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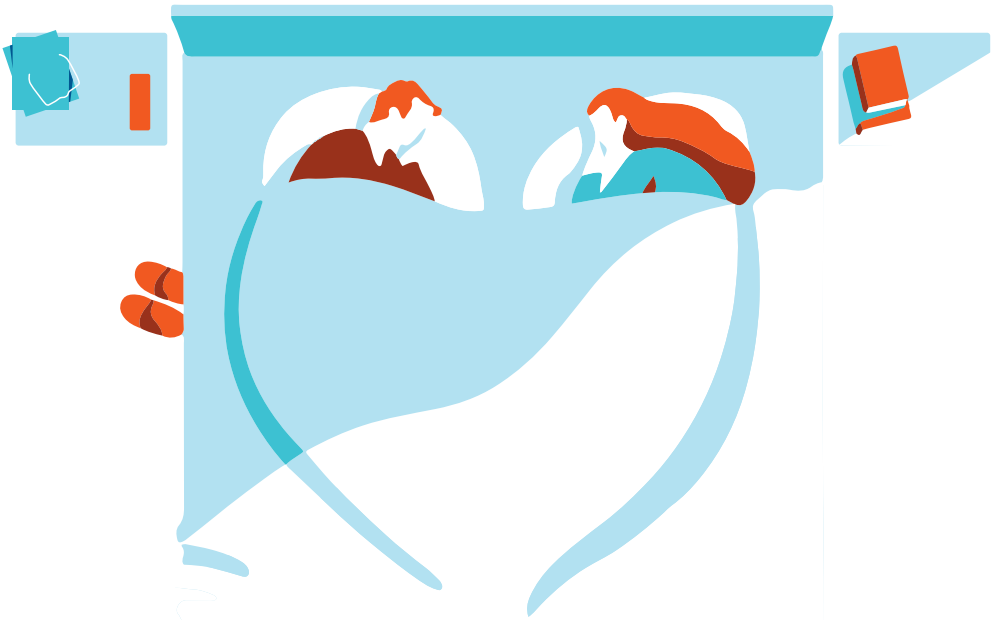

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EDITORIAL

El arte como terapia en salud psicofísica

Art as therapy in psychophysical health

Mª Teófila Vicente Herrero

Médico especialista en Medicina del Trabajo

De la Salud a la Enfermedad. Imagen cedida por Francisca Lita. Plumilla, 60 × 50 cm (1997).

La Asociación Británica de Terapeutas de Arte define la terapia artística como *una forma de psicoterapia que utiliza los medios artísticos como su principal modo de comunicación*. Ajustándose a esta definición, la terapia artística permite a los individuos utilizar el arte para expresarse creativamente y comunicarse de manera diferente con ellos mismos, con los demás y con su realidad.

En el Reino Unido existen actualmente varios proyectos que ofrece *Arts on Prescription* para personas con problemas de salud mental y aislamiento social. El objetivo de estos programas no es sustituir las terapias convencionales, sino actuar como complemento, ayudando a las personas en su recuperación a través de la creatividad y aumentando el compromiso social.

El término *arte* incluye una amplia gama de actividades que en este caso en concreto se enfocan o dirigen para que la creación artística actúe como un medio de apoyo que facilite cambios positivos en la salud tanto individual como colectiva. Sin embargo, resulta complejo medir el impacto que el arte como terapia tiene sobre la salud, a pesar de que su uso cada vez más extendido indica que la expresión artística puede contribuir a resolver problemas evidenciables en la práctica sanitaria y en la integración social.

Las terapias mediante cualquier tipo de actividad creativa tienen, cuando se enfocan hacia problemas de salud/enfermedad, un objetivo de promoción del concepto de salud global definido por la Organización Mundial de la Salud: *La salud es un estado de completo bienestar físico, mental y social, y no solamente la ausencia de afecciones o enfermedades.*

Esta cita procede del Preámbulo de la Constitución de la Organización Mundial de la Salud, adoptada por la Conferencia Sanitaria Internacional, celebrada en Nueva York del 19 de junio al 22 de julio de 1946 y firmada el 22 de julio de 1946 por los representantes de 61 Estados, no habiéndose modificado desde 1948.

Ajustándose a ella, el arte facilita, o bien la curación tras una enfermedad de la esfera física o psíquica, o la compatibilidad con una integración social, yendo más allá en la búsqueda de bienestar y cambios personales.

Todo esto es imposible si no se cuenta con personas formadas en este campo, con una capacitación y unos estándares profesionales como los exigibles a los terapeutas implicados en los entornos de la atención médica.

De forma tradicional, el uso del arte como herramienta de apoyo en temas de salud se ha enfocado hacia patologías crónicas, graves y especialmente en las enfermedades psiquiátricas y en casos de desarraigo social.

Resulta de especial interés su utilización como herramienta de apoyo en situaciones extremas como ocurre con las víctimas de torturas, en abusos sexuales, tanto más cuando los implicados son niños o personas con deficiencias psíquicas. Lo mismo ocurre con las situaciones de violencia de género.

Experiencias reseñables en nuestro país han marcado un camino abierto a una proyección mucho más amplia en el futuro. Es el caso de la colaboración mantenida durante dos años entre la Facultad de Bellas Artes de la Universidad Complutense de Madrid y el Organismo Autónomo Madrid Salud del Ayuntamiento de Madrid, que ha permitido desarrollar un proyecto de colaboración conjunta multiprofesional entre sanitarios, docentes y artistas iniciando lo que pueden ser venideras colaboraciones en arte, salud y prevención.

Quizás la mejor forma de concluir esta editorial es preguntarnos como Suely Rolnik *¿El arte cura?* y su enfoque como el desafío de una interrogación que involucra cuestiones fundamentales acerca de lo que es el vivir, crear, transformar, y de la relación que se puede establecer entre estos tres verbos si es que, como de hecho él mismo se cuestiona, existe alguna relación.

Referencias

1. Asociación profesional española de arteterapeutas. Disponible en: https://arteterapia.org.es/que-es-arteterapia/

2. Bungay H, Clift S. Arts on prescription: a review of practice in the U.K. Perspect Public Health. 2010 Nov;130(6):277-8.

3. Vicente Herrero MT. Arte y Terapia en el contexto valenciano de la crisis 2008-2018. En: De la Calle, R. Entre la crisis, la resistencia y la creatividad. Ed: Universidad Politécnica de Valencia; 2020, p:310-496.

4. Hartwell H. Arts and health. Perspect Public Health. 2013 Jan;133(1):2.

5. Adeane M. Is there a place for the arts in our modern healthcare system? Perspect Public Health. 2013 Jan;133(1):19-20.

6. Avila N, Orellana A, Cano MG, Antúnez N, Claver D. Arte, salud y prevención: primeras colaboraciones. Gac Sanit. 2014;28(6):501-4.

7. Suely Rolnik ¿El arte cura? Quaderns portàtils 02. Disponible en: http://www.medicinayarte.com/img/rolnik_arte_cura.pdf

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ORIGINAL

The study of Pap smear conduction and its related factors based on health belief model in women referred to health services center of Qom University of Medical Sciences during year 2020

El estudio de la conducción de la prueba de Papanicolaou y sus factores relacionados basado en el modelo de creencias de salud en mujeres remitidas al Centro de Servicios de Salud de la Universidad de Ciencias Médicas de Qom durante el año 2020

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Abstract

Cervical cancer is caused by the human papillomavirus (HPV). Pap smear is a test to diagnose cervical cancer in women. Up to 60% of deaths from cervical cancer have been identified by test. The purpose of this study was to investigate the prevalence of this test and its associated parameters among females visiting health centers in Qom. In this study, 320 women with health records who were referred to health centers in Qom in 2020 were chosen using a multistage random sample approach and inclusion and exclusion criteria. A robust and reliable researcher-made questionnaire with demographic variables, awareness questions and health belief model questions were developed. The data were finally analyzed by SPSS software with 0.05 significance level. Overall, %11.25 of the subjects regularly underwent Pap smear screening, %51.87 irregularly participated in cervical cancer screening programs, and %36.88 did not undergo. Cervical cancer was not seen as a serious condition by the participants. Even ladies who felt vulnerable attempted to conceal their feelings. As a result, while they had a low perception of susceptibility and the severity of disease risk, they had a higher perception of barriers, which led to a lower level of Pap smear use.

Key words: Cervical cancer, Pap smear, human papillomavirus.

Resumen

El cáncer de cuello uterino es causado por el virus del papiloma humano (VPH). La prueba de Papanicolaou es una prueba para diagnosticar el cáncer de cuello uterino en mujeres. Hasta el 60% de las muertes por cáncer de cuello uterino se han identificado mediante pruebas. El propósito de este estudio fue investigar la prevalencia de esta prueba y sus parámetros asociados entre las mujeres que visitan los centros de salud en Qom. En este estudio, 320 mujeres con registros médicos que fueron remitidas a centros de salud en Qom en 2020 fueron elegidas utilizando un enfoque de muestreo aleatorio de múltiples etapas y criterios de inclusión y exclusión. Se desarrolló un cuestionario robusto y confiable elaborado por investigadores con variables demográficas, preguntas de concienciación y preguntas del modelo de creencias de salud. Los datos fueron finalmente analizados por el software SPSS con un nivel de significancia de 0.05. En general, el 11,25% de los sujetos se sometieron con regularidad a la prueba de Papanicolaou, el 51,87% participó de forma irregular en los programas de detección del cáncer de cuello uterino y el 36,88% no se sometió. Los participantes no consideraron el cáncer de cuello uterino como una afección grave. Incluso las mujeres que se sentían vulnerables intentaron ocultar sus sentimientos. Como resultado, aunque tenían una baja percepción de susceptibilidad y la gravedad del riesgo de enfermedad, tenían una mayor percepción de las barreras, lo que llevó a un menor nivel de uso de la prueba de Papanicolaou.

Palabras clave: Cáncer de cuello uterino, frotis de Papanicolaou, virus del papiloma humano.

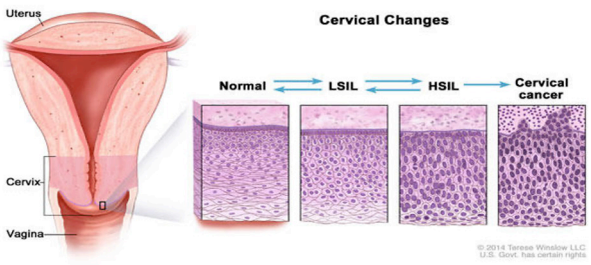
Introduction

Human papillomavirus (HPV) is sexually transmitted and is common in young people. They are usually cleared by the immune system. when high-risk types persist, they can cause abnormal cervical cell. If at least two-thirds of the surface layer of the cervix is affected, it can be termed cervical precancerous lesions[1]. Precancerous lesions can develop into cervical cancer after several years. Not all people with precancerous lesions of the cervix develop cervical cancer, but it is difficult to predict who will develop the condition. There are a number of different types of HPV that can cause precancerous lesions and cervical cancer. HPV16 and HPV18 are the most important high-risk types because they are responsible for about 70% of cervical cancers in the world. Prophylactic vaccination stimulates the production of antibodies that protect against future HPV infections by injecting HPV-like particles into the muscle.[2]

HPV viruses could be transmitted through sexual intercourse if they came into touch with infected genital skin, mucous membranes or body fluids. According to their ability to cause cancer, human papillomavirus genotypes are classed as high risk or low risk. HPV 6 and 11 which cause benign warts are the most prevalent low-risk types. High risk HPV are associated with development of cervical carcinoma (types 16,18, 31, 33, 45, 52, and 58)[3&4]. Although there is no virus-specific treatment for HPV infection, screening and treatment for pre-invasive cervix illness is very effective in avoiding cervical cancer progression[5]. Cervarix which targets HPV types 16 and 18, was released in 2007 and Gardasil 9 which targets HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 was released in 2014. All of these vaccines are meant to be given before sexual activity begins, if at all possible[6]. According to current research, the three approved HPV vaccinations have equivalent effectiveness in preventing cervical cancer[7]. According to a WHO position document on HPV vaccines published in 2017, all countries should move forward with nationwide HPV immunization. Several studies have found that, despite the high prevalence of HPV, there is a lack of information or erroneous perceptions about the virus, even among informed people. Despite the dangers of HPV, most women are unaware of them and have never heard of the virus[8].

There is evidence that when parents or young women are fully informed on the dangers and advantages of HPV vaccination, they are more likely to accept it[9]. Knowledge and attitudes about HPV infection and vaccines will have a significant impact on the outcome of a cervical cancer immunization campaign[10].As a result, we conducted a systematic assessment of several literature databases to determine the Iranian population's knowledge and attitude toward HPV and the HPV vaccine[11].

Figure 1: These images show how cervical cells that have long-lasting infections with high-risk HPV can change over time and become abnormal. Abnormal cervical cells may also return to normal even without treatment, especially in younger women. LSIL and HSIL are two types of abnormal changes to cervical squamous cells.



Methods

The present study is a descriptive and analytical study The statistical population included all women living in Qom. It was in 2020. In this study, 320 women were referred to health centers in the city of Qom was selected. This rate is according to the formula for estimating the sample size in descriptive studies with 95% confidence level, accuracy 0.05 and the prevalence of using Pap smear test is 30% based similar study. Inclusion criteria include being Iranian, age 20 to 60 years old, married, including spouse, deceased spouse or was separated from his wife. Mmethod in this study was a multi-stage randomization. Use a researcher questionnaire to collect data. For this purpose, after extensive study and search internet, question bank was prepared and the initial questionnaire to obtained and used after confirming its validity and reliability it placed. This questionnaire consists of 7 parts Demographic characteristics, awareness questions (14 questions), Questions based on the Health Belief Model include sensitivity Perceived 5 questions (perceived intensity) 5 questions (perceived benefits) 4 questions (perceived obstacles) 5 questions (action guide)
(8 questions).

Results and Analysis

According to the completion of the questionnaire by 30 women with similar characteristics to the studied samples Cronbach's alpha internal consistency coefficient of awareness questions 0.72, perceived sensitivity 0.79, perceived intensity, 0.81, Perceived benefits 0.78, perceived barriers 0.76 and guidance Action 0.77. The mean age of the samples was 33.74 8 8.71 years and with a minimum the age was 19 years and the maximum age was 56 years. 18.2% 7 people (illiterate, 6.56%) 21 people (educated) Elementary, 25.94%) 83 people (with secondary education, 94.40% (131 people) with secondary education and 24.38 Percentage (78 people)

had university education. 34.69Percent (111 people) they are employed and the rest is 65.31 percent 209 people (Khan Hadar. 15.94%) 51 people (no Children, 40%) 128 people (with one child, 26.87 86% (with two children and 17.19%) 55 (They had more than two children.) Is. The results also show 11.25% (36 people) had regular Pap smears and 51.87% (166 people) Irregularly in cervical cancer screening programs 36.88% (118 people) had never participated They did not use this test.

Discussion

To prevent cervical cancer some strategies, exist such as fast and successful treatment of vaginal and cervical infections to reduce the virus's transmission rate. The use of condoms to reduce the chance of transmission by up to 70%, reducing the number of sexual partners, and HPV vaccination are really effective[12]. Possible causes of cervical cancer include: Increasing the number of sexual partners, starting sexual activity before the age of 20, multiple deliveries, smoking, history of weakened immune system, history of visceral malignancy especially in the genitals, radiation therapy, condition Low socio-economic status, taking oral contraceptive pills, viral infections such as HPV and not participating in HPV Pap screening programs [Smear test] and especially doing it in the last 5 years[13]. Mean age in patients studied is 49. The average age of onset of cervical cancer is 47 years. Age of 39, 35 and 60, 64 are at risk. According to studies In Iran, the incidence of this cancer is 4.5 percent in year reported to indicate the importance of cervical cancer. The uterus is among the cancers of women in Iran[13]. Among these, Pap smears are among the most effective and least it is the most expensive final test for screening patients' cervical cancer is used. lesions only with biopsy in examination Colposcopy is detectable in the absence of Pap smear test[14].All women in a community cannot be called to a clinic for a biopsy and colposcopy, and it is time consuming and costly, Thus, Pap smear test of a cervical cancer screening method in women communities Various has been proposed and approved[15]. Acceptable proposed protocol for cervical cancer screening Uterus performed by the American Cancer Society in 2012[16]. Pap smear every three years in women 21 to 65 years old are necessary[17]. It is struck that only 5% of women in developing countries are participated in Pap smear screening programs while this rate in the United States is about 90%[18]. Now considering the importance of the issue, human behavior is affected by many different individual factors, social etc., this study utilizes Health Belief Model One of the models of studying behavior that show the relationship between health beliefs and health behavior[19]. The results of the present study indicated the fact that the percentage significantly (more than one third) of the women under study did not participate in a cervical cancer screening program. There were more than half of the irregularly pop tests. They had used smears and only a small percentage of them Regularly (every three years) screening schedule follow cervical cancer through a Pap smear they did. The results of other studies in our country indicates the status of cervical cancer screening Uterus through Pap smear is not desirable so in the study of absorption only 14.5% regularly they used Pap smear test[20]. This is the case in other developing countries as well[21&22]. Results of the present study along with other similar studies in the country shows the rate of Pap smear in our country is not desirable while in developed countries about 90% People are tested at least once for cervical cancer Pap smear used Hand[23].

In most industrialized countries, the reason for using Pap smear test is due to mortality. Cervical cancer has been significantly reduced. Differences in cervical cancer mortality rates in developed and developing countries resulting from doing or not performing a Pap smear. It should be noted that failure to perform regular cancer screening Cervical cancer risk increases two to six times that covers the cervix. The results of the present study showed that the knowledge of the women studied regarding Pap smear test is not in good condition.so that more than half of women have moderate awareness and a third had poor awareness[24&25].

In this study Fear of the outcome was found in testing and embarrassment were the biggest obstacles to doing it. These results can ring a risk to health planners because low perceived sensitivity and intensity can be the most important factor in not taking perform regular Pap smears as described earlier. Finally, it should be noted that the present study was done cross-sectionally and the conclusion was made cause and effect on results. Also using a self-reported questionnaire is another limited part of this study.

Table I: Achievable scores and how to classify the scores of knowledges and structures of the health belief model.

Structures	Achievable scores	good	medium	poor
0-4/6	4/6-9/2	9/2-14	0-14	Awareness
5-10	10-15	15-20	5-20	Perceived sensitivity
5-10	10-15	15-20	50-20	Perceived severity
5-10	10-15	15-20	5-20	Perceived benefits
5-10	10-15	15-20	5-20	Perceived Obstacles
8-16	16-24	24-32	8-32	Action guide

Table II: Comparison of mean and standard deviation of health belief model instruments according to the use of Pap smear test.

Significant level	No screening	Unregular screening	Regular screening	Awareness average
<0/001	5/32	6/11	8/31	Defiant deviation
	2/35	1/89	1/34	Perceived sensitivity
	8/31	11/01	14/22	average
	3/85	2/29	2/22	Defiant deviation
	8/31	11/01	14/22	Severely perceived
	10/01	12/00	14/05	average
	2/25	2/91	3/11	Defiant deviation
	11/99	13/20	14/11	Perceived barriers
	2/11	2/25	2/48	Average
	17/04	15/31	12/71	Defiant deviation
	3/35	2/96	2/51	Action guide
	15/2	18/21	24/48	Average
	5/66	3/62	4/31	Defiant deviation

Table III: Awareness correlation matrix, health belief model constructs and behavior towards Pap smear test.

Model Instruments	1	2	3	4	5	6
Awareness	125%	107%	-317%	69	123	156
Perceived sensitivity	144%	-118%	126%	108%	-11%	
Perceived intensity	138%	133%	221%	-133%		
Perceived benefits	106%	611%	-148%			
Perceived barriers						
Action guide	-297%	-166%				
Behavior	-	-	-	-	--	-

Conclusion

The results showed that divorced and widowed, number of marriages, marriages under the age of 16 and taking birth control pills is a risk factor of Cervical cancer. The use of treatments Cryoactivation can reduce the risk of infection. The results of this study are groups at risk of women. Findings of this study and similar studies are expressed takes a Pap smear every 6 months of women at risk are essential. This study showed that Women who have cancer tried to hide it. On the other hand, it showed that awareness and knowledge alone in women's participation in Pap tests Smear does not play a role due to the meaning of communication of model structures with the behavior of using this Pap smear test. In the present study, perceived barriers and perceived sensitivity are the most important reason for not having a Pap smear. Due to the high barriers, the rate of acceptance of this screening test was not desirable on the other hand with understanding of belief lack of vulnerability of their less studied subjects. They knew the risk of developing the disease and its complications and this kind of belief adopts any preventive behavior weakens.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Markowitz LE, Dunne EF, Saraiya M, Chesson HW, Curtis CR, Gee J, et al. Human papillomavirus vaccination:
recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2014;63(RR-05):1-30.

2. Bzhalava D. Human papillomavirus reference clones. International Human Papillomavirus Reference Center.
Available at: URL: http://www.hpvcenter.se/html/refclones.html, consulté en septembre; 2014.

3. Doorbar J, Quint W, Banks L, Bravo IG, Stoler M, Broker TR, et al. The biology and life-cycle of human papillomaviruses. Vaccine 2012; 30(Suppl 5): F55-70.

4. Lacey CJ, Lowndes CM, Shah KV. Chapter 4: burden and management of non-cancerous HPV-related conditions: HPV-6/11 disease. Vaccine 2006; 24(Suppl 3): S3/35-41.

5. Human papillomavirus vaccines: WHO position paper, October 2014. Wkly Epidemiol Rec 2014; 89(43):465-91.

6. Safaei A, Khanlari M, Momtahen M, Monabati A, Robati M, Amooei S, et al. Prevalence of high-risk human papilloma virus types 16 and 18 in healthy women with cytologically negative pap smear in Iran. Indian J Pathol Microbiol 2010; 53(4):681-5.

7. Shahramian I, Heidari Z, Mahmoudzadeh-Sagheb H, Moradi A, Forghani F. Prevalence of HPV infection and high-risk HPV genotypes (16, 18), among monogamous and polygamous women, in Zabol, Iran. Iran J Public Health 2011; 40(3):113–21.

8. Miryousefiata F, Alsadat Miryousefiata F. The effect of Familact probiotic supplement in patients with diabetes (Evaluation of Blood Glucose Parameters, Lipid Profile). ACADEMIC JOURNAL OF HEALTH SCIENCES. 2021; 36 (3): 52-63. doi: 10.3306/AJHS.2021.36.03.52 www.medicinabalear.org

9. Sohrabi A, Farzami MR, Samiee SM, Modarresi MH. An overview on papillomaviruses as the main cause of cervical cancer. Iran J Obstet Gynecol Infertil 2015; 18(145):14-25. (Persian).

10. Castellsagué X, Muñoz N, Pitisuttithum P, Ferris D, Monsonego J, Ault K, et al. End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24-45 years of age. Br J Cancer 2011; 105(1):28-37.

11. Smith JS, Lindsay L, Hoots B, Keys J, Franceschi S, Winer R, et al. Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: a meta-analysis update. Int J Cancer 2007; 121(3):621-32.

12. Fairley CK, Chen S, Tabrizi SN, McNeil J, Becker G, Walker R, et al. Prevalence of HPV DNA in cervical specimens in women with renal transplants: a comparison with dialysis-dependent patients and patients with renal impairment. Nephrol Dial Transplant 1994; 9(4):416-20.

13. Denny LA, Franceschi S, de Sanjose S, Heard I, Moscicki AB, Palefsky J. Human papillomavirus, human immunodeficiency virus and immunosuppression. Vaccine 2012; 30(Suppl 5): F168-74.

14. WHO Guidelines Approved by the Guidelines Review Committee. WHO guidelines for screening and treatment of precancerous lesions for cervical Cancer prevention. Geneva: World Health Organization; 2013.

15. WHO Guidelines Approved by the Guidelines Review Committee. WHO guidelines: use of cryotherapy for cervical intraepithelial neoplasia. Geneva: World Health Organization; 2011.

16. Khatibi M, Rasekh HR, Shahverdi Z, Jamshidi HR. Cost-effectiveness evaluation of quadrivalent human papilloma virus vaccine for HPV-related disease in Iran. Iran J Pharm Res 2014; 13(Suppl):225-34.

17. Joura E.A, Leodolter S, Hernandez-Avila M, Wheeler C.M, Perez G, Koutsky LA, Garland S.M, Harper D.M, and et al. Efficacy of a quadrivalent prophylactic human papillomavirus (types 6, 11, 16, and 18) L1 viruslike- particle vaccine against high-grade vulval and vaginal lesions: a combined analysis of three randomized clinical trials. Lancet.2007.369:9574:1693-702.

18. Petrosky E, Joseph A. Bocchini Jr, Hariri S, Chesson H, Curtis CR, Saraiya M, Unger ER, Markowitz LE. Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices. Morbidity and Mortality Weekly Report (MMWR). 2015: 64(11);300-4

19. Goldie SJ, Kohli M, Grima D, Weinstein MC, Wright TC, Bosch FX, Franco E. Projected Clinical Benefits and Cost-effectiveness of a Human Papillomavirus 16/18 Vaccine. Jnl of National Cancer Institute.2004;.96;604-6015.

20. National and state vaccination coverage among adolescents aged 13-17 years--United States, Centers for Disease Control and Prevention (CDC). Morb Mortal Wkly Rep. 2013 Aug 30;62(34):685-93.

21. Dobson S.R.M, McNeil S, Dionne M, Dawar M, Ogilvie G, Krajden M, Sauvageau C, Scheifele D.W. Kollmann TR .et al Immunogenicity of 2 Doses of HPV Vaccine in Younger Adolescents vs 3 Doses in Young WomenA Randomized Clinical Trial. JAMA. 2013;309(17):1793-802

22. Szarewsk A.HPV Vaccination and Cervical Cancer. Cancer Prevention. Current Oncology Reports.2012; 14 : 559-67

23. Giuliano A.R. Palefsky J.M. Goldstone S, Moreira E.D. Penny M.E. Aranda C, Vardas E, Moi H, Jessen H. Hillman R. and et al. Efficacy of Quadrivalent HPV Vaccine against HPV Infection and Disease in Males. N Engl J Med 2011; 364:401-11

24. Reiter P. L, Brewer NT, Gottlieb S. L, McRee A.L.Smith J.S. How much will it hurt? HPV vaccine side effects and influence on completion of the three-dose regimen. Vaccine 2009:27:6840-4.

25. Miryousefiata F, Sangy S. Assessing the Correct Understanding of Families about the Occurrence of Marital Cancer (Statistical Population: Denmark, Sweden and Iran), J. Med. Chem. Sci., 2021, 4(1) 60-74 DOI: 10.26655/JMCHEMSCI.2021.1.8
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ORIGINAL

Developing and teaching the deontology and consequentialism ethics foundations of healthcare whistleblowing

Desarrollar y enseñar los fundamentos éticos de la deontología y el consecuencialismo en la denuncia de irregularidades en la sanidad

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Abstract

Background: The importance of whistleblowing in health systems is examined in this study.
Methods: First, a brief definition and history of whistleblowing are said, especially in health systems. Then the lack of a proper place for whistleblowing in the education of medical students is studied. Then, the status and acceptance of whistleblowing in deontological and consequentialist ethical schools are examined.
Results: It is pointed out that almost all normative ethical schools agree with disclosure and whistleblowing and consider it an ethical matter. Therefore, whistleblowing training for students and medical staff is important to improve medical services and increase public confidence in the medical system.
Conclusion: The educational systems must take appropriate measures to train and integrate this method with other methods.

Key words: Developing, deontology, consequentialism ethics, healthcare whistleblowing.

Resumen

Antecedentes: En este estudio se examina la importancia de la denuncia de irregularidades en los sistemas sanitarios.
Métodos: En primer lugar, se hace una breve definición e historia de la denuncia de irregularidades, especialmente en los sistemas sanitarios. A continuación, se estudia la falta de un lugar adecuado para la denuncia de irregularidades en la formación de los estudiantes de medicina. A continuación, se examina la situación y la aceptación de la denuncia de irregularidades en las escuelas de ética deontológica y consecuencialista.
Resultados: Se señala que casi todas las escuelas éticas normativas están de acuerdo con la divulgación y la denuncia de irregularidades y la consideran una cuestión ética. Por lo tanto, la formación en materia de denuncia de irregularidades para estudiantes y personal médico es importante para mejorar los servicios médicos y aumentar la confianza del público en el sistema médico.
Conclusión: Los sistemas educativos deben tomar las medidas adecuadas para formar e integrar este método con otros.

Palabras clave: Desarrollo, deontología, ética consecuencialista, denuncia de irregularidades sanitarias.

Introduction

Medical, pharmaceutical, and health centers are exposed to all kinds of corruption, especially financial corruption, due to the high volume of capital turnover. Apart from financial and possibly life-threatening damage, corruption in health systems can undermine public and patient trust in medical systems. One of the methods to fight and prevent corruption is whistleblowing. According to some studies, medical students are less inclined to whistleblowing, and even as they progress to higher levels, their inclination decreases[1]. Perhaps one of the reasons is the lack of education and reminders of this important issue in medical ethics courses, so in this study, the role of whistleblowing in the normative medical ethical schools is examined to increase the awareness of students and medical staff about the importance of whistleblowing.

For example, one of these economic corruptions in medicine is related to GlaxoSmithKline. This company sells drugs through deceptive information that has not yet received the necessary licenses and bribes physicians that prescribe the company's drugs and hired an institute to write an article praising the company's drugs. Eventually, four of the company's employees exposed the company's corruption by whistleblowing[3].

Another example, at Pfizer Inc., nine company employees whistled illegal and unconventional manufacturing of a type of osteoarthritis drug, which led to the company being convicted. There are various methods to prevent corruption, fraud, and professional abuse, such as internal auditing, independent auditing, and internal control[4]. However, the most common method, which is often the least expensive method, is disclosure or whistleblowing. Such abnormalities are revealed by whistleblowing staff.

Totally, 83% of these disclosures are internal, and 17% are publicly disclosed, with whistleblowers reporting their information in various ways to a third party, which could be a senior manager, government official, or media.

In defining whistleblower, four components are usually considered as essential components of this phenomenon:

A. The intention and will of a person to make information public
B. Transferring information to parties outside an institution and registering and publishing them in public.
C. The significance of the transmitted information in terms of their potential or actual performance.
D. The current membership or prediction of the whistleblower in that institution

From the four elements mentioned, it is concluded that accidental information leakage is not a case of disclosure and must have been determined based on a specific plan and program. While the general public views whistleblowers' activities as largely positive, the assessments of representatives of government agencies are often quite critical. For example, the revelations of Julian Paul Assange and Edward Joseph Snowden created a heated debate in the media about the ethics of such activities[5].

Revival of whistleblowing in the twentieth century

Ralph Nader, a four-term US presidential candidate, American activist, author, lecturer, and lawyer, coined the word whistleblowing in 1970 to fight corruption in the United States[6]. He began his work by whistleblowing about Automobile Manufacturing Companies by writing the book "Unsafe at Any Speed." His actions and initiatives in the fight against corruption and protecting people's rights led him to repeatedly place in the list of 100 most influential American men. Although Ralph Nader revived the word, it has its roots in the 19th century when British police whistled to inform people and other colleagues of the existence of a criminal. Of course, some people associate the word whistle with the whistling of a football referee. Regardless of where the word originated and its history, the importance of this process is whistleblowing in preventing crime and corruption and any unpleasant events that are not necessarily crime or corruption[7].

The physician who unjustly became a victim in the whistleblowing:

Perhaps the greatest disclosure in medicine at a time when even many of the simplest codes of ethics did not exist was in the case of the Hungarian physician and surgeon Ignaz Philipp Semmelweis (1818-1865)[8]. Today, however, he is revered and glorified. Countries turn to documents to recognize him as belonging to their country, naming their largest universities after him and erecting statues of him in universities and squares and even coins for him.

At that time, disinfection of the hands was not yet accepted by physicians and surgeons. At that time, surgeons went to the surgery room without disinfecting the same hands that autopsied the bodies and operated on pregnant women. He found that if surgeons disinfected their hands after dissecting the corpses of dead patients and before attending the surgery room, the disease would not be transmitted to mothers, and the death rate would be reduced by 1:6 to 1:10. However, although he did not refrain from any action or disclosure, he was unfortunately ignored by the medical community and was labeled a mental illness. It was later, with the work of Pasteur, Koch, and Lister, that we understood his correct words[9].

Semmelweis Reflex

The impact of what the Hungarian physician did was immortalized in the history of medicine and disclosure history. Even a phenomenon called the Semmelweis reflex was perpetuated in the history of medical philosophy due to the importance of the subject.

This term is an allusion to the tendency to reject new evidence or knowledge that does not conform to known rules and beliefs of the day. In some cases, innovations in science lead to punishment rather than corresponding rewards because these innovations conflict with fixed paradigms and behavior patterns[10].

Although it is not known when this term was first used, it can be found in the writings of Robert Anton Wilson. Timothy Francis Leary (October 22, 1920 - May 31, 1996), in his book The Game of Life, describes Semmelweis's reaction as follows: "It is a collective behavior seen between primates and precocious humans on an underdeveloped planet in which the discovery of scientific facts is repressed and condemned[11]. Today, the term has also found its way into philosophy and theological studies and is referred to as "Hume's complete skepticism about causality[11].

Of course, this phenomenon has a long history. When Edward Jenner asked the Royal Society of England to publish his findings on vaccination, the society's president advised him to refrain from commenting on things that are very different from current science and do not jeopardize the reputation[12].

Galileo Gambit

In contrast to the Semmelweis reflex is the term Galileo gambit.

A term is a form of association fallacy often used by those who deny a well-established scientific or historical proposition. Scholars define this argument as follows: Galileo was ridiculed and even tried in his time for his scientific observations, but a few years later, his legitimacy became clear to everyone. Proponents argue that since their views and discoveries are not so consistent with the evidence of the time, this would lead to ridicule and rejection by other scientists, who would later be recognized as righteous scholars like Galileo. Of course, this is a false argument because most of those ridiculed or rejected have gone the wrong way[13].

Whistleblowing position among medical students and staff:

As mentioned, the attitude towards the issue of whistleblowing does not have a good place among medical students and physicians because students learn everything from their professors.

Contemporary medical ethics has not yet developed a strong theoretical concept of what is known as "whistleblowing" in healthcare. When medical students with the same ethical scenarios were challenged in the first and last weeks of a four-year medical course, the number of people who made the "right" ethical decision remained unchanged at 40%. Even worse, the percentage of students who confirm that they are reporting unethical behavior has decreased from 13% in the early weeks to less than 5% in the final weeks. The probable cause of such a decline in what might be called "whistleblowing" is the "hidden curriculum" that is passed on to students through the actions, attitudes, and opinions of senior physicians that they encounter in clinical rotations[14].

Acceptability of whistleblowing from the perspective of ethical theory

In this study, the acceptability of whistleblowing in the theories of ethical philosophy was examined. It was hoped that in this way, the acceptance of whistleblowing would be introduced more and more in students' ethics courses so that they are familiar with this subject. Many scholars have commented on the philosophical view of virtuosity about whistleblowing. For the lack of non-repetition, we will not deal with the ethical virtuosity school about which there are more or fewer articles.

Deontological view on whistleblowing

Deontological ethics is one of the theories proposed in normative ethics, and in answer to the question "What is the criterion of ethical do's and don'ts?" it is formed. This theory emphasizes the relationship between duty and the ethicality of action. Those who believe in deontological ethics will be an ethical act that is inherently ethical in nature, not necessarily one that has ethical consequences. According to this view, regardless of its results and consequences, the criterion of correctness and incorrectness depends on the action itself and its characteristics[15].

According to Kant, every action must be universal. However, an action that does not take into account the circumstances of others is in itself an unethical act, and universality is sometimes itself an unethical act[16].

Kant refers to the subject as an absolute issue as meaning the Absolute means that we must always behave so that our rule of action can be a general law for all human beings. From Kant's point of view, ethical principles are unchangeable, but rules depend on whether one wants to do an ethical or unethical act, and this life depends on the person himself[17].

The consequentialist view on whistleblowing

This approach, firstly, instead of focusing on the intrinsic characteristics of the act, focuses on its consequence. Secondly, it emphasizes actions and behaviors in ethical values and attaches primary importance to actions. Among the theories of consequentialism, the wisest theory is general ethical utilitarianism. This theory seeks ethical value in the emergence of the greatest good for most human beings. There is disagreement among proponents of utilitarianism as to the greatest good we seek[18].

According to Russian transhumanists Viktor Ugryumo, a key turning point in this path should be discovering the neural relation of pleasure. This physiological parameter

uniquely determines the level of pleasure (or pain) experienced by an organism[19].

Consequentialism is based on two principles:

- Whether an action is right or wrong, or whether an action is, in fact, ethical, depends only on the consequence of that action.
- The more action, the better the consequence, the more correct the action.

The utilitarianism of John Stuart Mill or Jeremy Bentham is a well-known example of consequentialism. In contrast, deontological ethics or deontological theories of John Locke and Emmanuel Kant are examples of non-consequentialism[19].

Support for whistleblowers should be institutionalized in health systems, and whistleblowers should be treated with acceptable incentives. Although ethical work should not be based on material rewards, at least whistleblowers should avoid potential. Put together, Despite high advances occurred in medical sciences[20-27], some diseases and disorders remain health threating[28-36]. However, by observing the ethical principles in medical sciences and technologies, appropriate solutions can be suggested to solve them.

Conclusions

Training students is essential in advancing medical knowledge and expanding and promoting health services. This training should be 360 degrees, and all aspects of human psychology should be used. However, teaching a book is effective; what the student learns secretly and in practice from his professors is very important. If a student has an ethics-oriented professor, he will also pay attention to ethics and law, which will establish in him. By teaching the acceptability of whistleblowing in the various normative ethics schools, a range will be created in which all tastes, each of which may be inclined to a normative ethics school, become more and more aware of its importance. Different aspects of whistleblowing should be explained to students, such as philosophical principles and related laws and their merits, and students should be encouraged to do so from the beginning. The use of new technologies in creating a suitable platform for whistleblowing, especially for communication and messaging, and creating legal and cultural infrastructure for whistleblowing can help spread this phenomenon and reduce corruption, fraud, and injustice. Hidden education and what students learn indirectly from professors and managers are very important.

Conflict of Interest

The author declare that he have no conflict of interest.

References

1. Radulovic U. Academic dishonesty and whistleblowing in a higher education institution: A sociological analysis (Doctoral dissertation, University of Johannesburg (South Africa)). 2017.

2. Bishop TJ, Hydoski FE. Corporate resiliency: managing the growing risk of fraud and corruption. John Wiley and Sons; 2009.

3. Lexchin J, Kohler JC, Gagnon MA, Crombie J, Thacker P, Shnier A. Combating corruption in the pharmaceutical arena. Indian Journal of Medical Ethics. 2018 Jul 1;3(3):234-9.

4. Noor MN, Mansor N. Whistleblowing Practice in the Public Sector and Internal Audit Effectiveness. In Proceedings of the International Conference on Islam and Global Issues 2018. 423-8.

5. Friedman M. Edward Snowden: Hero or Traitor: Considering the Implications for Canadian National Security and Whistleblower Law. Dalhousie J. Legal Stud. 2015;24:1.

6. Olesen T. The Birth of an Action Repertoire: On the Origins of the Concept of Whistleblowing. Journal of Business Ethics. 2021:1-2.

7. Chaloat I, Carrión-Crespo C, Licata M. Law and practice on protection whistle-blowers in the public and financial services sectors. ILO working paper. 2019;328:25.

8. Schreiner S. Ignaz Semmelweis: a victim of harassment?. Wiener Medizinische Wochenschrift. 2020;170(11):293-302.

9. Wilkinson G. Epidemics: wash your hands! The asylum delivery and violent death of Professor Ignaz Philipp Semmelweis; and, the cursed Semmelweis reflex–psychiatry in history. The British Journal of Psychiatry. 2021;218(5):242-.

10. Wilson RA. The Game of Life. New Falcon Publications. 1991.

11. Berti L. Early reception of smallpox inoculation in Italy: insights from the correspondence of the Fellows of the Royal Society. Diciottesimo Secolo. 2021;6:5-18.

12. Collins L. Bullspotting: finding facts in the age of misinformation. Prometheus Books; 2012.

13. Bolsin S, Faunce T, Oakley J. Practical virtue ethics: healthcare whistleblowing and portable digital technology. Journal of medical ethics. 2005;31(10):612-8.

14. Popa D, Ristea GA. Theoretical and practical aspects regarding the universities'codes of professional ethics and deontology. International Journal of Communication Research. 2020;10(3):257-65.

15. Benlahcene A, Zainuddin RB, Syakiran N, Ismail AB. A Narrative Review of Ethics Theories: Teleological & Deontological Ethics. Journal of Humanities and Social Science (IOSR-JHSS). 2018;23(1):31-2.

16. Dursun S, Mankolli H. The Value of Nature: Virtue Ethics Perspective. GNOSI: An Interdisciplinary Journal of Human Theory and Praxis. 2021;41-5.

17. Hooper S. Understanding the ethics of whistleblowing by nurses. Journal of the Australasian Rehabilitation Nurses' Association (JARNA). 2011;14(3):10-15.

18. Argonov VY. The pleasure principle as a tool for scientific forecasting of human self-evolution. Journal of Ethics and Emerging Technologies. 2014;24(2):63-78.

19. Mill JS. Utilitarianism and on liberty: Including Mill's' Essay on Bentham'and selections from the writings of Jeremy Bentham and John Austin. John Wiley & Sons; 2008.

20. Dehkordi FS, Tirgir F, Valizadeh Y. Effects of Guajol® ointment synthesized from medicinal smoke condensate of jennet feces on burn wound healing on Wistar rat. Veterinary Research Forum. 2017; 8(3):215.

21. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of Brucella abortus and Brucella melitensis in aborted bovine, ovine, caprine, buffaloes and camelid fetuses by application of conventional and real-time polymerase chain reaction. The Thai Journal of Veterinary Medicine. 2012;42(1):13.

22. Dehkordi FS, Momtaz H, Doosti A. Application of Real-Time PCR for detection of Aspergillus species in aborted ruminant foetuses. Bulgarian Journal of Veterinary Medicine. 2012;15(1):30-6.

23. Dehkordi FS. Prevalence study of Coxiella burnetii in aborted ovine and caprine fetuses by evaluation of nested and real-time PCR assays. American Journal of Animal and Veterinary Sciences. 2011;6(4):180-6.

24. Dehkordi FS, Tavakoli-Far B, Jafariaskari S, Momtaz H, Esmaeilzadeh S, Ranjbar R, et al. Uropathogenic Escherichia coli in the high vaginal swab samples of fertile and infertile women: virulence factors, O-serogroups, and phenotyping and genotyping characterization of antibiotic resistance. New Microbes and New Infections. 2020;38:100824.

25. Dehkordi FS, Haghighi N, Momtaz H, Rafsanjani MS, Momeni M. Conventional vs real-time PCR for detection of bovine herpes virus type 1 in aborted bovine, buffalo and camel foetuses. Bulgarian Journal of Veterinary Medicine. 2013;16(2):102-12.

26. Dehkordi FS, Yazdani F, Mozafari J, Valizadeh Y. Virulence factors, serogroups and antimicrobial resistance properties of Escherichia coli strains in fermented dairy products. BMC Research Notes. 2014c;7(1):1-8.

27. Dehkordi FS, Barati S, Momtaz H, Ahari SN, Dehkordi SN. Comparison of shedding, and antibiotic resistance properties of Listeria monocytogenes isolated from milk, feces, urine, and vaginal secretion of bovine, ovine, caprine, buffalo, and camel species in Iran. Jundishapur Journal of Microbiology. 2013a;6(3):284.

28. Ghorbani F, Gheisari E, Dehkordi FS. Genotyping of vacA alleles of Helicobacter pylori strains recovered from some Iranian food items. Tropical Journal of Pharmaceutical Research. 2016;15(8):1631-6.

29. Dehkordi FS, Gandomi H, Basti AA, Misaghi A, Rahimi E. Phenotypic and genotypic characterization of antibiotic resistance of methicillin-resistant Staphylococcus aureus isolated from hospital food. Antimicrobial Resistance & Infection Control. 2017;6(1):1-1.

30. Dehkordi FS. Prevalence study of Bovine viral diarrhea virus by evaluation of antigen capture ELISA and RT-PCR assay in Bovine, Ovine, Caprine, Buffalo and Camel aborted fetuses in Iran. AMB Express. 2011;1(1):1-6.

31. Dehkordi FS, Parsaei P, Saberian S, Moshkelani S, Hajshafiei P, Hoseini SR, et al. Prevalence study of Theileria annulata by comparison of four diagnostic Techniques in shouthwest Iran. Bulgarian Journal of Veterinary Medicine. 2012;15(2): 123-30.

32. Dehkordi FS, Haghighi Borujeni MR, Rahimi E, Abdizadeh R. Detection of Toxoplasma gondii in raw caprine, ovine, buffalo, bovine, and camel milk using cell cultivation, cat bioassay, capture ELISA, and PCR methods in Iran. Foodborne Pathogens and Disease. 2013;10(2):120-5.

33. Dehkordi FS, Khamesipour F, Momeni M. Brucella abortus and Brucella melitensis in Iranian bovine and buffalo semen samples: The first clinical trial on seasonal, Senile and geographical distribution using culture, conventional and real-time polymerase chain reaction assays. Kafkas Univ Vet Fak Dergisi. 2014;20(6):821-8.

34. Dehkordi FS, Valizadeh Y, Birgani TA, Dehkordi KG. Prevalence study of Brucella melitensis and Brucella abortus in cow's milk using dot enzyme linked immuno sorbent assay and duplex polymerase chain reaction. Journal of Pure and Applied Microbiology. 2014b;8(2):1065-9.

35. Sheikhshahrokh A, Ranjbar R, Saeidi E, Dehkordi FS, Heiat M, Ghasemi-Dehkordi P, et al. Frontier therapeutics and vaccine strategies for sars-cov-2 (COVID-19): A review. Iranian Journal of Public Health. 2020;49(Suppl 1):18.

36. Nejat S, Momtaz H, Yadegari M, Nejat S, Safarpour Dehkordi F, Khamesipour F. Seasonal, geographical, age and breed distributions of equine viral arteritis in Iran. Kafkas Univ Vet Fak Derg. 2015;21(1):111-6.

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ORIGINAL

Distribution of bacteria isolated from the cases of maxillofacial surgery

Distribución de las bacterias aisladas en cirugía maxilofacial

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Abstract

Background: Maxillofacial infections after the surgical operation are common dental complications. It is important to know the bacterial species responsible for these kinds of infections. The present survey aimed to evaluate prevalence of bacterial pathogens a isolated from post surgical maxillofacial infections.
Methods: One-hundred and eighty patients were evaluated. All patients with post maxillofacial surgeries, including deep fascial infections, dentoalveolar abscess and neck and head pus localization were included in the study. Distribution of bacterial pathogens in collected samples were studied using culture method and biochemical tests.
Results: 150 out of 180 (83.33%) patients were included in the study. The mean age of the examined patients was 49.7 years. The male to female ratio was 92/85 (P <0.05). Histories of smoking and alcohol were determined in 40% and 18% of cases, respectively. *S. aureus* (26.66%), *S. mutans* (25.33%), *Prevotella dentalis* (13.33%), *Stereptococcus viridans* (13.33%), Enterobacter aerogenes (12%), and *Prevotella buccalis* (11.33%) had the highest distribution. *Bacteroides forsythus* (2%), *Fusobacterium nucleatum* (3.33%), *Acinetobacter baummanii* (4%), and *Veillonella spp*. (4%) had the lowest distribution.
Conclusion: Aerobic bacteria had the higher distribution than anaerobics. Accurate prescription of antimicrobial drugs can diminish the risk of maxillofacial infections after surgical operation.

Key words: Maxillofacial surgery, bacteria, prevalence.

Resumen

Antecedentes: Las infecciones maxilofaciales tras la intervención quirúrgica son complicaciones dentales frecuentes. Es importante conocer las especies bacterianas responsables de este tipo de infecciones. El presente estudio tiene como objetivo evaluar la prevalencia de los patógenos bacterianos aislados en las infecciones maxilofaciales postquirúrgicas.
Métodos: Se evaluaron ciento ochenta pacientes. Se incluyeron en el estudio todos los pacientes con cirugías maxilofaciales posteriores, incluidas las infecciones fasciales profundas, los abscesos dentoalveolares y la localización de pus en el cuello y la cabeza. Se estudió la distribución de los patógenos bacterianos en las muestras recogidas mediante el método de cultivo y pruebas bioquímicas.
Resultados: Se incluyeron en el estudio 150 de 180 (83,33%) pacientes. La edad media de los pacientes examinados era de 49,7 años. La proporción entre hombres y mujeres fue de 92/85 (P <0,05). Se determinaron antecedentes de tabaquismo y alcohol en el 40% y el 18% de los casos, respectivamente. *S. aureus* (26,66%), *S. mutans* (25,33%), *Prevotella dentalis* (13,33%), *Stereptococcus viridans* (13,33%), *Enterobacter aerogenes* (12%) y *Prevotella buccalis* (11,33%) tuvieron la mayor distribución. *Bacteroides forsythus* (2%), *Fusobacterium nucleatum* (3,33%), *Acinetobacter baummanii* (4%) y *Veillonella spp*. (4%) tuvieron la menor distribución.
Conclusión: Las bacterias aerobias tuvieron mayor distribución que las anaerobias. La prescripción precisa de fármacos antimicrobianos puede disminuir el riesgo de infecciones maxilofaciales tras una operación quirúrgica.

Palabras clave: Cirugía maxilofacial, bacterias, prevalencia.

Introduction

Infections are considered one of the most critical causes of morbidity and mortality in the last century[1-5]. Maxillofacial infections are one of the most critical complications after the face, neck and oral surgeries. The importance of this infection are high due to their comolications, anatomical positions near to brain, respiratory system and mediastine and high occurrence[6].

Bacteria arge the most common cause of maxillofacial infections[7]. In this regard, *Stereptococcus mutans* (S. mutans), *S. viridans*, *S. oralis*, *S. pneumoniae*, *S. mitis*, *Staphylococcus aureus* (S. aureus), *Klebsiella pneumonia*, *Enterobacter aerogenes*, *Acinetobacter baummanii*, *Prevotella buccalis*, *Prevotella dentalis*, *Bacteroides forsythus*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, and *Veillonella spp*. are considered to be the most common causes of maxillofacial infections after surgical operation[7-10].

In keeping with the high imoportance of maxillofacial infections in the dental and head and neck surgical operations, their causes and epidemiology are still unknown. Thus, the present research was done to assess the distribution of bacterial pathogens isolated from the post maxillofacial infections.

Materials and methods

Population

From January to July 2020, a total of 180 patients with post maxillofacial infections were examined in the study. All patients with post maxillofacial surgeries, including deep fascial infections, dentoalveolar abscess and neck and head pus localization were included. Among them, those with fungal and viral infections, tumors, neoplasmic lesions, pregnancy, Human Immunodeficiency Virus (HIV), coronavirus disease 2019 (COVIUD-19), and those received antibiotic therapy and antiseptic solutions were excluded from the survey.

Samples collection

Aspiration sites were cleaned with ethanol (70%, Merck, Germany). Pus aspiration was done using a sterile needle. In some cases, a sterile swab was used. Samples were transferred to the laboratory using the thioglycolate broth (Merck, Germany) media were used for samples transmission to the laboratory.

Isolation and identification of bacteria

Blood agar media (Merck, Germany) were used for an initial examination of samples in an aerobic and anaerobic conditions. Chocolate agar media (Merck, Germany) were used for an initial examination of samples in microaerophilic condition. Totally, 5% defibrinated sheep blood was added into blood agar media. Isolates were Gram-stained after 24 h of growth in air and CO2 conditions at 37ºC, respectively. Isolates growth on the anaerobic blood agar were Gram-stained after 48 h incubation at 37ºC. Gram-negative and Gram-positive bacteria were tested rendering the Analytical Profile Index (API 20E) system[11]. Gram-positive coccoid bacteria were tested by catalase test. catalase-negative strains were tested for the hemolytic reaction, and growth in media contained 6.5% NaCl. Catalase-positive strains were tested for resistance to Novobiocinm, coagulase production, and mannitol fermentation on mannitol salt agar (Merck, Germany). Anaerobic strains were identified by AP120A procedures[12].

Numerical evaluation

Statistical data were tested by SPSS/21.0 software (SPSS Inc., Chicago, IL)[13-17]. Chi-square test and Fisher'sexact two-tailed tests were used for data analysis. P-value less than 0.05 was determined as a significance level[17-22].

Results

Demographical features

Demographical properties of the examined patients are specified in **table I**. Of 180 patients tested in the study, 150 (83.33%) met our inclusion critria. The mean age of the studied patients was 49.7 years. The male to female ratio of the examined population was 92/85 (P <0.05). Histories of smoking and alcohol were determined in 40% and 18% of included patients, respectively.

Table I: Demographic properties of examined patinets.

Demographic characters	Individuals (150 people included)
Mean age (SD) (year)	49.7 (10.2)
Sex (M/F)	92/58
Mean weight (SD)	73.2 (8.2)
Smoking (%)	40
Alcohol (%)	18

Table II: Bacterial distribution amongst the cases of maxillofacial infections.

Bacteria	Distribution (%)
Stereptococcus mutans	38 (25.33)
Stereptococcus viridans	20 (13.33)
Stereptococcus oralis	9 (6)
Stereptococcus pneumoniae	12 (8)
Stereptococcus mitis	15 (10)
Staphylococcus aureus	40 (26.66)
Klebsiella pneumonia	8 (5.33)
Enterobacter aerogenes	18 (12)
Acinetobacter baummanii	6 (4)
Prevotella buccalis	17 (11.33)
Prevotella dentalis	20 (13.33)
Bacteroides forsythus	3 (2)
Fusobacterium nucleatum	5 (3.33)
Porphyromonas gingivalis	9 (6)
Veillonella spp.	6 (4)

Bacterial distribution

Table II shows the bacterial distribution amongst the cases of maxillofacial infections. *S. aureus* (26.66%), *S. mutans* (25.33%), *Prevotella dentalis* (13.33%), *Stereptococcus viridans* (13.33%), *Enterobacter aerogenes* (12%), and *Prevotella buccalis* (11.33%) were the most commonly isolated bacteria. *Bacteroides forsythus* (2%), *Fusobacterium nucleatum* (3.33%), *Acinetobacter baummanii* (4%), and *Veillonella spp.* (4%) had the lowest distribution.

Discussion

Dental sciences have been developed in recent years[23-30]. However, some complications remain health threating issues[30-36].

The present survey showed that post surgical maxillofacial infections are threating among patients. In this regard, *S. aureus* (26.66%), *S. mutans* (25.33%), *Prevotella dentalis* (13.33%), *Stereptococcus viridans* (13.33%), *Enterobacter aerogenes* (12%), and *Prevotella buccalis* (11.33%) were the most commonly isolated bacteria. Similarly, Kityamuwesi et al. (2015)[37] reported that *S. aureus* (23.50%) and *S. viridans* (19.40%) were the most commonly detected bacteria in odontogenic infections. Similar distribution of bacterial pathogens in the cases of maxillofacial surgeries were reported from Taiwan[38], Austria[39], Denmark[40], and Japan[41]. Similarly, Nóbrega et al. (2016)[42] mentioned that Peptostreptococcus spp., Prevotella, and *P. gingivalis* were the most commonly detected bacteria amongst endodontic infections in Brazil. The profile of anaerobic bacterial distribution of our survey was similar to United States[43], United Kingdom44, and Japan[45].

The present survey is the first report of distribution of causes of maxillofacial infections in Armenia. The present survey was limited to the low numbers of isolated bacteria, absence of the analysis of the location of maxillofacial infections and types of surgery and finally absence of the evaluation of antibiotic resistance pattern of bacterial isolates.

Conclusions

The main attainment of the present survey was determination of the distri bution of the most important bacterial pathogens in the cases of maxillofacial infections after head and neck surgical operation. As shown, *S. aureus, S. mutans, Prevotella dentalis, Stereptococcus viridans, Enterobacter aerogenes*, and *Prevotella buccalis* were the main pathogens isolated from the examined cases. Using sterile condition in the sutrgical operation and application of suitable antimicrobialk drugs can diminish the risk of maxillofacial infections.

Conflict of Interest

The author declare that he have no conflict of interest.

References

1. Dehkordi FS, Tavakoli-Far B, Jafariaskari S, Momtaz H, Esmaeilzadeh S, Ranjbar R, et al. Uropathogenic Escherichia coli in the high vaginal swab samples of fertile and infertile women: virulence factors, O-serogroups, and phenotyping and genotyping characterization of antibiotic resistance. New Microbes and New Infections. 2020;38:100824.

2. Dehkordi FS, Yazdani F, Mozafari J, Valizadeh Y. Virulence factors, serogroups and antimicrobial resistance properties of Escherichia coli strains in fermented dairy products. BMC Research Notes. 2014c;7(1):1-8.

3. Dehkordi FS, Barati S, Momtaz H, Ahari SN, Dehkordi SN. Comparison of shedding, and antibiotic resistance properties of Listeria monocytogenes isolated from milk, feces, urine, and vaginal secretion of bovine, ovine, caprine, buffalo, and camel species in Iran. Jundishapur Journal of Microbiology. 2013a;6(3):284.

4. Ghorbani F, Gheisari E, Dehkordi FS. Genotyping of vacA alleles of Helicobacter pylori strains recovered from some Iranian food items. Tropical Journal of Pharmaceutical Research. 2016;15(8):1631-6.

5. Dehkordi FS, Gandomi H, Basti AA, Misaghi A, Rahimi E. Phenotypic and genotypic characterization of antibiotic resistance of methicillin-resistant Staphylococcus aureus isolated from hospital food. Antimicrobial Resistance & Infection Control. 2017;6(1):1-1.

6. Taub D, Yampolsky A, Diecidue R, Gold L. Controversies in the management of oral and maxillofacial infections. Oral and Maxillofacial Surgery Clinics. 2017 Nov 1;29(4):465-73.

7. Kim SK, Kook MS, Han CH, Ryu SY. Bacteriologic features and antibiotic susceptibility in isolates from oral and maxillofacial infections. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2005;31(4):322-8.

8. Strachan DD, Williams FA, Bacon WJ. Diagnosis and treatment of pediatric maxillofacial infections. General dentistry. 1998 Mar 1;46(2):180-2.

9. Rastenienė R, Pūrienė A, Aleksejūnienė J, Pečiulienė V, Zaleckas L. Odontogenic maxillofacial infections: A ten-year retrospective analysis. Surgical infections. 2015 Jun 1;16(3):305-12.

10. Wilson M. Lethal photosensitisation of oral bacteria and its potential application in the photodynamic therapy of oral infections. Photochemical & Photobiological Sciences. 2004;3(5):412-8.

11. Shayegani ME, Maupin PS, McGlynn DM. Evaluation of the API 20E system for identification of nonfermentative Gram-negative bacteria. Journal of Clinical Microbiology. 1978 Jun 1;7(6):539-45.

12. Karachewski NO, Busch EL, Wells CL. Comparison of PRAS II, RapID ANA, and API 20A systems for identification of anaerobic bacteria. Journal of clinical microbiology. 1985 Jan 1;21(1):122-6.

13. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of Brucella abortus and Brucella melitensis in aborted bovine, ovine, caprine, buffaloes and camelid fetuses by application of conventional and real-time polymerase chain reaction. The Thai Journal of Veterinary Medicine. 2012;42(1):13.

14. Dehkordi FS, Momtaz H, Doosti A. Application of Real-Time PCR for detection of Aspergillus species in aborted ruminant foetuses. Bulgarian Journal of Veterinary Medicine. 2012;15(1):30-6.

15. Dehkordi FS. Prevalence study of Coxiella burnetii in aborted ovine and caprine fetuses by evaluation of nested and real-time PCR assays. American Journal of Animal and Veterinary Sciences. 2011;6(4):180-6.

16. Dehkordi FS, Haghighi N, Momtaz H, Rafsanjani MS, Momeni M. Conventional vs real-time PCR for detection of bovine herpes virus type 1 in aborted bovine, buffalo and camel foetuses. Bulgarian Journal of Veterinary Medicine. 2013;16(2):102-12.

17. Dehkordi FS. Prevalence study of Bovine viral diarrhea virus by evaluation of antigen capture ELISA and RT-PCR assay in Bovine, Ovine, Caprine, Buffalo and Camel aborted fetuses in Iran. AMB Express. 2011;1(1):1-6.

18. Dehkordi FS, Parsaei P, Saberian S, Moshkelani S, Hajshafiei P, Hoseini SR, Babaei M, Ghorbani MN. Prevalence study of Theileria annulata by comparison of four diagnostic Techniques in shouthwest Iran. Bulgarian Journal of Veterinary Medicine. 2012;15(2): 123-30.

19. Dehkordi FS, Haghighi Borujeni MR, Rahimi E, Abdizadeh R. Detection of Toxoplasma gondii in raw caprine, ovine, buffalo, bovine, and camel milk using cell cultivation, cat bioassay, capture ELISA, and PCR methods in Iran. Foodborne Pathogens and Disease. 2013;10(2):120-5.

20. Dehkordi FS, Khamesipour F, Momeni M. Brucella abortus and Brucella melitensis in Iranian bovine and buffalo semen samples: The first clinical trial on seasonal, Senile and geographical distribution using culture, conventional and real-time polymerase chain reaction assays. Kafkas Univ Vet Fak Dergisi. 2014;20(6):821-8.

21. Dehkordi FS, Valizadeh Y, Birgani TA, Dehkordi KG. Prevalence study of Brucella melitensis and Brucella abortus in cow's milk using dot enzyme linked immuno sorbent assay and duplex polymerase chain reaction. Journal of Pure and Applied Microbiology. 2014b;8(2):1065-9.

22. Dehkordi FS, Tirgir F, Valizadeh Y. Effects of Guajol® ointment synthesized from medicinal smoke condensate of jennet feces on burn wound healing on Wistar rat. Veterinary Research Forum. 2017; 8(3):215.

23. Monajem Zade SM, Elyaskhil M, Fathi A, Asadinejad SM. Evaluate Risk Markers For Periodontal Disease In Children With Type 1 Diabetes: A Systematic Review And Meta-Analysis. 2021;12:5715-5722.

24. Ashtiani AH, Mardasi N, Fathi A. Effect of multiple firings on the shear bond strength of presintered cobalt-chromium alloy and veneering ceramic. The Journal of Prosthetic Dentistry. 2021;126(6):803-e1.

25. Mosharraf R, Molaei P, Fathi A, Isler S. Investigating the Effect of Nonrigid Connectors on the Success of Tooth-and-Implant-Supported Fixed Partial Prostheses in Maxillary Anterior Region: A Finite Element Analysis (FEA). International Journal of Dentistry. 2021;2021:1-12.

26. Abolhasani M, Ghasemi E, Fathi AH, Hayatizadeh MJ. Color Change of Ceramill Zolid FX Following Abrasion with/without Toothpaste. Journal of Iranian Dental Association. 2021;33(3):51-7.

27. Maalekipour M, Safari M, Barekatain M, Fathi A. Effect of Adhesive Resin as a Modeling Liquid on Elution of Resin Composite Restorations. International Journal of Dentistry. 2021;2021:1-9.

28. Fathi A, Salehi A. Antimicrobial resistance properties of Helicobacter pylori strains isolated from dental plaque and saliva samples. Academic Journal of Health Sciences. 2021;36 (4):51-55.

29. Khamisi N, Fathi A, Yari A. Antimicrobial resistance of Staphylococcus aureus isolated from dental plaques. Academic Journal of Health Sciences. 2022;37(1):136-40.

30. Fathi A, Ebadian B, Dezaki SN, Mardasi N, Mosharraf R, Isler S, Tabatabaei SS. An Umbrella Review of Systematic Reviews and Meta-Analyses Evaluating the Success Rate of Prosthetic Restorations on Endodontically Treated Teeth. International Journal of Dentistry. 2022 Feb 22;2022.

31. Ghasemi E, Fathi AH, Parvizinia S. Effect of three disinfectants on dimensional changes of different impression materials. Journal of Iranian Dental Association. 2019;31(3):169-76.

32. Monirifard R, Abolhasani M, Tahani B, Fathi A, Choobdaran A. Relationship of Personality Traits and Patient Satisfaction with Fixed Implant Prosthodontic Treatments. Journal of Iranian Dental Association. 2019;31(4):182-8.

33. Abolhasani M, Givehchian P, Fathi A, Goudarzi S. Relationship of Life Satisfaction and Satisfaction with Fixed Implant-Supported Prostheses in the Elderly. Journal of Iranian Dental Association. 2021;33(1):17-21.

34. Ebadian B, Fathi A, Khodadad S. Comparison of the effect of four different abutment screw torques on screw loosening in single implant-supported prosthesis after the application of mechanical loading. International Journal of Dentistry. 2021;2021:1-6.

35. Ebadian B, Fathi A, Savoj M. In Vitro Evaluation of the Effect of Different Luting Cements and Tooth Preparation Angle on the Microleakage of Zirconia Crowns. International Journal of Dentistry. 2021;2021:1-7.

36. Barakati B, Khodadadi R, Asadi P, Fathi A. Evaluate The Effect Of Various Titanium Abutment Modifications On The Behavior Of Peri-Implant Soft Tissue Healing, Inflammation, And Maintenance: A Systematic Review And Meta-Analysis. Turkish Onilne Journal of Qualitative Inquiry. 2021; 12:11401-10.

37. Kityamuwesi R, Muwaz L, Kasangaki A, Kajumbula H, Rwenyonyi CM. Characteristics of pyogenic odontogenic infection in patients attending Mulago Hospital, Uganda: a cross-sectional study. BMC microbiology. 2015 Dec;15(1):1-0.

38. Tsai YW, Liu YH, Su HH. Bacteriology of peritonsillar abscess: the changing trend and predisposing factors. Brazilian journal of otorhinolaryngology. 2018 Sep 1;84(5):532-9.

39. Poeschl PW, Spusta L, Russmueller G, Seemann R, Hirschl A, Poeschl E, et al. Antibiotic susceptibility and resistance of the odontogenic microbiological spectrum and its clinical impact on severe deep space head and neck infections. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;110:151-6.

40. Klug TE, Henriksen JJ, Fuursted K, Ovesen T. Significant pathogens in peritonsillar abscesses. European journal of clinical microbiology & infectious diseases. 2011 May;30(5):619-27.

41. Takenaka Y, Takeda K, Yoshii T, Hashimoto M, Inohara H. Gram staining for the treatment of peritonsillar abscess. International journal of otolaryngology. 2012 Jan 1;2012.

42. Nóbrega LM, Montagner F, Ribeiro AC, Mayer MA, Gomes BP. Bacterial diversity of symptomatic primary endodontic infection by clonal analysis. Brazilian oral research. 2016;30(1).

43. Brook I. Microbiology of acute and chronic maxillary sinusitis associated with an odontogenic origin. The Laryngoscope. 2005 May;115(5):823-5.

44. Haque M, Sartelli M, Haque SZ. Dental infection and resistance—global health consequences. Dentistry journal. 2019 Mar;7(1):22.

45. Kuriyama T, Karasawa T, Nakagawa K, Nakamura S, Yamamoto E. Antimicrobial susceptibility of major pathogens of orofacial odontogenic infections to 11 β-lactam antibiotics. Oral microbiology and immunology. 2002 Oct;17(5):285-9.

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ORIGINAL

Effect of astronomy on treatment of diseases; narrative review

Efecto de la astronomía en el tratamiento de enfermedades; revisión narrativa

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Abstract

Introduction: According to ancient hypothesis, location of starts in the sky can determine different events in the earth. The present survey was done to assess the effects of astronomy on the treatment of diseases.
Methods: A comprehensive searches were done on different databases such as Pubmed, Scopus, ScienceDirect, Directory of Open Access Journals (DOAJ) and … to find relevant researches about the effect of astronomy on treatment of diseases. Collected data were analyzed and categorized to write this paper.
Results: According to the results, the location of stars in space can lead to a series of meta-mental effects on Earth, which in turn can lead to or prevent the occurrence of some diseases. Among these, the most superficial effects of mental illness have been identified. Also, the use of some types of drugs at certain times and hours leads to better therapeutic results, all of which are affected by the position of the stars in space and their interaction with each other.
Conclusion: Unfortunately, very few studies have been done in this field and the role of stars in the treatment of diseases is not well understood. But it seems that more and more detailed studies can effectively determine the role of this science in the treatment of a wide range of diseases.

Key words: Effect, astronomy, treatment, medicine, diseases.

Resumen

Introducción: Según las antiguas hipótesis, la ubicación de las estrellas en el cielo puede determinar diferentes acontecimientos en la tierra. El presente estudio se realizó para evaluar los efectos de la astronomía en el tratamiento de las enfermedades.
Métodos: Se realizó una búsqueda exhaustiva en diferentes bases de datos como Pubmed, Scopus, ScienceDirect, Directory of Open Access Journals (DOAJ) y ... para encontrar investigaciones relevantes sobre el efecto de la astronomía en el tratamiento de enfermedades. Los datos recogidos se analizaron y clasificaron para escribir este artículo.
Resultados: Según los resultados, la ubicación de las estrellas en el espacio puede provocar una serie de efectos meta-mentales en la Tierra, que a su vez pueden provocar o prevenir la aparición de algunas enfermedades. Entre ellas, se han identificado los efectos más superficiales de las enfermedades mentales. Asimismo, el uso de algunos tipos de medicamentos en determinados momentos y horas conduce a mejores resultados terapéuticos, todo ello afectado por la posición de los astros en el espacio y su interacción entre ellos.
Conclusión: Desgraciadamente, se han realizado muy pocos estudios en este campo y no se conoce bien el papel de los astros en el tratamiento de las enfermedades. Sin embargo, parece que estudios más detallados pueden determinar efectivamente el papel de esta ciencia en el tratamiento de una amplia gama de enfermedades.

Palabras clave: Efecto, astronomía, tratamiento, medicina, enfermedades.

Introduction

Throughout history, humans have looked to the sky to navigate the vast oceans, to decide when to plant their crops and to answer questions of where we came from and how we got here. It is a discipline that opens our eyes, gives context to our place in the universe and that can reshape how we see the world. Astronomy is a natural science that studies celestial objects and phenomena and also locations of starts in the sky. It uses mathematics, physics, and chemistry in order to explain their origin and evolution. Stars, moons, planets, galaxies, nebulae, and comets are the main subjects in this science. More generally, astronomy studies everything that originates beyond Earth's atmosphere. Cosmology is a branch of astronomy that studies the universe as a whole[1].

Astronomy has so many applications in different sciences, such as physic, chemistry, earth sciences, climate and etc. Its applications are in different parts of the human life, such as industry, technology, aerospace sector, energy sector, international collaboration, and even medicine[2]. However, rare considerations were focused on the applications of astronomy in medical sciences.

For a long time astronomers and other scientists supposed that the position of their work was evident to society. But in these difficult days of financial severity, even the most obvious benefits of science have to undergo careful scrutiny. So, now more than ever is the time to highlight the importance of astronomy as a field in terms of its contributions to our technology, our mind sets and our lives. It is clear that astronomy and its related fields are at the forefront of science and technology; answering fundamental questions and driving innovation. The importance of this contribution to science and to society has been highlighted here and the sheer breadth of what astronomy has to offer will ensure that it continues to be of great importance to the scientific community[3].

Astronomy and medicine in ancient world

Astronomy has numerous characters to play in ancient medicine. There were two words "astronomy" and "astrology". Astronomy, measured and recorded celestial bodies and events scientifically and astrology means the application of astronomy in the human life to predict future events.

Hellenistic physicians rely on both astronomical and astrological information. In Mesopotamia, celestial events were correlated with human events in the practice of medicine and even more generally. The same was true in the Greco-Roman world. Neither Babylonian nor Greek medical practice depended only on astronomy/astrology, but both were an important component of medicine in both civilizations. Although this chapter will focus primarily on astronomy and astrology in Greco-Roman medicine, the Babylonian material provides an important precursor and counterpart to the Greek material and, thus, will also be treated here[4].

The natural cycle of the seasons due to the Sun's apparent annual motion and the natural phenomena due to its apparent daily motion (such as day/ night) and the Moon's motion (such as the month) all influenced earthly life. The courses of the planets, as well as celestial phenomena such as eclipses and meteorological phenomena such as the formation of clouds, rain, and comets (understood as sublunary phenomena) were influential as well. In an ancient medicine, Greek physicians employed the doctrine of humors (blood, phlegm, bile, and black bile), which could also be correlated with seasonal cycles and the planets, as well as the elements (earth, air, fire, and water) and qualities (hot, cold, wet, and dry). The application of astrological doctrines and principles was found previously, which tended to be applied in an individual way to a particular patient. These could include the casting of horoscopes to interpret the cause, progress, and resolution of disease —a practice called decumbiture (decubitus) and the use of astrological techniques in prescribing a therapeutic regimen[6].

In Iranian folk medicine[7,8], the times and locations of the stars and even the planets had a great impact on the healing of diseases. The position of the Sun, Saturn, Jupiter, Mercury and Venus in the sky leads to their gravitational and supernatural forces on each other, which results in a series of supernatural events on Earth. Also, with the change of seasons, many changes are made in human temperament which affect human diseases. During the day and night, the secretion of melatonin, which is due to the presence of light during the day or its absence at night from the enigmatic pineal gland can have a great impact on the effectiveness of drugs and health measures in improving and treating diseases. Astronomers were aware of this but did not know its main mechanism.

Astronomy and medicine in modern world

Astronomy has so many applications in the modern medicine. In this regard, several classifications, including radio astronomy, infrared astronomy, optical astronomy, ultraviolet astronomy, X-ray astronomy, Gamma-ray astronomy, and astrobiology, have been developed in the medical astronomy. Astronomy helps medical practitioners to diagnose and treat several types of cancer cells using several newly developed X-ray and Gamma-ray[9].

Astronomers struggle continually to see objects that are ever dimmer and further away. Medicine struggles with similar issues: to see things that are obscured within the human body. Both disciplines require high-resolution, accurate and detailed images. Perhaps the most notable example of knowledge transfer between these two studies is the technique of aperture synthesis, developed by the radio astronomer and Nobel Laureate, Martin Ryle (Royal Swedish Academy of Sciences, 1974). This technology is used in computerized tomography (also known as CT or CAT scanners), magnetic resonance imaging, positron emission tomography (PET) and many other medical imaging tools.

Along with these imaging techniques, astronomy has developed many programming languages that make image processing much easier, specifically IDL and IRAF. These languages are widely used for medical applications[10]. Another important example of how astronomical research has contributed to the medical world is in the development of clean working areas. The manufacture of space-based telescopes requires an extremely clean environment to prevent dust or particles that might obscure or obstruct the mirrors or instruments on the telescopes (such as in NASA's STEREO mission)[11]. The cleanroom protocols, air filters, and bunny suits that were developed to achieve this are now also used in hospitals and pharmaceutical labs[12].

Additionally, several modern applications have in medical sciences have been developed using the astrology. Radio astronomers developed a method that is now used as a non-invasive way to detect tumors. Small thermal sensors initially developed to control telescope instrument temperatures are now used to control heating in neonatology units - units for the care of newborn babies[13]. A low-energy X-ray scanner developed by NASA is currently used for outpatient surgery, sports injuries, and in third world clinics. It has also been used by the US Food and Drugs Administration (FDA) to study whether certain pills were contaminated[13]. Software for processing satellite pictures taken from space is now helping medical researchers to establish a simple method to implement wide-scale screening for Alzheimer's disease[14]. Looking through the fluid-filled, constantly moving eye of a living person is not that different from trying to observe astronomical objects through the turbulent atmosphere, and the same fundamental approach seems to work for both. Adaptive optics used in astronomy can be used for retinal imaging in living patients to study diseases such as macular degeneration and retinitis pigmentosa in their early stages[15].

Effects of astronomy on the treatment of diseases

One of the well-known aspects of the effect of astrology in treatment of diseases is its effects on humors and temperament. Temperament is a "commixture" (synkrasis) of the qualities of hot, cold, wet, and dry in every person, which affect its life and moods and also people resistance or sensitive against some diseases[16].

Ptolemy assigned planets one or more qualities based on their intrinsic nature, or their orientality or occidentality. The seasons, solstices and equinoxes, angles of the chart, and moon phases were also given qualities, as in the table above (**Table I**).

Ptolemy's instructions is used for delineating temperament from the birthchart, using the Ascendant (the sign rising on the eastern horizon at the time of birth), planets in the Ascendant sign and their rulers, and the Moon for the shape of the body. Fixed stars rising with the Ascendant were also incorporated to a lesser degree[18]. Other astrologers of Late Antiquity also assigned qualities and elements to the planets and zodiac signs, but except for Hephaestio (who quoted Ptolemy extensively), the use of astrological temperament was not discussed. Nevertheless, the importance given to temperament in medicine by such renowned physicians as Galen, coupled with the use of astrology in medical practice, led to further development of humors, elements and qualities in astrology, primarily under Arabic-language astrologers of the early Medieval period. By the end of the Middle Ages, astrologers began to incorporate astrological formulae for temperament into their work.

Conclusion

According to this study the movement and location of stars and planets relative to Earth can affect many factors related to human health. In this regard, the main role is played by human nature, which can change with the change of seasons. Also, being exposed day and night due to the effect of melatonin can strengthen or weaken the treatments performed against some diseases.

Table I: Ptolemy's assignment of qualities[17].

Angles		Solstice/equinox	Moon phase	Planet phase	Planets	Seasons
Cold	Imum Coeli	Winter solstice	New moon	Conjunction	Saturn	Autumn, winter
Hot	Midheaven	Summer solstice	Full moon	Opposition	Sun, Venus, Mars, Jupiter, Moon (slightly)	Spring, summer
Dry	Ascendant	Autumnal equinox	Last quarter	2nd station/ square	Sun, Mars, Saturn	Summer, autumn
Wet	Descendant	Vernal equinox	First quarter	1st station/ square	Moon, Venus, Jupiter	Winter, spring

The influence of planets and stars may play a role in the treatment of diseases through their effect on the melatonin gland. But achieving this goal requires more extensive studies.

Conflict of Interest

The author declare that he have no conflict of interest.

References

1. Feigelson ED, Babu GJ. Modern statistical methods for astronomy: with R applications. Cambridge University Press; 2012.

2. Rosenberg M, Baldon G, Russo P, Christensen LL. Astronomy in everyday life. Communicating Astronomy to the Public Journal. 2014;14:30-6.

3. Meher SK, Panda G. Deep learning in astronomy: a tutorial perspective. The European Physical Journal Special Topics. 2021;230(10):2285-317.

4. Greenbaum DG. Hellenistic Astronomy in Medicine. InHellenistic Astronomy 2020; pp. 350-380). Brill.

5. Ossendrijver M. Hellenistic Astronomy and the Babylonian Scribal Families. InHellenistic Astronomy 2020;426-439. Brill.

6. Geller MJ. Hellenistic Astronomy: The Science in Its Contexts edited by Alan C. Bowen and Francesca Rochberg. Aestimatio: Sources and Studies in the History of Science. 2021;2(1):188-94.

7. Sina I. Kitab Al-Qanun Fi Al-Tibb (The Canon of Medicine). Boulaq edition of the Canon. 1877.

8. Zakariya Al Razil (Rhazes). Kitab Al-Hawi fi al-Tibb (Liber Continens). 1094.

9. Report of Science Payloads Technology Division, Research and Science Support Department, ESA's science, technology and engineering research centre (ESTEC), Netherlands. 2001. Available at: https://www.esa.int/Newsroom/Press_Releases/Astronomy_helps_advance_medical_diagnosis_techniques.

10. Shasharina SG, Volberg O, Stoltz P, Veitzer S. GRIDL: high-performance and distributed interactive data language. InHPDC-14. Proceedings. 14th IEEE International Symposium on High Performance Distributed Computing, 2005. 2005 Jul 24 (pp. 291-292). IEEE.

11. Gruman JB. Image Artifacts-Telescope and Camera Defects, 2011. http://stereo.gsfc. nasa.gov/artifacts/artifacts_camera.shtml, Retrieved August 2013

12. Clark H. Modern-day cleanroom invented by Sandia physicist still used 50 years later, 2012. https://share.sandia.gov/news/ resources/news_releases/cleanroom_50th, Retrieved June 2013

13. National Research Council 1991, Working Papers: Astronomy and Astrophysics Panel Reports, (Washington, DC: The National Academies Press)

14. ESA 2013, Identifying Alzheimer's using space software, http://www.esa.int/Our_Activities/ Technology/TTP2/Identifying_Alzheimer's_ using_space_software, Retrieved July 2013

15. Boston Micromachines Corporation, http:// www2.bostonmicromachines.com/Portals/1703/docs/AO_101_White_Paper.pdf, 2010

16. Naseri M, Rezaeiazdeh H, Taheripanah T, Naseri V. Temperament theory in the iranian traditional medicine and variation in therapeutic responsiveness, based on pharmacogenetics. Journal of Islamic and Iranian traditional medicine. 2010;1(3):237-42.

17. Greenbaum DG. Astronomy, Astrology, and Medicine. Handbook of Archaeoastronomy and Ethnoastronomy. 2015:117.

18. Greenbaum DG. Temperament: astrology's forgotten key. The Wessex Astrologer, Bournemouth, UK. 2005.

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ORIGINAL

Study of maternal and fetal outcomes in gestational diabetes mellitus, tertiary care hospital, India

Estudio de los resultados maternos y fetales en la diabetes mellitus gestacional, hospital de atención terciaria, India

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Abstract

Objective: The main objective of the research was to assess the maternal and fetal outcome of subjects with Gestational Diabetes Mellitus. The other objectives of the study were to assess the KAP of subjects, Nutritional assessment of subjects with Gestational Diabetes Mellitus.

Methodology: This was an observational study, carried out over a period of 6 months among in-patients of the department of Obstetrics & Gynecology. Based on the inclusion and exclusion criteria, 130 subjects were selected and informed the purpose of the study and details were collected using the proforma developed. KAP questionnaire was filled by the subject to assess the knowledge, attitude and practice.

Results: A total of 130 patients were enrolled in the study based on the inclusion and exclusion criteria. The mean age of the study subjects was found to be 29.56 ± 4.64 years. Majority of the subjects belonged to the age group of 25-32 years (46.15%). Maternal distress (84.61%) was the most common maternal complication followed by cesarean section (73.84%). Jaundice (27.69%), followed by NICU admissions and Respiratory distress each with (16.92%) were the fetal complications. Subjects were administered the self-designed KAP questionnaire, to assess the knowledge, attitude and practice. Using statistical analysis, a weak positive correlation was observed between knowledge and attitude was statistically not significant, a weak negative correlation was observed between attitude and practice was not statistically significant, and a moderate positive correlation was observed between knowledge and practice which was statistically significant. Majority of the subject's showed poor physical activity (49.23%)

Conclusion: Pregnancies complicated with GDM are associated with adverse maternal and fetal outcome in terms of maternal distress, LSCS, hypertensive disorders, prolonged labor, infections, IUGR, macrosomia, jaundice, respiratory distress, low birth weight, low Apgar score at birth and high rates of admission to NICU. Low birth weight due to prematurity, IUGR and fetal distress are the main reasons for NICU admissions. Majority of the subjects had good knowledge, positive attitude and good practice regarding the disease condition and its management. Knowledge and practice were found to be interdependent.

Key words: Gestational diabetes, KAP questionnaire, pregnancy.

Resumen

Objetivo: El objetivo principal de la investigación fue evaluar el resultado materno y fetal de los sujetos con Diabetes Mellitus Gestacional. Los otros objetivos del estudio fueron evaluar el KAP de los sujetos, la evaluación nutricional de los sujetos con Diabetes Mellitus Gestacional.

Metodología: Se trata de un estudio observacional, llevado a cabo durante un período de 6 meses entre los pacientes internos del departamento de Obstetricia y Ginecología. Sobre la base de los criterios de inclusión y exclusión, se seleccionaron 130 sujetos, a los que se informó del propósito del estudio y se recopilaron datos utilizando el formulario elaborado. Los sujetos rellenaron el cuestionario KAP para evaluar sus conocimientos, actitudes y prácticas.

Resultados: Un total de 130 pacientes se inscribieron en el estudio según los criterios de inclusión y exclusión. La edad media de los sujetos del estudio fue de 29,56 ± 4,64 años. La mayoría de los sujetos pertenecían al grupo de edad de 25-32 años (46,15%). El sufrimiento materno (84,61%) fue la complicación materna más frecuente, seguida de la cesárea (73,84%). Las complicaciones fetales fueron la ictericia (27,69%), seguida de los ingresos en la UCIN y el sufrimiento respiratorio (16,92%). Se administró a los sujetos el cuestionario KAP diseñado por ellos mismos, para evaluar los conocimientos, la actitud y la práctica. Mediante un análisis estadístico, se observó una correlación positiva débil entre los conocimientos y la actitud, que no fue estadísticamente significativa, una correlación negativa débil entre la actitud y la práctica, que no fue estadísticamente significativa, y una correlación positiva moderada entre los conocimientos y la práctica, que fue estadísticamente significativa. La mayoría de los sujetos mostraron una actividad física deficiente (49,23%).

Conclusiones: Los embarazos complicados con DMG se asocian con resultados maternos y fetales adversos en términos de sufrimiento materno, LSCS, trastornos hipertensivos, parto prolongado, infecciones, RCIU, macrosomía, ictericia, sufrimiento respiratorio, bajo peso al nacer, baja puntuación de Apgar al nacer y altas tasas de ingreso en la UCIN. El bajo peso al nacer debido a la prematuridad, el RCIU y el sufrimiento fetal son las principales razones de los ingresos en la UCIN. La mayoría de los sujetos tenían un buen conocimiento, una actitud positiva y una buena práctica respecto a la condición de la enfermedad y su manejo. Se comprobó que los conocimientos y la práctica son interdependientes.

Palabras clave: Diabetes gestacional, cuestionario KAP, embarazo.

Introduction

Gestational diabetes mellitus (GDM) is defined as "hyperglycemia first detected during pregnancy that is clearly not preexisting or overt diabetes"[1]. It is believed to be the drastically increased prevalence of GDM had a negative impact on various short- and long-term maternal and neonatal adverse outcomes[2].

Gestational diabetes mellitus has been related with an expanded risk for pregnancy-induced hypertension (PIH) with relative risk going from 1.4 to 4.15[3-5] albeit a few examinations propose that the connection between PIH and GDM isn't surely known[6]. It additionally builds the pace of cesarean delivery by up to 57.4% and has a more noteworthy effect in instances of obesity as well as past history of cesarean area[7,8].

Gestational diabetes mellitus (GDM) is diabetes that is analyzed during the second or third trimester of pregnancy and isn't obviously clear diabetes[9]. As indicated by American Diabetes Association, Gestational Diabetes mellitus (GDM) has been defined as any level of glucose bigotry with beginning or starting determination during pregnancy.[10] Many risk factors for creating GDM are like those for type 2 diabetes mellitus (T2DM), including obesity, family background of diabetes and high-risk nationalities. Extra risk factors incorporate expanded maternal age, past macrocosmic infant, and individual history of GDM[11].GDM not only influences immediate maternal complications (hypertensive disorders such as preeclampsia, gestational hypertension and chronic hypertension, need for cesarean section, Hypoglycemia, Abortion, polyhydramnios,) and neonatal complications (hypoglycemia, respiratory distress, macrosomia, Jaundice, Hypothermia and still birth), but also increases the risk of future type 2 diabetes in mother as well as the baby[12]. There is no specific prevention for gestational diabetes but more healthy habits adopted before pregnancy can be a benefit. Some possible measures that can be considered are, eating healthy foods, being active and fit.[13] Worldwide there are many guidelines with recommendations for appropriate management strategies for GDM. Most guidelines recommend screening all patients for GDM at 24-28 weeks of gestation. GDM can be diagnosed using fasting glucose reading, glucose challenge test (GCT) or oral Glucose tolerance test (OGTT)[14]. According to American college of obstetricians and gynecologist (ACOG), once patient has been diagnosed with GDM, they should receive proper diet plan and exercise counselling[15]. It is estimated that 70-85% of cases, can be controlled with lifestyle modifications alone. If treatment targets are not met, pharmacotherapy should be initiated. Insulin is generally the recommended first line therapy as it does not cross placenta. Glyburide and Metformin are both pregnancy category B drugs which makes them safe and effective for a long- term use[16]. Approximately 7% of all pregnancies are confounded by GDM, which brings about in excess of 200,000 cases every year. The pervasiveness might go from 1 to 14% of all pregnancies, contingent upon the population contemplated and diagnostic tests employed. The predominance of high blood glucose (hyperglycemia) in pregnancy increases quickly with age and is most noteworthy in ladies beyond 45 years old.[15] In 2017, there were an estimated 204 million ladies living with diabetes. This number is projected to increase to 308 million by 2045. 1 out of 3 ladies with diabetes was of regenerative age.16.2% of live births had some type of hyperglycemia in pregnancy. An estimated 85.1% were because of Gestational diabetes and 1 of every 7 births were impacted by gestational diabetes. It is important for women with diabetes in pregnancy or GDM to carefully control and monitor their blood glucose levels to reduce the risk of adverse effect during pregnancy[17]. The present study is aimed to understand the effect of Gestational Diabetes Mellitus in maternal and fetal outcomes. Our study identifies the most significant factors that are responsible for developing Gestational Diabetes mellitus.

Materials and methods

This was an observational study, where according to the inclusion and exclusion criteria the subjects were identified from the in-patient department of obstetrics and gynecology. The purpose of the study was explained to the subjects and the consent was obtained. The subject was followed from the date of admission till delivery and maternal outcomes like placental abruption, oligohydramnios, mode of delivery, complications etc. and fetal outcomes like Apgar score, NICU admission, IUGR etc. was assessed. Relevant data (demographic details, laboratory investigations and medication chart) was reviewed with the case report form, and study tools were administered to obtain relevant information. The data thus obtained was entered in a Microsoft Excel sheet and was analyzed appropriately.

Data collected for this study was entered into Microsoft excel and analyzed statistically by computing proportion for all qualitative data and mean, standard deviation, for quantitative data. The result is also expressed in terms of 95% confidence interval. It is presented in the form of frequency format and diagrammatic representation wherever necessary. Statistical analysis was performed using Chi-square test to find the association between low birth weight and NICU admission. Fisher's exact probability test was done to find the association between Apgar score and NICU admission. Pearson correlation was done to find the interdependence between knowledge and attitude, knowledge and practice and attitude and practice. For inferential statistics the relationship between NICU admission and variables (Apgar score and low birth weight) the results were considered statistically significant wherever p value is less than 0.05.

Result

The study was conducted for a period of 6 months, included 130 subjects who were fulfilling the inclusion criteria and admitted in the patient wards of the department of Obstetrics and Gynecology in ESIC-MC-PGIMSR, Bengaluru. Gestational age plays an important role in the maternal and fetal outcome, 78 subjects delivered at 36-38 weeks (60%), followed by 52 subjects at 38-40 weeks (38.46%). The mean gestational age was found to be 37.78 ± 1.268 weeks. Hypothyroidism was the most common diagnosis 34(26.15%), followed by Gestational Hypertension 26 (20%), 6 (4.61%) candidiasis, 2 (1.53%) anaemia, 2 (1.53/%) Epilepsy, Lower Respiratory Tract Infection 2 (1.53%),Fever 2 (1.53%), Polio rescue paralysis 2 (1.53%) and 70 (53.84%) had No co-morbidities. Gestational Diabetes Mellitus Type A2 was the most common diagnosis 72 (55.38%), followed by Gestational Diabetes Mellitus Type A1 58 (44.61%). Maternal complications of the subjects were assessed and the most common complication was Maternal distress 110 subjects (84.61%) followed by Cesarean Section 96 (73.84%), 72 subjects (55.38%) with other co-morbidities,28 subjects with Lactational failure (13.4%), 24 (18.46%) subjects with Pre-mature Rupture of Membrane (PROM),18 (13.85%) with Polyhydramnios and 12 (9.23%) each with oligohydramnios and infection,10 (7.69%) subjects with obesity and 2 (1.53%) subjects with An hydramnios, hypoglycemia, Intra Uterine Growth Restricted in each category. Detailed distribution of subjects based on maternal complication is represented in **table I**.

Table I: Distribution of subjects based on maternal complications.

Complication	Number of subjects	Percentage (%)
Co-morbidity	72	55.38
Cesarean section	96	73.84
Oligohydramnios	12	9.23
polyhydramnios	18	13.85
Anhydramnios	2	1.53
Hypoglycemia	2	1.53
PROM	24	18.46
Pre-term	12	9.23
Maternal Distress	110	84.61
Obesity	10	7.69
Infection	12	9.23
Lactational Failure	28	13.4
IUGR	2	1.53

Fetal complications were assessed and the most common fetal complications were Jaundice 36 (27.69) followed by NICU admission and Respiratory Distress each with 22 (16.92%) subjects ,8 (6.15%) subjects has been found to have birth injuries, Hypoglycemia has been recorded in 10(7.69%) subjects 6 (4.62%) macrosomia and premature birth was recorded followed by 2 (1.53%) large for gestational age and 18 (13.8%) with other minor complications such as hypothermia, Infection etc. Detailed distribution of subjects based on fetal complications is represented in **table II**.

Table II: Distribution of subjects based on fetal complications.

Complication	Number of subjects	Percentage (%)
Hypoglycemia	10	7.69
Large for Gestational Age	2	1.53
Macrosomia	6	4.62
Respiratory Distress	22	16.92
Jaundice	36	27.69
Birth Injuries	8	6.15
Premature Birth	6	4.62
NICU Admission	22	16.92
Others	18	13.8

The APGAR score describes the condition of the new-born baby immediately after birth and if it is accordingly applied, it can be a standardized instrument for assessment. The APGAR is affected by many factors such as gestational age, Medications taken during pregnancy, any other co morbidity conditions etc.

Majority of the neonates 90 (69.23%) had APGAR score of greater than 14 (Normal) ,followed by 40 (30.77%) subjects had APGAR score between 4-6 (Mild asphyxia) at 1 min.APGAR score of 5 min was assessed and 130 (100%) neonates had APGAR score >7 (Normal). Detailed distribution of subjects based om APGAR score is displayed in **table III**.

Table III: Distribution of subjects based on Apgar score.

APGAR range	1 min (number of subjects)	1 min (%)	5 min (number of subjects)	5 min (%)
Normal (>7)	90	69.23	130	100
Mild Asphyxia (4-6)	40	30.77	0	0
Grand Total	130	100	130	100

Assessment of knowledge of disease in subjects with Gestational Diabetes Mellitus (Table IV).

The Knowledge possessed by the subject is a representation of their understanding about the disease and it greatly shows their approach to disease condition and its management.

The following questions were administered to the subjects:

Question K1: Do You Know normal level of Random Blood Sugar
Question K2: What are the known Risk factors for GDM?
Question K3: GDM is a risk factor for future type 2 DM?
Question K4: Do you know the name of the drug you are taking for your GDM?
Question K5: What are the long-term health consequences for the child born to GDM mothers?

Table IV: Distribution of response received for assessment of knowledge.

Response	K1		K2		K3		K4		K5	
	n	%	n	%	n	%	n	%	n	%
Correct answer	74	56.92	74	56.92	54	41.54	118	87.69	70	53.85
Incorrect answer	56	43.07	56	43.07	76	58.46	16	12.31	60	46.15

Assessment of Attitude in Subjects with Gestational Diabetes Mellitus

The attitude of the subject towards the disease and its management was assessed using Likert scale. Question A1: Regular checking of Glucose is important.

Out of 130 subjects of **Question A1** (58.46%, 76) strongly agreed and 36 (27.69%) agreed Regular checking of Glucose in Important, where as 1.53%, 2 disagreed and 16 (12.30%) had a neutral feeling. The graphical representation shown above specifies that majority of the subject had a positive attitude and part of the study population had a neutral or had mixed feeling.

In **Question A2**, 74 (58.46%) strongly agreed and 36 (27.69%) subjects agreed that Regular medications will improve the disease condition, while 18 (13.84%) had a neutral opinion, which means they were unaware that medication could improve the disease condition. Above graphical representation indicates that most of the subjects with GDM were aware that the regular medications does improve the disease conditions, which explains majority of the study population had a positive attitude towards the disease.

In **Question A3**, 78 (60%) strongly agreed and 48 (36.92%) agreed that sweet/sugar reduction/restriction could control GDM, while 4 (3.08%) had a neutral opinion or were unaware that medication could improve the disease condition. The graphical representation from figure above indicates that most of the study population were aware that sugar/sweet restriction/reduction help control GDM to certain extent, showing majority of the subjects had a positive attitude towards the disease.

In **Question A4**, majority of the study population disagreed 52 (40%) and 40 (30.77%) strongly disagreed that GDM should not be treated in pregnancy due to fear of risk to the baby and 34 (26.15%) had neutral response while very few subjects strongly agreed and agreed 2 (1.53%) that GDM should not be treated in pregnancy due to feat of the risk to the baby. According to the study population it is seen that majority of them had a negative attitude towards the disease condition and very few of them had positive attitude.

In **Question A5**, majority (27.69%, 36) disagreed and 32 (24.62%) strongly disagreed that emotional stress does not have any role in causing GDM, while 22 (16.92%) strongly agreed and 16 (12.31%) agreed that emotional stress does not have any role in causing GDM. The graphical representation from table below indicated that most of the subject were not sure that emotional Stress does have a role in causing GDM 28 (21.54%). This shows a mixed attitude towards the disease condition.

In **Question A6**, 46 (35.38%) and 40 (30.76%) strongly disagreed and disagreed that they take OTC medications during pregnancy, while only few 12 (9.23%) agreed and 6 (4.62%) strongly agreed that they take OTC medications during pregnancy and is safe to take, whereas 26 (20%) were neutral. The graphical representation above shows that most of the subjects were aware that OTC medications should not be taken during pregnancy. This shows that majority of the study population had positive attitude towards the disease and the medications they were taking. **table V**.

Table V: Distribution of subject's response to Question.

Distribution of subject's response to Question A1		
Response	*Number of subjects*	*Percentage (%)*
Strongly disagree	0	0
Disagree	2	1.53
Neutral	16	12.31
Agree	36	27.69
Strongly agree	74	58.46
Distribution of subject's response to Question A2		
Strongly disagree	0	0
Disagree	0	0
Neutral	18	13.85
Agree	36	27.69
Strongly agree	76	58.46
Distribution of subject's response to Question A3		
Strongly disagree	0	0
Disagree	0	0
Neutral	4	3.08
Agree	48	36.92
Strongly agree	78	60
Distribution of subject's response to Question A4		
Strongly disagree	40	30.77
Disagree	52	40
Neutral	34	26.15
Agree	2	1.53
Strongly agree	2	1.53
Distribution of subject's response to Question A5		
Strongly disagree	32	24.62
Disagree	36	27.69
Neutral	28	21.54
Agree	16	12.31
Strongly agree	22	16.92
Distribution of subject's response to Question A6		
Strongly disagree	46	35..38
Disagree	40	30.76
Neutral	26	20
Agree	12	9.23
Strongly agree	6	4.62

Table VI: Distribution of practice in subjects with hypertensive disorders of pregnancy.

Response	P1		P2		P3		P4	
	n	%	n	%	n	%	n	%
Yes	100	76.92	122	93.85	118	89.23	128	98.46
No	30	23.08	8	6.15	14	10.77	2	1.53

Table VII: Distribution of response received for assessment of Nutrition.

Response	NAQ1		NAQ 2		NAQ 3		NAQ 4		NAQ 5	
	n	%	n	%	n	%	n	%	n	%
Correct answer	112	86.15	98	75.38	104	80	120	92.31	100	76.92
Incorrect answer	18	13.85	32	24.62	26	20	10	7.69	30	23.08

Assessment of Practice in subjects with Gestational Diabetes Mellitus. (Table VI)

Knowledge of correct practice and its application is important for higher therapeutic outcomes. The following questions were administered:

Question P1: Do You do Regular follow up and Glucose monitoring?
Question P2: I make sure the drugs that has been prescribed to me is safe to me and baby
Question P3: I am following the instructions provided regarding proper medicine Use
Question P4: Are you avoiding extra added sugar/ sweet?

Question P1: Out of 130 Subjects, majority 100 (76.92%) did regular follow up and Glucose monitoring Question P2: Almost all of the subjects 122 (93.85%) made sure the drugs that has been prescribed to them during pregnancy Is safe to them as well as to the baby.
Question P3: Most of the subjects 118 (89.23%) followed the instruction provided to them regarding proper use of medicines prescribed
Question P4 : Almost all of the subjects 128 (98.46%) avoided extra added sugar in their daily food intake Detailed.
Using statistical analysis a positive correlation was observed between Knowledge and attitude (r=0.07) with p value 0.355497776 (>0.05) which was statistically significant, a positive correlation was observed between Knowledge and practice (r=0.075) with p value 0.057924406 (>0.05) which was statistically significant ,and a weak positive correlation was observed between attitude and practice (r=0.002) with p value 0.00000004(<0.05) which was statistically insignificant.
Subjects were administered the Self-designed Nutrition Assessment Questionnaire (NAQ) to assess the knowledge. The Questionnaire contained 5 questions which were developed as a tool to know their knowledge on Nutrition intake during GDM.

The following Questions were administered to the Subjects:
Question NAQ 1: Which diet plan should you be following to control GDM?
Question NAQ 2: What are the food sources of Iron?
Question NAQ 3: What all supplements should be taken during Pregnancy?
Question NAQ 4: What all foods you should avoid during 1 st trimester?
Question NAQ 5: What is the food Source of calcium?
Table VII

NAQ1: Most of the subjects 112 (86.15%) were aware of the diet plan they should be following to control GDM
NAQ 2: 98 (75.38%) of the subjects knew the food sources of Iron
NAQ 3: Most of the subjects 104(80%) were knowledgeable about the supplements that should be taken during pregnancy
NAQ 4 :120 (92.31%) had good idea about what food to avoid during the 1 st trimester
NAQ 5 : More than half of the subjects 100 (76.92%) knew the food sources of Calcium.

Assessment of Nutrition Practice in Subjects with Gestational diabetes Mellitus. (Table VIII)

Appropriate practice and its implementation is crucial for better therapeutic outcomes. The following questions were administered
Question NP1: How often do you eat Fruits?
Question NP 2: How often do you drink any carbonated beverages?
Question NP 3: How often do you eat from outside?
Question NP 4: How often do you take Vitamin Supplements?
Question NP 5: How often do you consume packaged snacks, cakes, pastries or sugars/sweetened drinks?

Question NP1: Out of 130 subjects 54 (41.54%) ate fruits oncea day and 48 (36.92%) had 2 or more times per day, while 6 (4.61%) never had ate fruits during their gestation period. The graphical representation above indicates that most of the subjects either had fruits 2 or more times per day or at least once a day. This showed that majority of the study population has a positive nutrition practice and very few have negative practice.

In Question NP2, more than majority (76.92%,100) Never drunk any carbonated beverages whereas 28 (21.54%) did once a week during pregnancy and GDM condition.

Table VIII: Distribution of subject's response to Question NP.

Distribution of subject's response to Question NP1		
Response	*Number of subjects*	*Percentage (%)*
Never	6	4.61
Once a day	54	41.54
2 or more times per day	48	36.92
1 time per week	22	16.92
Distribution of subject's response to Question NP2		
Never	100	76.92
Once a week	28	21.54
2 or more times per day	0	0
Often	2	1.53
Distribution of subject's response to Question NP3		
Never	60	46.15
Once a week	60	46.15
More than twice a week	6	4.62
Often	4	3.08
Distribution of subject's response to Question NP4		
Never	0	0
Everyday	102	78.46
Once in a while	14	10.77
Often	8	6.15
Distribution of subject's response to Question NP5		
Never	62	47.69
Everyday	0	0
Once in a while	64	49.23
Often	4	3.08

The Graphical representation above indicates that most of the study population were aware of the consequences of drinking carbonated beverages during pregnancy and especially in case of GDM which shows a positive practice towards the disease condition.

In Question NP3, there is an equal proportion of subjects Never 60(46.15%) and Once a week 60 (46.15%) eating from outside whereas only few subjects to mention eat more than twice a week 6 (4.62%) and often 4 (3.08%) from outside during GDM conditions. The graphically representation above shows a positive practice of subjects towards the disease condition

In Question NP4 ,102 (78.46%) subjects out of 130 total study population takes Vitamin Supplements Every day and very few took Once in a while (14,10.77%) or Often (8,6.15%). The graphical representation above shows a positive practice of study population towards the disease condition.

In Question NP5 ,64 (49.23%) subject's out of 130 subjects consume packaged snacks and other sweetened/ sugared products Once in a while, whereas 62 (47.69%) subjects mentioned that they Never consumed any packaged snacks or other sweetened products. The graphical representation indicates majority of the study population had Positive practice towards the disease condition. Detailed Explanation is presented in **table VIII**

Assessment of Pregnancy Anxiety scale in Subjects with Gestational Diabetes Mellitus.

The following Questions were administered:

Question PAS 1: I feel relaxed about the health of my baby
Question PAS 2: I feel nervous thinking about the pain of childbirth
Question PAS 3: I feel worried that I won't get my figure back after my baby is born
Question PAS 4: I feel secure that people I know care about me and will help me
Question PAS 5: I feel concerned about losing control during labor
Question PAS 6: I Feel nervous that my baby will have a deformity or a disease
Question PAS 7: I feel confident that the doctors and midwives will take good care of me
Question PAS 8: I feel Secure knowing that my husband finds me sexually attractive
Question PAS 9: I feel worried that I don't have enough support People living near me
Question PAS 10: I feel Satisfied with my Husband's Involvement in Pregnancy
Question PAS 11: I feel secure knowing my husband support me
Question PAS 12: I feel Confident that my baby will be born healthy
Question PAS 13: I feel uncertain about the physical changes occurring in my body
Question PAS 14: I feel Scared about Feeling Helpless during Labour?

Anxiety during pregnancy was assessed and the data showed that 104 (80%) were anxious about their baby's health, 104 (80%) were also anxious about labour pain, 90 (69%) were anxious about their physical appearance after delivery,32 (24.6%) were anxious about the amount of support they will be receiving from their family and 16 (12%) were anxious about their marital life. Detailed distribution is presented in **table IX.**

A total number of 830 drugs were prescribed to the 130 subjects admitted to the Obstetrics and Gynecology department of ESIC-PGIMSR, Bengaluru. The largest class of medications prescribed were Analgesics 316 (38%), followed by Antibiotics 306 (37%), Anti-Diabetic drugs 122 (14%), Thyroid medications 38 (5%), Anti-Hypertensive drugs 36 (4%) and Anti-Fungal drugs 14 (2%). Detailed distribution is given in **table IX.**

Table IX: Distribution of drugs used by respondents based on pharmacological classification.

Class of drugs	Number of drugs prescribed	Percentage (%)
Anti-Diabetic drugs	122	14%
Antibiotics	306	37%
Analgesics	316	38%
Anti-Hypertensive drugs	34	4%
Thyroid medications	38	5%
Anti-Fungal drugs	14	2%

Discussion

According to Dudhwadkar R et al,18pregnancy complicated with GDM, has adverse maternal and fetal outcomes, whose results show incidence of pre-eclampsia (26%), hypothyroidism (6%) and Polyhydramnios (20%) in GDM patients, which can complicate the course of pregnancy and has adverse effects on maternal and fetal outcomes. In another study conducted by Odar E et al,[19] similar results were found which stated that the mothers with GDM were four times more likely to have hypertensive disorders and nine times more likely to have vaginal candidiasis. Thus, all five studies indicate that women with GDM are at increased risk of Adverse Obstetric outcomes.

Jaundice was the most commonly seen fetal complication in our study which is very similar to the study done by Singla, M. et al[20] where as in a study done by Shukla et al[17], Macrosomia was the most commonly observed complication. According to a study done by IRC Barbosa et al,[21] fetal deaths were the commonly occurring complication. Where as in our study, NICU admission followed by Respiratory distress were also seen as the second most common complication. NICU admission in our study was due to Low birth weight and low APGAR score. Birth weight >3.5kg and <2.5kg was seen in 4.62% while 90.76% had weight between 2.5-3.5kg. In a study done by Singla, M et al,2067% of the subjects had birth weight >2.5kg and 6.1% had weight less than 1.5Kg .The Apgar score >7 at 1 and 5 minutes occurred in 69.23% and 100% respectively in neonates of Gestational Diabetes Mellitus mothers, Apgar score of 4-6 at 1 and 5 minutes occurred in 30.77%. Nevertheless, there was a considerable improvement in the Apgar scores of neonates at 5 minutes and this could ascribe a more effective neonatal resuscitation from appropriate care during the change to the uterine life. According to the study by Crowther, C. A et al[22], significantly low 1-minute Apgar score in babies is consistent. The above findings suggest that there should be a proper preparation for neonatal resuscitation at the time of childbirth in pregnancies complicated with GDM.

Chi square test (χ^2) was done to asses between low Apgar score and NICU admission, the result was seen as statistically significant. Fisher's exact probability test was done to find out the association between Low Birth weight and NICU admission, which is not significant at 5% level of significance.

The study conducted by Crowther AC et al[22], concluded that treatment of GDM (which include dietary advice, blood glucose monitoring and insulin or metformin therapy) reduces serious perinatal morbidity and may also improve women's health related QOL which is comparable to our study results which concludes the same on the basis of KAP of women treated for GDM and their positive response on satisfaction regarding treatment provided for GDM that helped subjects in achieving reduced adverse perinatal outcomes.

Among the responses received for Question K1 of KAP Questionnaire which checks whether the subject knows the normal level of Random blood sugar levels, (56.92%) of the respondents knew the normal level. In Question K2 which checks the awareness of patient about risk factors for GDM, (56.92%) were aware of it. In Question K3 which checks whether the patient know that GDM is a risk factor for future Type 2 DM, (41.54%) knew the correct response. In Question K4, which determines whether the patient knows the name of the antidiabetic drug they are taking, most of the subjects (87.69%) knew the name of antidiabetic drug they were taking. In Question K5, which determines whether the patient know the long-term health consequences of the child born to GDMmother, (53.85%) knew the consequences. Majority subjects had good knowledge about GDM whereas, remaining lack the knowledge of GDM, which may alter the attitude and practice towards disease management. Clinical activities such as patient counselling, medication review and pharmaceutical care program helps to increase the subject's knowledge about the disease condition. It was found out that most of the subjects had a positive attitude towards the disease condition and treatment given. Majority (76.92%) of the subjects had regular practice of checking their blood sugar levels, (93.85%) tried to find out whether the medicines taken by them (OTC or prescribed) is safe during pregnancy, (89.23%) followed the instructions regarding proper medicine use and (98.46%) reduced sugar/sweet intake as advised by the doctor. Our study results show, Good Knowledge Attitude and Practice towards disease condition, which is contrary to a study done by Odar E et al,[19], whose study results show only a small proportion of rural antenatal women (17.5%) had good knowledge about GDM.

According to data collected in our study, about nutrition assessment, majority of the subjects (86.15%) knew that diabetic diet should be followed to control GDM, (75.38%) subjects knew the food sources of iron, (80%) subjects knew the supplements that should be taken during pregnancy, most of them (92.31%) knew the fruits which should be avoided during pregnancy and (76.92%) knew the food sources of calcium. And according to the data obtained from Nutrition Practice Questionnaire, most of them (41.54%) ate fruits once a day, (36.92%) twice a day, (16.92%) once in a week and few of them (4.61%) never ate fruits during pregnancy. During pregnancy most of them (76.92%) never drank carbonated beverages. (46.15%) never ate food from outside, equal number of subjects (46.15%) ate once in week and few (7.7%) subjects had more often from outside. Most of them (78.46%) took vitamin supplements (including folic acid, calcium and iron supplements) every day as prescribed. Half of the subjects (49.23%) had packaged snacks

once in a while and (47.69%) of them never had. In our study, the results of Nutrition Knowledge assessment and Nutrition practice questionnaires, shows a positive Nutrition practice and assessment towards the disease condition where the knowledge on importance of right nutrition was provided. These results are comparable to the study conducted by Khushpreet K et al,[23] that concludes that, Nutrition counselling significantly improved the fetal outcome and KAP score of GDM.

Conclusion

Gestational Diabetes Mellitus associated with Pregnancy include maternal and fetal outcomes such as Macrosomia, Hyperbilirubinemia, NICU admission, Shoulder dystocia, polyhydramnios, premature birth, etc. Prior diagnosis, role of diet and correct treatment options and regular checkups plays a very important role in the prevention of Gestational Diabetes Mellitus. Low Apgar score and Low birth weight are the major complications for NICU admission.

Maternal distress was the most common maternal complication and Jaundice and respiratory distress is the most common fetal complications.

Assessment of knowledge Attitude and practice showed that majority of the subjects had good knowledge, a positive attitude and good practice regarding the disease condition and its management. Knowledge and attitude were found to be dependent.

Majority of the subjects had an adequate knowledge, Attitude and practice towards the intake of diet to follow during Gestational Diabetes Mellitus.

Assessment of physical activity showed that majority of the subjects had Poor physical activity which has an increased risk of Gestational diabetes Mellitus.

Pregnancy anxiety scale were assessed based on how anxious subject is about the health of the baby, labor pain, physical appearance after delivery, support received during gestation period and lastly about the marital life. According to the study, majority of the subjects were anxious about the baby's health and very less anxious about marital life.

830 drugs were prescribed to all the subjects. Most prescribed medication was Analgesic followed by antibiotics, anti-diabetic drugs, thyroid medication, anti-hypertensive drugs and few anti- fungal drugs as well.

Conflict of Interest

The author declare that he have no conflict of interest.

References

1. World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. World Health Organization; 2013.

2. Wang Z, Kanguru L, Hussein J, Fitzmaurice A, Ritchie K. Incidence of adverse outcomes associated with gestational diabetes mellitus in low-and middle-income countries. International Journal of Gynecology & Obstetrics. 2013 Apr 1;121(1):14-9.

3. Roglic G. Diabetes in women: the global perspective. International Journal of Gynecology & Obstetrics. 2009 Mar 1;104:S11-3.

4. Yogev Y, Xenakis EM, Langer O. The association between preeclampsia and the severity of gestational diabetes: the impact of glycemic control. American journal of obstetrics and gynecology. 2004 Nov 1;191(5):1655-60.

5. Wakwoya EB, Fita FU. Adverse maternal outcome and its association with gestational diabetes among women who gave birth in selected public hospitals in Eastern Ethiopia. Tropical Journal of Obstetrics and Gynaecology. 2018 Oct 10;35(1):58-62.

6. Jensen DM, Sørensen B, Feilberg-Jørgensen N, Westergaard JG, Beck-Nielsen H. Maternal and perinatal outcomes in 143 Danish women with gestational diabetes mellitus and 143 controls with a similar risk profile. Diabetic medicine. 2000 Apr;17(4):281-6.

7. Abu-Heija AT, Al-Bash M, Mathew M. Gestational and pregestational diabetes mellitus in Omani women: comparison of obstetric and perinatal outcomes. Sultan Qaboos University Medical Journal. 2015 Nov;15(4):e496.

8. Gascho CL, Leandro DM, Silva TR, Silva JC. Predictors of cesarean delivery in pregnant women with gestational diabetes mellitus. Revista Brasileira de Ginecologia e Obstetrícia. 2017;39:60-5.

9. American Diabetes Association. Erratum. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes-2016. Diabetes Care 2016; 39 (Suppl. 1): S13-S22. Diabetes care. 2016 Sep 1;39(9):1653.

10. Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L, Heller SR, Rodriguez H, Rosenzweig J, Vigersky R. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and the Endocrine Society. The Journal of Clinical Endocrinology & Metabolism. 2013 May 1;98(5):1845-59.

11. Lee ET, Howard BV, Savage PJ, Cowan LD, Fabsitz RR, Oopik AJ, Yeh J, Go O, Robbins DC, Welty TK. Diabetes and impaired glucose tolerance in three American Indian populations aged 45-74 years: the Strong Heart Study. Diabetes care. 1995 May 1;18(5):599-610.

12. Dempsey JC, Butler CL, Sorensen TK, Lee IM, Thompson ML, Miller RS, Frederick IO, Williams MA. A case-control study of maternal recreational physical activity and risk of gestational diabetes mellitus. Diabetes research and clinical practice. 2004 Nov 1;66(2):203-15.

13. Imam A. Current Status of Diabetes in Palestine: Epidemiology, Management, and Healthcare System. Cham, Switzerland: Springer. 2019.

14. Toft JH, Bleskestad IH, Skadberg Ø, Gøransson LG, Økland I. Glycated albumin in pregnancy: lc-ms/ms-based reference interval in healthy, nulliparous scandinavian women and its diagnostic accuracy in gestational diabetes mellitus. Scandinavian Journal of Clinical and Laboratory Investigation. 2022 Feb 9:1-9.

15. Hillier TA, Pedula KL, Ogasawara KK, Vesco KK, Oshiro CE, Lubarsky SL, Van Marter J. A pragmatic, randomized clinical trial of gestational diabetes screening. New England Journal of Medicine. 2021 Mar 11;384(10):895-904.

16. Kelley KW, Carroll DG, Meyer A. A review of current treatment strategies for gestational diabetes mellitus. Drugs in context. 2015;4.

17. Shukla A, Burute S, Meena A. Maternal and fetal outcome in gestational diabetes-A retrospective study. Int J Appl Res. 2017;3(9):305-9.

18. Dudhwadkar AR, Fonseca MN. Maternal and fetal outcome in gestational diabetes mellitus. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2016 Oct 1;5(10):3317-22.

19. Odar E, Wandabwa J, Kiondo P. Maternal and fetal outcome of gestational diabetes mellitus in Mulago Hospital, Uganda. African Health Sciences. 2004 Nov 10;4(1):9-14.

20. Singla M, Ahuja A, Juneja SK. Maternal and foetal outcomes in gestational diabetes mellitus. Journal of Evolution of Medical and Dental Sciences. 2016 Oct 20;5(84):6239-42.

21. Barbosa IR, Silva WB, Cerqueira GS, Novo NF, Almeida FA, Novo JL. Maternal and fetal outcome in women with hypertensive disorders of pregnancy: the impact of prenatal care. Therapeutic advances in cardiovascular disease. 2015 Aug;9(4):140-6.

22. Crowther CA. Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med. 2005;352:2477-86.

23. Khushpreet S, Rajesh K, Bilawal S, Manoj S, Ravdeep S, Verma HK. Impact of specialized goat training programme on knowledge level and adoption. Indian Veterinary Journal. 2018;95(3):30-2.

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ORIGINAL

Psychological determinants and their relationship with activities carried out by health sciences students during confinement by COVID-19

Determinantes psicológicos y su relación con actividades realizadas por estudiantes de ciencias de la salud durante el confinamiento por COVID-19

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Abstract

Objectives: During lockdown by COVID-19, some individuals engaged in behaviours generating a greater sense of positivity and control. The objective was to identify relationships between affect, coping strategies, and resilience with task management, distress caused by lockdown, and difficulty observing public health restrictions.
Methods: A cross-sectional observational study (May 2020) was carried out in the Complutense University of Madrid. The sample consisted of 50 first-year Health Sciences students, wich were assessed during lockdown by COVID19. The followins scales were used: the Positive and Negative Affect Schedule (PANAS), the Coping Orientation to Problems Experienced inventory, the Connor-Davidson Resilience Scale, and the Escala de Gestión de Actividades en Situación de Confinamiento (Activity Management during Lockdown Scale).
Results: Thirty-five students (70%) displayed a score of ³6 on the scale measuring the distress caused by the public health restrictions. Associations with r values of ≥0.5 were: distress caused by the pandemic and positive affect (r=0.512); seeking new hobbies and seeking social support (r=0.567); seeking new hobbies and humour (r=0.56); reading and active problem-focused coping (r=0.5).
Conclusions: Positive affect is influenced by behaviours linked to helping neighbours. Strategies allowing subjects to occupy their time more constructively were: active problem-focused coping, seeking psychosocial support, and acceptance and personal growth. The factors related to negative affect were alcohol consumption and/or drug use, humour.

Key words: Coping; COVID-19, lockdown, health science students, psychological resilience, social isolation.

Resumen

Objetivos: Durante el confinamiento por la COVID-19, algunas personas se involucraron en comportamientos que generaron una mayor sensación de positividad y control. El objetivo del presente estudio fue identificar relaciones entre el afecto, las estrategias de afrontamiento y la resiliencia con la gestión de tareas, la angustia causada por el encierro y la dificultad para observar las restricciones de salud pública.
Métodos: Se realizó un estudio observacional transversal (mayo de 2020) en la Universidad Complutense de Madrid. La muestra estuvo conformada por 50 estudiantes de primer año de Ciencias de la Salud, los cuales fueron evaluados durante el confinamiento por la COVID19. Se utilizaron las siguientes escalas: Positive and Negative Affect Schedule (PANAS), Coping Orientation to Problems Experienced Inventory, Connor-Davidson Resilience Scale y Escala de Gestión de Actividades en Situación de Confinamiento (Activity Management during Lockdown Scale).
Resultados: 35 estudiantes (70%) presentaron una puntuación mayor de 6 en la escala que mide el malestar causado por las restricciones de salud pública. Las asociaciones con valores de r ≥0,5 fueron: angustia por la pandemia y afecto positivo (r=0,512); búsqueda de nuevos pasatiempos y búsqueda de apoyo social (r=0,567); búsqueda de nuevos pasatiempos y humor (r=0,56); lectura y afrontamiento activo centrado en el problema (r=0,5).
Conclusiones: El afecto positivo está influido por conductas vinculadas a la ayuda al prójimo. Las estrategias que permitieron a los sujetos ocupar su tiempo de manera más constructiva fueron: afrontamiento activo centrado en el problema, búsqueda de apoyo psicosocial y aceptación y crecimiento personal. Los factores relacionados con el afecto negativo fueron el consumo de alcohol y/o drogas, el humor.

Palabras clave: Afrontamiento; COVID-19, confinamineto por pandemia, estudiantes de ciencias de la salud, resiliencia psicológica, asilamiento social.

Introduction

Spain spent 99 days under lockdown as a result of the pandemic. During this period, individuals engaged in a variety of behaviours, some of which led to a greater sense of positivity and control, as reported in a study by Sandín et al.[1] Another study with a Spanish sample showed that these positive effects were particularly strong during the first few weeks of lockdown, exceeding those observed in a sample of 990 Spaniards in 2013 following five years of one of the worst economic recessions seen in recent decades[2]. In the same vein, 61% of a sample of 657 healthcare workers reported an increased sense of meaning/purpose since the COVID-19 outbreak, according to Shechter et al.[3]

However, another section of the population experienced highly negative emotions such as stress and overwhelm, hopelessness, sleep problems, and even depression. One review showed that people in China experienced boredom, loneliness, and anger during lockdown, as well as an increase in psychological problems such as anxiety, stress, and depression[4]. Brooks et al. state that the predominant feelings experienced by people in lockdown are depression, fear, guilt, and anger[5].

To explain these results, several authors have analysed the influence of factors such as coping through physical activity[4], individual resilience[6], the influence of affect on certain behaviours and fears during the pandemic[1], and the association between behaviours such as social media use and higher levels of anxiety[7].

The objective of this study was to identify significant relationships between psychological factors, coping strategies, and resilience factors and each of the following: task management, perceived distress levels, and difficulty observing public health restrictions during the COVID-19 lockdown.

Methods

Design. Population. Sample.

This is a cross-sectional observational study involving Health Sciences students during the stay-at-home lockdown.

The target population comprised 370 first-year nursing and physiotherapy students. Initially, the aim was to explore stress coping strategies at various times during the 2019-2020 academic year. The sudden onset of the pandemic and the ensuing lockdown presented a new scenario, offering an opportunity for exploration that was not to be wasted. After informing students of the study's objectives, 116 agreed to participate.

The Epidat 4.2 tool was used to calculate the required sample size. For an expected mean resilience of 70 points and a standard deviation of 10 points, a 2% accuracy and 95% confidence, the required sample size was 53 subjects. Stratified random sampling by age and sex was carried out, resulting in a final sample of 50 participants.

Measurement scales and variables

Data were collected on sociodemographic variables and other variables such as people with whom the student spent the lockdown and difficulties experienced by the student in observing the restrictions (scale from 0 to 10).

The following validated, self-report questionnaires were used to assess various psychological factors and coping strategies:

1. The Positive and Negative Affect Schedule (PANAS) assesses, separately, the positive and negative emotional experiences lived recently[8]. This is a 20-item questionnaire where participants respond using Likert scales. The items are organised into two groups: 10 items refer to *positive aspects*, and 10 refer to *negative aspects*. The Spanish version has a good reliability index (Cronbach's α >.87) and construct validity[9].
2. The COPE (Coping Orientation to Problems Experienced) inventory. The Spanish version of the COPE-48 scale assesses the following 9 coping strategies using a Likert scale ranging from 1 = "I never do that" to 4 = "I do that frequently"[10]. The mean internal consistency of the Spanish version is 0.8.
3. The Connor-Davidson Resilience Scale. The Spanish adaptation consists of 25 items which participants evaluate using Likert scales ranging from 0 (not at all) to 4 (almost always). The items are grouped into 5 dimensions: *Persistence-Tenacity-Self-Efficacy; Control Under Pressure; Adaptability and Support Networks; Control and Meaning; Spirituality*. The sum of these values constitutes the total value for Resilience, whose thresholds are: less than 70 (low); 70 to 87 (intermediate); greater than 88 (high). The internal consistency of the Spanish version was optimal[11], with a Cronbach's α coefficient = 0.86.
4. The Emotion Thermometer is part of the American National Comprehensive Cancer Network Guidelines for Distress Management[12] and measures the overall emotional distress experienced by patients on a scale from 0 to 10. It has a sensitivity between 75% and 80%, and a specificity close to 60%[13]. Patients are considered to be in emotional distress if they score 6 or more.
5. The Escala de Gestión de Actividades en Situación de Confinamiento (Activity Management during Lockdown Scale) is a list of behaviours performed during lockdown, some of which were provided by the Official Psychologists' Association of Madrid[14]. Responses were collected on a Likert scale ranging from 1 (never) to 5 (almost always).

Ethical and legal aspects

The principles enshrined in the Helsinki Declaration on Biomedical Research Involving Human Subjects were

observed at all times. All the students were informed of the objectives and terms of implementation of the research and signed an informed consent form which explained that participation was completely voluntary and anonymous, that they could freely withdraw from the study at any time without giving a reason, and that such participation did not entail any benefit or harm for students. The confidentiality and privacy of their information were preserved in compliance with current regulations on the protection of personal data. The data were entered in secure databases and access to the data was restricted to the researchers. Data analysis was limited to the purposes of this study. This research was approved by the Institutional Review Board of Complutense University of Madrid.

Data analysis

Means and standard deviations were calculated for quantitative variables. Absolute and relative frequencies (percentages) were calculated for qualitative variables. The assumption of normality of the data was checked using graphical representation tests (histograms and Q-Q and P-P plots) and statistical significance tests such as the Shapiro-Wilk test.

For statistical comparisons, the χ-squared test was used (applying Fisher's exact test, if indicated) and the Z-test for qualitative variables. For the comparison of two means, Student's t-test or Mann-Whitney's U-test was used, depending on whether or not the data in question were parametric. The homoscedasticity of the data was checked using Levene's test. To analyse the degree of association between quantitative variables, Pearson's or Spearman's correlation coefficient was used depending on the parametric nature of the data.

All hypothesis tests were two-tailed and were conducted with a statistical significance threshold of alpha error <5% ($p < .05$). Confidence intervals were calculated with 95% certainty. SPSS v. 22 and Epidat v. 4.2. were used for data analysis.

Results

Description of the characteristics of the sample

Of the 50 students, 49 were women (98%). According to the distribution by Degree, 46 corresponded to Nursing (92%) and 4 to Physiotherapy (8%). The mean age was 19.9 (5.1) years, 95% CI (18.5-21.4). 32% of the participants declared that they were working while they were studying, 92% indicated that they passed the confinement with their family, 54% that it did not cost them anything to follow the restrictions imposed during the confinement. In terms of discomfort caused by the confinement situation, 35 students (70%) indicated a value equal to or greater than 6, with a mean score of 6 (2.2) 95% CI 5.4 -6.7. **Table I** shows the final characteristics of the sample.

Table I: Characteristics of the sample.

Variable	Mean or *n* (SD or %)
Female	49 (98)
Age (years)	19.9 (5.1)
Employed	16 (32)
Nursing students	46 (92)
With whom are you spending the lockdown?	
With my family	46 (92%)
Other	4 (8%)
I find it difficult to observe the restrictions	
Never	27 (54%)
Rarely	14 (28%)
Sometimes	6 (12%)
Often	3 (6%)
Almost always	0
Distress caused by the restrictions imposed (from 0 to 10)	6 (2.2)
	0-5 15 (30%)
	6-10 35 (70%)

Table II: Results of the PANAS, COPE-48, and Resilience scales during the COVID-19 lockdown.

	Mean, SD	95% CI
	PANAS	
POS. AFFECT	24.9, 7.7	22.7 - 27.1
NEG. AFFECT	26.3, 7.7	24.1 - 28.5
	COPE-48	
APC	25.3, 3.8	24.2 - 26.4
ACD	4.6, 1.6	4.1 - 5.1
FVE	10.5, 2.6	9.8 - 11.2
SSS	22.3, 5.7	20.7 - 23.9
HUM	9.3, 3.3	8.4 - 10.2
REL	7.2, 4.6	5.9 - 8.5
DEN	5.3, 2.1	4.7 - 5.9
REC	9.6 (2.3)	9 - 10.3
APG	21.2 (3.6)	20.2 - 22.2
	RESILIENCE	
PTS	23, 4.9	21.6 - 24.4
CUP	17, 4.4	15.8 - 18.3
ASN	16.1, 3.5	15.1 - 17.1
CAP	8.7, 2.3	8.05 - 9.4
SPI	4.3, 2.5	3.6 - 5
RSC	69.2, 13.7	65.3 - 73.1

APC: Active problem-focused coping; ACD: Alcohol consumption and/or drug use; FVE: Focus on and Venting of Emotions; SSS: Seeking Social Support; HUM: Humour; REL: Religion; DEN: Denial; REC: Restraint Coping; APG: Acceptance and personal growth; PTS: Persistence, Tenacity, and Self-Efficacy; CUP: Control Under Pressure; ASN: Adaptability and Support Networks; CAP: Control And Purpose; SPI: Spirituality; RSC: Resilience.

Through the PANAS, COPE-48 and Connor-Davidson scales, the psychological situation of the participants was analyzed about their affective state (positive or negative), coping strategies in the face of stress caused by confinement and resilience in the face of exceptionality confinement due to the pandemic, respectively (**Table II**). As can be seen, the mean score for the entire sample was 69.2 (13.7) 95% CI 65.3 - 73.1 as estimated for calculating the sample size.

Table III: Activities carried out during lockdown.

ACTIVITY DURING LOCKDOWN	Mean (SD)	95% CI
Watching the news	3.6 (1.2)	3.3 - 4
Watching TV	3.4 (1.1)	3.1 - 3.7
Listening to music	4.4 (0.95)	4.1 - 4.7
Carrying out university study	4.3 (0.8)	4 - 4.5
Reading	3.3 (1.2)	2.9 - 3.6
Seeking new hobbies	3.2 (1.2)	2.9
Doing household chores	3.9 (0.95)	3.6 - 4.1
Connecting with friends and family online	4.3 (1.05)	3.6 - 4.1
Completing pending tasks that they would not normally do	3.8 (0.96)	3.5 - 4.1
Keeping to a set timetable	3.6 (1.2)	3.3 - 3.9
Helping neighbours	2.4 (1.4)	2 - 2.8
Volunteering for social causes related to the pandemic	1.8 (1.2)	1.5 - 2.1
Working in healthcare during the pandemic	1.4 (1)	1.2 - 1.7
Working remotely in non-healthcare sectors	1.7 (1.1)	1.2 - 1.7
Performing routine hygiene and cleaning	4.2 (0.95)	3.95 - 4.5
Doing physical exercise	4 (1.1)	3.7 - 4.3
Talking to the people they live with	4.4 (0.86)	4.2 - 4.6
Creating a private space	4.2 (1.1)	3.9 - 4.5
Playing online games with friends	2.3 (1.4)	1.9 - 2.7

Table IV: Activities carried out during lockdown (comparison of means) and psychological state.

ACTIVITY DURING LOCKDOWN		PANAS		COPE-48									RESILIENCE					
		POS. AFFECT	NEG. AFFECT	APC	ACD	FVE	SSS	HUM	REL	DEN	REC	APG	PTS	CUP	ASN	CAP	SPI	RESC
Watching the news	≤ Mean	24.4	26.2	24.9	4.4	10.4	21.7	9.3	8.2	5.1	9.2	20.6	23.5	16.5	16.2	9.2	3.6	39
	> Mean	25.3	26.4	25.7	4.9	10.6	22.7	9.3	6.5	5.4	9.3	21.7	22.7	17.4	16	8.4	4.8	69.3
Watching TV	≤ Mean	23.8	26.1	25.3	4.5	10.4	22.5	8.6*	6.7	4.8*	9.6	21.8	22.2	17.3	15.8	8.4	4.3	68.1
	> Mean	26	26.6	25.4	4.8	10.7	22.1	10*	7.7	5.8*	9.6	20.7	23.8	16.8	16.4	9.1	4.2	70.3
Listening to music	≤ Mean	24.3	26	23.8*	4.7	10.5	22.7	7.4*	9.6	5.1	9	19.8*	22.6	17.6	16.1	8.7	4.4	69.4
	> Mean	25.3	26.5	26.2*	4.6	10.5	22	10.5*	7	5.3	10	22.1*	23.6	16.7	16.1	8.7	4.2	69.1
Carrying out university study	≤ Mean	26.2	24.1*	24.4	4.9	10.9	21.4	9	7.2	5.3	9.4	20.3*	21.7*	16.1	15.9	8.2	3.9	65.8*
	> Mean	23.2	29.2*	26.5	4.4	10.1	23.5	9.7	7.2	5.3	9.9	22.4*	24.7*	18.2	16.5	9.4	4.7	73.5*
Reading	≤ Mean	25.3	24.8	24.1*	4.9	10.5	21.8	9.2	6.9	5.6	9.8	20.5	23.1	16.6	15.9	8.8	4.3	68.6
	> Mean	24.2	28.8	27.4*	4.3	10.5	23.2	9.5	7.6	4.7	9.3	22.4	23	17.8	16.5	8.6	4.3	70.2
Seeking new hobbies	≤ Mean	25.8	23.4*	24.1*	4.9	10.9	20*	8.6*	7.2	5.3	9.6	20.1*	22.9	16.4	15.7	9	4.4	70.4
	> Mean	23.7	30.3*	27*	4.4	10	25.5*	10.3*	7.2	5.2	9.7	22.8*	23.2	16.4	15.7	8.3	4	67.6
Doing household chores	≤ Mean	25.8	25.4	24.6*	4.8	10.8	21.7	9.3	6.7	5.6	9.5	20.3*	22.7	16.9	16.1	8.5	4.3	68.5
	> Mean	22.8	28.4	27.1*	4.4	9.9	23.8	9.4	8.3	4.4	9.9	23.3*	23.8	17.3	16.3	9.2	4.3	70.8
Connecting with friends and family online	≤ Mean	25.6	24.5	24.1*	4.7	11.1	19.7*	8.7	7.3	4.8	9.7	20.8	22.7	17.5	16.9	9.3*	3.9	70.3
	> Mean	24.4	27.8	26.3*	4.6	10	24.3*	9.8	7.1	5.6	9.6	21.5	23.3	16.7	15.5	8.3*	4.5	68.4
Completing pending tasks	≤ Mean	24.8	24.9*	24.1*	4.8	10.8	21*	9.2	7.5	5.6	9.5	20.6*	23.7	17.9*	16.7*	9.1*	4.3	71.8*
	> Mean	25.3	30.1*	28.8*	4.2	9.8	25.9*	9.5	6.4	4.3	10	23*	21.2	14.6*	14.5*	7.5*	4.2	61.9*
Keeping to a set timetable	≤ Mean	25.4	24.9*	24.8	4.9*	10.6	21.8	9.2	7.1	5.5	9.6	20.8	23.1	17.3	16.2	8.8	4.4	69.8
	> Mean	24.6	30.8*	26.7	4*	10.3	23.1	9.6	8.4	5.1	9.6	22.4	23	16.4	15.9	8.4	4	67.7
Helping neighbours	≤ Mean	23.8*	26.3	24.7*	4.8	10.6	21.8	9.2	7.1	5.5	9.5	20.6*	23.3	17.5*	16.5	8.7	4.6	70.7
	> Mean	28.5*	26.4	27.5*	4.3	10.4	23.9	9.5	7.5	4.4	10	23.1*	22.1	15.6*	14.9	8.8	3.2	64.6
Volunteering for charity	≤ Mean	24.5	26.6	25.6	4.6	10.4	22.1	9.3	7.3	5.3	9.8	21.1	23.4	17.3	16.3	8.8	4.5	70.3
	> Mean	26.7	28.9	24.8	5	10.9	23.3	9.1	6.9	4.9	9	21.9	21.6	15.7	15.2	8.4	3.3	64.2
Working in healthcare	≤ Mean	24.4	26.9	24.4	4.6	10.6	22.4	9.3	7.2	5.2	9.6	21.1	23.3	17.3	16.5	8.8	4.2	69.9
	> Mean	29	22.3	25	5.3	10	21.8	9	7.3	6	9.7	21.8	21.3	15.5	13.3	8.5	5	63.7
Working remotely in non-healthcare sectors	≤ Mean	24.1	27.5*	25.2	4.6	10.5	22.3	9.2	6.8	4.9*0	9.4	21.1	23.6	17.4	16.7	8.9	4.1	70.7
	> Mean	27.9	22.2*	25.9	5	10.5	22.2	9.6	8.5	6.4*	10	21.8	21	15.8	14	8.1	4.9	63.8
Performing routine hygiene and cleaning	≤ Mean	23.3	26.2	24.8	5	10.3	21	9.6	6.9	5.4	9.6	21.1	22.6	17	16.3	8.6	39.6	68.5
	> Mean	26.5	26.4	25.9	4.4	10.7	23.6	9	7.5	5.1	9.6	21.4	23.5	17	16	8.8	4.6	69.9
Doing physical exercise	≤ Mean	25.2	22.8*	24.4*	4.9	10.2	20.3*	9	6.7	5.3	10	21.4	22.8	17.3	16.1	8.8	4.7	69.8
	> Mean	24.6	30.9*	26.5*	4.4	10.9	24.9*	9.7	7.8	5.3	9.1	22.3	23.4	16.7	16.1	8.6	3.7	68.5
Talking to the people they live with	≤ Mean	27.3	23.6*	24.2*	5	11	20.9	8.2	7.8	5.3	9.3	20	21.9	16.4	15.4	8.6	4.4	66.7
	> Mean	23.2	28.3*	26.1*	4.4	10.2	23.3	10.1	6.8	5.2	9.8	22.1	23.9	17.5	16.6	8.8	4.2	71
Creating a private space	≤ Mean	27.1*	23.9*	24.3	4.8	11	20.5	8.4	7.1	5.2	9.3	20.5	21.6	16.5	15.5	8.3	4.4	66.2
	> Mean	23.2*	28.2*	26.2	4.6	10.2	23.7	10	7.3	5.3	9.9	22.8	24.1	17.5	16.6	9.1	4.2	71.6
Playing online games with friends	≤ Mean	25.8	25.3	25.2	4.5	10.6	22.2	9.3	6.9	5.5	9.8	20.9	22.6	16.7	16.1	8.5	4.7	68.5
	> Mean	23.3	28.2	25.5	5	10.3	22.6	9.2	7.7	4.9	9.4	21.8	23.9	17.8	16.2	9.2	3.5	70.5
Finds it difficult to observe restrictions	≤ Mean	24.5	26.4	25.8*	4.6	10.3	22.3	9.4	6.9	5.1	9.9	21.4	23.2	17.1	16.1	8.7	4.3	69.3
	> Mean	26.4	26	23.3*	5.1	11.6	22.2	8.9	8.4	5.8	8.4	20.3	22.4	16.6	16.3	8.9	4.3	68.6
Distress caused by the pandemic	≤ Mean	21.5*	27.2	26.3	4.3*	10.1	21.8	10.2*	7.7	4.7	9.8	21.8	23.6	18.6*	17.3*	9.3	4.³	73*
	> Mean	28.1*	25.5	24.5	5*	10.9	22.8	8.5*	6.8	5.8	9.4	20.7	22.5	15.6*	15.1*	8.2	4.3	65.7*

APC: Active problem-focused coping; ACD: Alcohol consumption and/or drug use; FVE: Focus on and Venting of Emotions; SSS: Seeking Social Support; HUM: Humour; REL: Religion; DEN: Denial; REC: Restraint Coping; APG: Acceptance and personal growth; PTS: Persistence, Tenacity, and Self-Efficacy; CUP: Control Under Pressure; ASN: Adaptability and Support Networks; CAP: Control And Purpose; SPI: Spirituality; RSC: Resilience; * significant differences ($p<0.05$)

Table V: Correlation between activities performed during lockdown and psychological state.

ACTIVITY		PANAS		COPE-48									RESILIENCE					
		POS.	NEG.	APC	ACD	FVE	SSS	HUM	REL	DEN	REC	APG	PTS	CUP	ASN	CAP	SPI	RESC
Watching TV	Correlat. Coeff. Sig. (two-tailed)							0.21 0.14		.279 .050								
Listening to music	Correlat. Coeff. Sig. (two-tailed)			.315 .026				.409 .003				0.342 0.01						
Carrying out university study	Correlat. Coeff. Sig. (two-tailed)		.320 .024									0.193 0.18	.242 .090					.188 .190
Reading	Correlat. Coeff. Sig. (two-tailed)			.50 .000														
Seeking new hobbies	Correlat. Coeff. Sig. (two-tailed)		.401 .004	.336 .017			.567 .000	0.56 .08				0.334 0.018						
Doing household chores	Correlat. Coeff. Sig. (two-tailed)			.288 .043								0.303 0.01						
Connecting with friends and family online	Correlat. Coeff. Sig. (two-tailed)			.298 .035			.430 .002									.341 .015		
Completing pending tasks	Correlat. Coeff. Sig. (two-tailed)		.320 .023	.462 .001			.384 .006					0.403 0.004		-.125 .386	-.114 .431	-.257 .071		-.131 .363
Keeping to a set timetable	Correlat. Coeff. Sig. (two-tailed)		.450 .001		-.236 .099													
Helping neighbours	Correlat. Coeff. Sig. (two-tailed)	.246 .085		.140 .332								0.13 0.35		-0.30 0.03				
Volunteering for charity	Correlat. Coeff. Sig. (two-tailed)			-.190														
Working remotely in non-healthcare sectors	Correlat. Coeff. Sig. (two-tailed)		-0.14 0.31							0.243 0.09								
Doing physical exercise	Correlat. Coeff. Sig. (two-tailed)		.471 .001	.206 .152			.406 .003											
Talking to the people they live with	Correlat. Coeff. Sig. (two-tailed)		.297 .036	.360 .010														
Creating a private space	Correlat. Coeff. Sig. (two-tailed)		.302 .033															
Finds it difficult to observe restrictions	Correlat. Coeff. Sig. (two-tailed)			-.240 .093														
Distress caused by the pandemic	Correlat. Coeff. Sig. (two-tailed)	.512 .000			.215 .134			.357 .011						.322 .023	-.277 .052			-.248 .083

APC: Active problem-focused coping; ACD: Alcohol consumption and/or drug use; FVE: Focus on and Venting of Emotions; SSS: Seeking Social Support; HUM: Humour; REL: Religion; DEN: Denial; REC: Restraint Coping; APG: Acceptance and personal growth; PTS: Persistence, Tenacity, and Self-Efficacy; CUP: Control Under Pressure; ASN: Adaptability and Support Networks; CAP: Control And Purpose; SPI: Spirituality; RSC: Resilience

Activities carried out during confinement and their relationship with the psychological state

About the activities carried out by the students during home confinement (**Table III**), the most frequently carried out activities (mean ≥ 4 out of a total of 5 points) stand out: listening to music, performing university obligations (academic), being connected to the network of friends, family, carry out a routine of hygiene and personal cleaning caused by the pandemic, talk with the people with whom the student lives and create an intimate space. On the contrary, the least carried out activities have been (average ≤ 2 out of a total of 5 points): collaborating with solidarity volunteering or in health work related to the Covid-19 pandemic and teleworking in non-health activities.

The psychological situation was then analysed according to participants' degree of involvement in the activities they carried out during the stay-at-home lockdown. To this end, they were divided into two groups: those with scores above the mean frequency of performance for each of the activities and those with scores below the mean. The results are shown in **table IV**.

Finally, Pearson's correlation coefficients for the variables that were significantly associated (**Table V**) were analysed to determine the strength of the association between the activity performed during lockdown and the psychological situation.

Only watching the news, working in healthcare, performing routine hygiene and cleaning, and playing online games with friends were not correlated with any of the psychological situations.

Discussion

Positive and negative affect

Negative affect was correlated with the activities suggested by the Official Psychologists' Association of Madrid to improve individuals' ability to cope with the pandemic[14]. This suggests that, at least in terms of affect, it may not be particularly beneficial to follow these recommendations. In research on a population similar to that of this study, Ubillos et al. concluded that there is a relationship between negative affect and seeking new activities during lockdown[15].

In terms of spending time on carrying out university study, the data from our study echo those reported by Cleland et al., who shows that carrying out university study during lockdown was a stressor for many students[16].

Positive affect was primarily related to helping neighbours. These results are very similar to those obtained from volunteers in the Chinese population by Sun et al.[17] Positive affect was also associated with distress caused by the pandemic, which may be explained by the fact that subjects who have positive affect tend to maintain it and strive to maintain it in spite of the circumstances. This is in line with Sandín et al.[1] who described positive affect as a protective factor against negative affect during the COVID-19 lockdown along with age, income level, working outside the home, and having a private garden at home. However, these variables behave more erratically and their predictive power is much lower than that of vulnerability or risk factors.

Coping

The participants who spent their time most constructively were those correlated with active problem-focused coping, seeking psychosocial support, and acceptance and personal growth.

As in Main et al. active problem-focused coping was associated with behaviours linked to greater productivity over time[18].

Meanwhile, seeking psychosocial support was significantly associated with tasks that helped to create a more favourable environment for fulfilling participants' health and social needs. These results are similar to those obtained by Seiffge-Krenke[19]. in an adolescent population, with females being more likely to use this coping strategy. When the findings for a Finnish study population were compared to German and Israeli populations using the same assessment instrument, the coping behaviours observed were strikingly similar despite cultural differences.

Although Cassaretto et al.[20] note that acceptance and personal growth (AC) is often used in chronic and terminal illnesses, other authors such as Sandín et al.1 observe that a number of subjects rated the lockdown experience positively in a test on 'positive experiences'. This may be due to the uncontrollability and chronicity of the stressor (lockdown), which means that the resources used by individuals are similar to those used in chronic and terminal illnesses.

Humour was associated with unproductive and distracting behaviours that require minimal effort such as watching TV and listening to music, as well as with seeking new hobbies, which requires high levels of effort. Humour has also been associated with lower levels of anxiety[21] and displays a moderating effect on stress[22].

No significant relationships were found between behaviours during lockdown and the following coping mechanisms: focus on and venting of emotions (FVE), religion (REL), and restraint coping (REC). These results are very similar to those obtained from samples of Spanish students, scoring especially low in religion[23] and contrasting sharply with samples of practising nurses when faced with the death of patients[24].

One of the least useful adaptive coping strategies was alcohol consumption and/or drug use, which was associated with distress caused by the pandemic (r=0.215). A number of authors reported an increase in alcohol consumption and/or drug use among Spanish university students during lockdown[25]. Several studies have also documented this type of coping among adolescents and young adults in response to natural disasters[26] and as a way of coping with traumatic situations[27]. This can be interpreted as an avoidance behaviour[28] or as a pleasurable behaviour[29]. Interestingly, its relationship with keeping to a set timetable was negative, which suggests that the latter is a protective factor against drug use as a coping mechanism.

Finally, denial (DEN) was associated with working remotely in non-healthcare sectors and watching TV. Denial has been more frequently associated with traumatic events and inversely associated with age[30].

Resilience

Regarding resilience, the factors associated with more constructive activities were, firstly, persistence, tenacity, and self-efficacy (PTS), which were significantly associated with carrying out university study (r=.242), and secondly, control under pressure (CUP). Interestingly, this factor was negatively correlated with completing pending tasks and helping neighbours, and positively correlated with distress caused by the pandemic. This indicates that scoring high on this factor does not protect against distress, but it makes individuals approach lockdown in a more constructive way by supporting the community through caring behaviours.

The resilience (RESC) factor helps participants to focus on university activities and to avoid negative emotions

caused by the pandemic. These results are similar to those obtained by other authors, who have reported significant relationships between resilience and life satisfaction during the pandemic[31] and between resilience and traumatic events such as earthquakes[32], hurricanes[33], and suicide rates[34]. Resilience is also related to optimism, life satisfaction, and perceived wellbeing[35,36].

Adaptability and support networks (ASN) appears to be a protective factor against distress caused by the pandemic, but does not make task management during lockdown more constructive.

The factors that were least helpful in managing activities during lockdown were control and purpose (CAP), which were negatively associated with connecting with friends and family online (r=-0,341) and completing pending tasks (r= -0.257).

Curiously, all factors with the exception of spirituality (SPI) were negatively correlated with completing pending tasks, suggesting that resilient individuals are more focused on the present and the future. No significant relationships were found between spirituality and behaviours performed during lockdown.

Finally, it is worth noting that the correlations identified in our study are very strong for several factors and are even stronger than those found in similar studies (Puigt et al., 2011).

Limitations

The study limitations include the small population size and the voluntary nature of participation in the study. Future studies should include larger samples from different academic years.

Conclusions

Positive affect is influenced by behaviours associated with helping neighbours, while negative affect is influenced by seeking new hobbies, doing physical exercise, keeping to a set timetable, carrying out university study, creating a private space, reading, and completing pending tasks. The strategies that led to a more constructive approach to time management were: active problem-focused coping (which also helps in observing lockdown restrictions), seeking psychosocial support, and acceptance and personal growth. The factors related to negative affect caused by the pandemic were: alcohol consumption and/or drug use, humour, and the resilience factor control under pressure. The protective factors against negative affect caused by the pandemic were resilience and the resilience factor adaptability and support networks.

Given that spending time on helping neighbours within the lockdown constraints generated higher levels of positive affect, a more caring culture towards the groups closest to students could be fostered in disaster situations, such as service-learning. The study data highlight the importance of further training on time management during lockdown in order to avoid coping strategies such as alcohol consumption and/or drug use and watching TV excessively, as this can negatively affect health and lead to increased distress. We believe that these findings can help to create programmes targeting different psychological profiles to ensure that lockdowns are not experienced as a deprivation of individuals' freedom but are instead perceived as an opportunity to become stronger and glean satisfaction from helping others.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Sandín B, Valiente R, García-Escalera J, Chorot P. Psychological impact of the COVID-19 pandemic: Negative and positive effects in Spanish people duringthe mandatory national quarantine. *Journal of Psychopathology and Clinical Psychology / Revista de Psicopatología y Psicología Clínica*, 2020; 25 (1): 1-22.

2. Hervás G, Vázquez C. Construction and validation of a measure of integrative well-being in seven languages: The Pemberton Happiness Index. *Health and quality of life outcomes*, 2013; 11(1): 66-79. https://doi.org/10.1186/1477-7525-11-66.

3. Shechter A, Diaz F, Moise N. Psychological distress, coping behaviors, and preferences for support among New York healthcare workers during the COVID-19 pandemic. *Gen Hosp Psychiatry*, 2020; 66: 1- 8

4. Duan L, Zhu G. Psychological interventions for people affected by the COVID-19 epidemic. *Lancet Psychiatry*, 2020; 7(4): 300-302. https://doi.org/10.1016/S2215-0366(20)30073-0

5. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: Rapid review of the evidence. *Lancet*, 2020; 395: 912-20. DOI:https://doi.org/10.1016/S0140-6736(20)30460-8

6. Kavčič T, Avsec A, Zager Kocjan, G. Psychological Functioning of Slovene Adults during the COVID-19 Pandemic: Does Resilience Matter?. *The Psychiatric quarterly*, 2020; 21(1): 1-10. https://doi.org/10.1016/j.ijchp.2020.08.002

7. Gao J, Zheng P, Jia Y, Chen H, Mao Y, Chen S, et al. Mental health problems and social media exposure during COVID-19 outbreak. *Plos One*, 2020; 15 (4): e0231924. https:// doi.org/10.1371/journal.pone.0231924.

8. López-Gómez I, Hervás G, Vázquez C. Adaptación de las "escalas de afecto positivo y negativo" (panas) en una muestra general Española. *Behavioral Psychology/ Psicologia Conductual*, 2015; 23(3): 529-48.

9. Sandín B, Chorot P, Lostao L, Joiner T, Santed M, Valiente RM. Escalas PANAS de afecto positivo y negativo: validación factorial y convergencia transcultural. *Psicothema*, 1999; 11: 37-51.

10. Martínez-Ortega Y, Gomà-i-Freixanet M, Fornieles A. The COPE-48: An adapted version of the COPE inventory for use in clinical settings. Psychiatry Res., 2016; 246: 808-814.doi: http://dx.doi.org/10.1016/j.psychres.2016.1 0.031

11. García-León M, González-Gómez A, Robles-Ortega H, Padilla J, Peralta-Ramírez MI. Propiedades psicométricas de la Escala de Resiliencia de Connor y Davidson (CD-RISC) en población española. *Anales de Psicología*, 2019; 35(1): 33-40. http://dx.doi.org/10.6018/analesps. 35.1.31411

12. Holland JC, Andersen B, Breitbart WS, Dabrowski M, Dudley MM, Fleishman S, et al. Distress management: Clinical practice guidelines in Oncology™. JNCCN *Journal of the National Comprehensive Cancer Network*, 2007; 5(1): 66-98. https://doi.org/10.6004/jnccn.2007.0009

13. Patel D, Sharpe L, Thewes B. Using the distress thermometer and hospital anxiety and depression scale to screen for psychosocial morbidity in patients diagnosed with colorectal cancer. *J Affect Disord*., 2011; 131:412-6.

14. Colegio Oficial de Psicología de Madrid. Orientaciones para la gestión psicológica de la cuarentena por el coronavirus. Madrid. 2020 https://www.copmadrid.org/web/publicaciones/orientaciones-para-la-gestion-psicologica-de-la-cuarentena-por-el-coronavirus

15. Ubillos S, Gonzaléz J. Afrontando el impacto del COVID-19: Resultados Preliminares III. Burgos. Universidad de Burgos. Facultad de ciencias de la salud y facultad de ciencias de la educación; 2020 https://riubu.ubu.es/bitstream/handle/10259/5360/Afrontando_el_impacto_del%20COVID19-3.pdf?

16. Cleland C, McKimm J, Fuller R, Taylor D, Janczukowicz J. Adapting to the impact of COVID-19: Sharing stories, sharing practice. Medical Teacher; 2020.

17. Sun N, Wei L, Shi S, Jiao, D, Son R, Ma L, Wang H, Wang Z, You Y, Liu S. Wang A qualitative study on the psychological experience of caregivers of COVID-19 patients. *Am. J. Infect. Control*, 2020; (48), 592–598 doi: 10.1016/j.ajic.2020.03.018

18. Main A, Zhou Q, Ma Y, Luecken L, Liu X. Relations of SARS-Related Stressors and Coping to Chinese College Students Psychological Adjustment During the 2003 Beijing SARS Epidemic. *Journal of Counseling Psychology*, 2011; 58: 1410-1423. doi: 10 lO37/aOO23632

19. Seiffge-Krenke I. Coping behavior of Finnish adolescents: Remarks on a cross-cultural comparison. *Scandinavian Journal of Psychology*, 2020; 33 (4): 301-14.

20. Cassaretto M, Paredes R. Afrontamiento a la enfermedad crónica: estudio en pacientes con insuficiencia renal crónica terminal. *Revista De Psicología*, 2006; 24(1): 109-140. https://doi.org/10.18800/psico.200601.005

21. Savitsky B, Findling Y, Ereli A, Hendel T. Anxiety and coping strategies among nursing students during the covid-19 pandemic. Nurse Educ Pract., 2020;(46) doi: 10.1016/j.nepr.2020.102809.

22. Penson, R, Partridge R, Rudd P, Seiden M, Nelson J, Chabner Lynch, T. Update: laughter: the best medicine? *The Oncologist*, 2007; 10 (8): 651-60, https://doi.org/10.1634/theoncologist.10-8-651

23. Barrios N, Sánchez L, Salamanca Y. Patrones de personalidad patológica y estrategias de afrontamiento en estudiantes de psicología. *Psychologia: avances de la disciplina*, 2013; 7(2): 45-53.

24. Betriana F, Kongsuwan W. Lived experiences of grief of Muslim nurses caring for patients who died in an intensive care unit: A phenomenological study. Intensive And Critical Care Nursing, 2019; 52: 9-16. https://doi.org/10.1016/j.iccn.2018.09.003

25. Lázaro-Pérez C, Martínez-López J, Gómez-Galán J. Adicciones en estudiantes universitarios españoles en tiempos de encierro: perspectiva preventiva y social. *Ciencias sociales* ,2020; 9 (11): 195.

26. Reijneveld S, Crone M, Schuller A, Verhulst F, Verloove-Vanhorick, S. The changing impact of a severe disaster on the mental health and substance misuse of adolescents: follow-up of a controlled study. *Psychological Medicine*, 2005; 35 (3): 367-376, doi: 10.1017/s0033291704003575.

27. Hagan J. (2005) American Academy of Pediatrics Committee on Psychosocial Aspects of Child and Family Health, & Task Force on Terrorism. Psychosocial implications of disaster or terrorism on children: a guide for the pediatrician. Pediatrics, 2005; 116 (3): 787-95, 10.1542/peds.2005-1498

28. Brunner F, Neumann I, Yoon D, Rettenberger M, Stück E, Briken P. Determinants of Dropout From Correctional Offender Treatment. Front. Psychiatry,2019; 10(142). doi: 10.3389/fpsyt.2019.00142

29. Filbey F. The Neuroscience of Addiction. Cambridge: Cambridge University Press; 2019

30. Piñar-Navarro E, Cañadas-De la Fuente G, González-Jiménez E, Hueso-Montoro C. Anxiety and strategies for coping with stress used by first responders and out-of-hospital emergency health care staff before the COVID-19 pandemic . *Emergencias* 2020;32(5):369-73

31. Lozano-Díaz A, Fernández-Prados JS, Figueredo-Canosa V, Martínez-Martinez AM. Impactos del confinamiento por el COVID-19 entre universitarios: Satisfacción Vital, Resiliencia y Capital Social Online. *Revista Internacional de Sociología de la Educación*, 2020; 79-104.

32. González-Muzzio C. El rol del lugar y el capital social en la resiliencia comunitaria posdesastre. Aproximación mediante un estudio de caso después del terremoto del 23/F. EURES, *Revista Latinoamericana de Estudios Urbanos Regionales*, 2013; 39(117): 25-48. http://dx.doi.org/10.4067/S0250-71612013000200002

33. Elliott J, Haney T, Sams-Abiodun P. Limits to social capital: Comparing network assistance in two New Orleans neighborhoods devastated by hurricane Katrina, *The Sociological Quarterly*, 2010; 51(4): 624–648. https://doi.org/10.1111/j.1533- 8525.2010.01186.x

34. Lee J. Municipal-level determinants of suicide rates in South Korea: exploring the role of social capital and local government policies. *Journal of Asian Public Policy*, 2019; 1-18. https://doi.org/10.1080/17516234.2019.15653367

35. Cazalla-Luna N, Molero D. Inteligencia emocional percibida, disposición al optimismo-pesimismo, satisfacción vital y personalidad de docentes en su formación inicial. Revista de Investigación Educativa, 2016; 34(1): 241–258. https://doi.org/10.6018/rie.34.1.220701

36. Denovan A, Macaskill A. Stress and subjective well-being among first year UK undergraduate students. Journal of Happiness Studies, 2017; 18(2): 505–525. https://doi.org/10.1007/s10902-016-9736-y

37. Puigt RF, Ferré GG, Cebollero MP. Propiedades psicométricas del instrumento de valoración de riesgos psicosociales del instituto nacional de seguridad e higiene en el trabajo (FPSICO). Universidad de Barcelona; 2011. https://precoinprevencion.com/wp-content/uploads/2018/10/Estudio-sobre-las-propiedades-psicom%C3%A9tricas.pdf

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ORIGINAL

Status of non-enzymatic antioxidant vitamins (C and E) in patients either with type 2 diabete mellitus or hypertension alone and coexisted diabetes and hypertension

Estado de las vitaminas antioxidantes no enzimáticas (C y E) en pacientes con diabetes mellitus de tipo 2 o con hipertensión sola y con diabetes e hipertensión coexistentes

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Abstract

Aim: Oxidative stress is implicated as cause and consequence of both hypertension and diabetes. Antioxidant vitamins play a vital role in maintaining redox balance both in health and disease. Therefore we have estimated and compared the level of non-enzymatic antioxidant vitamin C and vitamin E status in healthy control subjects,T2DM, hypertensive patients and patients with coexisted diabetes and hypertension.

Methods: 30-40 years old male volunteered were divided in 4 groups (n=30 in each group); group I: Healthy controls, group II: T2DM patients, group III: Hypertensive patients and group IV: Patients with co-existed type 2 diabetes and hypertension. The anthropometric parameters, blood pressure, fasting and postparendial blood sugar, serum lipid peroxide, vitamin C and E were evaluated in this study.

Results: In our study the mean concentration of serum vitamin C and E in T2DM and hypertensive patients and patients with coexisted T2DM and hypertension was found to be significantly lower and serum lipid peroxide was higher than healthy control subjects (p <0.05).

Coclusion: The oxidative stress in T2DM and hypertensive male patients is reflected by lower serum concentration of antioxidant vitamin C and E as compared to non-diabetic, normotensive healthy male counterparts. In addition, the percentage decrease of these antioxidant vitamins was more in patients with coexisted T2DM with hypertension compared to T2DM or hypertension alone. Early onset type 2 diabetes mellitus and hypertension in young age has more adverse impact on cardiovascular health. Hence supplementation of vitamin C and E may be considered as an adjuvant therapy in the management of T2DM and hypertension and also to prevent premature cardiovascular related complications in young patients.

Key words: Vitamin C, vitamin E, oxidative stress, Type 2 diabetes mellitus, hypertension, coexisted diabetes and hypertension.

Resumen

Objetivo: El estrés oxidativo está implicado como causa y consecuencia tanto de la hipertensión como de la diabetes. Las vitaminas antioxidantes desempeñan un papel fundamental en el mantenimiento del equilibrio redox tanto en la salud como en la enfermedad. Por lo tanto, hemos estimado y comparado el nivel de vitamina C y vitamina E antioxidante no enzimática en sujetos sanos de control, DMT2, pacientes hipertensos y pacientes con diabetes e hipertensión coexistentes.

Métodos: Se dividió a los voluntarios de entre 30 y 40 años en 4 grupos (n=30 en cada grupo); grupo I: controles sanos, grupo II: pacientes con DMT2, grupo III: pacientes hipertensos y grupo IV: pacientes con diabetes tipo 2 e hipertensión coexistentes. En este estudio se evaluaron los parámetros antropométricos, la presión arterial, la glucemia en ayunas y postparto, el peróxido lipídico sérico y la vitamina C y E.

Resultados: En nuestro estudio, la concentración media de vitamina C y E en suero en los pacientes con DMT2 e hipertensos y en los pacientes con DMT2 e hipertensión coexistentes resultó ser significativamente menor y el peróxido lipídico en suero fue mayor que en los sujetos de control sanos (p <0,05).

Coclusión: El estrés oxidativo en los pacientes varones con DMT2 e hipertensión se refleja en una menor concentración sérica de vitaminas C y E antioxidantes en comparación con los varones sanos no diabéticos y normotensos. Además, el porcentaje de disminución de estas vitaminas antioxidantes fue mayor en los pacientes con DMT coexistente con hipertensión en comparación con la DMT o la hipertensión solas. La diabetes mellitus de tipo 2 y la hipertensión de aparición temprana tienen un impacto más adverso en la salud cardiovascular. Por lo tanto, la administración de suplementos de vitamina C y E puede considerarse un tratamiento coadyuvante en el tratamiento de la DMT2 y la hipertensión, así como para prevenir las complicaciones cardiovasculares prematuras en pacientes jóvenes.

Palabras clave: Vitamina C, vitamina E, estrés oxidativo, diabetes mellitus tipo 2, hipertensión, diabetes e hipertensión coexistentes.

Introduction

Diabetes and hypertension are two important lifestyle related diseases affecting around 285 million and 1 billion people, respectively around the world[1]. As a result of increased global population, prevalence of early onset of overweight/obesity and unhealthy lifestyle, these figures are expected to increase by approximately 50% over the next 20 years[2-4]. Cardiovascular diseases account for 40-80% of deaths in diabetic patients and about 12 million deaths each year; known to be one of major killer diseases in the world[5]. Hypertension is one of the most common cardiovascular diseases and it is a serious public health issue affecting more than 25% of adult population in both economically underdeveloped as well as developed countries[6]. About 85% of T2DM patients have blood pressure more than 130/80 mmHg. Understanding, why hypertension is a prevailing comorbidity among T2DM patients is a serious issue in the research community today. Hence, it would be of significant use to find out the association between these two catstrophic diseases early in their pathophysiological process in checking their major complications. Previous clinical and experimental research studies have reported that oxidative stress, through excess free radical formation, plays a significant role in the onset of T2DM and hypertension[7]. Oxidative stress causes destruction of cellular membrane lipids, has been attributed along with other types of intracellular and DNA oxidative damage in the normal senescent process and in pathogenesis of a number of chronic diseases. The integrated antioxidant mechanisms, including endogenous antioxidant enzymes and exogenous antioxidant vitamins, exist to restrict the harmful implications of oxidative stress. An inadequate intake of dietary antioxidant micronutrients may compromise redox homeostasis, thus aggravate overall oxidative stress[8]. Hence, the aim of this study is to estimate and inspect the level of non-enzymatic antioxidant vitamin C and vitamin E status in patients with T2DM, hypertension and coexisted diabetes and hypertension.

Materials and methods

Source of data

Known patients of type 2 diabetes, hypertension and co-existed type-2 diabetes with hypertension visiting Al-Ameen Medical College Hospital Vijayapur, Luqman Unani Medical Hospital Vijayapur and District Hospital Vijayapur were selected for the study.

Inclusion criteria

Control group: Healthy adult men, between 30-40 years, non-diabetic, normotensive no history or evidence of renal, cardiorespiratory and other chronic diseases. All participants were non-smokers, non-alcoholic and no history of long-term drug intake.

Patients with Type 2 diabetes: Confirmed type 2 diabetic, male, normotensive patients between 30-40 years attending the clinic for regular follow up for more than 6 months were included in this group.

Patients with hypertension: Hypertensive male patients between 30-40 years, with normal blood glucose (normoglycemic) attending the clinic for regular follow up for more than 6 months were included in this group.

Patients with co-existed Type 2 diabetes and hypertension: 30-40 years old, male patients visiting the OPD for more than six months

Exclusion Criteria

Patients with type 1 diabetes mellitus, other endocrinal disorder like Cushing's syndrome, thyroid disorder, chronic respiratory, coronary artery diseases, abnormal renal function or hepatic dysfunction were excluded from the study. Healthy men or patients below 30 years or above 40 years, smokers, alcoholic, with a history of long term multi vitamin intake were also excluded from this study.

Sample size

Total 120 cases i.e., sample size of 30 in each group was calculated by taking co-existed type- 2 diabetes and hypertension with alpha error of 0.05 and power of 90.

Study design

Group I: Healthy individuals non diabetic and normotensive (Controls)
Group II: Patients with type 2 diabetes (T2DM)
Group III: Patients with hypertension (HTN)
Group IV: Patients with co-existed type 2 diabetes and hypertension (T2DM + HTN)

Methods of collection of data

Details of the study was explained to the subjects/ patients and informed written consent was obtained from volunteers. The entire study was conducted as per the guidelines mentioned in the Declaration of Helsinki. The research protocol was approved by the institutional ethical committee.

Physical Parameters

Height was measured by using wooden stadiometer and weight was measured by using weighing scale (Tokyo, Japan) as per WHO international guidelines[9]. Body mass index (BMI) was calculated by Quetelet's index. Body surface area (BSA) was recorded by Dubois' nomogram.

Physiological Parameters

Systolic and diastolic blood pressure of each participatant was recorded in right arm in supine position using a standardized sphygmomanometer (Elko, India). An average of two recordings of both systolic and diastolic blood pressure was calculated. Hypertension (HTN) was defined following the criteria of the Joint National Committee on Prevention, Detection, Evaluation and

Treatment of High Blood Pressure (JNC 7 criteria)[10].
Biochemical Parameters

Five millilitres of blood sample was collected from each participant after overnight fast in a clean sterile plain tube and blood sample was allowed to stand at room temperature for 2 hours. The sample was centrifuged at 3000rpm for half an hour to collect serum. Postprandial plasma glucose was measured 2 hours after meal. Fasting and postprandial blood glucose levels were estimated by Auto analyser EM 360 (Transasia, ERBA Mannheim, Germany). The serum lipid peroxide was measured by the method of Satoh K[11]. Serum vitamin C was estimated by the Roe and Koether, 1943 Method[12]. Serum vitamin E (α-tocopherol) was determined by using non-antibody coated microplate with ELISA reader (ERBA-Lisa Scan II, Mannheim, Germany), Jargar et al, 2012 method[13].

Statistical Analysis

The results of each group were expressed in terms of mean + standard deviation. To determine the significance of inter-group differences, one way analysis (ANOVA) followed by 'post hoc t test' were done. A value of $p < 0.05$ was interpreted as statistically significant. The mean values of the groups were subtracted from the respective control group and the differences were calculated in terms of percent change.

Results

The clinical investigations and anthropometric parameters of group I (control), group II (type 2 diabetic patients), group III (hypertensive patients) and group IV (coexisted type 2 diabetic and hypertensive patients) are presented in **table I**.

Table I shows mean weight of group II-T2DM (82.43 + 28.13 kg) and group IV-T2DM + HTN (87.82 + 14.32 kg) patients was significantly more than healthy control men (75.12 + 23.04 kg); the mean values of BMI and BSA group II (T2DM), group III (HTN) and group IV (T2DM + HTN) patients were significantly greater than control group ($p < 0.05$). In physiological parameters the systolic and diastolic blood pressure was significantly higher in group III (HTN) and group IV (T2DM + HTN) patients than group II (T2DM) patients and group I control subjects ($p < 0.05$). The fasting and postprandial blood glucose was higher in group II (T2DM) and group IV (T2DM + HTN) patients than group III (HTN) patients and group I control subjects.

Table II shows biochemical investigation results in our study. The serum concentration of lipid peroxide in group II (T2DM), group III (HTN) and group IV (T2DM + HTN) patients was significantly more than group I (control subjects) ($p < 0.05$). The percentage increase of serum lipid peroxide in group I (control subjects) vs group II (T2DM) patients was 76.72%; group I (control subjects) vs group III (HTN) patients was 62.07% and group I (control subjects) vs group IV (T2DM + HTN) patients was highest 90.52% as depicted in **figure 1**. The serum concentration of vitamin C in group II (T2DM), group III (HTN) and group IV (T2DM + HTN) patients were significantly lower than group I control subjects ($p < 0.05$). The percentage decrease of serum vitamin C in group I (control subjects) vs group II (T2DM) patients was -42.96%; group I (control subjects) vs group III (HTN) patients was -38.8% and group I (control subjects) vs group IV (T2DM + HTN) patients was lowest -68% as shown in **figure 1**. The serum concentration of vitamin E in group II (T2DM), group III (HTN) and group IV (T2DM + HTN) patients was significantly lesser than group I (control subjects) ($p < 0.05$). The percentage decrease of serum

Table I: Clinical investigations in study groups with healthy controls.

Clinical Investigations	Group I (Controls)	Group II (T2DM)	Group III (HTN)	Group IV (T2DM + HTN)
Height (cm)	171.13 + 7.67[a]	169.46 + 5.24[a]	170.55 + 10.07[a]	172.23 + 6.21[a]
Weight (kg)	75.12 + 23.04[a]	82.43 + 28.13[b]	78.31 + 22.32[a]	87.82 + 14.32[c]
BMI (kg/m^2)	23.88 + 2.76[a]	26.04 ± 4.25[b]	26.71 ± 5.18[b]	27.37 ± 4.51[b]
BSA (m^2)	1.89 + 0.14[a]	1.96 + 0.32[b]	1.92 + 0.28[b]	2.04 + 0.19[c]
SBP (mmHg)	112.76 ± 8.21[a]	121.23 ± 11.78[b]	154.55 ± 16.98[c]	154.46 ± 19.18[c]
DBP (mmHg)	80.11 ± 10.09[a]	81.32 ± 9.97[a]	98.11 ± 12.15[b]	94.81 ± 16.09[b]
Fasting blood glucose (mg/dL)	86.94 ± 8.14[a]	146.65 ± 49.86[b]	89.97 ± 12.02[a]	143.76 ± 61.43[b]
Postprandial blood glucose (mg/dL)	110.24 ± 20.22[a]	229.42 ± 94.87[b]	116.77 ± 19.95[a]	230.04 ± 90.22[b]

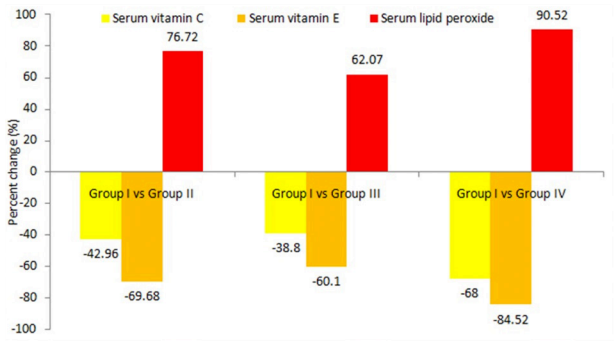
T2DM- Type 2 diabetic, HTN- Hypertensive, BMI-Body mass index, BSA-Body surface area, SBP- Systolic blood pressure, DBP- Diastolic blood pressure. Each value is mean +SD of 30 cases in each group (n=30). In each row, values with different superscripts (a, b, c, d) were significantly different from each other ($p < 0.05$). *Post-hoc* t-test analysis was used to test for differences among the means when analysis of variance (ANOVA) indicated a significant *p* value.

Table II: Serum levels of non-enzymatic antioxidant vitamins (C & E) and lipid peroxide in study groups with healthy controls.

Biochemical Investigations	Group I (Controls)	Group II (T2DM)	Group III (HTN)	Group IV (T2DM + HTN)
Serum lipid peroxide (µmol/L)	1.16 ± 0.12[a]	2.05 ± 0.21[b]	1.88 ± 0.05[c]	2.21 ± 0.22[d]
Serum vitamin C (mg/dL)	13.22 ± 2.76[a]	7.54 ± 1.92[b]	8.09 ± 2.81[b]	4.23 ± 3.06[c]
Serum vitamin E (µg/dL)	18.67 ± 1.82[a]	5.66 ± 2.20[b]	7.45 ± 1.97[c]	2.89 ± 2.14[d]

T2DM- Type 2 diabetic, HTN- Hypertensive. Each value is mean + SD of 30 cases in each group. In each row, values with different superscripts (a, b, c, d) were significantly different from each other ($p < 0.05$). *Post-hoc* t-test analysis was used to test for differences among the means when analysis of variance (ANOVA) indicated a significant *p* value.

Figure 1: Percent change graph of non-enzymatic antioxidant vitamins (C & E) and lipid peroxide in study groups verses healthy controls.



vitamin E in group I (control subjects) vs group II (T2DM) patients was -69.68%; group I (control subjects) vs group III (HTN) patients was -60.1% and group I (control subjects) vs group IV (T2DM + HTN) patients was again lowest -84.52% as shown in **figure 1**.

Discussion

This study emphasizes on the influence of non-enzymatic antioxidants like vitamin C and vitamin E on T2DM, hypertension and co-existed diabetes and hypertension and may explain the mechanism of disease pathogenesis.

The concentration of antioxidant vitamins C and E in a biological system also serve as oxidative stress biomarkers. The significant reduction of serum vitamin C and E and increase in lipid peroxide in young type 2 diabetic patients in our study indicates increase production of free radicals more than its clearance. Many other investigators have also reported that oxidative stress increases insulin resistance and plays an important role in pathogenesis of type 2 diabetes[14]. Hyperglycemia induced oxidative stress causes cellular and molecular changes like protein oxidation, lipid peroxidation and DNA damage and play a major role in progression of micro-vascular and macro-vascular complications in type 2 diabetes, causing systemic manifestations like retinopathy, nephropathy, neuropathy and accelerated coronary artery disease. The severity of tissue damage and complications are directly corelated with level/duration of hyperglycemia and consequently oxidative stress[15,16]. In research studies and meta-analysis conducted previously on type 2 diabetic male patients revealed that supplementation of vitamin C and E has improved redox balance, fasting blood glucose, lipid profile, insulin resistance, glycemic control and clinical condition of diabetic patients[17,18].

Serum lipid peroxide is well known oxidative stress biomarker, increased in hypertensive patients compared to normotensive subjects in this study suggestive of role of free radicals in pathogenesis of human hypertension. The experimental studies conducted on animal models also suggest that ROS are one of the key factors associated with endothelial dysfunction, modulators and mediators of angiotensin II induced vasoconstriction, hence play a vital role in pathogenesis of hypertension. The increased generation of free radicals in vascular smooth muscle/ endothelial cells and decreased NO bioavailability may be responsible for vascular remodeling and arterial stiffness in hypertensive patients[19,20]. In healthy individuals the vascular tissue is protected from the assault of ROS by both endogenous antioxidant enzymes and exogenous antioxidant vitamins found in vascular smooth muscles and adventitia[21]. The serum concentration of antioxidant vitamins; vitamin C and E were decreased in hypertensive patients compare to normotensive subjects in our study, probably these antioxidant vitamins were utilized for quenching of free radicals and termination of chain reactions in vascular cells to counteract oxidative stress. Previous experimental studies have showed that the supplementation of vitamin C and E has improved the plasma antioxidant status and reduced the progression of hypertension in animal model[22]. The. vitamin C and E are potent antioxidants and also believed to increases the activity of eNOS and bioavailability of nitric oxide (NO) and thereby improves endothelial dysfunction in hypertensive models[23].

In our study the oxidative stress markers were significantly more affected in patients with coexisted T2DM with hypertension than patients either with T2DM or hypertension alone as reflected by increase serum lipid peroxidation and decreased vitamin C and E concentration. The prevalence of coexisted T2DM with hypertension is around 30 to 60% of patients with T2DM at the time of diagnosis. Obesity, oxidative stress, insulin resistance, dyslipidemia and metabolic syndrome share common pathophysiological pathways for both type 2 diabetes mellitus and hypertension[24,25]. Onset T2DM and hypertension at younger age between 30-40 years as evident in our study may be adversely corelated with premature cardiovascular morbidity and mortality in their middle age[26]. The antioxidant vitamin C and E play crucial roles in maintaining redox homeostasis in cells and physiological system. Specific therapies targeting free radicals using these antioxidant vitamins in young hypertensive and T2DM patients might help to improve beta cell and vascular endothelial dysfunction; thus, may reduce the long-term complications, morbidity and mortality in T2DM and hypertensive patients. These vitamins may be considered as an adjuvant therapy for the management of diabetes and hypertension. However Long-term clinical trials and placebo/case control studies are needed to demonstrate their safety and efficacy in such patients.

Conclusion

The oxidative stress is evident in young age (30-40 years old) type 2 diabetes and hypertensive male patients as reflected by lower serum concentration of antioxidant vitamin C and E as compared to non-diabetic, normotensive healthy male counterparts. In addition, the percentage decrease of these antioxidant vitamins was more in patients with coexisted T2DM with hypertension compared to T2DM or hypertension alone. Early onset of type 2 diabetes mellitus and hypertension in young age has more adverse impact on cardiovascular health. Hence supplementation of vitamin C and E may be considered as an adjuvant therapy in the management of T2DM and hypertension and also to prevent premature cardiovascular related complications in young patients.

Author's contributions

Jameel J. Jargar designed and performed the research. Shaheenkousar Hattiwale analyzed the data and prepared final manuscript. Haroon Rashid Hattiwale Mohammad Muzammil Ahmed and Mohammed Nazeer crtically revised the manuscript and approved final version.

Conflict of interest

The authors declare that there is no conflict of interest.

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References

1. World Health Organization. Global status report on non-communicable diseases 2014. World Health Organization; 2014.

2. Schofield D, Shrestha RN, Cunich MM, Passey ME, Veerman L, Tanton R, et al. The costs of diabetes among Australians aged 45-64 years from 2015 to 2030: projections of lost productive life years (PLYs), lost personal income, lost taxation revenue, extra welfare payments and lost gross domestic product from Health & Wealth MOD2030. BMJ open 2017;7(1):e013158.

3. Vinothiya K, Ashokkumar N. Modulatory effect of vanillic acid on antioxidant status in high fat diet-induced changes in diabetic hypertensive rats. Biomed Pharmacotherap 2017;87:640-52.

4. Seravalle G, Grassi G. Sympathetic nervous system, hypertension, obesity and metabolic syndrome. High Blood Pressure & Cardiovascular Prevention 2016;23(3):175-9.

5. Rossi A, Zoppini G, Benfari G, Geremia G, Bonapace S, Bonora E, et al. Mitral Regurgitation and Increased Risk of All-Cause and Cardiovascular Mortality in Patients with Type 2 Diabetes. American J Med 2017;130(1):70-6.

6. Oh JY, Allison MA, Barrett-Connor E. Different impacts of hypertension and diabetes mellitus on all-cause and cardiovascular mortality in community-dwelling older adults: the Rancho Bernardo Study. J Hypertension 2017;35(1):55-62.

7. Rahman T, Hosen I, Islam MT, Shekhar HU. Oxidative stress and human health. Adv Biosci Biotech 2012;3(7A):997.

8. Bjørklund G, Chirumbolo S. Role of oxidative stress and antioxidants in daily nutrition and human health. Nutrition 2017;33:311-21.

9. World Health Organization, "Physical Status: The Use and Interpretation of Anthropometry. Report of the WHO Expert Committee." World Health Organization Technical Report Series, Vol. 854, Geneva, 1995, pp. 1-416.

10. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The JNC 7 Report. J Am Med Asso 2003;289(19):2560-72.

11. Satoh K. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. Clin Chim Acta 1978;90:37-43.

12. Roe JH, Koether CA. The determination of ascorbic acid in whole blood and urine through the 2,4-dinitrophenylhydrazine derivative of dehydroascorbic acid. J Biol Chem 1943;147:399-407.

13. Jargar JG, Hattiwale SH, Dhundasi SA, Das S, Das KK. A modified simple method for determination of serum α-tocopherol (Vitamin E). J Basic Clin Physiol Pharmacol 2012;23(1):45-8.

14. Asmat U, Abad, K, & Ismail K. Diabetes mellitus and oxidative stress—A concise review. Saudi pharmaceutical journal 2016; 24(5), 547-53.

15. Butkowski EG, Jelinek HF. Hyperglycaemia, oxi¬dative stress and inflammation markers. Redox Rep 2017; 22: 257-64.

16. Oguntibeju OO. Type 2 diabetes mellitus, oxidative stress and inflammation: examining the links. Int J Physiol Pathophysiol Pharmacol. 2019;11(3):45-63. Published 2019 Jun 15.

17. El-Aal AA, El-Ghffar EAA, Ghali AA, Zughbur MR, Sirdah MM. The effect of vitamin C and/or E supplementations on type 2 diabetic adult males under metformin treatment: A single-blinded randomized controlled clinical trial. Diabetes Metab Syndr. 2018;12(4):483-489. doi:10.1016/j.dsx.2018.03.013

18. Balbi ME., Tonin FS., Mendes AM. et al. Antioxidant effects of vitamins in type 2 diabetes: a meta-analysis of randomized controlled trials. Diabetol Metab Syndr 10, 18 (2018). https://doi.org/10.1186/s13098-018-0318-5

19. Touyz RM, Yao G, Quinn MT, Pagano PJ, Schiffrin EL. p47phox associates with the cytoskeleton through cortactin in human vascular smooth muscle cells: role in NAD(P)H oxidase regulation by angiotensin II. Arterioscler Thromb Vasc Biol 2005; 25: 512-8.

20. Touyz, RM., Briones, AM. Reactive oxygen species and vascular biology: implications in human hypertension. Hypertens Res 34, 5-14 (2011). https://doi.org/10.1038/hr.2010.201

21. Pizzino G, Irrera N, Cucinotta M, et al. Oxidative Stress: Harms and Benefits for Human Health. Oxid Med Cell Longev. 2017;2017:8416763. doi:10.1155/2017/8416763

22. Chen X, Touyz RM, Park JB, Schiffrin EL. Antioxidant effects of vitamins C and E are associated with altered activation of vascular NADPH oxidase and superoxide dismutase in stroke-prone SHR. Hypertension. 2001;38(3 Pt 2):606-611. doi:10.1161/hy09t1.094005

23. Ulker S, McKeown PP, Bayraktutan U. Vitamins reverse endothelial dysfunction through regulation of eNOS and NAD(P)H oxidase activities. Hypertension. 2003;41(3):534-539. doi:10.1161/01.HYP.0000057421.28533.37

24. Baradaran A, Nasri H, Rafieian-Kopaei M. Oxidative stress and hypertension: Possibility of hypertension therapy with antioxidants. J Res Med Sci. 2014;19(4):358-67.

25. Pouvreau C, Dayre A, Butkowski EG, de Jong B, Jelinek HF. Inflammation and oxidative stress markers in diabetes and hypertension. J Inflamm Res. 2018;11:61-68. Published 2018 Feb 19. doi:10.2147/JIR.S148911

26. Hillier TA, Pedula KL. Complications in young adults with early-onset type 2 diabetes: losing the relative protection of youth. Diabetes care. 2003;26(11):2999-3005.

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ORIGINAL

Genotyping of *Campylobacter jejuni* isolates from raw meat of animal species

Genotipado de aislados de Campylobacter jejuni procedentes de carne cruda de especies animales

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Abstract

Background: *Campylobacter jejuni* strains are important causes of foodborne diseases globally, the present survey was done to assess the prevalence and genotypic profile of *C. jejuni* strains isolated from raw meat samples.
Methods: Two-hundred raw meat samples were collected and analysis. Culture and biochemical tests were used for identification of *C. jejuni*. Isolates were also confirmed using the PCR test. PCR was also used to assess the distribution of virulence genes.
Results: 13.50% of samples were contaminated with *C. jejuni* strains. Raw cattle meat had the highest (25%), while raw goat meat (7.14%) had the lowest prevalence of *C. jejuni*. Significant difference was found amid the type of samples and prevalence of *C. jejuni* ($P< 0.05$). cafF (55.55%), cdtA (51.85%), and ciaB (44.44%) were the most commonly detected genes. Amongst the combined genotyping patterns, cadF+cdtA (25.92%) and ciaB+cdtA (18.51%) were the most commonly detected genetic properties. Additionally, cadF+ciaB+cdtA was identified amongst the 11.11% of isolates.
Conclusion: Role of raw meat, particularly raw cattle meat as a reservoir of *C. jejuni* strains was determined in the survey.

Key words: Campylobacter jejuni, prevalence, raw meat, epidemiology, virulence characters.

Resumen

Antecedentes: Las cepas de *Campylobacter jejuni* son importantes causas de enfermedades transmitidas por los alimentos a nivel mundial, el presente estudio se realizó para evaluar la prevalencia y el perfil genotípico de las cepas de *C. jejuni* aisladas de muestras de carne cruda.
Métodos: Se recogieron y analizaron 200 muestras de carne cruda. Se utilizaron pruebas de cultivo y bioquímicas para la identificación de *C. jejuni*. Los aislamientos también se confirmaron mediante la prueba PCR. También se utilizó la PCR para evaluar la distribución de los genes de virulencia.
Resultados: El 13,50% de las muestras estaban contaminadas con cepas de *C. jejuni*. La carne cruda de bovino fue la más alta (25%), mientras que la carne cruda de caprino (7,14%) tuvo la menor prevalencia de *C. jejuni*. Se encontró una diferencia significativa entre el tipo de muestras y la prevalencia de *C. jejuni* ($P< 0,05$). cafF (55,55%), cdtA (51,85%) y ciaB (44,44%) fueron los genes más comúnmente detectados. Entre los patrones de genotipado combinados, cadF+cdtA (25,92%) y ciaB+cdtA (18,51%) fueron las propiedades genéticas más comúnmente detectadas. Además, cadF+ciaB+cdtA se identificó en el 11,11% de los aislados.
Conclusión: En el estudio se determinó el papel de la carne cruda, en particular de la carne cruda de vacuno, como reservorio de cepas de *C. jejuni*.

Palabras clave: Campylobacter jejuni, Prevalencia, Carne cruda, Epidemiología, Caracteres de virulencia.

Introduction

Foods with animal origins are determined as causative agent of different types of zoonotic diseases[1-5]. In this regard, Campylobacter species are the predominant cause of acute bacterial enteritis in both developing and developed countries[6]. It has been estimated that 32,086 cases were notified in Australia with an incidence rate of 130 cases per 100,000 population[7]. Among species, Campylobacter jejuni is considered for more than 80% of cases of campylobacteriosis characterized by fever, diarrhea, and abdominal cramps[8].

During slaughter and processing, cross-contamination and further spread of *C. jejuni* can occur. Even after chilling and cutting of meat products, high contamination rates with *C. jejuni* are possible[9].

Researches revealed that some virulence factors are responsible for the pathogenesis of Campylobacter infections. Among them, Campylobacter adhesin to Fn (*cadF*), campylobacter invasion antigen B (*ciaB*), cytolethal distending toxin genes (*cdtA*), and Phospholipase A1 (*pldA*) are responsible for adhesion and invasion to host cells[10].

Rendering the high importance of the *C. jejuni*, as a causative agent of campylobacteriosis and Guillain-Barré syndrome (GBS)[11], it is essential to assess its epidemiology and routes of transmission into the human population. Thus, the present survey was done to assess the distribution and virulence characters of the *C. jejuni* strains isolated from raw meat samples of sheep, goat and cattle species.

Materials and methods

Samples

200 raw meat samples of sheep (n= 70), goat (n= 70) and cattle (n= 60) species were collected and examined from January 2019 to January 2020. Thigh muscle was collected fro this purpose. In this regard, 100 g of meat samples were collected separately in sterile plastic bags and transferred to laboratory.

Isolation and identification of *C. jejuni*

25 g of each raw meat sample was homogenized and transferred to 225 mL of Preston enrichment broth base containing Campylobacter-selective supplement IV (HiMedia, India) with 5% defibrinated sheep blood. After inoculation at 42 C for 24 h in a microaerophilic condition (85% N2, 10% CO2, 5% O2), 0.1 mL of the enrichment was then streaked onto the Campylobacterselective agar base (HiMedia, India) supplemented with an antibiotic supplement for the selective isolation of Campylobacter spp. (HiMedia, India) and 5% defibrinated sheep blood and incubated at 42 C for 48 h under the same condition. One presumptive Campylobacter colony from each selective agar plate was subcultured, and identification of presumptive Campylobacter spp. was performed using standard microbiological and biochemical procedures including Gram staining, hippurate hydrolysis, production of catalase, urease activity, oxidase test, indoxyl acetate hydrolysis, and susceptibility to cephalotin.

DNA extraction and analysis

DNA was extracted from *C. jejuni* isolates using DNA extraction kit (Cinnagene, Iran)[12-15]. Purity and quality of extracted DNA were then checked using the method described previously[16-20]. *C. jejuni* strains were identified another time using the PCR (**Table I**)[21].

Identified DNA, were subjected to several PCR procedures to obtain the profile of genetic properties as shown in **table II**[22].

Electrophoresis was done using the procedure reported previously[23-25].

Statistical analysis

Chi-square test was used for data analysis in a SPSS software. $P< 0.05$ was considered significant[26-30].

Results

Figure 1 shows the PCR electrophoresis of *C. jejuni* identification.

Table III shows the distribution of *C. jejuni* amongst raw meat samples of animal species. Total prevalence of *C. jejuni* was 13.50%. Raw cattle meat had the highest (25%), while raw goat meat (7.14%) had the lowest prevalence of *C. jejuni*. Significant difference was found amid the type of samples and prevalence of *C. jejuni* ($P< 0.05$).

Table I: PCR for detection of *C. jejuni*.

PCR programs	PCR Volume (50µL)	PCR product (bp)	Primer sequence (5'-3')	Target gene
1 cycle: 94 °C ---------- 1 min 35 cycle: 94 °C ---------- 30 s 60 °C ---------- 30 s 72 °C ---------- 40 s 1 cycle: 72 °C ---------- 3 min	5 µL PCR buffer 10X 2 mM $Mgcl_2$ 150 µM dNTP (Fermentas) 0.75 µM of each primers F & R 1.5 U Taq DNA polymerase (Fermentas) 3 µL DNA template	589	F: CTATTTTATTTTTGAGTGCTTGTG R: GCTTTATTTGCCATTTGTTTTATTA	MapA (*C. jejuni*)

Table II: PCR for determination of *C. jejuni* genetic properties.

PCR programs	PCR Volume (50µL)	PCR product (bp)	Primer sequence (5'-3')	Target gene
1 cycle: 94 °C ---------- 2 min. 35 cycle: 94 °C ---------- 40 s 43 °C ---------- 50 s 72 °C ---------- 4600 s 1 cycle: 72 °C ---------- 8 min	5 µL PCR buffer 10X 2 mM $MgCl_2$ 150 µM dNTP 0.75 µM of each primers F & R 1.5 U Taq DNA polymerase 3 µL DNA template	400	F: TTGAAGGTAATTTAGATATG R: CTAATACCTAAAGTTGAAAC	*cadF*
1 cycle: 94 °C ---------- 1 min. 35 cycle: 94 °C ---------- 60 s 54 °C ---------- 60 s 72 °C ---------- 60 s 1 cycle: 72 °C ---------- 10 min	5 µL PCR buffer 10X 2 mM $MgCl_2$ 150 µM dNTP 0.75 µM of each primers F & R 1.5 U Taq DNA polymerase 3 µL DNA template	527	F: TGCGAGATTTTTCGAGAATG R: TGCCCGCCTTAGAACTTACA	*ciaB*
1 cycle: 95 °C ---------- 2 min. 35 cycle: 94 °C ---------- 50 s 49 °C ---------- 60 s 72 °C ---------- 40 s 1 cycle: 72 °C ---------- 7 min	5 µL PCR buffer 10X 2 mM $MgCl_2$ 150 µM dNTP 0.75 µM of each primers F & R 1.5 U Taq DNA polymerase 3 µL DNA template	370	F: CCTTGTGATGCAAGCAATC R: ACACTCCATTTGCTTTCTG	*cdtA*
1 cycle: 94 °C ---------- 1 min. 35 cycle: 95 °C ---------- 60 s 46 °C ---------- 60 s 72 °C ---------- 60 s 1 cycle: 72 °C ---------- 8 min	5 µL PCR buffer 10X 2 mM $MgCl_2$ 150 µM dNTP 0.75 µM of each primers F & R 1.5 U Taq DNA polymerase 3 µL DNA template	385	F: AAGAGTGAGGCGAAATTCCA R: GCAAGATGGCAGGATTATCA	

Figure 1: PCR electrophoresis of *C. jejuni* identification. PC: Positive control, NC: Negative control, M: Marker (100 bp). Others: Positive samples.

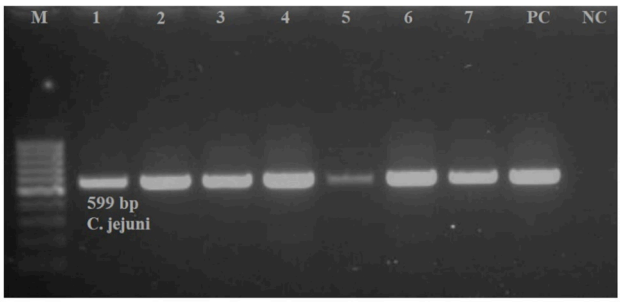

Table III: *C. jejuni* distribution amongst raw meat samples of animal species.

Raw meat samples	N. collected	N. positive (%)
Sheep	70	7 (10)
Goat	70	5 (7.14)
Cattle	60	15 (25)
Total	200	27 (13.50)

Table IV shows the genetic properties of *C. jejuni* strains isolated from raw meat samples. According to this table, *cafF* (55.55%), *cdtA* (51.85%), and *ciaB* (44.44%) were the most commonly detected genes. Amongst the combined genotyping patterns, *cadF+cdtA* (25.92%) and *ciaB+cdtA* (18.51%) were the most commonly detected genetic properties. Additionally, *cadF+ciaB+cdtA* was identified amongst the 11.11% of isolates. Significant difference was found amid the type of samples and distribution of *C. jejuni* genetic properties ($P< 0.05$).

Discussion

Medical sciences have been developed in recent years[31-36]. However, some diseases remain complicated[37-40]. Campylobacteriosis is one of the most dangerous diseases transmitted from animal

Table IV: *C. jejuni* genetic properties.

Raw meat samples (N. positive)	N. isolates harbored each gene (%)												
	cadF	*ciaB*	*cdtA*	*pldA*	*cadF +ciaB*	*cadF +cdtA*	*cadF +pldA*	*ciaB +cdtA*	*ciaB +pldA*	*cdtA +pldA*	*cadF +ciaB +cdtA*	*cadF +cdtA +plda*	*ciaB +cdtA +pldA*
Sheep (7)	3 (42.85)	3 (42.85)	3 (42.85)	2 (28.57)	1 (14.28)	2 (28.57)	1 (14.28)	2 (28.57)	1 (14.28)	1 (14.28)	1 (14.28)	-	-
Goat (5)	3 (60)	1 (20)	2 (40)	1 (20)	1 (20)	-	1 (20)	-	-	-	-	-	-
Cattle (15)	9 (60)	8 (53.33)	9 (60)	5 (33.33)	4 (26.66)	5 (33.33)	2 (13.33)	3 (20)	1 (6.66)	2 (13.33)	2 (13.33)	1 (6.66)	1 (6.66)
Total (27)	15 (55.55)	12 (44.44)	14 (51.85)	8 (29.62)	6 (22.22)	7 (25.92)	4 (14.81)	5 (18.51)	2 (7.40)	3 (11.11)	3 (11.11)	1 (3.70)	1 (3.70)

to human owing to the consumption of raw and undercooked products[41].

This survey showed that 13.50% of examined raw meat samples were contaminated with *C. jejuni*. Alike studies have been performed in this field. Hussain et al.[42] showed that among meat samples, the highest prevalence (48%) of Campylobacter was recorded in raw chicken meat followed by raw beef (10.9%) and raw mutton (5.1%). Korsak et al.[43] showed that Campylobacter species were detected in 690 (49.3%) of 1,400 poultry samples collected from retail trade. Strains were isolated from 50.2 and 41.1% of raw chicken and turkey meat samples, respectively, and from 50.1 and 42.6% of raw chicken and turkey giblets. The incidence of Campylobacter spp. on pork (10.6%) and beef (10.1%) was significantly lower than on poultry. *C. jejuni* was the most prevalent Campylobacter species in chicken (46.6%), pork (68.6%), and beef (66.7%), and Campylobacter coli was the most frequently isolated Campylobacter species in turkey meat (71.2%).

Whole incidence of *C. jejuni* amongst the poultry samples collected from Iraq[44], Pakistan[45], India[46], Korea[47], and China[48] was 10%, 40%, 26.30%, 36.30%, and 1.82% to 56.00%, respectively.

In the present survey high distribution of combined virulence genes was detected amongst the *C. jejuni* isolates. These factors are responsible for adhesion of bacteria into the epithelial cells of the gastric mucosa and invasion to them. In this regard, *cadF*, *ciaB*, *cdtA*, and *pldA* were detected in 55.55%, 44.44%, 51.85%, and 29.62% of isolates. Zheng et al.[49] revealed that All Campylobacter isolates possessed *flaA*, *cadF*, *pldA*, *cdtA*, *cdtB*, and *cdtC*, and most (91%) also contained the *ciaB* gene. However, the *virB11* gene, carried by virulence plasmid *pVir*, was absent in almost all the Campylobacter isolates. Melo et al.[50] reported that The genes *flaA*, *pldA*, *cadF*, and *ciaB* and the CDT complex were detected in 41/55 (74.5%), 35/55 (63.6%), 37/55 (67.3%), 37/55 (67.3%) and 36/55 (65.5%) strains respectively, and transcripts for the *ciaB* and *dnaJ* genes evaluated in 46 strains were detected in 60.9%.

Conclusion

Findings of this survey showed that Raw meat samples of sheep, goat and cattle species are reservoirs for transmission of virulent strains of *C. jejuni* into the human population. Proper cooking of meat before consumption can diminish the risk of Campylobacteriosis in human population. Cattle meat had the higher attitude for *C. jejuni* transmission.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of Brucella abortus and Brucella melitensis in aborted bovine, ovine, caprine, buffaloes and camelid fetuses by application of conventional and real-time polymerase chain reaction. The Thai Journal of Veterinary Medicine. 2012;42(1):13.

2. Dehkordi FS, Momtaz H, Doosti A. Application of Real-Time PCR for detection of Aspergillus species in aborted ruminant foetuses. Bulgarian Journal of Veterinary Medicine. 2012;15(1):30-6.

3. Dehkordi FS. Prevalence study of Coxiella burnetii in aborted ovine and caprine fetuses by evaluation of nested and real-time PCR assays. American Journal of Animal and Veterinary Sciences. 2011;6(4):180-6.

4. Dehkordi FS, Tavakoli-Far B, Jafariaskari S, Momtaz H, Esmaeilzadeh S, Ranjbar R, et al. Uropathogenic Escherichia coli in the high vaginal swab samples of fertile and infertile women: virulence factors, O-serogroups, and phenotyping and genotyping characterization of antibiotic resistance. New Microbes and New Infections. 2020;38:100824.

5. Dehkordi FS, Haghighi N, Momtaz H, Rafsanjani MS, Momeni M. Conventional vs real-time PCR for detection of bovine herpes virus type 1 in aborted bovine, buffalo and camel foetuses. Bulgarian Journal of Veterinary Medicine. 2013;16(2):102-12.

6. Thomas KM, de Glanville WA, Barker GC, Benschop J, Buza JJ, Cleaveland S, et al. Prevalence of Campylobacter and Salmonella in African food animals and meat: A systematic review and meta-analysis. International journal of food microbiology. 2020 Feb 16;315:108382.

7. Australian Government Department of Health. National Notifiable Diseases Surveillance System—notification rate of campylobacteriosis. Available at: http://www9.health.gov.au/cda/source/cda-index.cfm. Accessed 3 March 2019.

8. Ogden ID, Dallas JF, MacRae M, Rotariu O, Reay KW, Leitch M, et al. Campylobacter excreted into the environment by animal sources: prevalence, concentration shed, and host association. Foodborne pathogens and disease. 2009 Dec 1;6(10):1161-70.

9. Hull DM, Harrell E, van Vliet AH, Correa M, Thakur S. Antimicrobial resistance and interspecies gene transfer in Campylobacter coli and Campylobacter jejuni isolated from food animals, poultry processing, and retail meat in North Carolina, 2018–2019. PLoS One. 2021 Feb 11;16(2):e0246571.

10. Bolton DJ. Campylobacter virulence and survival factors. Food microbiology. 2015 Jun 1;48:99-108.

11. Zhang MJ, Zhang JZ. Campylobacteriosis and Guillain Barre syndrome. Zhonghua liu Xing Bing xue za zhi= Zhonghua Liuxingbingxue Zazhi. 2008 Jun 1;29(6):618-21.

12. Dehkordi FS, Yazdani F, Mozafari J, Valizadeh Y. Virulence factors, serogroups and antimicrobial resistance properties of Escherichia coli strains in fermented dairy products. BMC Research Notes. 2014c;7(1):1-8.

13. Dehkordi FS, Barati S, Momtaz H, Ahari SN, Dehkordi SN. Comparison of shedding, and antibiotic resistance properties of Listeria monocytogenes isolated from milk, feces, urine, and vaginal secretion of bovine, ovine, caprine, buffalo, and camel species in Iran. Jundishapur Journal of Microbiology. 2013a;6(3):284.

14. Ghorbani F, Gheisari E, Dehkordi FS. Genotyping of vacA alleles of Helicobacter pylori strains recovered from some Iranian food items. Tropical Journal of Pharmaceutical Research. 2016;15(8):1631-6.

15. Dehkordi FS, Gandomi H, Basti AA, Misaghi A, Rahimi E. Phenotypic and genotypic characterization of antibiotic resistance of methicillin-resistant Staphylococcus aureus isolated from hospital food. Antimicrobial Resistance & Infection Control. 2017;6(1):1-1.

16. Dehkordi FS. Prevalence study of Bovine viral diarrhea virus by evaluation of antigen capture ELISA and RT-PCR assay in Bovine, Ovine, Caprine, Buffalo and Camel aborted fetuses in Iran. AMB Express. 2011;1(1):1-6.

17. Dehkordi FS, Parsaei P, Saberian S, Moshkelani S, Hajshafiei P, Hoseini SR, et al. Prevalence study of Theileria annulata by comparison of four diagnostic Techniques in shouthwest Iran. Bulgarian Journal of Veterinary Medicine. 2012;15(2): 123-30.

18. Dehkordi FS, Haghighi Borujeni MR, Rahimi E, Abdizadeh R. Detection of Toxoplasma gondii in raw caprine, ovine, buffalo, bovine, and camel milk using cell cultivation, cat bioassay, capture ELISA, and PCR methods in Iran. Foodborne Pathogens and Disease. 2013;10(2):120-5.

19. Dehkordi FS, Khamesipour F, Momeni M. Brucella abortus and Brucella melitensis in Iranian bovine and buffalo semen samples: The first clinical trial on seasonal, Senile and geographical distribution using culture, conventional and real-time polymerase chain reaction assays. Kafkas Univ Vet Fak Dergisi. 2014;20(6):821-8.

20. Dehkordi FS, Valizadeh Y, Birgani TA, Dehkordi KG. Prevalence study of Brucella melitensis and Brucella abortus in cow's milk using dot enzyme linked immuno sorbent assay and duplex polymerase chain reaction. Journal of Pure and Applied Microbiology. 2014b;8(2):1065-9.

21. Gharbi M, Béjaoui A, Ben Hamda C, Jouini A, Ghedira K, Zrelli C, et al. Prevalence and antibiotic resistance patterns of Campylobacter spp. isolated from broiler chickens in the North of Tunisia. BioMed research international. 2018 Dec 23;2018.

22. Reddy S, Zishiri OT. Genetic characterisation of virulence genes associated with adherence, invasion and cytotoxicity in Campylobacter spp. isolated from commercial chickens and human clinical cases. Onderstepoort Journal of Veterinary Research. 2018 Jan 1;85(1):1-9.

23. Dehkordi FS, Tirgir F, Valizadeh Y. Effects of Guajol® ointment synthesized from medicinal smoke condensate of jennet feces on burn wound healing on Wistar rat. Veterinary Research Forum. 2017; 8(3):215.

24. Safarpordehkordi F, Yahaghi E, Khodaverdi Darian E. Prevalence of antibiotic resistance in Escherichia coli isolated from poultry meat supply in Isfahan. Iranian Journal of Medical Microbiology. 2014;8(2):41-7.

25. Safarpour Dehkordi F, Hosseini S, Rahimi E, Momeni M, Yahaghi E, Khodaverdi Darian E. Investigate the frequency of virulence genes Vibrio parahaemolyticus isolated from fish, lobsters and crabs caught from Persian Gulf. Iranian Journal of Medical Microbiology. 2014;8(2):1-7.

26. Safarpour Dehkourdi F, Momtaz H, Esmailzade S, Khayyat Khameneie M, Yahaghi E. Detection of virulence factors of Uropathoigenic Escherichia coli isolates from infertile women high vaginal swabs. Iranian Journal of Medical Microbiology. 2014;7(4):1-8.

27. Nejat S, Momtaz H, Yadegari M, Nejat S, Safarpour Dehkordi F, Khamesipour F. Seasonal, geographical, age and breed distributions of equine viral arteritis in Iran. Kafkas Univ Vet Fak Derg. 2015;21(1):111-6.

28. Ranjbar R, Seif A, Dehkordi FS. Prevalence of antibiotic resistance and distribution of virulence factors in the shiga toxigenic Escherichia coli recovered from hospital food. Jundishapur J Microbiol. 2019;12(5):8.

29. Rahi A, Kazemeini H, Jafariaskari S, Seif A, Hosseini S, Dehkordi FS. Genotypic and phenotypic-based assessment of antibiotic resistance and profile of staphylococcal cassette chromosome mec in the methicillin-resistant Staphylococcus aureus recovered from raw milk. Infection Drug Res. 2020;13:273.

30. Ranjbar R, Yadollahi Farsani F, Safarpoor Dehkordi F. Antimicrobial resistance and genotyping of vacA, cagA, and iceA alleles of the Helicobacter pylori strains isolated from traditional dairy products. Journal of Food Safety. 2019 Apr;39(2):e12594.

31. Monajem Zade SM, Elyaskhil M, Fathi A, Asadinejad SM. Evaluate Risk Markers For Periodontal Disease In Children With Type 1 Diabetes: A Systematic Review And Meta-Analysis. 2021;12:5715-5722.

32. Ashtiani AH, Mardasi N, Fathi A. Effect of multiple firings on the shear bond strength of presintered cobalt-chromium alloy and veneering ceramic. The Journal of Prosthetic Dentistry. 2021;126(6):803-e1.

33. Mosharraf R, Molaei P, Fathi A, Isler S. Investigating the Effect of Nonrigid Connectors on the Success of Tooth-and-Implant-Supported Fixed Partial Prostheses in Maxillary Anterior Region: A Finite Element Analysis (FEA). International Journal of Dentistry. 2021;2021:1-12.

34. Abolhasani M, Ghasemi E, Fathi AH, Hayatizadeh MJ. Color Change of Ceramill Zolid FX Following Abrasion with/without Toothpaste. Journal of Iranian Dental Association. 2021;33(3):51-7.

35. Maalekipour M, Safari M, Barekatain M, Fathi A. Effect of Adhesive Resin as a Modeling Liquid on Elution of Resin Composite Restorations. International Journal of Dentistry. 2021;2021:1-9.

36. Fathi A, Salehi A. Antimicrobial resistance properties of Helicobacter pylori strains isolated from dental plaque and saliva samples. Academic Journal of Health Sciences. 2021;36 (4):51-5.

37. Fathi A, Ebadian B, Dezaki SN, Mardasi N, Mosharraf R, Isler S, et al. An Umbrella Review of Systematic Reviews and Meta-Analyses Evaluating the Success Rate of Prosthetic Restorations on Endodontically Treated Teeth. International Journal of Dentistry. 2022 Feb 22;2022.

38. Monirifard R, Abolhasani M, Tahani B, Fathi A, Choobdaran A. Relationship of Personality Traits and Patient Satisfaction with Fixed Implant Prosthodontic Treatments. Journal of Iranian Dental Association. 2019;31(4):182-8.

39. Ebadian B, Fathi A, Khodadad S. Comparison of the effect of four different abutment screw torques on screw loosening in single implant-supported prosthesis after the application of mechanical loading. International Journal of Dentistry. 2021;2021:1-6.

40. Ebadian B, Fathi A, Savoj M. In Vitro Evaluation of the Effect of Different Luting Cements and Tooth Preparation Angle on the Microleakage of Zirconia Crowns. International Journal of Dentistry. 2021;2021:1-7.

41. Hermans D, Pasmans F, Messens W, Martel A, Van Immerseel F, Rasschaert G, et al. Poultry as a host for the zoonotic pathogen Campylobacter jejuni. Vector-Borne and Zoonotic Diseases. 2012 Feb 1;12(2):89-98.

42. Hussain I, Mahmood MS, Akhtar M, Khan A. Prevalence of Campylobacter species in meat, milk and other food commodities in Pakistan. Food microbiology. 2007 May 1;24(3):219-22.

43. Korsak D, Maćkiw E, Rożynek E, Żyłowska M. Prevalence of Campylobacter spp. in retail chicken, turkey, pork, and beef meat in Poland between 2009 and 2013. Journal of food protection. 2015 May;78(5):1024-8.

44. Ghaffoori MH. Prevalence of Campylobacter jejuni In Chicken Meat Marketed In Baghdad Province. Int. J. Adv. Res. Biol. Sci. 2017;4(6):1-1.

45. Samad A, Abbas F, Ahmed Z, Akbar A, Naeem M, Sadiq MB, et al. Prevalence, antimicrobial susceptibility, and virulence of Campylobacter jejuni isolated from chicken meat. Journal of Food Safety. 2019 Apr;39(2):e12600.

46. Khan JA, Rathore RS, Abulreesh HH, Qais FA, Ahmad I. Prevalence and antibiotic resistance profiles of Campylobacter jejuni isolated from poultry meat and related samples at retail shops in Northern India. Foodborne Pathogens and Disease. 2018 Apr 1;15(4):218-25.

47. Kang YS, Cho YS, Yoon SK, Yu MA, Kim CM, Lee JO, et al. Prevalence and antimicrobial resistance of Campylobacter jejuni and Campylobacter coli isolated from raw chicken meat and human stools in Korea. Journal of Food Protection. 2006 Dec;69(12):2915-23.

48. Jun WA, Guo YC, Ning LI. Prevalence and risk assessment of Campylobacter jejuni in chicken in China. Biomedical and Environmental Sciences. 2013 Apr 1;26(4):243-8.

49. Zheng J, Meng J, Zhao S, Singh R, Song W. Adherence to and invasion of human intestinal epithelial cells by Campylobacter jejuni and Campylobacter coli isolates from retail meat products. Journal of food protection. 2006 Apr;69(4):768-74.

50. Melo RT, Nalevaiko PC, Mendonça EP, Borges LW, Fonseca BB, Beletti ME, et al. Campylobacter jejuni strains isolated from chicken meat harbour several virulence factors and represent a potential risk to humans. Food Control. 2013 Sep 1;33(1):227-31.

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ORIGINAL

Estado funcional y calidad de vida en supervivientes de la COVID-19 que no han requerido hospitalización

Functional status and quality of life in nonhospitalized COVID-19 survivors

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Resumen

Antecedentes y objetivos: Los pacientes hospitalizados con COVID-19 pueden presentar síntomas persistentes a largo plazo, pero se desconocen las secuelas en los no hospitalizados. El objetivo del estudio fue describir la funcionalidad y calidad de vida en supervivientes de la COVID-19 no hospitalizados. Secundariamente, se evaluó actividad física, disnea, discapacidad y ansiedad/depresión, así como la relación entre ellas.

Material y métodos: Se realizó un estudio transversal multicéntrico en Atención Primaria donde se valoró la funcionalidad con la escala Estado Funcional Post-COVID-19 (PCFS) y el test 1- Minute-Sit-to-Stand (1MSTS). La calidad de vida se midió con el cuestionario EuroQol (EQ-5D- 5L). La actividad física se cuantificó con el Cuestionario Internacional de Actividad Física (IPAQ), la disnea con la escala modificada Medical Research Council (mMRC), la discapacidad con el Indicador General de Limitación de Actividad (GALI) y la ansiedad/depresión con la escala de Ansiedad y Depresión Hospitalaria (HADS).

Resultados: El estudio incluyó 120 participantes con 6,33±3,15 meses de evolución. Según la escala PCFS el 2,5% mostró limitación funcional severa y 31,7% moderada. El 45,8% tuvo valores por debajo del percentil 25 en el test 1MSTS y el 63,3% presentó disminución en la calidad de vida. El 43,3% mostró nivel de actividad física bajo. El 57,5% tuvo disnea, el 24,2% ansiedad/depresión y 46,6% declaró sentirse limitado.

Conclusión: Las personas que han padecido la COVID-19 sin requerir hospitalización, presentan limitaciones funcionales y un descenso en la calidad de vida a los 6 meses tras la infección, así como mayor nivel de discapacidad, disnea y ansiedad/depresión.

Palabras clave: Infecciones por coronavirus, sobrevivientes, atención ambulatoria, evaluación de la discapacidad, actividades cotidianas, calidad de vida, actividad motora, disnea, depresión, ansiedad.

Abstract

Background: Hospitalized patients with COVID-19 can have persistent symptoms a medium term. However, it is unknown the consequences a long term of survivors none hospitalized. The aim of this study was to describe the functional state and the quality of life in COVID-19 survivors that did not require hospitalisation. After this, physical activity, dyspnoea, disability and anxiety/depression was evaluated and relationship between them.

Methods: A multicentre cross-sectional study with Primary Care patients was carried out. By means of an interview, status functional was valued with Post-COVID-19 Functional Status Scale (PCFS) and the 1-Minute-Sit-to-Stand (1MSTS) test. Health-Related Quality of life was measured with EuroQol (EQ-5D-5L). Level of physical activity was quantified with International Physical Activity Questionnaire (IPAQ). Dyspnoea was valued with Modified Medical Research Council scale (mMRC). Disability was measured with General Activity Limitation Indicator (GALI). And, anxiety/depression was calculated with Hospital Anxiety and Depression scale (HADS).

Results: The study included 120 patients with an evolution time of 6.33±3.15 months. According to PCFS scale, 2.5% of patients showed severe functional limitations, 31.7% moderate and 16.7% slight. 45.8% had a score in 1-MSTS test lower for percentile 25 and 63,3% showed decline of quality of life. 43.3% showed a low physical activity level and 50% moderated. 57.5% had dyspnoea, 24.2% suffer from anxiety/depression and 46.6% claimed that they felt limited.

Conclusion: Results suggest that people who had suffered from mild COVID-19, who have not required hospitalisation, they show functional limitations and a decrease in Health-Related Quality of life.

Key words: COVID-19, survivors, ambulatory care, disability evaluation, functional status, Health-Related Quality of life, motor activity, dyspnea, depression, anxiety.

Introducción

El 11 de marzo de 2020 la Organización Mundial de la Salud declaró pandemia a la infección por SARS-CoV-2 causante de la enfermedad COVID-19. La evolución de la pandemia ha puesto de manifiesto la persistencia de signos y síntomas prolongados más allá de las 12 semanas tras el inicio de síntomas. Esta entidad clínica se ha definido como COVID-persistente y su prevalencia se sitúa en torno al 10-16% de los casos[1-3].La fisiopatología de estos síntomas persistentes aún se encuentra en período de estudio, aunque se barajan tres posibles causas: presencia de reservorios del virus causante de la enfermedad (SARS-CoV-2) en diferentes tejidos como el intestino delgado donde permanecería activo, papel patológico de los anticuerpos con respuesta inmune exagerada y fenómenos autoinmunes con linfopenia asociada[4-6].

Los signos y síntomas persistentes son muy numerosos y variados. Estudios observacionales realizados en diferentes países han reflejado que los supervivientes a la COVID-19 muestran con mayor frecuencia tos, disnea, fatiga, algias musculares, articulares, presión en el pecho, mareos, diarreas y parestesias[1-3]. A nivel cognitivo, destacan la pérdida de memoria, ansiedad y síndrome de estrés postraumático[1-2]. Además, han reportado un descenso en la calidad de vida y una incapacidad para realizar las actividades habituales[2].

Otro problema que ha surgido dentro de la comunidad científica es conocer que herramientas son más adecuadas para valorar objetivamente dichos síntomas persistentes. Las escalas que se han seleccionado para aplicarlas en población post-COVID-19 han sido: el Índice de Barthel (IB), el test 1-Minute-Sit-to-Stand (1-MSTST) y el Test de 6 Minutos Marcha (T6MM)[7-9] , entre otros. Además, se han incluido cuestionarios para valorar el grado de disnea, la calidad de vida, el nivel de actividad física y el grado de estrés y ansiedad[7,9-10]. Sin embargo, ninguna de ellas mide la capacidad funcional del sujeto para realizar de forma autónoma las acciones que componen el quehacer cotidiano a nivel individual y social incluyendo dentro de ella actividades básicas de la vida diaria, instrumentales y avanzadas. En este sentido, Klok et al.[11] diseñaron la escala Estado Funcional Post-COVID-19 (PCFS) que permite monitorizar de forma sencilla la evolución de los síntomas y el impacto de los mismos en el estado funcional del paciente que ha sufrido la COVID- 19. Estas escalas se han utilizado para medir secuelas a largo plazo en población hospitalizada por lo que resulta fundamental determinar el impacto de la COVID-19 que no ha requerido hospitalización, que supone el 80-90% de las casos[12], en la calidad de vida y el estado funcional mediante el uso de cuestionarios validados. Conocer dichas alteraciones permitiría establecer programas preventivos y terapéuticos que aborden de forma específica estas secuelas en el ámbito de la Atención Primaria.

Por todo lo anterior expuesto, el objetivo principal del estudio fue describir el estado funcional y la calidad de vida en personas que hayan superado la COVID-19 sin requerir ingreso hospitalario. De forma secundaria, se determinó el nivel de actividad física, disnea, el grado de ansiedad/depresión y discapacidad post-COVID-19, así como la relación entre ellas.

Material y método

Población de estudio

Se realizó un estudio transversal multicéntrico que incluyó a pacientes que habían sufrido la COVID-19 y cuyo seguimiento se realizó desde Centros de Atención Primaria de la Comunidad de Madrid, España. Los criterios de inclusión fueron: a) mayor de 18 años, b) infección por COVID-19 confirmada mediante técnicas de Reacción en Cadena de la Polimerasa con Transcriptasa Inversa (PCR) o test antigénicos rápidos (Ag-RDT), c) pertenecer a un Centro de Atención Primaria en Madrid, d) aceptar participar mediante la firma del consentimiento. Los criterios de exclusión fueron: a) ingreso hospitalario desde la fecha de confirmación del diagnóstico, b) dificultad para comunicarse en castellano, c) ser asintomáticos en el momento de la confirmación del diagnóstico.

El estudio fue realizado respetando los principios éticos de la Declaración de Helsinki y aprobado por el Comité de Ética e Investigación Clínica del Hospital Clínico San Carlos y la Comisión Local de Investigación Este de la Gerencia Asistencial de Atención Primaria. Todos los participantes expresaron su conformidad mediante la firma del consentimiento informado y los datos fueron tratados cumpliendo la normativa de Protección de Datos vigente.

La captación se llevó a cabo desde las consultas de medicina, enfermería y fisioterapia de los diferentes Centros de Atención Primaria mediante un muestreo por conveniencia. La recogida de datos se realizó desde el 1 Febrero al 1 Junio de 2021 a través de una entrevista presencial.

Variables

Se recogió información sociodemográfica (edad, sexo, nivel de estudios, ocupación y estado civil), hábito tabáquico y comorbilidades asociadas (diabetes, enfermedad pulmonar obstructiva crónica, asma, hipertensión arterial, cardiopatía, dislipemia y obesidad). Además, se registró el tiempo desde la confirmación de la enfermedad COVID-19.

La capacidad funcional se midió con la escala Estado Funcional Post-COVID-19 (PCFS) y el test 1- Minute-Sit-to-Stand (1-MSTST). La escala PCFS es una escala ordinal con 6 grados: grado 0 (sin limitación funcional), grado 1 (limitación funcional no significativa), grado 2

(limitación funcional leve), grado 3 (limitación funcional moderada), grado 4 (limitación funcional severa) y grado 5 (fallecido). El grado de alteración se asigna a través de una entrevista estructurada siendo la calificación final el peor estado funcional obtenido en alguna de las preguntas[11]. El test 1-MSTST consiste en cuantificar el número de veces que el paciente es capaz de levantarse y sentarse de una silla durante un minuto de tiempo. Para ello se utilizó una silla sin apoyabrazos y se cuantificó el número de ciclos completos sin la utilización de los brazos[8]. Se tomaron los valores de referencia normativos para identificar los participantes que presentaban disminución de la fuerza de los miembros inferiores[13].

La calidad de vida relacionada con la salud se cuantificó a través del cuestionario EuroQol (EQ- 5D-5L). Este instrumento consta de 2 partes: el sistema descriptivo y la Escala Visual Analógica (EQ-EVA)[14]. El sistema descriptivo integra 5 dimensiones: movilidad, autocuidado, actividades habituales, dolor/malestar y ansiedad/depresión, con 5 niveles de gravedad cada una: 1 sin problemas, 2 problemas leves, 3 problemas moderados, 4 problemas severos y 5 extremos. La EQ-EVA puntúa la salud global de 0-100 siendo peor y mejor estado de salud imaginables respectivamente. Además, el EQ-5D-5L define un índice sintético único (Index-EQ) que va desde 0 (muerte) a 1 (salud completa) que se define a partir de fórmulas ponderadas de muestras de población general. Para determinar si existía o no alteración en la calidad de vida, se tomó como referencia los datos obtenidos en población general española en la Encuesta Nacional de Salud[15].

El nivel de actividad física se midió mediante el Cuestionario Internacional de Actividad Física versión corta (IPAQ-S) y la versión Elderly (IPAQ-E). El IPAQ-S es una herramienta que consta de 7 preguntas acerca de la frecuencia, duración e intensidad de la actividad física (moderada e intensa) realizada en los últimos 7 días, así como el caminar y el tiempo sentado en un día laboral. Así establece 3 niveles de actividad física: baja, moderada y alta[16]. El IPAQ-E procede de la adaptación a personas mayores de 65 años del IPAQ-S, añadiendo en las actividades moderadas limpiar cristales y baldosas y en las vigorosas cavar en el huerto[17].

El grado de disnea se objetivó mediante la escala modificada del Medical Research Council (mMRC) que valora el grado de disnea de 0-4 según la limitación funcional que provoca en las actividades de la vida diaria[18].

El nivel de ansiedad y depresión fue evaluado mediante la escala de Ansiedad y Depresión Hospitalaria (HADS). Esta escala está compuesta por 2 subescalas, una para depresión y otra para ansiedad, que constan de 7 ítems que se puntúan de 0 (ausencia de síntoma) a 3 (máxima presencia) puntos[19]. Se tomó como punto de corte óptimo una puntuación ≥ 12[19] .

El grado de discapacidad se valoró a través del Índice Barthel (IB) y el Indicador General de Limitación de la Actividad (GALI). El IB valora 10 actividades de la vida diaria: comer, lavarse, vestirse, arreglarse, control de heces y orina, uso retrete, trasladarse, deambular y subir/bajar escaleras. Dichas actividades se valoran de forma diferente entre 0-15 puntos obteniendo un rango global que puede variar entre 0 (completamente dependiente) y 100 puntos (completamente independiente)[20]. El indicador GALI mide la limitación percibida para las actividades cotidianas en los últimos 6 meses, estableciendo tres grados; gravemente limitado, sí limitado pero no gravemente y no, nada limitado[21].

Análisis estadístico

Los cálculos estadísticos fueron realizados con el software IBM SPSS® (Statistical Package for the Social Sciences 22, SPSS Inc., Chicago, IL USA). Los resultados obtenidos en las variables cualitativas se expresaron como frecuencias absolutas y relativas y las variables cuantitativas como media y desviación estándar (o en medianas y rangos intercuartílicos). Se efectuaron test de normalidad a través de la prueba Kolmogorov-Smirnov. El coeficiente de correlación de Spearman (Rho) fue usado para determinar correlaciones entre variables categóricas y variables continuas que no seguían una distribución normal. Se consideró baja correlación a valores inferiores a 0,30, moderada entre 0,30 y 0,60 y fuerte en valores superiores a 0,6[22]. La interpretación de los test estadísticos se realizó en base a un nivel de significancia del 5% ($p < 0,05$) para un intervalo de confianza del 95%.

Resultados

Se identificaron 135 personas de todas las zonas básicas de Salud de la Comunidad de Madrid, de las cuales 5 declinaron participar y 10 no cumplían los criterios de inclusión por lo que la muestra final fue de 120 participantes (60% mujeres). La edad media fue de 45,58±13,44 años y el tiempo medio desde la confirmación del diagnóstico hasta la valoración inicial fue de 6,33±3,15 meses. En la **Tabla I** se muestran las características sociodemográficas y clínicas de la población de estudio.

Estado funcional y calidad de vida

Las puntuaciones en la escala PCFS reflejaron que el 21,7% (n=26) de los participantes mostró un grado 1 con limitación funcional no significativa, el 16,7% (n=20) un grado 2 con limitación funcional leve, el 31,7% grado 3 (n=38) con limitación moderada y el 2,5% (n=3) grado 4 con limitación severa.

En el test 1-MSTS la media de ciclos completos de levantarse y sentarse de la silla fue de 26,98±8,73 (**Tabla II**). El 34,2% de los sujetos tenía valores por debajo del percentil 2,5 y el 45,8% del percentil 25.

Tabla I: Características sociodemográficas y clínicas de la muestra.

Total (n=120)	Media± DE	n (%)
Edad (años)	45,58±13,44	
Peso (kg)	70,87±13,56	
Talla (m)	1,68±0,09	
Sexo (n,%)		
Mujer		48 (40%)
Hombre		72 (60%)
Nivel estudios		
Graduado escolar		37 (30,8%)
Grado medio		20 (16,7%)
Grado superior		8 (6,7%)
Universitario		55 (45,8%)
Ocupación		
Activo		78 (65%)
Desempleo		13 (10,8%)
Incapacidad temporal		13 (10,8%)
Jubilado		9 (7,5%)
Estudiante		7 (5,8%)
Estado civil		
Soltero		37 (30,8%)
Casado		77 (64,2%)
Divorciado		4 (3,3%)
Viudo		2 (1,7%)
Hábito tabáquico		
Fumador		14 (11,7%)
Exfumador		87 (72,5%)
No fumador		19 (15,8%)
Co-morbilidades		
Diabetes		2 (1,7%)
HTA		14 (11,7%)
Cardiopatía		5 (4,2%)
EPOC		3 (2,5%)
Asma		8 (6,7%)
Dislipemia		20 (16,7%)
Obesidad		11 (9,2%)
Tiempo desde el diagnóstico (meses)	6,33±3,15	

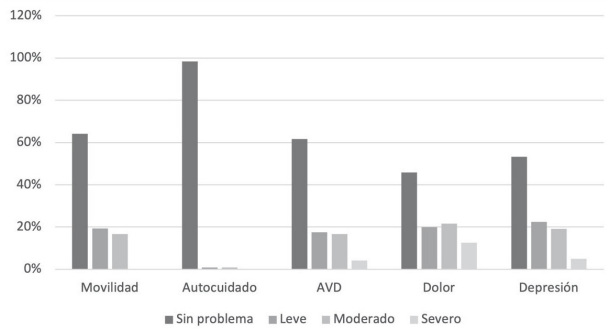
HTA= hipertensión arterial; EPOC= enfermedad pulmonar obstructiva crónica.

Tabla II: Calidad de vida, estado funcional, niveles de ansiedad y depresión, actividad física y discapacidad de la muestra.

Variable n=120	Media± d.e	IC
1-MSTS (repeticiones)	26,98±8,73	25,40-28,55
Calidad de vida (puntos)		
EQ-Index	0,82±0,19	0,78-0,85
EQ-EVA	70,50±19,23	67,02-73,98
Nivel de actividad física (METS)	1359,08±1167,45	1148,06-1570,11
IPAQ-S	1387,94±1187,28	1167,63-1608,24
IPAQ-E	810,83±448,12	340,56-1281,11
HADS (puntos)		
Depresión	4,46±4,23	3,69-5,22
Ansiedad	7,22±4,70	6,37-8,07
Índice de Barthel (puntos)	100	100-100

1MSTS= test 1-Minute-Sit-to-Stand; EQ-EVA= Escala Visual Analógica; IPAQ-S=Cuestionario Internacional de Actividad Física versión Corta; IPAQ-E= Cuestionario Internacional de Actividad Física versión Ederly; HADS=Escala de Ansiedad y Depresión Hospitalaria.

Figura 1: Categorización de la muestra según el sistema descriptivo EQ-5D-5L.



En lo referente a la calidad de vida, los resultados obtenidos en el sistema descriptivo se reflejan en la **Figura 1**. La media de las puntuaciones obtenidas en la EQ-EVA y en el Index-EQ fueron de 70,5±19,23 y 0,82±0,19, respectivamente (**Tabla II**). El 63,3% presentó una disminución del Index EQ y en la EQ-EVA respecto a valores de referencia de población general.

Niveles de actividad física y grado de disnea

El 42,1% (n=48) de los participantes presentó un nivel bajo de actividad física, el 50,9% (n=58) moderado y el 7% (n=8) alto según el cuestionario IPAQ-S. Los datos obtenidos en el IPAQ-E, sugieren que el 66,7% (n=4) de los mayores de 65 años tuvo un nivel bajo de actividad física (**Tabla II**). La actividad semanal medida en METS se observa en la **Tabla II**. Además, según la escala de disnea mMRC, el 27,5% (n=33) de los entrevistados mostró grado 1 de disnea, el 28,3% (n=34) grado 2 y el 1,7% (n=2) grado 3.

Síntomas de ansiedad y depresión

De todos los participantes, el 17,5% (n=21) se categorizó como caso de ansiedad y el 6,7% (n=8) de depresión según los puntos de corte de la escala HADS (**Tabla II**).

Discapacidad

Todos los participantes fueron totalmente independientes para realizar las actividades básicas de la vida diaria según el Índice de Barthel (**Tabla II**). El 8,3% (n=10) declaró sentirse gravemente limitado para llevar a cabo las actividades que realizaba habitualmente y el 38,3% (n=46) limitado según el indicador GALI.

Correlación entre variables

Se observó una correlación fuerte entre la escala PCFS y la EQ-EVA (rho= -0,736; $p < 0,01$) y el Index-EQ (rho= -0,816; $p < 0.01$) y moderada con el test 1-MSTS (rho= -0,379; $p < 0,01$). Además, el test 1-MSTS mostró una correlación moderada con la EQ-EVA (rho= 0,369; $p < 0,01$) y el Index- EQ (rho= 0,389; $p < 0,01$) respectivamente. Las correlaciones entre calidad de vida y estado funcional con las variables secundarias se pueden observar en **Tabla III**.

Tabla III: Correlación entre funcionalidad y calidad de vida con variables secundarias.

	PCFS		1MSTS		EQ-Index		EQ-EVA	
	Rho	p.valor	Rho	p.valor	Rho	p.valor	Rho	p.valor
Funcionalidad								
PCFS			**-0,379	0	**-0,816	0	**-0,736	0
1-MSTS					**0,389	0	**0,369	0
Calidad de vida								
EQ-Index							**0,810	0
Nivel de actividad física								
IPAQ-S	-0,165	0,08	**0,34	0	*0,196	0,037	**0,275	0,003
IPAQ-E	-0,25	0,633	0,207	0,694	0,414	0,414	0,32	0,537
Grado de disnea	**0,749	0	**-0,39	0	**-0,776	0	**-0,663	0
HADS								
Depresión	**0,664	0	**-0,388	0	**-0,673	0	**-0,671	0
Ansiedad	**0,473	0	-0,114	0,214	**-0,484	0	**-0,477	0
GALI	**-0,808	0	**-0,342	0	**-0,828	0	**-0,77	0

*p<0,05 **p<0,01

PCFS=Escala Estado Funcional Post-COVID-19; 1MSTS= test 1-Minute-Sit-to-Stand; EQ-EVA= Escala Visual Analógica; IPAQ-S=Cuestionario Internacional de Actividad Física versión Corta; IPAQ-E=Cuestionario Internacional de Actividad Física versión Ederly; HADS=escala de Ansiedad y Depresión Hospitalaria; GALI=Indicador General de Limitación de la Actividad.

Discusión

Hasta donde los autores conocen, esta investigación es el primer estudio realizado a largo plazo que describe la calidad de vida y funcionalidad en población española que ha sufrido la COVID- 19 sin requerir ingreso hospitalario. La mayoría de los estudios publicados a día de hoy se han centrado en medir prevalencia de signos y síntomas persistentes en población hospitalizada. Los hallazgos obtenidos en la investigación rebelan que casi la mitad de los supervivientes a la COVID-19 sin necesidad de hospitalización presentan una limitación funcional leve (16,7%) y moderada (31,7%) que les provoca tener que reducir la intensidad de las actividades habituales o les obliga a modificarlas teniendo que ser asumidas por otra persona. Además, existe una limitación en los roles sociales habituales y en cuanto a los niveles de calidad de vida el 63,3% de los participantes mostró un descenso tanto en el Index-EQ como en la EQ-EVA siendo el dolor y la ansiedad/depresión las dimensiones más afectadas.

La limitación funcional que muestran los participantes del estudio es el reflejo del impacto que tiene la gran variedad de signos y síntomas persistentes en el desempeño de las actividades cotidianas. El porcentaje de personas con limitación funcional es menor al obtenido con los datos ofrecidos en el estudio de validación de la escala PCFS en los Países Bajos (limitación leve 16,7% vs 33,31%, limitación moderada 31,7% vs 52,20%)[23]. Esta diferencia podría deberse a que el tiempo medio transcurrido desde el inicio de síntomas es menor que en nuestro estudio (79 días vs 189 días) y que la valoración se realizó a través de una web con participantes sin prueba de confirmación de diagnóstico en su mayoría.

En lo referente a la funcionalidad medida a través del test 1-MSTS, los participantes del estudio completaron de media 26,98±8,73 ciclos. El número de ciclos obtenidos fue 6 unidades superior a los datos aportados por Núñez-Cortés et al.[8]. Esta diferencia podría deberse a que en dicho estudio se valoraba a pacientes que habían requerido ingreso hospitalario al mes del alta. Además, la mayoría de la muestra (45,8%) obtuvo puntuaciones por debajo del percentil 25 respecto a los valores normativos. Esto implica debilidad de la musculatura de los miembros inferiores, lo que podría explicar la limitación reportada en la realización de las actividades de la vida diaria[24].

A nivel de calidad de vida los datos de nuestro estudio son congruentes con la evidencia disponible que refiere un descenso de la misma en personas post-COVID-19[2,9-10]. Las dimensiones del sistema descriptivo EQ-5D-5L que han mostrado mayor afectación son la depresión/ansiedad y el dolor/malestar. Estos resultados coinciden con los síntomas persistentes referidos con mayor frecuencia en personas que padecen COVID-persistente[2-3]. Si comparamos las puntuaciones del Index-EQ y la EQ-EVA con las de estudios realizados en población que no ha requerido ingreso hospitalario por la infección, estas fueron superiores a los reflejados por Meys et al.[9] (0,82 vs 0,62 puntos y 70,5 vs 50,71 puntos). Esto podría deberse a que el tiempo transcurrido desde el inicio de los síntomas en nuestro estudio es de 6 meses frente a los 2,5 meses del citado estudio. Por otro lado, los resultados obtenidos son muy similares a los que muestran pacientes que requirieron ingreso hospitalario por la COVID-19 a los 4 meses tras el alta hospitalaria (Index EQ: 0,82 vs 0,86 y EQ-EVA 70,5 vs 69,9 puntos)[25]. Estos resultados implican que probablemente a medio-largo plazo la disminución en la calidad de vida esté más relacionada con las secuelas persistentes de la propia enfermedad como dolor, disnea, fatiga, etc., más que por la gravedad inicial de la misma[26]. Por otro lado, la calidad de vida de los participantes del estudio muestra un descenso en todos los apartados del cuestionario EQ-5D- 5L cuando se compara con los

datos obtenidos en la Encuesta Nacional de Salud de población española de referencia[15].

En lo referente al nivel de actividad física, el 57,9% de los participantes mostró un nivel de actividad física moderado-alto. Estos resultados contrastan con el dato reportado por Anastasio et al.[27] en población hospitalizada y no hospitalizada en la que el 81,7% de los sujetos declararon un adecuado nivel de actividad física. En comparación con los datos suministrados por la Encuesta Nacional de Salud en España los resultados de nuestro estudio muestran un descenso en todos los niveles de actividad física siendo el nivel alto de actividad física el que presenta una mayor disminución de en torno al 17%[28]. Esto podría deberse a que para alcanzar un nivel alto se precisa la realización de actividades vigorosas como levantar objetos pesados, ejercicio aeróbico intenso o pedalear rápido en bicicleta cuya ejecución estaría más condicionada por la disnea y la debilidad muscular reportados por esta población.

En cuanto al grado de disnea, según la escala mMRC, el 55,8% de los entrevistados presentó un grado 1 y 2. Estos datos concuerdan con los obtenidos en los estudios de Garrigues et al.[25] y Raman et al.[26] cuya prevalencia fue del 53,4% y 64,3% aunque en ellos se incluían pacientes que habían requerido hospitalización. A nivel de ansiedad y depresión los valores presentados por los participantes son superiores a los hallazgos obtenidos por Halpin et al.[10] (17,5 puntos vs 29,27 puntos) y Rass et al.[29] (6,7 puntos vs 11 puntos) en pacientes hospitalizados por COVID- 19. Por último, todos los participantes refirieron ser totalmente independientes para la realización de las actividades básicas de la vida diaria medidas a través del Índice de Barthel. Los estudios publicados que han utilizado como variable esta escala obtuvieron una puntuación menor de 60 puntos, es decir, dependencia moderada[7,24]. Estos índices tan bajos podrían explicarse a que fueron evaluados cuando los pacientes aún estaban ingresados y presentaban un deterioro general importante tras la infección, ya que más de la mitad de ellos no podía caminar y el 80% requería algún tipo de soporte ventilatorio. Esto podría sugerir, que el Índice de Barthel no es una herramienta sensible para detectar la discapacidad no grave ya que solamente analiza la capacidad para realizar actividades básicas de la vida diaria y no tiene en cuenta actividades instrumentales y avanzadas como la escala PCFS que podría ser útil para detectar alteraciones en la capacidad funcional con independencia de su severidad[23]. Sin embargo, los resultados del indicador GALI reflejan que un 46,6% de los participantes declara presentar limitación en los últimos 6 meses para realizar las actividades habituales que hacía anteriormente, lo cual es superior en un 23,8% superior al porcentaje de individuos que declara sentirse limitado según los datos de referencia de la población española[30].

Implicaciones clínicas

La importancia de este estudio recae en que las consecuencias post-COVID-19 se han cuantificado a nivel funcional, dando importancia a la repercusión que la infección leve tiene en las actividades cotidianas tanto en el hogar, en el trabajo/estudio y en el rol social. Resulta fundamental visibilizar que los pacientes que han padecido la COVID-19 de forma leve, sin requerir ingreso hospitalario y cuyo manejo ha sido exclusivamente desde las consultas de Atención Primaria, también pueden presentar secuelas a largo plazo derivadas de la infección.

Limitaciones

Las principales limitaciones del presente estudio recaen en la heterogeneidad de los participantes y que se ha realizado un muestreo por conveniencia por lo que la muestra no es representativa de toda la población. Además, al tratarse de un estudio transversal no permite conocer la evolución de las alteraciones post-COVID-19 en el tiempo ni establecer causalidad. A partir de los hallazgos obtenidos, podría resultar interesante establecer futuras líneas de investigación que permitan monitorizar todas las variables de forma longitudinal estableciendo su posible asociación.

Conclusiones

Los resultados del presente estudio sugieren que las personas que han tenido COVID-19 sin requerimiento de ingreso hospitalario, presentan limitaciones funcionales y un descenso en la calidad de vida a los 6 meses tras la infección. Además, manifiestan un mayor nivel de discapacidad, disnea, ansiedad y depresión.

Conflicto de intereses

Los autores del manuscrito declaran que no existe ningún tipo de conflicto de intereses.

Bibliografía

1. National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19 [Internet]. Escocia; 2020. [Actualizado 18-12-2020; consultado 12-01-2021]. Disponible en: https://www.nice.org.uk/guidance/ng188

2. Semg.es. Resultados Encuesta COVID-19 persistente [Internet]. 2020 [Actualizado 11- 11-2020; consultado 20-12-2020]. Disponible en: https://www.semg.es/images/2020/Noticias/20201111_Resultados_Encuesta_COVID_ Persistente.pdf

3. Cirulli E, Schiabor-Barrett KM, Riffle S, Bolze A, Neveux I, Dabe S, et al. Long-term COVID-19 symptoms in a large unselected population. medRxiv. [Preprint]. 2020:2020.10.07.20208702.

4. Gaebler C, Wang Z, Lorenzi JCC, Muecksch F, Finkin S, Tokuyama M, et al. Evolution of antibody immunity to SARS-CoV-2. Nat Med. 2021; 591:639-44.

5. Wang EY, Mao T, Klein J, Dai Y, Huck JD, Liu F, et al. Diverse Functional Autoantibodies in Patients with COVID-19. Nat Med. 2021; 595: 283-8.

6. Patterson BK, Guevara-Coto J, Yogendra R, Francisco EB, Long E, Pise A, et al. Immune- Based Prediction of COVID-19 Severity and Chronicity Decoded Using Machine Learning. Front Immunol. 2021; 12:700782.

7. Curci C, Pisano F, Bonacci E, Camozzi DM, Ceravolo C, Bergonzi R et al. Early rehabilitation in post-acute COVID-19 patients: data from an Italian COVID-19 rehabilitation unit and proposal of a treatment protocol. A cross-sectional study. Eur J Phys Rehabil Med. 2020; 56:633-41.

8. Núñez-Cortés R, Rivera-Lillo G, Arias-Campoverde M, Soto-García D, García-Palomera R, Torres-Castro R. Use of sit-to-stand test to assess the physical capacity and exertional desaturation in patients post COVID-19. Chron Respir Dis. 2021; 18:1479973121999205.

9. Meys R, Delbressine JM, Goërtz YMJ, Vaes AW, Machado FVC, Van Herck M, Burtin C, Posthuma R, Spaetgens B, Franssen FME, Spies Y, Vijlbrief H, Van't Hul AJ, Janssen DJA, Spruit MA, Houben-Wilke S. Generic and Respiratory-Specific Quality of Life in Non- Hospitalized Patients with COVID-19. J Clin Med. 2020;9:3993.

10. Halpin, SJ, McIvor, C, Whyatt, G, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. J Med Virol. 2020; 1-10.

11. Klok FA, Boon GJAM, Barco S, et al. The Post-COVID-19 Functional Status scale: a tool to measure functional status over time after COVID-19. Eur Respir J. 2020; 56: 2001494.

12. Pascarella G, Strumia A, Piliego C, Bruno F, Del Buono R, Costa F et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med. 2020; 288:192-206.

13. Strassmann A, Steurer-Stey C, Lana KD, Zoller M, Turk AJ, Suter P, et al. Population-based reference values for the 1-min sit-to-stand test. Int J Public Health. 2013;58: 949-53.

14. Herdman M, Badia X, Serra S. El EuroQol-5D: una alternativa sencilla para la medición de la calidad de vida relacionada con la salud en Atención Primaria. Aten Primaria. 2001;28:425-30.

15. Ministerio de Sanidad, Servicios Sociales e Igualdad. Encuesta Nacional de Salud España 2011/2012. Serie Informes monográficos no3. Calidad de vida relacionada con la salud en adultos: EQ-5D-5L [Internet]. Madrid: Ministerio de Sanidad, Servicios Sociales e Igualdad; 2014. Disponible en: https://www.mscbs.gob.es/estadEstudios/estadisticas/encuestaNacional/encuestaNac 2011/informesMonograficos/CVRS_adultos_EQ_5D_5L.pdf

16. Van Dyck D, Cardon G, Deforche B, De Bourdeaudhuij I. IPAQ interview version: convergent validity with accelerometers and comparison of physical activity and sedentary time levels with the self-administered version. J Sports Med Phys Fitness.2015;55: 776-86.

17. Rubio-Castañeda FJ, Tomás-Aznar C, Muro-Baquero C. Medición de la actividad física en personas mayores de 65años mediante el IPAQ-E: validez de contenido, fiabilidad y factores asociados. Rev Esp Salud Pública. 2017;91: 201701004.

18. Perez T, Burgel PR, Paillasseur JL, Caillaud D, Deslée G, Chanez P, et al. Modified Medical Research Council scale vs Baseline Dyspnea Index to evaluate dyspnea in chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2015;10: 1663-72.

19. Terol-Cantero MC, Cabrera-Perona V, Martín-Aragón M. Revisión de estudios de la Escala de Ansiedad y Depresión Hospitalaria (HAD) en muestras españolas. Anal Psicol. 2015;31: 494-503.

20. Cabañero-Martínez MJ, Cabrero-García J, Richart-Martínez M, Muñoz-Mendoza CL. The Spanish versions of the Barthel index (BI) and the Katz index (KI) of activities of daily living (ADL): a structured review. Arch Gerontol Geriatr. 2009;49:e77-e84.

21. Julià Sanchís R. Validez del indicador general de limitación de la actividad (GALI) para medir el funcionamiento en la población: un análisis comparativo con salud percibida a través de encuestas de Salud en España. [tesis doctoral]. Alicante: Universidad de Alicante; 2016.

22. Carter R, Lubinsky J, Domholdt E. Rehabilitation research: principles and applications. 4th ed. St. Louis (MO): Elsevier Saunders; 2011.

23. Machado FVC, Meys R, Delbressine JM, Vaes AW, Goërtz YMJ, van Herck M, et al. Construct validity of the Post-COVID-19 Functional Status Scale in adult subjects with COVID-19. Health Qual Life Outcomes. 2021; 19:1-10.

24. Belli S, Balbi B, Prince I, Cattaneo D, Masocco F, Zaccaria S, et al. Low physical functioning and impaired performance of activities of daily life in COVID-19 patients who survived hospitalisation. Eur Respir J.2020;56: 2002096.

25. Garrigues E, Janvier P, Kherabi Y, Le Bot A, Hamon A, Gouze H, Doucet L, Berkani S, Oliosi E, Mallart E, Corre F, Zarrouk V, Moyer JD, Galy A, Honsel V, Fantin B, Nguyen Y. Post- discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. J Infect. 2020; 81: e4-e6.

26. Raman B, Cassar MP, Tunnicliffe EM, Filippini N, Griffanti L, Alfaro-Almagro F, et al. Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. EClinicalMedicine. 2021; 31:100683.

27. Anastasio F, Barbuto S, Scarnecchia E, Cosma P, Fugagnoli A, Rossi G, Parravicini M, Parravicini P. Medium-term impact of COVID-19 on pulmonary function, functional capacity and quality of life. Eur Respir J. 2021; 11:2004015.

28. Ministerio de Sanidad, Consumo y Bienestar Social. Encuesta Nacional de Salud ENSE, España 2017. Serie informes monográficos no2 –ACTIVIDAD FÍSICA, DESCANSO Y OCIO. Madrid: Ministerio de Sanidad, Consumo y Bienestar Social; 2019. Disponible en: https://www.mscbs.gob.es/estadEstudios/estadisticas/encuestaNacional/encuestaNac 2017/ACTIVIDAD_FISICA.pdf

29. Rass V, Beer R, Schiefecker AJ, Kofler M, Lindner A, Mahlknecht P, et al. Neurological outcome and quality of life three months after COVID-19: a prospective observational cohort study. Eur J Neurol. 2021; 28(10): 3348-59.

30. Ministerio de Sanidad, Consumo y Bienestar Social. Encuesta Nacional de Salud ENSE, España 2017. Serie informes monográficos no3 LIMITACIÓN Y DISCAPACIDAD [Internet]. Madrid: Ministerio de Sanidad, Consumo y Bienestar Social; 2019. Disponible en: https://www.mscbs.gob.es/estadEstudios/estadisticas/encuestaNacional/encuestaNac 2017/LIMITACION_Y_DISCAPACIDAD.pdf

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ORIGINAL

Investigation of education based on self-regulation model on fallow ups postpartum in women with gestational diabetes

Investigación de la educación basada en el modelo de autorregulación sobre los barbechos posparto en mujeres con diabetes gestacional

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Abstract

Background: Gestational diabetes as a silent disease, a phenomenon that affects pregnancy, the mother and the fetus. The prevalence of type 2 diabetes after gestational diabetes have been reported from 30 to 70 percent. This study examines the effect of education based on the self-regulation model on fallow ups postpartum in women with a history of gestational diabetes.
Materials and methods: Current study is an experimental study. The sampling is a multi-stage. method in this study was that of the urban areas Qom (4 area), Region 2 Qom was selected as the research community. Then the community health centers in the area between two randomly (as a test and the other one as a control) were selected. In each center by referring to the case of pregnant women, 46 patients were randomly selected and their phone calls were invited to participate in study. After selecting subjects, while acquiring informed consent and provide a full description of the purpose of this study, questionnaires were given to them in the (demographic, self-regulation, Psychometric Study of the Exercise Procrastination Scale, Healthy Diet Procrastination Scale) Baseline information was taken from them.
Results: Overall, 92 subjects with mean age 29.93 ± 4.9 participated in the study. More participants had secondary and high school education (46.7 percent), housewives (77.2 percent), overweight (52.2 percent), with 2 children (43.5 percent) and middle-income status (62 percent). Friedman test result showed that the experimental group, the average of all three measures have changed significantly, while there was no significant change in the control group.
Conclusions: According to the findings of this study, education based on models of self-regulation training enhances physical activity and nutritional status of women with Gestational Diabetes.

Key words: Self-regulation model, gestational diabetes, on fallow ups postpartum.

Resumen

Antecedentes: la diabetes gestacional como enfermedad silenciosa, fenómeno que afecta al embarazo, a la madre y al feto. Se ha informado que la prevalencia de diabetes tipo 2 después de la diabetes gestacional es del 30 al 70 por ciento. Este estudio examina el efecto de la educación basada en el modelo de autorregulación en los barbechos posparto en mujeres con antecedentes de diabetes gestacional.
Materiales y métodos: El estudio actual es un estudio experimental. El muestreo es de varias etapas. El método en este estudio fue el de las áreas urbanas Qom (área 4), la Región 2 Qom fue seleccionada como la comunidad de investigación. Luego se seleccionaron los centros de salud comunitarios en el área entre dos al azar (como prueba y el otro como control). En cada centro al referirse al caso de las embarazadas, se seleccionaron aleatoriamente 46 pacientes y se invitó a sus llamadas telefónicas a participar en el estudio. Luego de seleccionar a los sujetos, mientras se obtenía el consentimiento informado y se brindaba una descripción completa del propósito de este estudio, se les entregaban cuestionarios en el (demográfico, autorregulación, Estudio psicométrico de la Escala de procrastinación del ejercicio, Escala de procrastinación de dieta saludable) Se tomó información de referencia de ellos.
Resultados: En total, 92 sujetos con una edad media de 29,93 ± 4,9 participaron en el estudio. Más participantes tenían educación secundaria y preparatoria (46,7 por ciento), amas de casa (77,2 por ciento), sobrepeso (52,2 por ciento), con 2 hijos (43,5 por ciento) y situación de ingresos medios (62 por ciento). El resultado de la prueba de Friedman mostró que en el grupo experimental, el promedio de las tres medidas ha cambiado significativamente, mientras que no hubo cambios significativos en el grupo de control.
Conclusiones: De acuerdo con los hallazgos de este estudio, la educación basada en modelos de entrenamiento de autorregulación mejora la actividad física y el estado nutricional de las mujeres con Diabetes Gestacional.

Palabras clave: Modelo de autorregulación, diabetes gestacional, en barbechos posparto.

Introduction

The increasing prevalence of type 2 diabetes in the young population in particular has led to an increase in the number of pregnancies complicated by diabetes. Many women with gestational diabetes already have type 2 diabetes that has not been diagnosed before. Pregnant patients with diabetes can be divided into two categories: people whose diabetes is diagnosed before pregnancy and people whose disease is diagnosed during pregnancy. 59% of all deaths in the world and 46% of diseases are due to non-communicable diseases and statistics show an increase in the prevalence of these diseases. The damage caused by these diseases and their staggering costs to health systems have always been a serious and powerful stimulus for the design and implementation of prevention programs at various levels. Meanwhile, diabetes is one of the predominant goals of preventive policies as a disease with debilitating effects that is initially contagious. Especially in the case of diabetes (type 2) there are effective and useful methods of prevention[1&2]. In this regard, due to the high sensitivity of the health care system to prevention programs in Iran, many procedures have been taken to prevent it by the health networks of the Islamic Republic of Iran. Control of diabetes and its problems has been a priority since 1991.

Today, chronic diseases are one of the main causes of disability and mortality in many countries of the world. Diabetes is one of the most serious non-communicable diseases worldwide and is classified as a disease with a global epidemic[3]. The number of people with diabetes worldwide in 2010 is estimated at 285 million[4]. By 2030, the number of people with diabetes is expected to double, and this "diabetic epidemic" includes pregnant women[5].

Decreased insulin secretion, decreased glucose uptake due to insulin resistance, and increased glucose uptake to varying degrees are involved in each type of diabetes. Diabetes causes premature and late changes that result in disability, cost of treatment, and ultimately increase mortality. Diabetes is the fifth leading cause of death in the world and the number one cause of chronic renal failure, non-traumatic amputation and blindness in many societies[6].

In the past, diabetes-related deaths were estimated at 800,000 per year; However, it has long been known that this estimate is much lower than the actual amount. A more reasonable estimate is that 4,000,000 deaths from the disease occur worldwide each year. Diabetes is the leading cause of 9% of all deaths worldwide[7]. The prevalence of diabetes has increased significantly in the last two decades. Although the prevalence is seen in both types of diabetes, the increase in the prevalence of type 2 diabetes has been far greater than in type 1 diabetes. In the 21st century, the prevalence of type 2 diabetes and impaired glucose tolerance (IGT) has become epidemic due to decreased physical activity and weight gain and obesity[8]. The incidence of type 1 diabetes is lower than that of type 2 diabetes, and is generally between 3 and 35 per 100,000 people per year. The incidence of type 1 diabetes in Canada and the United States is reported to be between 8 and 20 per 100,000 people. In general, type 1 diabetes is rare in people in Japan, China, the Philippines, as well as in Asian Indians, African Africans, and Eskimos, and is more common in whites. Type 1 diabetes is difficult to diagnose per 100,000 people in a year, and therefore many studies are incomplete in terms of defining indicators and their results should be considered with caution[9]. The prevalence of type 2 diabetes in the general population is between 1 to 4% and in people over 40 years between 5 to 10%. Given the growing prevalence of type 2 diabetes in the world, the World Health Organization declared it a latent epidemic and since 1993 has called on all countries to fight diabetes[10].

The types of diabetes are divided according to its pathological process. The most common types of diabetes are types 1 and 2, which differ in etiology, epidemiology and many other dimensions. In addition to type 1 and type 2 diabetes, diabetes may appear for other reasons such as genetic disorders, some diseases, etc. Gestational diabetes is different from type 1 and type 2 diabetes because it is diagnosed for the first time in a pregnant woman. The side effects for mothers and fetuses are similar to those who already have diabetes and then become pregnant, and may become completely normal after termination of pregnancy. There are three ways to diagnose type 2 diabetes today:

1. The venous plasma glucose concentration is equal to or greater than 200 mg / dL two hours after ingestion of 75 g of glucose.
2. Venous plasma glucose concentration in a random sample equal to or greater than 200 mg / dL with a clear sign of diabetes
3. Intravenous plasma glucose concentration in two fasting sessions equal to or greater than 126 mg / dL.

Normal plasma glucose levels in the fasting state and 2 hours after eating 75 g of glucose are 100 and 140 mg/dL, respectively. The American Diabetes Association prefers fasting plasma glucose levels because it is more practical, more proportionate, and more reproducible. If fasting plasma is between 100. 125 It is called " Impaired fasting glucose (IFG)". If the glucose concentration is between 140 and 200 two hours after glucose consumption, it is called "g Impaired glucose tolerance (IGT)". In these two groups, the incidence of diabetes is higher. Although two-thirds of them may not always have the symptoms of diabetes, they are more likely to have cardiovascular complications. Lifestyle changes can reduce the risk of developing diabetes in these groups[11].

Hemoglobin A1C is closely related to blood sugar levels, but is not currently used as a diagnostic test for diabetes because its normal nature cannot rule out impaired glucose tolerance or mild diabetes.

Literature of Review

The articles reviewed in this study include two Persian articles and one English article. By searching for terms such as: postpartum diabetes, self-regulation, postponement, in Iran Doc, Magiran, SID databases and searching for terms such as, screening, diabetes, type 2 diabetes, follow up, postpartum, procrastination, Gestational diabetes was obtained in PubMed, science direct, ProQuest, ISI databases in the period 2016-2005. The following studies are sorted by the closest time.

Rashidi et al. (2013), a cross-sectional study entitled Factors related to postpartum screening in women with a history of gestational diabetes in Kermanshah and performed on 150 subjects. The objectives of this study included determining the frequency of referrals for postpartum diabetes screening in women with a history of gestational diabetes and determining the relationship between demographic and reproductive characteristics, diabetes profile, and how to provide health services with individual referral for postpartum diabetes screening in women. She had a history of gestational diabetes. Personal and fertility characteristics: age, occupation, education, number of pregnancies and deliveries and abortions, number of children, number of household members, type of last pregnancy, income, receiving maternity care, smoking, having insurance, type of insurance, place of delivery, History of high birth weight (more than 4000 g), abnormal birth history, recent live birth and recent baby weight. Characteristics of diabetes: Age of onset of gestational diabetes, Diagnostic test for gestational diabetes, Gestational age, onset of insulin use, type of insulin, diet use, history of diabetes in previous pregnancies, type of diabetes in the family, family history, hospitalization history in pregnancy to control blood sugar. The research sample included 150 women who had given birth with a history of gestational diabetes in a recent pregnancy who had passed at least 6 months from the date of their delivery and were under pregnancy care in Kermanshah clinics and had a health record. Had no pre-gestational diabetes and at least 6 months from the date of delivery. The researcher, by referring to the files of the research units, obtained their telephone numbers with the permission of the University Ethics Committee and made telephone calls to them. And completed the questionnaire. In the end, the authors concluded that due to the low rate of female referral for screening for postpartum diabetes, it is necessary to identify the factors associated with female referral for screening, remove the barriers and with timely diagnosis, an opportunity to Prevent or delay the onset of type 2 diabetes in the future[12].

The methodology of this study and its expression is helpful in advancing the objectives of our study, but the innovation of the present study is the implementation of an educational intervention based on the self-regulatory model, the effect of which on postpartum follow-up in women with a history of gestational diabetes.

Peyman et al. (2012) conducted a study in 2012 to determine the effect of self-regulatory education on physical activity in women with type 2 diabetes. This study was a randomized controlled trial. The study population was women with type 2 diabetes referred to health centers in Mashhad. Inclusion criteria include: type 2 diabetes based on the evidence in the health record, age 35 to 65 years, not having any of the complications of diabetes, willingness to participate in the study, ability to read and write, physical activity and no treatment with It was insulin. Exclusion criteria included: suffering from complications of diabetes during the implementation of an educational intervention that restricts physical activity and absence of more than two sessions in theory sessions. The results showed that the mean age of participants was 49.07 years. In the intervention group, there was a significant difference in goal setting ($P < 0.001$), planning ($P = 0.001$) in the intervention evaluation courses; Knowledge ($P < 0.001$) and physical activity ($P < 0.001$) were observed. Also, there was a significant decrease in fasting blood sugar and body mass index at follow-up compared to before the intervention, which was not observed in the control group. At the end of the training, the researchers concluded that the educational intervention, using self-regulatory strategies, increases physical activity, improves blood sugar and body mass index in type 2 diabetic women[13].

Safarzadeh et al. (2014) conducted an experimental study entitled "The effect of training on postpartum sports activities using the health belief model" in women referring to health centers in Bandar Abbas. It turned out that 191 women referring to selected health centers in Bandar Abbas during the years 91 to 92 were selected. Then, these women were randomly divided into three groups: test, first control and second control. The above study refers to the effectiveness of educational intervention based on health belief model, but since the structures of self-care model as well as gestational diabetes are different categories to answer the question of whether self-regulatory model education can improve the level of physical activity Whether or not women with a history of gestational diabetes need a separate study is the subject of this study.[14]

Coppola et al. (2013) conducted a cross-sectional study of 6770 pregnant women at Pugliese-Ciaccio Hospital in Caucasian, southern Italy. The statistical population of this study included women who participated in gestational diabetes screening from January 2004 to December 2011. The aim of this study was to "accurately determine

the prognostic factors in performing postpartum glucose tolerance test in women with a history of gestational diabetes". Out of 1159 women diagnosed with gestational diabetes, 374 (32.3%) were screened for postpartum participated, attended, took part in. A significant increase in referral rates was observed following counseling. Other predictive factors included: previous history of gestational diabetes, higher education, and insulin therapy during pregnancy. Also, there was no significant difference between body mass index, family history of type 2 diabetes and number of deliveries with the rate of participation. Overall, the data of this study showed that the intervention as a counseling is an effective, inexpensive, and simple tool in increasing the rate of oral glucose tolerance test for women with a history of gestational diabetes. However, despite counseling, some women still do not participate. Polycystic ovary syndrome was also a strong predictor of women's participation in the postpartum diabetes test. The authors conclude that further studies are needed to determine whether their findings are common to other populations.[15]

Material and Methods

The present study is a quasi-experimental study. The study population in this study included all women with a history of gestational diabetes in District 2 of Qom. The research samples in this study include women with a history of gestational diabetes in the second region of Qom who have been pregnant for at least 6 weeks and have the characteristics of the research units. The following formula was used to determine the sample size. This formula is used to determine the sample size in intervention studies where the dependent variable is quantitative. Here, too, the dependent variables are the values of self-regulation, procrastination in physical activity, and procrastination in diet, all of which are quantified. According to previous studies[15], the alpha value was 5%, the beta value was 20%, and the average difference was 10 acceptable. In addition, some studies show that the average score of self-regulation in Iranian women is 112 and its standard deviation is 16.7.

Taking into account the 10% drop, the sample size of 46 people for each group (92 people in total) was determined.

$$n = \frac{2\sigma^2 (Z_{1-\beta} + Z_{1-\alpha/2})^2}{u1 - u2}$$

$$n = \frac{2 * 16.7^2 (Z_{\beta} + Z_{\alpha/2})^2}{u1 - u2}$$

$$n = \frac{2 * 278.89\ (1.96 + 0.8)^2}{10^2} = \frac{4250.28}{100} = 42.50$$

$$n = 42.50$$

The sampling method in the present study is multi-stage. The research method in the present study was that among the urban areas of Qom (4 regions), region 2 of Qom city was selected as the research community. Then, from the health centers of this region, two centers were randomly selected (one as a test and the other as a control). Then, in each center, referring to the files of pregnant women, 46 people were randomly selected and they were invited to participate in the research project by phone. If a case did not wish to participate in the study or did not meet the inclusion criteria, the next case number would be selected as an alternative. After selecting the subjects, while obtaining informed consent and providing complete explanations of the purpose of the study, the relevant questionnaires were provided to them (demographic information, self-regulatory questionnaire, postpartum physical activity postponement questionnaire, diet postponement questionnaire). After delivery) and information was obtained from them before the intervention.

In the next step, the intervention group underwent training based on self-regulatory model. The trainings were held in 4 sessions during one month and the duration of each class was 60 minutes. The trainings were held in the form of classes of 5-10 people, in other words, the intervention group was divided into 6 class groups and all the same trainings were provided by fixed people (researcher and nutrition expert). Immediately after the full implementation of the educational intervention and also 6 weeks after the intervention, both experimental and control groups were evaluated again and questionnaires were administered.

Inclusion criteria include:

1. Having gestational diabetes based on the documents in the health record
2. Women with a history of gestational diabetes who are at least 12 weeks old
3. The identity of the landline or mobile phone in the health record
4. Willingness to participate in the study
5. Ability to read and write

Exclusion criteria include:

1. Reluctance to cooperate
2. Absence from a training session
3. History of receiving training in this field

Using the demographic information questionnaire (age, level of education, employment status, number of children, family income, previous history of gestational diabetes), the main research tools included three self-regulatory questionnaires, Miller and Brown, physical activity delay questionnaire and diet delay questionnaire. Mourning. Due to the fact that procrastination questionnaires had not been localized before, so in the present study, the validity and reliability of these tools were assessed, and the steps of its preparation are as follows. The same

method was used in the process of preparing and determining the validity and reliability of the deferrals. While obtaining the consent of the main designers of the questionnaires, the Forward-Backward method was used for the translation process of the questionnaires. In this method, first the questionnaire was translated into Persian by two people with a focus on midwifery and fluent in English, then a Persian version was prepared while comparing the two translated versions. This Persian version was provided separately to two other translators to be translated into English. Finally, in a meeting with the presence of midwifery experts and health education and health promotion, the necessary corrections were made in terms of appropriateness and compliance with the original text.

In order to assess the content validity index (Content Validity Index), the questionnaire was given to 8 specialists (4 midwives, including 1 master and 3 PhDs, 2 epidemiologists and 2 PhDs in health education). In order to determine the content validity index, three criteria of "simplicity and fluency", "relevance" and "clarity or clarity" were used using a 4-point Likert spectrum for each item (58, 59), which in this method Due to the number of experts, questions with a score less than 0.80 are eliminated. Face validity of the questionnaires was provided to 8 women with a history of gestational diabetes and the reported ambiguities were resolved.

In the next step, cronbach's alpha coefficien method was used to determine internal consistency and stability and Test-Retest method was used to confirm time reliability. In this method, questionnaires were given to 20 women with a history of pregnancy and Cronbach's alpha was determined. Then, ten days later, the questionnaires were given to the same people again and the correlation between the scores obtained from the two studies was determined by calculating Pearson correlation coefficient and coefficient internal correlation.

Material analysis

Descriptive statistics (frequency, percentage and mean) are used to describe the status and frequency of the subject in terms of demographic variables. So that each structure in both groups were compared. Chi-square test was also used to compare the two groups in terms of demographic variables. Analysis of variance was used to compare the means in the two independent groups and also to compare the means in the multiple procedures. To compare the mean structures of the self-regulatory model, the mean deferral of physical activity and the mean deferral of diet in three-time stages (before intervention, immediately after intervention and 6 weeks after intervention), repeated measures analysis of variance was used.

Findings

A total of 92 patients with a mean age of 29.93. 4.9 participated in the study. Most participants had middle and high school education (46.7%), housewife (77.2%), were overweight (52.2%), had 2 children (43.5%) and had an average income status (62%). The mean number of deliveries in the participants was 2.20. 0.92. Regarding the insurance status, 85.9% of the participants had at least one type of insurance, 90.2% had no history of gestational diabetes in the previous delivery, 90.2% reported their recent delivery to public hospitals and no One participant did not use the glucose test at home during pregnancy.

In the evaluation of participants before the intervention, the results showed that the mean SRQ scale in all subjects was 147.7 34 34.7 n = 92. The mean of acceptance, evaluation, commissioning, review, planning, implementation and measurement structures was Respectively 24/47 ‘, 4, 24 ± 22/24, 21/32 2 2.5, 20/67 7 5.7, 17.57 4 5.4, 13.82 5 5.5 and 8/5 It was 22.4 , 4 and it can be said that the acceptance structure and the implementation structure were the best and the weakest means, respectively. On the other hand, the mean postponement of physical activity and postponement of diets were 23.26 , 3.3 and 3.3, respectively. It was 20.93.

The mean of SRQ scores was directly and significantly related to education (P 00 001) and income (P = 0.001). In women with higher education and higher family income, the average SRQ status was also better.

There was a significant relationship between the mean scores of physical activity delay (EPS) at different levels of education (P≥001) and income (P = 0.001). The mean EPS was lower in women with higher education and higher family income (Table 4-4). The mean scores of diet postponement (HDPS) were also significantly different at different levels of education (P = 0.003) and the mean HDPS was lower in people with higher education. Although the mean HDPS was lower in people with higher income, but the difference was not significant at the level of 0.05 (P = 0.07).

Prior to the intervention, different statistical tests showed that the experimental and control groups were equal in terms of demographic variables as well as the mean scores of SRQ, EPS and HDPS and no significant differences were observed between the two groups.

In Pearson correlation analysis, the results showed that there was a significant inverse correlation between SRQ scores and EPS and HDPS instruments that Pearson coefficient was r = -0.58 and r = 0.79, respectively (P <0.0001)). Also, all SRQ constructs were found to have a direct and significant relationship with the whole

SRQ scale, which Pearson correlation coefficients are. No significant correlation was found between start-up structures (P = 0.15) and evaluation (P = 0.07) with acceptance structures.

Immediately after the intervention and also 6 weeks after the intervention, the scores of SRQ scale and its structures, the mean of EPS and HDPS in the experimental and control groups were re-measured. The result of Friedman test showed that in the experimental group, the mean of all three scales changed significantly, so that at the level of P = 0.01, the mean SRQ scores both immediately after the intervention (168.41 45 45.7) and at 6 weeks after the intervention (164.43 42 42.4) was more than before the intervention (149.15 33 33.8). On the other hand, the mean SRQ in the control group did not show a significant change.

The mean scores of EPS and HDPS were also significantly reduced so that the mean scores of EPS were significantly in the stage immediately after the intervention (15.54 8 5.8) and 6 weeks after the intervention (15.76 5 5.5). It was lower than before the intervention (23.11 ± 3.1). There was a significant change in Haykeh in the control group (P = 0.14).

Also, the mean of HDPS scores was significantly (P <0.001) in the immediate stage (14.48 ± 3.1) and 6 weeks after the intervention (14.83 3 3.1) lower than the pre-intervention stage (3.3). 20.96 3), while no significant change was observed in the control group (P = 0.17).
In addition to the above scales, the two groups of test and control were compared in terms of performing screening tests after the intervention and the results showed that the rate of screening in the experimental group was significantly (P = 0.002) higher than the control group. In the experimental group, 40 women participated in screening tests, while only 27 in the control group).

Discussion and conclusion

The aim of this study was to evaluate the effectiveness of self-regulatory model-based education on postpartum follow-up in women with gestational diabetes. Diet and postpartum screening test.

Findings and evaluations before the intervention showed the unfavorable status of SRQ scale scores, its structures, mean EPS and HDPS scores. The score obtained from the SRQ scale in the total number of participants was 46% of the total score. The scores obtained by the participants in the admission and evaluation structures were 53% of the total score, which obtained an average score from these two structures, but in the scores of the commissioning, review, planning, implementation and assessment structures, 47, 44, 40, 31 and 48%, respectively. The total score was possible, which in this regard, the situation of the participants is unfavorable and weak. The lowest score of the participants was related to the execution structure.

It seems that the self-efficacy of these people in performing self-care and health behaviors is low and this issue causes the poor scores of these people in the implementation structure. On the other hand, the level of education of most participants in middle school and high school is (47%), which can be one of the main reasons for low scores in various structures of self-regulatory scale, especially in the construction structure. Santiago et al. Showed that pregnant women with Higher education levels have a more favorable self-regulatory status[16]. Education is directly related to the level of health literacy, responsibility for health, self-efficacy and health attitudes of individuals, and people with higher education have more self-care behaviors than people with lower education. On the other hand, the economic situation is directly related to receiving and benefiting from health services, regular visits, performing diagnostic tests and using medical services. In the present study, only 6.5% of the participants had a good income, and 31.5% reported a low income and 62% reported a moderate income. Economic factors seem to be among the determining factors in the health status of people and the group of pregnant women. The results of the present study showed the unfavorable status of the scores of the Physical Delay and Diet Delay scales. The mean scores of participants' physical activity delay before the intervention were 77% of the total possible score, while on this scale, a higher score means an unfavorable situation. It can be said that women with a history of diabetes in the present study were in a very unfavorable position in terms of physical activity. It seems that cultural and economic factors, the level of awareness and attitude of individuals play an important role in performing physical activities. These findings are consistent with the study of Shakeri et al.[17]

Regarding the average score of diet postponement, the situation was better than the postponement of physical activity, but the status of this item was also unfavorable, so that the average score of the participants was 70% of the total score. It seems necessary to provide more education and remove existing barriers to adopting healthy eating programs in women with gestational diabetes, and it is necessary to pay more attention to this issue in the programs of the Ministry of Health.

Prior to the intervention, the results of correlation analysis between the variables of self-regulatory scale, physical activity delay scale and diet postponement scale in all participants (n = 92) showed a strong and significant relationship between them. Pearson correlation coefficient between self-regulation scale and physical activity delay was -0.58, which indicates that people with higher self-regulation score have lower physical activity delay score and therefore are in better condition. On

the other hand, the relationship between self-regulation scale and diet postponement was statistically stronger as the Pearson correlation coefficient was -0.79, indicating that individuals whose scores were higher than the self-regulation scale were firmly on the diet scale scores. They are less, in other words, they have a better diet. This important finding is consistent with the study of Jalili et al., So that in the study, the mean of self-regulatory scores was recognized as one of the most important predictors of healthy eating behaviors[18].

On the other hand, all structures of the self-regulatory model, with the exception of the acceptance structure, were inversely and significantly correlated with the scales of physical activity and diet. It seems that the acceptance construct as the first construct of the self-regulatory process does not have a significant correlation with the deferral scales, although due to the small sample size (92 participants) this can be attributed to random error. The results of the analysis 6 weeks after the intervention showed that the mean scores obtained from the self-regulatory scale in the experimental group increased by 15 points, in other words, before the intervention, the mean scores of participants was 47% of the total score of the scale, while 6 One week after the intervention, the participants' mean scores were 52% of the total self-regulatory scale. In addition, all structures of this model were associated with a significant increase.

The results of the present study showed that the educational intervention based on the self-regulatory model improves the mean scores of physical activity delay in women with a history of gestational diabetes. The statistical comment is very significant. However, no change was observed in the control group. On the other hand, the educational intervention based on the self-regulatory model had reduced the mean scores of the participants in the diet delay scale so that in the experimental group a decrease of 6 points was observed in the mean of this scale but in the control group no change was observed.

It seems that self-regulatory model training allows a person to consciously define and set goals and be able to control their emotions and thoughts in order to achieve goals. The trained person interprets and examines his behaviors in terms of alignment with his goals, and if he sees the desired behavior as positive, he acquires it or continues it, but if he does not find a behavior that fits his goals, he cuts it off. This ability and skill were presented to the study group in the present study through training based on self-regulatory model and the results of analysis 6 weeks after the intervention show the effectiveness of these trainings. In the present study, 6 weeks after the intervention, all participants were screened for postpartum screening tests and the results showed that 40 (87%) of the experimental group had performed screening tests, but in the control group had only 27 patients (59%) who had taken the necessary steps to perform screening tests. In the control group, individuals probably received routine follow-up in health centers performed by health personnel, and in the intervention group, in addition to receiving these routine services, they underwent model-based training. In general, according to the findings of the present study, training according to the self-regulatory model improves the physical activity and nutritional status of women with a history of gestational diabetes and it is recommended that this model in the programs of the Ministry of Health and at different levels of Use clinical centers and provide training packages based on this model to the health team, especially midwives, nurses, health workers and even doctors.

Declaration

Hereby I declare that the present thesis is exclusively my own work, based on my research in the department Maternal and Health Child of at the Faculty of Nursing and Midwifery, Tehran University of Medical Sciences Tehran, Iran. I also declare that no part of this thesis has been submitted in this form to any other university or Institution of higher education for an academic degree. Information delivered from the published or unpublished work of others has been acknowledge in text and a list of references is given. All thesis is reserved for the Tehran University of Medicine Sciences. Criticism by mentioning the source is allowed.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Beaglehole R, Bonita R, Horton R, Adams C, Alleyne G, Asaria P, et al. Priority actions for the non-communicable disease crisis. The Lancet. 2011;377(9775):1438-47.

2. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. The Lancet. 1997;349(9064):1498-504.

3. Currie SL. Applying the Theory of Planned Behaviour to persons with prediabetes and diabetes: An examination of intention and behaviour for healthy eating and physical activity: Library and Archives Canada= Bibliothèque et Archives Canada; 2011.

4. Didarloo A, Shojaeizadeh D, Ardebili HE, Niknami S, Hajizadeh E, Alizadeh M. Factors influencing physical activity behavior among iranian women with type 2 diabetes using the extended theory of reasoned action. Diabetes & metabolism journal. 2011;35(5):513-22.

5. Ghazanfari Z, Niknami S, Ghofranipour F, Hajizadeh E, Montazeri A. Development and psychometric properties of a belief-based Physical Activity Questionnaire for Diabetic Patients (PAQ-DP). BMC medical research methodology. 2010;10(1):104.

6. Group UPDS. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ: British Medical Journal. 1998:703-13.

7. Morris AP, Voight BF, Teslovich TM, Ferreira T, Segre AV, Steinthorsdottir V, et al. Large-scale association analysis provides insights into the genetic architecture and pathophysiology of type 2 diabetes. Nature genetics. 2012;44(9):981.

8. Gray A, Raikou M, McGuire A, Fenn P, Stevens R, Cull C, et al. Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41). Bmj. 2000;320(7246):1373-8.

9. Redekop WK, Koopmanschap MA, Stolk RP, Rutten GE, Wolffenbuttel BH, Niessen LW. Health-related quality of life and treatment satisfaction in Dutch patients with type 2 diabetes. Diabetes care. 2002;25(3):458-63.

10. Norris SL, Engelgau MM, Narayan KV. Effectiveness of self-management training in type 2 diabetes. Diabetes care. 2001;24(3):561-87.

11. Panzram G. Mortality and survival in type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia. 1987;30(3):123-31.

12. Rashidi k VRF, Pakgohar M. Factors associated with postpartum diabetes screening in women with GDM. Theses of Master, medicine tehran university. 2014.

13. Peyman N, Taghipour A, Mahdizadeh M, Esmaeely H. The effect of educational intervention based on self-regulation strategies on physical activity in women with type 2 diabetes. Evidence Based Care. 2013;2(4):7-17

14. Safarzade S, Behboodi MZ, Saffari M. The Impact of Education on Performing Postpartum Exercise Based on Health Belief Model. 2014.

15. Capula C, Chiefari E, Vero A, Iiritano S, Arcidiacono B, Puccio L, et al. Predictors of postpartum glucose tolerance testing in Italian women with gestational diabetes mellitus. ISRN endocrinology. 2013;2013.

16. Aghaie Meybodi HR, Azizi F. The assessment of relation between lipid distribution and weight change with diabetes incidence in a group of Tehran, district 13 population. Research in Medicine 2008, 32(2): 105-113

17. Shakeri M, Fekri S, Shahnavaz A, Shakibazadeh E. Effectiveness of a Group-based Educational Program on Physical Activity among Pregnant Women. Hayat. 2012;18(3):1-9.

18. Jalily M, Barati M, Bashirian S. Using social cognitive theory to determine factors predicting nutritional behaviors in pregnant women visiting health centers in Tabriz, Iran. Journal of Education and Community Health. 2015;1(4):11-21.

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ORIGINAL

Parámetros antropométricos relacionados con valores de alto riesgo de diferentes escalas de hígado graso no alcohólico y fibrosis hepática en 146.318 adultos españoles

Anthropometric parameters related to high-risk values of different scales of nonalcoholic fatty liver disease and liver fibrosis in 146.318 spanish adults

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Resumen

Introducción y objetivos: El hígado graso es una alteración muy frecuente, que puede estar o no asociada con el consumo de alcohol, y que consiste en la acumulación de grasa en el hígado. El objetivo del trabajo es valorar como afectan variables sociodemográficas y el exceso de peso en la prevalencia de hígado graso no alcohólico y fibrosis hepática determinados mediante escalas de riesgo.
Material y métodos: Estudio descriptivo y transversal en 146318 españoles de diferentes regiones. Se valora el riesgo de hígado graso no alcohólico y de fibrosis hepática empleando el fatty liver index, el hepatic steatosis index, el fatty liver disease index, el lipid accumulation index y el BARD score. Como variables sociodemográficas se analizan la edad, el sexo y la clase social.
Resultados: Todas las escalas estudiadas, tanto de hígado graso no alcohólico como de fibrosis hepática, ven incrementados sus valores medios y la prevalencia de valores de alto riesgo a medida que se incrementa la edad, a medida que se desciende en la clase social y paralelamente al incremento de las escalas de sobrepeso y obesidad.
Conclusiones: En población española hay una clara influencia de la edad, el sexo, la clase social y la obesidad en los valores de las escalas que determinan el hígado graso no alcohólico y la fibrosis hepática.

Palabras clave: Hígado graso no alcohólico, fibrosis hepática, obesidad, clase social.

Summary

Introduction and objectives: Fatty liver is a very frequent alteration, which may or may not be associated with alcohol consumption, and which consists of the accumulation of fat in the liver. The aim of this study is to evaluate how sociodemographic variables and excess weight affect the prevalence of nonalcoholic fatty liver disease and hepatic fibrosis determined by means of risk scales.

Methods: Descriptive and cross-sectional study in 146318 Spaniards from different regions. The risk of nonalcoholic fatty liver disease and hepatic fibrosis was assessed using the fatty liver index, the hepatic steatosis index, the fatty liver disease index, the lipid accumulation index and the BARD score. Age, sex and social class were analyzed as sociodemographic variables.

Results: All the scales studied, both for non-alcoholic fatty liver disease and liver fibrosis, increased their mean values and the prevalence of high-risk values as age increased, as social class decreased and in parallel with the increase in the overweight and obesity scales.

Conclusions: In the Spanish population there is a clear influence of age, sex, social class and obesity on the values of the scales that determine nonalcoholic fatty liver disease and liver fibrosis.

Key words: Nonalcoholic fatty liver disease, liver fibrosis, obesity, social class.

Introducción

El hígado graso se presenta cuando se acumula mucha grasa en las células hepáticas. Aunque es normal tener una pequeña cantidad de grasa en estas células, se considera que es graso cuando está conformado por más de 5% de grasa. El patrón típico es una lesión central hepatocelular con inflamación lobulillar con o sin fibrosis[1].

Hay dos tipos principales:
- Enfermedad del hígado graso no alcohólico
- Enfermedad del hígado graso por alcohol, también llamada esteatosis hepática alcohólica

Como su nombre lo indica, la enfermedad del hígado graso por alcohol se debe al alto consumo de alcohol (>20 g al día para mujeres y >30 g al día para hombres). El hígado descompone la mayor parte del alcohol que bebe para que sea eliminado del cuerpo, pero el proceso de descomposición puede generar sustancias nocivas. Estas sustancias pueden dañar las células del hígado, provocar inflamación y debilitar las defensas naturales del cuerpo. Cuanto más alcohol se consume, más se daña el hígado. La enfermedad del hígado graso por alcohol es la etapa más temprana de la enfermedad del hígado por el alcohol (o hepatopatía alcohólica). Las siguientes etapas son la hepatitis alcohólica y la cirrosis.

Varias afecciones relacionadas entran en la amplia categoría de enfermedades del hígado graso no alcohólico (EHGNA) que es la enfermedad hepática más común en adultos y niños en los países occidentales llegando a tener una prevalencia del 25,5%[2]. El hígado graso no alcohólico o HGNA (NAFL, en inglés) es la etapa inicial, reversible de la enfermedad hepática. Desafortunadamente, con frecuencia no se diagnostica. Con el tiempo, la EHGNA puede causar una afección hepática más grave conocida como esteatohepatitis no alcohólica, o EHNA (NASH, en inglés). La EHNA involucra mayor acumulación de grasa e inflamación que daña las células hepáticas. Esto puede provocar fibrosis, o cicatrización tisular, a medida que las células hepáticas son lesionadas repetidamente y mueren. Desafortunadamente, es difícil predecir si el hígado graso progresará a EHNA, lo que puede aumentar significativamente el riesgo de cirrosis y cáncer de hígado, concretamente en Estados Unidos la tasa anual de muerte por cirrosis aumentó en un 65% y se duplicó la de hepatocarcinoma[3]. La EHGNA también se relaciona con un aumento en el riesgo de desarrollar otras afecciones, incluyendo enfermedad cardíaca, diabetes y enfermedad renal.

Existen varios factores que pueden causar o contribuir para desarrollar hígado graso como son la obesidad, el exceso de grasa abdominal, la resistencia a la insulina, la ingesta elevada de carbohidratos refinados y de bebidas azucaradas y el deterioro de la salud intestinal.

Existen varios signos y síntomas de hígado graso, aunque puede que no todos estén presentes: fatiga y debilidad, dolor leve o sensación de llenura en el área abdominal derecha o central, niveles elevados de enzimas hepáticas, como AST y ALT, niveles elevados de insulina y triglicéridos.

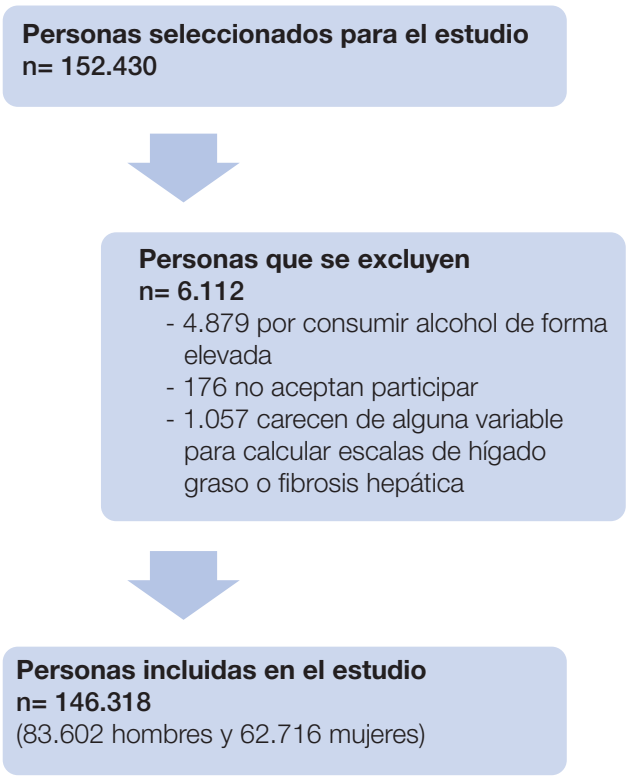
Si el hígado graso progresa a EHNA, se pueden desarrollar los siguientes síntomas: pérdida de apetito, náusea y vómitos, dolor abdominal de moderado a intenso y ojos y piel de color amarillento.

El objetivo de este trabajo fue conocer la relación entre diferentes parámetros antropométricos y escalas que valoran el riesgo de presentar hígado graso no alcohólico y fibrosis hepática en población española y determinar la prevalencia de alto riesgo de hígado graso no alcohólico y de fibrosis hepática en población española.

Material y métodos

Se realiza un estudio descriptivo y transversal en 152430 personas incluidas en una base de datos anonimizada, de ellas se excluyen 6112 por diferentes motivos (ver flujograma en la **figura 2**) con lo que finalmente quedan 146.318 (83.602 hombres y 62.716 mujeres) con edades comprendidas entre 18 y 79 años.

Figura 2: Flujograma de los participantes en el estudio.



Criterios de inclusión

- Edad entre 18 y 79 años.
- Aceptar participar en el estudio.
- Contar con los parámetros necesarios para calcular las escalas de hígado graso y fibrosis hepática.
- No consumir alcohol en cantidades elevadas

Las determinaciones antropométricas, clínicas y analíticas, las realiza el personal sanitario de las distintas unidades de salud laboral participantes en el estudio, después de homogenizar las técnicas de medición.

Para la medición del peso, que se expresa en kilogramos, y la altura, que se expresa en cm, se emplea una báscula con tallímetro: modelo SECA 700. El perímetro de cintura abdominal (en cm) se mide con una cinta métrica: SECA modelo 20 con la persona en bipedestación, pies juntos y tronco recto, abdomen relajado y extremidades superiores colgando a ambos lados del cuerpo. La cinta métrica se coloca paralela al suelo a nivel de la última costilla flotante. Perímetro de cadera se mide con la misma cinta métrica y adoptando la misma posición que en el perímetro de la cintura y pasando la cinta de forma horizontal a nivel de la cadera. El índice cintura/altura se obtiene dividiendo el perímetro de cintura entre la altura considerándose alto a partir de 0,50[4].

Se utilizaron otras escalas antropométricas:
- IMC se calcula dividiendo el peso entre la altura^2 (en metros). Se considera obesidad a partir de 30.
- CUN BAE (Estimador de Adiposidad Corporal de la Clínica Universitaria de Navarra)[5]

-44,988 + (0,503 x edad) + (10,689 x sexo) + (3,172 x IMC) - (0,026 x IMC2) + (0,181 x IMC x sexo) - (0,02 x IMC x edad) - (0,005 x IMC2 x sexo) + (0,00021 x IMC2 x edad)
Hombre = 0 Mujer = 1
- Fórmula de Deurenberg[6]

1,2 x (IMC) + 0,23 x (edad) - 10,8 x (sexo) - 5,4 Hombre = 0 Mujer = 1
- Masa grasa relativa[7].

Mujeres: 76- (20 x (altura/cintura)) Hombres: 64- (20 x (altura/cintura))

Como escalas de hígado graso no alcohólico se emplean:
- Índice de hígado graso[8] (fatty liver index FLI).

FLI = (e0,953*log (triglicéridos) + 0,139*IMC + 0,718*log (GGT) + 0,053*circunferencia de la cintura - 15,745) / (1 + e0,953*log (triglicéridos) + 0,139*IMC + 0,718*log (GGT) + 0,053*circunferencia de la cintura - 15,745) x 100
- Índice de esteatosis hepática (HSI)[9]

HSI = 8 x ALT/AST + IMC (+ 2 si hay diabetes tipo 2, + 2 si es mujer)
- Índice de hígado graso (FLD)[10]

IMC + Triglicéridos + 3 × (ALT/AST) + 2 × Hiperglucemia (presencia= 1; ausencia = 0)

Los valores <28,0 o >37,0 excluyen la posibilidad de NAFLD
IMC ≥ 28 = 1 punto, AST/ALT ≥0,8 = 2 puntos, diabetes mellitus tipo 2 = 1 punto.

Corte de alto riesgo 2 puntos
- Producto de la acumulación de lípidos[11].
- Hombres: (cintura (cm) - 65) x (triglicéridos (mMol)).
- Mujeres: (cintura (cm) - 58) x (triglicéridos (mMol)).

Para valorar el riesgo de fibrosis hepática se emplea la escala BARD score[12]

El IMC ≥28 = 1 punto, la relación GOT/GPT ≥0,8 = 2 puntos, diabetes mellitus tipo 2 = 1 punto. Se considera alto riesgo valores a partir de 2 puntos.

La presión arterial se obtiene en decúbito supino con un esfigmomanómetro automático OMRON M3 calibrado y tras 10 minutos de descanso. Se realizan tres mediciones con intervalos de un minuto obteniéndose la media de las tres. Los análisis de sangre se obtienen por venopunción periférica tras un ayuno de 12 horas. Las muestras se remiten a los laboratorios de referencia y se procesan en un tiempo máximo de 48-72 horas. Para glucemia, colesterol total y triglicéridos se emplean métodos enzimáticos automatizados. Los valores se expresan en mg/dl. El HDL se determina por precipitación con dextrano-sulfato Cl2Mg, y los valores se expresan en mg/dl. El LDL se calcula empleando la fórmula de Friedewald (siempre que los triglicéridos sean inferiores a 400 mg/dl). Los valores se expresan en mg/dl.

Fórmula de Friedewald: LDL= colesterol total –HDL– triglicéridos/5

Las cifras de glucemia se clasifican según las recomendaciones de la Asociación Estadounidense para la Diabetes[13], se calificaron como diabéticos los pacientes con diagnóstico previo, los que tras obtener una cifra de glucemia superior a 125 mg/dl presentaron una Hemoglobina glicosilada ≥ 6,5% o si la persona toma tratamiento hipoglucemiante.

Se consideró como fumador a aquella persona que había consumido de forma regular al menos 1 cigarrillo/día (o el equivalente en otros tipos de consumo) en el último mes, o había dejado de fumar hace menos de un año.

Para la clase social se utiliza la Clasificación Nacional de Ocupaciones del año 2011 (CNO-11) y de la propuesta realizada por el grupo de determinantes sociales de la Sociedad Española de Epidemiología[14]. Se opta por la clasificación en 3 categorías: Clase I. Directores/gerentes, profesionales universitarios, deportistas y artistas. Clase II. Ocupaciones intermedias y trabajadores por cuenta propia sin asalariados. Clase III. Trabajadores no cualificados.

Análisis estadístico

Se realiza un análisis descriptivo de las variables categóricas, calculando la frecuencia y distribución de respuestas de cada una de ellas. Para las variables cuantitativas, se calcula la media y la desviación estándar y para las variables cualitativas se calcula el porcentaje. El análisis de asociación bivariante se realiza mediante el test de la χ^2 (con corrección del estadístico exacto de Fisher cuando las condiciones lo requirieran) y la *t* de *Student* para muestras independientes. Para valorar la correlación entre los valores de las diferentes escalas se emplea el coeficiente de correlación de Pearson. La concordancia entre los resultados de todas las escalas se valora con el índice Kappa de Cohen. Se determinan las curvas ROC estableciéndose las áreas debajo de la curva, los puntos de corte, sensibilidad, especificidad e índice Youden de los diferentes patrones antropométricos en relación con las escalas de hígado graso y fibrosis hepática. Para el análisis multivariante se ha utilizado la regresión logística binaria con el método de Wald, con el cálculo de las Odds-ratio y se realiza la prueba de bondad de ajuste de Hosmer-Lemeshow. El análisis estadístico se realiza con el programa SPSS 27.0 siendo el nivel de significación estadística aceptado de 0,05.

Consideraciones y aspectos éticos

El estudio fue aprobado por el Comité de ética de investigación clínica del área de salud de Illes Balears nº IB 4383/20. Todos los procedimientos se realizaron de acuerdo con las normas éticas del comité de investigación institucional y con la Declaración de Helsinki de 2013. Todos los pacientes firmaron documentos de consentimiento informados por escrito antes de participar en el estudio.

Resultados

La edad media de los participantes es de 41 años, más del 76% pertenecen a la clase social III y casi un 33% son fumadores.

Tanto los parámetros antropométricos (IMC, cintura/altura) como los clínicos (tensión arterial) y los analíticos (perfil lipídico, glucemia, perfil hepático y perfil renal) muestran valores más desfavorables en los hombres siendo en todos los casos las diferencias estadísticamente significativas. Los datos completos se presentan en la **tabla I**.

En las mujeres, tal como se aprecia en la **tabla II a**, los valores de todas las escalas de hígado graso no alcohólico y de fibrosis hepática van incrementando su valor a medida que lo hace la edad. También se observa un incremento en las escalas a medida que se desciende en la clase social.

El incremento de los valores de las escalas de sobrepeso y obesidad se acompaña de una elevación de los valores de las escalas de hígado graso y fibrosis hepática.

Tabla I: Características sociodemográficas, antropométricas, analíticas y clínicas de la población.

	Hombres n=83602 Media (de)	Mujeres n=62716 Media (de)	Total n=146318 Media (de)	p
Edad (años)	41,8 (10,5)	39,9 (10,5)	41,0 (10,5)	<0.0001
Altura (cm)	175,2 (6,8)	162,3 (6,3)	169,7 (9,2)	<0.0001
Peso (kg)	82,6 (15,0)	68,0 (14,7)	76,3 (16,5)	<0.0001
IMC (kg/m²)	26,9 (4,5)	25,8 (5,4)	26,4 (4,9)	<0.0001
Cintura (cm)	87,6 (10,2)	75,1 (10,5)	82,3 (12,0)	<0.0001
Cintura/altura	0,50 (0,06)	0,46 (0,06)	0,48 (0,06)	<0.0001
TAS (mmHg)	126,1 (15,6)	115,4 (15,5)	121,5 (16,5)	<0.0001
TAD (mmHg)	77,3 (11,1)	72,3 (10,5)	75,2 (11,1)	<0.0001
Colesterol (mg/dl)	195,6 (37,9)	192,1 (35,5)	194,1 (36,9)	<0.0001
HDL (mg/dl)	52,1 (9,8)	57,2 (10,3)	54,2 (10,3)	<0.0001
LDL (mg/dl)	118,7 (34,9)	116,4 (33,4)	117,7 (34,3)	<0.0001
Triglicéridos (mg/dl)	125,7 (76,0)	93,1 (45,6)	111,8 (66,7)	<0.0001
Glucemia (mg/dl)	93,4 (21,5)	88,3 (16,0)	91,2 (19,5)	<0.0001
GPT (U/L)	29,0 (17,5)	18,7 (11,6)	24,6 (16,1)	<0.0001
GOT (U/L)	24,4 (13,3)	18,2 (7,9)	21,7 (11,7)	<0.0001
GGT (U/L)	32,7 (31,8)	18,8 (16,3)	26,7 (27,2)	<0.0001
Creatinina (mg/dl)	0,86 (0,17)	0,68 (0,14)	0,79 (0,18)	<0.0001
	n (%)	**n (%)**	**n (%)**	**p**
18-29 años	12004 (14,4)	12180 (19,4)	24184 (16,5)	<0.0001
30-39 años	22274 (26,6)	18126 (28,9)	40400 (27,6)	
40-49 años	28128 (33,6)	20082 (32,0)	48210 (32,9)	
50-59 años	17970 (21,5)	10516 (16,8)	28486 (19,5)	
60-79 años	3226 (3,9)	1812 (2,9)	5038 (3,4)	
Clase social I	5082 (6,1)	4696 (7,5)	9778 (6,7)	<0.0001
Clase social II	12158 (14,5)	12856 (20,5)	25014 (17,1)	
Clase social III	66362 (79,4)	45164 (72,0)	111526 (76,2)	
Fumadores	56428 (67,5)	41805 (66,7)	98233 (67,1)	<0.0001
No fumadores	27174 (32,5)	20911 (33,3)	48085 (32,9)	

IMC índice de masa corporal. TAS Tensión arterial sistólica. TAD Tensión arterial diastólica. HDL Lipoproteína de alta densidad LDL Lipoproteína de baja densidad. GOT Transaminasa glutámico oxalacética. GPT Transaminasa pirúvico oxalacética. GGT Gamma Glutamil Transpeptidasa

Tanto en las variables sociodemográficas como en las escalas de sobrepeso-obesidad las diferencias observadas siempre han sido estadísticamente significativas (p<0.0001)

En los hombres también se observa el incremento de los valores medios de todas las escalas de hígado graso no alcohólico y fibrosis hepática a medida que se incrementa la edad. No se aprecia un empeoramiento de los valores de estas escalas, como hemos visto e las mujeres, a medida que bajamos en la clase social ya que en algunos casos los valores son peores en la clase social III y en otros en la clase social II.

También observamos un empeoramiento de las escalas hepáticas a medida que se incrementan los valores de las escalas de sobrepeso y obesidad.

Como ocurría en las mujeres las diferencias observadas en todos los casos son estadísticamente significativas (p<0.0001). Los datos completos se presentan en la **tabla II b**.

Tabla II a: Valores medios de las diferentes escalas de hígado graso y fibrosis hepática según variables sociodemográficas y escalas de sobrepeso-obesidad en mujeres.

Mujeres	n	FLI Media (de)	HSI Media (de)	FLD Media (de)	LAP Media (de)	BARD score Media (de)
18-29 años	12180	14,3 (19,7)	34,4 (6,5)	28,4 (5,7)	15,9 (15,9)	0,29 (0,53)
30-39 años	18126	18,0 (22,5)	35,9 (7,1)	29,7 (6,2)	18,2 (17,8)	0,39 (0,61)
40-49 años	20082	20,1 (22,2)	36,7 (6,6)	30,4 (5,6)	19,7 (18,1)	0,45 (0,65)
50-59 años	10516	25,3 (24,1)	38,0 (6,8)	31,6 (5,7)	23,5 (20,6)	1,65 (0,78)
60-79 años	1812	26,9 (23,7)	38,6 (6,6)	32,1 (5,5)	24,2 (19,2)	1,69 (0,77)
Clase social I	4696	13,0 (17,4)	34,2 (5,6)	28,2 (4,8)	14,5 (15,8)	0,43 (0,70)
Clase social II	12856	17,0 (20,9)	35,7 (6,6)	29,4 (5,5)	17,2 (16,9)	0,55 (0,78)
Clase social III	45164	20,8 (23,2)	36,7 (7,0)	30,4 (6,1)	20,4 (18,7)	0,68 (0,84)
Cintura/altura <0,50	48088	9,9 (9,6)	33,9 (5,0)	27,7 (3,7)	12,9 (9,8)	0,42 (0,68)
Cintura/altura ≥ 0,50	14628	50,8 (24,2)	44,2 (6,3)	37,7 (5,3)	40,3 (23,2)	1,37 (0,83)
Bajo peso IMC	1896	2,2 (1,3)	27,1 (3,0)	21,2 (1,4)	4,7 (4,2)	0,13 (0,38)
Normopeso IMC	30722	6,0 (4,5)	32,2 (3,9)	26,1 (2,3)	10,2 (7,2)	0,24 (0,49)
Sobrepeso IMC	18060	19,1 (11,3)	37,9 (3,9)	31,5 (2,1)	20,7 (12,5)	0,74 (0,82)
Obesidad IMC	12038	57,1 (21,6)	45,9 (5,7)	39,3 (4,5)	42,6 (23,9)	1,56 (0,75)
Normal CUN BAE	13682	3,8 (2,6)	29,8 (3,4)	23,9 (1,9)	8,4 (6,3)	0,09 (0,31)
Sobrepeso CUN BAE	16328	6,81 (4,7)	33,2 (3,5)	27,0 (1,8)	11,0 (7,6)	0,24 (0,48)
Obesidad CUN BAE	32706	32,3 (24,7)	40,6 (6,3)	34,1 (5,2)	28,0 (20,8)	1,06 (0,87)
No obesidad RFM	32110	6,4 (5,5)	32,6 (4,6)	26,5 (3,1)	9,1 (6,5)	0,28 (0,55)
Obesidad RFM	30606	33,2 (25,2)	40,2 (6,8)	33,8 (5,9)	30,0 (20,4)	1,01 (0,89)
Normal Deuremberg	3582	2,9 (1,9)	28,2 (3,1)	22,4 (1,7)	7,1 (6,0)	0,06 (0,25)
Sobrepeso Deuremberg	13836	4,7 (3,0)	31,1 (3,4)	25,1 (2,0)	9,2 (6,3)	0,08 (0,28)

FLI Fatty liver index. HSI Hepatic steatosis index. FLD Fatty liver disease. LAP Lipid accumulation product. IMC Índice de masa corporal. CUN BAE Clínica Universitaria de Navarra Body Adiposity Estimator. RFM Relative Fat Mass. En todos los casos las diferencias observadas con todas las variables son estadísticamente significativas p<0.0001

Tabla II b: Valores medios de las diferentes escalas de hígado graso y fibrosis hepática según variables sociodemográficas y escalas de sobrepeso-obesidad en hombres.

Hombres	n	FLI Media (de)	HSI Media (de)	FLD Media (de)	LAP Media (de)	BARD score Media (de)
18-29 años	12004	26,9 (24,2)	34,5 (6,7)	29,8 (5,2)	23,8 (21,2)	0,56 (0,79)
30-39 años	22274	36,4 (26,4)	36,4 (6,8)	31,6 (5,3)	32,0 (29,4)	0,79 (0,90)
40-49 años	28128	43,3 (26,7)	37,4 (6,8)	32,6 (5,3)	36,7 (31,0)	0,98 (0,95)
50-59 años	17970	45,5 (25,9)	37,6 (6,4)	32,9 (5,2)	37,1 (28,9)	2,02 (0,93)
60-79 años	3226	46,0 (25,2)	37,7 (6,1)	33,2 (4,9)	37,4 (26,2)	2,09 (0,89)
Clase social I	5082	38,1 (25,5)	36,6 (6,6)	31,7 (4,9)	32,4 (28,0)	1,10 (1,06)
Clase social II	12158	39,7 (25,5)	37,1 (6,4)	32,2 (5,0)	33,3 (27,2)	1,15 (1,05)
Clase social III	66362	39,8 (27,1)	36,7 (6,8)	32,0 (5,5)	33,8 (29,4)	1,13 (1,05)
Cintura/altura <0,50	45802	23,3 (16,3)	33,7 (5,1)	29,1 (3,5)	20,3 (14,7)	0,72 (0,85)
Cintura/altura ≥ 0,50	37800	59,6 (23,3)	40,6 (6,5)	35,6 (5,1)	49,9 (33,5)	1,64 (1,06)
Bajo peso IMC	624	5,4 (4,6)	25,7 (3,0)	21,7 (1,4)	8,1 (8,0)	0,33 (0,54)
Normopeso IMC	29986	16,8 (11,5)	31,8 (4,2)	27,4 (2,4)	17,4 (12,6)	0,50 (0,69)
Sobrepeso IMC	35834	41,9 (18,5)	37,3 (4,6)	32,5 (2,5)	34,6 (23,0)	1,17 (0,98)
Obesidad IMC	17158	76,2 (15,7)	44,8 (5,9)	39,6 (4,3)	61,2 (38,5)	2,18 (0,86)
Normal CUN BAE	14054	11,6 (7,9)	30,0 (3,9)	25,7 (2,1)	14,4 (10,3)	0,60 (0,54)
Sobrepeso CUN BAE	23876	23,7 (13,8)	33,9 (4,3)	29,3 (2,2)	22,0 (15,4)	0,58 (0,71)
Obesidad CUN BAE	45672	56,7 (23,0)	40,4 (6,1)	35,4 (4,6)	45,7 (32,5)	1,68 (1,00)
No obesidad RFM	51786	25,0 (17,4)	34,0 (5,3)	29,4 (3,6)	21,7 (16,0)	0,76 (0,88)
Obesidad RFM	31816	63,5 (21,9)	41,4 (6,4)	36,3 (5,0)	53,1 (34,5)	1,74 (1,04)
Normal Deuremberg	14750	12,4 (8,5)	30,5 (4,1)	26,1 (2,4)	14,9 (10,8)	0,26 (0,49)
Sobrepeso Deuremberg	25668	26,1 (15,6)	34,3 (4,6)	29,6 (2,6)	23,7 (16,8)	0,59 (0,71)
Obesidad Deuremberg	43184	57,1 (23,5)	40,4 (6,3)	35,5 (4,7)	46,0 (33,1)	1,76 (0,97)

FLI Fatty liver index. HSI Hepatic steatosis index. FLD Fatty liver disease. LAP Lipid accumulation product. IMC Índice de masa corporal. CUN BAE Clínica Universitaria de Navarra Body Adiposity Estimator. RFM Relative Fat Mass. En todos los casos las diferencias observadas con todas las variables son estadísticamente significativas p<0.0001

Algo similar a lo observado para los valores medios se aprecia con la prevalencia de valores de alto riesgo de las escalas de hígado graso no alcohólico y fibrosis hepática, es decir se incrementa la prevalencia a medida que aumenta la edad, a medida que descendemos en la clase social y cuando se incrementan los valores de las escalas de sobrepeso-obesidad. Esta situación se observa tanto en hombres como en mujeres y en ambos las diferencias observadas son estadísticamente significativas en todos los casos (ver **tablas III a** y **III b**).

Destacan las muy altas correlaciones siguiendo la escala de Landis y Koch[15] de FLI con FLD (0,864) y LAP (0,809) y de HSI con FLD (0,928). También hay alta correlación entre FLI con HSI (0,712) y BARD score (0,731), entre FLD con BARD score (0,669) y LAP (0,681) y entre BARD score y LAP (0,617). Todos los datos se muestran en la **tabla IV**.

Los más altos niveles de concordancia se aprecian entre FLI con LAP y BARD score. (ver **tabla V**)

Tabla III a: Prevalencia de valores altos de las diferentes escalas de hígado graso y fibrosis hepática según variables sociodemográficas y escalas de sobrepeso-obesidad en mujeres.

Mujeres	n	FLI alto % (95% CI)	HSI alto % (95% CI)	FLD alto % (95% CI)	LAP alto % (95% CI)	BARD score alto % (95% CI)
18-29 años	12180	5.6 (5.5-5.7)	32.5 (32.4-32.6)	34.7 (34.6-34.8)	20.1 (20.0-20.2)	3.4 (3.3-3.5)
30-39 años	18126	8.3 (7.9-8.7)	40.6 (40.2-41.0)	39.9 (39.5-40.3)	25.6 (25.1-26.0)	5.7 (5.3-6.1)
40-49 años	20082	8.7 (8.3-9.1)	47.5 (47.1-47.9)	48.2 (47.8-48.6)	29.4 (29.0-29.8)	7.5 (7.1-7.9)
50-59 años	10516	11.8 (11.2-12.4)	57.4 (56.8-58.0)	54.0 (53.4-54.6)	37.9 (37.3-38.5)	48.6 (48.0-49.2)
60-79 años	1812	12.0 (10.9-13.1)	62.9 (61.8-64.0)	60.7 (59.6-61.8)	39.8 (38.7-40.9)	52.2 (51.1-53.3)
Clase social I	4696	4.1 (3.3-4.9)	30.2 (29.4-31.0)	37.2 (36.4-38.0)	16.1 (15.3-16.9)	7.7 (6.9-8.5)
Clase social II	12856	6.7 (6.2-7.2)	40.7 (40.2-41.2)	42.5 (40.0-41.0)	23.1 (22.6-23.6)	11.8 (11.3-12.3)
Clase social III	45164	9.6 (9.5-9.7)	47.4 (47.3-47.5)	45.8 (45.7-45.9)	30.9 (30.8-31.0)	15.8 (15.7-15.9)
Cintura/altura <0.50	48088	0.3 (0.2-0.4)	30.1 (30.0-30.2)	43.1 (43.0-43.2)	12.1 (12.0-12.2)	7.9 (7.8-8.0)
Cintura/altura ≥ 0.50	14628	35.9 (35.4-36.4)	92.9 (92.4-93.4)	49.2 (48.7-49.7)	81.2 (80.7-81.7)	35.6 (35.1-36.1)
Bajo peso IMC	1896	0.0 (0.0-0.0)	0.8 (0.4-1.2)	0.2 (0.1-0.4)	0.1 (0.0-0.2)	1.3 (0.5-2.2)
Normopeso IMC	30722	0.0 (0.0-0.0)	12.6 (12.4-12.8)	18.9 (18.7-19.1)	4.4 (4.2-4.6)	2.6 (2.4-2.8)
Sobrepeso IMC	18060	0.7 (0.3-1.1)	67.3 (66.9-67.7)	37.4 (37.0-37.8)	34.3 (33.9-34.7)	17.0 (16.6-17.4)
Obesidad IMC	12038	43.6 (43.1-44.1)	99.7 (98.5-100.0)	97.4 (96.9-97.9)	84.3 (83.8-84.8)	42.6 (42.1-43.1)
Normal CUN BAE	13682	0.0 (0.0-0.0)	3.8 (3.3-4.3)	1.7 (1.2-2.2)	2.3 (1.8-2.8)	0.5 (0.3-0.8)
Sobrepeso CUN BAE	16328	0.0 (0.0-0.0)	16.4 (15.9-16.9)	26.5 (26.0-27.0)	5.9 (5.4-6.4)	2.3 (1.8-2.8)
Obesidad CUN BAE	32706	16.4 (6.2-16.6)	76.0 (75.8-76.2)	71.4 (71.2-71.6)	50.2 (50.0-50.4)	26.2 (26.0-26.4)
No obesidad RFM	32110	0.0 (0.0-0.0)	18.4 (18.2-18.6)	29.2 (29.0-29.4)	3.2 (3.0-3.4)	3.9 (3.7-4.1)
Obesidad RFM	30606	17.6 (17.4-17.8)	72.4 (72.2-72.6)	60.6 (60.4-60.8)	54.5 (54.3-54.7)	25.3 (25.1-25.5)
Normal Deuremberg	3582	0.0 (0.0-0.0)	1.6 (0.6-2.6)	0.4 (0.1-0.9)	1.9 (0.9-2.9)	0.3 (0.0-0.7)
Sobrepeso Deuremberg	13836	0.0 (0.0-0.0)	7.3 (6.8-7.8)	7.5 (7.0-8.0)	2.7 (2.2-3.2)	0.2 (0.0-0.5)
Obesidad Deuremberg	45298	11.9 (11.8-12.0)	59.6 (59.5-59.7)	59.3 (59.2-59.4)	38.1 (38.0-38.3)	19.8 (19.7-19.9)

FLI Fatty liver index. HSI Hepatic steatosis index. FLD Fatty liver disease. LAP Lipid accumulation product. IMC Índice de masa corporal. CUN BAE Clínica Universitaria de Navarra Body Adiposity Estimator. RFM Relative Fat Mass. En todos los casos las diferencias observadas con todas las variables son estadísticamente significativas p<0.0001

Tabla III b: Prevalencia de valores altos de las diferentes escalas de hígado graso y fibrosis hepática según variables sociodemográficas y escalas de sobrepeso-obesidad en hombres.

Hombres	n	FLI alto % (95% CI)	HSI alto % (95% CI)	FLD alto % (95% CI)	LAP alto % (95% CI)	BARD score alto % (95% CI)
18-29 años	12004	12.9 (12.5-13.3)	33.9 (33.4-34.4)	48.5 (48.0-49.0)	13.6 (13.1-14.1)	24.3 (23.8-24.8)
30-39 años	22274	21.5 (21.1-21.9)	45.8 (45.4-46.2)	59.9 (59.5-60.4)	21.0 (20.5-21.5)	37.5 (37.0-38.0)
40-49 años	28128	29.0 (28.6-29.4)	53.6 (53.2-54.0)	64.6 (64.2-65.0)	28.9 (28.5-29.3)	45.6 (45.2-46.0)
50-59 años	17970	31.6 (31.1-32.1)	56.3 (55.8-56.8)	65.1 (64.6-65.6)	65.1 (64.6-65.6)	49.2 (48.7-49.7)
60-79 años	3226	31.9 (30.9-32.9)	59.1 (58.1-60.1)	67.3 (66.3-68.3)	65.7 (64,7-66.7)	49.5 (48.5-50.5)
Clase social I	5082	22.3 (21.5-23.1)	49.4 (48.6-50.2)	64.9 (64.1-65.7)	32.4 (31.6-33.2)	38.0 (37.7-38.8)
Clase social II	12158	23.8 (23.3-24.3)	51.2 (50.7-51.7)	66.3 (65.8-66.8)	34.7 (34.2-35.2)	41.9 (41.4-42.4)
Clase social III	66362	25.8 (25.7-26.0)	49.2 (48.1-49.3)	58.6 (58.5-58.7)	33.7 (33.6-33.8)	41.5 (41.4-41.6)
Cintura/altura <0.50	45802	3.9 (3.8-4.0)	27.0 (26.9-27.1)	60.7 (60.6-60.8)	17.0 (16.9-17.1)	16.3 (16.2-16.4)
Cintura/altura ≥ 0.50	37800	51.3 (51.0-51.6)	76.7 (76.4-77.0)	62.0 (61.7-62.3)	54.0 (53.7-54.3)	71.6 (71.3-71.9)
Bajo peso IMC	624	0.0 (0,0-0.0)	0.3 (0.0-0.9)	0.0 (0,0-0.0)	3.5 (2.0-5.0)	1.0 (0.1-3.2)
Normopeso IMC	29986	0.9 (0.6-1.2)	11.7 (11.4-12.0)	39.5 (39.2-39.8)	9.3 (9.0-9.6)	10.5 (10.2-10.8)
Sobrepeso IMC	35834	18.4 (18.1-18.7)	58.5 (58.2-58.8)	41.7 (41.4-42.0)	34.3 (34.0-34.6)	46.6 (46.3-46.9)
Obesidad IMC	17158	83.3 (82.8-83.8)	98.6 (98.1-99.1)	95.2 (94.7-95.7)	76.4 (75.9-76.9)	85.6 (85.1-86.1)
Normal CUN BAE	14054	0.1 (0.0-0.9)	5.8 (5.3-6.3)	11.7 (11.2-12.2)	3.5 (3.0-4.0)	5.4 (4.9-5.9)
Sobrepeso CUN BAE	23876	2.4 (2.0-2.8)	22.4 (22.0-22.8)	70.6 (70.2-71.0)	11.0 (10.6-11.4)	19.8 (19.4-20.2)
Obesidad CUN BAE	45672	45.1 (44.9-45.3)	77.1 (76.9-77-3)	72.6 (72.4-72.8)	55.0 (54.8-55.2)	63.6 (63.4-63.8)
No obesidad RFM	51786	5.3 (5.2-5.4)	29.8 (29.7-30.0)	59.2 (59.1-59.3)	19.0 (18.9-19.1)	19.5 (19.4-19.6)
Obesidad RFM	31816	58.0 (57.7-58.3)	81.5 (81.2-81.8)	62.6 (62.3-62.9)	57.9 (57.6-58.2)	76.8 (76.5-77.1)
Normal Deuremberg	14750	0.2 (0.0-0.8)	7.7 (7.2-8.2)	20.6 (20.1-21.1)	2.4 (1.9-2.9)	6.2 (57.7-6.7)
Sobrepeso Deuremberg	25668	4.1 (3.7-4.5)	28.2 (27.8-28.6)	68.2 (67.8-68.6)	11.1 (10.7-11.5)	23.7 (23.3-24.1)
Obesidad Deuremberg	43184	46.5 (46.3-46.7)	76.4 (76.2-76.6)	73.0 (72.8-73.2)	57.9 (57.7-58.1)	63.8 (63.6-64.0)

FLI Fatty liver index. HSI Hepatic steatosis index. FLD Fatty liver disease. LAP Lipid accumulation product. IMC Índice de masa corporal. CUN BAE Clínica Universitaria de Navarra Body Adiposity Estimator. RFM Relative Fat Mass. En todos los casos las diferencias observadas con todas las variables son estadísticamente significativas p<0.0001

Destacan las muy altas correlaciones siguiendo la escala de Landis y Koch[15] de FLI con FLD (0,864) y LAP (0,809) y de HSI con FLD (0,928). También hay alta correlación entre FLI con HSI (0,712) y BARD score (0,731), entre FLD con BARD score (0,669) y LAP (0,681) y entre BARD score y LAP (0,617). Todos los datos se muestran en la **tabla IV**. Los más altos niveles de concordancia se aprecian entre FLI con LAP y BARD score. (ver **tabla V**)

En la **tabla VI** y **figuras 3a** y **3b** se muestran las diferentes curvas ROC de las escalas de hígado graso no alcohólico y fibrosis hepática en relación con las escalas de sobrepeso y obesidad. Destacamos las importantes áreas debajo de la curva del FLI, especialmente en mujeres. También son muy elevadas estas áreas para HSI y LAP. Los menores valores se aprecian para FLD.

Tabla IV: Coeficiente de correlación de Pearson de las diferentes escalas de hígado graso no alcohólico y fibrosis hepática.

	FLI	HSI	FLD	BARD score	LAP
FLI	1	0,712	0,864	0,731	0,809
HSI		1	0,928	0,587	0,513
FLD			1	0,669	0,681
BARD score				1	0,617
LAP					1

Tabla V: Concordancia de las diferentes escalas de hígado graso no alcohólico y fibrosis hepática empleando el índice Kappa de Cohen.

	FLI	HSI	FLD	BARD score	LAP
FLI	1	0.350	0.130	0.532	0.524
HSI		1	0.273	0.458	0.401
FLD			1	0.086	0.025
LAP				1	0.471
BARD score					1

Tabla VI: Curvas ROC de las diferentes escalas de hígado graso no alcohólico y fibrosis hepática.

Mujeres	FLI Área (IC 95%)	HSI Área (IC 95%)	FLD Área (IC 95%)	LAP Área (IC 95%)	BARD score Área (IC 95%)
IMC	0,981 (0,980-0,983)	0,929 (0,927-0,931)	0,762 (0,758-0,766)	0,899 (0,896-0,901)	0,840 (0,835-0,844)
Cintura/altura	0,972 (0,971.0,974)	0,852 (0,849-0,855)	0,654 (0,650-0,658)	0,924 (0,922-0,926)	0,788 (0,783-0,792)
CUN BAE	0,982 (0,981.0,983)	0,926 (0,924-0,928)	0,753 (0,749-0,758)	0,898 (0,895-0,901)	0,870 (0,867-0,873)
RFM	0,973 (0,971-0,974)	0,853 (0,850-0,856)	0,655 (0,651-0,660)	0,925 (0,923-0,927)	0,789 (0,784-0,793)
Deuremberg	0,976 (0,974-0,977)	0,910 (0,907-0,912)	0,733 (0,729-0,738)	0,886 (0,883-0,889)	0,892 (0,889-0,895)
Hombres	**Área (IC 95%)**	**Área (IC 95%)**	**Área (IC 95%)**	**Área (IC 95%)**	**Área (IC 95%)**
IMC	0,934 (0,932-0,935)	0,904 (0,902-0,906)	0,584 (0,579-0,589)	0,842 (0,839-0,844)	0,837 (0,834-0,840)
Cintura/altura	0,908 (0,906-0,910)	0,823 (0,820-0,825)	0,522 (0,518-0,527)	0,866 (0,863-0,868)	0,764 (0,760-0,767)
CUN BAE	0,932 (0,931-0,934)	0,896 (0,894-0,898)	0,577 (0,572-0,582)	0,840 (0,838-0,843)	0,863 (0,861-0,866)
RFM	0,909 (0,907-0,911)	0,823 (0,821-0,826)	0,522 (0,518-0,527)	0,867 (0,864-0,869)	0,765 (0,761-0,768)
Deuremberg	0,914 (0,912-0,916)	0,869 (0,867-0,871)	0,566 (0,561-0,571)	0,824 (0,821-0,827)	0,873 (0,871-0,876)

FLI Fatty liver index. HSI Hepatic steatosis index. FLD Fatty liver disease. LAP Lipid accumulation product. IMC Índice de masa corporal. CUN BAE Clínica Universitaria de Navarra Body Adiposity Estimator. RFM Relative Fat Mass.

Figura 3 a: Curva ROC en mujeres.

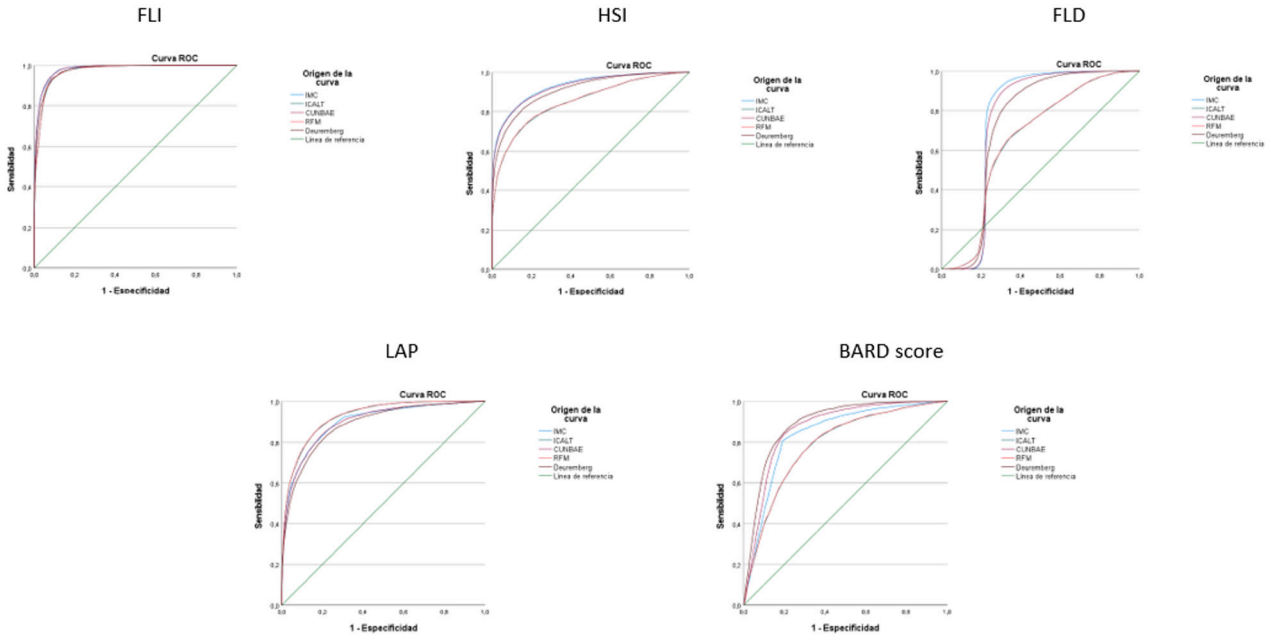
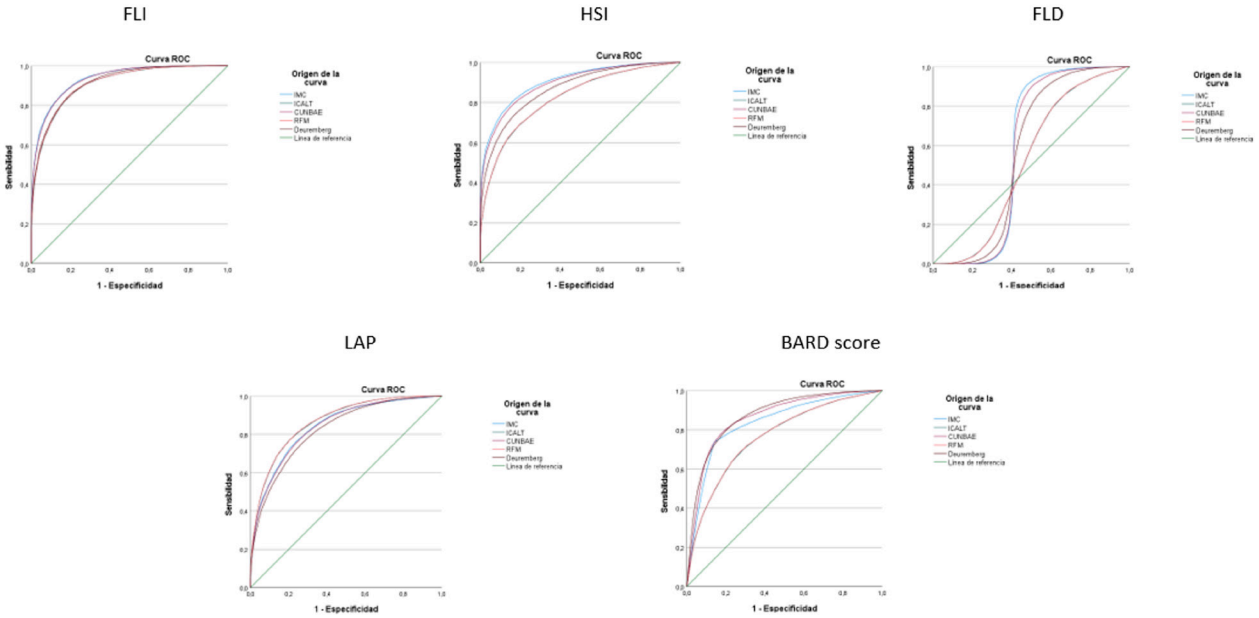


Figura 3 b: Curva ROC en hombres.



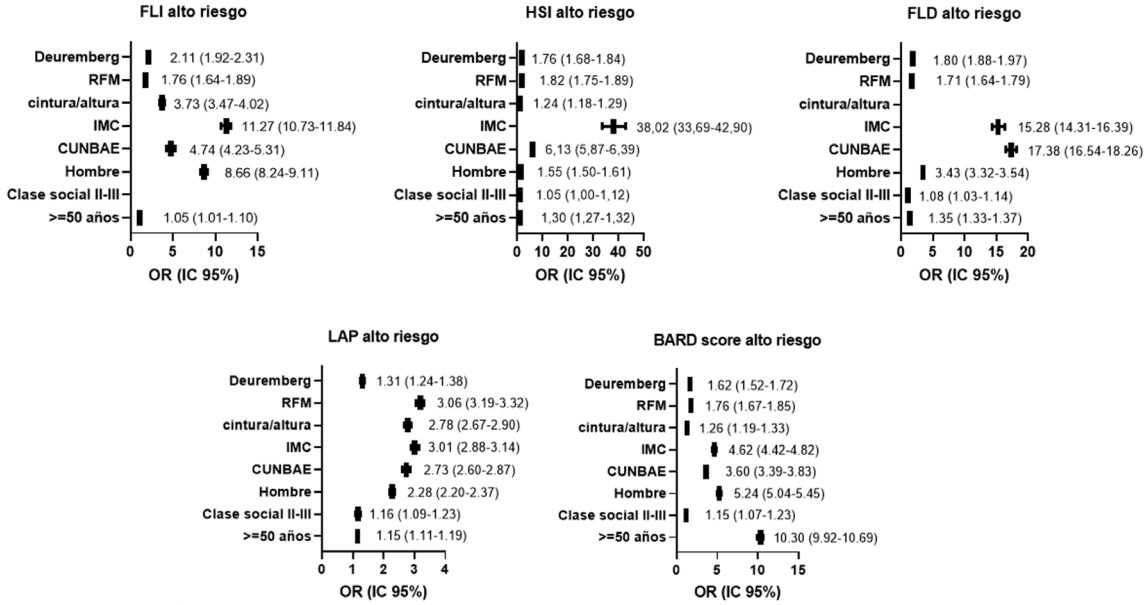
En la **tabla VII** se muestran los puntos de corte de las diferentes escalas de sobrepeso-obesidad para predecir la aparición de valores de alto riesgo de las escalas de hígado graso no alcohólico y fibrosis hepática. Los valores más elevados de sensibilidad, especificidad e índice Youden se aprecian con el FLI y especialmente en mujeres. Los valores más bajos se encuentran por el contrario para el FLD.

Tabla VII: Puntos de corte, sensibilidad, especificidad e índice Youden de escalas de sobrepeso y obesidad para cada una de las escalas de hígado graso no alcohólico y fibrosis hepática por sexo.

Mujeres	FLI alto Pcorte-Sen-Especif-Youden	HSI alto Pcorte-Sen-Especif-Youden	FLD alto Pcorte-Sen-Especif-Youden	LAP alto Pcorte-Sen-Especif-Youden	BARD score alto Pcorte-Sen-Especif-Youden
IMC	31,2-92,6-92,6-0,852	25,2-84,7-84,6-0,693	25,1-77,2-77,1-0,543	26,6-81,7-81,4-0,631	27,8-81,3-79,9-0,612
Cintura/altura	0,52-94,8-89,0-0,838	0,46-78,7-75,9-0,549	0,46-66,1-65,6-0,317	0,48-85,2-83,5-0,687	0,48-75,1-70,3-0,454
CUN BAE	43,9-93,0-92,9-0,859	36,0-84,8-84,1-0,689	36,0-76,0-75,9-0,519	38,0-82,0-81,7-0,637	40,0-82,2-81,4-0,636
RFM	38,2-92,9-91,7-0,846	32,2-77,9-77,8-0,559	32,0-66,1-65,6-0,317	34,0-84,4-84,3-0,687	34,0-73,8-71,8-0,456
Deuremberg	42,0-91,9-91,8-0,837	34,4-82,7-82,4-0,651	34,3-73,0-72,9-0,459	36,3-80,6-80,5-0,611	38,5-82,3-82,1-0,644
Hombres	**Pcorte-Sen-Especif-Youden**	**Pcorte-Sen-Especif-Youden**	**Pcorte-Sen-Especif-Youden**	**Pcorte-Sen-Especif-Youden**	**Pcorte-Sen-Especif-Youden**
IMC	28,1-85,6-84,4-0,700	26,3-82,3-80,7-0,630	26,0-60,0-58,9-0,189	26,7-76,4-75,9-0,523	27,2-78,7-78,0-0,567
Cintura/altura	0,51-85,8-80,2-0,660	0,51-76,8-76,7-0,535	0,49-0,60-0,50-0,104	0,50-79,2-77,1-0,563	0,51-70,6-70,4-0,410
CUN BAE	28,4-85,0-84,7-0,697	25,7-81,6-80,7-0,627	25,2-60,7-58,7-0,194	26,4-75,9-75,8-0,517	27,2-80,2-80,0-0,602
RFM	25,5-83,1-82,5-0,656	23,5-75,0-73,1-0,481	23,2-53,1-52,7-0,058	24,2-78,3-78,2-0,565	24,4-70,6-70,4-0,410
Deuremberg	27,8-82,6-82,5-0,651	25,3-78,3-78,0-0,563	25,0-57,9-52,7-0,154	25,8-74,4-74,0-0,484	26,7-80,0-79,6-0,596

Pcorte-Sen-Especif-Youden. Punto de corte, sensibilidad, especificidad, índice Youden. FLI Fatty liver index. HSI Hepatic steatosis index. FLD Fatty liver disease. LAP Lipid accumulation product. IMC Índice de masa corporal. CUN BAE Clínica Universitaria de Navarra Body Adiposity Estimator. RFM Relative Fat Mass.

Figura 4: Análisis multivariante mediante regresión logística binaria con el modelo Wald.



Discusión

En nuestro estudio se observa que los valores de todas las escalas que valoran el hígado graso no alcohólico y la fibrosis hepática presentan cifras más elevadas a medida que se incrementa la edad y a medida que se desciende en la escala social. Igualmente se aprecian valores más elevados de estas escalas en los varones y a medida que se incrementan las cifras de escalas que determinan sobrepeso y obesidad.

En nuestro estudio las personas con un nivel socioeconómico más bajo presentan una prevalencia de riesgo alto tanto de hígado graso como de fibrosis hepática mayor que aquellas personas con un estatus socioeconómico más favorable. Estos datos coinciden con los encontrados por Guoyu et al[16] en población china y por Das et al en población India[17].

Nuestro trabajo muestra que la prevalencia de riesgo alto de hígado graso y fibrosis hepática se va incrementando con la edad, estos datos coinciden con los obtenidos en una reciente revisión sistemática realizada en Japón[18].

Esta misma revisión mostró, al igual que nosotros, que la prevalencia de estas alteraciones hepáticas es mayor en los hombres y concluyó que la prevalencia de EHGNA es mayor en los hombres que en las mujeres premenopáusicas, mientras que lo contrario es cierto después de la menopausia. Por lo tanto, antes de la menopausia, el estrógeno puede tener efectos protectores contra la EHGNA.

La mayoría de estudios[19-23] consultados coinciden con nosotros en el incremento de la prevalencia de hígado graso y fibrosis hepática en las personas con obesidad mostrando que hasta el 80% de los pacientes con EHGNA son obesos, definidos como un índice de masa corporal (IMC) > 30 kg/m(2). Sin embargo, la distribución del tejido graso juega un papel más importante que el IMC. La gran cantidad de tejido adiposo visceral en individuos con obesidad mórbida (IMC > 40 kg/m(2)) contribuye a una alta prevalencia de EHGNA.

Como puntos fuertes del estudio tenemos el elevado tamaño muestral, más de 146000 personas, la gran cantidad de escalas de hígado graso no alcohólico y fibrosis hepática analizadas, en concreto 5, y la diversidad de escalas de sobrepeso y obesidad tenidas en cuenta, otras 5.

Como limitaciones podemos indicar que no se han empleado instrumentos objetivos de medida para evaluar el hígado graso no alcohólico y fibrosis hepática sino escalas validadas de riesgo.

Conclusiones

El hígado graso no alcohólico y la fibrosis hepática determinadas mediante escalas de riesgo en población española se ven influenciadas por diferentes variables sociodemográficas (edad, sexo y clase social) y por el exceso de peso y grasa corporal.

Conflicto de intereses

Los autores del manuscrito declaran que no existe ningún tipo de conflicto de intereses.

Bibliografía

1. Wahlang B, Beier JI, Clair HB, Bellis-Jones HJ, Falkner KC, McClain CJ, et al. Toxicant-associated steatohepatitis. Toxicol Pathol. 2013;41(2):343-60.

2. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatol Baltim Med. 2016;64(1):73-84.

3. Tapper EB, Parikh ND. Mortality due to cirrhosis and liver cancer in the United States, 1999-2016: observational study. BMJ. 2018 Jul 18;362:k2817.

4. Luengo Pérez LM , Juan Manuel Urbano Gálvez JM, Pérez Miranda M. Validación de índices antropométricos alternativos como marcadores del riesgo cardiovascular. Endocrinol Nutr. 2009;56(9):439-46

5. Gómez-Ambrosi J. Silva C. Catalán V. Rodríguez A. Galofré JC. Escalada J. et al. Clinical usefulness of a new equation for estimating body fat. Diabetes Care 2012;35(2):383-8.

6. Deurenberg P. Wetstrate JA. Seidell JC. Body mass index as a measure of body fatness: age- and sex- specific prediction formulas. Br J Nutr 1991; 65: 105-14.

7. Woolcott OO. Bergman RN. Relative fat mass (RFM) as anew estimator of whole-body fat percentage-A cross-sectional study in American adults individuals. Sci Rep. 2018;8(1):10980.

8. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, et al. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol. 2006; 6:33.

9. Lee JH, Kim D, Kim HJ, Lee CH, Yang JI, Kim W, et al. Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. Dig Liver Dis. 2010 ;42(7):503-8.

10. Fuyan S, Jing L, Wenjun C, Zhijun T, Weijing M, Suzhen W, et al. Fatty liver disease index: a simple screening tool to facilitate diagnosis of nonalcoholic fatty liver disease in the Chinese population. Dig Dis Sci. 2013;58(11):3326-34

11. Chiang JK, Koo M. Lipid accumulation product: a simple and accurate index for predicting metabolic syndrome in Taiwanese people aged 50 and over. BMC Cardiovasc Disord. 2012; 12:78

12. Raszeja-Wyszomirska J, Szymanik B, Ławniczak M, Kajor M, Chwist A, Milkiewicz P. Validation of the BARD scoring system in Polish patients with nonalcoholic fatty liver disease (NAFLD). BMC Gastroenterol. 2010 Jun 28;10:67.

13. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010;33(Suppl 1):S62-9.

14. Domingo-Salvany A, Bacigalupe A, Carrasco JM, Espelt A, Ferrando J, Borrell C. Propuesta de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011. Gac Sanit 2013;27(3):263-72

15. Landis J, Koch G: The measurement of observer agreement for categorical data. Biometrics 1977; 33:159-74.

16. Jia G, Li X, Wang L, Li Q, Yang L, Li N, et al. Relationship of socioeconomic status and non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus. Zhonghua Gan Zang Bing Za Zhi. 2015 Oct;23(10):760-4.

17. Das K, Mukherjee PS, Ghosh A, Ghosh S, Mridha AR, Dhibar T, et al. Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease. Hepatology. 2010 May;51(5):1593-602.

18. Tobari M, Hashimoto E. Characteristic Features of Nonalcoholic Fatty Liver Disease in Japan with a Focus on the Roles of Age, Sex and Body Mass Index. Gut Liver. 2020 Sep 15;14(5):537-45.

19. Milić S, Lulić D, Štimac D. Non-alcoholic fatty liver disease and obesity: biochemical, metabolic and clinical presentations. World J Gastroenterol. 2014 Jul 28;20(28):9330-7.

20. Ooi GJ, Burton PR, Bayliss J, Raajendiran A, Earnest A, Laurie C, et al. Effect of Body Mass Index, Metabolic Health and Adipose Tissue Inflammation on the Severity of Non-alcoholic Fatty Liver Disease in Bariatric Surgical Patients: a Prospective Study. Obes Surg. 2019 Jan;29(1):99-108.

21. Praveenraj P, Gomes RM, Kumar S, Karthikeyan P, Shankar A, Parthasarathi R, et al. Prevalence and Predictors of Non-Alcoholic Fatty Liver Disease in Morbidly Obese South Indian Patients Undergoing Bariatric Surgery. Obes Surg. 2015 Nov;25(11):2078-87.

22. Qureshi K, Abrams GA. Prevalence of biopsy-proven non-alcoholic fatty liver disease in severely obese subjects without metabolic syndrome. Clin Obes. 2016 Apr;6(2):117-23.

23. Caro-Sabido EA, Larrosa-Haro A. Efficacy of dietary intervention and physical activity in children and adolescents with nonalcoholic fatty liver disease associated with obesity: A scoping review. Rev Gastroenterol Mex (Engl Ed). 2019 Apr-Jun;84(2):185-94.

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ORIGINAL

Acute hypoglycemic and hypotensive effect of continuous and intermittent aerobic exercise in patients with type 2 diabetes

Efecto hipoglucemiante e hipotensor agudo del ejercicio aeróbico continuo e intermitente en pacientes con diabetes tipo 2

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Abstract

Objectives: Different modes of exercise could bring diverse acute responses. This study aimed to investigate the acute hypoglycemic and hypotensive effect to continuous and intermittent aerobic exercise in patients with type 2 diabetes (T2DM).
Methods: This study included one session of continuous jogging, one session of intermittent fast running, and one time of rest, which was defined as continuous group, intermittent group and control group respectively. The experiments were randomly carried out in three days with an interval of at least 72 hours between each two experimental days. Fifteen patients participated in a bout of 2 km continuous jogging, 2 km intermittent fast running, or no exercise (control) on three days with an interval of 72 h or more. Blood glucose, blood pressure (BP), and Physical Activity Enjoyment Scale (PACES) were measured.
Results: All the participants completed the study with no adverse event. Blood glucose was significant lower at post in two exercise groups ($p < 0.05$) and at 2 h post intermittent exercise than in control. Continuous and intermittent exercise significantly reduced systolic BP (by ~ 4.27 and 13.27 mmHg) and diastolic BP (by ~5.40 and 1.07 mmHg) ($p \leq 0.001$). Whereas, only intermittent exercise brought remarkably smaller pulse pressure (dropped by ~12.20 mmHg). Additionally, intermittent exercise yielded higher PACES score ($p < 0.01$).
Conclusions: Intermittent aerobic exercise produces slightly stronger acute hypoglycemic and remarkably stronger hypotensive effect than continuous exercise in patients with T2DM. Together with the better enjoyment feelings, intermittent exercise is worth to be recommended for patients with T2DM.

Key words: Blood glucose, blood pressure, aerobic exercise, type 2 diabetes.

Resumen

Objetivos: Los diferentes modos de ejercicio pueden aportar diversas respuestas agudas. Este estudio tiene como objetivo investigar el efecto hipoglucémico e hipotensor agudo al ejercicio aeróbico continuo e intermitente en pacientes con diabetes tipo 2 (T2DM).
Métodos: Este estudio incluyó una sesión de trote continuo, una sesión de carrera rápida intermitente y un tiempo de descanso, que se definieron como grupo continuo, grupo intermitente y grupo control respectivamente. Los experimentos se realizaron aleatoriamente en tres días con un intervalo de al menos 72 horas entre cada dos días experimentales. Quince pacientes participaron en una tanda de 2 km de trote continuo, 2 km de carrera rápida intermitente o ningún ejercicio (control) en tres días con un intervalo de 72 h o más. Se midieron la glucosa en sangre, la presión arterial (PA) y la escala de disfrute de la actividad física (PACES).
Resultados: Todos los participantes completaron el estudio sin ningún evento adverso. La glucosa en sangre fue significativamente más baja en los dos grupos de ejercicio ($p < 0,05$) y a las 2 h del ejercicio intermitente que en el control. El ejercicio continuo e intermitente redujo significativamente la PA sistólica (en ~ 4,27 y 13,27 mmHg) y la PA diastólica (en ~ 5,40 y 1,07 mmHg) ($p \leq 0,001$). En cambio, sólo el ejercicio intermitente aportó una presión de pulso notablemente menor (se redujo en ~12,20 mmHg). Además, el ejercicio intermitente produjo una mayor puntuación de PACES ($p < 0,01$).
Conclusiones: El ejercicio aeróbico intermitente produce un efecto hipoglucemiante agudo ligeramente más fuerte y un efecto hipotensor notablemente más fuerte que el ejercicio continuo en pacientes con DMT2. Junto con la mejor sensación de disfrute, el ejercicio intermitente merece ser recomendado para los pacientes con DMT2.

Palabras clave: Glucemia, presión arterial, ejercicio aeróbico, diabetes tipo 2.

Introduction

Type 2 diabetes is a metabolic disorder characterized by chronic hyperglycemia caused by insulin secretion defects and/or insulin resistance, which has become one the most pressing and prevalent issue of worldwide. The deteriorating glycemic control lead to adverse heath outcomes and multisystem complications[1], including impairments with cardiovascular system. The presence of diabetes increases the mortality risk from cardiovascular diseases (CVDs) across different ethnicity groups and sex[2].

As one of the basic therapies for T2DM, exercise can improve glycemic metabolism, confer wide-ranging health benefits, and delay the progress of disease. However, the optimal exercise style, intensity and duration, etc. were not fully discovered. Traditionally recommended exercise approaches usually include low to moderate intensity sustained physical activity. Continuous aerobic exercise is proven to be able to reduce blood glucose, decrease blood pressure, and improve lipid profile by increasing heat consumption, elevating muscle glycogen content, regulating neuroendocrine and reducing insulin resistance[3-5]. However, recent research has shown that high-intensity interval training (HIIT) can promote improvements in glucose control and cardiovascular health in individuals with T2DM[6]. Compared with continuous exercise, there are studies demonstrating that intermittent aerobic exercise has better effect in improving body composition, blood glucose and energy consumption and oxygen consumption[7-9]. Studies have found that intermittent fast running can quickly improve glucose metabolism and prolong insulin sensitivity6. Meanwhile, it positively affects the metabolic system of patients and improve their cardiopulmonary adaptability[10].

Studies on intermittent exercise applied in T2DM treatment so far at present are insufficient, and only couple of studies compared the acute effect of intermittent and continuous exercises on glycometabolism and associated parameters in patients with T2DM. Santiago et al. examined the acute glycemia and pressure response of continuous and interval aerobic exercise in patients with T2DM[11]. However, some limitations make further studies are still necessary. Firstly, the subjects in Santiggo et al's study had a eight-week pre-training, thereby they were slightly trained instead of sedentary. The responses may be different in these people. Secondly, the study lack a control group (no exercise) which made it hard to differentiate the effects of exercise. Thirdly, the observation of glycemia was limited to 30 minutes after the end of exercise and longer time response was missed. Additionally, although pulse pressure has been shown to be an important predictor, better than systolic blood pressure, for the risk of CVDs in diabetes[12,13], it was missing in Santiggo's study.

The main purpose of the present study is to explore the acute hypoglycemic and hypotensive effect of continuous and intermittent aerobic exercise in patients with T2DM. Clarifying the role of single exercise in regulating blood glucose and blood pressure will help to enhance patients' confidence about the benefits of exercise to the health outcome and be helpful for appropriate, efficient and safe exercise prescription.

Material and methods

Subjects

Patients with T2DM in Department of Endocrinology at the Second People's Hospital of Changshu were recruited through convenience sampling. All participants were screened based on their health history and the American College of Sports Medicine guidelines to ensure their suitability and safety in participating exercise. Eligible participants were 18 to 65 years old and met the diagnostic criteria of T2DM in Guideline for Preventions and Treatment of Type 2 Diabetes in China (2013 Edition)[14]. Exclusion criteria include the patients who had any underlying complications unsuitable for exercise or could not tolerate moderate intensity exercise, including but not limiting to the diseases of heart, vascular, brain, kidney, eye, foot, nervous system, and malignant tumor; who had rest heart rate > 120 beats/min, rest blood pressure > 160/100 mmHg, or fasting blood glucose >16.7 mmol/L[15].

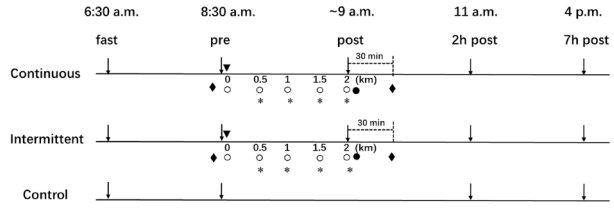
Fifteen qualified patients participated in this study. The study protocol was reviewed and approved by the Medical Ethics Committee of the Second People's Hospital of Changshu, and conducted in compliance with the guidelines stated in the World Medical Association (WMA) Declaration of Helsinki. All patients were fully informed orally and in writing of the nature of the study as well as the possible risks, and signed the informed consent.

Research design and procedure

This study included one session of continuous jogging, one session of intermittent fast running, and one time of rest, which was defined as continuous group, intermittent group and control group respectively. The experiments were randomly carried out in three days with an interval of at least 72 hours between each two experimental days. The experiment orders were defined as the following four kinds: 1. control—continuous—intermittent 2. control—intermittent—continuous 3. continuous—intermittent—control 4. intermittent—continuous—control. Four lots of each order were prepared and the subjects decided the experimental order by drawing lots. In the continuous and intermittent groups, patients had continuous and intermittent exercise respectively and in the control group the patients did not do any exercise training and maintain their usual daily activities.

All patients accepted the measurements of fasting blood glucose at fast (6.30 a.m.), and thereafter had the identical breakfast delivered by the Nutrition Department of the hospital. During the exercise day, the patients start to exercise at 8:30 a.m. Patients' blood glucose, the rate of perceived exertion (RPE), heart rate (HR), blood pressure (BP) and Physical Activity Enjoyment Scale (PACES) were measured at different time points. The measurement time points for each parameter were presented in **figure 1**.

Figure 1: Detection time points of each parameter.↓: blood glucose, ▼:: exercise start, ◆: blood pressure, ❍: heart rate, *: RPE, ●: Physical Activity Enjoyment Scale.



Exercise intervention

At 6 days before the first formal test day, the patients were asked to do 500 m running exercise once a day for 3 days as adaptational training. The running time and speed were not strictly prescribed, and it was specified that patients should keep their rating of perceived exertion (RPE) within 12~15 and the exercise should not bring over fatigue. In the 3 days before the first formal test, patients were required to rest without specially prescribed exercise.

For the formal test, the patients in the continuous group were required to continuously jog at a speed close to or reach a moderate degree of rating of perceived exertion (RPE) 12~15. According to the results of the pre-trial test, the exercise speed was set at 4-6 km/h, and the exercise time was expected to be 20-30 min. The patients were instructed to finish the jogging in the continuous exercise session and avoid fast walking.

In the intermittent exercise session, patients were required to run at a preset speed of 6-8 km/h for 3 minutes and rested for 4 minutes and then completed the whole exercise process following this pattern. The total running time for the intermittent group was expected to be 15-20 minutes, and the total rest time 9-12 minutes, with a total experiment time being 24-32 minutes.

Research scientists were responsible for supervise exercise sessions. For the subjects whose jogging or running speed out of the specified range, they were reminded to speed up or down to meet the requirement. Both continuous and intermittent exercise sessions included warm-up and cool-down period. The warm-up consisted of 5 min of jogging and gentle stretching and the cool-down consisted of 5 min of walking and gentle stretching. Patients were asked to put on their jogging shoes and cotton socks during exercise. In the 2 h before exercise, patients were encouraged to consume 400~500 ml water to ensure the adequate hydration.

Measurements

Subjects' basic information, including age, sex, BMI, course of disease, and complication were asked or measured and recorded. Some blood biochemical indexes, were recorded from patients' current hospitalization medical record.

In the two exercise groups, patients put on a polar heart rate meter (FR1, Boneng company, Finnish) during exercise to continuously monitor the heart rate. The heart rate before exercise (HR-0), at 0.5 km (HR-0.5), 1 km (HR-1.0), 1.5 km (HR-1.5) and 2 km (HR-2.0) during exercise were recorded. Meanwhile, Borg rating of perceived exertion (RPE) was evaluated at every 500 m, thus the RPE scores at 0.5 km (RPE-0.5), 1 km (RPE-1.0), 1.5 km (RPE-1.5) and 2 km (RPE-2.0) were recorded respectively.

Fingertip blood glucose was tested in fast state (~6.30 a.m.), immediately before (pre, at 8.30 a.m.) and after exercise (post, ~9.10 a.m.), 2h and 7h post exercise (at ~11:00 a.m. and 4:00 p.m.). Blood glucose was detected by Ritter blood glucose meter (glucose peroxidase method, GM300, Daqing plant of Huaguang Biotechnology Co., Ltd., China) and corresponding reagent strips.

Blood pressure was measured before exercise (BP-0) and 30 minutes after exercise (BP-30) on left upper limb in supine position. Pulse pressure was calculated by systolic and diastolic blood pressure.

After exercise finished, patients were asked to fill in the PACES scores according to their own feelings. The PACES contains 18 items and each item is divided into 7 levels with a total score of 126. The higher the total score means the higher acceptance of the physical activity.

Safety consideration

Before exercise, the researchers provided exercise education for the patients, and helped to check the feet, shoes and socks of the patients. During exercise, all patients and researchers carried candy in case of hypoglycemia and water was accessible all the time. When the patient has dizziness, nausea, palpitations, chest pain and other discomfort, or the patient's self-reported exercise is beyond the tolerance range, extremely tired, unable or unwilling to continue exercise, the exercise would be stopped immediately. Medical doctors and nurses were responsible for supervise one-to-one the whole exercise process. The heath history investigation during screening, and the HR, RPE and BP monitored during exercise also ensure the safety.

Statistical analysis

Data were analyzed using SPSS 22.0 software (IBM, NY). Descriptive data are presented as mean ± standard deviation (SD). Differences of blood glucose at different time points among the three groups were analyzed using two factor repeated measurement analysis of variance, when needed, the Bonferroni *post hoc* was used. Paired t test was used to compare the difference of exercise execution, RPE, HR, blood pressure and PACES scores at the same monitoring points between the two exercise sessions. One way ANOVA was used to compare the differences of HR and RPE among different monitoring points in the exercise groups. If the data does not conform to the normal distribution, nonparametric test is used. $P < 0.05$ showed that the difference was statistically significant.

Results

1. General characteristics of subjects

Anthropometric and physiologic characteristics of the study patients (n = 15) are outlined in **table I**. In the 15 subjects (11 males, 4 females), 6 had hypertension, 1 fatty liver, 2 hepatitis B and 1 gastritis. All patients were treated with insulin, and 9 of them took additional oral hypoglycemic drugs.

Table I: Study population characteristics.

Variable	Mean ± SD	Range
Age (years)	48.87 ± 6.77	33-56
Body weight (kg)	72.07 ± 13.57	50-103
Height (cm)	167.53 ± 9.65	150-183
BMI (kg/m²)	25.33 ± 3.22	22-34
Course of disease (years)	5.53 ± 4.52	1-14
Glycosylated hemoglobin (%)	9.03 ± 2.65	5.1-16.4
C-peptide (ng/ml)	2.40 ± 1.05	1-4.82
Insulin (ng/ml)	6.64 ± 4.49	0.91-18.41
Triglyceride (mmol/L)	2.47 ± 2.57	0.75-11.1
Cholesterol (mmol/L)	4.76 ± 1.37	2.11-6.68

Values are mean ± SD

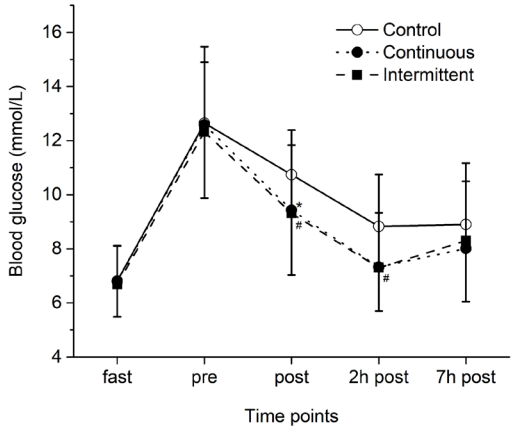
2. Exercise execution data and physical response of HR and RPE

There was no hypoglycemia (blood glucose < 3.9mmol/l) happened in the two groups at each time point in this study.

Patients in both exercise sessions finished a 2-km distance running or jogging. The speed in the intermittent group (7.25 ± 0.67 km/h) was significantly larger than that in the continuous group (6.06 ± 0.50 km/h) ($P < 0.001$). The running time was 19.53 ± 1.81 min and 16.40 ± 1.35 min in continuous and intermittent groups respectively and there was an additional intermittent rest time of 10.40 ± 1.55 min in the latter.

Heart rate of the patients during continuous and intermittent exercise were presented in **Figure 2**. There was no significant difference in the baseline heart rate (HR-0) between two exercise groups ($P > 0.05$). However, the heart rate during the whole period of exercise was significantly higher in the intermittent group than those in the continuous group ($P < 0.01$). Intra-group comparison showed, compared with HR-0, significantly higher HR-0.5, HR-1.0, HR-1.5 and HR-2.0 were found in both exercise groups ($P < 0.01$), whereas no significant difference among HR-0.5, HR-1.0, HR-1.5 and HR-2.0 in either group ($P > 0.05$) (**Figure 2**).

Figure 2: Blood glucose levels at different time points in the three experimental groups, $\bar{x}\pm S$. *: continuous group compared with control group, $P< 0.05$; #: intermittent group compared with control group, $P< 0.05$. To avoid confusion, the significance of intra-group comparison in each group were not marked.



Percentage of maximal heart rate (HRmax) which equals to (220-age) was calculated, and the values during continuous exercise session were more than 70% and during intermittent exercise more than 80% (**Table II**).

Table II: $\%HR_{max}$ at different time points of two exercise groups (%).

	Continuous group	Intermittent group	*t*	*P*
%HRmax-0	45.2 ± 3.7	45.6 ± 3.7	-1.580	0.136
%HRmax-0.5	71.6 ± 3.3	80.8 ± 3.7**	-12.198	<0.001
%HRmax-1.0	72.9 ± 3.4	81.4 ± 3.7**	-10.563	<0.001
%HRmax-1.5	73.4 ± 3.8	81.9 ± 3.8**	-10.975	<0.001
%HRmax-2.0	73.7 ± 3.8	82.5 ± 3.6**	-16.793	<0.001

**: compared with Continuous group, $P< 0.001$

There was no significant difference with RPE between the two exercise groups except for the larger RPE-0.5 in the intermittent group than that of continuous group ($P < 0.01$). Intra-group comparison, RPE increased with the extension of exercise time in both exercise groups, and the score at each time point was significantly higher than the previous one ($P < 0.01$) (**Table III**).

Table III: RPE scores during exercise in two exercise groups (points).

	Continuous group	Intermittent group	*t*	*P*
RPE-0.5	11.00 ± 1.00	12.73 ± 1.10**	-3.926	<0.001
RPE-1.0	13.73 ± 1.94	13.93 ± 1.62	-0.276	0.787
RPE-1.5	14.93 ± 2.12	15.00 ± 1.81	-0.098	0.923
RPE-2.0	16.87 ± 1.13	17.07 ± 1.03	-0.494	0.629

**: compared with Continuous group, $P< 0.001$.

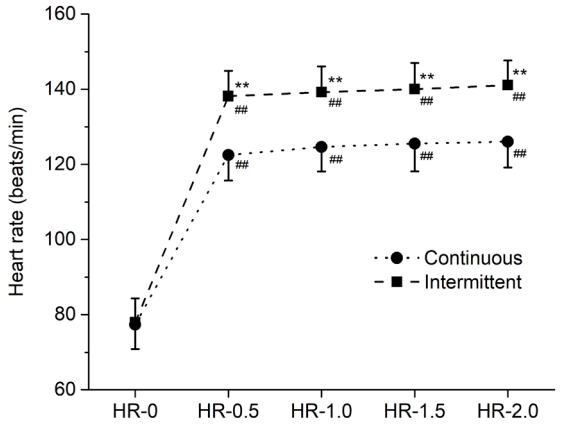
3. Blood glucose

The exercise x time interaction (P = 0.311) was not existed. Therefore, main effect of exercise and time were analyzed respectively. There was a significant main effect of exercise (P = 0.027) and of time (P < 0.001).

Pairwise comparison results showed that the intermittent exercise caused slightly lower blood glucose from control which close to be significant (P = 0.085), whereas the continuous exercise did not (P = 0.132). There was no significant difference of fasting, pre and 7h post blood glucose among the three groups (all P > 0.05); the post blood glucose of the two exercise groups was significantly lower than that of the control group (P =0.033 and 0.012, respectively); the 2h post blood glucose of the intermittent group was significantly lower than that of the control group (P = 0.040) (**Figure 3**).

Intra-group pairwise comparison found that blood glucose at pre and post were significantly increased compared with fasting blood glucose in all three groups (P < 0.01); 2h and 7h post blood glucose in the control group were significantly higher than fasting blood glucose (P < 0.01, P < 0.05); the 2h post blood glucose of continuous group and 7h post blood glucose of intermittent group were significantly higher than fasting blood glucose (P <0.05) (**Figure 3**).

Figure 3: HR at different time points of two exercise groups,$\bar{x}$±S. **: compared with continuous group, P< 0.01; ##: compared with HR-0 of the corresponding group, P< 0.01.



4. Blood pressure

Both SBP and DBP decreased significantly at 30 min after the exercise in two groups. SBP at 30 min (SBP-30) after intermittent group was lower than that of continuous group (P < 0.01), while DBP-30 was higher (P < 0.01). The pulse pressure became significantly smaller in intermittent group (dropped by ~12.20 mmHg, P < 0.01), whereas had no change in continuous group (**Table IV**).

5. PACES

PACES scores in the continuous and intermittent groups were 81.4 ± 1.84 and 92.7 ± 1.62 respectively and the latter was significantly higher than the former (P < 0.001).

Discussion

In this study, acute reduction response of glycemia and blood pressure to two different modes of exercise, continuous jogging and intermittent fast running, in patients with T2DM were explored. The results found that both continuous and intermittent aerobic exercise significantly decreased blood glucose and systolic and diastolic blood pressure levels. Moreover, intermittent exercise caused remarkably smaller pulse pressure whereas continuous exercise did not.

During exercise execution, the heart rate immediately after exercise in the continuous jogging group (73.7% ± 8.0% of HR_{max}) and the intermittent fast running group (82.5% ± 6.0% of HR_{max}) demonstrated that the exercise has reached moderate and high intensity respectively. RPE gradually increased with the extension of exercise time. Except for the higher value in intermittent exercise when running to 0.5 km, no difference in RPE scores between the two groups in the later period, suggesting that intermittent aerobic exercise did not lead to increased subjective exertion in the case of higher intensity. Through communication with patients, we learned that patients felt more difficult in the early stage of intermittent exercise because of the faster speed. However, in the middle and late stage during the continuous jogging, fatigue continued to increase, and some patients felt difficult to complete the prescribed distance without encouragement, whereas in the intermittent exercise, due to recovery of physical vigor after a short rest period, subject felt easier to complete the whole distance. Guiraud et al.[16] showed that, when healthy young people were trained with intermittent exercise and continuous exercise with same energy consumption, the RPE score during the intermittent exercise was lower, and it was easier to accept this kind of exercise. Although there was no significant difference in the final RPE score in this study, from communication

Table IV: BP before and 30 minutes after exercise in two exercise groups (mmHg)

	SBP-0	SBP-30	DBP-0	DBP-30	Pulse pressure-0	Pulse-pressure-30
Continuous	125.6±10.82	120.2±10.06#	75.3±8.61	71.0±7.96#	50.33±12.32	49.20±11.39
Intermittent	125.7±8.42	112.5±9.33#**	75.5±8.96	74.5±9.01#**	50.20±9.63	38.00±10.64##**
T(Z)	-0.081	4.864	-0.647	-3.344		
P	0.937	< 0.001	0.518	0.001		

#, ##: compared with the corresponding value before exercise, P < 0.05 and < 0.001.
**: compared with the corresponding value at the Continuous group, P < 0.001.

with patients, we know that intermittent fast running was easier to complete than continuous jogging.

The study found that, with similar blood glucose at fasting and pre-exercise in the three groups, no difference in blood glucose in the each time point post exercise between the continuous jogging and the intermittent fast running groups, suggesting that the transient regulatory effects of two kinds of exercise on blood glucose were similar. Entin et al.[17] pointed out that, when exercise intensity exceeds 60% $VO2_{max}$, sugar is the main energy material of skeletal muscle. According to the correlation between oxygen uptake volume and percentage of maximum heart rate[18], it is concluded that the exercise intensity in continuous jogging and intermittent fast running (~71.6-82.5%, except for the rest intervals) is above 60% $VO2_{max}$. The same exercise volume (2 km of distance) may be the main reason contributing to the similar hypoglycemic effect. Chao et al.[19] found no difference in fasting blood glucose, glycosylated hemoglobin, and lipid profile after the continuous jogging and the intermittent fast running aerobic exercise intervention for 12 weeks in 45 patients with T2DM. Our results showed that the blood glucose changes after a single continuous jog and intermittent fast run were similar, which is consistent with results from Santiago et al[11].

However, intermittent exercise caused slightly lower blood glucose from control, whereas the continuous exercise did not, and blood glucose at 2h post in the intermittent group instead of in the continuous group was significantly lower than that in the control group. These results suggested that intermittent exercise might had more pronounced influence on blood glucose in couple of hours post exercise. Previous research found that intermittent fast running causes increased energy consumption not only during exercise, but also after exercise, whereas continuous exercise has no such effect[20]. This may account for the lower blood glucose level found in intermittent group in this study. There was no significant difference in 7h post blood glucose level among the three groups, suggesting that the regulatory effect of single acute exercise on blood glucose in patients with T2DM may last for only short time (probably couple of hours).

One of the widely recognized important risk for CVDs in patients with T2DM is hypertension[12]. Our result found that, at 30 minutes after 2km exercise training, systolic and diastolic blood pressure levels were significantly lower than before exercise in both exercise groups. This is consistent with the existing study which has proved that a single acute exercise can reduce the systolic and diastolic blood pressure of patients with hypertension after exercise[11,21]. In this study, we observed that a much remarkable systolic blood pressure reduction in the intermittent group while a slightly less reduction of diastolic blood pressure than continuous group, demonstrating that two modes of exercise lead to different hemodynamics and neural regulation. Additionally, pulse pressure became significantly smaller following intermittent exercise instead of continuous exercise. Ramírez-Vélez found that single intermittent exercise and continuous exercise with the same amount can improve the elasticity of arterial blood vessels and vascular function parameters, while intermittent exercise has a stronger effect[22]. This may be the reason for the greater reduction of systolic blood pressure and the significantly smaller pulse pressure after intermittent exercise. The reduction of blood pressure after a single exercise suggests that repeated regular exercise is likely to produce antihypertensive or other cardiovascular improvement effects in such patients and the intermittent exercise has superior effects in this aspect than continuous exercise. More studies are needed to confirm the conclusion.

PACES score, as a secondary observation, was found to be larger after intermittent fast running than after continuous jogging, demonstrating that patients were more willing to engage in intermittent exercise. This is consistent with the conclusion from Bartlett et al[23]. The running time in intermittent exercise time is short, and the rest time is a buffer period, which helps to relieve runner's difficult feeling, increase exercise interest and improve exercise compliance[24]. The combination of rest and exercise is more relaxed and lead to less psychological pressure, brings more enthusiasm for exercise participants to join in exercise and persist[25]. The long running time during continuous jogging causes some patients' lack of confidence to finish the whole process and little pleasure of exercise. There was no hypoglycemia (blood glucose < 3.9mmol/l) happened in the two groups at each time point in this study. However, due to the small sample size, the safety of patients with T2DM needs to be further confirmed with larger sample size.

Conclusions

The more significantly reduced blood glucose, remarkably decreased systolic blood pressure and significantly smaller pulse pressure prove that the intermittent aerobic exercise produces slightly stronger acute hypoglycemic and remarkably stronger hypotensive effect than continuous exercise in patients with T2DM. Together with the better enjoyment feelings, intermittent exercise is worth to be recommended for patients with T2DM. Our result has major implications for the practice of diabetes education in clinical rehabilitation. Patients can easily adopt the exercise method in this study making it possible to start exercise and continue exercise in their daily life.

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Interests conflict
The authors declare that they have no conflict of interest.

References

1. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321(7258):405-12. doi: 10.1136/bmj.321.7258.405.

2. Glovaci D, Fan W, Wong ND. Epidemiology of Diabetes Mellitus and Cardiovascular Disease. Curr Cardiol Rep. 2019;21(4):21. doi: 10.1007/s11886-019-1107-y.

3. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. Diabetes Care. 2016;39(11):2065-79. doi: 10.2337/dc16-1728.

4. Bello AI, Owusu-Boakye E, Adegoke BO, Adjei DN. Effects of aerobic exercise on selected physiological parameters and quality of life in patients with type 2 diabetes mellitus. Int J Gen Med. 2011;4:723-7. doi: 10.2147/IJGM.S16717.

5. Li Z, Hu Y, Yan R, Li H, Zhang D, Li F, et al. Twenty Minute Moderate-Intensity Post-Dinner Exercise Reduces the Postprandial Glucose Response in Chinese Patients with Type 2 Diabetes. Med Sci Monit. 2018;24:7170-7. doi: 10.12659/MSM.910827.

6. Francois ME, Little JP. Effectiveness and safety of high-intensity interval training in patients with type 2 diabetes. Diabetes Spectr. 2015;28(1):39-44. doi: 10.2337/diaspect.28.1.39.

7. Alvarez C, Ramirez-Campillo R, Martinez-Salazar C, Mancilla R, Flores-Opazo M, Cano-Montoya J, et al. Low-Volume High-Intensity Interval Training as a Therapy for Type 2 Diabetes. Int J Sports Med. 2016;37(9):723-9. doi: 10.1055/s-0042-104935.

8. Karstoft K, Winding K, Knudsen SH, Nielsen JS, Thomsen C, Pedersen BK, et al. The effects of free-living interval-walking training on glycemic control, body composition, and physical fitness in type 2 diabetic patients: a randomized, controlled trial. Diabetes Care. 2013;36(2):228-36. doi: 10.2337/dc12-0658.

9. Karstoft K, Wallis GA, Pedersen BK, Solomon TP. The effects of interval- vs. continuous exercise on excess post-exercise oxygen consumption and substrate oxidation rates in subjects with type 2 diabetes. Metabolism. 2016;65(9):1316-25. doi: 10.1016/j.metabol.2016.05.017.

10. Káfuňková P, Kvapil M. Interval Training and Compensation of Type 2 Diabetes. Open Journal of Clinical Diagnostics. 2017;7(1):20-30. doi: 10.4236/ojcd.2017.71003.

11. Santiago E, Delevatti RS, Bracht CG, Netto N, Lisboa SC, Vieira AF, et al. Acute glycemic and pressure responses of continuous and interval aerobic exercise in patients with type 2 diabetes. Clin Exp Hypertens. 2018;40(2):179-85. doi: 10.1080/10641963.2017.1339075.

12. Narita K, Hoshide S, Kario K. Hemodynamic Stress, Pulse Pressure, and Blood Pressure Variability May Be Strong Triggers of Cardiovascular Events in Diabetes. Am J Hypertens. 2019;32(11):1045-7. doi: 10.1093/ajh/hpz131.

13. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Meta-analysis of the quantitative relation between pulse pressure and mean arterial pressure and cardiovascular risk in patients with diabetes mellitus. Am J Cardiol. 2014;113(6):1058-65. doi: 10.1016/j.amjcard.2013.12.005.

14. Weng JP. Guideline for prevention and treatment of type 2 diabetes in China (2013 Edition). Chin J Endocrinol Metab. 2014;30(10):893-942. doi: 10.3760/cma.j.issn.1000-6699.2014.10.020.

15. American Diabetes A. Physical activity/exercise and diabetes. Diabetes Care. 2004;27 Suppl 1:S58-62. doi: 10.2337/diacare.27.2007.s58.

16. Guiraud T, Nigam A, Juneau M, Meyer P, Gayda M, Bosquet L. Acute Responses to High-Intensity Intermittent Exercise in CHD Patients. Med Sci Sports Exerc. 2011;43(2):211-7. doi: 10.1249/MSS.0b013e3181ebc5de.

17. Entin PL, Gest C, Trancik S, Richard Coast J. Fuel oxidation in relation to walking speed: influence of gradient and external load. Eur J Appl Physiol. 2010;110(3):515-21. doi: 10.1007/s00421-010-1523-6.

18. Li XY. Study on the expression types of exercise intensity and their correlation. J Phys Adult Educ. 2010;26(01):38-41. doi: 10.3969/j.issn.1672-268X.2010.01.015.

19. Chao M, Liang F, Wang Z, Wang L, Ouyang G, Wang XD. Effects of aerobic exercise with different intensities on Physiological Indexes of patients with type 2 diabetes mellitus. Chin J Rehabil Med. 2015;30(09):883-7. doi: 10.3969/j.issn.1001-1242.2015.09.004.

20. Bahr R. Excess postexercise oxygen consumption--magnitude, mechanisms and practical implications. Acta Physiol Scand Suppl. 1992;605:1-70. doi:

21. Viana AA, Fernandes B, Alvarez C, Guimaraes GV, Ciolac EG. Prescribing high-intensity interval exercise by RPE in individuals with type 2 diabetes: metabolic and hemodynamic responses. Appl Physiol Nutr Metab. 2019;44(4):348-56. doi: 10.1139/apnm-2018-0371.

22. Ramirez-Velez R, Hernandez-Quinones PA, Tordecilla-Sanders A, Alvarez C, Ramirez-Campillo R, Izquierdo M, et al. Effectiveness of HIIT compared to moderate continuous training in improving vascular parameters in inactive adults. Lipids Health Dis. 2019;18(1):42. doi: 10.1186/s12944-019-0981-z.

23. Bartlett JD, Close GL, MacLaren DP, Gregson W, Drust B, Morton JP. High-intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: implications for exercise adherence. J Sports Sci. 2011;29(6):547-53. doi: 10.1080/02640414.2010.545427.

24. Thum JS, Parsons G, Whittle T, Astorino TA. High-Intensity Interval Training Elicits Higher Enjoyment than Moderate Intensity Continuous Exercise. PLoS One. 2017;12(1):e0166299. doi: 10.1371/journal.pone.0166299.

25. Heisz JJ, Tejada MG, Paolucci EM, Muir C. Enjoyment for High-Intensity Interval Exercise Increases during the First Six Weeks of Training: Implications for Promoting Exercise Adherence in Sedentary Adults. PLoS One. 2016;11(12):e0168534. doi: 10.1371/journal.pone.0168534.

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ORIGINAL

Evaluation of the effectiveness of herbal composition (fennel, anise and bamboo cane) in the treatment of polycystic ovaries

Evaluación de la efectividad de la composición de hierbas (hinojo, anís y caña de bambú) en el tratamiento de ovarios poliquísticos

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Abstract

Polycystic ovary syndrome is one of the most common endocrine disorders. The most common cause of infertility is ovulation. The aim of this study was to evaluate the effectiveness of plant composition (fennel, anise and Bamboo Cane) in the treatment of polycystic ovaries. This double-blind, randomized placebo study was performed in the years 1300-1400. In this study, a controlled clinical trial on 20 patients with PCO referred to Sajjad Clinic in Tehran was randomly divided into two groups. The first group was treated with 19 drops of plant extract (fennel, anise, Bamboo Cane) once a day and the second group were treated with metformin and 1000 mg daily. The duration of treatment was 2 weeks for the first group and 3 months for the second group. The results of sonography showed that in the group receiving the compound (fennel, anise and Bamboo Cane) 50% of the subjects, the appearance of the ovaries was free of cysts. The results of jujube consumption with metformin in patients with polycystic ovary syndrome seem to be similar. Complications of metformin (nausea, vomiting, and diarrhea) were reported.

Key words: fennel, anise, bamboo cane, polycystic ovary.

Resumen

El síndrome de ovario poliquístico es uno de los trastornos endocrinos más comunes. La causa más común de infertilidad es la ovulación. El objetivo de este estudio fue evaluar la efectividad de la composición vegetal (hinojo, anís y caña de bambú) en el tratamiento de los ovarios poliquísticos. Este estudio de placebo aleatorizado y doble ciego se realizó en los años 1300-1400. En este estudio, un ensayo clínico controlado en 20 pacientes con PCO remitidos a la Clínica Sajjad en Teherán se dividió al azar en dos grupos. El primer grupo se trató con 19 gotas de extracto vegetal (hinojo, anís, caña de bambú) una vez al día y el segundo grupo se trató con metformina y 1000 mg diarios. La duración del tratamiento fue de 2 semanas para el primer grupo y de 3 meses para el segundo grupo. Los resultados de la ecografía mostraron que en el grupo que recibió el compuesto (hinojo, anís y caña de bambú) el 50% de los sujetos, la apariencia de los ovarios estaba libre de quistes. Los resultados del consumo de azufaifo con metformina en pacientes con síndrome de ovario poliquístico parecen ser similares. Se informaron complicaciones de la metformina (náuseas, vómitos y diarrea).

Palabras clave: hinojo, anís, caña de bambú, ovario poliquístico.

Introduction

Polycystic ovary syndrome is one of the most common endocrine disorders. The most common cause of infertility is lack of ovulation. With a prevalence of 5-24% depending on the diagnostic criteria. The name of this syndrome is due to the presence of large ovaries containing a large number of small cysts (in most women and not all) that are located on the outer layer of each ovary. This problem occurs due to changes in the structure of intra-ovarian hormones and enzyme issues that cause the level of these hormones to rise. In this syndrome, the levels of female hormones (such as estrogen, progesterone, LH, FSH) are unbalanced. And increases male hormones (androgens) and insulin hormone. Signs and symptoms of polycystic ovary syndrome may vary, including: Irregular periods: The patient may have a period less than once a month (usually less than 8 times a year) and the patient may not have a period at all. The patient may also have heavy menstrual bleeding. Weight gain, excess hair growth on the face, chest, back, abdomen, arms or inside the thighs. Acne is oily skin. Today, due to the side effects of chemical drugs, the use of complementary medicine in the treatment of diseases such as polycystic ovaries have been considered. These medicinal plants include fennel, anise and Bamboo Cane[1].

Botanical characteristics

Bamboo Cane

Bamboo Cane is a white, hard, crystalline material made of silica, which is taken from the nodes and stems of bamboo or bamboo. This substance has medicinal properties and is also known as bamboo sugar, black bamboo, Indian bamboo, razor bamboo, formal bamboo, golden bamboo and Indian reed. It is a plant of the genus Grain and has several different species. The roots of this plant are in the form of underground stems (rhizomes), the leaves are narrow and pointed, and its aerial stems are banded, reaching a height of several meters. The most important medicinal properties of this plant are: Forearm News: Treatment of intestinal and duodenal ulcers, strengthening the heart, improving the relief of pregnant women[2].

Anise or Roman anise

Anise or Roman anise, belonging to the umbrella family, Pimpinella anisum with the scientific name (Umbelliferae) is one of the oldest medicinal plants. The Arabic name of this plant is Bozralrazianj Roman or Alrazianj Shami and also Hab Al-Halwa. This herbaceous plant is one year old with a height of 30-50 cm and has small white flowers in the form of umbel inflorescences and yellowish green fruits, the upper part of which is pointed and has five prominent lines on it. It is grown in the eastern Mediterranean, western Asia, the Middle East, Mexico, Egypt and Spain[3&4]. The part used in this plant is its seeds (Aniseeds). From the perspective of traditional medicine, fresh seeds that have not been peeled are better; Because there are many properties in the skin of seeds 5. In the books of Iranian traditional medicine, anise is considered to have a warm and dry nature. Other organs have been used as a cleanser, analgesic and anti-inflammatory, and as a facelift. These seeds also strengthen the kidneys and open the obstructions of the liver, spleen, bladder and uterus[6&7].

Fennel

Fennel plant Foeniculum vulgare Mill is one of the most important and widely used aromatic and medicinal plants. Its seeds are the most important organ producing essential oil and its most important composition is anethole (50 to 75%). The active ingredients of this plant are used in pharmacy to treat cough, heartburn, bloating, indigestion in children and stimulate breastfeeding in lactating mothers[8].

Materials and Methods

Extraction

After preparing fennel, anise and Bamboo Cane seeds, extraction was done by soaking with 80% ethanol solvent. This double-blind, randomized placebo study was performed in the years 1300-1400. In this study, a controlled clinical trial was performed on 20 patients with PCO referred to Sajjad Clinic in Tehran. Written and informed consent was obtained from all patients to participate in the study and the study protocol was approved by the ethics committee[9].

Randomization and Medical prescribing

All women of childbearing age who referred to Sajjad Clinic with complaints of oligomenorrhea and infertility were collected and a complete clinical examination was performed. Individuals who did not meet the inclusion criteria were excluded from the study. Vaginal ultrasonography was performed on individuals who met these criteria. Those who did not have positive ultrasound symptoms were excluded from the study and those with these conditions were randomly divided into two groups: the first group treated with 19 drops of plant extract (fennel, anise, Bamboo Cane) once a day and the second group treated with metformin and 1000 mg daily. The duration of treatment was 2 weeks for the first group and 3 months for the second group. Twenty patients with oligomenorrhea and infertility referred to Sajjad Clinic were evaluated as appropriate in terms of inclusion criteria. The age range was 17-33 years with an average of 24.12 years. They were oligomenorrhea[10&11].

Statistical Analysis

After the simulation test, the therapeutic effects and side effects of the two groups were statistically judged by Fisher's exact test.

Findings

The study was conducted on 20 people in 2 groups of 10 people. The people in the 2 groups were similar in terms of economic and social status (referrals to a center) and age. Clinical treatment results in 2 groups were presented in **table I**.

Their differences were not statistically significant. (P≤0.2)

Table I: Distribution of samples according to clinical results of treatment by group therapy.

Medicine	Pregnancy	Regular menstruation	Oligomenorrhea	Exit the plan	p-value
Metformin	(10%)1	(33%)3	(50%)5	(10%)1	86/0
Extract fennel-anise and Bamboo Cane	(10%)1	(60%)6	(10%)1	(20%)2	46/0

The results of the ultrasound view of the ovaries after treatment are presented in **table II** and show that there are still no differences in the condition of the ovaries after treatment and this difference was not statistically significant.

Table II: Distribution of samples according to clinical results of treatment by group therapy.

Medcine	clear	Pco	P-value
Metformin N=10	(50%)5	(50%)5	14/0
Extract (fennel-anise and Bamboo Cane N=10	(5/87%)7	(5/12%)1	07/0

Clinical results showed that while taking the drug drops (fennel, anise, Bamboo Cane), 2 people were out of the plan. One case occurred. 6 people had regular periods and 1 person remained oligomenorrhea. The results of ultrasound showed that in 87.5% of people, all ovaries were free of cysts. It happened. Five people remained oligomenorrhea and three people had regular periods. In the ultrasound obtained in 50% of people, the appearance of the ovaries was free of cysts.

Discussion

The study showed that the therapeutic effects of the extract (fennel, anise, Bamboo Cane) were similar to metformin and did not differ. From the perspective of Iranian traditional medicine, anise seeds have analgesic and inflammatory properties and due to their anti-inflammatory effects can be effective in the prevention and treatment of many diseases in which inflammation is a major factor[3&4]. Also, the analgesic effects of anise essential oil were comparable to morphine and aspirin. Fixed oils of anise also had good analgesic and anti-inflammatory effects[12] which is consistent with the present study. On the other hand, anise extracts and excellent analgesic effects in heat and writing tests induced by studying anise seeds have effects. It has hypoglycemic, hyperlipidemic, lipid peroxidation control (oxidative stress index) and antioxidants in patients with type 2 diabetes[13&14]. In another study, anise extract significantly reduced the number and severity of hot flashes in postmenopausal women[15].

In a study, oral administration of methanolic extract of fennel seeds in rats showed inhibitory effects on acute and non-acute inflammation of this plant by inhibiting two pathways of cyclooxygenase and lipoxygenase. Also, in increasing milk, reducing menstrual pain, facilitating childbirth It is also used to increase sexual desire. Its essential oil also shows potential hypoglycemic and antioxidant effects[15].

In another study, it was shown that fennel seed is a potential source of antioxidant activity. 100 mg of ethanolic and aqueous extracts of this plant are 99.1% and 77.5% of antioxidant activity, respectively, which is the amount of alpha antioxidant activity. Tocopherol was 36.1% higher with the same dose[16].

In another study, Moradi et al. In a review study in 1398 found that the effect of medicinal plants such as fennel by reducing insulin resistance; Bamboo Cane with menstrual regulation; Anise with oligomenorrhea recovery; Also, fennel root is effective with anti-androgenic effects and increased FSH against polycystic ovary syndrome[17], which is consistent with the present study.

Conclusion

Although this study has introduced medicinal plants affecting polycystic ovary syndrome, the use of medicinal plants can also be associated with side effects, so comprehensive clinical trial studies are recommended in relation to the introduced plants.

Conflict of interest

Authors do not have any conflict of interest to declare.

References

1. Surmaghi S. Medicinal Plants and Phototherapy. Tehran, Iran: Donyaei Taghziah Publication; 2010: 81-2. [In Persian].

2. Berjis K, Ghiasi M, Sangy S. "Health need assessment in female adolescents, in Qom: A cross sectional study." Journal of education and health promotion vol. 8 39. 15 Feb. 2019, doi: 10.4103/jehp.jehp_11_18

3. Tonkaboni SM. AlMomenin T. Tehran, Iran: Traditional Medicine & Materia Medica Research Center, Shahid Beheshti University of Medical Sciences Publication; 2008. p. 65-6.[In Persian].

4. Sahraei H, Ghoshooni H, Hossein SS, Mohseni AA, Shafaghi B, Falahi M, et al. The effects of fruit essential oil of the Pimpinella anisum on acquisition and expression of morphine induced conditioned place preference in mice. J Ethnopharmacol 2002; 80(1): 43-7.

5. Twaij HA, Elisha EE, Khalid RM, Paul NJ. Analgesic Studies on some Iraqi Medicinal Plants. Pharmaceutical Biology 1987; 25(4): 251-4.

6. Nahidi F, Taherpoor M, Mojab F, Majd H. Effect of Anise extract on hot flush of menopause. Pajoohandeh 2008; 13(3): 167-73.

7. Rajeshwari U, Shobha I, Andallu B. Comparison of aniseeds and coriander seeds for antidiabetic, hypolipidemic and antioxidant activities. Spatula DD 2011; 1(1): 9-16.

8. Kataoka H, Horiyama S, Yamaki M, Oku H, Ishiguro K, Katagi T, Takayama M, Semma M and Ito Y. Anti-inflammatory and anti-allergic activities of hydroxylamine and related compounds. Biological and Pharmaceutical Bulletin 2002; 25 (11): 1436-1441.

9. Oktay M, Gülçin İ and Küfrevioğlu Ö İ. Determination of in vitro antioxidant activity of fennel (Foeniculum vulgare) seed extracts.LWT-Food Science and Technol. 2003; 36 (2): 263-71.

10. Koppula S and Kumar H. Foeniculum vulgare Mill (Umbelliferae) attenuates stress and improves memory in wister rats.Tropical Journal of Pharmaceuti

11. Miryousefiata F, Sangy S. Assessing the Correct Understanding of Families about the Occurrence of Marital Cancer (Statistical Population: Denmark, Sweden and Iran), J. Med. Chem. Sci., 2021, 4(1) 60-74 DOI: 10.26655/JMCHEMSCI.2021.1.8
URL: http://www.jmchemsci.com/article_120965.htm

12. Eskandari N , Alipour Z, Ahmari Tehran H, Eshagh Hossaini K, Sangi S. Effect of vocal stimulation on responses of premature infants: A randomized controlled trial. Health Spiritual Med Ethics 2013;1(1):9-16

13. Surmeli Oz, Miryousefiata F. Neonatal Findings Of Infants Born To Mothers With Toxoplasma Seroconversion: A Single Center Experience. Baskent Pediatry Gunleri Journal. Pediatrics Department, Faculty of Medicine, Baskent University, Ankara, Turkey.2021:38-40.

14. Miryousefiata F, Alsadat Miryousefiata F. The effect of Familact probiotic supplement in patients with diabetes (Evaluation of Blood Glucose Parameters, Lipid Profile). ACADEMIC JOURNAL OF HEALTH SCIENCES. 2021; 36 (3): 52-63. doi: 10.3306/AJHS.2021.36.03.52 www.medicinabalear.org

15. SangyS, Miryousefi Ata F, Miryousefiata F. Study of Thymus and T-cell Development and Tumor Immunology Budapest International Research in Exact Sciences. 2021; 3,(3) :162-170
DOI: https://doi.org/10.33258/birex.v3i3.2081

16 Moradi F, Anjazab B, Ghadiri Anari A, The effect of medicinal plants on polycystic ovary syndrome: A review study, National Conference on Women's Health Promotion, 1398

17. Standley JM. A meta-analysis of the efficacy of music therapy for premature infants. J PediatrNurs 2002; 17:107-13

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ORIGINAL

Variables antropométricas, sociodemográficas y clínicas que influyen en el grado de control de la glucemia en 10.794 diabéticos tipo 2 en tratamiento hipoglucemiante

Anthropometric, sociodemographic and clinical variables that influence the degree of glycemic control in 10.794 type 2 diabetics under hypoglycemic treatment

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Resumen

Introducción: La diabetes tipo 2 es una enfermedad crónica multifactorial muy frecuente en el mundo y cuya prevalencia va en aumento. Es importante lograr un adecuado control de la glucemia en los pacientes diabéticos para evitar la aparición de complicaciones clínicas.
Objetivo: Se pretende conocer el grado de control de la glucemia en pacientes diabéticos en tratamiento hipoglucemiante valorando además que variables pueden influir en el grado de control.
Material y métodos: Estudio transversal en 10794 diabéticos tipo 2 en tratamiento con fármacos hipoglucemiantes. Se valora el grado de control mediante los criterios de la Asociación Americana de Diabetes (glucemia basal en ayunas inferior a 126 mg/dl o hemoglobina glicosilada inferior a 7%). Se valora la influencia que pueden tener en el grado de control de la glucemia en estos pacientes de variables sociodemográficas como edad, sexo y clase social, variables antropométricas como el IMC, consumo de tabaco y tratamientos concomitantes de patologías como la dislipemia o la hipertensión arterial.
Resultados: Un 35,4% de los varones se consideran bien controlados aplicando como criterio los valores de glucemia y un 50,1% si el criterio empleado es la hemoglobina glicosilada. En las mujeres estas cifras son del 45,9% y 58,3% respectivamente. Las variables que incrementan el riesgo de presentar un mal control empleando uno u otro criterio son la edad a partir de 55 años, el sexo masculino, pertenecer a la clase social III y ser obeso.
Conclusiones: El grado de control de la glucemia en pacientes diabéticos en tratamiento hipoglucemiante en nuestro estudio no se puede considerar muy elevado.

Palabras clave: diabetes mellitus, fármacos antidiabéticos, obesidad.

Abstract

Introduction: Type 2 diabetes is a multifactorial chronic disease that is very common in the world and whose prevalence is increasing. It is important to achieve adequate glycemic control in diabetic patients to avoid the appearance of clinical complications.
Objective: The aim of this study was to determine the degree of glycemic control in diabetic patients under hypoglycemic treatment and to assess the variables that may influence the degree of control.
Material and methods: Cross-sectional study in 10794 type 2 diabetics under treatment with hypoglycemic drugs. The degree of control was assessed according to the criteria of the American Diabetes Association (fasting basal glycemia less than 126 mg/dL or glycosylated hemoglobin less than 7%). The influence that sociodemographic variables such as age, sex and social class, anthropometric variables such as BMI, tobacco consumption and concomitant treatment of pathologies such as dyslipidemia or arterial hypertension may have on the degree of glycemic control in these patients was assessed.
Results: 35.4% of the men were considered to be well controlled using glycemia values as a criterion and 50.1% if the criterion used was glycosylated hemoglobin. In women, these figures were 45.9% and 58.3%, respectively. The variables that increase the risk of presenting poor control using one or other criterion are age over 55 years, male sex, belonging to social class III and being obese.
Conclusions: The degree of glycemic control in diabetic patients under hypoglycemic treatment in our study cannot be considered very high.

Key words: diabetes mellitus, antidiabetic drugs, obesity.

Introducción

La diabetes tipo 2 o diabetes mellitus es una enfermedad crónica que se produce cuando el páncreas secreta una cantidad insuficiente de insulina o bien cuando nuestro cuerpo no utiliza de forma eficaz esta insulina que produce. La insulina es una hormona que se encarga de regular la glucemia. El efecto de la diabetes no controlada es lo que conocemos como hiperglucemia que si se mantiene en el tiempo puede provocar graves alteraciones en diferentes órganos y sistemas, especialmente los nervios y los vasos sanguíneos[1].

La diabetes mellitus tipo 2 en estos momentos se considera uno de los problemas de salud más graves de nuestro tiempo[2]. En España diferentes estudios valoraron la prevalencia de diabetes tipo 2, situándola entre el 6 y el 10%[3]. Un gran estudio epidemiológico nacional (di@bet.es)[4] elevó esa cifra al 13,8% de los adultos indicando que el 7,8% era diabetes conocida y el 6% era desconocida para las personas que la sufren.

Muchos son los factores que influyen en la aparición de la diabetes, así diferentes investigaciones han encontrado al menos 45 genes relacionados con la diabetes tipo 2, aunque todavía no se conoce el mecanismo real por el que estos genes aumentan la aparición de esta patología.

En la fisiopatología de la diabetes tipo 2 uno de los elementos clave es la resistencia a la insulina o lo que es lo mismo la deficiente respuesta de nuestro cuerpo a la insulina, hormona que va a facilitar la síntesis de glucosa. Esta resistencia a la insulina puede ser una consecuencia de la evolución de algunos genes "ahorrativos" que ayudarían al cuerpo a acumular energía para periodos posteriores de escasez. En nuestra sociedad, donde existe una gran accesibilidad a cualquier tipo de alimento este factor genético constituye un escenario óptimo para la diabetes.

La resistencia insulínica, el sobrepeso y la obesidad y un deficiente control glucémico se pueden encontrar en los grupos familiares, de manera que si un familiar presenta diabetes, nosotros tendremos mayor riesgo de sufrirla. El sexo también influye, siendo el masculino más propenso a padecerla.

Se sabe que los factores de riesgo de enfermedad cardiovascular como la hipertensión arterial, la hipertrigliceridemia y la hipercolesterolemia incrementan el riesgo de sufrir diabetes tipo 2. En la génesis de esta asociación se encuentran los estilos de vida poco saludables como el sedentarismo que suelen ocasionar sobrepeso. Sin embargo se cree que también existen otras razones asociadas, así existe evidencia científica que hace pensar que la diabetes tipo 2 provoca inflamación de las paredes sanguíneas que llevaran finalmente a un incremento de las patologías cardiovasculares. Un estudio danés mostró que el 40% de personas recientemente diagnosticadas de diabetes tipo 2 mostraban niveles elevados de un marcador de la inflamación como es la proteína C reactiva[5].

La lesión vascular renal que aparece en los pacientes diabéticos podría ser la causa por la cual la diabetes y la hipertensión arterial suelen aparecer simultáneamente. También se ha visto que en los diabéticos con vasos sanguíneos ya alterados hay mayor predisposición a sufrir alteraciones vasculares graves asociadas a la acumulación de lípidos y a la hipertensión, de manera que podemos concluir que aquellas personas que presentan factores de riesgo cardiovascular tienen un riesgo más elevado de tener diabetes tipo 2.

Se sabe que valores elevados de índice de masa corporal (IMC) predisponen a la aparición de diabetes tipo 2 ya que un exceso de grasa corporal puede generar resistencia a la insulina. Sin embargo uno de cada cinco personas obesas no presenta signos de la enfermedad y un 15% de las personas con diabetes tipo 2 muestran peso normal.

Se sabe que el riesgo de presentar diabetes tipo 2 aumenta con la edad. Aunque la mayoría de los nuevos diagnósticos se producen entre los 45 y 64 años cada vez se observan más en edades más tempranas. El hecho de que cada vez se diagnostique más en edades muy tempranas[6] nos habla de la influencia que tiene en su génesis el ambiente, relacionado principalmente con la mala alimentación y el escaso nivel de actividad física.

El estrés, ya sea doméstico o laboral, puede ser un factor relacionado con la aparición de diabetes tipo 2. Un estudio norteamericano[7] mostró que los varones con matrimonios no felices presentaban mayor riesgo de presentar diabetes tipo 2 que aquellos matrimonios felices.

Otro estudio indicó que el estrés crónico incrementaba los efectos nocivos de dietas poco saludables (ricas en azúcares y grasas) al aumentar la cantidad de grasa en el abdomen y el riesgo de presentar resistencia a la insulina[8]. Las hormonas relacionadas con el estrés como norepinefrina y cortisol se unen a los receptores celulares y modificar su respuesta.

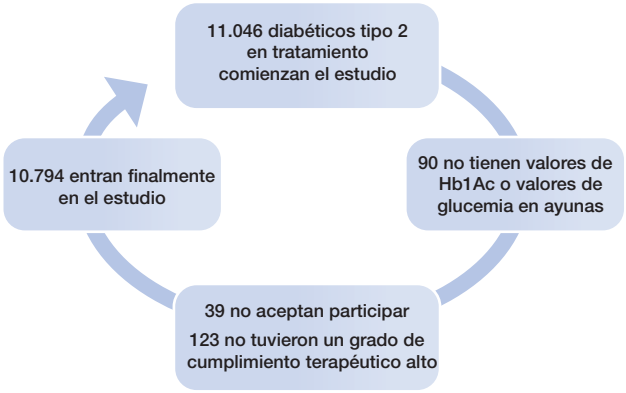
El objetivo de este estudio fue determinar las variables que influyen en el grado de control de la glucemia en diabéticos tipo 2 en tratamiento con fármacos hipoglucemiantes y establecer el porcentaje de personas diabéticas tipo 2 en tratamiento que se pueden considerar controladas.

Material y métodos

Se lleva a cabo un estudio descriptivo y transversal en 10923 diabéticos tipo 2 españoles en tratamiento

con fármacos hipoglucemiantes durante el periodo comprendido entre enero de 2019 y diciembre de 2019. Del total 129 se excluyen (39 al no aceptar participar y 90 por no tener los valores de hemoglobina glicosilada o glucemia en ayunas) quedando finalmente 10.794 (4.300 mujeres y 6.494 hombres). Los datos se muestran en el diagrama de flujo (**Figura 1**).

Figura 1: Diagrama de flujo de los participantes en el estudio.



Criterios de inclusión

- Ser diabético tipo 2
- Recibir tratamiento hipoglucemiante
- Tener un grado de cumplimiento terapéutico alto.
- Aceptar participar en el estudio

Para eliminar el sesgo inter observador, las mediciones tantos antropométricas, clínicas y analíticas, las realiza el personal sanitario que participa en el estudio, tras homogenizar las técnicas de medición.

La edad se clasifica en 4 grupos: 18-34 años, 35-44 años, 45-54 años y ≥55 años.

El peso (en kilogramos), y la altura (en cm) se determinan con una báscula con tallímetro modelo SECA 700 con capacidad para 200 kg que lleva anexo un tallímetro telescópico SECA 220 con división milimétrica e intervalo 60-200 cm.

El IMC se calcula dividiendo el peso en kg entre la altura en metros al cuadrado:
IMC= peso (kg)/altura^2 (metros)
El IMC se clasifica en normopeso (< 25kg/m^2), sobrepeso (25-29,9 kg/m^2) y obesidad (≥30 kg/m^2).

La presión arterial se determina en decúbito supino con un esfigmomanómetro automático OMRON M3 calibrado después de 10 minutos de descanso. Se obtienen tres mediciones con intervalos de un minuto obteniéndose la media de las tres. Los análisis de sangre se obtienen tras 12 horas de ayuno. Las muestras se envían a los laboratorios de referencia. Glucemia, colesterol total y triglicéridos emplean métodos enzimáticos automatizados y los valores se expresan en mg/dl. El HDL se determina por precipitación con dextrano-sulfato Cl2Mg, y los valores se expresan también en mg/dl. El LDL se calcula empleando la fórmula de Friedewald (siempre que los triglicéridos sean inferiores a 400 mg/dl). Los valores se expresan en mg/dl.

Fórmula de Friedewald: LDL= colesterol total –HDL– triglicéridos/5

Para llegar al diagnóstico de diabetes tipo 2 y siguiendo los criterios de la American Diabetes Association9 (ADA) existen diferentes posibilidades:

- Hemoglobina glicosilada (HbA1c). Valora el nivel promedio de glucemia de los últimos dos o tres meses. Valores a partir de 6,5 indican diabetes, cifras entre 5,7 y 6,4 prediabetes y cifras por debajo de 5,7 se consideran normales. Suele utilizarse para comprobar el grado de eficacia con la que se controla la glucemia elevada en tratamiento.
- Glucosa aleatoria en sangre. Muestra los valores de glucosa en sangre en el momento que se realiza la determinación. Valores a partir de 200 mg/dl hablan de diabetes.
- Glucosa plasmática en ayunas. Valores a partir de 126mg/dl indican diabetes.
- Test de tolerancia oral de glucosa. Se realiza una determinación antes de tomar una bebida azucarada y otra dos horas después. Valores a partir de 200mg/dl indican diabetes.

Consideramos fumador a aquella persona que regularmente ha consumido al menos 1 cigarrillo/día (o el equivalente en otros tipos de consumo) en el último mes, o ha dejado de fumar hace menos de un año.

La clase social se obtiene a partir de la Clasificación Nacional de Ocupaciones del año 2011 (CNO-11) partiendo de la propuesta realizada por el grupo de determinantes sociales de la Sociedad Española de Epidemiología[10]. Elegimos la clasificación en 3 categorías: Clase I. Directores/gerentes, profesionales universitarios, deportistas y artistas. Clase II. Ocupaciones intermedias y trabajadores por cuenta propia sin asalariados. Clase III. Trabajadores no cualificados.

El tratamiento para la dislipemia y para la hipertensión arterial se determina mediante entrevista clínica. En esta misma entrevista clínica se preguntó a las personas por su grado de cumplimiento con el tratamiento.

Existen múltiples definiciones del término cumplimiento terapéutico. De forma simple se puede decir que representa la concordancia entre las instrucciones dadas y las conductas seguidas. La definición más comúnmente aceptada es la propuesta inicialmente por Haynes et al[11] y avalada posteriormente por un grupo de expertos de

la Organización Mundial de la Salud (OMS) que define al cumplimiento como "el grado hasta el cual la conducta del paciente, en términos de tomar medicamentos, seguir dietas o realizar cambios en el estilo de vida, coinciden con la prescripción clínica". Existe cierto acuerdo al considerar como cumplidor a aquél que sigue dichas recomendaciones en al menos un 80%.

Análisis estadístico

Se realiza un análisis descriptivo de las variables categóricas, calculando la frecuencia y distribución de respuestas de cada una de ellas. Para las variables cuantitativas, se calcula la media y la desviación estándar y para las variables cualitativas se calcula el porcentaje. El análisis de asociación bivariante se realiza mediante el test de la χ^2 (con corrección del estadístico exacto de *Fisher* cuando las condiciones lo requirieran) y la t de *Student* para muestras independientes. Para el análisis multivariante se ha utilizado la regresión logística binaria con el método de Wald, con el cálculo de las Odds-ratio y se realiza la prueba de bondad de ajuste de Hosmer-Lemeshow. La correlación entre el grado de control del tratamiento mediante glucemia basal y hemoglobina glicosilada se realiza empleando el índice kappa de Cohen. El análisis estadístico se realiza con el programa SPSS 27.0 siendo el nivel de significación estadística aceptado de 0,05.

Consideraciones y aspectos éticos

El estudio fue aprobado por el Comité de ética de investigación clínica del área de salud de Illes Balears nº IB 4383/20. Todos los procedimientos se realizaron de acuerdo con las normas éticas del comité de investigación institucional y con la Declaración de Helsinki de 2013. Todos los pacientes firmaron documentos de consentimiento informados por escrito antes de participar en el estudio.

Resultados

En la **tabla I** se muestran las características de los participantes en el estudio, incluyendo los valores medios y las prevalencias de los diferentes parámetros antropométricos, analíticos, clínicos y sociodemográficos.

Como datos más destacados señalaremos que la mayoría de personas incluidas en el estudio pertenecen a la clase social III (72,4%), la prevalencia de obesidad es muy elevada (42,5%), los fumadores representan el 29,1% y que entre un 16,5% y un 18,3% están en tratamiento por comorbilidades asociadas. Todos los datos se pueden consultar en la **tabla I**.

Los valores medios de glucemia en las personas diabéticas tipo 2 que están en tratamiento hipoglucemiante muestran que los valores más elevados aparecen en las personas de menor edad y van incrementándose a medida que la persona va envejeciendo, esto se observa en ambos sexos.

También se observan valores más elevados entre las personas de las clases sociales más desfavorecidas (clase social III). A medida que se incrementa el valor del IMC van aumentando los valores medios de la glucemia. En cuanto al valor de la glucemia basal según existan o no comorbilidades asociadas a la diabetes tipo 2 podemos decir que en los varones los peores resultados se obtienen en los que sólo reciben tratamiento para diabetes mientras que en las mujeres estos peores resultados se obtienen en el grupo con diabetes tipo 2 e hipertensión arterial. Los resultados completos se presentan en la **tabla II**.

Tabla I: Características de la muestra.

	Hombre n=6494 Media (DE)	Mujer n=4300 Media (DE)	Total n=10794 Media (DE)	p
Edad (años)	51,0 (9,3)	47,8 (11,0)	49,7 (10,2)	<0.0001
Altura (cm)	172,4 (7,1)	159,6 (6,8)	167,3 (9,4)	<0.0001
Peso (kg)	87,5 (16,8)	75,7 (16,6)	82,8 (17,7)	<0.0001
IMC (kg/m²)	29,4 (5,2)	29,7 (6,2)	29,5 (5,6)	<0.0001
TAS (mmHg)	136,4 (17,8)	126,9 (18,4)	132,6 (18,6)	<0.0001
TAD (mmHg)	81,6 (10,9)	75,9 (11,0)	79,3 (11,3)	<0.0001
Colesterol (mg/dl)	183,9 (38,7)	193,4 (37,9)	187,7 (38,7)	<0.0001
HDL (mg/dl)	50,6 (10,6)	55,9 (11,8)	52,7 (11,4)	<0.0001
Triglicéridos	170,4 (129,6)	140,1 (98,9)	158,5 (119,5)	<0.0001
Glucemia (mg/dl)	152,3 (57,0)	143,6 (60,6)	148,9 (58,6)	<0.0001
	n (%)	**n (%)**	**n (%)**	**p**
18-34 años	6,8	13,8	9,6	<0.0001
35-44 años	14,9	19,5	16,7	
45-54 años	35,6	34,2	35,1	
≥55 años	42,7	32,5	38,6	
Clase social I	6,7	4,6	5,9	<0.0001
Clase social II	20	24,2	21,7	
Clase social III	73,3	71,2	72,4	
Normopeso	19,9	25,3	22,1	<0.0001
Sobrepeso	39,1	30	35,4	
Obesidad	41	44,7	42,5	
No fumadores	69,2	73,3	70,9	<0.0001
Fumadores	30,8	26,7	29,1	
Diabetes	45,2	53,3	48,4	<0.0001
Diabetes+dislipemia	16,8	15,9	16,5	
Diabetes+HTA	21,2	14	18,3	
Diabetes+dislipemia+HTA	16,8	16,7	16,8	

Tabla II : Valores medios de glucemia basal en ayunas en diabéticos tipo 2 en tratamiento hipoglucemiante según las diversas variables sociodemográficas, antropométricas, consumo de tabaco y tratamientos de comorbilidades asociadas por sexo.

	Hombres			Mujeres		
	n	Media (DE)	p	n	Media (DE)	p
18-34 años	440	158,7 (72,7)	<0.0001	592	146,5 (74,3)	0.006
35-44 años	968	158,1 (68,8)		840	137,2 (68,4)	
45-54 años	2312	151,4 (54,8)		1472	144,5 (57,9)	
≥55 años	2774	150,1 (50,9)		1396	145,4 (51,0)	
Clase social I	432	145,2 (44,0)	<0.0001	200	124,0 (43,2)	<0.0001
Clase social II	1300	147,3 (51,7)		1040	136,3 (57,1)	
Clase social III	4762	154,4 (59,3)		3060	147,4 (62,3)	
Normopeso	1294	156,1 (70,5)	<0.0001	1088	137,1 (66,2)	<0.0001
Sobrepeso	2538	148,1 (53,5)		1288	148,2 (64,1)	
Obesidad	2662	154,6 (52,5)		1924	144,2 (54,3)	
No fumadores	4496	152,1 (54,9)	0.586	3152	145,7 (59,9)	<0.0001
Fumadores	1998	152,9 (61,5)		1148	137,9 (62,2)	
Diabetes	2936	155,5 (61,9)	<0.0001	2292	144,3 (68,0)	0.014
Diabetes + dislipemia	1092	147,9 (52,9)		684	141,1 (51,7)	
Diabetes + HTA	1092	151,8 (53,3)		604	149,2 (53,0)	
Diabetes + dislipemia + HTA	1374	149,5 (51,5)		720	139,1 (47,8)	

Tabla III : Grado de control de glucemia basal en ayunas y de hemoglobina glicosilada en diabéticos tipo 2 en tratamiento hipoglucemiante según las diversas variables sociodemográficas, antropométricas, consumo de tabaco y tratamientos de comorbilidades asociadas por sexo.

	Hombres					Mujeres				
	Glucemia <126 mg/dl			HbA1c <7%		Glucemia <126 mg/dl			HbA1c <7%	
	n	% (IC 95%)	p	% (IC 95%)	p	n	% (IC 95%)	p	% (IC 95%)	p
18-34 años	440	36,8 (34,0-39,6)	0.136	51,1 (48,3-53,9)	0.047	592	52,7 (50,1-55,3)	<0,0001	63,2 (61,6-64,8)	<0.0001
35-44 años	968	37,0 (34,9-39,1)		52,5 (50,4-54,6)		840	56,2 (54,0-58,4)		66,0 (63,8-68,2)	
45-54 años	2312	36,4 (34,9-37,9)		51,3 (49,8-52,8)		1472	44,8 (43,0-46,6)		58,0 (56,2-59,8)	
≥55 años	2774	33,8 (32,4-35,2)		48,2 (45,8-50,6)		1396	37,8 (36,0-39,6)		51,9 (50,1-53,7)	
Clase social I	432	34,3 (31,5-37,1)	0.068	57,4 (54,6-60,2)	<0.0001	200	60,0 (57,0-63,0)	<0,0001	70,0 (67,0-73,0)	<0.0001
Clase social II	1300	38,2 (36,4-40,0)		58,8 (57,0-60,6)		1040	52,3 (50,3-54,3)		63,8 (61,8-65,8)	
Clase social III	4762	34,8 (33,8-35,8)		47,1 (45,5-48,7)		3060	42,7 (41,4-44,0)		55,7 (52,4-57,0)	
Normopeso	1294	37,7 (35,5-39,9)	<0.0001	51,7 (49,5-53,9)	<0.0001	1088	57,4 (55,4-59,4)	<0,0001	66,5 (64,5-68,5)	<0.0001
Sobrepeso	2538	38,1 (36,6-39,6)		52,8 (51,3-54,3)		1288	43,2 (41,3-45,1)		55,7 (53,7-57,7)	
Obesidad	2662	31,7 (30,3-33,1)		46,8 (45,3-48,3)		1924	41,2 (39,5-42,9)		55,4 (53,7-57,1)	
No fumadores	4496	34,5 (33,2-35,8)	0.013	50,0 (48,7-51,3)	0.400	3152	43,8 (42,2-45,4)	<0,0001	56,4 (54,8-58,0)	<0.0001
Fumadores	1998	37,4 (35,7-39,1)		50,4 (48,6-52,2)		1148	51,6 (49,7-53,5)		63,5 (61,6-65,4)	
Diabetes	2936	35,0 (33,7-36,3)	0.104	49,9 (48,6-51,2)	0.964	2292	49,2 (47,7-50,7)	<0,0001	60,5 (59,0-62,0)	<0.0001
Diabetes + dislipemia	1092	38,6 (36,6-40,6)		50,5 (48,5-52,5)		684	45,0 (43,3-46,7)		60,2 (58,5-61,9)	
Diabetes + HTA	1092	34,6 (32,6-36,6)		50,6 (48,6-52,6)		604	43,3 (41,6-45,0)		52,8 (51,1-54,5)	
Diabetes + dislipemia +HTA	1374	34,4 (32,6-36,2)		49,9 (48,1-51,7)		720	37,1 (35,4-38,8)		54,0 (52,3-55,7)	
Total	6494	35,4 (34,4-36,4)		50,1 (49,1-51,1)		4300	45,9 (44,6-47,2)		58,3 (57-0-59,6)	

El grado de control general de las personas diabéticas tipo 2 en tratamiento oscila entre un 35,4% de los hombres si aplicamos criterios de glucemia basal y un 50,1% si el criterio aplicado es la hemoglobina glicosilada. Estas cifras son algo superiores en las mujeres con valores que van del 45,9% al 58,3% según el criterio empleado.

Para considerar que una persona diabética tipo 2 que está en tratamiento hipoglucemiante está bien controlada emplearemos los criterios de la ADA (glucemia basal en ayunas inferior a 126 mg/dl o hemoglobina glicosilada inferior a 7%).

En nuestro estudio observamos que, en ambos sexos, el peor grado de control se obtiene en las personas de mayor edad, y esto se produce tanto si aplicamos como referencia la glucemia basal como la hemoglobina glicosilada.

En los varones el mayor porcentaje de diabéticos bien controlados se encuentra entre los pertenecientes a la clase social II tanto si consideramos glucemia basal como hemoglobina glicosilada. En las mujeres por el contrario los mejores resultados se obtienen entre las pertenecientes a las clases sociales más favorecidas (clase I).

Las personas con exceso de peso, tanto hombres como mujeres y aplicando cualquiera de los dos indicadores de control, presentan peores resultados.

En los varones no se observan diferencias en el grado de control de la glucemia entre aquellos que sólo están

en tratamiento para la diabetes tipo 2 o también lo están para otras patologías cardiovasculares (dislipemia e hipertensión arterial). En las mujeres sin embargo si se aprecian diferencias entre los grupos según el tratamiento, de manera que aquellas que sólo reciben tratamiento para la diabetes tipo 2 o para la diabetes y la dislipemia muestran mayor grado de control).

Llama la atención que en este análisis bivariante los fumadores muestren un mejor grado de control glucémico que los no fumadores.

Todos los resultados se pueden consultar en la **tabla III**. Cuando realizamos un análisis de concordancia mediante el Índice Kappa de Cohen entre el grado de control obtenido mediante la glucemia basal y mediante la hemoglobina glicosilada el valor que se obtiene es 0,728 que se clasifica como considerable según la escala de Landis y Koch[12]. (**Tabla IV**)

Tabla IV : Coeficiente Kappa de Cohen.

Coeficiente kappa	Nivel de concordancia
0.0-0.20	Pobre
0.21-0.40	Baja
0.41-0.60	Aceptable
0.61-0.79	Buena
0.80-0.91	Muy buena
0.92-1.0	Excelente

En el análisis multivariante mediante regresión logística binaria con el modelo de Wald se emplean como covariables la obesidad determinada con IMC, la clase social III, la edad a partir de 55 años, el consumo de tabaco, el estar en tratamiento de la diabetes tipo 2 y de otro patología cardiovascular y el sexo masculino que fueron las variables que mostraron significación estadística en los análisis bivariantes.

Cuando empleamos la glucemia basal a partir de 126 mg/dl como criterio de control encontramos que la variable que más incrementa el riesgo de tener un mal control es el sexo masculino con una OR de 1.54 (IC 95% 1.42-1.66).

Si el criterio es la hemoglobina glicosilada a partir de 7% la variable que más aumenta el riesgo de un mal control es pertenecer a la clase social III con una OR de 1.53 (IC 95% 1.40-1.67).

En ambos casos, tanto si empleamos la glucemia basal como si utilizamos la hemoglobina glicosilada, todas las covariables, salvo el consumo de tabaco y la existencia de tratamientos de otras patologías cardiovasculares concomitantes, aumentan el riesgo de tener un mal control de la glucemia en diabéticos tipo 2 en tratamiento hipoglucemiante.

Los datos completos se muestran en la **figura 2**.

Discusión

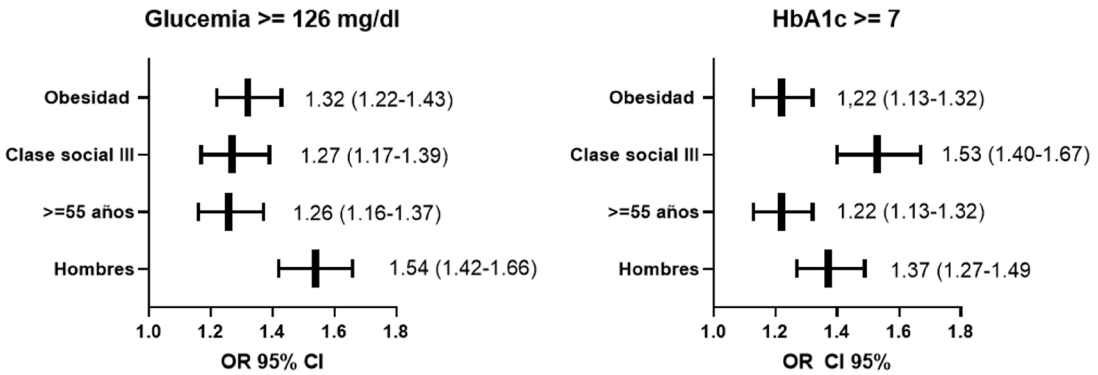
En nuestro estudio realizado en 10.794 diabéticos tipo 2 en tratamiento hipoglucemiante el grado de control de la glucemia se puede considerar entre bajo y moderado, siendo mejor en las mujeres. Otros estudios parten de grupos sujetos menores que los voluntarios participantes en el presente trabajo.

El sexo masculino, la edad a partir de 55 años, pertenecer a la clase social III y ser obeso incrementan el riesgo de tener un mal control glucémico.

En estudios previos al presente trabajo se investigó la adherencia al tratamiento en pacientes con DM2. Se observó que una buena adherencia al tratamiento estaba acompañada de bajos valores de IMC, mejor perfil lipídico, así como mejor desempeño profesional. Los autores concluyeron que el desempeño emocional y físico son determinantes de la buena adherencia al tratamiento diabético lo cual tiene un impacto beneficioso sobre el IMC, los lípidos y el control glucémico[13].

Otros autores señalan que la diabetes suele ir acompañada de dislipidemia no diagnosticada. En base a esto y con resultados comparables con nuestro

Figura 2: Análisis multivariante mediante regresión logística binaria con el método de Wald para control del tratamiento según valores de glucemia basal y según valores de hemoglobina glicosilada.



trabajo, se realizó un estudio retrospectivo con 140 pacientes con DM2 durante un período de un año, con el objetivo de investigar la relevancia clínica de los perfiles y las proporciones lipídicas como modelos bioquímicos predictivos para el control glucémico en pacientes con diabetes mellitus tipo 2 (DM2). Los hallazgos del perfil lipídico como colesterol total (CT), colesterol unido a lipoproteínas de baja densidad (C-LDL), triglicéridos (TG) y parámetro de relación de lípidos (relación C-LDL a colesterol unido a lipoproteínas de alta densidad (C-HDL)) fueron más altos en los pacientes con control glucémico deficiente (p <0,05) y el cHDL fue significativamente menor en los pacientes con control glucémico deficiente. Estos resultados corroboran lo encontrado por otros autores, señalando que los perfiles de lípidos (LDL-C) y las proporciones de lípidos (LDL-C / HDL-C y TC / HDL-C ratio) muestran marcadores potenciales que pueden usarse para predecir el control glucémico en pacientes con DM2[14]. También otros autores han evaluado la asociación de la relación triglicéridos a colesterol HDL (TG / HDL-C) y el índice de glucosa triglicéridos (TyG) con la HbA1c y evaluar su papel potencial como predictores del control glucémico en pacientes con DM2. Ese estudio transversal incluyó un total de 113 pacientes clasificados según sus valores de HbA1c en dos grupos: pacientes con buen control glucémico (HbA1c <7%) y con mal control glucémico (HbA1c >7%). Los pacientes con mal control glucémico mostraron mayores valores de TG/HDL-C y de índice TyG. Un análisis de regresión lineal estableció la relación TG / HDL-C y el IMC, así como el índice TyG y el IMC, se asociaron significativamente de forma independiente con la HbA1c incluso después de controlar la edad, el sexo, la duración de la diabetes y el tabaquismo[15].

Aunque las características sociodemográficas de los sujetos participantes se estructuran de un modo diferente al de nuestro trabajo, también se comprobó que en los hombres era menor el control glucémico en un estudio descriptivo transversal retrospectivo dirigido a detectar factores modificables y poblaciones diana asociados al mal control de la diabetes tipo 2 (DM2) en atención primaria realizado en Tenerife. Además del control de la DM2, se obtuvieron datos sociodemográficos, clínicos, hábitos de vida y seguimiento de medidas preventivas y terapéuticas. Fueron evaluados 587 pacientes tratados con fármacos antidiabéticos, una parte de los cuales partían de incumplimiento terapéutico o padeciendo inercia terapéutica; el mal control de DM2 era peor en los hombres menores de 65 años, con ratio Triglicéridos/ HDL ≥ 3 o con síndrome metabólico y en los que tenían indicados mayor número de fármacos para DM2[16].

Por otra parte, el tratamiento terapéutico puede establecer diferencia en los resultados, lo cual no fue abordado en nuestro trabajo. Así se evaluó la eficacia hipoglucemiante de la adición de empagliflozina frente a los medicamentos existentes que aumentan la dosis en pacientes con diabetes tipo 2 no controlada (DT2). Después del tratamiento, la reducción de HbA1c fue significativamente mayor en el grupo de empagliflozina que en los controles. La empagliflozina disminuyó la presión arterial sistólica y diastólica, los triglicéridos y los niveles de alanina y aspartato aminotransferasa. El peso corporal, el IMC, la circunferencia de la cintura, la masa grasa y el área de grasa visceral abdominal disminuyeron significativamente mientras se mantuvo la masa corporal magra[17].

Al igual que el tratamiento hipoglucemiante, es importante recalcar hacia hábitos de alimentación, modificación en la dieta, realización de ejercicios, todo lo cual puede beneficiar el control glucémico en pacientes de DM2. Estudios observacionales han puesto en evidencia que la ingesta de ácidos grasos poliinsaturados (PUFA) reduce el riesgo de DM2, sin embargo, en cuanto al control de la glucemia, no todos los estudios coinciden al señalar que una dieta rica en aceites de pescado pueda favorecer dicho control. las intervenciones dietéticas no ofrecen una solución definitiva dado que los estudios parten de condiciones muy variadas, no siempre se obtiene regulación de los parámetros glucémicos e incluso en algunos casos se ha obtenido un incremento de los niveles de glucosa[18].

También se ha probado el uso de dietas cetogénicas (KD) pues no solo tiene un efecto terapéutico sobre el control de la glucemia y los lípidos en pacientes con DM2, sino que también contribuye significativamente a la pérdida de peso. Mediante metaanálisis se ha encontrado que el nivel de glucosa en sangre en ayunas y la hemoglobina glicosilada disminuyeron después de la intervención de KD[19].

Una dieta baja en carbohidratos ha resultado ser efectiva para reducir los niveles de glucosa en sangre para pacientes portadores de DM2 en América e Inglaterra; similares resultados se observaron en pacientes chinos, pudiéndose también regular los niveles de lípido, disminuye el IMC, así como la dosis de insulina que requirieron dichos pacientes[20].

Otros estudios han empleado ejercicios físicos para regular parámetros bioquímicos de insulina/ glicemia basal y poscarga en pacientes obesos con insulinorresistencia, encontrando mejoría los parámetros de glicemia e insulina en ayuno y poscarga[21].

Como puntos fuertes del estudio destacaremos el gran tamaño muestral (más de 10000 diabéticos tipo 2), el que la valoración del grado de control se realiza no sólo con valores de glucemia basal sino también con valores de hemoglobina glicosilada y que se han tenido en cuenta bastantes variables que podrían influir en el grado de control como edad, sexo, clase social, IMC, tabaco y tratamiento con patologías concomitantes.

Como limitaciones destacaríamos que se ha realizado en población laboral (entre 18-69 años) por lo que los resultados no son extrapolables a la población general ya que faltaría por analizar los no incluidos en este rango de edad. Tampoco se ha tenido en cuenta el tipo de fármaco empleado, ya que la diversidad era enorme, por lo que no sabemos si este factor podría influir o no en el grado de control glucémico. Otra limitación es que la valoración del grado de cumplimiento ha sido autoreportada.

Bibliografía

1. Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Emerging Risk Factors Collaboration. Lancet. 2010; 26;375:2215-22

2. Campbell AW. The diabetes pandemic. Altern Ther Health Med. 2011 Nov-Dec;17(6):8-9.

3. Goday A. Epidemiología de la diabetes y sus complicaciones no coronarias, Rev Esp Cardiol 2002;55(6):657-70

4. Soriguer F, Goday A, Bosch-Comas A, Bordiú E, Calle-Pascual A, Carmena R, et al. Prevalence of diabetes mellitus and impaired glucose regulation in Spain: the Di@bet.es Study. Diabetologia. 2012 Jan;55(1):88-93.

5. Svensson E, Mor A, Rungby J, Berencsi K, Nielsen JS, Stidsen JV, et al. Lifestyle and clinical factors associated with elevated C-reactive protein among newly diagnosed Type 2 diabetes mellitus patients: a cross-sectional study from the nationwide DD2 cohort. BMC Endocr Disord. 2014 Aug 28;14:74.

6. Amy S. Shah, Kristen J. Nadeau. The changing face of paediatric diabetes. Diabetologia 2020; 63:683-91

7. Whisman MA, Rhee SH, Hink L, Boeldt DL, Johnson DP. Genetic and Environmental Influences on the Association between Subjective Well-Being and Marital Adjustment. Couple Family Psychol. 2014;3(1):48-64.

8. Aschbacher K, Kornfeld S, Picard M, Puterman E, Havel PJ, Stanhope K, et al. Chronic stress increases vulnerability to diet-related abdominal fat, oxidative stress, and metabolic risk. Psychoneuroendocrinology. 2014 Aug;46:14-22.

9. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021 Jan;44(Suppl 1):S15-S33.

10. Domingo-Salvany A, Bacigalupe A, Carrasco JM, Espelt A, Ferrando J, Borrell C. Propuesta de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011. Gac Sanit 2013;27(3):263-72

11. Haynes RB, Yao X, Degani A, Kripalani S, Grag A, McDonald HP. Intervenciones para mejorar el cumplimiento con la medicación (Revisión Cochrane traducida). En: La Biblioteca Cochrane Plus, 2006 Número 1. Oxford.

12. Landis J, Koch G: The measurement of observer agreement for categorical data. Biometrics 1977; 33:159-74.

13. Marinho FS, Moram CBM, Rodrigues PC, Leite NC, Salles GF, Cardoso CRL. Treatment Adherence and Its Associated Factors in Patients with Type 2 Diabetes: Results from the Rio de Janeiro Type 2 Diabetes Cohort Study. J Diabetes Res. 2018;2018:8970196.

14. Artha IMJR, Bhargah A, Dharmawan NK, Pande UW, Triyana KA, Mahariski PA, et al. High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. Vasc Health Risk Manag. 2019;15:149-157. Published 2019 Jun 5. doi:10.2147/VHRM.S209830

15. Babic N, Valjevac A, Zaciragic A, Avdagic N, Zukic S, Hasic S. The Triglyceride/HDL Ratio and Triglyceride Glucose Index as Predictors of Glycemic Control in Patients with Diabetes Mellitus Type 2. Med Arch. 2019;73(3):163-168. doi:10.5455/medarh.2019.73.163-8

16. Cuevas Fernández FJ, Pérez de Armas A, Cerdeña Rodríguez E, Hernández Andreu M, Iglesias Girón MJ, García Marrero MR, et al. Mal control de la diabetes tipo 2 en un centro de salud de atención primaria: factores modificables y población diana. Aten Primaria. 2021;53(9):102066.

17. Shin Y, Moon JH, Chin HJ, Ferrannini E, Lim S. Glycemic Efficacy and Metabolic Consequences of an Empagliflozin Add-on versus Conventional Dose-Increasing Strategy in Patients with Type 2 Diabetes Inadequately Controlled by Metformin and Sulfonylurea. Endocrinol Metab (Seoul). 2020;35(2):329-38.

18. Telle-Hansen VH, Gaundal L, Myhrstad MCW. Polyunsaturated Fatty Acids and Glycemic Control in Type 2 Diabetes. Nutrients. 2019;11(5):1067.

19. Yuan X, Wang J, Yang S, Gao M, Cao L, Li X, et al. Effect of the ketogenic diet on glycemic control, insulin resistance, and lipid metabolism in patients with T2DM: a systematic review and meta-analysis. Nutr Diabetes. 2020;10(1):38.

20. Wang LL, Wang Q, Hong Y, Ojo O, Jiang Q, Hou YY, et al. The Effect of Low-Carbohydrate Diet on Glycemic Control in Patients with Type 2 Diabetes Mellitus. Nutrients. 2018;10(6):661.

21. Dalmazzo V, Ponce Á, Delgado Floody PA, Carrasco Alarcón VC, Martínez Salazar C. Efectos del ejercicio físico intervalado en la mejora del control glicémico de adultos obesos con insulinorresistencia [Effects of interval exercise in the improvement of glycemic control of obese adults with insulin resistance]. Nutr Hosp. 2019;36(3):578-82.

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ORIGINAL

Evaluation the relationship between serum levels of interleukin_37 and liver aminotransferase enzymes in acute and chronic stages of hepatitis B infection in Iraq

Evaluación de la relación entre los niveles séricos de interleucina_37 y las enzimas aminotransferasa hepáticas en las etapas aguda y crónica de la infección por hepatitis B en Irak

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Abstract

Background: Hepatitis B is liver inflammation that can be caused by viruses, medicines, or toxic substances. Inflammatory chemokines and cytokines, epithelial cells, PBMCs, and macrophages all produce interleukin IL-37, which has been associated with liver injury known as)IL-1 family member 7). The "AST and ALT" levels of aminotransferase enzymes "AST and ALT" are useful in the diagnosis of liver disease.
Methods: Interleukin-37, ALT, and AST concentrations in the blood serum of three distinct groups (anti- core (+), HB patients and healthy volunteers) were assessed using a variety of methodologies in this research.
Results: According to the findings of this research, The anti- core (+)group IL-37 serum levels differed significantly from those of the HB patients and healthy controls , While serum IL-37 levels did not differ significantly between HB patients and the healthy control group, "ALT" and "AST" serum levels were found to be significantly greater in the anti- core (+) group than in the other two groups, highly significant positive correlation between IL-37and "ALT" ($r=0.510$ and $P < 0.01$) and also with "AST" ($r=0.445$ and $P < 0.01$).
Conclusion: According to this study, which looked at three separate groups of patients, the anti- core (+) had the greatest levels of interleukines-37 and aminotransferase enzymes (ALT and AST), and the two appeared to be positively associated.

Key words: ALT, AST, IL-37, hepatitis B.

Resumen

Antecedentes: La hepatitis B es una inflamación del hígado que puede ser causada por virus, medicamentos o sustancias tóxicas. Las quimiocinas y citoquinas inflamatorias, las células epiteliales, las PBMC y los macrófagos producen la interleucina IL37, que se ha asociado a la lesión hepática conocida como (IL-1 family member 7). Los niveles de las enzimas aminotransferasas "GOT y GPT" son útiles en el diagnóstico de la enfermedad hepática.
Métodos: En esta investigación se evaluaron las concentraciones de interleucina-37, GOT y GPT en el suero sanguíneo de tres grupos distintos (anti-core (+) , pacientes con HB y voluntarios sanos) utilizando diversas metodologías.
Resultados: Según los resultados de esta investigación, los niveles séricos de IL-37 de los pacientes con core difieren significativamente de los de los pacientes con HB y de los controles sanos , Mientras que los niveles séricos de IL-37 no difieren significativamente entre los pacientes con HB y el grupo de controles sanos, los niveles séricos de "GOT" y "GPT" resultaron ser significativamente mayores en el grupo anti-core (+) que en los otros dos grupos, correlación positiva altamente significativa entre IL-37y "GOT" ($r=0.510$ y $P < 0,01$) y también con "AGPT" ($r= 0,445$ y $P < 0,01$).
Conclusiones: Según este estudio, en el que se analizaron tres grupos distintos de pacientes, los antinucleares (+) presentaban los mayores niveles de interleucinas-37 y de enzimas aminotransferasas (GOT y GPT), y ambos parecían estar positivamente asociados.

Palabras clave: GOT, GPT, IL-37, hepatitis B.

Introduction

As a result of exposure to blood and blood products as well as other bodily fluids and the use of sharps objects, people get hepatitis B, a liver inflammation[1]. Globally, 116 million people are chronically infected with hepatitis B, the WHO Western Pacific and African regions that number rises to 81 million. WHO A total of 60 million people in the WHO Eastern Mediterranean Region, 18 million in WHO south-east Asia, 14 million in WHO Europe, and 14 million in WHO Africa are ill. An estimated 5 million people in the Americas region have been affected[2]. Acute and chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC) can all be caused by the human (HBV). For a diagnosis of HBV infection and the disease it causes, a combination of clinical, biochemical and histological data is used. After HBV infection, a variety of viral antigens and antibodies can be found in the blood, and careful interpretation of the results is critical for the correct diagnosis of many clinical types of HBV infection[3,4.] AST and ALT, two enzymes found primarily in the liver but also in red blood cells, heart cells, muscle tissue, and other organs like the pancreas and kidneys, are involved in the metabolism of aspartate and alanine[5]. "Serum glutamic oxaloacetic transaminase (GOT) and serum glutamic pyruvic transaminase (GPT)" were previously referred to as "AST" and "ALT"[6]. AST and ALT readings can be used to diagnose liver disease. The normal range for AST and ALT blood levels is 5-40 u/l and 5-35 u/l, respectively. However, when tissues or organs such as the liver or heart are ill or injured, additional "AST" and "ALT" are released into the circulation, causing the enzyme levels to rise[7]. Serum alanine and aspartate aminotransferase "(ALT, AST)" levels begin to rise and jaundice may emerge within a few weeks of the appearance of viral indicators[8]. To put it another way, the degree of tissue damage is exactly proportional to blood levels of "AST" and "ALT". "AST" levels can rise by up to 20 times their normal value following serious injury, While it is possible for "ALT" levels to rise even further (up to 50 times greater than normal). Testing for the "AST/ALT" ratio (AST/ALT) can reveal whether or not someone's liver or another organ has been damaged[9,10]. ALT, inflammation, and/or fibrosis on liver biopsy may affect serum levels of certain of hepatic enzymes, bilirubin and albumin in patients with evidence of chronic hepatitis[11]. Hepatic function and disease severity can be evaluated and assessed using biomarkers[12]. "Natural killer (NK) cells", monocytes, and activated B cells all express "IL-37", an emerging member of the IL-1 family of cytokines[13,14]. Splice variants (a-e) are included in this set[15]. Pro-inflammatory cytokines and inflammation-inducing events can cause an increase in the IL-37 protein[16]. Macrophage or epithelial cell production of IL-37 effectively prevented the generation of pro-inflammatory and innate immunocytes[16,17]. In a variety of disorders, IL-37 inhibits inflammation and innate immunity[18]. There is still a lack of understanding of the role of IL-37 in the immunological response to chronic hepatitis B and C. In this research, the serum levels of IL-37, ALT, and AST were evaluated to see if there was a correlation between them at different phases of hepatitis B infection, as well as IL-37's role in hepatitis B virus pathogenesis.

Materials and methods

Blood samples collection

The anti –core (+) group consisted of 100 blood samples that tested negative for hepatitis B surface antigen (HBsAg(-)) using an immunoassay ELISA (HBsAg) (Imbian ELISA kit, Novosibirsk, Russia), but positive (+) anti-HBc by utilizing the anti-HBc II kit (Abbott Diagnostics, USA). Iraq's National Blood Transfusion Center was the source of this. Another 80 samples were taken from patients at Baghdad's gastrointestinal and hepatitis teaching hospital, while the third group acquired 20 samples from healthy people. Using centrifugation, the serum from each sample was divided into two 1.5-ml tubes and stored at a low temperature (-70°C) until testing.

Laboratory testing

Measured of the Interleukin -37, " (ALT)" and "(AST)"

An enzyme-linked immunosorbent assay (ELISA) kit from Cusabio was used to measure "IL-37" levels in the blood of each of the three study groups (the U.S.).Units per liter (U/L) is the most frequent way to measure ALT. (The U.S.A.: GenWay's ALT Assay Kit). Aspartate Aminotransferase is nearly commonly measured in units/ liter (U/L). Making Use of Activity Assay Kit (SIGMAALDRICH, US.A.).

Statistical analysis:

For both the descriptive and inferential analyses, SPSS software (version 20) was used. The average and standard deviation of the data were used to represent the findings. The statistical significance of the relationships between the variables was assessed through the application of one-way analysis of variance (ANOVA).

Results

Anti-inflammatory properties and the capacity to reduce the immune system's reaction to a number of ailments have made IL-37 a popular supplement (Akdis and others 2011). The relationship between HBV infection and IL-37 has not yet been investigated. Serum IL-37 concentrations in healthy individuals, HB patients, and core patients were all measured as part of this study. Results from this study show that IL-37 levels in the core group patients were significantly higher than those in HB patients and healthy groups, although there was no significant difference between patients and healthy groups in IL-37 serum levels, **table I**.

Table I: "IL-37" levels in three groups.

Groups	Mean + S.D	
Anti-Core (+)	404.49 + 166.8	a
HB Patients	245.87 + 84.73	b
Healthy	201.22 + 23.36	b
P value	< 0.01	

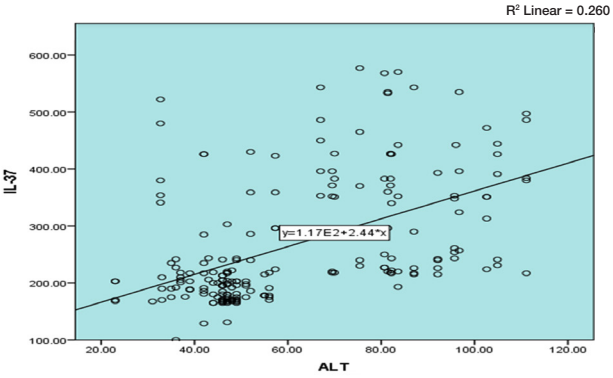
Serum "ALT" levels were also examined across three groups: core patients, patients with a diagnosis of hepatitis B, and healthy individuals. According to the results in the table, the ALT levels in serum were significantly higher in the Anti-core(+) group than in the other two, despite the fact that there were no differences between the HB patients and healthy groups, **table II**.

Table II: "ALT" levels in three groups.

Groups (ALT)	Mean + S.D	
Anti-Core (+)	78.15 + 20.27	a
HB Patients	45.36 + 7.46	b
Healthy	41.10 + 4.93	b
P value	< 0.01	

The correlation between IL-37 and ALT levels in three groups was studied according to the study, the serum levels of IL-37 (r = 0.510 and P: <0.001) were highly correlated with ALT (r = 0.510), **figure 1**.

Figure 1: The relationship between serum levels of interleukin-37 and aminotransferase (ALT).



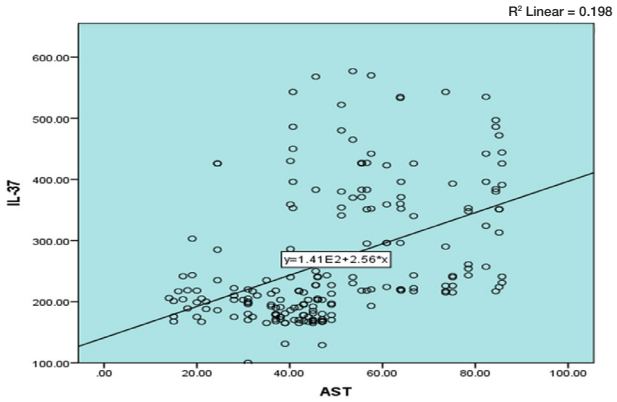
Anti-core (+) group had greater AST concentrations than patients and healthy people, whereas those in the HB group had higher AST concentrations than those in the healthy group but lower levels than those in the HB patients group (**Table III**).

Table III: "AST" levels in three groups.

Groups (AST)		
Anti-Core (+)	62.27 + 16.68	a
HB Patients	40.61 + 6.06	b
Healthy	19.35 + 4.10	c
P value	< 0.01	

It was revealed that serum levels of "IL-37" and "AST" were higher positively correlated (r =0.45) in three groups of samples, **figure 2**.

Figure 2: The relationship between serum levels of interleukin-37 and aspartate aminotransferase (AST).



Discussion

This inflammation is brought on by the hepatocyte and immune cell release of cytokines in response to the HBV core protein[19]. Donors who had (anti –HBc+) were shown to have considerably greater levels of serum IL-37 and their association to liver enzymes (ALT and AST) in this study compared to patients with HBV and healthy control groups. levels of IL-37, also were found to be positive correlated with ALT (r =0.510 and P:<0.01) and AST (r=0.445 and P<0.01) after using correlation analysis. Other researchers have discovered that the anti-inflammatory cytokine "IL-37" reduces the immune system's response to a variety of disorders because it is ability to inhibit both the natural and adaptive immune systems[20]. Study after study has shown that IL-37 inhibits a wide range of functions, such as antigen presentation and macrophage activation[21]. Previous studies have connected the "IL-37" to HB inflammation[22]. Proinflammatory and anti-inflammatory cytokines were found at significant concentrations in individuals with CAHB in the current study[22].

It is possible that patients with elevated levels of "IL-37" may have HB-specific immune responses. Increased "IL37" dramatically decreased expression of IFN-alpha (IL1beta) and TNF-alpha (IL-6) in PBMCs[23]. This shows that proinflammatory cytokines may increase the synthesis of "IL-37" in core patients, and that "IL-37" may initiate a negative feedback loop to reduce the excessive production of proinflammatory cytokines. Up regulation of antiinflammatory cytokines, such as "IL-37", could thus be a possible underlying mechanism for reducing inflammation and easing illness symptoms. However, the amounts of these anti-inflammatory cytokines may not be high enough to offset the negative effects of proinflammatory cytokines in individuals with progressive core disease[24,25].

Previous research discovered that individuals with achronic HB infection had much greater amounts of "IL-37" in their serum than healthy controls, and these higher levels of "IL-37" were found to be associated with higher levels of "(ALT)", which matched the findings of this study26. The aminotransferase enzymes "(ALT and AST)" are a sensitive marker for hepatocyte necrosis. Increased "ALT" levels are a better indicator of liver damage than decreased "ALT." The third zone of the liver acini contains a larger concentration of "AST", and injury to this zone can result in more severe alterations in "AST" levels[27]. Other investigations discovered that AST may be a more accurate predictor of liver parenchymal inflammation and necrosis, liver fibrosis and chronic hepatitis B consequences than "ALT". These findings are consistent with those of prior research[28] and contradict those of other studies that found a strong correlation between ALT levels and inflammatory grade[29].

Conclusion

This study measured the serum levels of interleukin-37 and liver aminotransferase enzymes (ALT and AST) this study found that serum levels of interleukin -37 in The anti –core (+) group was significantly higher than the other two groups (HB patients and healthy control)and there was a strong correlation between serum levels of interleukin-37 liver aminotransferase enzymes ("ALT" and "AST")in the donors who had the anti-HBc (+) / HBs Ag (-) or chronic HBV infection, which indicates the persistence of inflammation in the liver even when HBs Ag is not present.

Conflict of interest

Authors do not have any conflict of interest to declare.

References

1. Kim HS, Rotundo L, Yang JD, Kim D, Kothari N, Feurdean M, et al. Racial/ethnic disparities in the prevalence and awareness of Hepatitis B virus infection and immunity in the United States. J Viral Hepat. 2017;24(11):1052-66. doi:10.1111/jvh.12735

2. Hepatitis B: Word Health Organization 2021 [27 July]. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b

3. Kuhns MC, Busch MP. New strategies for blood donor screening for hepatitis B virus: nucleic acid testing versus immunoassay methods. Mol Diagn Ther. 2006;10(2):77-91. doi:10.1007/bf03256447

4. Chang MH. Chronic hepatitis virus infection in children. J Gastroenterol Hepatol. 1998;13(5):541-8. doi:10.1111/j.1440-1746.1998.tb00685.x

5. Jacobs DS, Kasten B, Demott W. Laboratory test handbook. LWW; 1991.

6. Witjes CD, JN IJ, van der Eijk AA, Hansen BE, Verhoef C, de Man RA. Quantitative HBV DNA and AST are strong predictors for survival after HCC detection in chronic HBV patients. Neth J Med. 2011;69(11):508-13.

7. Schumann G, Aoki R, Ferrero CA, Ehlers G, Férard G, Gella FJ, et al. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 degrees C. Clin Chem Lab Med. 2006;44(9):1146-55. doi:10.1515/cclm.2006.212

8. Liang TJ, Ghany M. Hepatitis B e Antigen--the dangerous endgame of hepatitis B. N Engl J Med. 2002;347(3):208-10. doi:10.1056/NEJMe020060

9. http://www.medfriendly.com/aspartateaminotransferase.html

10. http://www.medfriendly.com/alanineaminotransferase.html.

11. Abulude OA, Ahmed I, Sadisu FU. Assessment of Hepatitis B Viral Infection as a Predictor of Hepatic Enzymes and Compounds Alteration among Antenatal Patients. Med Sci (Basel). 2017;5(4). doi:10.3390/medsci5040024

12. Liang TJ. Hepatitis B: the virus and disease. Hepatology. 2009;49(5 Suppl):S13-21. doi:10.1002/hep.22881

13. Dunn E, Sims JE, Nicklin MJ, O'Neill LA. Annotating genes with potential roles in the immune system: six new members of the IL-1 family. Trends Immunol. 2001;22(10):533-6. doi:10.1016/s1471-4906(01)02034-8

14. Bufler P, Azam T, Gamboni-Robertson F, Reznikov LL, Kumar S, Dinarello CA, et al. A complex of the IL-1 homologue IL-1F7b and IL-18-binding protein reduces IL-18 activity. Proc Natl Acad Sci U S A. 2002;99(21):13723-8. doi:10.1073/pnas.212519099

15. Sharma S, Kulk N, Nold MF, Gräf R, Kim SH, Reinhardt D, et al. The IL-1 family member 7b translocates to the nucleus and down-regulates proinflammatory cytokines. J Immunol. 2008;180(8):5477-82. doi:10.4049/jimmunol.180.8.5477

16. Nold MF, Nold-Petry CA, Zepp JA, Bufler P, Dinarello CA. 120 The IL-1 family member IL-1F7 reduces innate immunity by inhibiting Toll-like receptor and IL-1 signaling pathways. Cytokine. 2008;3(43):264.

17. Boraschi D, Lucchesi D, Hainzl S, Leitner M, Maier E, Mangelberger D, et al. IL-37: a new anti-inflammatory cytokine of the IL-1 family. Eur Cytokine Netw. 2011;22(3):127-47. doi:10.1684/ecn.2011.0288

18. Akdis M, Burgler S, Crameri R, Eiwegger T, Fujita H, Gomez E, et al. Interleukins, from 1 to 37, and interferon-γ: receptors, functions, and roles in diseases. J Allergy Clin Immunol. 2011;127(3):701-21.e1-70. doi:10.1016/j.jaci.2010.11.050

19. Lin YJ, Huang LR, Yang HC, Tzeng HT, Hsu PN, Wu HL, et al. Hepatitis B virus core antigen determines viral persistence in a C57BL/6 mouse model. Proc Natl Acad Sci U S A. 2010;107(20):9340-5. doi:10.1073/pnas.1004762107

20. Li S, Neff CP, Barber K, Hong J, Luo Y, Azam T, et al. Extracellular forms of IL-37 inhibit innate inflammation in vitro and in vivo but require the IL-1 family decoy receptor IL-1R8. Proc Natl Acad Sci U S A. 2015;112(8):2497-502. doi:10.1073/pnas.1424626112

21. Ye L, Ji L, Wen Z, Zhou Y, Hu D, Li Y, et al. IL-37 inhibits the production of inflammatory cytokines in peripheral blood mononuclear cells of patients with systemic lupus erythematosus: its correlation with disease activity. J Transl Med. 2014;12:69. doi:10.1186/1479-5876-12-69

22. Dinarello CA, Nold-Petry C, Nold M, Fujita M, Li S, Kim S, et al. Suppression of innate inflammation and immunity by interleukin-37. Eur J Immunol. 2016;46(5):1067-81. doi:10.1002/eji.201545828

23. Palomo J, Dietrich D, Martin P, Palmer G, Gabay C. The interleukin (IL)-1 cytokine family--Balance between agonists and antagonists in inflammatory diseases. Cytokine. 2015;76(1):25-37. doi:10.1016/j.cyto.2015.06.017

24. Li C, Ji H, Cai Y, Ayana DA, Lv P, Liu M, et al. Serum interleukin-37 concentrations and HBeAg seroconversion in chronic HBV patients during telbivudine treatment. J Interferon Cytokine Res. 2013;33(10):612-8. doi:10.1089/jir.2013.0001

25. Meng JP, Luo P, Bai Y, Cui F. Entecavir downregulates interleukin-37 in patients with chronic active hepatitis B infection. J Int Med Res. 2020;48(1):300060519884157. doi:10.1177/0300060519884157

26. Dinarello CA. Introduction to the interleukin-1 family of cytokines and receptors: Drivers of innate inflammation and acquired immunity. Immunol Rev. 2018;281(1):5-7. doi:10.1111/imr.12624

27. Henriksen JH, Siemssen O, Krintel JJ, Malchow-Møller A, Bendtsen F, Ring-Larsen H. Dynamics of albumin in plasma and ascitic fluid in patients with cirrhosis. J Hepatol. 2001;34(1):53-60. doi:10.1016/s0168-8278(00)00009-x

28. Hasanjani Roushan MR, Hajiahmadi M, Shafaie S. Histopathological features of liver and its relation to serum transaminase levels in 91 cases of anti-HBe-positive chronic hepatitis B. Int J Clin Pract. 2005;59(7):791-4. doi:10.1111/j.1742-1241.2005.00416.x

29. Wang ZL, Liu WP, Wang GQ. [Relationship among pathological changes in liver tissues and level of serum ALT, virology of patients with chronic HBV infection]. Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi. 2008;22(5):388-90.

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ORIGINAL

Papel de la enfermeria del trabajo en la detección precoz de personas con alto riesgo de resistencia a la insulina

Role of occupational nursing in the early detection of people at high risk of insulin resistance

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Resumen

Introducción: La resistencia a la insulina (RI) es un importante problema de salud pública debido a su estrecha relación con elevaciones de la glucemia, ya sea con prediabetes o con diabetes mellitus.
Objetivo: El objetivo de este trabajo es doble, por una parte conocer las variables que influyen en la aparición de la RI y por otro establecer un perfil de persona de alto riesgo sobre la que pueden actuar los profesionales de salud laboral, especialmente el personal de enfermería.
Material y métodos: Estudio descriptivo y transversal en 418343 trabajadores españoles en los que se determina la RI aplicando tres escalas diferentes: Score Metabólico para la Resistencia a la Insulina (METS-IR), índice triglicéridos/HDL y el índice triglicéridos glucosa (TyG index). Se valora como influyen en los valores de estas escalas variables sociodemográficas (sexo, edad y clase social), el consumo de tabaco y el índice de masa corporal.
Resultados: La prevalencia de RI varia en las mujeres de 6,4% al emplear METS-IR, 7,1% si utilizamos triglicéridos/HDL y 12,5% si la escala empleada es el TyG index. En los varones la prevalencia es de 11,4%, 26,7% y 27,3% respectivamente. La variable que más incrementa el riesgo de presentar alto riesgo de RI con las tres escalas es la obesidad y la que menos el tabaquismo. El perfil de persona considerada de alto riesgo es un varón con 50 o más años, fumador, de clase social II o III y obeso.
Conclusiones: El establecimiento de un perfil de personas con alto riesgo de presentar RI puede permitir que los profesionales de salud laboral, especialmente de enfermería, pueda desarrollar estrategias de prevención y de diagnóstico precoz para disminuir la prevalencia de RI.

Palabras clave: Resistencia a la insulina, obesidad, diagnóstico precoz, prevención, salud ocupacional.

Abstract

Introduction: Insulin resistance (IR) is a major public health problem because of its close association with elevations in blood glucose, either with pre-diabetes or diabetes mellitus.
Objective: The aim of this study is twofold: on the one hand, to determine the variables that influence the onset of IR and, on the other, to establish a profile of high-risk individuals on whom occupational health professionals, especially nurses, can take action.
Methods: Descriptive and cross-sectional study in 418343 Spanish workers in which IR was determined by applying three different scales: Metabolic Score for Insulin Resistance (METS-IR), triglycerides/HDL index and the triglycerides/glucose index (TyG index). The influence of sociodemographic variables (sex, age and social class), tobacco consumption and body mass index on the values of these scales was assessed.
Results: The prevalence of IR varies in women from 6.4% when using METS-IR, 7.1% when using triglycerides/HDL and 12.5% if the scale used is the TyG index. In men the prevalence is 11.4%, 26.7% and 27.3% respectively. The variable that most increases the risk of presenting a high risk of IR with the three scales is obesity and the one that least increases the risk of smoking. The profile of a person considered to be at high risk is a male aged 50 or over, smoker, social class II or III and obese.
Conclusions: The establishment of a profile of people at high risk of developing IR may allow occupational health professionals, especially nurses, to develop prevention and early diagnosis strategies to reduce the prevalence of IR.

Key words: Insulin resistance, obesity, early diagnosis, prevention, occupational health.

Introducción

La resistencia a la insulina (RI) es un problema de salud que se relaciona con elevaciones de la glucemia, inicialmente con prediabetes y finalmente con diabetes tipo 2[1]. La RI aparece cuando el cuerpo no reacciona a la acción de la insulina, de manera que se eleva la glucemia y con ello se incrementa la necesidad de más insulina. Se genera un círculo vicioso, que puede desencadenar diabetes cuando el páncreas es incapaz de producir más insulina.

Las causas de la RI no se conocen del todo aunque se han identificado numerosos factores de riesgo que pueden contribuir a su desarrollo. En los últimos años, la RI ha ido aumentado en paralelo a la elevación del sobrepeso y la obesidad[2], lo que hace pensar en el importante papel que tienen las células grasas en este proceso. Otros factores involucrados en la génesis de la RI son la baja actividad física[3], las dietas ricas en carbohidratos[4], el estrés crónico[5], dosis altas de esteroides durante mucho tiempo[6] y situaciones patológicas como el ovario poliquístico[7] y la enfermedad de Cushing[8].

Es importante detectar precozmente la RI ya que se puede revertir si se produce un cambio en los estilos de vida que incluyen ejercicio físico y alimentación saludable. La reducción del consumo de azúcares provoca una disminución de la producción de insulina y, por lo tanto, de la resistencia a su acción.

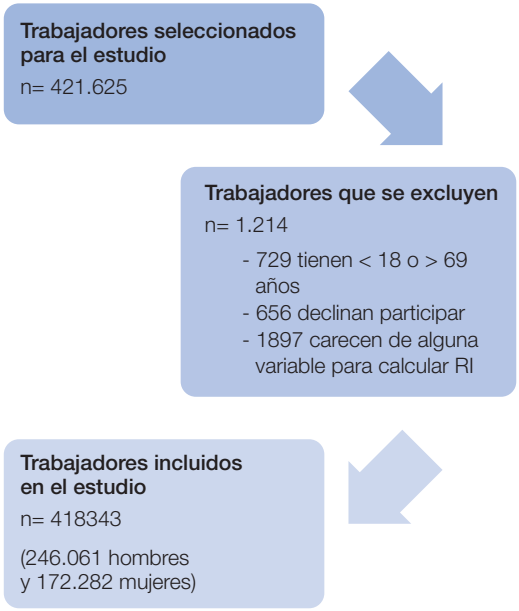
Poco se ha estudiado como afectan variables sociodemográficas como la edad, el sexo, o la clase social en la RI, por ello uno de los objetivos de este trabajo es determinar cómo influyen estas variables, además del consumo de tabaco y la obesidad, en que se incremente el riesgo de padecer RI. El otro objetivo es valorar el papel de los profesionales de enfermería de las unidades de salud en la detección precoz de personas con alto riesgo de presentar resistencia a la insulina estableciendo un perfil de persona sobre el que plantear estrategias de intervención y/o prevención.

Material y métodos

Se realizó un estudio descriptivo y transversal en 421625 trabajadores que acudieron a los reconocimientos médicos laborales periódicos entre enero de 2016 y junio de 2020, en empresas de diferentes regiones españolas. El flujograma se presenta en la **figura 1**.

Los datos se obtuvieron de una base anonimizada de trabajadores depositada en un repositorio universitario homologado. En esta base se incluyen los reconocimientos médicos laborales realizados entre los años 2016-2020 en diversos servicios de prevención de riesgos laborales de todo el territorio nacional (RD 688/2005 de 10 de junio y Ley 31/95 de Prevención de Riesgos Laborales). El Comité de Ética de Investigación de Illes Balears aprobó el estudio (IB 4383/20). Todos los procedimientos se realizaron de acuerdo con las normas éticas del comité de investigación institucional y con la Declaración de Helsinki de 2013.

Figura 1: Flujograma de los participantes en el estudio.



Criterios de inclusión:

Se incluyeron los trabajadores en activo, entre 18 y 69 años de edad, que aceptaron participar en el estudio previa firma del correspondiente consentimiento informado.

Las determinaciones antropométricas, clínicas y analíticas las realizaron el personal sanitario de las diferentes unidades de salud laboral participantes en el estudio, tras homogenizar las técnicas de medición.

El peso (expresado en kilogramos) y la altura (expresada en centímetros) se determinaron con una báscula-tallímetro modelo SECA 700 con capacidad para 200 kg y divisiones de 50 gramos, con tallímetro telescópico añadido SECA 220 de división milimétrica e intervalo 60-200 cm.

La circunferencia de cintura se midió en centímetros con una cinta métrica SECA modelo 20, con intervalo de 1-200 cm y división milimétrica. Para su valoración, la persona se sitúa en bipedestación, pies juntos y tronco erguido, abdomen relajado y extremidades superiores colgando a ambos lados del cuerpo. Se coloca la cinta métrica paralela al suelo a nivel de la última costilla flotante.

La presión arterial se determinó en decúbito supino con un esfigmomanómetro automático OMRON M3 calibrado tras 10 minutos de reposo (tamaño del manguito ajustado a la circunferencia del brazo). Se realizaron tres mediciones con intervalos de un minuto y se calculó la media de las tres.

Las muestras de sangre se obtuvieron por venopunción periférica tras ayuno de 12 horas y se remitieron a los laboratorios de referencia donde fueron procesadas en un tiempo máximo de 48-72 horas. Las cifras de glucemia, colesterol total y triglicéridos se determinaron por métodos enzimáticos automatizados, expresando los valores en mg/dL. El nivel de colesterol HDL (mg/dL) se calculó por precipitación con dextrano-sulfato Cl2Mg, y el de colesterol LDL (mg/dL) mediante la fórmula de Friedewald (siempre que el nivel de triglicéridos fuera inferior a 400 mg/dL): LDL= colesterol total – HDL – (triglicéridos/5).

El índice de masa corporal (IMC) se calculó dividiendo el peso entre el cuadrado de la altura en metros; se consideró obesidad a partir de 30 Kg/m^2.

Las escalas que valoran resistencia a la insulina son:

- Triglicéridos/HDL. Se calcula dividiendo los triglicéridos entre el HDL colesterol. Se considera alto riesgo de RI cuando los valores son superiores a 3,1 en varones y 2,2 en mujeres[9].
- TyG index.= LN (Triglicéridos [mg/dL] × glucemia [mg/dL]/2)[9]. Se establecen como puntos de corte para riesgo alto de RI 8,8 3n varones y 8,7 en mujeres.
- Score Metabólico para la Resistencia a la Insulina. METS-IR[10]. LN (2 x glucemia +Triglicéridos) x IMC/LN (HDL-c). Se considera riesgo alto de RI a partir de 50.

La clase social se obtuvo de la Clasificación Nacional de Ocupaciones (CNO-11) de 2011, a partir de la propuesta realizada por el grupo de determinantes sociales de la Sociedad Española de Epidemiología[11]. Se optó por la clasificación en 3 categorías: Clase I, Directores/gerentes, profesionales universitarios, deportistas y artistas. Clase II, Ocupaciones intermedias y trabajadores por cuenta propia sin asalariados. Clase III, Trabajadores no cualificados.

El consumo de tabaco se consideró como una variable dicotómica y podía tener el valor de sí/no. Un fumador era una persona que había consumido regularmente al menos 1 cigarrillo/día (o su equivalente en otros tipos de consumo) en el mes anterior o había dejado de fumar menos de un año antes. Una persona que no había fumado durante más de 12 meses o que nunca había fumado se consideraba no fumadora.

Análisis estadístico

Se realizó un análisis descriptivo de las variables categóricas, calculando la frecuencia y la distribución de las respuestas para cada una de ellas. Para las variables cuantitativas se calculó la media y la desviación estándar, mientras que para las cualitativas se calculó el porcentaje. El análisis de asociación bivariante se realizó mediante la prueba de Chi cuadrado (con corrección del estadístico exacto de Fisher cuando las condiciones lo requerían) y la prueba t de Student para muestras independientes. Para el análisis multivariante se utilizó la regresión logística binaria con el método de Wald, con cálculo de la Odds ratio y la prueba de bondad de ajuste de Hosmer-Lemeshow. La correlación entre los diferentes modelos se establece con el coeficiente de correlación de Pearson y la concordancia con el índice Kappa de Cohen. Para determinar el valor predictivo del IMC sobre los valores de alto riesgo de RI se realizan curvas ROC. El análisis estadístico se realizó con el programa SPSS 27.0, con un nivel de significación estadística aceptado de 0,05.

Resultados

Los valores de todas las variables antropométricas, clínicas y analíticas de los trabajadores incluidos en el estudio presentan valores más desfavorables en los hombres, siendo en todos los casos las diferencias observadas estadísticamente significativas.

Los grupos más numerosos en ambos sexos son las edades entre 30 y 49 años y los pertenecientes a la clase social III. La prevalencia global de fumadores es del 33,2%, siendo algo más elevado entre los hombres. Los datos completos se presentan en la **tabla I.**

Los valores medios de las tres escalas que valoran el riesgo de RI (TyG index, METS-IR y triglicéridos/HDL) van aumentando a medida que lo hace la edad, esta situación se repite en ambos sexos. Estos valores medios también van empeorando a medida que bajamos en la escala social. El incremento en los valores de IMC se traduce en un aumento de los valores medios de las escalas de RI. El consumo de tabaco sólo incrementa los valores medios de triglicéridos/HDL en hombres y de METS-IR en mujeres. Los datos completos se pueden consultar en las **tablas IIa** y **IIb**.

Algo similar a lo observado con los valores medios lo encontramos cuando se valora el efecto de las variables sociodemográficas y el IMC sobre la prevalencia de valores de alto riesgo de RI, es decir se aprecia un incremento de la prevalencia a medida que envejece la población y a medida que aumenta el peso y una elevación del riesgo de RI a medida que se desciende en la clase social. El tabaco no parece afectar a la prevalencia de valores de alto riesgo de RI en ninguno de los dos sexos. Todos los datos se presentan en las **tablas IIIa** y **IIIb**.

Tabla I: Características sociodemográficas, antropométricas, clínicas y analíticas de la muestra.

	Mujeres n=172.282 Media (DE)	Hombres n=246.061 Media (DE)	Total n=418.343 Media (DE)	p
Edad (años)	39,6 (10,8)	40,6 (11,1)	40,2 (11,0)	<0.0001
Altura (cm)	161,8 (6,5)	174,6 (7,0)	169,4 (9,3)	<0.0001
Peso (kg)	66,2 (14,0)	81,4 (14,7)	75,1 (16,2)	<0.0001
IMC (kg/m²)	25,3 (5,2)	26,7 (4,5)	26,1 (4,8)	<0.0001
Cintura (cm)	74,8 (10,6)	86,2 (11,1)	81,5 (12,2)	<0.0001
TAS (mm Hg)	117,4 (15,7)	128,2 (15,5)	123,7 (16,5)	<0.0001
TAD (mm Hg)	72,6 (10,4)	77,8 (11,0)	75,6 (11,0)	<0.0001
Colesterol	190,6 (35,8)	192,6 (38,9)	191,8 (37,7)	<0.0001
HDL-c	56,8 (8,7)	50,3 (8,5)	53,0 (9,1)	<0.0001
LDL-c	116,1 (34,8)	118,0 (36,7)	117,2 (35,9)	<0.0001
Triglicéridos	89,1 (46,2)	123,7 (86,4)	109,5 (74,6)	<0.0001
Glucemia	87,8 (15,1)	93,3 (21,3)	91,0 (19,2)	<0.0001
	%	%	%	p
18-29 años	20,7	18,8	19,6	<0.0001
30-39 años	29,7	27,6	28,4	
40-49 años	29,6	30,0	29,9	
50-59 años	16,8	19,7	18,5	
60-79 años	3,2	3,9	3,6	
Clase social I	6,9	4,9	5,7	<0.0001
Clase social II	23,4	14,9	18,4	
Clase social III	69,7	80,3	75,9	
No fumadores	67,2	66,6	66,9	<0.0001
Fumadores	32,8	33,4	33,2	

Tabla IIa: Valores medios de escalas que valoran el riesgo de resistencia a la insulina según variables sociodemográficas, consumo de tabaco e IMC en mujeres.

Mujeres		TyG index		METS-IR		TG/HDL	
	n	Media (DE)	p	Media (DE)	p	Media (DE)	p
18-29 años	35617	8,0 (0,4)	<0.0001	32,4 (7,7)	<0.0001	1,4 (0,8)	<0.0001
30-39 años	51115	8,1 (0,4)		34,2 (8,3)		1,5 (0,9)	
40-49 años	51017	8,2 (0,5)		36,0 (8,4)		1,7 (1,0)	
50-59 años	28951	8,4 (0,5)		37,96 (8,4)		2.0 (1,2)	
60-69 años	5582	8,5 (0,5)		39,1 (8,1)		2,1 (1,2)	
Clase social I	11894	8,0 (0,4)	<0.0001	32,7 (7,3)	<0.0001	1,5 (0,9)	<0.0001
Clase social II	40266	8,1 (0,5)		33,8 (7,7)		1,6 (0,9)	
Clase social III	120122	8,2 (0,5)		35,9 (8,7)		1,7 (1,0)	
No fumadores	115727	8,2 (0,5)	0.611	35,0 (8,5)	<0.0001	1,6 (1,0)	0.566
Fumadores	56555	8,2(0,5)		35,2 (8,4)		1,6 (1,0)	
Bajo peso	5768	7,9 (0,4)	<0.0001	23,7 (1,5)	<0.0001	1,3 (0,6)	<0.0001
Normopeso	91309	8,0 (0,4)		29,9 (2,9)		1,4 (0,7)	
Sobrepeso	47032	8,3 (0,5)		37,9 (3,0)		1,8 (1,1)	
Obesidad	28173	8,5 (0,5)		49,8 (6,9)		2,3 (1,3)	

Tabla IIb: Valores medios de escalas que valoran el riesgo de resistencia a la insulina según variables sociodemográficas, consumo de tabaco e IMC en hombres.

Mujeres		TyG index		METS-IR		TG/HDL	
	n	Media (DE)	p	Media (DE)	p	Media (DE)	p
18-29 años	46215	8,2 (0,5)	<0.0001	34,9 (7,4)	<0.0001	1,8 (1,3)	<0.0001
30-39 años	67798	8,4 (0,6)		38,1 (7,9)		2,4 (1,9)	
40-49 años	73935	8,6 (0,6)		40,6 (8,5)		2,9 (2,3)	
50-59 años	48522	8,7 (0,6)		42,4 (8,5)		3,2 (2,4)	
60-69 años	9591	8,8 (0,6)		43,4 (8,3)		3,2 (2,0)	
Clase social I	11950	8,4 (0,5)	<0.0001	38,6 (7,5)	<0.0001	2,5 (1,8)	<0.0001
Clase social II	36590	8,5 (0,6)		39,0 (7,9)		2,6 (2,0)	
Clase social III	197521	8,5 (0,6)		39,4 (8,7)		2,6 (2,1)	
No fumadores	163920	8,5 (0,6)	0.435	39,3 (8,6)	0.087	2,6 (2,1)	<0.0001
Fumadores	82141	8,5 (0,6)		39,3 (8,6)		2,6 (2,2)	
Bajo peso	2448	8,1 (0,5)	<0.0001	24,5 (1,6)	<0.0001	1,6 (1,1)	<0.0001
Normopeso	93186	8,3 (0,5)		32,2 (3,1)		1,9 (1,4)	
Sobrepeso	48245	8,6 (0,6)		39,9 (3,7)		2,7 (2,0)	
Obesidad	102182	8,8 (0,6)		52,2 (7,0)		3,8 (2,8)	

Tabla IIIa: Prevalencia de valores altos de escalas que valoran el riesgo de resistencia a la insulina según variables sociodemográficas, consumo de tabaco e IMC en mujeres.

Mujeres		TyG index alto		METS-IR alto		TG/HDL alto	
	n	% (IC 95%)	p	% (IC 95%)	p	% (IC 95%)	p
18-29 años	35617	6,3 (6,2-6,5)	<0.0001	3,8 (3,7-3,9)	<0.0001	3,3 (3,2-3,4)	<0.0001
30-39 años	51115	8,4 (8,4-8,4)		5,7 (5,7-5,7)		4,8 (4,8-4,8)	
40-49 años	51017	12,9 (12,9-12,9)		7,2 (7,2-7,2)		7,6 (7,6-7,6)	
50-59 años	28951	23,2 (23,0-23,4)		8,9 (8,7-9,1)		13,2 (13,0-13,4)	
60-69 años	5582	29,8 (29,2-30,4)		10,0 (9,4-10,6)		16,2 (15,6-16,8)	
Clase social I	11894	7,9 (7,4-7,9)	<0.0001	3,4 (2,9-3,9)	<0.0001	4,4 (3,9-4,9)	<0.0001
Clase social II	40266	10,9 (10,8-11,0)		4,4 (4,3-4,5)		6,3 (6,2-6,4)	
Clase social III	120122	13,4 (13,4-13,4)		7,4 (7,4-7,4)		7,6 (7,6-7,6)	
No fumadores	115727	12,5 (12,5-12,5)	0.262	6,5 (6,5-6,5)	0.338	7,1 (7,1-7,1)	0.427
Fumadores	56555	12,5 (12,5-12,5)		6,5 (6,5-6,5)		7,1 (7,1-7,1)	
Bajo peso	5768	3,7 (3,1-4,3)	<0.0001	0,0 (0,0-0,0)	<0.0001	1,6 (1,1-2,1)	<0.0001
Normopeso	91309	6,1 (6,1-6,1)		0,0 (0,0-0,0)		2,8 (2,8-2,8)	
Sobrepeso	47032	15,9 (15,7-16,1)		0,1 (0,1-0,1)		8,8 (8,7-8,9)	
Obesidad	28173	29,2 (28,8-29,6)		39,1 (38,7-39,5)		19,1 (18,7-19,5)	
Total	172282	12,5 (12,5-12,5)		6,4 (6,4-6,4)		7,1 (7,1-7,1)	

Tabla IIIb: Prevalencia de valores altos de escalas que valoran el riesgo de resistencia a la insulina según variables sociodemográficas, consumo de tabaco e IMC en hombres.

Hombres		TyG index alto		METS-IR alto		TG/HDL alto	
	n	% (IC 95%)	p	% (IC 95%)	p	% (IC 95%)	p
18-29 años	46215	10,7 (10,6-10,8)	<0.0001	4,9 (4,8-5,0)	<0.0001	11,0 (10,9-11,1)	<0.0001
30-39 años	67798	21,9 (21,9-21,9)		8,4 (8,4-8,4)		21,9 (21,9-21,9)	
40-49 años	73935	32,1 (32,1-32,1)		13,2 (13,2-13,2)		31,3 (31,3-31,3)	
50-59 años	48522	39,9 (39,8-40,0)		17,4 (17,3-17,5)		38,1 (38,0-38,2)	
60-69 años	9591	45,7 (45,1-46,3)		19,6 (19,0-20,2)		42,6 (42,0-43,2)	
Clase social I	11950	24,1 (23,6-24,6)	<0.0001	8,1 (7,6-8,6)	<0.0001	23,7 (23,2-24,2)	<0.0001
Clase social II	36590	25,9 (25,6-26,2)		9,5 (9,2-9,8)		25,4 (25,1-25,7)	
Clase social III	197521	27,8 (27,8-27,8)		12,0 (12,0-12,0)		27,1 (27,1-27,1)	
No fumadores	163920	27,3 (27,3-27,3)	0.191	11,5 (11,5-11,5)	0.125	26,6 (26,6-26,6)	0.117
Fumadores	82141	27,4 (27,4-27,4)		11,3 (11,3-11,3)		26,8 (26,8-26,8)	
Bajo peso	2448	7,3 (6,0-8,6)	<0.0001	0,0 (0,0-0,0)	<0.0001	6,2 (5,2-7,4)	<0.0001
Normopeso	93186	13,3 (13,3-13,3)		0,0 (0,0-0,0)		11,6 (11,6-11,6)	
Sobrepeso	48245	23,3 (23,2-23,4)		2,1 (2,0-2,2)		60,2 (60,1-60,3)	
Obesidad	102182	64,0 (64,0-64,0)		26,5 (26,5-26,5)		25,1 (25,1-25,1)	
Total	246061	27,3 (27,3-27,3)		11,4 (11,4-11,4)		26,7 (26,7-26,7)	

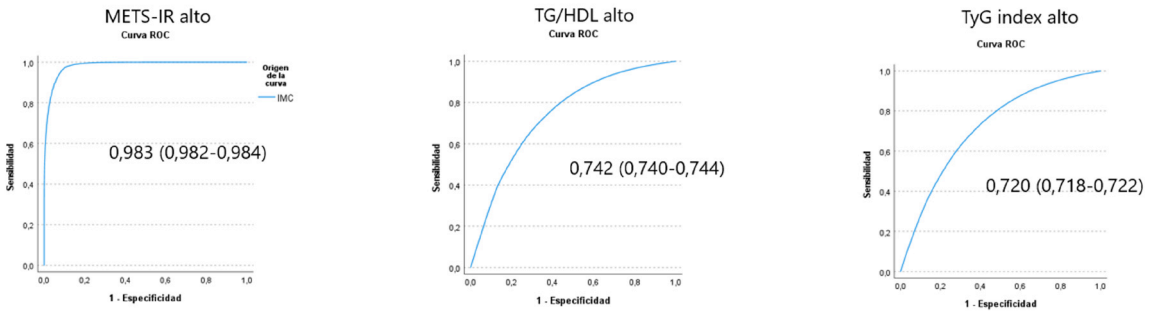
Nos interesa valorar como el IMC puede predecir la aparición de valores elevados de las tres escalas de riesgo de RI, para ello se calculan las curvas ROC, determinado el área debajo de la curva y los puntos de corte con sus respectivos niveles de sensibilidad, especificidad e índice Youden.

El METS-IR es el indicador que presenta mejor valor predictivo con un área debajo de la curva muy elevada (0,983 IC 95% 0,982-0,984), mientras que tanto el TyG index como el índice triglicéridos/HDL presentan áreas debajo de la curva algo inferiores. Los datos completos se encuentran en la **tabla IV** y **figura 2**.

Tabla IV: Curvas ROC de IMC para los diferentes indicadores de resistencia a la insulina altos.

	Área debajo curva	Punto de corte	Sensibilidad	Especificidad	Índice Youden
METS-IR alto	0,983 (0,982-0,984)	30	97,2	90,0	0,872
TyG index alto	0,720 (0,718-0,722)	26,5	66,8	66,5	0,333
TG/HDL alto	0,742 (0,740-0,744)	26,5	70,7	66,3	0,370

Figura 2: Curvas ROC de IMC para los diferentes indicadores de resistencia a la insulina altos.



En el análisis multivariante mediante regresión logística binaria con el modelo de Wald se establecen como covariables todas aquellas variables que presentaron diferencias estadísticamente significativas en los análisis bivariantes, es decir edad a partir de 50 años, clase social II y III, sexo masculino, fumadores y personas obesas según el IMC.

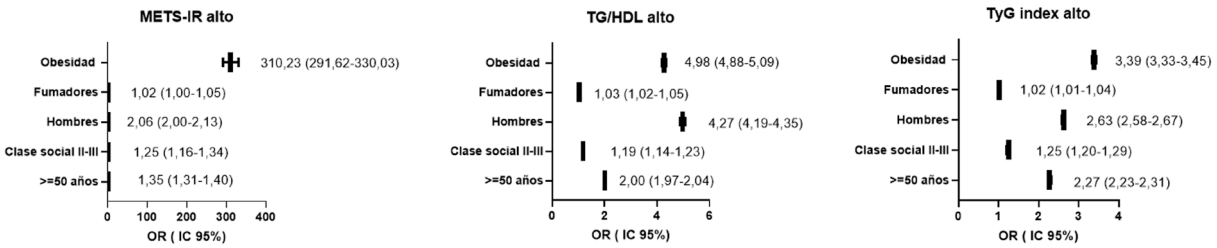
Entre los resultados más interesantes que encontramos en este análisis podríamos destacar que todas las covariables han mostrado incrementar el riesgo de presentar valores alto de las tres escalas de RI.

La covariable que más incrementa el riesgo con las tes escalas es la obesidad, siendo el efecto especialmente notable cuando se emplea la escala METS-IR (OR 310,23 IC 95% 291,62-330,03). La variable que tiene un menor efecto es el tabaco ya que las OR superan por poco el valor de 1. Todos los datos se pueden consultar en la **tabla V** y en la **figura 3**.

Tabla V: Análisis multivariante mediante regresión logística binaria.

	METS-IR alto		TG/HDL alto		TyG alto	
	OR (IC 95%)	p	OR (IC 95%)	p	OR (IC 95%)	p
≥ 50 años	1,35 (1,31-1,40)	<0.0001	2,00 (1,97-2,04)	<0.0001	2,27 (2,23-2,31)	<0.0001
Clase social II-III	1,25 (1,16-1,34)	<0.0001	1,19 (1,14-1,23)	<0.0001	1,25 (1,20-1,29)	<0.0001
Hombres	2,06 (2,00-2,13)	<0.0001	4,98 (4,88-5,09)	<0.0001	2,63 (2,58-2,67)	<0.0001
Fumadores	1,02 (1,00-1,05)	0.048	1,03 (1,02-1,05)	0.040	1,02 (1,01-1,04)	0.041
Obesidad	310,23 (291,62-330,03)	<0.0001	4,27 (4,19-4,35)	<0.0001	3,39 (3,33-3,45)	<0.0001

Figura 3: Análisis multivariante mediante regresión logística binaria.



Interesa también conocer el grado de correlación y de concordancia de las tres escalas de RI, para ello empleamos el coeficiente de correlación de Pearson y la escala de concordancia kappa de Cohen.

Observamos que el grado de correlación es muy bueno con la escala de Landis y Koch12 entre TyG index y triglicéridos/HDL y aceptable entre METS-IR y las otras dos escalas. Los resultados se pueden ver en la **tabla VI**.

Cuando determinamos la concordancia entre las tres escalas vemos que los valores del índice kappa de Cohen oscilan entre 0,281 (METS-IR y TyG index), 0,328 (METS-IR y triglicéridos/HDL) y 0,759 (TyG index y triglicéridos/HDL).

En base a los resultados obtenidos en los diferentes análisis realizados podemos establecer un perfil de persona de alto riesgo para padecer RI: Varón de 50 o más años, perteneciente a la clase social II o III, obeso y fumador.

Tabla VI: Coeficiente de correlación de Pearson entre las diferentes escalas de resistencia a la insulina.

		Correlaciones		
		IATGHDL	TyGindex	METSIR
IATGHDL	Correlación de Pearson Sig. (bilateral) N	1 418343	,820** ,000 418343	,537** ,000 418343
TyGindex	Correlación de Pearson Sig. (bilateral) N	,820** ,000 418343	1 418343	,566** ,000 418343
METSIR	Correlación de Pearson Sig. (bilateral) N	,537** ,000 418343	,566** ,000 418343	1 418343

** La correlación es significativa en el nivel 0,01 (bilateral).

Discusión

La prevalencia de riesgo alto de RI que hemos encontrado varía según la escala que se aplique, oscilando entre el 6,4% y el 12,5% en las mujeres y entre el 11,4% y el 27,3% en los hombres. Todas las variables analizadas incrementan el riesgo de aparición de RI con las tres escalas, siendo la obesidad la que muestra un efecto mayor. El grado de correlación y de concordancia entre las tres escalas es muy variable observándose los mejores resultados entre TyG index y triglicéridos/HDL.

En nuestro estudio las personas de las clases sociales menos favorecidas presentan mayor prevalencia de RI este resultado se observa también en varios trabajos, así Volaco[13] en una revisión sistemática encontró que el nivel socioeconómico más bajo se asociaba a implicaciones metabólicas que están relacionadas con la resistencia a la insulina y posiblemente también puede interferir con la capacidad de las células beta para secretar insulina y cambiar la microbiota intestinal, aumentando aún más el riesgo futuro de desarrollar diabetes. Kyrou[14] también encontró esa asociación entre bajo nivel socioeconómico y RI.

En sentido contrario a lo obtenido por nosotros Paudel[15] en un estudio realizado en casi 2000 personas de Nepal encontró que los individuos con estudios superiores, con un empleo remunerado y perteneciente a grupos étnicos favorecidos tenían más probabilidades de padecer RI.

Nosotros hemos encontrado que a medida que aumenta la edad se produce un incremento en la prevalencia de la RI, esto mismo se ha observado en un estudio realizado por Pucci[16] en el año 2017. También un estudio que examinaba los efectos del envejecimiento en la regulación de la glucosa en hombres y mujeres chinos de edad avanzada[17] concluyó que el envejecimiento se asocia con el desarrollo de resistencia a la insulina.

Nuestros resultados muestran que el consumo de tabaco incrementa ligeramente el riesgo de presentar RI, algo similar hemos encontrado en una revisión de Mukharjee[18]

En la cual el investigador identificó que la resistencia a la insulina se produce en los fumadores debido a la fosforilación del sustrato del receptor de insulina1 (IRS1) en la posición Ser-636. Un estudio coreano[19] realizado en 10568 personas que empleaba el TyG index como marcado de RI encontró incrementos en el valor de este indicador en las personas fumadoras si se comparaba con las no fumadoras.

La prevalencia de RI encontrada por nosotros es superior en los varones algo similar a lo encontrado en un estudio realizado en Murcia[20], sin embargo este resultado no coincide con el estudio de Pucci[16] y con un estudio realizado en Turquía[21] donde la prevalencia en mujeres era superior.

El incremento del IMC en nuestro trabajo se relaciona con un aumento de la RI, en este mismo sentido se expresan diferentes autores como Demir[21] o Polsky[22].

Como puntos fuertes del estudio destacaríamos el elevadísimo tamaño muestral (más de 418000 personas), el número de escalas de RI analizadas (tres) y la gran cantidad de variables que se han tenido en cuenta para valorar su influencia en la aparición de RI. También es interesante que se haya establecido un perfil de personas de alto riesgo de presentar RI ya que esto nos puede permitir a los profesionales de salud laboral, especialmente a los de enfermería, y a otros profesionales sanitarios como los de atención primaria el establecer estrategias de prevención y de diagnóstico precoz con el objetivo de disminuir la aparición en nuestra población de la RI.

Como limitaciones encontramos que se ha realizado en un área geográfica concreta y en población laboral (entre 18 y 69 años) lo que impide la extrapolación de los resultados a otras zonas geográficas y a la población general ya que se han excluido a las personas de menos de 18 a y más de 69 años.

Conclusiones

En la aparición de RI pueden influir diferentes factores entre los que podemos destacar la edad, el sexo, la clase social, el consumo de tabaco y la obesidad.

El poder establecer un perfil de personas con alto riesgo de presentar RI permitirá a los profesionales de salud laboral, principalmente a los de enfermería, el elaborar estrategias de prevención y de diagnóstico precoz para disminuir la prevalencia de RI.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

Bibliografía

1. Tang Q, Li X, Song P, Xu L. Optimal cut-off values for the homeostasis model assessment of insulin resistance (HOMA-IR) and pre-diabetes screening: Developments in research and prospects for the future. Drug Discov Ther. 2015 Dic; 9(6): 380-5.

2. Barazzoni R, Gortan Cappellari G, Ragni M, Nisoli E. Insulin resistance in obesity: an overview of fundamental alterations. Eat Weight Disord. 2018 Apr;23(2): 149-57.

3. Sampath Kumar A, Maiya AG, Shastry BA, Vaishali K, Ravishankar N, Hazari A, et al. Exercise and insulin resistance in type 2 diabetes mellitus: A systematic review and meta-analysis. Ann Phys Rehabil Med. 2019 Mar;62(2): 98-103.

4. Jung CH, Choi KM. Impact of High-Carbohydrate Diet on Metabolic Parameters in Patients with Type 2 Diabetes. Nutrients. 2017 Mar 24;9(4):322.

5. Onyango AN. Cellular Stresses and Stress Responses in the Pathogenesis of Insulin Resistance. Oxid Med Cell Longev. 2018 Jul 9;2018:4321714.

6. Vejrazkova D, Vcelak J, Vankova M, Lukasova P, Bradnova O, Halkova T, et al. Steroids and insulin resistance in pregnancy. J Steroid Biochem Mol Biol. 2014 Jan;139:122-9.

7. Concha C F, Sir P T, Recabarren SE, Pérez B F. Epigenética del síndrome de ovario poliquístico. Rev Med Chil. 2017 Jul;145(7):907-15.

8. Ježková J, Ďurovcová V, Wenchich L, Hansíková H, Zeman J, Hána V, et al. The relationship of mitochondrial dysfunction and the development of insulin resistance in Cushing's syndrome. Diabetes Metab Syndr Obes. 2019 Aug 19;12:1459-71.

9. Unger G, Benozzi SF, Peruzza F, Pennacchiotti GL. Triglycerides and glucose index: A useful indicator of insulin resistance. Endocrinol Nutr. 2014;61(10):533-40

10. Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, Viveros-Ruiz T, Cruz-Bautista I, Romo-Romo A, et al METS-IR a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. Eur J Endocrinol 2018;178(5):533-44

11. Domingo-Salvany A, Bacigalupe A, Carrasco JM, Espelt A, Ferrando J, Borrell C. Propuesta de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011. Gac Sanit 2013;27(3):263-72

12. Landis J, Koch G: The measurement of observer agreement for categorical data. Biometrics 1977; 33:159-74.

13. Volaco A, Cavalcanti AM, Filho RP, Précoma DB. Socioeconomic Status: The Missing Link Between Obesity and Diabetes Mellitus? Curr Diabetes Rev. 2018;14(4):321-6.

14. Kyrou I, Tsigos C, Mavrogianni C, Cardon G, Van Stappen V, Latomme J, et al Sociodemographic and lifestyle-related risk factors for identifying vulnerable groups for type 2 diabetes: a narrative review with emphasis on data from Europe. BMC Endocr Disord. 2020 Mar 12;20(Suppl 1):134.

15. Paudel S, Tran T, Owen AJ, Smith BJ. The contribution of physical inactivity and socioeconomic factors to type 2 diabetes in Nepal: A structural equation modelling analysis. Nutr Metab Cardiovasc Dis. 2020 Sep 24;30(10):1758-67.

16. Pucci G, Alcidi R, Tap L, Battista F, Mattace-Raso F, Schillaci G. Sex- and gender-related prevalence, cardiovascular risk and therapeutic approach in metabolic syndrome: A review of the literature. Pharmacol Res. 2017 Jun;120:34-42.

17. Liu J, Wu YY, Huang XM, Yang M, Zha BB, Wang F, et al. Ageing and type 2 diabetes in an elderly Chinese population: the role of insulin resistance and beta cell dysfunction. Eur Rev Med Pharmacol Sci. 2014;18(12):1790-7.

18. Mukharjee S, Bank S, Maiti S. Chronic Tobacco Exposure by Smoking Develops Insulin Resistance. Endocr Metab Immune Disord Drug Targets. 2020;20(6):869-77.

19. Baek W, Lee JW, Lee HS, Han D, Choi SY, Chun EJ, et al. Concurrent smoking and alcohol consumers had higher triglyceride glucose indices than either only smokers or alcohol consumers: a cross-sectional study in Korea. Lipids Health Dis. 2021 May 11;20(1):49.

20. Candela JM, Romero Ortiz J, Cánovas Domínguez C, Gallardo Martín A. Prevalencia del síndrome metabólico y resistencia insulina en la población adulta de Yecla. Boletin Epidemiológico de Murcia. 2006: 27(682).

21. Demir AK, Şahin Ş, Kaya SU, Bütün İ, Çıtıl R, Önder Y, et al. Prevalence of insulin resistance and identifying HOMA1-IR and HOMA2-IR indexes in the Middle Black Sea region of Turkey. Afr Health Sci. 2020 Mar;20(1):277-86.

22. Polsky S, Ellis SL. Obesity, insulin resistance, and type 1 diabetes mellitus. Curr Opin Endocrinol Diabetes Obes. 2015 Aug;22(4):277-82.

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ORIGINAL

Evaluation of the results of platelet-rich plasma (PRP) treatment in the treatment of complex perianal fistula: a prospective study

Evaluación de los resultados del tratamiento con plasma rico en plaquetas (PRP) en el tratamiento de la fístula perianal compleja: un estudio prospectivo

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Abstract

Background: Platelet-rich plasma (PRP) has therapeutic effects in accelerating the healing of soft tissue injuries. Due to the side effects of the existing treatment methods in the management of complex anal fistula and the limited research in the field of alternative therapies using new technologies, the present study was conducted to investigate the application of autologous PRP in the treatment of anal fistula.

Methods: In this descriptive-prospective study, patients with complex anal fistula were studied. After excision of external orifice and curettage of the tract, PRP was injected into the tract and finally the inside of the tract was filled with PRP material. After surgery, patients underwent 1-week, 1-month, 6-month and 1-year follow-ups to evaluate their recovery status. Outcomes of this study included success rate, recovery time, satisfaction, return to work, readmission, and recurrence.

Results: Overall, the results of the study showed that the success rate of PRP treatment in patients with complex anal fistula is 66.7%. In 16.7% of patients, the result was "continuous external discharge" and in 16.7% of patients the result was "abscess formation after healing". Recovery time was 24.29 (8.69) days. Rate of return to work, satisfaction, readmission was 79.2%, 79.2% and 16.37%, respectively. Also, the recurrence rates in the first month, sixth month and first year were 16.37%, 10% and 11.1%, respectively.

Conclusion: The present study suggests that PRP treatment is associated with high success rate in the treatment of anal fistula.

Key words: Anal fistula, platelet-rich plasma.

Resumen

Antecedentes: El plasma rico en plaquetas (PRP) tiene efectos terapéuticos en la aceleración de la curación de las lesiones de tejidos blandos. Debido a los efectos secundarios de los métodos de tratamiento existentes en el manejo de la fístula anal compleja y a la limitada investigación en el campo de las terapias alternativas con nuevas tecnologías, el presente estudio se realizó para investigar la aplicación del PRP autólogo en el tratamiento de la fístula anal.

Métodos: En este estudio descriptivo-prospectivo se estudiaron pacientes con fístula anal compleja. Tras la escisión del orificio externo y el legrado del tracto, se inyectó PRP en el tracto y finalmente se rellenó el interior del tracto con material de PRP. Después de la cirugía, los pacientes se sometieron a seguimientos de 1 semana, 1 mes, 6 meses y 1 año para evaluar su estado de recuperación. Los resultados de este estudio incluyeron la tasa de éxito, el tiempo de recuperación, la satisfacción, la vuelta al trabajo, el reingreso y la recidiva.

Resultados: En general, los resultados del estudio mostraron que la tasa de éxito del tratamiento con PRP en pacientes con fístula anal compleja es del 66,7%. En el 16,7% de los pacientes, el resultado fue "secreción externa continua" y en el 16,7% de los pacientes el resultado fue "formación de abscesos después de la curación". El tiempo de recuperación fue de 24,29 (8,69) días. La tasa de retorno al trabajo, satisfacción y readmisión fue del 79,2%, 79,2% y 16,37%, respectivamente. Asimismo, las tasas de recidiva en el primer mes, el sexto mes y el primer año fueron del 16,37%, el 10% y el 11,1%, respectivamente.

Conclusión: El presente estudio sugiere que el tratamiento con PRP se asocia con una alta tasa de éxito en el tratamiento de la fístula anal.

Palabras clave: Fístula anal; Plasma rico en plaquetas.

Introduction

Anal sepsis is one of the most common benign anorectal diseases managed by surgeons. Of all patients who present with perianal abscess, up to 65% will develop a chronic or recurrent anal fistula. Operative intervention remains the only effective modality to treat this condition. Although the principal goal of treatment is to eradicate the fistula, it is also important to preserve anal continence, minimize postoperative complications, and decrease risk of recurrence.

Surgical therapy is the main method used to treat anal fistula. The best treatment criterion is to eradicate the infected lesion, ensure sufficient drainage, and promote the closure of the fistula, while minimizing damage to the anal sphincter. The integrity of the internal anal sphincter (IAS) and external anal sphincter (EAS) is the most important guarantee for keeping normal anal function of patients[1,2].

Anal fistula refers to a duct between the perianal skin and the anorectal canal, a common surgical problem usually occurring after the treatment of perianal abscesses. Continuous discharge of pus, pain, itching, as well as contamination of underwear are among its significant characteristics[1,2]. Fistula treatment options include fistulotomy, fistulectomy (with or without sphincteroplasty surgery), endorectal advancement flap, anocutaneous advancement flap, fistula plug, fibrin glue injection, Fistula-tract Laser Closure (FiLaC) and (LIFT)[3,4]. One of new treatment options in this field is blood-derivatives-based methods. One of the significant blood derivatives of this bioactive substance is Platelet-Rich Plasma (PRP), with more than 20 growth factors and other protein molecules such as binding molecules and chemokines involved in processes like proliferation, differentiation, as well as cell regeneration[5]. The PRP potentials such as its therapeutic ability depend on the amount of growth factors it has. With the addition of certain activating agents like thrombin and calcium chloride that induce and stimulate the growth factors release from granules Alpha's in PRP, the platelets collected in PRP start secreting growth factors[1]. Platelets existing in PRP enhance the level of growth factors in the environment by secreting these factors in this environment[6]. Growth factors perform as a mitogen cell division stimulant in cells like endothelial cells and fibroblast cells, initiating the angiogenesis processes, as well as differentiation and proliferation of fibroblasts. Moreover, growth factors regulate collagen synthesis besides promoting cell proliferation as well as cell differentiation processes[7]. More than 95% of the synthesized growth factors are released in an explosive process during the first hours after activation. Given the impacts of platelet-enriched plasma on acceleration of healing the soft tissue injuries in addition to its autologous nature (prepared from the patient's own blood), the treatment cost is reduced, and it is time-effective for the surgeon and the patient[8]. Hence, given the complications of therapeutic methods for anal fistula beside the limited research on alternative therapies through new technologies, the current study was performed to investigate the use of autologous PRP in the anal fistula treatment.

Materials and Methods

Patient Population

This was a descriptive-prospective study performed on patients with complex anal fistula referring to Shahid Beheshti University of Medical Sciences from 2019 to 2020.

Inclusion criteria were age between 18 and 80 years and diagnosis of high trans sphincteric fistula.

Exclusion criteria were patients with ASA score 4, inflammatory bowel disease, fistula with multiple tracts or active perianal sepsis, lower and middle intrasphincteric fistula, as well as pregnant and lactating patients.

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran and registered with the protocol number "IR.SBMU.MSP.REC.1398.566".

After obtaining the patient's consent, preparation of PRP was the first step. In autologous PRP preparation, 30 cc of patient's whole blood was sampled on the day of treatment. Blood coagulation and secretion of platelet granules were controlled by addition of an anticoagulant like dextrose citrate. The whole blood sample was centrifuged (850G) at a constant speed to form three different layers by means of a two-stage centrifuge or by double spin method. The lower layer contained red blood cells; the middle layer has white blood cells, while the upper layer contains plasma-soluble platelets. In the second round of the centrifuge (1200G), the upper and middle layers were then removed and centrifuged. The obtained solution contained pellet platelets. Moreover, the pellet was re-dissolved in plasma in order to reach a volume of 12 cc, with its final volume depended on the volume needed for treatment.

Prior to the operation, the patient was recommended to use four Bisacodyl suppositories the day before surgery. After spinal anesthesia and in lithotomy position anoscopy was performed by colorectal surgeon. After accurate determination of the internal orifice, main tract and the external orifice, the external orifice and a part of the tract at the ischioanal fossa was excised, followed by the curettage of the trans sphincteicr tract. The internal orifice was closed by Vicryl suture 2/0 Subsequently, PRP was injected into the tract; and finally the tract was filled with PRP material.

Outcomes

A questionnaire including age, sex, type of fistula, and treatment methods was data collection tool.
Patients underwent follow-ups of 1 week, 1 month, 6 months, and 1 year after surgery in order to assess their recovery status. The studied outcomes in this review included intensity of pain (based on VAS), success rate, recovery time (days), satisfaction of patient with treatment, return to work, readmission, and recurrence.

Statistical Analysis

All registered data were analyzed using SPSS software version 20 for Windows (SPSS, Chicago, IL). For descriptive statistics, the Mean ± SD index was used for quantitative variables with normal distribution.

Sampling

The census method was used as the sampling method and all patients with perianal fistula with an age range of 18-80 years referring to hospitals affiliated to Shahid Beheshti University of Medical Sciences over the years 2019-2020 were investigated considering the exclusion criteria.

Result

In total, 24 patients with perianal fistula were included in the study and treated with PRP. Among these, (66.7%) 16 patients were male and (33.3%) 8 patients were female. The mean age of the patients was 41.66±11.99 years with a minimum age of 22 and a maximum age of 60 years.

The results of the study on the Mean pain severity one week after surgery, postoperative recovery time (days) are shown in **table I**.

The results of the study on the frequency distribution of response to treatment, return to work, patient satisfaction with treatment, postoperative readmission, recurrence in the first month, sixth month and first year are shown in **table II**.

Discussion

Several; developments have been occurred in medical sciences, particularly in the management of diseases[9-16]. Fistula surgery remains a matter for colorectal surgeons and an exhausting process for patients with impaired quality of life. Simple fistula is treated usually by fistulotomy, that provides healing for about 90% of patients with low risk of incontinence. The main problem lies in the treatment of complex perianal fistula, as fistulotomy represents an unacceptable risk of incontinence in these patients.

Platelet α-granules contain mitogenic and chemotactic growth factors (GF) and associated healing molecules in an inactive form, important in wound healing, such as platelet-

Table I: Mean pain severity one week after surgery & postoperative recovery time in patients.

Variables	Minimum	Maximum	Mean	Standard deviation
Pain severity one week after surgery	2	8	4.7	1.58
Postoperative recovery time(days)	10	40	24.29	8.69

Table II: frequency distribution of response to treatment, return to work, patient satisfaction with treatment, postoperative readmission, recurrence in the first month, sixth month and first year.

Variables	Frequency	Percent
Response to treatment		
Improved without abscess formation	16	66.7%
Continuous external discharge	4	16.7%
Abscess formation after healing	4	16.7%
Return to work		
have no	5	20.8%
have	19	79.2%
Patient satisfaction		
have no	5	20.8%
have	19	79.2%
Postoperative readmission		
have	4	16.3%
have no	20	83.3%
Recurrence in the first month		
have	4	16.3%
have no	20	83.3%
Recurrence in the sixth month		
have	2	10%
have no	18	90%
Recurrence in the first year		
have	2	11.1%
have no	16	88.9%

derived growth factor (PDGF), transforming growth factors β1, β2, β3, platelet-derived angiogenesis factor, insulin-like growth factor 1, platelet factor 4 (PF-4), epidermal growth factor, epithelial cell grow factor, vascular endothelial cell growth factor (VEGF), basic fibroblast growth factor and others cytokines. During normal wound healing, trapped platelets become activated and degranulate, resulting in releasing of α-granule content. The secreted growth factors immediately bind to the external surface of cell membranes in the wound via transmembrane receptors in mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells.

This work aimed to evaluate the effect of the use PRP in when it is used as adjunct in the treatment of high perianal fistula.

In 2019, a randomized, double-blind clinical trial was performed by de la Portilla et al. in order to compare the clinical implications of using autologous PRP vs. fibrin glue in treating cryptoglandular anal fistula. Patients were clinically and endoscopically assessed at 1 week, and 3, 6, and 12 months after operation. The main outcome of this study included the rate of fistula recovery (complete, partial, and no improvement) while the secondary outcomes were fistula recurrence, fecal status, quality of life (QoL), and pain. Out of 56 patients enrolled in the present study, 32 were assigned to the PRP group and 24 to the fibrin glue group. The results revealed the overall improvement rate of 71% in the PRP group and 58.3% in the fibrin glue group. In the PRP group, the complete and partial recovery rates were 48.4% and 22.6%, and they were 41.7% and 16.7% in the fibrin glue group. The rate of pain and thus the QoL in the PRP group was significantly better. All complications were minor and no adverse effects were seen in the fecal status[17]. In 2021, Madbouly et al. performed a prospective trial examining the effect of PRP on the treatment of transsphincteric fistula. In the present study, patients with a transsphincteric fistula that involved more than 50% of their anal sphincter were included. They were randomly assigned to two groups of Ligation of Intersphincteric fistula tract (LIFT) with and without PRP. Each group included 49 patients. The complete closure of the fistula and the time needed for recovery were the main outcomes of this study. Forty-two patients in the PRP group and 32 patients in the group without PRP showed complete recovery of fistula, with a significant difference between the two groups. In the PRP group, the mean postoperative recovery time was significantly shorter (15.7 days) compared to that in the group without PRP (21.6 days). Four patients in the PRP group and three in the group without PRP exhibited one-year recurrence. In the PRP group and on days 1 and 7 after surgery, pain was better, like QoL rate one month after surgery[18]. Moreno-Serrano et al. (2016) investigated the effect of PRP on the recovery of complex anal fistulas. This study was performed from 2011 to 2013. Its outcomes included fistula recovery, treatment complications, as well as QoL. Twenty-three patients (12 men and 11 women) were included in the present study and followed up for at least 12 months, two of whom were excluded from the study. Seventeen out of the remaining 21 patients had low fistulas. In this research, the success rate of treatment was 62%. No patient experienced incontinence after treatment. The QoL improved in all patients except two of them[19]. In 2019, a study was performed by Orban et al. in order to assess the impact of PRP on the treatment of high anal fistula. Their prospective study was conducted on patients with fistula from 2016 to 2019, in which nine males and seven females were included. The success rate was 75%, i.e. twelve patients completely recovered with no recurrence while two patients developed postoperative abscess and two patients experienced continuous discharge from the surgery site[20].

In our study, we used autologous platelet rich plasma as adjunct in the treatment of high perianal fistula and obtained cure rates of66/7%. As regard incontinence, our study we had no case develop fecal incomitance.

Conclusion

Overall, the results of the present study showed that the use of PRP is associated with high success in the treatment of high perianal fistula; without affection of fecal continence. Therefore, the use of this treatment is recommended in the treatment of anal fistula.

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Conflict of Interest

The authors declare that there is no conflict of interest in the publication of this paper.

References

1. Buchanan GN, Bartram CI, Phillips RK, Gould SW, Halligan S, Rockall TA, et al. Efficacy of fibrin sealant in the management of complex anal fistula: a prospective trial. Diseases of the colon and rectum. 2003;46(9):1167-74.

2. Steele SR, Kumar R, Feingold DL, Rafferty JL, Buie WD. Practice parameters for the management of perianal abscess and fistula-in-ano. Diseases of the colon and rectum. 2011;54(12):1465-74.

3. Ritchie RD, Sackier JM, Hodde JP. Incontinence rates after cutting seton treatment for anal fistula. Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland. 2009;11(6):564-71.

4. Tozer P, Sala S, Cianci V, Kalmar K, Atkin GK, Rahbour G, et al. Fistulotomy in the tertiary setting can achieve high rates of fistula cure with an acceptable risk of deterioration in continence. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract. 2013;17(11):1960-5.

5. van Onkelen RS, Gosselink MP, Schouten WR. Is it possible to improve the outcome of transanal advancement flap repair for high transsphincteric fistulas by additional ligation of the intersphincteric fistula tract? Diseases of the colon and rectum. 2012;55(2):163-6.

6. Dhurat R, Sukesh M. Principles and Methods of Preparation of Platelet-Rich Plasma: A Review and Author's Perspective. Journal of cutaneous and aesthetic surgery. 2014;7(4):189-97.

7. Sunitha Raja V, Munirathnam Naidu E. Platelet-rich fibrin: evolution of a second-generation platelet concentrate. Indian journal of dental research: official publication of Indian Society for Dental Research. 2008;19(1):42-6.

8. Lara FJ, Serrano AM, Moreno JU, Carmona JH, Marquez MF, Pérez LR, et al. Platelet-rich fibrin sealant as a treatment for complex perianal fistulas: a multicentre study. J Gastrointest Surg. 2015;19(2):360-8.

9. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of Brucella abortus and Brucella melitensis in Aborted Bovine, Ovine, Caprine, Buffaloes and Camelid Fetuses by application of conventional and real-time polymerase chain reaction. The Thai Journal of Veterinary Medicine. 2012 Mar 1;42(1):13.

10. Sheikhshahrokh A, Ranjbar R, Saeidi E, Dehkordi FS, Heiat M, Ghasemi-Dehkordi P, Goodarzi H. Frontier therapeutics and vaccine strategies for sars-cov-2 (COVID-19): A review. Iranian Journal of Public Health. 2020 Jul 11.

11. Ranjbar R, Seif A, Dehkordi FS. Prevalence of antibiotic resistance and distribution of virulence factors in the shiga toxigenic Escherichia coli recovered from hospital food. Jundishapur Journal of Microbiology. 2019;12(5):8.

12. Nejat S, Momtaz H, Yadegari M, Nejat S, Safarpour Dehkordi F, Khamesipour F. Seasonal, geographical, age and breed distributions of equine viral arteritis in Iran. Kafkas Univ Vet Fak Derg. 2015 Jan 1;21(1):111-6.

13. Rahimi E, Yazdanpour S, Dehkordi FS. Detection of Toxoplasma gondii antibodies in various poultry meat samples using enzyme linked immuno sorbent assay and its confirmation by polymerase chain reaction. J Pure Appl Microbiol. 2014;8(1):421-7.

14. Dehkordi FS. Prevalence study of Bovine viral diarrhea virus by evaluation of antigen capture ELISA and RT-PCR assay in Bovine, Ovine, Caprine, Buffalo and Camel aborted fetuses in Iran. AMB express. 2011 Dec;1(1):1-6.

15. Dehkordi FS, Haghighi N, Momtaz H, Rafsanjani MS, Momeni M. Conventional vs real-time PCR for detection of bovine herpes virus type 1 in aborted bovine, buffalo and camel foetuses. Bulgarian Journal of Veterinary Medicine. 2013 Jun 1;16(2).

16. Ranjbar R, Farsani FY, Dehkordi FS. Phenotypic analysis of antibiotic resistance and genotypic study of the vacA, cagA, iceA, oipA and babA genotypes of the Helicobacter pylori strains isolated from raw milk. Antimicrobial Resistance & Infection Control. 2018 Dec;7(1):1-4.

17. de la Portilla F, Muñoz-Cruzado MVD, Maestre MV, García-Cabrera AM, Reyes ML, Vázquez-Monchul JM, et al. Platelet-rich plasma (PRP) versus fibrin glue in cryptogenic fistula-in-ano: a phase III single-center, randomized, double-blind trial. International journal of colorectal disease. 2019;34(6):1113-9.

18. Madbouly KM, Emile SH, Issa YA, Omar W. Ligation of intersphincteric fistula tract (LIFT) with or without injection of platelet-rich plasma (PRP) in management of high trans-sphincteric fistula-in-ano: Short-term outcomes of a prospective, randomized trial. Surgery. 2021;170(1):61-6.

19. Moreno-Serrano A, García-Díaz JJ, Ferrer-Márquez M, Alarcón-Rodríguez R, Álvarez-García A, Reina-Duarte Á. Using autologous platelet-rich plasma for the treatment of complex fistulas. Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva. 2016;108(3):123-8.

20. Yasser A. Orban, Goda A. Effectiveness of autologous platelet rich plasma in the treatment of hight perianal fistula. Int J of Adv Res. 2019; 7: 59-64.

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ORIGINAL

The anterior cruciate ligament (ACL) reconstruction in athletes and non-athletes: single- or double-bundle; review

La reconstrucción del ligamento cruzado anterior (LCA) en atletas y no atletas: un solo paquete o doble paquete; revisión

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Abstract

Background: The anterior cruciate ligament (ACL) consists of two functional bundles, the anteromedial bundle, and the posterolateral bundle. Furthermore, these bundles work synergistically to provide knee anteroposterior and rotational stability. ACL injury causes reduce the function, balance, and destruction of the knee joint. This review was performed to describe current information on anterior cruciate ligament reconstruction and its effect on activities of athletes and non-athletes as well as express the difference between "single-bundle" and "double-bundle".
Methods: Different databases were checked and analyzed to wrote this review.
Results: Anterior cruciate ligament injury is common among athletes and even non-athletes. Because of the prevalence of ACL rupture, the reconstruction of the anterior cruciate ligament is one of the most frequently performed orthopedic surgeries. Reconstruction of the anterior cruciate ligament has evolved significantly over the past 40 years. Reconstruction of ACL in the double-bundle technique is advocated more closely restore the function of the native ligament than the conventional single-bundle technique. Previous research has shown that double-bundle anterior cruciate ligament replacement has a considerable advantage in anterior and rotational stability when compared to single-bundle anterior cruciate ligament restoration. However, because to the difficulty of the double-bundle, most surgeons consider the single-bundle to be the preferable method of ACL reconstruction.
Conclusion: ACL Injuries in athletes were extensively studied, however many ACL lesions are seen in non-athletes as a result of low-grade recreational activities which is not well addressed. Because performing the appropriate method of the anterior cruciate ligament reconstruction will be related to the continuation of activities and the life quality of individuals.

Key words: ACL reconstruction, athletes, single-bundle, double-bundle.

Resumen

Antecedentes: El ligamento cruzado anterior (LCA) consta de dos haces funcionales, el haz anteromedial y el haz posterolateral. Además, estos haces trabajan de forma sinérgica para proporcionar estabilidad anteroposterior y rotacional a la rodilla. Las lesiones del LCA reducen la función, el equilibrio y la destrucción de la articulación de la rodilla. Esta revisión se realizó para describir la información actual sobre la reconstrucción del ligamento cruzado anterior y su efecto en las actividades de los atletas y los no atletas, así como para expresar la diferencia entre el "haz simple" y el "haz doble".
Métodos: Se revisaron y analizaron diferentes bases de datos para redactar esta revisión.
Resultados: La lesión del ligamento cruzado anterior es común entre los atletas e incluso entre los no atletas. Debido a la prevalencia de la rotura del LCA, la reconstrucción del ligamento cruzado anterior es una de las cirugías ortopédicas más frecuentes. La reconstrucción del ligamento cruzado anterior ha evolucionado considerablemente en los últimos 40 años. Se defiende que la reconstrucción del LCA con la técnica de doble haz restablece más estrechamente la función del ligamento nativo que la técnica convencional de un solo haz. Investigaciones anteriores han demostrado que la sustitución del ligamento cruzado anterior con doble haz tiene una ventaja considerable en cuanto a la estabilidad anterior y rotacional en comparación con la restauración del ligamento cruzado anterior con un solo haz. Sin embargo, debido a la dificultad del doble haz, la mayoría de los cirujanos consideran que el haz único es el método preferible para la reconstrucción del LCA.
Conclusión: Las lesiones del LCA en los atletas fueron ampliamente estudiadas, sin embargo, muchas lesiones del LCA se ven en los no atletas como resultado de actividades recreativas de bajo grado que no se aborda bien. Porque realizar el método adecuado de la reconstrucción del ligamento cruzado anterior estará relacionado con la continuación de las actividades y la calidad de vida de los individuos.

Palabras clave: Reconstrucción del LCA, deportistas, ligamento simple, ligamento doble.

Introduction

One of the most important knee stabilizing ligaments is the anterior cruciate ligament[1]. The anterior cruciate ligament (ACL) helps maintain dynamic-static stability and knee joint coordination. ACL injury has a severe effect on knee mobility and balance[2]. This injury causes effective sensory feedback in the injured knee which can reduce the function and balance of knee joint[3]. Among the joint injuries associated with sports movements, the knee accounts for about 10-25 % of all injuries, and among knee injuries, about 45% are related to ligament injuries[4]. ACL injury is common among athletes and even non-athletes, to the extent that one in 3,000 people in the United States suffers from ACL injury annually[5]. ACL injury, is one of the most devastating orthopedic diseases, which can result in a lot of time lost from sport[6].

Because of the prevalence of ACL injuries, ACL reconstruction is one of the most frequently performed orthopedic surgeries[7,8]. Surgical procedures conducted to reconstruct ACL are usually "single-bundled" or "double-bundled". In general, anterior cruciate ligament reconstruction using the appropriate method was associated with the continuation of activities and the life quality of patients.

Therefore, our goals in this paper are to provide a brief overview of describe current information on anterior cruciate ligament reconstruction and its effect on activities of athletes and non-athletes, as well as express the difference between "single bundle" and "double bundle" technique. We performed the literature review within the PubMed database using the keywords: "ACL Reconstruction, Athletes, Single-Bundle, Double-Bundle" with dates from 2000 to 2021. This paper describes the complications of anterior cruciate ligament injuries and provides an overview of the ACL reconstruction technique. We then present a review on the reconstruction of ACL in athletes and non-athletes as well as a comparison of the single-bundled and double-bundled as surgical procedures performed to reconstruct the ACL.

ACL injuries

ACL is one of the most important elements to stabilize the knee and is vital for the stability of the knee joint during running and sports activities. ACL consists of two major functional bundles, the smaller anteromedial (AM) and the larger posterolateral (PL) bundle. When the knee is extended, the PL bundle is tight, and the AM bundle is quite lax. As the knee is flexed, the AM bundle is tight, and the PL bundle is relax (Figure 1&2). With the knee flexed the AM bundle is the primary resistance against the anterior translation of the tibia, while the bulky PL bundle tends to stabilize the knee near full extension, particularly against rotation[9,10].

ACL injuries are among the most frequent knee ligament injuries in the world with an incidence of 8 per 100,000 cases per year[11-15]. The most affected are between 15 and 25 years old and athletes.

Regarding the low average of age in the Iranian population, the frequency of ACL tear is high, but there is no accurate estimate of this injury in Iran16. In the United States, about 200,000 ACL tear occurs per year[17-20]. Tears of this ligament are linked to knee instability and other ligament injuries. Long-term effects from ACL injury include meniscus tears and articular cartilage degradation. As a result, in the majority of cases, ACL rupture necessitates ligament reconstruction surgery. Because of the operation and subsequent complications, the athlete must take at least six months off from their major sports activity.

Figure 1: Anterior cruciate ligament injury.

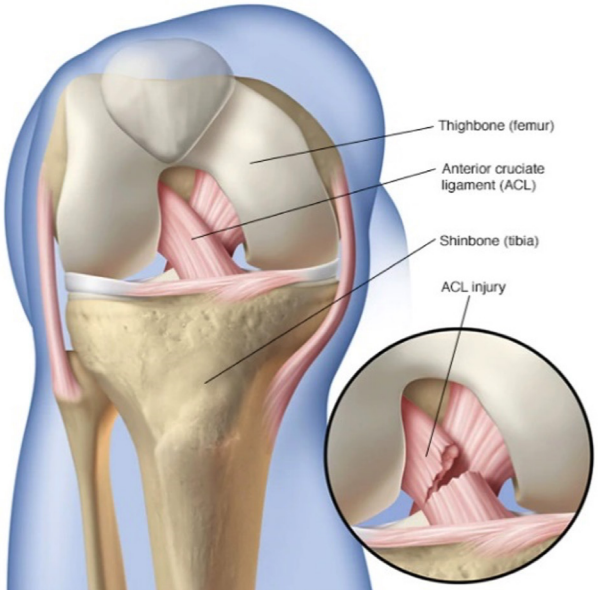
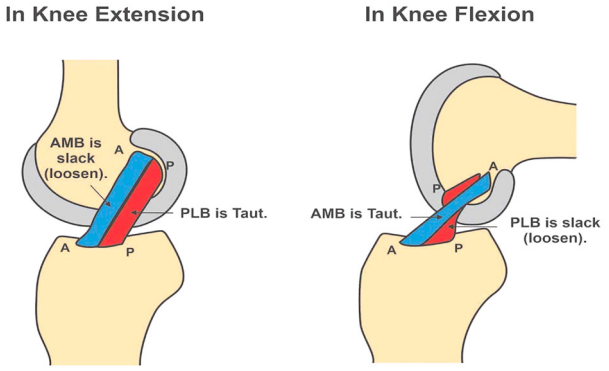


Figure 2: AM and Pl bundles of Acl in extension and flexion*.



* Retrieved from: https://physio-study.com/anterior-cruciate-ligament-anatomy-biomechanics/#more-2031

ACL reconstruction

ACL reconstruction has significantly evolved over the past 40 years with debate regarding the timing of reconstruction[18]. The surgery method is the common treatment for athletes because it restores stability and limits the potential for progressive degeneration and instability of the knee.

Early surgery may facilitate back to work or sporting; conversely, delayed reconstruction of ACL can be associated with delayed early rehabilitation due to increased muscle atrophy and reduced strength[21]. There is no consensus on the optimal time to perform ACL reconstruction surgery[22]. Early studies have recommended that early reconstruction may facilitate an early return to work but may increase the incidence of post-operative complications[23]. Smith et al., (2010) in a study entitled 'Early versus delayed surgery for ACL reconstruction: a systematic review and meta-analysis' based on the current literature found there was no difference in clinical outcome among the patients who underwent early compared with delayed ACL reconstruction[22]. Although in a survey of 101 consultant orthopedic surgeons, 81% reported that they considered the ideal time span from injury to operation to be between 1 and 6 months[24]. Probably early surgical intervention during the initial weeks post-injury resulted in restoring tibiofemoral stability that can minimize the risk of further meniscal injury which may be associated with degenerative joint changes[25]. On the other hand, some research suggest that delaying surgical intervention potentially reduce the incidence of post-operative arthrofibrosis in terms of the optimization of pre-operative knee range of motion and recovery of surrounding soft tissues from the initial injury[26].

ACL reconstruction in athletes and non-athletes

Previous studies showed that physical activity is the most common risk factor for ACL injuries in young people. Today, public health guidance programs strongly recommend regular physical activity to improve health and reduce the risk of chronic disease. Therefore, the number of athletes is rapidly increasing[27]. As a result, the risk of ACL injury is increased, and such injuries now involve significant amounts of public health costs[28]. A descriptive study of communities can identify people at risk in society, identify harmful situations and mechanisms, and help intervention programs to mitigate these harms. It is demonstrated that ACL injuries are one of the most frequent types of sports injury[29]. Although the need for reconstruction of ACL in athletes is explicit; however, there are some differences of opinion on managing ACL injuries in non-athlete persons[30]. Injuries of the ACL in athletes were studied extensively in orthopedic sports medicine, however many ACL lesions are seen in non-athletes as a result of accidents or low-grade recreational activities, which is not well addressed[31].

Reconstruction of ACL is readily offered to athletes, whereas this treatment is sometimes conservatively for non-athletes[32,33]. The treatment of injuries of the ACL in athletes was widely performed. But, the outcome of non-operative management in the general population was neglected.

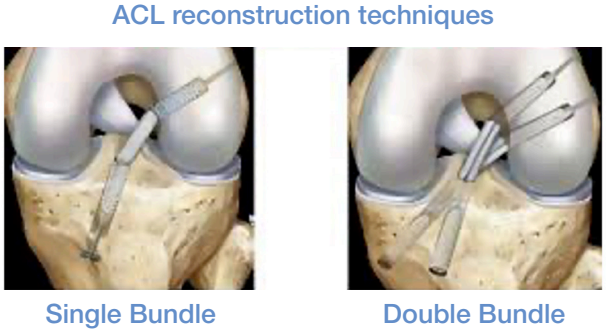
Many ACL injuries in non-athletes may be lost in terms of the conservative management, assuming that non-athletes do not have a significant degree of instability. In fact, there may be a high rate of instability and meniscus injuries in non-athletes.

Double-bundle versus single-bundle

Early reports of ACL reconstruction were first published 30 years ago[34]. Surgical procedures performed to reconstruct the ACL are usually "single-bundled" or "double-bundled"[35]. The single-bundled is widely accepted as the standard surgical option to reconstruct ACL injuries. The single bundled is effective in restoring anterior stability and has favorable postoperative clinical results. However, several studies have linked the single-bundled method to an increased risk of osteoarthritis and rotational instability problems. The focus of advances in ACL reconstructive techniques is to reduce these complications. Therefore, double blinded ACL reconstruction is considered by many surgeons as an attractive option[34].

The technique of replicating the complex anatomy of ACL in a double-bundle technique was first described in 1983[36]. Then, many technical variations of the procedure were added in recent decades (**Figure 3**).

Figure 3: Single vs. double bundle technique[38].



However, the literature review showed that most of the methods of ACL reconstruction focused on using a single bundle so that various single-bundle techniques have still dominated during the past years. Although this technique has high success rates but 30% of patients experience persistent knee pain or instability[37].

Double bundle and single bundle techniques could be compared from various aspects. Different studies have evaluated the return to the preinjury level according to the

Lysholm score, the functionality of the knee according to Subjective International Knee Documentation Committee (IKDC) score, active reincorporation, anteroposterior and rotational stability, development of osteoarthritis, and graft rupture.

Anterior and rotational stability in ACL reconstruction is very important as it may be correlated with the risk of meniscus and cartilage injury, as well as graft rupture and osteoarthritis changes[39]. Some research showed that single- bundle and double bundle surgery provide anterior stability as these two techniques could closely imitate AMB in ACL reconstruction, and there is no significant difference between these two techniques in this regard[40] However, there are some concerns regarding the failure of single bundle technique to provide adequate rotational stability in the knee[41]. To improve rotational stability, surgical procedures in "double bundles" were modified to reconstruct not only the anteromedial bundle but also the posterolateral bundle[42]. Therefore, the reconstruction of ACL using Double-bundle method was developed to reconstruct both the anteromedial and posterolateral bundles. Theoretically, the double bundle technique reconstructed PLB, in addition to AMB, which functions at extension and contributed more to rotational stability. Some studies have revealed improving in rotational stability for double-bundle reconstruction compared with single-bundle[43], and Biomechanical studies show a significant advantage in anterior and rotational stability with double-bundle compared to single-bundle ACL reconstruction[36]. The concept behind this result is that rotational stability increase significantly with the additional reconstruction of the PLB when compared to a single bundle ACL reconstruction[35]. However, more recent systematic reviews and meta-analysis show that there was no significant difference between the double-bundle and single-bundle techniques in rotational stability[40]. An explanation for this result is that perhaps the other peripheral structures, such as the collateral ligaments and the muscles that cross the joint play an important role in rotational stability[44].

In more recent systematic review and meta-analysis study, with a total of 1707 patients, the qualitative and quantitative analysis showed that there is no clear difference between these two techniques in knee function or sports incorporation and the true difference is in the subjective assessment by the patient and not the objective assessment[45]. The higher subjective feeling of the patient in the double-bundle technique allows the patient greater confidence in their return to physical activities. Therefore, the evaluation of the patient and activity levels should be considered when choosing the double-bundle technique.

Graft failure is another factor to consider to compare double-bundle and single-bundle techniques. It increases the individual suffering, recurrent instability, and future economic burden[46]. A meta-analysis conducted in 2018 showed that double-bundle technique has no advantage over single bundle regarding graft failure rate. The latter is mostly affected by other factors including new knee trauma, infection of implanted graft, returning too soon to pivoting sports, and radical rehabilitation programs rather than the technique[47].

Regarding osteoarthritis changes, again most recent meta-analysis did not show any statistically significant difference between double-bundle and single-bundle technique. Theoretically, single-bundle might result in a smaller patellofemoral and tibiofemoral contact area and greater pressures and subsequent osteoarthritis changes[48]. However, delay from the primary injury to ACL reconstruction, concomitant injury, such as meniscal or another ligament tear, influence osteoarthritis changes more than the single or double technique[43,49].

In conclusion, it seems that double-bundle technique has no significant superiority over single bundle. In one hand, double-bundle seems to be associated with better subjective functionality; on the other hand, probably because of the complexity of the double-bundle, still the single-bundle is considered the preferred choice for most of surgeons for ACL reconstruction[50]. Some of the studies on the superiority of these reconstruction techniques over each other have a follow-up period less than three to five years, a follow-up period that is too short to observe the natural history of the injured ACL repair and the postoperative changes to the knee and this may be a reason for the existed controversy.

Conclusion

Because of the prevalence of anterior cruciate ligament tears, ACL reconstruction is one of the most frequently performed orthopedic surgeries. Anterior cruciate ligament damage is widespread in both athletes and non-athletes, and it is poorly treated. Some clinical data revealed that "double-bundle" surgery provided greater anterior-posterior and rotational stability than "single-bundle" surgery. Other studies have shown no significant difference between a "single-bundle" and a "double-bundle." Probably because of the complexity of the double-bundle, the single-bundle considered the preferred choice for most of the surgeons for ACL reconstruction. Although it seems that this choice may have more anatomical and biomechanical reasons related to the complexity of the surgical procedure.

Conflict of Interest

The authors declare that there is no conflict of interest in the publication of this paper.

Table I: Studies on anterior cruciate ligament reconstruction.

First Author (year)	Title	Aim	Conclusion	Ref
Maestro (2021)	Subjective assessment reported by the patients shows differences between single-bundle and double-bundle anterior cruciate ligament reconstruction, systematic review and meta-analysis	To compare the functional recovery, active reincorporation, and anteroposterior and rotational stability of patients undergoing ACL reconstruction using techniques of simple-bundle or double-bundle	There is no clear or significant difference in the clinical stability and knee function or in sports incorporation	45
Chen (2020)	Single-bundle versus double-bundle autologous anterior cruciate ligament reconstruction: a meta-analysis of randomized controlled trials at 5-year minimum follow-up	Compare the mid- to long-term outcome of single bundle and double bundle ACL reconstruction concerning knee stability, clinical function, graft failure rate, and osteoarthritis (OA) changes.	The double bundle was not superior to the single bundle in ACL reconstruction regarding knee stability, clinical function, graft failure rate, and OA changes with a mid- to long-term follow-up	40
Dong (2019)	Long-term results after double and single bundle ACL reconstruction: Is there any difference? A meta - analysis of randomized controlled trials	Compare the longer-term efficacy between double-bundle and single-bundle techniques.	Single-bundle and double-bundle techniques could yield similar efficacy. No superiority was founded in double bundle ACL reconstruction with a minimal 5-year follow-up	44
Chowdhury (2019)	Anterior Cruciate Ligament Reconstruction Using Autologous Hamstring Double Bundle Graft Compared with Single Bundle Graft Procedures	Comparing the clinical and functional outcome of autologous double bundle and single bundle reconstruction for ACL injury.	Compared to single bundle the post-operative symptoms and signs were more improved in double bundle. Rotational and anterior stability of the knee was better in the double bundle group although not significant and all patients in our study were able to return their activity.	51
Grassi (2018)	New Trends in Anterior Cruciate Ligament Reconstruction: A Systematic Review…	Analyzing national surveys of orthopedic surgeons on ACL reconstruction to determine their preferences related to the preferred graft	Single-bundle reconstruction with anteromedial portal technique and suspension femoral fixation and screws fixation for the tibia seem the preferred solution.	52
Kay (2018)	Over 90 % of children and adolescents return to sport after anterior cruciate ligament reconstruction…	Evaluating the rate at which children and adolescent athletes return to sporting activities after ACL reconstruction	There is a high rate of return to sport following ACL reconstruction in children and adolescent. However, this is associated with a relatively high rate of graft tears and a similar rate of contralateral ACL injury.	53
Jarvela (2017)	Double-Bundle Versus Single-Bundle Anterior Cruciate Ligament Reconstruction.	Evaluating the rate of graft failure, knee stability and OA in double bundle and single bundle ACL reconstruction at 10-year follow-up	Double-bundle resulted in significantly fewer graft failures than single-bundle. Knee stability and OA rates were similar.	54
Devgan (2016)	A prospective study to evaluate the clinico-radiological outcomes of arthroscopic single bundle versus double bundle anterior cruciate ligament reconstruction	Compare clinical and radiological outcomes of arthroscopic single-bundle versus double-bundle ACL reconstruction	No statistically significant difference in knee stability, knee scores, subjective evaluations, and MRI evaluation between single- and double-bundle ACL reconstruction	55
Grassi (2016)	Returning to sport after ACL reconstruction: a survey between the Italian Society of Knee…	To survey among Italian Society of Knee, Arthroscopy, Sport, Cartilage and Orthopedic Technologies members in order to evaluate their approaches to the return to sport after ACL reconstruction	Six months was generally considered adequate by most of the members for the most demanding activities. The most used criteria to allow return to sport were manual testing.	56
Ambra (2016)	Anterior cruciate ligament reconstruction: how do we perform it? ...	Evaluating the current trends and common practice of Brazilian orthopedic surgeons, while selecting approaches for ACL reconstruction surgery.	Surgeons' preferences for ACL reconstruction are variable, and are influenced by learning time and availability of tools rather than research evidence.	57
Middleton (2014)	Anatomic anterior cruciate ligament reconstruction: a global perspective	To discuss current concepts, approaches, and techniques in the field of ACL reconstruction among leading surgeons in the field.	The most popular graft choice is hamstring tendon autograft. Nearly half of the surgeons surveyed performed both single- and double-bundle ACL reconstructions depending on certain criteria.	14
Smith (2010)	Early versus delayed surgery for ACL reconstruction: a systematic review and meta-analysis	To determine whether ACL reconstruction should be performed acutely following tears.	There was no difference in clinical outcome between patients who underwent early compared to delayed ACL reconstruction.	22
Carola (2009)	Anatomic Single- and Double-Bundle ACL Reconstruction Flowchart	To define anatomic ACL reconstruction as the functional restoration of the ACL to its native dimensions, collagen orientation, and insertion sites.	A flowchart was developed that can help orthopedic surgeons perform anatomic ACL reconstruction. This flowchart is applicable to both single- and double-bundle reconstruction and is accompanied by informative tables, figures, videos, and valuable literature	58

First Author (year)	Title	Aim	Conclusion	Ref
Joseph (2008)	Is ACL reconstruction only for athletes?	To compare the incidence of meniscal and cartilage injuries in an athlete and non-athlete population in relation to time of presentation since injury	Both athletes and non-athletes are equally susceptible for long-term meniscal and cartilage injuries if ACL reconstruction is not carried out early.	29
Siebold (2008)	Prospective Randomized Comparison of Double-Bundle Versus Single-Bundle ACL Reconstruction	To evaluate the clinical results of four-tunnel Double-Bundle ACL reconstruction	The results show a significant advantage in the anterior and rotational stability for Double-Bundle ACL reconstruction compared to Single-Bundle ACL reconstruction	36
Jarvela (2007)	Double-bundle versus single-bundle ACL reconstruction…	To compare the outcomes of ACL reconstruction when using either double-bundle or single-bundle technique	The rotational stability was significantly better in the double-bundle group than in the single-bundle group. In anterior stability of the knee, there was no significant difference between the groups.	34
Drosos (2004)	The causes and mechanisms of meniscal injuries in the sporting and non-sporting environment …	To establish the etiology and circumstances of meniscal injuries in the general adult population	In an unselected general adult population nearly one third of meniscal injuries occur in the course of non-sporting activities of daily living and one third in the absence of any recognized injury.	33

References

1. Tegner Y, Lysholm J, Lysholm M, Gillquist J. A performance test to monitor rehabilitation and evaluate anterior cruciate ligament injuries. The American journal of sports medicine. 1986;14(2):156-9.

2. Brownstein B, Bronner S. Functional movement in orthopaedic and sports physical therapy: evaluation, treatment, and outcomes: Churchill Livingstone; 1997.

3. Kennedy JC, Alexander IJ, Hayes KC. Nerve supply of the human knee and its functional importance. The American journal of sports medicine. 1982;10(6):329-35.

4. Fong DT-P, Lam M-H, Lai P-K, Yung PS-H, Fung K-Y, Chan K-M. Effect of anticipation on knee kinematics during a stop-jump task. Gait & posture. 2014;39(1):75-9.

5. Gabler CM. The Effectiveness of Neuromuscular Training on a Modifiable Anterior Cruciate Ligament Injury Risk Factor: Ohio University; 2012.

6. Dick R, Putukian M, Agel J, Evans TA, Marshall SW. Descriptive epidemiology of collegiate women's soccer injuries: National Collegiate Athletic Association Injury Surveillance System, 1988-1989 through 2002–2003. Journal of athletic training. 2007;42(2):278.

7. Gianotti SM, Marshall SW, Hume PA, Bunt L. Incidence of anterior cruciate ligament injury and other knee ligament injuries: a national population-based study. Journal of Science and Medicine in Sport. 2009;12(6):622-7.

8. Barrett D. Proprioception and function after anterior cruciate reconstruction. The Journal of bone and joint surgery British volume. 1991;73(5):833-7.

9. Purnell ML, Larson AI, Clancy W. Anterior cruciate ligament insertions on the tibia and femur and their relationships to critical bony landmarks using high-resolution volume-rendering computed tomography. Am J Sports Med. 2008;36(11):2083-90.

10. Petersen W, Zantop T. Anatomy of the anterior cruciate ligament with regard to its two bundles. Clin Orthop Relat Res. 2007;454:35-47.

11. Shafiei E, Mohammad Javadi M, Kariminasab MH, Shayesteh Azar M, Daneshpour M, Mohammadpour RA, et al. Analysis of the outcome of Anterior Cruciate Ligament reconstruction surgery on knee in athletes from Sari, 2007-2008. Journal of Mazandaran University of Medical Sciences. 2010;19(74):2-7.

12. Badiezadeh K. How long athletes remain athletes after anterior cruciate ligament reconstruction? 2004.

13 TAHMASBI M, Panjavi B. Operative results of arthroscopic and open ACL reconstruction by bone-patellar tendon-bone graft. 2001.

14. Middleton K, Hamilton T, Irrgang J, Karlsson J, Harner C, Fu F. Anatomic anterior cruciate ligament (ACL) reconstruction: a global perspective. Part 1. Knee Surgery, Sports Traumatology, Arthroscopy. 2014;22(7):1467-82.

15. Clayton RA, Court-Brown CM. The epidemiology of musculoskeletal tendinous and ligamentous injuries. Injury. 2008;39(12):1338-44.

16. Tahmasebi MN, Firoozabadi MA, Panjavi B, Kaseb MH. Knee stabiligy after ACL reconstruction through graft fixation in femoral tunnel: transfemoral pinning versus endobutton techniques. Tehran University Medical Journal. 2011;69(2).

17. Kurosaka M, Kuroda R, Kubo S, Hoshino Y, Araki D, Yoshiya S. Double-bundle anatomic anterior cruciate ligament reconstruction: the technique and clinical experience. Operative Techniques in Sports Medicine. 2008;16(3):125-30.

18. Kocher MS, Steadman JR, Briggs KK, Sterett WI, Hawkins RJ. Relationships between objective assessment of ligament stability and subjective assessment of symptoms and function after anterior cruciate ligament reconstruction. The American journal of sports medicine. 2004;32(3):629-34.

19. Jomha NM, Borton DC, Clingeleffer AJ, Pinczewski LA. Long-term osteoarthritic changes in anterior cruciate ligament reconstructed knees. Clinical Orthopaedics and related research. 1999(358):188-93.

20. Mall NA, Chalmers PN, Moric M, Tanaka MJ, Cole BJ, Bach Jr BR, et al. Incidence and trends of anterior cruciate ligament reconstruction in the United States. The American journal of sports medicine. 2014;42(10):2363-70.

21. Fithian DC, Paxton EW, Stone ML, Luetzow WF, Csintalan RP, Phelan D, et al. Prospective trial of a treatment algorithm for the management of the anterior cruciate ligament-injured knee. The American journal of sports medicine. 2005;33(3):335-46.

22. Smith TO, Davies L, Hing CB. Early versus delayed surgery for anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Knee Surgery, Sports Traumatology, Arthroscopy. 2010;18(3): 304-11.

23. Melikoglu MA, Balci N, Samanci N, Filiz MB, Gurbuz U, Dagseven T, et al. Timing of surgery and isokinetic muscle performance in patients with anterior cruciate ligament injury. Journal of Back and Musculoskeletal Rehabilitation. 2008;21(1):23-8.

24. Francis A, de WM Thomas R, McGregor A. Anterior cruciate ligament rupture: reconstruction surgery and rehabilitation.: A nation-wide survey of current practice. The Knee. 2001;8(1):13-8.

25. Sgaglione NA, Del Pizzo W, Fox JM, Friedman MJ. Arthroscopically assisted anterior cruciate ligament reconstruction with the pes anserine tendons: comparison of results in acute and chronic ligament deficiency. The American journal of sports medicine. 1993;21(2):249-56.

26. Shelbourne K, Patel D. Timing of surgery in anterior cruciate ligament-injured knees. Knee Surgery, Sports Traumatology, Arthroscopy. 1995;3(3):148-56.

27. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. Jama. 1995;273(5):402-7.

28. Pasanen K, Parkkari J, Kannus P, Rossi L, Palvanen M, Natri A, et al. Injury risk in female floorball: a prospective one-season follow-up. Scandinavian journal of medicine & science in sports. 2008;18(1):49-54.

29. Joseph C, Pathak SS, Aravinda M, Rajan D. Is ACL reconstruction only for athletes? International orthopaedics. 2008;32(1):57-61.

30. Nebelung W, Wuschech H. Thirty-five years of follow-up of anterior cruciate ligament—deficient knees in high-level athletes. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2005;21(6):696-702.

31. Casteleyn P-P, Handelberg F. Non-operative management of anterior cruciate ligament injuries in the general population. The Journal of bone and joint surgery British volume. 1996;78(3):446-51.

32. Chick RR, Jackson DW. Tears of the anterior cruciate ligament in young athletes. JBJS. 1978;60(7):970-3.

33. Drosos G, Pozo J. The causes and mechanisms of meniscal injuries in the sporting and non-sporting environment in an unselected population. The Knee. 2004;11(2):143-9.

34. Järvelä T. Double-bundle versus single-bundle anterior cruciate ligament reconstruction: a prospective, randomize clinical study. Knee Surgery, Sports Traumatology, Arthroscopy. 2007;15(5):500-7.

35. Gabriel MT, Wong EK, Woo SLY, Yagi M, Debski RE. Distribution of in situ forces in the anterior cruciate ligament in response to rotatory loads. Journal of orthopaedic research. 2004;22(1):85-9.

36. Siebold R, Dehler C, Ellert T. Prospective randomized comparison of double-bundle versus single-bundle anterior cruciate ligament reconstruction. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2008;24(2):137-45.

37. Buoncristiani AM, Tjoumakaris FP, Starman JS, Ferretti M, Fu FH. Anatomic double-bundle anterior cruciate ligament reconstruction. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2006;22(9):1000-6.

38. Amin MF, Abd El Kareem H, Sadek AF, Saleh AN. MRI evaluation of the knee post double bundle ACL reconstruction: Association of graft findings and comparison with arthroscopy. The Egyptian Journal of Radiology and Nuclear Medicine. 2016;47(2):521-9.

39. Jiang H, Ma G, Li Q, Hu Y, Li J, Tang X. Cortical Button Versus Cross-pin Femoral Fixation for Hamstring Anterior Cruciate Ligament Reconstruction: A Meta-analysis of Randomized Controlled Trials. Am J Sports Med. 2018;46(9):2277-84.

40. Chen H, Chen B, Tie K, Fu Z, Chen L. Single-bundle versus double-bundle autologous anterior cruciate ligament reconstruction: a meta-analysis of randomized controlled trials at 5-year minimum follow-up. Journal of Orthopaedic Surgery and Research. 2018;13(1):50.

41. Hemmerich A, van der Merwe W, Batterham M, Vaughan CL. Knee rotational laxity in a randomized comparison of single-versus double-bundle anterior cruciate ligament reconstruction. The American journal of sports medicine. 2011;39(1):48-56.

42. Pena E, Calvo B, Martinez M, Palanca D, Doblare M. Influence of the tunnel angle in ACL reconstructions on the biomechanics of the knee joint. Clinical Biomechanics. 2006;21(5):508-16.

43. Song E-K, Seon J-K, Yim J-H, Woo S-H, Seo H-Y, Lee K-B. Progression of osteoarthritis after double-and single-bundle anterior cruciate ligament reconstruction. The American journal of sports medicine. 2013;41(10):2340-6.

44. Dong Z, Niu Y, Qi J, Song Y, Wang F. Long term results after double and single bundle ACL reconstruction: Is there any difference? A meta - analysis of randomized controlled trials. Acta Orthop Traumatol Turc. 2019;53(2):92-9.

45. Maestro A, Herruzo I, Varillas-Delgado D, Martín-Saborido C. Subjective assessment reported by patients shows differences between single-bundle and double-bundle anterior cruciate ligament reconstruction, systematic review and meta-analysis. Scientific Reports. 2021;11(1):15385.

46. Bach BR, Provencher M. ACL surgery: how to get it right the first time and what to do if it fails: SLACK Incorporated; 2010.

47. Jarvela S, Kiekara T, Suomalainen P, Jarvela T. Double-Bundle Versus Single-Bundle Anterior Cruciate Ligament Reconstruction A Prospective Randomized Study With 10-Year Results. AMERICAN JOURNAL OF SPORTS MEDICINE. 2017;45(11):2578-85.

48. Tajima G, Iriuchishima T, Ingham SJ, Shen W, van Houten AH, Aerts MM, et al. Anatomic double-bundle anterior cruciate ligament reconstruction restores patellofemoral contact areas and pressures more closely than nonanatomic single-bundle reconstruction. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2010;26(10):1302-10.

49. Adravanti P, Dini F, de Girolamo L, Cattani M, Rosa MA. Single-bundle versus double-bundle anterior cruciate ligament reconstruction: a prospective randomized controlled trial with 6-year follow-up. The journal of knee surgery. 2017;30(09):898-904.

50. Tiamklang T, Sumanont S, Foocharoen T, Laopaiboon M. Double-bundle versus single-bundle reconstruction for anterior cruciate ligament rupture in adults. Cochrane Database of Systematic Reviews. 2012(11).

51. Chowdhury AZ, Ali MH, Faisal MA, Kundu IK, Arifeen KN, Mahmood CI, et al. Anterior Cruciate Ligament Reconstruction Using Autologous Hamstring Double Bundle Graft Compared With Single Bundle Graft Procedures. Mymensingh Med J. 2019;28(1):126-36.

52. Grassi A, Carulli C, Innocenti M, Mosca M, Zaffagnini S, Bait C, et al. New trends in anterior cruciate ligament reconstruction: a systematic review of national surveys of the last 5 years. Joints. 2018;6(03):177-87.

53. Kay J, Memon M, Marx RG, Peterson D, Simunovic N, Ayeni OR. Over 90% of children and adolescents return to sport after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Knee surgery, sports traumatology, arthroscopy. 2018;26(4):1019-36.

54. Järvelä S, Kiekara T, Suomalainen P, Järvelä T. Double-Bundle Versus Single-Bundle Anterior Cruciate Ligament Reconstruction: A Prospective Randomized Study With 10-Year Results. The American Journal of Sports Medicine. 2017;45(11):2578-85.

55. Devgan A, Rohilla R, Singh A, Tanwar M, Devgan R, Siwach K. A prospective study to evaluate the clinico-radiological outcomes of arthroscopic single bundle versus double bundle anterior cruciate ligament reconstruction. J Clin Orthop Trauma. 2016;7(Suppl 2):236-42.

56. Grassi A, Vascellari A, Combi A, Tomaello L, Canata GL, Zaffagnini S, et al. Return to sport after ACL reconstruction: a survey between the Italian Society of Knee, Arthroscopy, Sport, Cartilage and Orthopaedic Technologies (SIGASCOT) members. European Journal of Orthopaedic Surgery & Traumatology. 2016;26(5):509-16.

57. Ambra LFM, Rezende FC, Xavier B, Shumaker FC, da Silveira Franciozi CE, Luzo MVM. Anterior cruciate ligament reconstruction: how do we perform it? Brazilian orthopedic surgeons' preference. International orthopaedics. 2016;40(3):595-600.

58. van Eck CF, Lesniak BP, Schreiber VM, Fu FH. Anatomic single- and double-bundle anterior cruciate ligament reconstruction flowchart. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2010;26(2):258-68.

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ORIGINAL

Lesiones traumáticas orales como signo de violencia. Importancia de la detección en la visita dental

Oral traumatic injuries as a sign of violence. Importance of detection at the dental visit

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Resumen

La violencia interpersonal es un grave problema de la sociedad actual, las lesiones consecuencia de este tipo de violencia afectan al área facial y bucodental, siendo los Odonto-Estomatólogos los encargados de diagnosticar y tratar las lesiones de este área, sin embargo no profundizan en la situación de violencia que causó las lesiones. Exponemos en este artículo el marco legal que rodea al especialista ante este problema, así como los signos de detección e identificación de estos pacientes, la exploración oral y la realización del parte de lesiones. Incidiendo en la necesidad de formación y preparación curricular así como en la realización de cursos de formación en este tema para la detección del problema, resaltando la importancia de disponer de protocolos de actuación.

Palabras clave: Traumatismo dental, violencia interpersonal, protocolos, odontología.

Abstract

Interpersonal violence is a serious problem in today's society, the injuries resulting from this type of violence affect the facial and oral area, being the Odonto- Stomatologists in charge of diagnosing and treating injuries in this area, however they do not delve into the situation of violence that caused the injuries. We present in this article the legal framework that surrounds the specialist in the face of this problem, as well as the signs of detection and identification of these patients, the oral examination, and the performance of the injury report. Influencing the need for training and curricular preparation as well as conducting training courses on this issue to detect the problem, highlighting the importance of having action protocols.

Key words: Dental trauma, interpersonal violence, protocols, dentistry.

Introducción

El concepto de violencia está sometido a distintas interpretaciones que se rigen por los códigos sociales culturales por lo que es difícil establecer un concepto de violencia a nivel mundial. La OMS[1] define la violencia como: El uso deliberado de la fuerza física o el poder, ya sea en grado de amenaza o efectivo, contra uno mismo, otra persona o un grupo o comunidad, que cause o tenga muchas probabilidades de causar lesiones, muerte, daños psicológicos, trastornos del desarrollo o privaciones".

Las estadísticas de lesiones causadas por la violencia interpersonal son preocupantes por sus elevadas cifras. En el año 2000 la tasa de mortalidad atribuida a este tipo de violencia fue de 8,8 por cada 100000 habitantes, pero es mucho mayor la incidencia de lesiones no mortales. Todos los profesionales sanitarios tienen la obligación de emitir informes y partes de lesiones ante la sospecha de casos[2]. La profesión dental puede y debe detectar estas situaciones de violencia interpersonal, ya que frecuentemente las lesiones se centran en la región facial.

Coelho et al[3] estudió 790 historias clínicas de casos de violencia con el objetivo de determinar los patrones de lesiones provocadas por la violencia interpersonal, concluyendo que las lesiones más frecuentes fueron: contusión facial y laceración, conmoción cerebral, fractura dental y mandibular. En los casos debidos a violencia urbana se detectó contusión facial y concusión dental en el 87,5% de los casos, laceración facial en el 57% y fractura mandibular en el 32,5%, lo que pone de manifiesto la importancia de las lesiones que afectan al área bucodental.

Las lesiones en la cabeza y en el cuello representan 65-75 % del trauma físico que ocurre durante los incidentes de violencia doméstica[4]. Nelms et al[5] demostraron la gran presencia de lesiones bucodentales con la afectación de lesiones en labios en el 29%, dientes fracturados en el 15%, fractura mandibular en el 7%, dientes perdidos en el 5% y lesiones en la lengua en el 5%. Fuera del área oral se constataron un 21% de lesiones faciales, 14% de lesiones en cuello y un 3% otro tipo de lesiones.

En un estudio realizado sobre la población brasileña víctima de la violencia interpersonal, Nóbrega et al[6] concluyeron que la prevalencia de trauma oral-maxilofacial fue alta, estando presente en el 46,4% de los casos. Casi la mitad de las mujeres de este estudio presentaron traumatismo maxilofacial, lo que centra esta región, nuevamente, como un área importantísima en las lesiones causadas por este tipo de violencia. Otras investigaciones también ponen de manifiesto la alta incidencia de traumatismos máxilo- faciales con especial incidencia en fracturas mandibulares como consecuencia de violencia interpersonal[7,8,9].

Los dentistas y otros profesionales del cuidado dental tienen un papel particularmente relevante en la identificación de estos casos. Sin embargo, la falta de formación curricular en el tema para la identificación y manejo de los casos de violencia, el desconocimiento legal, el miedo personal a la denuncia y la antigua percepción social de la violencia doméstica como una cuestión familiar y que afecta a la esfera privada de los ciudadanos hace que sea un grupo profesional que elude el problema. Ya en 1994, la Asociación Americana de Escuelas de Odontología (AADS), ahora Asociación Americana de Educación Dental, aprobó una resolución recomendando que todos los currículos de higiene dental y de Odontología incluyeran formación sobre el maltrato.

Este artículo tiene por objetivo exponer la importancia de la detección de las lesiones provocadas por la violencia interpersonal y la necesidad de establecer protocolos de actuación que a fecha de hoy no están estandarizados para el personal sanitario de esta especialidad

Marco legal

Legislación aplicable al odonto-estomatólogo en tanto que personal sanitario

a) Código Penal: Artículo 196: Delito de omisión del deber de socorro del personal sanitario
b) Código Penal: Artículo 450: Delito contra la Administración de Justicia por omisión del deber de impedir delitos o promover su persecución
c) Código Civil (Real Decreto de 24 de julio de 1889): Art.1902 y siguientes: Obligaciones que nacen de culpa o negligencia y que causan responsabilidad civil profesional cuando se acredita tanto el nexo de causalidad entre la actuación y el resultado como la existencia de negligencia. Debe distinguirse entre la *culpa del profesional* y la *culpa profesional* propiamente dicha.
d) Ley General de Sanidad 14/1986, de 25 de abril.
e) Decreto 1030/2006, de 15 de septiembre, por el que se establece la obligación de servicios comunes del Sistema Nacional de Salud y el procedimiento para su actualización, incluyendo el diagnóstico y la atención a la violencia de género, tanto en asistencia primaria como en la especializada (Anexos II y III del mismo).
f) Código Español de ética y deontología dental del Consejo de Dentistas, Organización colegial de dentistas de España (2012).
g) Leyes relacionadas con el derecho a la intimidad del paciente:
a. Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y Garantía de los Derechos Digitales
b. Reglamento Europeo (UE) 2016/679 del Parlamento Europeo y del Consejo, de 27 de abril de 2016, relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación

de estos datos y por el que se deroga la Directiva 95/46/CE (Reglamento General de Protección de Datos)
c. Ley Orgánica 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y obligaciones en materia de información y documentación clínica, que define el concepto y contenido de la historia clínica (artículos 14 y 15) y se refiere a su uso (artículo 16)
h) Legislación de lucha y protección ante la violencia de género y la violencia doméstica:
a. Ley Orgánica 1/2004, de 28 de diciembre, de Medidas de Protección Integral contra la Violencia de Género.
b. Ley Orgánica 3/2007, de 22 de marzo, para la Igualdad Efectiva de Hombres y Mujeres.
i) Legislación de protección del menor: Ley Orgánica 1/1996, de 15 de enero, de Protección Jurídica del menor, que reconoce el principio de atención inmediata en caso de desprotección (artículo 14), de las actuaciones de protección (artículo 12), así como la obligación de comunicación de las situaciones de maltrato (artículo 13).

Obligaciones legales y responsabilidad

El odontólogo tiene la obligación legal de cumplir el marco legal anteriormente expuesto, siendo garantes de la seguridad y atención del paciente, protegiendo su derecho a la intimidad, independientemente del área en el que ejerza la profesión ya sea de ámbito privado o público.

El Profesional tiene la obligación de cumplimentar la historia Clínica, que debe conservar conforme a las Leyes de autonomía del paciente y de protección de datos y a la vez el paciente tiene derecho a obtener un informe clínico.

Si no se cumplen estas obligaciones, puede darse lugar a distintos tipos de infracciones que pueden llevar hasta la inhabilitación profesional. Como consecuencia de la legislación expuesta, el Odonto-Estomatologos tiene distintos tipos de responsabilidades:

a. Responsabilidad Profesional: La obligación del Odonto-Estomatólogo de reparar, responder y resarcir los daños que hayan producido a los pacientes como consecuencia de actos u omisiones, voluntarias o involuntarias, de acuerdo con la definición clásica acuñada por el profesor Juan Antonio Gisbert Calabuig[10]
b. Responsabilidad penal: Surge al infringir el código penal.
c. Responsabilidad civil: Contractual, extracontractual y derivada del daño causado por el delito.
d. Responsabilidad Contencioso-administrativa: cuando el daño es causado por el personal de la Administración Sanitaria.
e. Responsabilidad en el ámbito sanitario: suele vincularse a los medios puestos a disposición del paciente.

Signos de detección-identificación de casos de violencia

Recepción del paciente

La victima puede presentarse en los servicios sanitarios inmediatamente después de la agresión o tiempo después. Los pacientes cuyas lesiones orales son debidas a accidentes fortuitos suelen acudir inmediatamente, sin embargo, los pacientes que han sufrido violencia especialmente interpersonal no suelen acudir en el momento de la lesión, sino tiempo después.

La relación del paciente con sus familiares puede reflejar un comportamiento interfamiliar que nos puede hacer sospechar que existe un problema de relación entre los miembros de la familia. El cuidado extremadamente excesivo por parte de los familiares hacia el paciente puede ocultar una situación de dominio o maltrato. El impedimento de los familiares para que el paciente nos comunique lo que le pasa, así como la voz impositora del familiar también son signos de sospecha. La manifestación de miedo, llanto, tartamudez, inseguridad y la falta de explicaciones coherentes suelen acompañar estas situaciones. Si se trata de un niño la presencia de comportamientos muy pasivos o disruptivos pueden hacernos sospechar que estamos frente a maltratos o abusos infantiles. Es importante observar al paciente al entrar en el consultorio, la forma de andar puede reflejar otras lesiones corporales, deben observarse las zonas de piel no cubiertas por la ropa para detectar signos de traumatismos recientes o antiguos. La falta de cuidado personal del paciente, con aspecto poco limpio y ropa inadecuada suele ser frecuente.

La historia clínica debe registrar todos los datos referentes al accidente que provocó las lesiones, día, hora, lugar del accidente, forma en que se produjo, elementos con los que se golpeó y dirección de la caída o del golpe. Es importante la toma de fotografías.

El 50% de los niños maltratados presentan trauma orofacial, por lo que es muy importante diferenciarlo de las lesiones traumáticas causadas accidentalmente, estas últimas suelen estar relacionadas con las estructuras óseas y tienen un relato coherente y acorde con el desarrollo del niño. Hay que estar muy atentos a discrepancias entre los hechos relatados y las consecuencias traumáticas[11,12].

Exploración oral

En el momento de la exploración suele observarse lesiones en los tejidos blandos que podrían estar en distintas fases de cicatrización.

En niños suele haber presencia de caries en dientes definitivos y temporales que no han sido tratados,

pérdida de algún diente anticipadamente al momento del recambio dental y ausencia de mantenedores de espacio, problemas de maloclusión y ausencia de tratamientos restauradores. Lesiones en el frenillo labial o lingual en niños pequeños deben alertarnos pues para muchos autores estas lesiones no son accidentales[13,14]. En este colectivo además de los maltratos también debemos tener en cuenta el concepto de negligencia dental definido en 2016 por la Academia Americana de Odontología Pediátrica como: "Dental neglect is willful failure of parent or guardian to seek and follow through with treatment necessary to ensure a level of oral heath essential for adequate function and freedom from pain and infection"[15].

En mujeres y/o adultos el estado oral suele ser deficiente con la presencia de candidiasis y lesiones en las mucosas por parafunciones como mordedura de la mucosa yugal o bruxismo, lo que indica el nivel de estrés emocional al que están sometidos. Suelen tener tratamientos que no se han realizado en su totalidad, dando explicaciones poco claras de por qué no se finalizaron. La presencia de complicaciones de traumatismos como cambio del color de los dientes, desplazamientos dentales y fístulas suelen ser comunes.

En pacientes geriátricos dependientes se suele observar falta de higiene oral, pérdida de dientes que no han sido sustituidos y suelen ser portadores de prótesis muy antiguas y deterioradas, lo que indica la falta de cuidado y la dejadez por parte de sus familiares en el bienestar del paciente.

En pacientes con necesidades especiales suele observarse la presencia de patología periodontal debido al acúmulo de sarro por la falta de cuidado oral, la ausencia de tratamientos conservadores y la falta de controles dentales habituales.

La cavidad oral también puede presentar signos que indiquen abuso sexual. Las petequias en paladar suelen estar presentes en casos de felaciones forzadas, así mismo pueden detectarse condilomas acuminados, chancros sifilíticos y otras manifestaciones de enfermedades de transmisión sexual.

Exponemos en este apartado como ejemplo, el caso clínico de una paciente de 43 años que sufrió una agresión de su pareja dentro de lo que se denomina violencia de género. (**Figura 1**)

La paciente acude a visita a las 3 horas de la agresión. A la exploración clínica se puede observar el 2.1 desplazado, en el eje vertical, hacia coronal, dificultando la oclusión a la paciente. La mucosa presenta herida vertical en la zona vestibular distal del 2.1, sin dehiscencia de los bordes, también presenta ligero sangrado en el margen gingival (**Figura 1- A**). A la palpación la paciente manifiesta dolor, presentando movilidad y dando la sensación de debilidad en el 2.1. Las pruebas de vitalidad son negativas. Se descartan facturas radiculares mediante exploración radiográfica en diferentes proyecciones, observándose un agrandamiento del espacio periodontal en la zona apical. No se observan lesiones en otros dientes. Diagnosticando el caso clínico de luxación extrusiva traumática del 2.1 como consecuencia de agresión por violencia de género.

Se realiza reposición del diente en el alveolo y se procede a la ferulización, que se mantiene durante 15 días. Se realizó tratamiento endodóntico y se fueron realizando controles para verificar la buena evolución del caso.

El pronóstico de los traumatismos dentales que tienen como consecuencia la luxación del diente, tienen una evolución incierta, pudiendo presentar diferentes complicaciones, que podrían llevar a la pérdida del diente.

Parte de lesiones

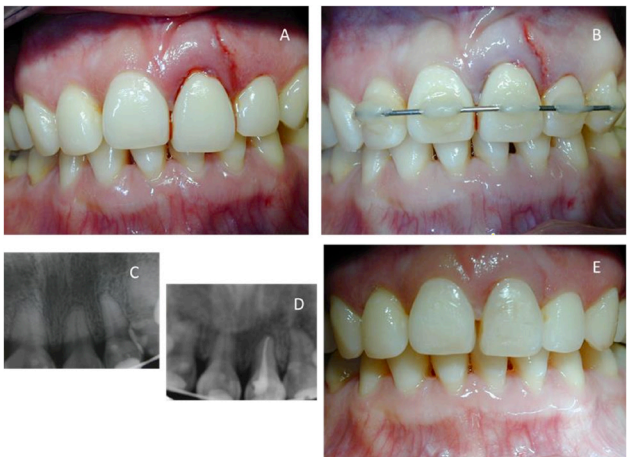
El parte de lesiones es un documento sanitario breve, médico-legal, que se traslada a la autoridad judicial y que sirve de medio de prueba para comunicar un hecho, debiendo ser remitido obligatoriamente al Juzgado. En ningún caso se solicitará el consentimiento del paciente ni de los tutores para realizarlo.

La estructura está compuesta por un preámbulo y cuerpo:

Preámbulo:

- Identificación del profesional e institución para la que presta los servicios
- Identificación del lesionado

Figura 1: Paciente que sufrió una luxación extrusiva tras una agresión por violencia de género. A: Imagen clínica inicial B. Reposicionamiento del diente en el alveolo y ferulización. C: RX periapical tras el reposicionamiento del diente. D: RX periapical a la semana de la luxación tras el tratamiento endodóntico E: Imagen clínica al mes de la lesión.



Cuerpo:

- Fecha y hora de atención
- Descripción de las lesiones: número, localización, extensión, naturaleza, morfología, número de puntos de sutura, con aportación de documentos gráficos si fuera posible
- Descripción del estado emocional del paciente
- Inclusión del diagnóstico, tratamiento prescrito y destino del paciente
- Emisión de un pronóstico: leve, moderado, grave
- Referencia a quién se notifica: juez de guardia, servicios sociales, etc.

En la sanidad pública el parte de lesiones suele consistir en un documento autocopiativo del que se hacen tres copias: una se envía al Juzgado de Guardia en menos de 24 horas, otra queda en la historia clínica del paciente y una última es entregada a éste. No existen formularios específicos para el Odonto-Estomatólogo, sería de gran ayuda tener formularios estandarizados[16] que faciliten la toma de datos.

Discusión

De lo anteriormente expuesto, por tanto, se extrae que actualmente nos encontramos ante una aparente paradoja: el personal sanitario tiene la obligación legal de detectar, prevenir e identificar indicios de violencia, pero no se nutre a este personal de los medios educativos y formativos necesarios para cumplir con este deber.

Una de las formas de prevención de la violencia es la educación, tanto de la sociedad en general como de los profesionales sanitarios en particular. La sociedad debe recibir actuaciones educativas enfocadas al respeto, la tolerancia, la igualdad, la no violencia intrafamiliar y la promoción de una cultura igualitaria entre clases sociales y géneros. Así mismo, la sociedad debe mostrarse intolerante con los causantes de la violencia.

Más allá de la obligación legal y en cuanto al deber social, el Artículo 12 del Código español de ética y deontología dental obliga al dentista a dar prioridad a los intereses del paciente, en relación con el principio de beneficencia, deben velar por la vida y beneficio de la salud del paciente.

Los Odonto-Estomatologos tanto por su condición de profesionales sanitarios como por ser los encargados de tratar las consecuencias de las agresiones en la cavidad oral, deben tener la preparación adecuada para enfrentarse a estos problemas. En concreto los Odontólogos del equipo de Atención primaria juegan un papel muy importante en el control y detección de estos pacientes.

Por tanto, resulta elemental poner énfasis en la formación de estas competencias, como de hecho ya requiere la Ley Orgánica 1/2004, de 28 de diciembre, de Medidas de Protección Integral contra la violencia de género, que establece que las administraciones educativas competentes asegurarán que en los ámbitos curriculares de las licenciaturas y diplomaturas, y en los programas de especialización de las profesiones sociosanitarias, se incorporarán contenidos dirigidos a la capacitación para la prevención, la detección precoz, la intervención y el apoyo a las víctimas[17].

Gibson-Howell et al[18] en su artículo "Instruction in Dental Curricula to Identify and Assist Domestic Violence Victims", en el que estudió la enseñanza que escuelas de odontología de Canadá y Estados Unidos, impartieron sobre la violencia doméstica entre los años 1996- 2007, pone de manifiesto la necesidad de aumentar cursos dedicados a los dentistas para mejorar la formación en el manejo de los estos temas, a pesar de que ya disponían de formación curricular, demostrando que cuando el dentista tiene más formación sobre el tema está más seguro en la identificación y manejo de la violencia interpersonal.

En otro estudio realizado en la universidad de Tennessee a los estudiantes de Odontología[19], expone que más de un tercio (36.0%) informaron no haber tenido capacitación en competencias de violencia. Un 20% reconoció tener alguna experiencia de violencia interpersonal en su vida, ya sea a través de la victimización personal o testigo de abuso o violencia dirigida a un miembro de su familia. Los estudiantes que habían recibido algún tipo de capacitación sobre manejo de la violencia se limitaban a sesiones entre 1-5 horas impartidas por las asignaturas de cirugía oral y maxilofacial, pediatría, y prostodoncia. Concluyendo que es interesante una enseñanza basada en 5R: "Recognizing, Responding, Referring to Resources, and being cognizant of mandated Reporting requirement", que fue aplicada en un proyecto de identificación de violencia familiar llamado "Healing Homes" con buenos resultados.

Otros estudios respecto a Violencia doméstica[20,21] confirman que dentistas, técnicos sanitarios y médicos generalmente no tienen el conocimiento necesario para la adecuada identificación y derivación de estos casos. Además, los profesionales de la odontología no se consideran lo suficientemente hábiles como para realizar preguntas sensibles y además desconocen las instituciones de apoyo a las víctimas, debido a la falta de formación. Otro ejemplo de ello es el estudio publicado sobre dentistas jordanos[22], la mitad de los entrevistados declararon haber sospechado maltrato infantil en al menos un caso en los últimos 5 años, pero solo el 12% de ellos lo comunicaron. Son necesarios protocolos de procedimiento en este colectivo, así como la formación continuada y formularios para registrar los

datos clínicos exploratorios y los índices de riesgo ante estas situaciones. En este sentido, debemos hacer referencia a un programa nacido en la Universidad James Cook, en Australia, para la formación de los Odontologos en la detección de la violencia doméstica[23]. La Facultad de Medicina y Odontología, en colaboración con profesorado de Trabajo Social de la James Cook University y el Servicio de Violencia Doméstica de Cairns, ha elaborado este nuevo programa: "Violencia doméstica: reconocer, responder y derivar" que nace en el año 2015. Dando mucha importancia a la formación de los profesionales en la escucha activa, protocolos específicos y la coordinación interinstitucional.

Estos estudios vienen a corroborar que, el trabajo del profesional de la salud bucodental ante los casos que se le plantean en su actividad diaria no debe centrar su atención únicamente en el resultado de la reparación del daño, sino también en las causas que han provocado la situación que presenta el paciente, y que para ser atendido adecuadamente tanto sanitaria como socialmente requiere de *algo más* que una formación científico-técnica, especialmente ante las situaciones de violencia.

Por último, y a modo de conclusión, queremos compartir con vosotros la reflexión que Nelson Mandela[1], incorpora al prólogo del Informe Mundial sobre la violencia y la salud, que nos parece viene a resumir del mejor modo posible el objetivo que quisiéramos alcanzar con este artículo: "*Arroja luz sobre los diversos rostros de la violencia, desde el sufrimiento "invisible" de los individuos más vulnerables de la sociedad a la tragedia tan notoria de las sociedades en conflicto. Hace progresar nuestro análisis de los factores que conducen a la violencia y las posibles respuestas de los distintos sectores de la sociedad, y con ello nos recuerda que la seguridad y las garantías no surgen de manera espontánea, sino como fruto del consenso colectivo y la inversión pública*".

Conclusiones

1. Es importante registrar en la historia clínica la información exhaustiva de cómo, dónde y de qué forma/ modo se produjo la lesión.
2. Es obligatorio dar parte a las autoridades ante la sospecha de lesiones causadas por violencia.
3. Es obligatorio emitir un parte de lesiones.
4. Debe priorizarse siempre el derecho de salvaguardar a la/s victima/s frente a cualquier otro bien jurídico protegido que pueda entrar en juego.
5. Son necesarios cursos de capacitación en competencia de violencia para Odonto- estomatólogos.
6. Es aconsejable disponer de modelos estandarizados de partes de lesiones.

Conflicto de intereses

Los autores declaran que no existen conflictos de intereses

Contribución de los Autores

Todos los autores han contribuido a la realización de este manuscrito, y han leído y aprobado la versión final del manuscrito.

Bibliografía

1. O. M. S. «Informe Mundial sobre la Violencia y la Salud,» Comercialización y Difusión, Organización Mundial de la Salud, Ginebra, Suiza, 2002 https://apps.who.int/iris/bitstream/handle/10665/67411/a77102_spa.pdf.

2. Park C, Welbury R. Current and historical involvement of dentistry in child protection and a glimpse of the future. Oral Dis 2016; 22(7): 605-8 DOI: 10.1111/odi.12485.

3. Coelho Ferreira M, Batista A, de Oliveira Ferreira F, Ramos-Jorge M, Silva Marques L. Pattern of oral–maxillofacial trauma stemming from interpersonal physical violence and determinant factors. Dent Traumatol 2014; 1: 215-21, DOI: 10.1111/edt.12047.

4. Le B, Dierks E, Ueeck B, Homer L, Potter B. Maxillofacial injuries associated with domestic violence. J Oral Maxillofac Surg 2001; 59(11): 1277-83. DOI:10.1053/joms.2001.27490.

5. Nelms E, Gutmann M, Solomon E, Janice J, DeWald P, Campbell P. What Victims of Domestic Violence Need from the Dental Profession. J Dent Educ 2009; 73(4): 490-6

6. da Nóbrega L, Bernardino I, Barbosa K, Silva J, Massoni A. Pattern of oral- maxillofacial trauma from violence against women and its associated factors. Dent Traumatol 2017; 33: 181-186 DOI: 10.1111/edt.12327.

7. Boffano P, Roccia F, Zavattero E. Assault-related maxillofacial injuries: the results from the European Maxillofacial Trauma (EURMAT) multicenter and prospective collaboration. Oral Surg Oral Med Oral Pathol Oral Radiol 2015; 119(4) 385-391 doi: 10.1016/j.oooo.2014.12.004

8. da Silva E, Matos F, Pimenta R, Rodrigues J, Marques J, Musse J. Epidemiological profile and characterization of oral and maxillofacial injuries in women victims of interpersonal violence. Int J Odontostomat 2016; 10:11-16

9. Kaura S, Kaur P, Bahl R, Bansal S, Sangha P. Retrospective Study of Facial Fractures, Ann Maxillofac Surg 2018; 17(8): 78-82. http://www.amsjournal.com/text.asp?2018/8/1/78/234303, 2018 DOI: 10.4103/ams.ams_73_17.

10. Gisbert Calabuig J. Adaptación de la definición clásica de responsabilidad profesional médica a la odontoestomatología, realizada por Juan Antonio Gisbert Calabuig, catedrático de medicina legal y toxicología (1960-1987), vicedecano de la facultad de medicina de Granada (1975).

11. Harris J, Sidebotham P, Welbury R. Child protectionand the dental team: an introduction to safeguarding children in dental practice. London, England: British Dental Association 2009 pp. 1-70

12. Doria A, Navarro M. La odontología en el diagnóstico del maltrato infantil. Univ Odontol 2016; 35(74): 49-63, 2016 https://doi.org/10.11144/Javeriana.uo35- 74.odmi.

13. Johnson J, Wright F. Dentalcare.com Child Maltreatment: The Role of a Dental Professional. 23 10 2019. [En línea]. Available: https://www.dentalcare.com/en-us/professional-education/ce-courses/ce599. [Último acceso: 06 11 2020].

14. Fisher-Owens SLJ, Tate A. Oral and Dental Aspect of Child Abuse and Neglect. Pediatrics. 2017; 140(2):e20171487. doi: 10.1542/peds.2017-1487.

15. Fisher-Owens S, James J, Lukefahr L, Rao Tate A. Oral and Dental Aspects of Child Abuse and Neglect. 2016 Pediatrics; 39(4): 278-283 DOI: 10.1542/peds.2017-1487.

16. Porro Pérez R, Labajo González E, Martínez Pérez E, Planells del Pozo P. Maltrato infantil y Odontología: de la identificación al reporte del caso. RCOE 2019; 24(3) https://rcoe.es/articulo/85/maltrato-infantil-y-odontologa-de-la-identificacin-al-reporte-del-caso, pp. 79-87, 2019 https://rcoe.es/articulo/85/maltrato-infantil-y-odontologa-de-la-identificacin-al-reporte-del-caso.

17. Artículo 15.3 de LO 1/2004.

18. Gibson-Howell J, Gladwin M, Hicks M, Tudor J, Rashid R. Instruction in Dental Curricula to Identify and Assist Domestic Violence Victims. Journal of Dental Education 2008; 72(11): 1277-89

19. Connor P, Nouer S, STN M, Banet M, Tipton N. Dental Students and Intimate Partner Violence: Measuring Knowledge and Experience to Institute Curricular Change. Journal of Dental Education 2011; 75(8): 1010-9

20. Othman S, Mat Adenan N. Domestic violence management in Malaysia: a survey on the the primary health care providers. Asia Pac Fam Med 2008; 7:71187–92 doi: 10.1186/1447-056X-7-2.

21. Furniss K, McCaffrey M, Parnell V, Rovi S. Nurses and barriers to screening for intimate partner violence. Am J Matern Child Nurs 2007; 32:238-43 doi: 10.1097/01.NMC.0000281964.45905.89.

22. Sonbol H, Bagain Z, Saman R. Knowledge, educational experiences and attitudes towards child abuse amongst Jordanian dentists. Eur J Dent Educ 2012; 16(1): 158-65 doi: 10.1111/j.1600-0579.2011.00691.x.

23. Cook UJ. «www.sbs.com,» 2015. [En línea]. Available at : https://www.sbs.com.au/language/spanish/un-programa-pionero-en-australia- forma-a-dentistas-para-detectar-violencia-domestica. [Último acceso: 06 11 2020].

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ORIGINAL

Lifestyle, overweight and obesity in spanish workers: related variables

Estilo de vida, sobrepeso y obesidad en los trabajadores españoles: variables relacionadas

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Abstract

Objective: To assess lifestyle habits related to diet and physical activity in workers and their impact on cardiovascular, metabolic and hepatic risk in relation to socio-demographic and occupational variables.
Design: Cross-sectional descriptive study in active labor forcé between March 2020 and June 2021. Site: occupational health services of the Balearic Islands.
Participants: 815 workers, aged 18-66 years, who attended regular health surveillance examinations in their companies. Interventions: Adherence to the Mediterranean Diet was estimated using the PREDIMED questionnaire and physical activity with the reduced IPAQ questionnaire. Regicor/Score was used to calculate cardiovascular risk and the online calculator for metabolic syndrome. The risk of hepatic repercussion was assessed with the Fatty Liver Index (FLI).
Results: There are greater adherence to MedDiet in women (56.89%) and greater physical activity in men (57.8%). Physical activity was related to improvement in all indicators of obesity and adiposity in men. In women only with body mass index and body fat ($p < 0.0001$). All sociodemographic variables showed a relationship with physical activity performed ($p < 0.0001$) but not with adherence to the MedDiet.
Conclusion: MedDiet adherence is higher in women and physical activity in men with an impact on BMI, but not on CVR or metabolic syndrome. Body fat is the adiposity parameter most correlated with physical activity in both sexes. Social class I and II and non-manual work were related to higher physical activity.

Key words: Mediterranean diet, physical activity, cardiovascular risk, metabolic syndrome.

Resumen

Objetivo: Evaluar los hábitos de vida relacionados con alimentación y actividad física en trabajadores y su impacto en el riesgo cardiovascular, metabólico y hepático relacionándolos con variables sociodemográficas y laborales.
Diseño: Estudio descriptivo transversal en trabajadores en activo laboralmente desde marzo 2020-junio de 2021. Emplazamiento: servicios de salud laboral de Islas Baleares.
Participantes: 815 trabajadores, entre 18-66 años que acudieron a los exámenes periódicos de vigilancia de la salud de sus empresas. Intervenciones: Se estimó la adherencia a la Dieta Mediterránea mediante el cuestionario PREDIMED y la actividad física con el cuestionario reducido IPAQ. Para el cálculo de Riesgo cardiovascular se utilizó Regicor/Score, y para el síndrome metabólico la calculadora on line. El riesgo de repercusión hepática se valoró con el índice de hígado graso (FLI).
Resultados: Mayor adherencia a MedDiet en mujeres (56,89%) y mayor actividad física en hombres (57,8%). Se observa mejora con la actividad física en todos los indicadores de obesidad y adiposidad en hombres. En mujeres sólo con el IMC y la grasa corporal ($p < 0,0001$). Todas las variables sociodemográficas mostraron relación con la actividad física realizada ($p < 0,0001$), no con la adherencia a MedDiet.
Conclusión: La adherencia MedDiet es mayor en mujeres y la actividad física en hombres con impacto en el IMC, pero no en RCV o Síndrome metabólico. La grasa corporal es el parámetro de adiposidad que más se correlaciona con la actividad física en ambos sexos. La clase social I y II y el trabajo no manual se relacionaron con mayor actividad física.

Palabras clave: Dieta mediterranea, actividad física, riesgo cardiovascular, syndrome metabólico.

Introduction

More than three hundred years ago, Bernadino Ramazzini made certain observations on the relationship between health problems, work habits and lifestyle. These observations are still valid, especially after the COVID-19 outbreak, we highlight his findings on risk prevention, health promotion and the influence of unhealthy lifestyle habits. Besides it is not easy to evaluate and compare studies performed at different times, the study of the relationship between past and current practices should encourage the implementation of improvements in this field[1].

An unhealthy lifestyle, apart from generating health problems, can also have a negative impact on the workplace: sickness leave, loss of productivity and reduced working capacity. Programs oriented on health promotion in the workplace are aimed to improve workers' health, but tend to minimize these negative consequences and the overall assessments of the effectiveness of these programs are hindered by a high degree of heterogeneity in interventions and study populations[2].

The adherence to the mediterranean diet (MedDiet) and physical activity (PA) are associated with beneficial effects on preventing cardiovascular diseases by reducing the risk of hepatic steatosis in subjects with Metabolic Syndrome (MetS) and obesity[3].

A fundamental part of a healthy lifestyle is based on the definition of what constitutes a varied healthy diet, which continuously changes. Scientific evidence supports that the intake of certain types of nutrients, specific groups of foods or general dietary patterns positively affects health and promotes the prevention of common non-communicable diseases. MedDiet is rich in plant-based foods, including fresh fruits and vegetables, whole grains, legumes, seeds and nuts; and with a smaller amount of animal origin meats, in particular fatty and processed meats. This diet demonstrated its effectiveness on preventing diseases, especially cardiovascular diseases, and positively affecting the overall health[4].

The 2020 WHO guidelines support PA as a healthy lifestyle, with the addition of the following statements: a) any quantity of PA is better than nothing, b) an increased PA promotes an optimal health and c) it is recommended to reduce sedentary habits[5].

The aim of this work is to analyze the lifestyle habits of Spanish workers during the pandemic in terms of food intake and PA, and their relationship with the following parameters: cardiovascular risk (CVR), MetS, fatty liver, obesity, and socio-demographic variables.

Method

A descriptive cross-sectional study was performed in a sample of 815 Spanish workers (481 males and 334 females), aged between 18 and 66 years from a total population of 1028 workers, of which 76 were excluded due to not satisfying the criteria and 137 that refused to participate. Occupational doctors from the participating companies of the services sector of the Balearic Islands collected the data during the regular health surveillance examinations performed between March 2020 and June 2021. Participation was voluntary with an informed consent to use the results for epidemiological purposes. Were inclusion criteria: being active in the company and not being under treatment for previous cardiovascular disease or having uncontrolled or compensated cardiovascular risk factors.

The Ethics Committee for Clinical Research of the Health Area of the Balearic Islands (IB 4383/20) approved the current study.

In order to determine weight and height, a SECA 700 scale and SECA 220 telescopic measuring device incorporated in the scale were used. The body mass index (BMI) ranges taken into account were the ones defined by the WHO. Being normal weight when the BMI is below 25; overweight when the BMI is equal or above 25 and below 30; obese class I when the BMI is equal or above 30 and below 40; and obese class II when the BMI is equal or above 40[6].

The hip and waistline perimeters were determined with a SECA 20 measuring tape, with a measuring range from 1 cm to 200 cm, divided on a millimetric scale. The TANITABC-420MA analyzer was used to determine body composition, estimating the percentage of body fat and visceral fat. The ranges for the waist circumference (WC) were considered normal in men when below 94 cm and below 80 cm in women. Waist to hip ratio (WHR) index was considered normal in men when below 0.94 and below 0.84 in women. The waist to height ratio (WtHR) was considered normal for both sexes when below <0.5. Total body fat percentage (TBF%) was considered normal for both sexes when below 20% and visceral fat (VF) was considered normal in men when below 20 and below 30 in women[7,8].

Social and occupational variables included in the study were as follows:

Age: Due to the sample size and taking into account that cardiovascular maturity is reached at 40 years old and cardiovascular decline starts at 50, individuals were classified under three different groups: between 18 and 39 years, between 40 and 50 years, and between 51 and 66 years.

Sex: A categorical variable, with individuals classified as male or female.

Social class and type of work: Determined on the basis of the National Classification of Occupations of the year 2011 (CNO-11) and on the basis of the proposal made by the Group of Social Determinants from the Spanish Society of Epidemiology[9]. For statistical analysis purposes, a reduced classification with three categories was defined from the original seven categories:

- Class I. Directors/managers, college professionals, sportsmen and artists.
- Class II. Intermediate occupations and self-employed persons without employees.
- Class III. Unskilled workers.

Type of work: manual (blue collar) and not manual (white collar).

Study level: according to the current education system in Spain and classified in three categories:

- Elementary school: consisting of six basic levels, from first to sixth grade of primary school.
- Intermediate: compulsory secondary education, with two cycles. The first cycle ranged from the first to third course, and the second cycle consisting of the fourth course.
- Superior: completed university degrees or superior vocational education, in any of the forms established and in accordance with the legislation in force when completed.

Workplace characteristics: i) manual handling of loads (MHL) and vehicle driving (at least 1/3 of the working day) and ii) sedentary work (seated at least 50% of the working day).

Cardiovascular risk (CVR) was calculated by using the Score and REGICOR tables[10,11], as these standards are available for the Spanish population and being the REGICOR the only one validated for the aforementioned population.

The presence of metabolic syndrome (MetS) was determined with an online multiplatform application, based on the ATP-III definition, validated in Spanish patients and taking into account the following variables: gender, abdominal perimeter, triglycerides, maximum and minimum blood pressure and basal glycaemia[12].

Fatty liver was estimated with the fatty liver index (FLI) calculator, algorithm based on PCi, BMI and triglyceride and γ-glutamyltransferase levels[13].

The assessment of dietary habits was evaluated with the validated PREDIMED survey of adherence to the Mediterranean diet (MedDiet)[14,15].

The reduced IPAQ validated survey was used to assess healthy living habits in terms of PA[16,17].

Statistical Analysis

A descriptive analysis of the categorical variables was made by calculating their frequencies and distributions. Regarding quantitative variables, the statistical analyses included calculations of means and standard deviations (SD) and in the case of qualitative variables, their percentages. Bivariant association analyses were carried out with the Chi-squared test (when required, data was corrected with Fisher's exact test), Student's t-test was used for independent samples and the Cohen Kappa test was used to assess the concordance between the different scales. Multivariant analyses were carried out with mutinomial logistic regressions.

Data were analyzed using the Statistical Package for the Social Sciences version 27 (SPSS Inc, Chicago), considering a p-value below 0.05 as statistically significant.

Results

The characteristics of the population sample are shown in **table I**, with a mean of 48 year old population, with men presenting higher BMI values and being classified as overweight; as well, all their adiposity indicators were higher (waist circumference, waist to height ratio, total body fat and visceral fat). There were no significant differences in the educational level between men and women. Concerning the social class and type of work, social class III and manual work was predominant in both sexes, but being significantly higher in men. There are significant differences observed in the characteristics of the workplace depending on the sex: vehicle driving with manual handling of loads (MHL) was predominant in male population, while women were majorly sedentary. There was a significant greater adherence to the MedDiet in women with; on the contrary, the level of PA was higher in men.

Regarding the diet content, the overall consumption of olive oil, butter, vegetables, nuts, fish and white meat was higher in women. Men reported higher consumption of rice and pasta, wine, soft drinks, red meat, fruits and vegetables (**Table II**).

PREDIMED assessment analyses revealed that there are no significant relationships between the MedDiet adherence and the following variables: adiposity and obesity parameters, cardiovascular risk, metabolic syndrome and fatty liver (**Table III**). However, and depending on the sex, significant relationships were observed between the degree of PA and the studied variables: in men, an increase of PA revealed a decrease in all adiposity and obesity parameters (overweight and obese BMI values, high total body fat, high visceral fat, high waist to height ratio and high waist to hip ratio). While in women, an increase of PA reduced their BMI values and total body fat (**Table IV**).

There were no significant relationships between the degree of adherence to the MedDiet and the socio-demographic variables, except in sex, where women showed a greater adherence to the MedDiet. Regarding the level of PA, significant differences were found in all sociodemographic parameters, with higher levels of PA in men, young people, with elementary studies, social class III and manual occupations (**Table V**).

As well, a significant relationship was observed between the type of occupation and the adherence to the MedDiet depending on the sex: being higher in women than in men. Likewise, women have a higher adherence to the MedDiet, regardless the nature of the job performed (sedentary/non-sedentary; with and without vehicle driving and MHL). Regarding PA, no significant relationship between PA and occupational characteristics were found in any case (**Table VI**).

Discussion

This study shows the degree of the adherence to the MedDiet and PA during the COVID-19 pandemic, being the first one quantified through the PREDIMED survey, and the most recent one with the reduced IPAC questionnaire. Significant differences were found between men and women: in terms of diet, women showed a greater adherence to the MedDiet both qualitatively and quantitatively, while men revealed to perform higher levels of PA.

Men and women show substantial differences, not only in terms of somatometric characteristics, but also in social conditions such as socioeconomic level and occupational variables. These circumstances make difficult to compare this population and skew the aforementioned results.

Table I: Characteristics of the Study Population. Comparison between sex.

Variable	Male (N = 481)	Female (N = 334)	P
Anthropometric and adiposity variables: mean (SD)			
Age	48.25 (8.35)	48.89 (8.16)	0.277
Weight	82.79 (13.93)	67.97 (11.98)	**<0.001**
Height	173.42 (6.81)	160.72 (5.98)	**<0.001**
BMI	27.49 (4.01)	26.33 (4.47)	**<0.001**
Waist	94.61 (10.96)	84.35 (11.43)	**<0.001**
Waist/height	0.55 (0.06)	0.53 (0.07)	**<0.001**
Hip	106.22 (58.83)	99.00 (10.13)	0.027
Waist/Hip	0.92 (0.07)	0.85 (0.06)	**<0.001**
Total body fat	24.70 (6.58)	36.08 (7.78)	**<0.001**
Visceral fat	11.35 (4.53)	7.53 (2.65)	**<0.001**
BMI classification (%)			
Normal	29.11	41.62	**<0.001**
Overweight	48.86	39.52	
Obesity	22.04	18.86	
Study level (%)			
Elementary	49.06	41.92	0.116
Intermediate	32.43	35.63	
Superior	18.50	22.46	
Social class and type of work (%)			
Class I	3.33	2.40	**<0.001**
Class II	20.58	36.83	
Class III	76.09	60.78	
Type of work (%)			
Non-manual work	23.91	39.22	**<0.001**
Manual work	76.09	60.78	
Workplace characteristics (%)			
sedentary work	25.16	41.92	**<0.001**
(seated > 50% working day)			
Driving of vehicles and MHL	71.93	53.29	**<0.001**
(at least 1/3 of the working day)			
Healthy lifestyle: MedDiet -PREDIMED	43.87	56.89	**<0.001**
High MedDiet adherence			
Healthy lifestyle: PA IPAQ			
Low exercise	1.87	3.29	0.041
Moderate exercise	40.33	47.31	
High exercise	57.80	49.40	

Values of p<0.05 are considered significant.

Table II: MedDiet adherence results (PREDIMET survey): total and partial.

Total results (%)		Males	Females	P
MedDiet adherence				
High adherence		43.87	56.89	<0.001
Low adherence		56.13	43.11	
Partial results (%)				
Survey items				
Olive oil use	yes	97.30	97.60	0.668
	no	2.70	2.40	
Olive oil quantity (spoons / day)	2 or more	89.60	94.31	0.030
	< 2	10.40	5.69	
Vegetables (Portions / day)	2 or more	36.59	60.68	<0.001
	< 2	63.41	39.22	
Fruits (Pieces / day)	3 or more	28.27	23.34	0.010
	<3	71.73	67.66	
Red meat (per day)	1 or more	3.95	2.40	<0.001
	<1	96.05	97.60	
Butter (per day)	1 or more	2.91	4.49	0.021
	<1	97.09	95.51	
Soft drinks (per day)	1 or more	17.46	8.38	<0.001
	<1	82.64	91.62	
Wine consumption (per week)	3 or more	9.56	3.29	<0.001
	<3	90.44	96.71	
Legumes (days / week)	3 or more	20.58	17.07	0.024
	<3	79.42	82.93	
Fish (days / week)	3 or more	28.27	34.73	0.033
	<3	71.73	65.27	
Industrial pastry (days / week)	3 or more	23.28	17.66	0.010
	<3	73.72	82.34	
Nuts (days / week)	1 or more	76.51	79.34	0.087
	< 1	23.49	20.66	
Other non-red meats (per week)	yes	95.63	97.01	0.112
	no	4.37	2.99	
Rice, pasta, lightly fried	2 or more	92.10	88.92	0.052
	< 2	7.90	11.08	

p<0.05 values are considered significant. PREDIMED questionnaire: < 9 low adherence >= 9 good adherence.

Table III: Relationship between MedDiet adherence and physical activity with high scores prevalence, CVR, MetS and FLI indicators.

Relationship between MedDiet adherence and MetS, CVR and FLI							
	Females				**Males**		
	Low n = 144	**High n = 190**	**P**		**Low n = 270**	**High n = 211**	**P**
MetS	18.06	15.79	0.595		22.22	18.96	0.197
High SCORE	6.03	9.82	0.011		36.48	45.20	0.156
High REGICOR	4.31	5.71	0.007		16.81	16.76	0.945
High risk FLI	13.89	11.64	0.758		34.81	28.71	0.165
Relationship between level of physical activity (IPAC survey) and MetS, CVR and FLI							
	Females				**Males**		
	Low n = 11	**Moderate n = 158**	**High n = 165**	**P**	**Low n = 9**	**Moderate n = 194**	**High n = 278**	**P**
MetS	27.27	21.02	12.12	0.161	44.44	27.98	15.16	0.006
High SCORE	9.09	9.56	7.04	0.671	11.11	43.43	38.94	0.009
High REGICOR	0.00	7.25	3.52	0.344	0	16.57	17.62	0.033
High risk FLI	19.18	14.65	10.30	0.010	33.33	39.38	27.08	0.010

MetS = Metabolic syndrome; CVR = Cardiovascular risk; FLI = Fatty liver index
It was considered high Score risk ≥ 5% and Framingham-REGICOR ≥10%. Metabolic syndrome (MetS) presence was positive with three or more altered parameters. Fatty liver value <30 is considered low probability and>60 is considered indicative of high steatosis risk.
Values of p<0.05 are considered significant.

Additional studies on the current subject have shown variable outcomes as well.

Some studies suggest that the adherence to the MedDiet increased slightly during the confinement, but also raised the consumption of non-healthy food. Also, the number of people that practice PA decreased, along with its weekly dedication[18].

Equivalent studies in terms of occupational health within a pandemic context obtained similar results, reassuring the idea that both PA and a healthy diet are key factors to avoid the main non-communicable diseases. During the confinement, workers were more likely to develop sedentary behaviors; however, this conduct was easier to revert if there was a health promotion program in the workplace that encouraged a moderate increase of PA.

Concerning the diet, health promotion programs and remote working also had positive effects by increasing the adherence to the MedDiet in working population, which highlights the relevance of this kind of programs in this population[19].

Likewise, additional studies conducted during the pandemic showed an increased adherence to the MedDiet, although no significant changes were reported in terms of BMI[20].

Table IV: Lifestyle relationships between food intake, physical activity, and adiposity indicators.

Relationship between MedDiet adherence with obesity parameters and adiposity indicators (%)						
	MedDiet adherence					
	Males			Females		
	High n = 211	Low n = 270	P	High n = 190	Low n = 144	P
BMI overweight/obesity	68.72	72.59	0.500	57.36	59.72	0.849
High body fat	71.90	79.18	0.178	71.58	85.07	0.072
High visceral fat	54.76	59.48	0.576	11.58	12.50	0.463
High waist to height ratio	75.36	80.37	0.113	60.00	60.42	0.515
High waist to hip ratio	31.28	38.89	0.040	57.89	56.94	0.475
Relationship between level of physical activity with obesity parameters and adiposity indicators (%)						
	Physical activity					
	Males			Females		
	High n = 203	Moderate-low n = 278	P	High n = 165	Moderate-low n = 169	P
BMI overweight/obesity	64.75	79.31	<0.001	60.61	65.09	0.024
High body fat	67.74	86.14	<0.001	65.45	84.02	<0.001
High visceral fat	49.10	68.81	<0.001	10.30	13.69	0.223
High waist to height ratio	70.86	88.18	<0.001	56.36	63.91	0.097
High waist to hip ratio	30.94	41.87	0.009	55.15	59.76	0.229

p<0.05 values are considered significant. PREDIMED questionnaire: < 9 low adherence >= 9 high adherence. IPAC: moderate physical activity at least 600 METs and high physical activity at least 3000 METs.

Table V: Relationships between diet and physical activity with sociodemographic variables: sex, age, study level, social class, occupation.

Relationship between MedDiet adherence and sociodemographic variables					
Sociodemographic variables		MedDiet adherence (%)			
		n	High	Low	P
Sex	Male	481	43.87	56.13	**<0.001**
	Female	334	56.88	43.12	
Age	18-39 years	129	13.72	17.87	0.075
	40-49 years	270	31.42	34.78	
	50-66 years	416	54.86	47.34	
Study level	Elementary	376	42.89	49.28	0.062
	Secondary	275	37.66	29.95	
	Higher education	164	19.45	20.77	
Social class	Class I	24	2.74	3.14	0.643
	Class II	222	28.68	25.85	
	Class III	569	68.58	71.01	
Occupation	Non-manual	246	31.42	28.99	0.248
	Manual	569	68.58	71.01	
Relationship between level of physical activity and sociodemographic variables					
Sociodemographic variables		Physical activity (%)			
		n	High	Moderate-low	P
Sex	Male	481	57.80	42.20	0.011
	Female	334	49.40	50.60	
Age	18-39 years	129	63.57	36.43	0.034
	40-49 years	270	55.56	44.44	
	50-66 years	416	50.72	49.28	
Study level	Elementary	376	59.57	40.43	0.007
	Secondary	275	52.73	47.27	
	Higher education	164	45.12	54.88	
Social class	Class I	24	25.00	75.00	**<0.001**
	Class II	222	30.18	69.82	
	Class III	569	65.03	34.97	
Occupation	Non-manual	246	29.67	70.33	**<0.001**
	Manual	569	65.03	34.97	

p<0.05 values are considered significant. PREDIMED questionnaire: < 9 low adherence >= 9 high adherence. IPAC: moderate physical activity at least 600 METs and high physical activity at least 3000 METs.

In this work, a link between the practice of PA and an improvement of adiposity indicators and BMI were observed, but no association was found with an increased adherence to the MedDiet.

Concerning the sociodemographic variables analyzed, there were no significant differences in terms of adherence to the MedDiet, except in sex, with greater adherence in women. On the contrary, the practice of PA showed statistical differences in all sociodemographic variables, with higher levels of exercise in young men, with elementary studies, belonging to a social class III and performing manual jobs. These findings contrast with earlier studies that suggest a positive relationship between the adherence to the MedDiet and higher social classes, with less adherence in lower socioeconomic levels[21].

Although the results of previous studies on this subject are variable, the beneficial effects of the MedDiet as a healthy diet and lifestyle is widely accepted. The differences seen between these studies can be explained by the variability of the alimentary systems in different parts of the world[22]. Therefore, additional multidisciplinary studies are needed to evaluate the sustainability of the MedDiet that include the aforementioned aspects[23].

Given that, the MedDiet has been revised in a simplified framework in order to adapt it to different nutritional and socioeconomic contexts of the Mediterranean region, by considering socioeconomical challenges, lifestyle, diet, environment and health population, and therefore, compiling these updated recommendations.

The new concept of "main meals" was introduced to reinforce the vegetal component of the dietary pattern, frugality and moderation is emphasized due to the public health challenge that obesity represents. As well, cultural and lifestyle elements such as coexistence, culinary habits, PA, adequate rest, proportion and frequency of food intake are considered. These new recommendations comprise additional factors such as seasonality, biodiversity, local, traditional and organic products availability. Thus, the MedDiet has been recognized as Intangible Cultural Heritage of Mankind by the UNESCO in 2010, taking into account its contribution to health and general well-being, adapted to the current reality with a new graphic representation[24].

In contrast, in the context of the COVID-19 pandemic, some authors examined the association between regional adherence to a MedDiet and COVID-19 cases and deaths by using an ecological study design, emphasizing that the adherence to the MedDiet was negatively associated with both COVID-19 cases and related deaths in 17 regions of Spain. This association remained valid when adjusted with welfare factors. Similarly, a negative association was found between the adherence to the MedDiet and COVID-19-related deaths in 23 countries, when adjusted with welfare and physical inactivity. The anti-inflammatory properties of MedDiet, probably due to its content of polyphenols, may be a biological basis that explains these findings. However, there are still confounding factors unrelated with dietary aspects that caused COVID-19 cases and related deaths that should be explored in future cohort studies[25].

Adult Spanish population, especially young adults, students and highly active individuals declared that they decreased their PA during the COVID-19 confinement[26]. This work opens new comparative options once the pandemic era ends, in order to evaluate the modified lifestyle habits of this population.

Table VI: Relationship between diet and physical activity with occupation characteristics.

Relationship between MedDiet adherence and occupation									
Occupation characteristics	**High adherence**				**Low adherence**				**P**
	Males		**Females**		**Males**		**Females**		
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	
Non sedentary > 50%	154	42.78	114	58.76	206	57.22	80	41.24	**<0.001**
Sedentary > 50%	57	47.11	76	54.29	64	52.89	64	45.71	
Non-driving and MLH	55	40.74	81	51.92	80	59.26	75	48.08	**<0.001**
Driving and MHL	156	45.09	109	61.25	190	54.91	109	38.76	
Relationship between level of physical activity and occupation									
Occupation characteristics	**High**				**Moderate-low**				**P**
	Males		**Females**		**Males**		**Females**		
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	
Non sedentary > 50%	239	66.39	130	67.01	121	33.61	64	32.99	0.132
Sedentary > 50%	39	32.23	35	25	82	67.77	105	75	
Non-driving and MLH	51	37.78	50	32	84	62.24	106	67.95	0.258
Driving and MHL	227	65.61	114	64.61	119	34.39	63	35.39	

MHL: Manual handling of loads. p<0.05 values are considered significant. PREDIMED questionnaire: < 9 low adherence >= 9 high adherence. IPAC: moderate physical activity at least 600 METs and high physical activity at least 3000 METs.
Values of p<0.05 are considered significant.

Due to the confinement period of the COVID-19 pandemic, some authors have reviewed the studies that explored the health impacts of several weeks of reduction in PA and daily step count, combined with altered eating habits. These studies identified an increased resistance to insulin, total body fat, abdominal fat and inflammatory cytokines as some of the main metabolic consequences. All these factors have been strongly associated with the development of metabolic syndrome, which in turn increases the risk of multiple chronic diseases[27].

In the present work, the adherence to the MedDiet has not shown any substantial relationship with adiposity parameters, nor with CVR or MetS. On the contrary, there were differences observed in terms of the level of PA (assessed through IPAQ), with a significant relationship between increased exercise level of PA and improved indicators of obesity and adiposity, especially in men.

Conclusions

The adherence to the MedDiet, assessed with the PREDIMED survey, showed a higher adherence in women in the population studied, while the PA assessed through the IPAQ questionnaire, showed greater levels of moderate to high PA in men. Social class and type of work were related with levels of PA, but not with the adherence to the MedDiet. Likewise, the level of PA was associated with obesity and adiposity indicators, especially in men.

The adherence to the MedDiet and the practice of PA showed an important relationship with cardiovascular risk, decreasing its prevalence when a healthy diet was adopted and moderate to high levels of PA are performed.

Working age people spend much of their time at work. Therefore, we highlight the importance of developing health promotion programs at the workplace, aimed to encourage an appropriate lifestyle mainly focused on encouraging heart-healthy diets and an increase of PA.

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Conflict of interest
Authors do not have any conflict of interest to declare.

What is known on the topic
Lifestyle in diet and exercise have been modified during the COVID-19 pandemic period.

Unhealthy lifestyle habits may generate cardiometabolic risks and increase the risk of overweight and obesity.
The joint study of BMI and adiposity indicators complements the definition of obesity.

What this study contributes:
The assessment of dietary and exercise habits by means of valid surveys facilitates action in risk prevention.

Adherence to the Mediterranean diet has less impact on cardiometabolic risk and hepatic repercussions rather than moderate-high physical activity, but complements it.

There are differences between men and women in lifestyle and its cardiovascular and obesity repercussions.

References

1. Franco G. Bernardino Ramazzini's De Morbis Artificum Diatriba on Workers' Health-the Birth of a New Discipline. J UOEH 2021;43(3):341-8.

2. Rongen A, Robroek SJW, van Lenthe FJ, Burdorf A. Workplace health promotion: a meta-analysis of effectiveness. Am J Prev Med 2013;44(4):406-15.

3. Bullón Vela MV, Abete I, Zulet MLÁ, Tur JA, Pintó X, Corbella E, et al. Risk factors differentially associated with non-alcoholic fatty liver disease in males and females with metabolic syndrome. Rev Esp Enferm Dig 2020;112(2):94-100.

4. Cena H, Calder PC. Defining a Healthy Diet: Evidence for The Role of Contemporary Dietary Patterns in Health and Disease. Nutrients 2020;12(2):334.

5. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med 2020;54(24):1451-62.

6. World Health organitation. Body mass index – BMI. Copenhagen, https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi ;2020[consultada el 1 de marzo de 2022].

7. Tutunchi H, Ebrahimi Mameghani M, Ostadrahimi A, Asghari Jafarabadi M. What are the optimal cut-off points of anthropometric índices for prediction of overweight and obesity? Predictive validity of waist circumferemce , waist-to-hip and waist-to-height ratios. Health Promotion Perspectives 2020;10(2)142-7.

8. Bello Chavolla OY, Antonio Vila NE, Vargas Vázquez A, Viveros Ruiz TL, Almeda Valdes P, Gómez Velasco D, et al. Metabolic Score for Visceral Fat (METS-VF), a novel estimator of intra-abdominal fat content and cardio-metabolic health. Clin Nutr 2020;39(5):1613-20.

9. Domingo-Salvany A, Bacigalupe A, Carrasco JM, Espelt A, Ferrando J, Borrell C. Propuestas de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011. Gac Sanit 2013;27(3):263-72. http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213-.

10. Registre Gironí del Cor. Validación de las tablas Framigrahm-Regicor;2022 https://regicor.cat/es/presentacion/tablas-de-framingham-regicor/

11. María Grau, Jaume Marrugat. Risk Functions and the Primary Prevention of Cardiovascular Disease. Rev Esp Cardiol. 2008;61(4):404-16.

12. Taberner R. Calculadora multiplataforma para síndrome metabólico y riesgo cardiovascular en pacientes con psoriasis [Multiplatform application to determine presence of metabolic syndrome and cardiovascular risk in patients with psoriasis]. Actas Dermosifiliogr 2012;103(2):111-9.

13. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, Tiribelli C. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol 2006;6:33.

14. Ros E. The PREDIMED study. Endocrinol Diabetes Nutr 2017;64(2):63-6.

15. Ferreira-Pêgo C, Nissensohn M, Kavouras SA, Babio N, Serra-Majem L, Martín Águila A, Mauromoustakos A, Álvarez Pérez J, Salas-Salvadó J. Beverage Intake Assessment Questionnaire: Relative Validity and Repeatability in a Spanish Population with Metabolic Syndrome from the PREDIMED-PLUS Study. Nutrients 2016;8(8):475.

16. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003;35(8):1381-95.

17. Román Viñas B, Ribas Barba L, Ngo J, Serra Majem L. Validación en población catalana del cuestionario internacional de actividad física [Validity of the international physical activity questionnaire in the Catalan population (Spain)]. Gac Sanit 2013;27(3):254-7.

18. Sánchez Sánchez E, Ramírez Vargas G, Avellaneda López Y, Orellana Pecino JI, García Marín E, Díaz Jimenez J. Eating Habits and Physical Activity of the Spanish Population during the COVID-19 Pandemic Period. Nutrients 2020;12(9):2826.

19. Franco E, Urosa J, Barakat R, Refoyo I. Physical Activity and Adherence to the Mediterranean Diet among Spanish Employees in a Health-Promotion Program before and during the COVID-19 Pandemic: The Sanitas-Healthy Cities Challenge. Int J Environ Res Public Health 2021;18(5):2735.

20. Tárraga López PJ, Panisello Royo JM, Carbayo Herencia JA, Carro A, Rosich N, Panisello M, Allins Presas J, Solera Albero J. Cambios observados en la adherencia a la dieta mediterránea en una población española durante el confinamiento debido a la pandemia ocasionada por el SARS-CoV-2. Nutr Hosp 2021;38(1):109-20.

21. Álvarez-Fernández C, Romero-Saldaña M, Álvarez-López Á, Molina-Luque R, Molina-Recio G, Vaquero-Abellán M. Adherence to the Mediterranean diet according to occupation-based social classifications and gender. Arch Environ Occup Health 2021;76(5):275-81.

22. Burlingame B, Dernini S. Sustainable diets: the Mediterranean diet as an example. Public Health Nutr 2011;14(12A):2285-7.

23. Dernini S, Berry EM, Serra-Majem L, La Vecchia C, Capone R, Medina FX, et al. Med Diet 4.0: the Mediterranean diet with four sustainable benefits. Public Health Nutr 2017;20(7):1322-30.

24. Bach-Faig A, Berry EM, Lairon D, Reguant J, Trichopoulou A, Dernini S, et al; Mediterranean Diet Foundation Expert Group. Mediterranean diet pyramid today. Science and cultural updates. Public Health Nutr 2011;14(12A):2274-84.

25. Greene MW, Roberts AP, Frugé AD. Negative Association Between Mediterranean Diet Adherence and COVID-19 Cases and Related Deaths in Spain and 23 OECD Countries: An Ecological Study. Front Nutr 2021;8:591964.

26. Castañeda Babarro A, Arbillaga Etxarri A, Gutiérrez Santamaría B, Coca A. Physical Activity Change during COVID-19 Confinement. Int J Environ Res Public Health 2020;17(18):6878.

27. Martinez Ferran M, de la Guía Galipienso F, Sanchis Gomar F, Pareja Galeano H. Metabolic Impacts of Confinement during the COVID-19 Pandemic Due to Modified Diet and Physical Activity Habits. Nutrients 2020;12(6):1549

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ORIGINAL

Placenta morphology and biomarkers in pregnancies with congenital heart disease. A systematic review

Morfología de la placenta y biomarcadores en embarazos con cardiopatías congénitas. Una revisión sistemática

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Abstract

Background: Congenital heart defect (CHD) is an influential factor that restricts intrauterine growth. One of the most critical complications in children with CHD is delayed nerve growth, which appears to begin from the fetal period. Delayed fetal neurodevelopment can be associated with or even explained by the impaired placenta in cases of CHD. This systematic study presents a literature review on placental growth with CHD.
Methods: We performed a regular search and used the Newcastle-Ottawa measure to evaluate data quality. Outcomes included size and weight of the placenta, vascular structure, immuno-histo-chemistry, expression of placental genes, and angiogenic biomarkers.
Results: 1308 studies were evaluated, and 21 articles were included. Studies with a genetic abnormality or multiple pregnancies were excluded. CHD cases had a lower weight of the placenta and an increased insertion rate in the umbilical cord. Further, microscopic characteristics of the abnormal placenta showed decreasing and increasing in angiogenic and anti-angiogenic biomarkers, respectively, in maternal serum and umbilical cord blood. The results showed Altered expression of genes affects placental and fetal growth pathways in placental and maternal serum tissues.
Conclusion: placental impairments were found in CHD cases. More researches are required to clarify the role of the abnormal placenta in delayed neurodevelopment.

Key words: Placenta morphology, placenta biomarkers, congenital heart disease, congenital heart defect.

Resumen

Antecedentes: La cardiopatía congénita (CC) es un factor influyente que restringe el crecimiento intrauterino. Una de las complicaciones más críticas en los niños con CC es el retraso en el crecimiento nervioso, que parece comenzar desde el periodo fetal. El retraso del neurodesarrollo fetal puede estar asociado o incluso explicarse por la alteración de la placenta en los casos de CC. Este estudio sistemático presenta una revisión de la literatura sobre el crecimiento de la placenta con la CC.
Métodos: Se realizó una búsqueda periódica y se utilizó la medida Newcastle-Ottawa para evaluar la calidad de los datos. Los resultados incluyeron el tamaño y el peso de la placenta, la estructura vascular, la inmunohistoquímica, la expresión de los genes placentarios y los biomarcadores angiogénicos.
Resultados: Se evaluaron 1308 estudios y se incluyeron 21 artículos. Se excluyeron los estudios con una anomalía genética o con embarazos múltiples. Los casos de CHD presentaban un menor peso de la placenta y una mayor tasa de inserción en el cordón umbilical. Además, las características microscópicas de la placenta anormal mostraron una disminución y un aumento de los biomarcadores angiogénicos y antiangiogénicos, respectivamente, en el suero materno y en la sangre del cordón umbilical. Los resultados mostraron que la expresión alterada de los genes afecta a las vías de crecimiento de la placenta y del feto en los tejidos de la placenta y del suero materno.
Conclusión: se encontraron alteraciones de la placenta en los casos de cardiopatía isquémica. Se requieren más investigaciones para aclarar el papel de la placenta anormal en el retraso del neurodesarrollo.

Palabras clave: Morfología de la placenta, biomarcadores de la placenta, cardiopatía congénita, defecto cardíaco congénito.

Introduction

As a common congenital aberration, congenital heart deficiency (CHD) affects five to eight per thousand infants[1]. CHDs are a significant cause of newborn mortality worldwide, and approximately half of the cases are severe1. However, survival rates of affected infants have improved Due to the continuous growth of ICU-care and cardiothoracic operation. For that purpose, the focus of discovery has turned from improving survival rates to increasing long-term developmental consequences[2]. The neurodevelopmental break has been announced in a significant number of children and adolescents affected with CHD, which is a considerable part of the CHD morbidity[3,4]. Much earlier literature associated this morbidity with the complicated cardiothoracic operation in early life and its adverse effects[3,4]. But more recently, fetal ultrasound and MRI technologies were discovered several impairments in CHDs fetuses and infants before the operation, such as decreasing fetal and newborn head circumference and delaying cortical maturation[3,4]. In addition, intrauterine growth restriction, pre-eclampsia, and pregnancy-induced hypertension have been detected in pregnancies with prenatal CHD[5-7]. Impairment signs in placental growth are detected by increased umbilical artery resistance and decreased global placental perfusion[8]. In prenatal CHD, the increased umbilical artery resistance may correlate with neurodevelopmental consequences and proposes whether this is a potential contributor to damaged neurodevelopment in these pregnancies[9]. The association of placenta features, placental biomarkers, and placental neurodevelopment in CHD remains unclear and has not been investigated accurately. In this systematic and meta-analysis review, a survey of the literature on CHD and placenta biomarkers is presented, intending to examine the use of the placenta biomarkers in the association with CHD and fetal neurodevelopment.

Materials and methods

Search strategy

We conducted a regular search in PubMed, Embase, Google Scholar, and Cochrane on Nov 15th, 2021. The search terms included “congenital heart deficiency,” “placenta,” “biomarkers,” “fetus,” “neurodevelopment,” “genetic,” “angiogenic. We admitted Papers from all years. The entire research sequence was: “Heart Defects”, “Placenta”,” Fetus”,” English”.

Study selection

Two independent researchers (MS, MA) screened the title/abstracts and consequently read the full text of selected articles. A third researcher (MH) was helping if there was disagreement. Eligibility criteria for inclusion were: 1) infants with CHD 2) placenta features concerning macroscopic analyses, immunohistochemistry, vascular and villous structure, immunoreactivity, angiogenic biomarkers, 3) description of placenta characteristics compared with evidence values or a control group. exclusion criteria for studies were: 1) articles associated with CHD and a genetic or syndrome disorder 2) articles associated with CHD and multiple pregnancies 3) articles with less than ten participants.

Assessment of data Quality and extraction

Quality assessment was evaluated utilizing the Newcastle Ottawa Scale (NOS) for estimating the degree of non-randomized studies Quality. Placenta features concerning macroscopic analyses, immunohistochemistry, vascular and villous structure, immunoreactivity, angiogenic biomarkers were extracted and investigated.

Results

Study screening

The performed search find1308 studies. Following title/abstract screening, 125 studies were read the full text, and finally, 18 studies were entered (**Figure 1**)[10-27].

The characteristics of included studies are presented in **table I**. There were differences in the categorization of CHDs types and comparing study groups within included studies (**Table I**).

According to cardiac intervention requirements, CHDs were categorized as full CHD, significant CHD (intervention in the first breath year), or only one specific congenital heart defect. Of the included articles, ten represented macroscopic placenta features, six represented microscopic placenta features, four expressed maternal/umbilical cord angiogenic biomarkers in serum samples, and five described gene expressions in placental tissue/maternal serum.

Assessment of data Quality

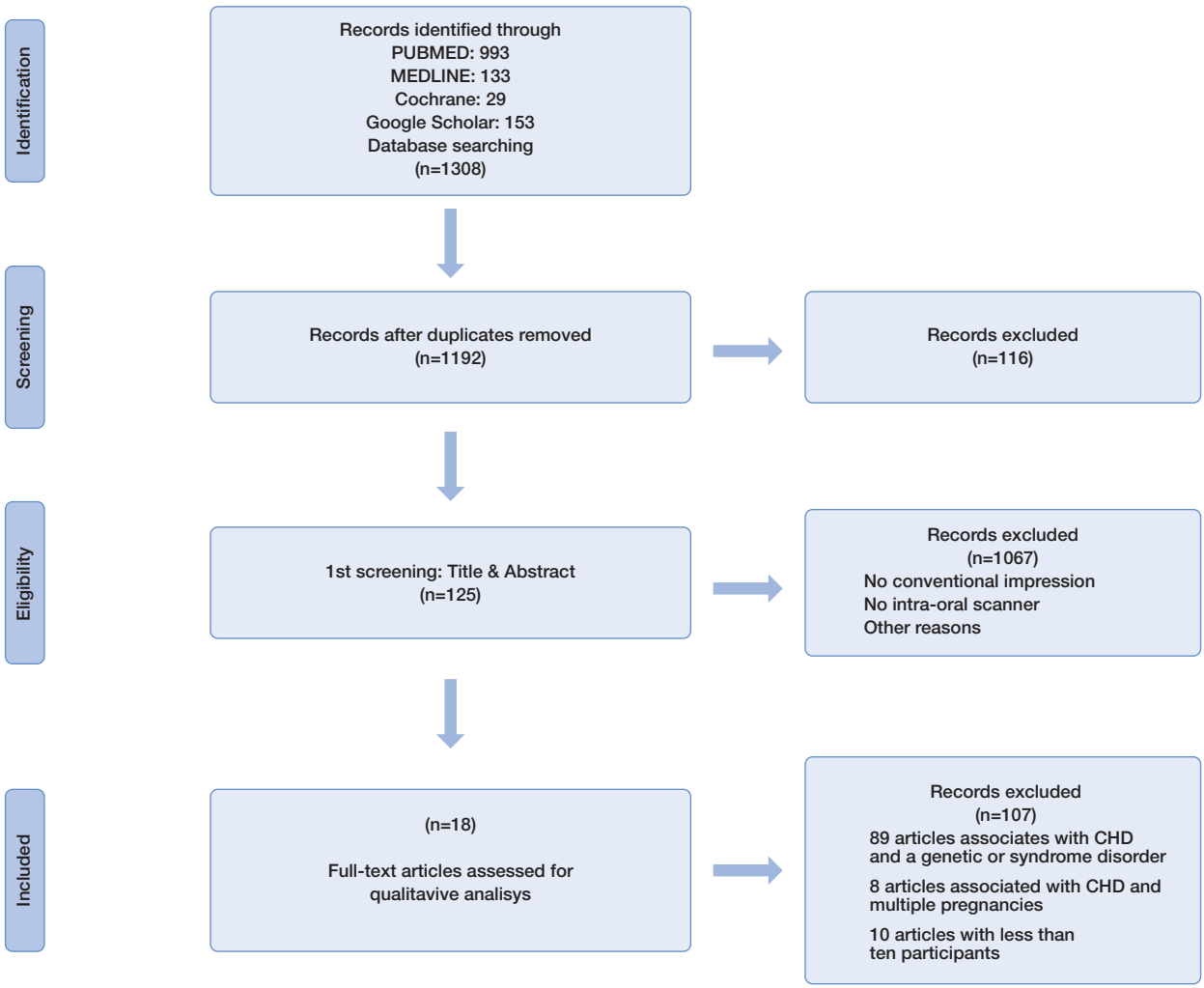
Assessing the Quality is presented in **table II**. In this systematic review, the quality ranking of Most included studies was satisfactory. Consistent with the quality grading of studies according to NOS, thirteen studies received five to six stars. However, one study received just one star because of the low cases and inadequate cohort/controls selections. Further, three studies received three stars due to not having a control group for comparing the measurements.

Results of included studies

At the birth time, a decrease in weight and percentiles of the Placenta was seen associated with ventricular septal defect (VSD), Tetralogy of Fallot (ToF), double-outlet right ventricle28, and hypoplastic left heart syndrome (HLHS) (**Table I**)[14]. At 18 and 39 weeks of pregnancy, the smaller volume of the Placenta was associated with CHD cases, but these changes were not statistically significant[13]. It is essential to distinguish

the placenta-to-birthweight rate because placenta weight does not differ between cases with and without intrauterine growth restriction. Five studies that reported conflicting data described the ratio of the placenta to the birth weight as an estimate of placental weight by adjusting for birth weight. Although, four studies detected No significant difference in the placenta-to birthweight rate[16,20,21,27], implying that smaller placentas in CHD only exist in subjects with low birth weight. According to the birth weight of CHD, three studies[19,24,25] reported that the placentas were smaller than anticipated, and there was a significantly lower ratio of placenta-to-birth weight. When CHD placentas are smaller than birthweight, the fetus can attain its growth potential; therefore, the placental preserves the function. Adverse outcomes have been detected for Abnormal umbilical cord insertion, such as intrauterine growth restriction and demise. In one study, 200 CHD cases were evaluated16 that were reported Significantly high percentages of abnormal umbilical cord insertion. However, in two studies that had analyzed, the HLHS (16 patients) and other types of CHD (32 cases)[14,21], probably due to the small number of inclusions, no high percentages of abnormal umbilical cord insertions were reported. In addition, placental disorders were found less than other macroscopic disorders in major CHD types26. defects in fetal-maternal relations are commonly observed in Histological reports of CHD gestations. Some studies reported the impaired microscopic in HLHS types, which described fibrin deposition and hypoplasia of distal villous, lower vascular area, and membrane counts of vascular-syncytial[14,25]. Subsequently, researchers detected other defects in CHD subjects that were not found in healthy placentae, like thrombosis, choriangiosis, infarction, and impaired maturation of villous[19,21,24,27]. However, the rate of microscopic abnormality in the placental did not show a significant difference between subjects PE, PIH, and IUGR[24]. Placental trophoblasts are responsible for the production of angiogenic biomarkers such as placental growth factor (PlGF) and pregnancy-associated plasma protein-A (PAPP-A)[29,30]. The concentrations of PlGF and

Figure 1: Flow charts for the studies were identified, displayed, and included in the study.



PAPP-A in maternal serum were significantly lower in CHD cases, so the decreased expression of angiogenic biomarkers may cause changes in placental vascular pathways in CHD[11,12,15]. In contrast, the concentrations of anti-angiogenic biomarkers such as fms-like soluble tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng) in maternal serum and umbilical cord blood were significantly higher in CHD[12]. These findings could explain dysfunction, perfusion, and placental weight loss in CHD cases due to alterations in the expression of these biomarkers. In CHD cases, placental tissue and maternal serum altered functional and developmental gene expression in mRNA levels. Altered expression of developmental genes of trophoblast, placental, and embryonic may indicate a correlation between CHD and genetic expression[10,15,17,22,25].

Table I: Study characteristics of included studies.

Author/year	Study design	Follow up time	Participants (N)			CHD type	Conclusion
			Total	Case	Control		
Ozcan et al, (2021)	R	Post-partum	139	47	92	MCCD	The highest risk is seen in fetal CHD with maternal risk factors
Giorgione et al, (2020)	R	Post-partum	936	480	456	MCCD	Major CHD are significantly associated with the risk of PE, SGA and PTB
Courtney et al, (2020)	R	Post-partum	42	24	18	HLHS	Despite common vascular disturbances in placentas from HLHAs
Schlatterer et al, (2019)	P	Post-partum	51	51	0	All type	These data suggest that placental abnormalities are common in CHD and may have a compounding effect on brain lesions in this high-risk population
Russell et al, (2019)	P	Post-partum	133	133	0	CHD requiring surgery	Damaging variants in proangiogenic genes may impact placental function and are associated with impaired fetal growth in pregnancies involving a fetus with congenital heart defect
Radhakrishna et al, (2019)	P	Post-partum	18	8	10	VSD	This is the first report in which placental analysis has been used for determining the pathogenesis of and predicting VSD
Miremberg et al, (2019)	R	Post-partum	66	32	34	Severe CHD	Placental vascular malperfusion lesions are more common in pregnancies complicated with CHD as compared with CNS malformations
Takemoto et al, (2018)	P	Post-partum	663	37	626	All type	Major anomalies may tend to aggregate in the 90th percentile of the BW/PW ratio
Rychik et al, (2018)	P	Post-partum	120	120	0	All type	Studies investigating the relationship between placental abnormalities and postnatal outcomes may offer insight into the fetal origins of outcome variability in CHD
Morano et al, (2018)	R	Second trimester	40	10	30	VSD	These data confirm previous studies on the specific association of mRNA species and type of congenital heart defect and confirm that ventricular septal defects are associated with abnormal mRNA for the tenascin-X gene
Contro et al, (2017)	R	Second trimester	78	36	42	LVOT	These data suggested that molecular screening of CNTRA and LVOT obstruction in the second trimester is feasible
Curti et al, (2016)	P	Second trimester	70	39	31	All type	These data represent a step forward in the screening of CHDs
Albalawi et al, (2016)	R	Post-partum	400	200	200	CHD requiring surgery	t cord insertion should be evaluated at routine obstetric sonography
Jones et al, (2015)	R	Post-partum	34	16	18	HLHS	Placentas from pregnancies complicated by fetal HLHS are characterized by abnormal parenchymal morphology, suggesting immature structure may be due to vascular abnormalities
Llurba et al, (2014)	P	Post-partum	269	65	204	MCCD	Data suggest that ani imbalance angiogenic-antiangiogenic factors is associated with developmental defects of the human heart
Andescavage et al, (2014)	P	Second trimester	135	41	94	All type	Abnormalities in placental development may contribute to the significant morbidity in this high-risk population. Assessment of placental volume by MRI allows for in vivo assessments of placental development
Llurba et al, (2013)	P	First trimester	408	68	340	MCCD	In pregnancies with isolated fetal heart defects there is evidence of impaired placental angiogenesis in the absence of impaired placental perfusion and function
Arcelli et al, (2010)	R	Second trimester	88	40	48	All type	Altered placental genetic expression was found at term delivery in affected fetuses. The aberration was also confirmed in maternal blood at the second trimester of women bearing a fetus with congenital heart disease

R: Retrospective; MCCD: Major congenital cardiac defects; HLHS: hypoplastic left heart syndrome; P: Prospective; VSD: ventricular septal defects; LVOT: Left Ventricular Outflow Tract

Table II: Quality of included studies based on the Newcastle-Ottawa assessment scale.

	Selection		Comparability	Outcome		
	Representativeness of exposed cohort	Selection of non-exposed cohort	Comparability of cohorts	Assessment of outcome	Adequacy of follow-up	Total score (0-6)
Ozcan (2021)	★	★	★	★	★	5
Giorgione (2020)	★	★	★	★	★	6
Courtney (2020)	★	★	★★		★	5
Schlatterer (2019)	★			★	★	3
Russell (2019)	★			★	★	3
Radhakrishna (2019)	★	★	★★	★	★	6
Miremberg (2019)				★		1
Takemoto (2018)	★	★	★★	★	★	6
Rychik (2018)	★			★	★	3
Morano (2018)	★	★	★★	★	★	6
Contro (2017)	★	★	★★	★	★	6
Curti (2016)	★	★	★★	★	★	6
Albalawi (2016)	★	★	★★	★	★	6
Jones (2015)		★	★★	★	★	5
Llurba (2014)	★	★	★★	★	★	6
Andescavage (2014)	★	★	★★	★		5
Llurba (2013)	★	★	★★	★	★	6
Arcelli (2010)	★	★	★★	★	★	6

Discussion

This systematic study showed an association between CHD disorder and the incidence of weight loss, abnormalities, and altered genes expression in the placenta. Comparable properties were seen in IUGR, PE, and PIH, all of which had abnormal trophoblast invasion and insufficiency in the placenta[25]. Subsequently, in CHD cases, placental defects could reduce oxygen and nutrients between the fetus and mother. Further, In CHD without PE and IUGR, the altered and insufficient placenta was also found. The probable reason for these results could be associated with the altered expression of genes involved in CHD development. In addition, insufficient trophoblast invasion may be responsible for pathological placenta alterations related to the classical defective phenotype.

Altered expression of molecules that affect vascular development can induce vascular changes in the placenta and fetus. Alteration of gene expression at the protein level was reported as having a local or systemic effect on cardiac tissue of the placenta and maternal serum. These findings indicate that alterations in gene expression and affecting cardiac and placental tissue also affect vascular growth pathways in other fetal tissues. Since environmental and genetic predisposition performs a significant function in developing CHD, this disorder is known to have multifactorial features. Epigenetic effects or hypoxic stress on early embryogenesis can explain angiogenic imbalance and vascular formation changes in CHD cases[19,25]. On the other hand, epigenetic changes in CHD may be due to the hemodynamic influences, which affect developmental pathways of vascular and causes alteration in angiogenesis and abnormalities in placental. The results show that the CHD pathogenesis factors can have epigenetic effects on placental tissue[23,25]. Typically, more placental weight loss is seen in CHD cases, so changes in the expression level of angiogenic biomarkers may be associated with the placental size. Further researches are needed to understand better the correlation between angiogenic biomarkers and placental weight in CHD cases. Since placental changes are also observed in cases of CHD without PE and IUGR, it can assume that vascular alterations delay the maturation of the fetal brain and growth in childhood[4]. Therefore, comparing the placental perfusion disorder, vascular genetic pathways, and angiogenic expression in CHD with PE and IUGR. Fetal tissue perfusion and hypoxia can be caused by placental dysfunction and alterations in vascular expression. There were so many issues in the veterinary and public health[31-45], which need additional studies.

Conclusion

The findings of this systematic study reveal an association between CHD cases with lower weight of placenta, macroscopic and microscopic abnormalities of the placenta, altered expression of genetic and angiogenic biomarkers in placental tissue, and maternal serum. These findings indicate defective development of vascular in the placenta and fetus. The neurodevelopmental disorder is also an essential complication of CHD. Thus, more research on impaired placental effects on consequences of these cases is needed in the future. Furthermore, there should be a correlation between morphology and placental function with neurodevelopmental results in the fetus, childhood and adulthood, and hemodynamic consequences of different types of CHD. Finally, the benefits of this information for CHD cases can help develop preventive measures in the entire lifespan.

Conflict of interest

Authors do not have any conflict of interest to declare.

References

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. Journal of the American college of cardiology. 2002 Jun 19;39(12):1890-900.

2. Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. The lancet. 2010 Feb 20;375(9715):649-56.

3. Everwijn SM, Namburete AI, van Geloven N, Jansen FA, Papageorghiou AT, Noble AJ, et al. Cortical development in fetuses with congenital heart defects using an automated brain-age prediction algorithm. Acta obstetricia et gynecologica Scandinavica. 2019 Dec;98(12):1595-602.

4. van Nisselrooij AE, Jansen FA, van Geloven N, Linskens IH, Pajkrt E, Clur SA, et al. Impact of extracardiac pathology on head growth in fetuses with congenital heart defect. Ultrasound in Obstetrics & Gynecology. 2020 Feb;55(2):217-25.

5. Gumusoglu SB, Chilukuri AS, Santillan DA, Santillan MK, Stevens HE. Neurodevelopmental outcomes of prenatal preeclampsia exposure. Trends in neurosciences. 2020 Apr 1;43(4):253-68.

6. Binder J, Carta S, Carvalho JS, Kalafat E, Khalil A, Thilaganathan B. Evidence for uteroplacental malperfusion in fetuses with major congenital heart defects. Plos one. 2020 Feb 5;15(2):e0226741.

7. Sun BZ, Moster D, Harmon QE, Wilcox AJ. Association of preeclampsia in term births with neurodevelopmental disorders in offspring. JAMA psychiatry. 2020 Aug 1;77(8):823-9.

8. Gol S, Pena RN, Rothschild MF, Tor M, Estany J. A polymorphism in the fatty acid desaturase-2 gene is associated with the arachidonic acid metabolism in pigs. Scientific reports. 2018 Sep 25;8(1):1-9.

9. Abeysekera JB, Gyenes DL, Atallah J, Robertson CM, Bond GY, Rebeyka IM, et al. Fetal Umbilical Arterial Pulsatility Correlates With 2-Year Growth and Neurodevelopmental Outcomes in Congenital Heart Disease. Canadian Journal of Cardiology. 2021 Mar 1;37(3):425-32.

10. Arcelli D, Farina A, Cappuzzello C, Bresin A, De Sanctis P, Perolo A, et al. Identification of circulating placental mRNA in maternal blood of pregnancies affected with fetal congenital heart diseases at the second trimester of pregnancy: implications for early molecular screening. Prenatal Diagnosis: Published in Affiliation With the International Society for Prenatal Diagnosis. 2010 Mar;30(3):229-34.

11. Llurba E, Syngelaki A, Sánchez O, Carreras E, Cabero L, Nicolaides KH. Maternal serum placental growth factor at 11–13 weeks' gestation and fetal cardiac defects. Ultrasound in Obstetrics & Gynecology. 2013 Aug;42(2):169-74.

12. Llurba E, Sanchez O, Ferrer Q, Nicolaides KH, Ruíz A, Domínguez C, et al. Maternal and foetal angiogenic imbalance in congenital heart defects. European heart journal. 2014 Mar 14;35(11):701-7.

13. Andescavage N, Yarish A, Donofrio M, Bulas D, Evangelou I, Vezina G, et al. 3-D volumetric MRI evaluation of the placenta in fetuses with complex congenital heart disease. Placenta. 2015 Sep 1;36(9):1024-30.

14. Jones HN, Olbrych SK, Smith KL, Cnota JF, Habli M, Ramos-Gonzales O, et al. Hypoplastic left heart syndrome is associated with structural and vascular placental abnormalities and leptin dysregulation. Placenta. 2015 Oct 1;36(10):1078-86.

15. Curti A, Lapucci C, Berto S, Prandstraller D, Perolo A, Rizzo N, et al. Maternal plasma mRNA species in fetal heart defects: a potential for molecular screening. Prenatal diagnosis. 2016 Aug;36(8):738-43.

16. Albalawi A, Brancusi F, Askin F, Ehsanipoor R, Wang J, Burd I, et al. Placental characteristics of fetuses with congenital heart disease. Journal of Ultrasound in Medicine. 2017 May;36(5):965-72.

17. Contro E, Stefani L, Berto S, Lapucci C, Arcelli D, Prandstraller D, et al. Circulating mRNA in maternal plasma at the second trimester of pregnancy: a possible screening tool for cardiac conotruncal and left ventricular outflow tract abnormalities. Molecular diagnosis & therapy. 2017 Dec;21(6):653-61.

18. Morano D, Berto S, Lapucci C, Baldinazzo LW, Prandstraller D, Farina A. Levels of circulating mRNA for the Tenascin-X (TNXB) gene in maternal plasma at the second trimester in pregnancies with isolated congenital ventricular septal defects. Molecular diagnosis & therapy. 2018 Apr;22(2):235-40.

19. Rychik J, Goff D, McKay E, Mott A, Tian Z, Licht DJ, et al. Characterization of the placenta in the newborn with congenital heart disease: distinctions based on type of cardiac malformation. Pediatric cardiology. 2018 Aug;39(6):1165-71.

20. Takemoto R, Anami A, Koga H. Relationship between birth weight to placental weight ratio and major congenital anomalies in Japan. Plos one. 2018 Oct 22;13(10):e0206002.

21. Miremberg H, Gindes L, Schreiber L, Raucher Sternfeld A, Bar J, Kovo M. The association between severe fetal congenital heart defects and placental vascular malperfusion lesions. Prenatal diagnosis. 2019 Oct;39(11):962-7.

22. Radhakrishna U, Albayrak S, Zafra R, Baraa A, Vishweswaraiah S, Veerappa AM, et al. Placental epigenetics for evaluation of fetal congenital heart defects: Ventricular Septal Defect (VSD). PloS one. 2019 Mar 21;14(3):e0200229.

23. Russell MW, Moldenhauer JS, Rychik J, Burnham NB, Zullo E, Parry SI, et al. Damaging variants in proangiogenic genes impair growth in fetuses with cardiac defects. The Journal of pediatrics. 2019 Oct 1;213:103-9.

24. Schlatterer SD, Murnick J, Jacobs M, White L, Donofrio MT, Limperopoulos C. Placental pathology and neuroimaging correlates in neonates with congenital heart disease. Scientific reports. 2019 Mar 11;9(1):1-1.

25. Courtney J, Troja W, Owens KJ, Brockway HM, Hinton AC, Hinton RB, et al. Abnormalities of placental development and function are associated with the different fetal growth patterns of hypoplastic left heart syndrome and transposition of the great arteries. Placenta. 2020 Nov 1;101:57-65.

26. Giorgione V, Fesslova V, Boveri S, Candiani M, Khalil A, Cavoretto P. Adverse perinatal outcome and placental abnormalities in pregnancies with major fetal congenital heart defects: A retrospective case-control study. Prenatal Diagnosis. 2020 Oct;40(11):1390-7.

27. Ozcan T, Kikano S, Plummer S, Strainic J, Ravishankar S. The association of fetal congenital cardiac defects and placental vascular malperfusion. Pediatric and Developmental Pathology. 2021 Jun;24(3):187-92.

28. Matthiesen NB, Henriksen TB, Agergaard P, Gaynor JW, Bach CC, Hjortdal VE, et al. Congenital heart defects and indices of placental and fetal growth in a nationwide study of 924 422 liveborn infants. Circulation. 2016 Nov 15;134(20):1546-56.

29. Sun IY, Overgaard MT, Oxvig C, Giudice LC. Pregnancy-associated plasma protein A proteolytic activity is associated with the human placental trophoblast cell membrane. The Journal of Clinical Endocrinology & Metabolism. 2002 Nov 1;87(11):5235-40.

30. Arroyo J, Torry RJ, Torry DS. Deferential regulation of placenta growth factor (PlGF)-mediated signal transduction in human primary term trophoblast and endothelial cells. Placenta. 2004 May 1;25(5):379-86.

31. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of Brucella abortus and Brucella melitensis in aborted bovine, ovine, caprine, buffaloes and camelid fetuses by application of conventional and real-time polymerase chain reaction. The Thai Journal of Veterinary Medicine. 2012;42(1):13.

32. Dehkordi FS, Momtaz H, Doosti A. Application of Real-Time PCR for detection of Aspergillus species in aborted ruminant foetuses. Bulgarian Journal of Veterinary Medicine. 2012;15(1):30-6.

33. Dehkordi FS. Prevalence study of Coxiella burnetii in aborted ovine and caprine fetuses by evaluation of nested and real-time PCR assays. American Journal of Animal and Veterinary Sciences. 2011;6(4):180-6.

34. Dehkordi FS, Tavakoli-Far B, Jafariaskari S, Momtaz H, Esmaeilzadeh S, Ranjbar R, et al. Uropathogenic Escherichia coli in the high vaginal swab samples of fertile and infertile women: virulence factors, O-serogroups, and phenotyping and genotyping characterization of antibiotic resistance. New Microbes and New Infections. 2020;38:100824.

35. Dehkordi FS, Haghighi N, Momtaz H, Rafsanjani MS, Momeni M. Conventional vs real-time PCR for detection of bovine herpes virus type 1 in aborted bovine, buffalo and camel foetuses. Bulgarian Journal of Veterinary Medicine. 2013;16(2):102-12.

36. Dehkordi FS, Yazdani F, Mozafari J, Valizadeh Y. Virulence factors, serogroups and antimicrobial resistance properties of Escherichia coli strains in fermented dairy products. BMC Research Notes. 2014c;7(1):1-8.

37. Dehkordi FS, Barati S, Momtaz H, Ahari SN, Dehkordi SN. Comparison of shedding, and antibiotic resistance properties of Listeria monocytogenes isolated from milk, feces, urine, and vaginal secretion of bovine, ovine, caprine, buffalo, and camel species in Iran. Jundishapur Journal of Microbiology. 2013a;6(3):284.

38. Ghorbani F, Gheisari E, Dehkordi FS. Genotyping of vacA alleles of Helicobacter pylori strains recovered from some Iranian food items. Tropical Journal of Pharmaceutical Research. 2016;15(8):1631-6.

39. Dehkordi FS, Gandomi H, Basti AA, Misaghi A, Rahimi E. Phenotypic and genotypic characterization of antibiotic resistance of methicillin-resistant Staphylococcus aureus isolated from hospital food. Antimicrobial Resistance & Infection Control. 2017;6(1):1-1.

40. Dehkordi FS. Prevalence study of Bovine viral diarrhea virus by evaluation of antigen capture ELISA and RT-PCR assay in Bovine, Ovine, Caprine, Buffalo and Camel aborted fetuses in Iran. AMB Express. 2011;1(1):1-6.

41. Dehkordi FS, Parsaei P, Saberian S, Moshkelani S, Hajshafiei P, Hoseini SR, et al. Prevalence study of Theileria annulata by comparison of four diagnostic Techniques in shouthwest Iran. Bulgarian Journal of Veterinary Medicine. 2012;15(2): 123-30.

42. Dehkordi FS, Haghighi Borujeni MR, Rahimi E, Abdizadeh R. Detection of Toxoplasma gondii in raw caprine, ovine, buffalo, bovine, and camel milk using cell cultivation, cat bioassay, capture ELISA, and PCR methods in Iran. Foodborne Pathogens and Disease. 2013;10(2):120-5.

43. Dehkordi FS, Khamesipour F, Momeni M. Brucella abortus and Brucella melitensis in Iranian bovine and buffalo semen samples: The first clinical trial on seasonal, Senile and geographical distribution using culture, conventional and real-time polymerase chain reaction assays. Kafkas Univ Vet Fak Dergisi. 2014;20(6):821-8.

44. Dehkordi FS, Valizadeh Y, Birgani TA, Dehkordi KG. Prevalence study of Brucella melitensis and Brucella abortus in cow's milk using dot enzyme linked immuno sorbent assay and duplex polymerase chain reaction. Journal of Pure and Applied Microbiology. 2014b;8(2):1065-9.

45. Dehkordi FS, Tirgir F, Valizadeh Y. Effects of Guajol® ointment synthesized from medicinal smoke condensate of jennet feces on burn wound healing on Wistar rat. Veterinary Research Forum. 2017; 8(3):215.

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ORIGINAL

Effect of hydrothermal aging on the optical properties of monolithic zirconia ceramics

Efecto del envejecimiento hidrotérmico sobre las propiedades ópticas de las cerámicas monolíticas de zirconio

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Abstract

Background/Purpose: Monolithic zirconia which have good optical properties and excellent mechanical properties such as flexural strength and fracture resistance. This study aimed to investigate the effect of hydrothermal aging on the optical properties of the monolithic zirconia.

Materials and methods: In this *in vitro* study, some groups of all-ceramic restorations were examined, of which monolithic zirconia with high translucency was used as the restorative material and three materials, grade 5 titanium and white and yellow zirconia, as substructure materials. Color standard characteristics, *l*, *a* and *b* values, were measured and recorded by a digital spectrophotometer before and after the aging process. Then, the mean values of data were compared by variance analysis.

Results: The statistical results show that the difference in mean values of color changes (ΔE) between the titanium group and yellow zirconia group was statistically significant. However, no significant difference was observed between titanium and white zirconia groups and between white zirconia and yellow zirconia groups. In all the groups, the differences in the mean ΔE in various thicknesses were significant. The differences between the mean *l*, *a*, and *b* indices were significant in all the groups before and after the aging process.

Conclusion: The color changes associated with the aging process were higher in the yellow zirconia group than in the other two groups. The *l* and ΔE indices decreased, and the *a* and *b* values increased due to the aging process. Restorations with the thickness of 1.5-mm and above exhibited greater color stability after aging.

Key words: Hydrothermal aging, optical properties, zirconia ceramics.

Resumen

Antecedentes/Propósito: La zirconia monolítica que tiene buenas propiedades ópticas y excelentes propiedades mecánicas como la resistencia a la flexión y a la fractura. Este estudio tiene como objetivo investigar el efecto del envejecimiento hidrotérmico en las propiedades ópticas de la zirconia monolítica.

Materiales y métodos: En este estudio in vitro, se examinaron algunos grupos de restauraciones de cerámica sin metal, de los cuales se utilizó circonio monolítico de alta translucidez como material de restauración y tres materiales, titanio de grado 5 y circonio blanco y amarillo, como materiales de subestructura. Se midieron las características de color estándar, los valores l, a y b, y se registraron con un espectrofotómetro digital antes y después del proceso de envejecimiento. A continuación, se compararon los valores medios de los datos mediante un análisis de varianza.

Resultados: Los resultados estadísticos muestran que la diferencia en los valores medios de los cambios de color (ΔE) entre el grupo de titanio y el grupo de circonio amarillo fue estadísticamente significativa. Sin embargo, no se observó ninguna diferencia significativa entre los grupos de titanio y de circonio blanco y entre los grupos de circonio blanco y de circonio amarillo. En todos los grupos, las diferencias en la media de ΔE en varios espesores fueron significativas. Las diferencias entre los índices medios l, a y b fueron significativas en todos los grupos antes y después del proceso de envejecimiento.

Conclusiones: Los cambios de color asociados al proceso de envejecimiento fueron mayores en el grupo de circonio amarillo que en los otros dos grupos. Los índices l y ΔE disminuyeron, y los valores a y b aumentaron debido al proceso de envejecimiento. Las restauraciones con un grosor de 1,5 mm y superior mostraron una mayor estabilidad del color tras el envejecimiento.

Palabras clave: Envejecimiento hidrotérmico, propiedades ópticas, cerámica de circonio.

Introduction

In recent years, dental ceramics have become an increasingly essential materials in tooth restoration[1]. The fabrication of anterior restorations with natural colors and appearances is an essential process in dentistry that is particularly important for patients[2].Metal-ceramic restorations with high fracture strength are successfully used in dentistry[3,4]. Obtaining natural translucency in metal-ceramic restorations is more difficult than that in all-ceramic restorations due to the opaqueness of metal substructure[5,6]. The materials of choice in modern dental ceramic are feldspathic porcelain, leucite-based material, lithium disilicate, and zirconia[7]. Among all-ceramic restorations, zirconia restorations have exhibited favorable physiological and mechanical properties[8,9]. However, despite advances in the esthetics and strength of ceramic materials, the color harmony between ceramics and natural teeth is still not easy to achieve, and it remains a challenge[10].

Manufacturers have been striving to improve the optical properties of all-ceramic materials for better aesthetic outcomes[11]. The color of zirconia can be affected by various factors, substructure color, cement type, zirconia type, zirconia thickness, staining process, sintering conditions, and aging process[11-18]. Although translucent zirconia has been introduced in dentistry, but the color matching of restoration with natural teeth is a problem. In clinical situations, when the tooth of patient is discolored or restored with opaque or costume post-core materials, the restorative material should be able to mask the underlying color of restoration to achieve esthetic results. Therefore, the high translucency of ceramics is not always an advantage[19-20]. The minimum thickness of monolithic zirconia for sufficient fracture resistance is recommended 0.5 mm, but there is no consensus on the minimum thickness of zirconia to provide the esthetic needs[21-24].

Studies have shown that when the surface of zirconia is exposed to water or water vapor, it undergoes a slow, spontaneous, and progressive phase transition. This phenomenon is known as the aging process or low-temperature degradation (LTD). This is one of the disadvantages of zirconia because, after the phase transition from tetragonal to monolithic phase, the surface becomes rough, and a successive displacement of particles with the subsequent micro-crack of cores is observed[25]. One of major research interest is evaluating the mechanical behavior of zirconia after the aging process in a humid environment. Many variables are contributed in the response of zirconia to the aging process, particle size, zirconia properties, and quality, distribution of stabilizing oxides, time, and atmospheric conditions during the sintering process[25].

Clinical and laboratory care are needed to maintain the integrity of the zirconia surface to minimize the effects of the aging process.

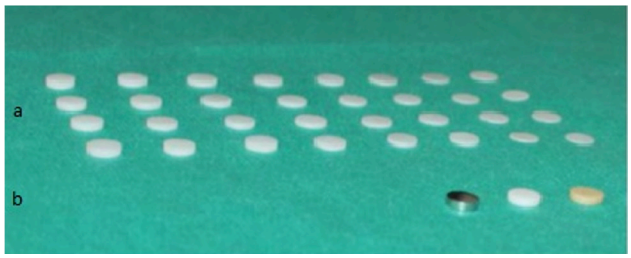
Today, ceramic systems have been introduced to improve the adaptation and color stability of restorations[26-28]. Monolithic zirconia restorations are a good choice in cosmetic dentistry because, in addition to good optical properties, they have excellent mechanical properties such as flexural strength and fracture resistance[29,30-32]. However, achieving the ideal esthetic outcome with these restorations remains a challenge[31-33].

This study aimed to investigate the effect of hydrothermal aging on the optical properties of the all-ceramic restorations. The null hypothesis of the study was that the aging process does not affect the final color of the restorations in different thicknesses of zirconia and on different sub-structures.

Materials and methods

In this experimental study, monolithic zirconia with high translucency (DD cubeX2; Dental Direkt GmbH, Germany) was used as the restorative material, and three materials; grade 5 titanium, white zirconia, and yellow zirconia (IPS e.max ZirCAD; Ivoclar Vivadent AG), were used as the substructure (**Figure 1**).

Fiogure 1: a. Translucent monolithic zirconia disks in different thicknesses, b. Titanium, white zirconia and yellow zirconia disks.



The samples number were considered at n=4 in each group and thickness, based on the study of Jirajariyavej B et al., using G-power software with $\alpha = 0.05$ and 90% test power[34]. High translucency monolithic zirconia was considered for the disks material, and they were fabricated by CAD/CAM method (Coritec 250i; imes-icore GmbH, Eiterfeld, Germany). The disks' diameter was considered 10 mm with the thickness of 0.5, 0.7, 0.9, 1.1, 1.3, 1.5, 1.7, and 1.9 mm, and for each thickness, four disks were prepared.34 Then the samples were immersed for 5 seconds in the paint liquid (DD Bio ZX2 monolithic zero A2 LZDD; Dental Direkt GmbH, Sponge, Germany).

The colored disks were dried with an ordinary bulb for 45 minutes, then the samples were sintered at a temperature of 1.520°C for 12 hours in a sintering furnace (iSINT HT;

imesicore GmbH), and their both sides were equalized by a polishing kit (BruxZir; Glidewell Direct, Irvine, CA, USA). The thickness of the samples was measured by a micrometer with the accuracy of ±0/02 mm (293 MDC-MX Lite; Mitutoyo Corp, Kawasaki, Japan).

A titanium disk with the thickness of 2 mm was prepared by lath as the substructure material, and 2-mm-thick disks were made of white and yellow zirconia, white shade MO 0 as white zirconia and yellow shade MO 2 as yellow zirconia, by the CAD/CAM technique. IPS e.max ZirCAD was crystallized according to the manufacturer's instructions in the furnace (inFire HTC Speed Dentsply Sirona). All the samples were cleaned in an ultrasonic bath (Elmasonic S-30; Dentec, North Shore, Australia), contains 98% ethanol for 20 minutes, and dried in an oil-free air current.

The samples were divided into three groups, all-ceramic restorations on a titanium substructure (Ti), all-ceramic restorations on a white zirconia substructure (W-ZrO_2), and all-ceramic restorations on a yellow zirconia substructure (Y-ZrO_2). The zirconia disks were placed on the three substructures, and a drop of glycerin was used at the interfaces to make proper contact. *l*, *a*, and *b* parameters in CIElab system were determined for zirconia samples in different thicknesses using a digital spectrophotometer (Ultrascan XE; Hunter Associates Laboratory, Inc.), To investigate the optical properties. The total color changes of the samples (ΔE) were calculated based on the changes of *l*, *a*, *b* according to the following formula:

$$\Delta E = [(\Delta a)^2 + (\Delta b)^2 + (\Delta l)^2]^{½}$$

Before the measurement procedure, the spectrophotometer was calibrated according to the manufacturer's instructions. For more accuracy, the color of all the samples was measured three times in the condition that the spectrophotometer tip was placed at the center of the sample.

After the first series of measurements, all the disks underwent the same aging process. All the samples were placed in a thermocycling device (PLC) containing two tanks, cool and hot water baths with temperatures of 5ºC and 55ºC, respectively. All samples were subjected to 10,000 thermal cycles. During each thermal cycle, samples were placed in a cold-water bath for 60 seconds and in a hot water bath for 60 seconds, and the transition time between hot and cold baths was considered 10 seconds. After completion of thermal aging, the samples were cleaned in an ultrasonic cleaner containing distilled water for 5 minutes, and then the second series of color measurements were performed.

Data were analyzed using SPSS software through paired t-test, Tukey Post Hoc test, and ANOVA.

Results

The experimental results show that the mean ΔE index was 1.11±0.52 in the Ti group, 1.49±0.53 in the Y-ZrO_2 group, and 1.35±0.51 in the W-ZrO_2 group; the differences among all groups were significant (P=0.014). Pairwise comparisons of the groups showed that the difference in the mean ΔE between the Ti group and the Y-ZrO_2 group was significant (P=0.004) but, no significant differences were observed between W-ZrO_2 and Ti groups (P=0.063) and also between W-ZrO_2 and Y-ZrO_2 groups (P=0.28). In all the groups, the differences in the mean ΔE in the different thicknesses were significant (**Table I**).

The differences in the mean *l*, *a*, and *b* indexes in all the groups before and after the aging process were significant (**Tables II** and **III**).

Values greater than 5.5 for the ΔE index are compared as clinically acceptable and more than 2.6 as the perceived limit of integrated zirconia color changes against thicknesses in different substructures due to the aging process in **Table IV.**

Table I: Mean color changes of ΔE in different thicknesses.

Group	Thickness	Mean	SD	P_Value
Ti	0.5	1.78	0.29	<0.001
	0.7	1.56	0.54	
	0.9	1.28	0.11	
	1.1	1.30	0.28	
	1.3	1.17	.22	
	1.5	0.72	0.25	
	1.7	0.61	0.22	
	1.9	0.42	0.27	
Y-ZrO_2	0.5	2.06	0.08	<0.001
	0.7	1.84	0.52	
	0.9	1.90	0.43	
	1.1	1.66	0.14	
	1.3	1.26	0.36	
	1.5	1.47	0.50	
	1.7	0.98	0.36	
	1.9	0.78	0.08	
W-ZrO_2	0.5	1.94	0.48	<0.001
	0.7	1.39	0.13	
	0.9	1.71	0.27	
	1.1	1.42	0.23	
	1.3	1.84	0.15	
	1.5	1.11	0.40	
	1.7	0.80	0.11	
	1.9	0.61	0.05	

Table II: Mean differences of *l*, *a*, and *b* indexes before and after hydrothermal aging.

Parameter	Group	Before	After	The difference	P_ Value
l	**Ti**	79.59±0.60	78.79±0.86	-0.77	<0.001
	Y-ZrO_2	79.76±0.39	79.20±0.76	-0.56	<0.001
	W-ZrO_2	81.22±0.66	80.60±0.47	-0.62	<0.001
a	**Ti**	-0.27±07	-0.16±.83	0.11	<0.001
	Y-ZrO^2	0.97±0.26	1.08±0.38	0.11	<0.001
	W-ZrO_2	0.13±.50	0.19±0.46	0.06	<0.001
b	**Ti**	17.26±0.81	17.92±0.45	0.66	<0.001
	Y-ZrO_2	19.33±0.74	20.53±1.05	1.2	<0.001
	W-ZrO_2	17.31±0.98	18.27±0.80	0.96	<0.001

Table III: Changes in *l*, *a*, and *b* in different thicknesses.

Variable		Ti			$Y\text{-}ZrO_2$			$W\text{-}ZrO_2$		
	Thickness	Mean	S.D	P_Value	Mean	S.D	P_Value	Mean	S.D	P_Value
Δl	0.5	-1.04	0.33	0.004	-1.06	0.36	<0.001	-0.94	0.42	0.002
	0.7	-0.98	0.25		-0.86	0.31		-0.94	0.09	
	0.9	-0.94	0.18		-0.77	0.44		-0.76	0.21	
	1.1	-1.10	0.35		-0.77	0.27		-0.65	0.32	
	1.3	-0.95	0.32		-0.30	0.21		-0.44	0.20	
	1.5	-0.57	0.33		-0.11	0.15		-0.52	0.11	
	1.7	-0.49	0.25		-0.17	0.09		-0.36	0.13	
	1.9	-0.30	0.25		-0.36	0.15		-0.30	0.13	
	Total	-0.80	0.38		-0.55	0.41		-0.61	0.31	
Δa	0.5	0.26	0.15	<0.001	0.43	0.07	<0.001	0.15	0.06	<0.001
	0.7	0.26	0.07		0.15	0.04		0.12	0.04	
	0.9	0.16	0.04		0.08	0.03		0.05	0.03	
	1.1	0.06	0.10		0.06	0.03		0.04	0.01	
	1.3	0.09	0.04		0.05	0.01		0.01	0.01	
	1.5	-0.02	0.04		0.03	0.01		0.01	0.012	
	1.7	0.06	0.05		0.01	0.01		0.07	0.009	
	1.9	-0.02	0.02		0.01	0.01		0.01	0.009	
	Total	0.10	0.12		0.10	0.13		0.05	0.06	
Δb	0.5	1.42	0.22	<0.001	1.66	0.33	0.014	1.66	0.39	0.027
	0.7	1.14	0.68		1.59	0.53		1.02	0.10	
	0.9	0.84	0.20		1.34	0.59		0.89	0.41	
	1.1	0.66	0.07		1.24	0.19		0.93	0.33	
	1.3	0.64	0.11		1.07	0.32		0.92	0.75	
	1.5	0.32	0.12		1.01	0.14		0.96	0.45	
	1.7	0.21	0.02		0.96	0.37		0.71	0.07	
	1.9	0.06	0.07		0.68	0.08		0.52	0.08	
	Total	0.66	0.50		1.19	0.45		0.95	0.46	

Table IV: Comparison of the color change of monolithic zirconia thicknesses on different substructures due to aging process with the 2.6 and 5.5 values.

Thickness	Mean ΔE	P-value (Perception limit, 2.6)	P-value (Perception limit, 5.5)
<1.5	1.61	<0.001	<0.001
>1.5	0.83	<0.001	<0.001

Discussion

The results showed that the differences in *l*, *a*, *b* and ΔE parameters of zirconia before and after aging were significant in association with thickness and substructure type. The null hypothesis of this study, the aging process no effect the final color of restorations in different zirconia thicknesses and substructure, was rejected. Therefore, the aging process could affect the color of zirconia in all the groups, especially in thicknesses less than 1.5 mm. In all the analyses, the effect of thickness on zirconia color changes concerning aging was significant. The substructure color affected the *a*, *l*, and *b* values in the translucent zirconia. The greatest changes in the index l, *a*, *b*, and *ΔE* due to aging process in all the groups were related to zirconia with a thickness of 0.5 mm and the lowest changes were related to the thickness of 1.9 mm (**Table III**). The *l* and *ΔE* indices decreased and a and b indexes increased due to aging (**Table II**).

The results showed that the difference in mean ΔE was significant due to the thickness of zirconia in all groups. Therefore, in all the groups (Ti, $Y\text{-}ZrO_2$, and $W\text{-}ZrO_2$) the color change decreased significantly with increasing the ceramic thickness. In the Ti group, the color changes at thicknesses less than 1.1 mm were significantly higher than those at thicknesses more than 1.3 mm. In the $Y\text{-}ZrO_2$ group, color changes at thicknesses less than 1.5 mm were significantly greater compared to thickness more than 1.7 mm and in the $W\text{-}ZrO_2$ group, color changes at thicknesses of less than 1.3 mm were significantly higher compared to the thicknesses of more than 1.5 mm (**Table III**). Therefore, the maximum change was concerned with the minimum zirconia thickness and vice versa, which is supported by the results of y Volpato *et al*[25]. In fact, the color changes in the samples after aging process can be attributed to changes in the microstructure of the zirconia surface due to the long aging process. Monolithic particles are larger than tetragonal particles and increase the roughness of zirconia surface, exposing the surface to more color changes. Dikicier *et al*, showed that the effect of aging process on color parameters, regardless of thickness was significant and for all the systems, a value increased and l and b values decreased with increasing thickness. They also indicated that the thickness of restoration significantly affected its color. Their results regarding changes in a and l values are consistent with this study[35]. Stevenson et al reported that the color of ceramic restorations are affected by tooth color, ceramic thickness, and the opacity of materials[36]. The present study showed that the mean ΔE in the $Y\text{-}ZrO_2$ group was higher than that in the $W\text{-}ZrO_2$ and Ti groups, which was significant.

These findings indicated that the use of $Y\text{-}ZrO_2$ as a substructure resulted in more color changes than $W\text{-}ZrO_2$ and Ti.

The color changes in zirconia samples after the aging process were significantly less at thicknesses more than 1.5 mm than 2.6 value, suggesting that this color change is imperceptible by the naked eye, and t than 2.6 value, suggesting that this color change is imperceptible by the naked eye this color change is imperceptible by the naked eye. Therefore, it is not important. On the other hand, the color change in zirconia samples with thicknesses less than 1.5 mm due to the aging process was significantly greater than the 2.6 value and significantly lower than the 5.5 value. Therefore, the color change in these samples is perceptible but clinically acceptable.

Zirconia has an internal chemical structure with high density, so that its porosity is less than 0.05%. 37,38 This property of zirconia explains its slight changes in its appearance due to the aging process. Changes probably occur only on the zirconia surface; therefore, creating a more uniform and homogeneous surface may reduce the aging effect. However, it should be noted that several factors can directly affect the transition from the tetragonal phase to the monolithic, including defects or the absence of oxygen, size, shape, and location of ZrO_2 particles as well as type and amount of stabilizing oxide, and presence of residual stress that are not clinically controllable[39-42]. Some laboratory and clinical factors that can be controlled include thermal changes, surface treatments, finishing line type, and polishing[44-47].

This study examined only one brand of monolithic zirconia in one shade. There may be additional value in future studies looking at other zirconia brands, other shades, and the effects of different cement types.

Conclusion

Within the limitation of this study, it could be concluded that the mean ΔE changes were significantly different among all groups (Ti, Y-ZrO_2, and W-ZrO_2). The color changes due to the aging process in the Y-ZrO_2 group were greater than the other two groups. The *l* and *ΔE* indexes decreased and *b* and *a* indexes increased due to the aging process. In all the groups, thicknesses more than 1.5 mm exhibited greater color stability after the aging process.

References

1. Kilic K, Kesim B, Sumer Z, Polat Z, Kesim S. In vitro cytotoxicity of all-ceramic substructural materials after aging. J Dent Sci 2013;8:231-8.

2. Lee YK, Yu B, Lee SH, Cho MS, Lee CY, Lim HN. Shade compatibility of esthetic restorative materials-A review. Dent Mater 2010;26:1119-26.

3. Walton TR. An up to 15-year longitudinal study of 515 metal-ceramic FPDs: Part 1. Outcome. Int J Prosthodont 2002;15:439-45.

4. Napankangas R, Raustia A. Twenty-year follow-up of metal-ceramic single crowns: A retrospective study. Int J Prosthodont 2008;21:307-11.

5. Heffernan MJ, Aquilino SA, Diaz-Arnold AM, Haselton DR, Stanford CM, Vargas MA. Relative translucency of six all-ceramic systems. Part I: Core materials. J Prosthet Dent 2002;88:4-9.

6. Heffernan MJ, Aquilino SA, Diaz-Arnold AM, Haselton DR, Stanford CM, Vargas MA. Relative translucency of six all-ceramic systems. Part II: Core and veneer materials. J Prosthet Dent 2002;88:10-5.

7. Weng JH, Chen HL, Chen G, Cheng CH, Liu JF. Original Article Compressive strength of lithium disilicate inlay cementation on three different composite resins. J Dent Sci 2021;16:994-1000.

8. Raigrodski AJ. Contemporary materials and technologies for all-ceramic fixed partial dentures: A review of the literature. J Prosthet Dent 2004;92:557-62.

9. Luthardt RG, Holzhuter M, Sandkuhl O, Herold V, Schnapp JD, Kuhlisch E, et al. Reliability and properties of ground Y-TZP-zirconia ceramics. J Dent Res 2002;81:487-91.

10. Vichi A, Louca C, Corciolani G, Ferrari M. Color related to ceramic and zirconia restorations: A review. Dent Mater 2011;27:97-108.

11. Bai XD, Yan YZ, Li Q. Spectrophotometric evaluation of color errors generated in the visual color duplication procedure for current ceramic veneers. J Dent Sci 2021;16:145-53.

12. Basso GR, Kodama AB, Pimentel AH, Kaizer MR, Della Bona A, Moraes RR, et al. Masking Colored Substrates Using Monolithic and Bilayer CAD-CAM Ceramic Structures. Oper Dent 2017;42:387-95.

13. Oh SH, Kim SG. Effect of abutment shade, ceramic thickness, and coping type on the final shade of zirconia all-ceramic restorations: in vitro study of color masking ability. J Adv Prosthodont 2015;7:368-74.

14. Tabatabaian F, Javadi Sharif M, Massoumi F, Namdari M. The color masking ability of a zirconia ceramic on the substrates with different values. J Dent Res Dent Clin Dent Prospects 2017;11:7-13.

15. Malkondu O, Tinastepe N, Kazazoglu E. Influence of type of cement on the color and translucency of monolithic zirconia. J Prosthet Dent 2016;116:902-8.

16. Tabatabaian F, Khodaei MH, Namdari M, Mahshid M. Effect of cement type on the color attributes of a zirconia ceramic. J Adv Prosthodont 2016;8:449-56.

17. Tuncel I, Turp I, Usumez A. Evaluation of translucency of monolithic zirconia and framework zirconia materials. J Adv Prosthodont 2016;8:181-6.

18. Kumagai N, Hirayama H, Finkelman MD, Ishikawa-Nagai S. The effect of translucency of Y-TZP based all-ceramic crowns fabricated with different substructure designs. J Dent 2013;41:E87-E92.

19. Tabatabaian F, Dalirani S, Namdari M. Effect of Thickness of Zirconia Ceramic on Its Masking Ability: An In Vitro Study. J Prosthodont 2019;28:666-71.

20. Kim HK, Kim SH. Optical properties of pre-colored dental monolithic zirconia ceramics. J Dent 2016;55:75-81.

21. Kim HK, Kim SH, Lee JB, Han JS, Yeo IS. Effect of polishing and glazing on the color and spectral distribution of monolithic zirconia. J Adv Prosthodont 2013;5:296-304.

22. Azer SS, Ayash GM, Johnston WM, Khalil MF, Rosenstiel SF. Effect of esthetic core shades on the final color of IPS Empress all-ceramic crowns. J Prosthet Dent 2006;96:397-401.

23. Karaagachoglu L, Yilmaz B. Influence of cement shade and water storage on the final color of leucite-reinforced ceramics. Oper Dent 2008;33:386-91.

24. Nakamura T, Saito O, Fuyikawa J, Ishigaki S. Influence of abutment substrate and ceramic thickness on the colour of heat-pressed ceramic crowns. J Oral Rehabil 2002;29:805-9.

25. Shokry TE, Shen C, Elhosary MM, Elkhodary AM. Effect of core and veneer thicknesses on the color parameters of two all-ceramic systems. J Prosthet Dent 2006;95:124-9.

26. Volpato CAM, Cesar PF, Bottino MA. Influence of Accelerated Aging on the Color Stability of Dental Zirconia. J Esthet Dent 2016;28:304-12.

27. Conrad HJ, Seong WJ, Pesun GJ. Current ceramic materials and systems with clinical recommendations: A systematic review. J Prosthet Dent 2007;98:389-404.

28. Kelly JR, Benetti P. Ceramic materials in dentistry: historical evolution and current practice. Aust Dent J 2011;56:84-96.

29. Zarone F, Russo S, Sorrentino R. From porcelain-fused-to-metal to zirconia: Clinical and experimental considerations. Dent Mater 2011;27:83-96.

30. Brizuela-Velasco A, Dieguez-Pereira M, Alvarez-Arenal A, Chavarri-Prado D, Solaberrieta E, Fernandez-Gonzalez FJ, et al. Fracture Resistance of Monolithic High Translucency Zirconia Implant-Supported Crowns. Implant Dent 2016;25:624-8.

31. Sulaiman TA, Abdulmajeed AA, Donovan TE, Cooper LF, Walter R. Fracture rate of monolithic zirconia restorations up to 5 years: A dental laboratory survey. J Prosthet Dent 2016;116:436-9.

32. Vichi A, Sedda M, Fonzar RF, Carrabba M, Ferrari M. Comparison of Contrast Ratio, Translucency Parameter, and Flexural Strength of Traditional and "Augmented Translucency" Zirconia for CEREC CAD/CAM System. J Esthet Dent 2016;28:S32-S9.

33. Zhang Y, Mai ZS, Barani A, Bush M, Lawn B. Fracture-resistant monolithic dental crowns. Dent Mater 2016;32:442-9.

34. Kurbad A. Microveneering technique for esthetic enhancement of monolithic zirconia restorations. Int J Comput Dent 2016;19:165-78.

35. Jirajariyavej B, Wanapirom P, Anunmana C. Influence of implant abutment material and ceramic thickness on optical properties. J Prosthet Dent 2018;119:819-25.

36. Dikicier S, Ayyildiz S, Ozen J, Sipahi C. Effect of varying core thicknesses and artificial aging on the color difference of different all-ceramic materials. Acta Odontol Scand 2014;72:623-9.

37. Stevenson B, Ibbetson R. The effect of the substructure on the colour of samples/restorations veneered with ceramic: a literature review. J Dent 2010;38:361-8.

38. Pecho OE, Ghinea R, Ionescu AM, Cardona JD, Paravina RD, Perez MD. Color and translucency of zirconia ceramics, human dentine and bovine dentine. J Dent 2012;40:E34-E40.

39. Ozturk O, Uludag B, Usumez A, Sahin V, Celik G. The effect of ceramic thickness and number of firings on the color of two all-ceramic systems. J Prosthet Dent 2008;100:99-106.

40. Kelly JR, Denry I. Stabilized zirconia as a structural ceramic: An overview. Dent Mater 2008;24:289-98.

41. Mesic K, Majnaric I, Mehulic K. Effect of Aging on the Microstructure and Optical Properties of Translucent ZrO2 Ceramics. Acta Stomatol Croat 2021;55:114-28.

42. Hallmann L, Mehl A, Ulmer P, Reusser E, Stadler J, Zenobi R, et al. The influence of grain size on low-temperature degradation of dental zirconia. J Biomed Mater Res B Appl Biomater 2012;100B:447-56.

43. Kosmac T, Dakskobler A, Oblak C, Jevnikar P. The strength and hydrothermal stability of Y-TZP ceramics for dental applications. Int J Appl Ceram Technol 2007;4:164-74.

44. Cattani-Lorente M, Scherrer SS, Ammann P, Jobin M, Wiskott HWA. Low temperature degradation of a Y-TZP dental ceramic. Acta Biomater 2011;7:858-65.

45. Borchers L, Stiesch M, Bach FW, Buhl JC, Hubsch C, Kellner T, et al. Influence of hydrothermal and mechanical conditions on the strength of zirconia. Acta Biomater 2010;6:4547-52.

46. Kosmac T, Oblak C, Marion L. The effects of dental grinding and sandblasting on ageing and fatigue behavior of dental zirconia (Y-TZP) ceramics. J Eur Ceram Soc 2008;28:1085-90.

47. Kim HK, Kim SH, Lee JB, Han JS, Yeo IS. Effect of polishing and glazing on the color and spectral distribution of monolithic zirconia. J Adv Prosthodont 2013;5:296-304.

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ORIGINAL

Efectos del entrenamiento de fuerza en la salud de adultos mayores

Health-related outcomes of strength training in older adults

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Resumen

Introducción: El proceso normal de envejecimiento se caracteriza por una progresión de eventos fisiológicos que ocurren a lo largo del ciclo de vida. Los cambios relacionados con la edad ocurren en todo el cuerpo y son más prominentes en los últimos años. Los objetivos y propósitos de este estudio fueron: i) proporcionar un resumen de la investigación existente y relevante, ii) evaluar las variables del programa de ejercicios y iii) brindar recomendaciones prácticas basadas en evidencia para la prescripción de ejercicios y el entrenamiento de fuerza en adultos mayores, de acuerdo con las pautas y recomendaciones internacionales.
Métodos: Usando un enfoque basado en evidencia, combinamos datos científicos, declaraciones de expertos y preocupaciones de los usuarios finales para mejorar las referencias de los intereses, valores, requisitos y opciones de la población que envejece. Así, la declaración de posición presenta una valoración de los principales estudios obtenidos tras un exhaustivo análisis de la literatura.
Resultados y conclusiones: En conclusión, destacamos que el entrenamiento de fuerza solo o combinado con entrenamiento aeróbico, es parte fundamental de la prevención primaria de muchas enfermedades crónicas en adultos mayores, además de retrasar la progresión y reducir los síntomas de las condiciones crónicas relacionadas. Los programas de ejercicios de componentes múltiples, especialmente los ejercicios de fuerza que incluyen el entrenamiento de la fuerza muscular, son las intervenciones más efectivas para amortiguar el impacto de la discapacidad física y otros resultados adversos relacionados con la salud, incluso en los ancianos.

Palabras clave: Actividad física, fuerza, bienestar.

Abstract

Introduction: The normal aging process is characterized by a progression of physiological events that occur throughout the life cycle. Age-related changes occur throughout the body and are most prominent in later years. the aims and purposes of this study were to: i) provide a summary of existing and relevant research, ii) assess exercise program variables, and iii) give practical evidence-based recommendations for exercise prescription and resistance training in older adults, according to international guidelines.
Methods: Using an evidence-based approach, we combined scientific data, experts' statements, and end-user concerns to improve references for the interests, values, requirements, and choices of the aging population. Thus, the position statement presents an assessment of the main studies obtained after a thorough analysis of the literature.
Results and conclusions: As conclusions we highlight that strength training alone or combined with aerobic training, is a fundamental part of the primary prevention of many chronic diseases in older adults, in addition to delaying the progression and reducing the symptoms of related chronic conditions. Multicomponent exercise programs, especially strength exercises that include muscle power training, are the most effective interventions for buffering the impact of physical disability and other adverse health-related outcomes, even in the oldest-old.

Key words: Physical activity, strength, wellbeing.

Introducción

Los adultos mayores representan el grupo de edad de más rápido crecimiento de la población. Los cambios fisiológicos asociados con el envejecimiento primario y las enfermedades crónicas concurrentes tienen un impacto adverso en la capacidad funcional, los resultados de salud y la calidad de vida[1]. El proceso normal de envejecimiento se caracteriza por una progresión de eventos fisiológicos que ocurren a lo largo del ciclo de vida. Los cambios relacionados con el envejecimiento ocurren en todo el cuerpo y son más prominentes en los últimos años.

La edad avanzada, incluso si no está asociada con el desarrollo de una enfermedad crónica grave, se acompaña de una multiplicidad de modificaciones biológicas que pueden contribuir a la reducción de la masa, la fuerza y la función del músculo esquelético, lo que lleva a una disminución general de la resistencia fisiológica (capacidad para pararse y recuperarse de los estresores). También está relacionado con la reducción del tamaño muscular (atrofia muscular), la pérdida de la unidad motora y la reducción de la velocidad de contracción, lo que a su vez conduce a una disminución de la fuerza muscular, la potencia y la resistencia[2-4].

Como un fenómeno multifacético y complejo, el envejecimiento se manifiesta de forma diferente entre los individuos a lo largo de la vida y está extremadamente condicionado por las interfaces entre las características genéticas, ambientales, de comportamiento y demográficas[5]. La literatura describe que la sarcopenia afecta al rendimiento motor y muscular[3,6-8]. Las pérdidas de la función muscular pueden reducir la aptitud física y la independencia en las actividades de la vida diaria. Además, los altos niveles de dependencia de los ancianos se asocian positivamente con un mayor temor y riesgo de caídas y niveles más bajos de calidad de vida[9].

Dado que la mayoría de los factores de riesgo asociados con las enfermedades crónicas aumentan con la edad (avanzada), la adopción de una actividad física regular es esencial para atenuar las disminuciones funcionales asociadas con el envejecimiento y para mejorar los resultados relacionados con la salud física y psicológica de los adultos mayores[1,10].

Como tal, y considerando que gran parte de la población de edad avanzada es sedentaria y tiene bajos niveles de aptitud física, los objetivos y propósitos de este estudio fueron: 1) presentar un resumen de los trabajos de investigación existentes y pertinentes, 2) evaluar las variables del programa de ejercicios, y 3) ofrecer recomendaciones prácticas basadas en la evidencia para la prescripción de ejercicios y el entrenamiento de fuerza en los adultos mayores, de acuerdo con las recomendaciones internacionales

Proceso

Mediante un enfoque de práctica basado en la evidencia, combinamos datos científicos, declaraciones de expertos y preocupaciones de los usuarios finales para mejorar las referencias de los intereses, valores, requisitos y selecciones de las personas mayores. Por lo tanto, la declaración de posición presenta una evaluación aguda del trabajo disponible principal pertinente obtenido a través de un análisis de alcance de la literatura.

Dado que existe una gran diferencia biológica entre los adultos mayores de edad cronológica relacionada y las modificaciones relacionadas con la edad en el músculo esquelético normalmente comienzan a lo largo de la mediana edad, no se consideró adecuada una designación estándar de edad avanzada basada en la edad cronológica. En cambio, debido a la amplia variedad fisiológica y funcional, y al comienzo de las consecuencias relacionadas con la edad para el músculo esquelético, se analizaron los estudios que incluyeron sujetos de 50 años en adelante.

Evidencia de las declaraciones resumidas

El entrenamiento de fuerza es el método más eficaz disponible para mantener y aumentar la masa corporal magra y mejorar la fuerza y la resistencia muscular[11]. Se recomienda como parte de las pautas de actividad física que incluyen trabajar todos los grupos musculares principales en dos o más días a la semana[10,12]. Los adultos mayores pueden obtener muchos beneficios para la salud del entrenamiento de fuerza, como el aumento de la fuerza muscular, el aumento de la masa muscular y el mantenimiento de la densidad ósea. Además, se ha demostrado que ciertas dimensiones de la calidad de vida relacionada con la salud mejoran en los adultos mayores debido a la intervención de entrenamiento de fuerza[13].

Teniendo en cuenta las consecuencias físicas, sociales y emocionales adversas del envejecimiento, las estrategias tanto de prevención como de tratamiento son esenciales para la salud y el bienestar de los adultos mayores[5,10,13]. Entre los factores que contribuyen al proceso de envejecimiento, el desuso muscular es un factor evitable y cambiante. El entrenamiento de fuerza se considera un elemento significativo de un programa completo de ejercicios para complementar los efectos positivos ampliamente reconocidos del entrenamiento aeróbico en la salud y las capacidades físicas[12]. Existe una evidencia sólida y convincente de que el entrenamiento de fuerza puede amortiguar los efectos del envejecimiento sobre la función neuromuscular y la capacidad funcional[12-17]. Diferentes formas de entrenamiento de fuerza tienen el potencial de aumentar la fuerza, la masa y la potencia muscular[12]. Además, la evidencia revisada disponible revela una asociación dosis-respuesta donde el

volumen y la intensidad están fuertemente relacionados con las adaptaciones al ejercicio de fuerza[14,18].

Teniendo esto en cuenta, diferentes instituciones sugieren que los adultos deben participar en actividades de fortalecimiento muscular de intensidad moderada a alta, lo que incluye trabajar todos los grupos musculares principales dos o más días a la semana[10,12]. Para el adulto de edad avanzada, se aplican las mismas pautas de fortalecimiento muscular, ya que el entrenamiento de fuerza puede promover beneficios aún mayores para esta población. Varios problemas de salud que afectan a los adultos mayores pueden mitigarse o incluso prevenirse mediante la adopción de un programa regular de entrenamiento de fuerza[13]. Por ejemplo, los adultos mayores tienen un mayor riesgo de muerte prematura debido a caídas, que a su vez se asocian con disminuciones de la aptitud y el equilibrio muscular relacionadas con la edad que pueden reducirse/mejorarse mediante diferentes formas de entrenamiento de fuerza[19-22].

Los adultos mayores pueden obtener muchos otros beneficios para la salud con el entrenamiento de fuerza, junto con más masa y fuerza muscular[13,23]. Los estudios han demostrado que el entrenamiento de fuerza puede beneficiar la densidad mineral ósea[24,25], los perfiles de lipoproteínas[26], el control de la glucemia[27], la composición corporal[28], los síntomas de fragilidad[29], los factores de riesgo del síndrome metabólico[30] y los marcadores de enfermedades cardiovasculares[31]. Esta creciente cantidad de evidencias ha proporcionado un apoyo adicional a los hallazgos inicialmente reportados en la revisión seminal de Pollock y Vincent[32] (ver **tabla I**), demostrando que el entrenamiento de fuerza juega un papel significativo en la mejora de muchos factores de salud asociados con la prevención de enfermedades crónicas a lo largo del curso de la vida.

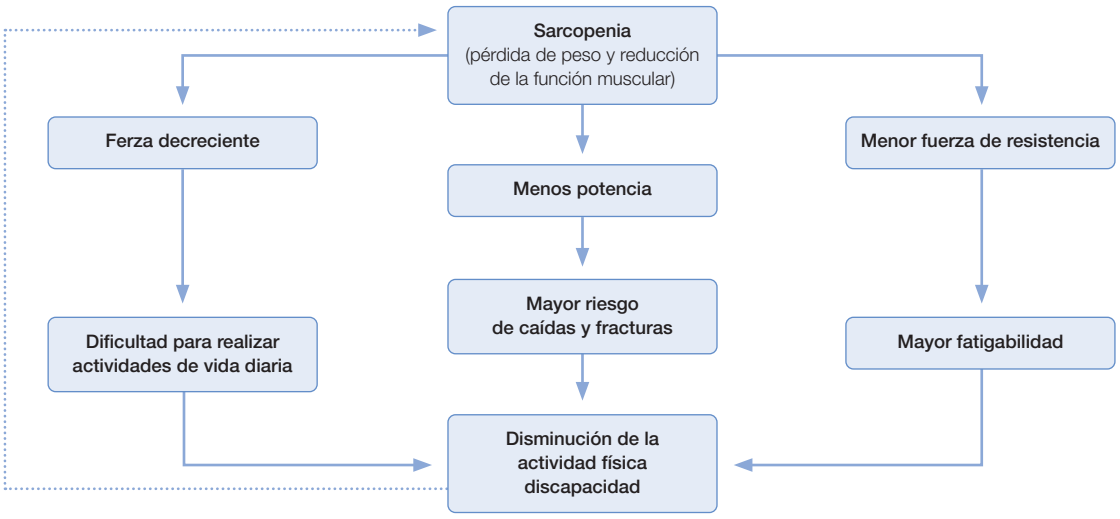
Tabla I: Efectos del entrenamiento de fuerza en las variables de salud y condición física.

Variable	Entrenamiento de fuerza
Densidad mineral ósea	↑↑
Riesgo de caídas	↓
Osteoartritis	↓
% de gasa	↓
Masa corporal magra	↑↑
Fuerza	↑↑↑
Resistencia muscular local	↑↑↑
Metabolismo de la glucosa	
Respuesta de la insulina	↓↓
Niveles de insulina basal	↓
Sensibilidad a la insulina	↑↑
Lípidos en sangre	
HDL	↑↔
LDL	↓↔
Ritmo cardíaco en reposo	↔
Volumen sistólico	↔
Presión sanguínea en reposo	
Sistólica	↔
Diastólica	↓↔
VO_{2max}	↑
Tiempo de resistencia	↑↑
Función física	↑↑↑
Movilidad/vida independiente	↑↑↑
Metabolismo basal	↑↑

En conjunto, la evidencia indica que el entrenamiento de fuerza mejora la salud física, la capacidad funcional y la calidad de vida en las personas mayores, incluso en presencia de fragilidad y enfermedades crónicas. Además, los niveles de entrenamiento de fuerza acordes con las pautas internacionales se han asociado con una mayor aptitud física, un mejor perfil de riesgo cardiovascular y una disminución de la mortalidad general (por todas las causas)[33-35].

De acuerdo con Hunter y otros[36], una parte sustancial de las reducciones en la fuerza relacionada con la edad y la función muscular está mediada por disminuciones en la actividad física diaria, que a su vez induce una mayor sarcopenia. Esto da como resultado un ciclo de retroalimentación positiva que empeora con el tiempo (**Figura 1**).

Figura 1: Modelo de los cambios funcionales relacionados con la edad en la sarcopenia (como se presenta en Hunter y otros36).



Por lo tanto, la interrupción de este ciclo es de suma importancia para mantener la capacidad funcional y la calidad de vida de los ancianos.

Todos los programas de ejercicios de fuerza deben ajustarse a las necesidades y competencias individuales de los adultos mayores. Se debe realizar una evaluación médica/física completa para descartar posibles comorbilidades y contraindicaciones del ejercicio físico (infarto de miocardio o angina inestable, hipertensión no controlada, insuficiencia cardíaca aguda y obstrucción arterial venosa completa). Además, también se debe realizar el seguimiento del plan/programa establecido y sus posibles efectos secundarios (lesiones musculares, articulaciones y fracturas). En resumen, la prescripción de ejercicios debe ser específica e individualizada (estado de salud, factores de riesgo de enfermedades crónicas, características de comportamiento, objetivos personales y preferencias de ejercicio) y progresiva para optimizar y maximizar la magnitud de las adaptaciones de fuerza en los ancianos[37-39].

No obstante, el entrenamiento de fuerza también se puede prescribir simultáneamente con el entrenamiento aeróbico, ya que ambos modos/tipos de ejercicio físico obtienen beneficios distintos, como mejoras en las funciones neuromusculares y cardiovasculares[16], respectivamente, y porque tanto la fuerza muscular como la aptitud aeróbica están inversamente asociadas con mortalidad por cualquier causa en personas mayores[12,37-39]. Con esto en mente, diferentes instituciones internacionales han sugerido pautas y recomendaciones de ejercicio que incluyen la combinación de ejercicios aeróbicos, entrenamiento de fuerza, agilidad / equilibrio y ejercicios de flexibilidad estática y dinámica para adultos[40-42] (ver **tabla II**).

Para promover y mantener la salud, todos los adultos sanos deben acumular al menos 150 minutos semanales de ejercicio aeróbico de intensidad moderada (60-70% de la frecuencia cardíaca máxima, o 12-13 en un rango de escala de esfuerzo percibido de 6 a 20 puntos), distribuidos por la mayoría de los días de la semana o, alternativamente, acumular al menos 75 minutos de actividad aeróbica vigorosa (70% a 90% de la frecuencia cardíaca máxima, o 14 a 16, en un rango de escala de esfuerzo percibido de 6 a 20 puntos). Los adultos deben seguir realizando actividades que mantengan o aumenten la fuerza muscular, al menos dos días a la semana, no consecutivos. Se recomienda a los ancianos, además de los niveles mínimos de ejercicios aeróbicos y de fuerza recomendados para los adultos, que realicen ejercicios de estiramiento y equilibrio al menos 2 a 3 veces por semana, a fin de evitar caídas y mantener y mejorar su autonomía y calidad de vida[12,38-44].

El entrenamiento de fuerza debe realizarse de 2 a 3 veces por semana, usando 3 series de repeticiones 8-12, con una intensidad inicial de 20-30% de 1RM, progresando hasta el 70% de 1RM. El entrenamiento de fuerza puede realizarse utilizando máquinas de resistencia que requieren grupos de músculos importantes (por ejemplo, la presión de las piernas y la extensión de la rodilla). Sin embargo, los ejercicios que implican movimientos monoarticulares tienen una respuesta cardiovascular más baja (aumento de la frecuencia cardíaca y de la presión sanguínea), siendo, al principio del proceso de entrenamiento, más adecuados para su uso en individuos con enfermedades cardiovasculares[38-40]. Para optimizar la mejora de la capacidad funcional del anciano, el programa de entrenamiento de fuerza debe incluir también ejercicios de fuerza que reproduzcan la actividad de la vida diaria, por ejemplo, levantarse y sentarse[45].

El entrenamiento de potencia muscular (alta velocidad) puede ser más beneficioso en términos de mejora funcional que un programa de entrenamiento de resistencia muscular (baja velocidad)[46]. Este tipo de entrenamiento, con cargas ligeras, realizando movimientos explosivos, debería incluirse en las actividades a prescribir en los ancianos, ya que se sugiere que se asocie a una (más) mejora de la capacidad funcional[38,39,46]. El entrenamiento de resistencia cardiovascular debe incluir conjuntos de caminatas en diferentes direcciones y ritmos, caminar en una cinta de correr y subir y bajar escaleras. Esta

Tabla II: Recomendaciones internacionales de la actividad física para adultos sanos.

Organización	Tipo	Modo	Duración	Intensidad	Frecuencia
American College of Sport Medicine [40]	Actividades aeróbicas	Marcha rápida	75' - 150' semana	Moderada a Vigorosa	Mínimo 3 días / semana
	Entrenamiento de fuerza	8 - 10 ejercicios 3 - 4 sets 8 - 12 Reps.		75% de 1RM	Mínimo 2 días / semana
	Flexibilidad	Complementario a otros tipos de ejercicio (estático y dinámico; grupos de músculos principales)			
American Heart Association [41]	Actividades aeróbicas	Marcha	150' semana	Moderada	3 - 7 días / semana
		Marcha rápida 2 días / semana	90' semana	Vigorosa	
	Entrenamiento de fuerza	2 - 4 sets 8 - 12 Reps.		75% de 1RM	3 días / semana

Tabla III: Guía de prescripción de ejercicio en ancianos[44].

Beneficios	Modalidad de ejercicio	Prescripción
Mejora de la resistencia cardiovascular	Caminar Pedalear	60-80% FCma (40-60% VO_{2max}) 5-30 min/sesión 3 días/semana
Aumento de masa muscular y fuerza	Pesos libres Máquinas resistencia variable	8-10 repeticiones por serie con un peso que pudiésemos realizar 20 repeticiones máximas (20 RM) o más y no sobrepasar la realización de 4-6 repeticiones por serie con un peso que pudiésemos realizar 15 RM (30-70% 1 RM) 6-8 ejercicios Grandes grupos musculares 8-10 repeticiones 2-3 series
Potencia y capacidad funcional	Incluir ejercicios de la vida diaria (levantarse y sentarse, subir/bajar escaleras) Incluir ejercicios de potencia (a altas velocidades con pesos ligeros/moderados)	En los ancianos (incluso en los más viejos) se puede mejorar la potencia mediante el entrenamiento al 60% de 1 RM y con la máxima velocidad a esta resistencia (p. ej: tan rápido como sea posible) que estará entre el 33-60% de la velocidad máxima sin resistencia
Flexibilidad	Estiramientos Yoga/pilates	10-15 min 2-3 días semana
Equilibrio	Debería incluir ejercicios en la posición de tándem, semitándem, desplazamientos multidireccionales con pesos extra (2-4 kg), caminar con apoyo talón punta, subir escaleras con ayuda, trasferencia de peso corporal (desde una pierna a la otra) y ejercicios de Tai Chi modificados	En todas las sesiones

actividad debería comenzar con 5-10 minutos, durante las primeras semanas, progresando a 15-30 minutos[47].

El entrenamiento del equilibrio debe incluir ejercicios en posición tándem, semitándem, movimientos multidireccionales bajo carga (2-4 kg), caminar con el apoyo de los dedos de los pies del talón, subir escaleras con ayuda y transferencia de masa corporal (de una pierna a la otra). Los ejercicios modificados de *Tai Chi*, el yoga, el estiramiento y el entrenamiento de equilibrio también pueden mejorar el funcionamiento físico y beneficiar a los pacientes con hipertensión, enfermedades cardíacas y artritis[16-25] (ver **tabla III**).

Los programas de entrenamiento multicomponente deben incluir aumentos graduales de volumen, intensidad y complejidad de los ejercicios cardiovasculares, de fuerza y de equilibrio. Para entrenar alternativamente, la fuerza muscular de un día y otra resistencia cardiovascular es un excelente estímulo para mejorar la fuerza, la potencia y la resistencia cardiovascular. Cuando se realizan programas de entrenamiento que combinan la fuerza y la resistencia cardiovascular, se debe realizar preferentemente un entrenamiento de fuerza antes del entrenamiento cardiovascular[39]. En individuos con bajos niveles de aptitud física y/o sin hábitos regulares de participación en el ejercicio, la aplicación de un volumen de entrenamiento bajo puede facilitar la adherencia al programa de entrenamiento[12].

Conclusiones

En las personas mayores, la actividad física es beneficiosa por cuanto respecta a los siguientes resultados de salud: mejora de la mortalidad por todas las causas y la mortalidad cardiovascular, la incidencia de hipertensión, la incidencia de cáncer en lugares específicos y la incidencia de diabetes de tipo 2, la salud mental (menor presencia de síntomas de ansiedad y depresión), la salud cognitiva y el sueño, y posible mejora de las mediciones de adiposidad. En las personas mayores, la actividad física sirve para prevenir caídas y las lesiones por caídas, así como el deterioro de la salud ósea y funcional.

El entrenamiento de fuerza solamente, o combinado con entrenamiento aeróbico, se supone como una parte fundamental de la prevención primaria de las enfermedades crónicas de muchos adultos mayores, pero también para retrasar la progresión / reducir los síntomas de las afecciones crónicas relacionadas.

Las personas mayores deben acumular a lo largo de la semana un mínimo de entre 150 y 300 minutos de actividad física aeróbica de intensidad moderada, o bien un mínimo de entre 75 y 150 minutos de actividad física aeróbica de intensidad vigorosa, o bien una combinación equivalente de actividades de intensidad moderada y vigorosa, con el fin de obtener beneficios notables para la salud. También deben realizar actividades de fortalecimiento muscular de intensidad moderada o

más elevada para trabajar todos los grandes grupos musculares dos o más días a la semana, ya que ello reporta beneficios adicionales para la salud. Dentro de su actividad física semanal, las personas mayores deben realizar actividades físicas multicomponente variadas que den prioridad al equilibrio funcional y a un entrenamiento de fuerza de intensidad moderada o más elevada tres o más días a la semana para mejorar su capacidad funcional y evitar caídas.

Los programas de ejercicios multicomponentes, y especialmente los ejercicios de fuerza que incluyen entrenamiento de potencia muscular, son las intervenciones más relevantes para amortiguar el impacto de la discapacidad física y otros resultados adversos relacionados con la salud, incluso en los más viejos. Estos programas también son intervenciones valiosas en otros dominios de fragilidad, como caídas y deterioro cognitivo.

El ejercicio físico y el entrenamiento de fuerza deben adaptarse a las características y contraindicaciones de cada individuo, y deben prescribirse con un plan individualizado progresivo, para tener beneficios continuos, al igual que otros tratamientos médicos. El entrenamiento de fuerza también debe adaptarse para que coincida con las necesidades y preferencias funcionales, basado en una estrategia pragmática que hace que el ejercicio sea sostenible y seguro. Dicha estrategia incorpora elementos motivacionales y conocimiento / monitoreo de beneficios alcanzables, utilizando un enfoque idiográfico.

Como conclusión en las personas mayores, se recomienda que limiten el tiempo que dedican a actividades sedentarias. Sustituir el tiempo sedentario por una actividad física de cualquier intensidad (incluso leve) se traduce en beneficios para la salud. Con el fin de reducir los efectos perjudiciales para la salud de un nivel alto de sedentarismo, las personas mayores deben procurar realizar más actividad física de intensidad moderada a vigorosa de la recomendada.

Referencias

1. Zaleski AL, Taylor BA, Panza GA, Wu Y, Pescatello LS, Thompson PD, et al. Coming of Age: Considerations in the Prescription of Exercise for Older Adults. Methodist Debakey Cardiovasc J. 2016;12(2):98-104. doi:10.14797/mdcj-12-2-98

2. Arakelian VM, Goulart CDL, Mendes RG, Sousa NM, Trimer R, Guizilini S, et al. Physiological responses in different intensities of resistance exercise - Critical load and the effects of aging process. J Sports Sci. 2019; 37(12):1420-28. doi: 10.1080/02640414.2018.1561389.

3. Frontera WR, Hughes VA, Fielding RA, Fiatarone MA, Evans WJ, Roubenoff R. Aging of skeletal muscle: a 12-yr longitudinal study. J Appl Physiol (1985). 2000; 88(4):1321-6. doi: 10.1152/jappl.2000.88.4.1321.

4. Traczyk A, Kuźba K, Chłystek J, Potyra K, Abramczyk A, Łakomski M. Resistance training for the elderly. Review of the literature. Journal of Education, Health and Sport 2018, 8(9), 1048-57.

5. Ben-Shlomo Y, Cooper R, Kuh D. The last two decades of life course epidemiology, and its relevance for research on ageing. Int J Epidemiol. 2016; 45(4):973-88. doi: 10.1093/ije/dyw096.

6. Greenlund LJ, Nair KS. Sarcopenia-consequences, mechanisms, and potential therapies. Mech Ageing Dev. 2003; 124(3):287-99. doi: 10.1016/s0047-6374(02)00196-3.

7. Moran J, Ramirez-Campillo R, Granacher U. Effects of Jumping Exercise on Muscular Power in Older Adults: A Meta-Analysis. Sports Med. 2018; 48(12):2843-57. doi: 10.1007/s40279-018-1002-5.

8. Vandervoort AA. Aging of the human neuromuscular system. Muscle Nerve. 2002; 25(1):17-25. doi: 10.1002/mus.1215.

9. Carrasco-Poyatos M, Rubio-Arias JA, Ballesta-García I, Ramos-Campo DJ. Pilates vs. muscular training in older women. Effects in functional factors and the cognitive interaction: A randomized controlled trial. Physiol Behav. 2019; 201:157-64. doi: 10.1016/j.physbeh.2018.12.008.

10. American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc. 2009; 41(7):1510-30.

11. Hass CJ, Feigenbaum MS, Franklin BA. Prescription of resistance training for healthy populations. Sports Med. 2001;31(14):953-964. doi:10.2165/00007256-200131140-00001

12. Fragala MS, Cadore EL, Dorgo S, Izquierdo M, Kraemer WJ, Peterson MD, et al. Resistance Training for Older Adults: Position Statement From the National Strength and Conditioning Association. J Strength Cond Res. 2019; 33(8):2019-052. doi: 10.1519/JSC.0000000000003230.

13. Hart P, Buck DJ. The effect of resistance training on health-related quality of life in older adults: Systematic review and meta-analysis. Health Promot Perspect. 2019;9(1):1-12. doi:10.15171/hpp.2019.01

14. Borde R, Hortobágyi T, Granacher U. Dose-Response Relationships of Resistance Training in Healthy Old Adults: A Systematic Review and Meta-Analysis. Sports Med. 2015; 45(12):1693-720. doi: 10.1007/s40279-015-0385-9.

15. Cadore EL, Casas-Herrero A, Zambom-Ferraresi F, Idoate F, Millor N, Gómez M, et al. Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. Age (Dordr). 2014; 36(2):773-85. doi: 10.1007/s11357-013-9586-z.

16. Cadore EL, Izquierdo M, Pinto SS, Alberton CL, Pinto RS, Baroni BM, et al. Neuromuscular adaptations to concurrent training in the elderly: effects of intrasession exercise sequence. Age (Dordr). 2013; 35(3):891-03. doi: 10.1007/s11357-012-9405-y.

17. Silva RB, Eslick GD, Duque G. Exercise for falls and fracture prevention in long term care facilities: a systematic review and meta-analysis. J Am Med Dir Assoc. 2013; 14(9):685-89.e2. doi: 10.1016/j.jamda.2013.05.015.

18. Steib S, Schoene D, Pfeifer K. Dose-response relationship of resistance training in older adults: a meta-analysis. Med Sci Sports Exerc. 2010; 42(5):902-14. doi: 10.1249/MSS.0b013e3181c34465.

19. Bergen G, Stevens MR, Burns ER. Falls and Fall Injuries Among Adults Aged ≥65 Years - United States, 2014. MMWR Morb Mortal Wkly Rep. 2016; 65(37):993-98. doi: 10.15585/mmwr.mm6537a2.

20. Ahmadiahangar A, Javadian Y, Babaei M, Heidari B, Hosseini SR, Aminzadeh M. The role of quadriceps muscle strength in the development of falls in the elderly people, a cross-sectional study. Chiropr Man Therap. 2018; 26(1):1-6. doi: 10.1186/s12998-018-0195-x.

21. Van Ancum JM, Pijnappels M, Jonkman NH, Scheerman K, Verlaan S, Meskers CGM, et al. Muscle mass and muscle strength are associated with pre-and post-hospitalization falls in older male inpatients: a longitudinal cohort study. BMC Geriatr. 2018; 18(1):116. doi: 10.1186/s12877-018-0812-5.

22. Skinner EH, Dinh T, Hewitt M, Piper R, Thwaites C. An Ai Chi-based aquatic group improves balance and reduces falls in community-dwelling adults: A pilot observational cohort study. Physiother Theory Pract. 2016; 32(8):581-90. doi: 10.1080/09593985.2016.1227411.

23. Westcott WL. Resistance training is medicine: effects of strength training on health. Curr Sports Med Rep. 2012; 11(4):209-16. doi: 10.1249/JSR.0b013e31825dabb8.

24. Huovinen V, Ivaska KK, Kiviranta R, Bucci M, Lipponen H, Sandboge S, et al. Bone mineral density is increased after a 16-week resistance training intervention in elderly women with decreased muscle strength. Eur J Endocrinol. 2016; 175(6):571-82. doi: 10.1530/EJE-16-0521.

25. Anek A, Kanungsukasem V, Bunyaratavej N. Effects of aerobic step combined with resistance training on biochemical bone markers, health-related physical fitness and balance in working women. J Med Assoc Thai. 2015; 98 Suppl 8:S42-51.

26. Ribeiro AS, Tomeleri CM, Souza MF, Pina FL, Schoenfeld BJ, Nascimento MA, et al. Effect of resistance training on C-reactive protein, blood glucose and lipid profile in older women with differing levels of RT experience. Age (Dordr). 2015; 37(6):109. doi: 10.1007/s11357-015-9849-y.

27. Takenami E, Iwamoto S, Shiraishi N, Kato A, Watanabe Y, Yamada Y, et al. Effects of low-intensity resistance training on muscular function and glycemic control in older adults with type 2 diabetes. J Diabetes Investig. 2019; 10(2):331-38. doi: 10.1111/jdi.12926.

28. Cavalcante EF, Ribeiro AS, do Nascimento MA, Silva AM, Tomeleri CM, Nabuco HCG, et al. Effects of Different Resistance Training Frequencies on Fat in Overweight/Obese Older Women. Int J Sports Med. 2018; 39(7):527-34. doi: 10.1055/a-0599-6555.

29. Nagai K, Miyamato T, Okamae A, Tamaki A, Fujioka H, Wada Y, et al. Physical activity combined with resistance training reduces symptoms of frailty in older adults: A randomized controlled trial. Arch Gerontol Geriatr. 2018; 76:41-47. doi: 10.1016/j.archger.2018.02.005.

30. Tomeleri CM, Souza MF, Burini RC, Cavaglieri CR, Ribeiro AS, Antunes M, et al. Resistance training reduces metabolic syndrome and inflammatory markers in older women: A randomized controlled trial. J Diabetes. 2018; 10(4):328-37. doi: 10.1111/1753-0407.12614.

31. Shaw BS, Gouveia M, McIntyre S, Shaw I. Anthropometric and cardiovascular responses to hypertrophic resistance training in postmenopausal women. Menopause. 2016; 23(11):1176-81. doi: 10.1097/gme.0000000000000687.

32. Pollock ML, Vincent KR. Resistance training for health. The President's Council on Physical Fitness and Sports Research Digest, 1996. http://fitness.foundation/s/Digest-1996_Resistance-Training-for-Health_Series-2-Number-8-December.pdf

33. Kamada M, Shiroma EJ, Buring JE, Miyachi M, Lee IM. Strength training and all-cause, cardiovascular disease, and cancer mortality in older women: a cohort study. J Am Heart Assoc. 2017;6(11). doi: 10.1161/jaha.117.007677.

34. Kraschnewski JL, Sciamanna CN, Poger JM, Rovniak LS, Lehman EB, Cooper AB, et al. Is strength training associated with mortality benefits? A 15-year cohort study of US older adults. Prev Med. 2016; 87:121-7. doi: 10.1016/j.ypmed.2016.02.038.

35. Mernitz H, McDermott AY. Exercise and the Elderly: A Scientific Rationale for Exercise Prescription. J Clin Outcomes Manag. 2004; 11(2): 106-16.

36. Hunter GR, McCarthy JP, Bamman MM. Effects of resistance training on older adults. Sports Med. 2004; 34(5):329-48. doi: 10.2165/00007256-200434050-00005.

37. Haff G, Triplett NT. Essentials of strength training and conditioning. 4th ed. Champaign, IL: Human Kinetics. 2016: 462

38. Cadore EL, Rodríguez-Mañas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: a systematic review. Rejuvenation Res. 2013; 16(2):105-14. doi: 10.1089/rej.2012.1397.

39. Cadore EL, Izquierdo M. How to simultaneously optimize muscle strength, power, functional capacity, and cardiovascular gains in the elderly: an update. Age (Dordr). 2013; 35(6):2329-44. doi: 10.1007/s11357-012-9503-x.

40. Pescatello LS. ACSM's Guidelines for Exercise Testing and Prescription. 10th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health, 2017.

41. Riegel B, Moser DK, Buck HG, Dickson VV, Dunbar SB, Lee CS, et al; American Heart Association Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; and Council on Quality of Care and Outcomes Research. Self-Care for the Prevention and Management of Cardiovascular Disease and Stroke: A Scientific Statement for Healthcare Professionals from the American Heart Association. J Am Heart Assoc. 2017; 6(9):e006997. doi: 10.1161/JAHA.117.006997.

42. American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. Med Sci Sports Exerc. 2009; 41(3):687-08. doi: 10.1249/MSS.0b013e3181915670.

43. Izquierdo M, Häkkinen K, Ibañez J, Garrues M, Antón A, Zúñiga A, et al. Effects of strength training on muscle power and serum hormonesin middle age and older men (2001). J Appl Phys-iol. 90(4), 1497-507. doi: 10.1152/jappl.2001.90.4.1497.

44. World Health Organization. Guidelines on Physical Activity and Sedentary Behaviour: at a glance. Geneva: World Health Organization. 2020: 6-7.

45. Casas Herrero Á, Cadore EL, Martínez Velilla N, Izquierdo Redin M. El ejercicio físico en el anciano frágil: una actualización [Physical exercise in the frail elderly: an update]. Rev Esp Geriatr Gerontol. 2015; 50(2):74-81. doi:10.1016/j.regg.2014.07.003.

46. Izquierdo M, Cadore EL. Muscle power training in the institutionalized frail: a new approach to counteracting functional declines and very late-life disability. Curr Med Res Opin. 2014; 30(7):1385-90. doi:10.1185/03007995.2014.908175.

47. Cadore EL, Moneo AB, Mensat MM, Muñoz AR, Casas-Herrero A, Rodriguez-Mañas L, et al. Positive effects of resistance training in frail elderly patients with dementia after long-term physical restraint. Age (Dordr). 2014; 36(2):801-11. doi: 10.1007/s11357-013-9599-7.

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SHORT ORIGINAL ARTICLE

The art in medicine. Jobs with electrical risk and pandemic

El arte en medicina. Trabajos con riesgo eléctrico y pandemia

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Abstract

This article presents a reflection about the risk by exposure to electricity for workers who work at height. This collective of workers –who are considered essential and whose activity requires a specific set of physical skills and adequacies– are now exposed to the added risks of the COVID-19 pandemic.

The consequences of work related accidents or injuries also implicate their families, and this is reflected in Francisca Lita's painting, which opens a door towards present and future hope, showing her belief that the COVID-19 virus will eventually be controlled.

Resumen

Este artículo reflexiona sobre el riesgo por exposición a la corriente eléctrica de trabajadores en alturas al que se añade el miedo por la pandemia en este grupo de trabajadores considerados esenciales y cuya actividad requiere de su presencia física.

Las consecuencias por accidentes o lesiones derivadas de su actividad implican también a sus familias y se refleja en la pintura de Francisca Lita, quien deja abierta la puerta a la esperanza en un control de la enfermedad por COVID-19 y refleja una esperanza presente y futura.

Introduction

Exposure to risk is part of everyone's daily work. However, the current preventive legislation in industrialised countries seeks to have those risks reduced, by applying protective measures at both individual and collective levels[1].

Essential workers such as those who carry out power cable maintenance have seen their working-at-height risk linked to the current risk of becoming infected by the COVID-19 virus.

In Spain, the preventive legislation establishes that working-at-height tasks must be performed by qualified workers, following previously established protocols. Such protocols, if their complexity requires it, need to be rehearsed on stable ground and adjusted to the necessary requirements of the situation. Jobs that are to be carried out in locations where communication may be hampered – due to geographical reasons, quarantining or other circumstances -, must be performed in the presence of at least two first aid trained workers[2].

These activities demand a high degree of specialisation, being performed by highly trained workers, using the appropriate machinery and tools[3].

The risks of working with exposure to electricity

Jobs in contact with electricity carry a very high occupational risk. Death following electrocution is mostly the consequence of ventricular fibrillation and asphyxia, and burns are the most frequent consequences of non-fatal accidents.

The severity of the injuries sustained by these workers depends on a variety of factors that are linked to the characteristics of the electric current (voltage and amperage), duration and type of contact and the resistance of the human body.

Mortality rates of electrical risk

The results are different depending on the country and the working sector.

In Saudi Arabia, data from 2020 shows that the most common accidents and injuries occured in the construction sector, and the most frequent causes were falls from height (>80%) and electrocutions (>60%)[4]. In Italy, between 2002-2016, 18,9% of fatal occupational

injuries were caused by a form of dangerous energy or process – mechanical, thermal, electrical or chemical in small construction and agricultural businesses[5]. In Spain, data from 2015 registered 2.486 accidents, of which 11 had fatal consequences, caused by contact with electricity during working hours[6].

Work during the pandemic

The COVID-19 pandemic has initiated a change in the life of workers around the world, but many of these workers were marked as essential and therefore had to continue their activities. Amongst them are those working with electricity. It was then necessary to adapt the working procedures, in order for the workers to stay apart as much as possible (travelling in separate vehicles, maintaining social distancing at all times, no access to changing rooms, eating restrictions at the workplace, etc.), which led to anxiety and fear of becoming infected by the virus. All these measures had an impact on the workers' job, home and health. Surveys are currently being conducted in order to discover and understand the real implications this unprecedented pandemic has had in people's work, private lives and health[7].

The electric risk, painted

Francisca Lita's image shows the shared work of two colleagues working on an power cable, with the threat and risk of exposure to electricity stretching it´s hand towards them - and the tears of suffering of their loved ones, conscious of the risks and awaiting their return.

The painting shows two clear sides, subtly separated by an electric post. On one side, the workers carry out their daily job, with their routines and their risks; on the other side, as if being part of a special universe, the pandemic risk is shown – present in society and added as a complementary risk to the workers usual activities, becoming part of their routines.

The pandemic risk side is shown with greater clarity and the tree flowers express the hope of a promising future where the disease will be controlled.

The security straps that keep the workers attached to each other, as well as the electrical structures, allude to the pandemic too. They show that, for those essential workers who are carrying out vital tasks for the rest of society, the risk is present in all their activities.

The figures of the two workers are not clear, but actually imprecise, reflecting their souls, feelings, fears and hesitations, which make them blurry as they feel the threatening risks. The figure of the loved ones and their tears are drawn with great precision and are the central focus of this symbolic composition, gathering the fears of the workers' relatives who long for them to come back safe: without having been in contact with the virus and having finished the work free of accidents or injuries.

Conflict of interest

Authors do not have any conflict of interest to declare.

Bibliography

1. España. Jefatura del Estado. Ley 31/1995, de 8 de noviembre, de prevención de Riesgos Laborales. Jefatura del Estado Boletín Oficial del Estado núm. 269, de 10 de noviembre de 1995 Referencia: BOE-A-1995-24292

2. España. Ministerio de la Presidencia. Real Decreto 614/2001, de 8 de junio, sobre disposiciones mínimas para la protección de la salud y seguridad de los trabajadores frente al riesgo eléctrico Boletín Oficial del estado núm. 148, de 21/06/2001.

3. España. INSST. Guía Técnica para la evaluación y prevención del riesgo eléctrico https://www.insst.es/documents/94886/96076/g_electr.pdf/46679419-d4cc-461e-8da1-4b2e65df9146

4. Abukhashabah E, Summan A, Balkhyour M. Occupational accidents and injuries in construction industry in Jeddah city. Saudi J Biol Sci. 2020 Aug;27(8):1993-1998. doi: 10.1016/j.sjbs.2020.06.033. Epub 2020 Jun 25.

5. Campo G, Cegolon L, De Merich D, Fedeli U, Pellicci M, Heymann WC, Pavanello S, Guglielmi A, Mastrangelo G. The Italian National Surveillance System for Occupational Injuries: Conceptual Framework and Fatal Outcomes, 2002-2016. Int J Environ Res Public Health. 2020 Oct 20;17(20):7631. doi: 10.3390/ijerph17207631.

6. España. Ministerio de trabajo y economía social. Estadística de Accidentes de Trabajo. https://www.mites.gob.es/estadisticas/eat/welcome.htm

7. Trougakos JP, Chawla N, McCarthy JM. Working in a pandemic: Exploring the impact of COVID-19 health anxiety on work, family, and health outcomes. J Appl Psychol. 2020 Nov;105(11):1234-1245. doi: 10.1037/apl0000739. Epub 2020 Sep 24.

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SPECIAL ARTICLE

Protein misfolding and medicinal strategies in neurodegenerative disorders

Mal plegamiento de proteínas y estrategias medicinales en los trastornos neurodegenerativos

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Abstract

Proteins that misfold may accumulate and cause disorders like Alzheimer's and Parkinson's. New medicines are also explored to forecast and even cure these illnesses' severe symptoms. Because they were misfolded during creation or maintenance, rogue proteins may harm a biological system. This causes over twenty human illnesses, including Alzheimer's, Huntington's, Parkinson's, and other neurodegenerative diseases. To create new therapies and medications, researchers will need to understand protein misfolding and aggregation formation. To summarize, protein misfolding causes aggregation and neurodegeneration. This suggests that nature employs protein aggregation to execute unique physiological activities in various biological conditions.

Key words: Protein misfolding, Alzheimer's disease, Huntington's disease, Parkinson's disease.

Resumen

Las proteínas que se pliegan mal pueden acumularse y causar trastornos como el Alzheimer y el Parkinson. También se exploran nuevos medicamentos para prever e incluso curar los graves síntomas de estas enfermedades. Las proteínas mal plegadas durante su creación o mantenimiento pueden dañar un sistema biológico. Esto provoca más de veinte enfermedades humanas, como el Alzheimer, el Huntington, el Parkinson y otras enfermedades neurodegenerativas. Para crear nuevas terapias y medicamentos, los investigadores deberán comprender el mal plegamiento de las proteínas y la formación de agregados. En resumen, el mal plegamiento de las proteínas causa agregación y neurodegeneración. Esto sugiere que la naturaleza emplea la agregación de proteínas para ejecutar actividades fisiológicas únicas en diversas condiciones biológicas.

Palabras clave: Mal plegamiento de proteínas, enfermedad de Alzheimer, enfermedad de Huntington, enfermedad de Parkinson.

Introduction

At several stages of the biological process, the ability of proteins to function properly depends on their coordinated interactions. The normal number of cell proteins is 30,000 and the linear chain of a protein consists of amino acids[1]. This linear chain can be used in its natural form. After translation, proteins begin to fold due to the interactions between amino acids. Proteins that fold themselves after production are more prone to misfolding and The crowded cell environment increases misfolding[2,3]. Also, the PQC mechanism ensures that proteins are folded, transported, and eliminated correctly in live creatures. Even when the original structure of a protein is present, misfolding occurs because numerous proteins do not have access to it. After partial unfolding of the protein, some critical intermediates are formed, which can then self-organise into oligomeric aggregates that eventually form amyloid fibrils. Protein degradation and lysosomal degradation are triggered when molecular chaperones fail to refold misfolded proteins. It can happen because of somatic or genetic mutations, age, changes in the cell environment (like temperature, pH, oxidative stress, and the presence of metal ions), and because of alterations in the cell environment. Diabetes type II, which occurs when amyloid fibrils accumulate in the pancreas, Alzheimer's

disease (AD), which occurs when the aggregates accumulate in brain cells, and other systemic diseases, which occur when amyloid fibrils accumulate in multiple organs such as the liver and heart, are all examples of human diseases associated with amyloid fibrils[4].

Alzheimer's, Parkinson's, Huntington's, and TSE are all induced by improper protein folding and aggregation[5-8]. The buildup of misfolded proteins in diverse brain areas causes CNS amyloidosis; researchers have found a pathogenic pathway connected with these disorders[9]. Proteins, which are very soluble in water, progressively convert into cruciform sheet filamentous polymers. In the cytoplasm and nucleus of afflicted brain cells, as well as in the extracellular space[10], amyloid fibrils develop. A robust quality control mechanism prevents misfolded and aggregated proteins from forming. Molecular chaperones prevent misfolding and aggregation of non-native proteins[11].

This article discusses protein misfolding and aggregation in neurodegenerative disorders. Protein misfolding causes neurodegeneration. To investigate the clinical and biological consequences of recent research supporting these concepts[12].

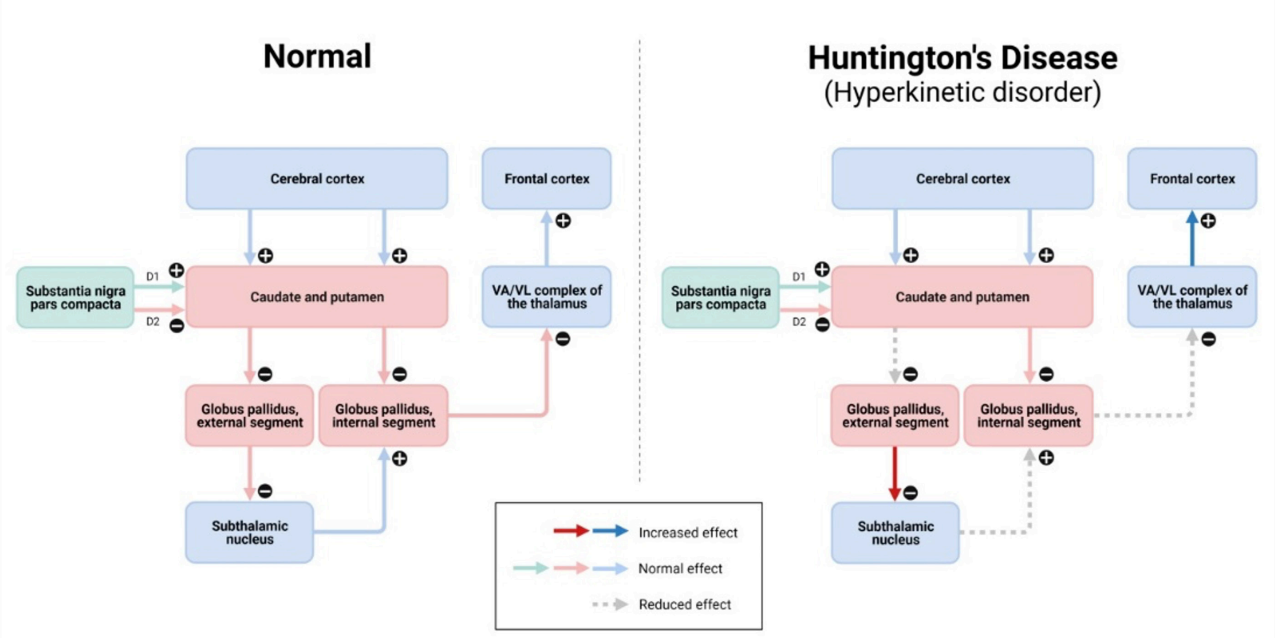
Cells Protein Folding

During folding, several aspects of the process are affected by the environment in which it occurs. After release from the ribosome, polypeptides are folded either in the cytoplasm or in other subcellular compartments such as the endoplasmic reticulum (ER) or mitochondria after being transported across membranes during cellular synthesis[13]. The carboxy-terminal region of a developing chain may also initiate the cotranslational folding of proteins, whereas the exit channel of the ribosome contains the carboxy-terminal segment[14]. Prior to folding, proteins face unique obstacles in the manufacturing process due to the tightly packed macromolecules in cells[15]. Due to the exposed hydrophobic surfaces of incompletely folded chains, they are more likely to bind with other molecules than fully folded chains. The accumulation is due to the fact that their concentration increases[15] and exceeds the first-order folding process that normally occurs in the concentrated environment of cells[16], making the situation even more difficult[17], Complex methods have been developed to prevent proteins from aggregating before folding. Molecular chaperones and the ubiquitin-proteasome system are two examples of systems that are not only independent but also work together in living cells. One of the best known neurodegenerative diseases will be briefly reviewed in this part to provide insight into the pathology that distinguishes it from other diseases[18].

Huntington's disease (HD)

Huntington's disease is a well-known hyperkinetic movement disorder defined by chorea-like movements. This hereditary disorder usually affects people between the ages of 30 and 50. Alzheimer's disease progresses to fatality. Children of Huntington's disease patients have a 50% probability of developing the illness. Frequent repeated actions include hand flapping, swaying, hitting the head, mouthing and choosing objects. Dependence to drugs or alcohol is not the cause of these unpredictable behavior[19]. Dementia and mortality occur within 15 to 20 years after the onset of this condition20 (**Figure 1**).

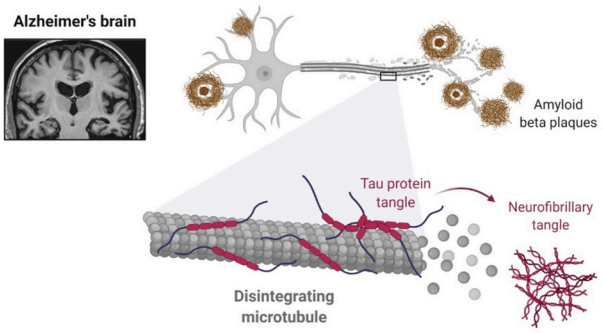
Figure 1: Schematic diagrams display Normal state and hyperkinetic disease (e.g. Huntington disease).



Alzheimer's disease (AD)

Alzheimer's disease (AD) is a neurodegenerative condition that progresses over time (**figure 2**)[21]. Age is a significant risk factor for neurodegenerative disorders such as Alzheimer's, which are characterized by aberrant protein aggregation. As a result, amyloid-beta plaques in the extracellular space and tau neurofibrillary tangles in the medial temporal region and cortex of afflicted neuronal tissues reflect two separate illnesses[22].

Figure 2: Alzheimer's disease is a degenerative neurological condition caused by extracellular amyloid-beta plaques and tau neurofibrillary tangles in the medial temporal region and brain.



Prion disease

Neurodegenerative illnesses induced by prion infection are known as transmissible spongiform encephalopathies (TSE)[23]. The condition is hypothesized to be caused by structural changes to the PrPc protein in the brain, which leads in the compulsive form of PrPTSE. The pathogenesis and emergence of an infectious prion are dependent on this change. Predatory prion infections have been proven to impact the central nervous system (CNS) of a wide range of species[24].

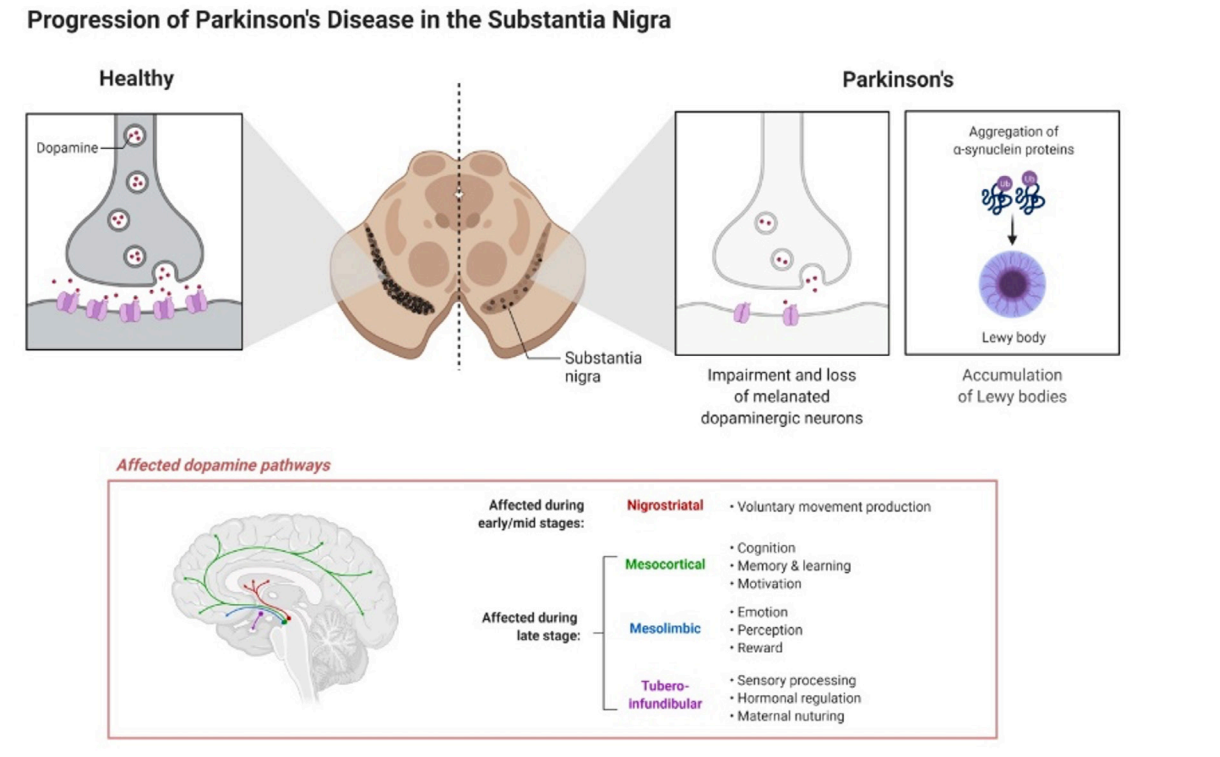
Amyotrophic lateral sclerosis (ALS)

Motor neuron degeneration in the brain stroma, motor cortex, and anterior horn of the spinal cord is a hallmark of ALS, which is lethal and occurs in the latter stages of the illness[25].

Parkinson's disease (PD)

Parkinson's disease is a progressive neurological illness. This second highest frequent neurological illness is caused by dopaminergic cell loss in the substantia nigra. Lewy bodies are a neurodegenerative characteristic of Parkinson's disease[26]. Recently, exosomes, extracellular nanovesicles, have been shown to transport aggregated proteins from one cell to another (**Figure 3**)[27].

Figure 3: Parkinson's disease is a progressive neurological disease. This second most frequent neurodegenerative illness is caused by dopaminergic cell loss in the substantia nigra. Lewy bodies are a neuropathological characteristic of Parkinson's disease.



Exosomes have long been thought to clear cells of waste products and thus play an active role in intercellular communication. In addition, these vesicles contain a variety of inflammatory and signalling substances as well as short RNAs. Prevention of Parkinson's disease could be as simple as targeting molecules such as these vesicles[28].

Medication strategies

The increasing prevalence of neurodegenerative diseases in the general population worldwide is a cause for concern[29]. As described above, neurodegeneration is exacerbated by protein misfolding and aggregation. Extensive research on potential treatments and countermeasures is needed[30-32].

Proteins Stabilization

It is possible to avoid protein misfolding and aggregation by using compounds that bind to the native protein. Examples of this strategy include transthyretin, PrP, and Ab. In the blood and cerebrospinal fluid (CSF), transthyretin (TTR) predominates[33]. T4 and RBP are transported by this transporter[34]. Stabilization of the tetramer by thyroxine could limit TTR fibril formation in vitro[34,35]. Preventing PrPTSE may need the study of chemicals that stabilize PrP c and alter its structure.

Protein aggregation disruption

Neurodegeneration progresses due in part to protein aggregation, which serves a key function. This pathway may also be stopped after protein misfolding has occurred[36]. Amyloid abnormalities are linked to an unique molecule that inhibits the spread of fibrils by binding to the end of a filament. There is one end of these molecules that binds to the fibril, while the other end has no apparent binding surface. Studies conducted in the laboratory using -leaf breakers have shown promising outcomes. It is possible to stop polypeptide chains from forming by using a blocker[37,38].

The self-recognition motif of a misfolded protein is included in these short synthetic peptides, which make use of foldable sheet structure. Synuclein, IAPP, Ab, PrP, and insulin have been found to alter the structure and aggregation of these proteins[39]. However, these inhibitors themselves form amyloid fibrils, which is a drawback to this technique. To avoid amyloid formation, hydrogen bonds may be disrupted in the backbone of the protein. N-methylation and other structural modifications, like streric hindrances to amyloid growth, decrease the stranding capacity of amyloids.

Conclusion

Conformational alterations in proteins are the primary cause of protein aggregation. When these alterations are made, the amyloidogenic amino acids become more accessible to the environment. Protein folding, misfolding, aggregation, and related disorders were the primary emphasis of this review in order to acquire a complete picture of neurodegenerative disease, as well as associated diseases and medicines. Aggregation is a key cause of many neurodegenerative illnesses, and it has to be explored more thoroughly in the future. For amyloids, hydrophobic interaction is an essential mechanism for stabilization, based to a research published in the journal ACS Nano. Despite the prevalence of neurodegenerative illnesses, there is presently no cure for them. Hydrophobic bonds between aromatic and hydrophobic amino acid residues, according to the study, may be weakened. Protein self-aggregation inhibitors might be developed using the findings of this study. A function for protein misfolding and aggregation is well-known in these disorders' underlying pathogenesis. Furthermore, new treatments for these incurable illnesses are very certain to be identified in the future.

Conflict of interest

Authors do not have any conflict of interest to declare.

References

1. Abbasbeigi S. Misfolded structures| A brief insight into protein aggregation criteria, which may lead to Proteopathy diseases. Journal of Chemical Reviews. 2020;3(1):97-108.

2. Alpaugh M, Denis HL, Cicchetti F. Prion-like properties of the mutant huntingtin protein in living organisms: the evidence and the relevance. Molecular psychiatry. 2021 Oct:1-2.

3. Aubi O, Knappskog PM, Martinez A. Early stage discovery and validation of pharmacological chaperones for the correction of protein misfolding diseases. InProtein Misfolding Diseases 2019 (pp. 279-292). Humana Press, New York, NY.

4. Ayers JI, Borchelt DR. Phenotypic diversity in ALS and the role of poly-conformational protein misfolding. Acta Neuropathologica. 2021 Jul;142(1):41-55.

5. Balakrishnan R, Azam S, Cho DY, Su-Kim I, Choi DK. Natural Phytochemicals as Novel Therapeutic Strategies to Prevent and Treat Parkinson's Disease: Current Knowledge and Future Perspectives. Oxidative Medicine and Cellular Longevity. 2021 May 25;2021.

6. Caballero AB, Gamez P. Nanochaperone-Based Strategies to Control Protein Aggregation Linked to Conformational Diseases. Angewandte Chemie. 2021 Jan 4;133(1):41-52.

7. Camacho MV, Telling G, Kong Q, Gambetti P, Notari S. Role of prion protein glycosylation in replication of human prions by protein misfolding cyclic amplification. Laboratory Investigation. 2019 Nov;99(11):1741-8.

8. Carbonell F, Iturria-Medina Y, Evans AC. Mathematical modeling of protein misfolding mechanisms in neurological diseases: a historical overview. Frontiers in Neurology. 2018 Feb 2;9:37.

9. Chang CW, Shao E, Mucke L. Tau: Enabler of diverse brain disorders and target of rapidly evolving therapeutic strategies. Science. 2021 Feb 26;371(6532):eabb8255.

10. Charvin D, Medori R, Hauser RA, Rascol O. Therapeutic strategies for Parkinson disease: beyond dopaminergic drugs. Nature Reviews Drug Discovery. 2018 Nov;17(11):804-22.

11. Cremades N, Dobson CM. The contribution of biophysical and structural studies of protein self-assembly to the design of therapeutic strategies for amyloid diseases. Neurobiology of Disease. 2018 Jan 1;109:178-90.

12. Dhouafli Z, Cuanalo-Contreras K, Hayouni EA, Mays CE, Soto C, Moreno-Gonzalez I. Inhibition of protein misfolding and aggregation by natural phenolic compounds. Cellular and molecular life sciences. 2018 Oct;75(19):3521-38.

13. Diteepeng T, Del Monte F, Luciani M. The long and winding road to target protein misfolding in cardiovascular diseases. European Journal of Clinical Investigation. 2021 May;51(5):e13504.

14. El Saghir A, Farrugia G, Vassallo N. The human islet amyloid polypeptide in protein misfolding disorders: Mechanisms of aggregation and interaction with biomembranes. Chemistry and Physics of Lipids. 2021 Jan 1;234:105010.

15. Elfawy HA, Das B. Crosstalk between mitochondrial dysfunction, oxidative stress, and age related neurodegenerative disease: Etiologies and therapeutic strategies. Life sciences. 2019 Feb 1;218:165-84.

16. Emwas AH, Alghrably M, Dhahri M, Sharfalddin A, Alsiary R, Jaremko M, et al. Living with the enemy: From protein-misfolding pathologies we know, to those we want to know. Ageing Research Reviews. 2021 Sep 1;70:101391.

17. Gámez A, Yuste-Checa P, Brasil S, Briso-Montiano Á, Desviat LR, Ugarte M, et al. Protein misfolding diseases: prospects of pharmacological treatment. Clinical genetics. 2018 Mar;93(3):450-8.

18. Gandhi J, Antonelli AC, Afridi A, Vatsia S, Joshi G, Romanov V, et al. Protein misfolding and aggregation in neurodegenerative diseases: a review of pathogeneses, novel detection strategies, and potential therapeutics. Reviews in the Neurosciences. 2019 Jun 1;30(4):339-58.

19. Hartl FU. Protein misfolding diseases. Annual review of biochemistry. 2017 Jun 20;86:21-6.

20. Gonzalez-Garcia M, Fusco G, De Simone A. Membrane interactions and toxicity by misfolded protein oligomers. Frontiers in Cell and Developmental Biology. 2021;9:395.

21. Guha S, Subramaniyam R. Amyloid beta peptides, tau protein acetylation and therapeutic strategies for treating Alzheimer's disease: a review. Life Research. 2021;4(1):9.

22. Guo S, Nguyen L, Ranum LP. RAN proteins in neurodegenerative disease: Repeating themes and unifying therapeutic strategies. Current opinion in neurobiology. 2022 Feb 1;72:160-70.

23. Harischandra DS, Ghaisas S, Zenitsky G, Jin H, Kanthasamy A, Anantharam V, et al. Manganese-induced neurotoxicity: new insights into the triad of protein misfolding, mitochondrial impairment, and neuroinflammation. Frontiers in neuroscience. 2019 Jun 26;13:654.

24. Hughes D, Mallucci GR. The unfolded protein response in neurodegenerative disorders–therapeutic modulation of the PERK pathway. The FEBS journal. 2019 Jan;286(2):342-55.

25. Lukas J, Pospech J, Oppermann C, Hund C, Iwanov K, Pantoom S, et al. Role of endoplasmic reticulum stress and protein misfolding in disorders of the liver and pancreas. Advances in medical sciences. 2019 Sep 1;64(2):315-23.

26. Niewiadomska-Cimicka A, Trottier Y. Molecular targets and therapeutic strategies in spinocerebellar ataxia type 7. Neurotherapeutics. 2019 Oct;16(4):1074-96.

27. Pande M, Srivastava R. Molecular and clinical insights into protein misfolding and associated amyloidosis. European Journal of Medicinal Chemistry. 2019 Dec 15;184:111753.

28. Pinheiro L, Faustino C. Therapeutic strategies targeting amyloid-β in Alzheimer's disease. Current Alzheimer Research. 2019 Apr 1;16(5):418-52.

29. Rochet JC. Novel therapeutic strategies for the treatment of protein-misfolding diseases. Expert reviews in molecular medicine. 2007 Jun;9(17):1-34.

30. Ryan P, Xu M, Davey AK, Danon JJ, Mellick GD, Kassiou M, et al. O-GlcNAc modification protects against protein misfolding and aggregation in neurodegenerative disease. ACS chemical neuroscience. 2019 Apr 15;10(5):2209-21.

31. Sharma R, Srivastava T, Pandey AR, Mishra T, Gupta B, Reddy SS, et al. Identification of Natural Products as Potential Pharmacological Chaperones for Protein Misfolding Diseases. ChemMedChem. 2021 Jul 6;16(13):2146-56.

32. Soto C, Pritzkow S. Protein misfolding, aggregation, and conformational strains in neurodegenerative diseases. Nature neuroscience. 2018 Oct;21(10):1332-40.

33. Stremmel W, Weiskirchen R. Therapeutic strategies in Wilson disease: pathophysiology and mode of action. Annals of Translational Medicine. 2021 Apr;9(8).

34. Tao YX, Conn PM. Pharmacoperones as novel therapeutics for diverse protein conformational diseases. Physiological Reviews. 2018 Apr 1;98(2):697-725.

35. Tchkonia T, Kirkland JL. Aging, cell senescence, and chronic disease: emerging therapeutic strategies. Jama. 2018 Oct 2;320(13):1319-20.

36. Verdile V, De Paola E, Paronetto MP. Aberrant phase transitions: side effects and novel therapeutic strategies in human disease. Frontiers in genetics. 2019 Mar 22;10:173.

37. Wang S, Zheng J, Ma L, Petersen RB, Xu L, Huang K. Inhibiting protein aggregation with nanomaterials: The underlying mechanisms and impact factors. Biochimica et Biophysica Acta (BBA)-General Subjects. 2022 Feb 1;1866(2):130061.

38. Weaver DF, Meek A, Gupta M, Wang YF. In Silico Search for Endogenous Inhibitors of Protein Misfolding.

39. Yang X, Ji Y, Wang W, Zhang L, Chen Z, Yu M, et al. Amyotrophic lateral sclerosis: molecular mechanisms, biomarkers, and therapeutic strategies. Antioxidants. 2021 Jul;10(7):1012.

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CASE REPORT

Investigating the effect of observing the health triangle on gallstone treatment; a case report

Investigación del efecto de la observación del triángulo de la salud en el tratamiento de los cálculos biliares; informe de un caso

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Abstract

Introduction: Gallstone disease is a highly prevalent disease in general population and is associated with high costs of treatment and morbidity. The major risk factors to develop gallstone include sedentary lifestyle, and a diet rich in simple. Cholecystectomy is considered the most recommended treatment for symptomatic gallstone by classic medicine. However, complications from cholecystectomy are significant and is not acceptable to many patients. Hence, introducing an alternative treatment for such patients is mandatory.
Methods: In this case report, considering the etiology of gallbladder disease, we presented a 92- years-old woman with gallstone disease treated with nutrition correction in line with the health triangle and also other traditional medicine remedies.
Results: After one year of treatment initiation the symptoms of the patient were resolved and the gallstone size reduced considerably until there was no sign of the gallstone in ultrasonography.
Conclusion: Performing health triangle along with nutrition correction and traditional medicine remedies, with the mechanism of changing the cell metabolism, could be an alternative medication for the treatment of gallstone disease.

Key words: Gallstone, health triangle, full health.

Resumen

Introducción: Los cálculos biliares son una enfermedad de alta prevalencia en la población general y se asocia con altos costes de tratamiento y morbilidad. Los principales factores de riesgo para el desarrollo de cálculos biliares son el estilo de vida sedentario y una dieta rica en grasas. La medicina clásica considera que la colecistectomía es el tratamiento más recomendado para los cálculos biliares sintomáticos. Sin embargo, las complicaciones de la colecistectomía son importantes y no son aceptables para muchos pacientes. Por lo tanto, es obligatorio introducir un tratamiento alternativo para estos pacientes.
Métodos: En este informe de caso, teniendo en cuenta la etiología de la enfermedad de la vesícula biliar, presentamos a una mujer de 92 años con enfermedad de cálculos biliares tratada con corrección nutricional de acuerdo con el triángulo de la salud y también con otros remedios de la medicina tradicional.
Resultados: Después de un año de inicio del tratamiento, los síntomas de la paciente se resolvieron y el tamaño del cálculo biliar se redujo considerablemente hasta que no hubo ningún signo del cálculo biliar en la ecografía.
Conclusión: La realización del triángulo de la salud junto con la corrección nutricional y los remedios de la medicina tradicional, con el mecanismo de cambio del metabolismo celular, podría ser una medicación alternativa para el tratamiento de la enfermedad de cálculos biliares.

Palabras clave: Cálculo biliar, triángulo de salud, salud completa.

Introduction

Gallstone disease is a highly prevalent disease in general population and is associated with high costs of treatment and morbidity. Gallstone disease is also one of the common causes of hospitalization worldwide[1]. The major risk factors to develop gallstone include genetic susceptibility, sedentary lifestyle, and a diet rich in simple sugars (monosaccharides, disaccharides). The interplay between numerous environmental factors and physiological intercellular responses to lipids, sugars, diet and hepatic and digestive function can cause the formation of gallstone[2,3].In individuals with both a sedentary lifestyle and a diet rich in refined sugars, the risk of gallstone formation is significantly increased[4]. Studies have shown that physical activity and healthy diet is associated with a decreased risk of gallstone formation and cholecystectomy[5,6].

Cholecystectomy (surgical removal of the gallbladder) is considered the most recommended treatment for symptomatic gallstone by modern medicine and it is one of the most common elective surgeries in the US. In the recent years, the laparoscopic techniques for cholecystectomy have significantly reduced the hospitalization and patient recovery time[7]. However, complications from laparoscopic cholecystectomy including bile duct injuries, the escape of gallstones into the peritoneum and preoperative symptoms following surgery are significant and is not acceptable to many patients[8]. Besides, for some patients, cholecystectomy does not correct the underlying mechanisms that lead to gallstone formation. Surgery in some patients is associated with high burden (e.g. in old ages) or may be contraindicated for some reasons[9]. Hence, introducing an alternative treatment for such patients is mandatory. In this case report, considering the etiology of gallbladder disease, we presented a case with gallstone disease treated with some alternative approaches.

Materials and methods

Case presentation

A 92-year-old woman without past medical history presented to our department with a history of abdominal pain in right upper quadrant (RUQ), nausea and vomiting. On examination she had a abdominal tenderness in RUQ but she did not present any signs of intestinal obstruction or peritonitis and her rectal examination was normal. The height and weight of the patient were 150 cm and 45 kg respectively. With gallbladder or bile duct stone as the most probable diagnosis, we ordered some laboratory tests and abdominal ultrasonography. The laboratory findings, including her aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin levels, were elevated and higher than normal range. In ultrasonography, a stone with a diameter of 27 mm was noted in 22.04.2017 (**Table I** and **table II**). With the results blood tests and ultrasonography of we came to definitive diagnosis of gallstone disease. The patient was candidate for cholecystectomy or endoscopic retrograde cholangiopancreatography (ERCP). However, the patient and her family were unwilling to undergo surgery or any classical medicine treatments. Hence, the patient was candidate for use of traditional medicine treatments.

At first visit (April 2017), the treatment approach was to modify the patient's diet and lifestyle according to the health triangle (treatment of food, species, manual procedures) in fact as part of six essentials and keep health (Hefze-el-Sehah) that has been mentioned in The Book of the Law of Wise Abu Ali Sina[10]. Also, oral and absorptive treatments were administrated with herbal remedies and nutrition correction including: pain relief by massaging with black seed oil and chamomile oil, using Docin syrup (combination of Fennel flower and honey), a table spoon, after each meal. Quit cold temper foods, cold temperature, replacing yellow bovine animal oil instead of industrial oils, to increase cell metabolism were also in our treatment approach. With mentioned above remedies and full compliance of health triangle, the patient's daily pain, vomiting and nausea were initially reduced to weekly, then once a month, once every two months, then once every nine months after the first visit to the traditional medicine center. Finally, the pain and other complications of the disease were completely resolved. The successive ultrasonography in following months after treatment initiation revealed a reduction in gallstone size until there was no sign of gallbladder stone. The laboratory tests also showed a significant reduction in AST, ALT, ALP and bilirubin (**Table I** and **table II**).

Table I: Ultrasonography results.

Date	Results
April 2017	stone with a diameter of 27mm
September 2017	stone with a diameter of 17mm with sludge around it (overall dimensions 22mm) in the middle of CBC
May 2018	no clear gallstones

Table II: Laboratory tests results.

	Apr. 2017	Sep 2017	Nov 2017	Normal range
AST	600	145	163	up to 40 U/L
ALT	230	72	45	up to 41.0 U/L
ALP	6210	2431	1692	up to 270 U/L
T Bili	3.5	3.4	2.6	Adult: 0.1 -1.2 mg/dl
D Bili	2.1	2.8	1.9	up to 0.3 mg/dl

Discussion

The pathophysiology of gallstone formation consists of three major stages. In the first stage, the composition of bile is altered and saturated with cholesterol, due to genetics, diet and other environmental causes (estrogens, multiple birth, birth control bills, obesity, rapid weight loss and terminal ileum diseases). These changes increase the chances of cholesterol precipitation

and crystallization. In the second stage of gallstone formation, the gallbladder emptying is impaired resulting in bile stasis and the formation of biliary sludge. In this stage the gallbladder shows signs of inflammation. In the final stage, cholesterol crystallizes around a pronucleus forming a gallbladder stone[11].

Some alternative strategies for treatment of gallstone may include reducing gallbladder inflammation and restoring normal bile composition and secretion. These objectives could be reached by some traditional medicine remedies which alter the cell metabolism, reduce inflammation of gallbladder and improve bile secretion. One of these treatments include dietary changes based on health triangle (treatment of food, spices, manual procedures)10. In both classic medicine and traditional medicine, mild cases of gallstone may be treated with a variety of methods, including herbal medicine, dietary changes, and manual procedures[12].

Studies have shown that some foods including eggs, red meat, onion, fowl, milk, coffee, oranges, corn, beans, nuts, apples, and tomatoes can cause the recurrence of gallstone even after surgery with the mechanism of allergy formation[13]. Eliminating these types of foods can halt the saturation of bile with cholesterol and reduce gallstone formation. Consuming more fruits and vegetables, less refined carbohydrates, yellow animal derived oil instead of industrial oil and eliminating cold tempered foods may also lower the formation of bile stone through correction of cell metabolism[12]. Physical activity is also have been shown to reduce and prevent gallstone in both men and women. The underlying mechanism is mostly due to changes in glucose metabolism. Following an exercise training program, fasting plasma insulin levels are significantly reduced and it is suggested to explain the protective effect of physical activity[12].

This approach not only treat gallbladder disease but also it can prevent it, therefore significantly reduced the medical, economic, psychological, physical and psychological costs due to this disease. However, further clinical studies on the impact of this traditional medicine approach and the health triangle guidelines on the treatment of gallstone is needed.

Conclusion

According to this case report, performing health triangle in fact part of six essentials and keep health (Hefze-el-Sehah) of Abu ALI Sina along with dietary changes and lifestyle modification and traditional medicine remedies, with the mechanism of changing the cell metabolism, could be an alternative medication for the treatment of gallstone disease. Further clinical studies on the impact of the health triangle guidelines on the treatment of gallstone is needed.

Conflict of interest

Authors do not have any conflict of interest to declare.

References

1. Peery AF, Crockett SD, Barritt AS, Dellon ES, Eluri S, Gangarosa LM, et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. Gastroenterology. 2015 ;149(7):1731-41.

2. Heaton KW, Braddon FE, Emmett PM, Mountford RA, Hughes AO, Bolton CH, et al. Why do men get gallstones? Roles of abdominal fat and hyperinsulinaemia. European Journal Of gastroenterology and hepatology. 1991;3:745-51.

3. Moerman CJ, Smeets FW, Kromhout D. Dietary risk factors for clinically diagnosed gallstones in middle-aged men A 25-year follow-up study (The Zutphen study). Annals of epidemiology. 1994 ;4(3):248-54.

4. Misciagna G, Centonze S, Leoci C, Guerra V, Cisternino AM, Ceo R, et al. Diet, physical activity, and gallstones—a population-based, case-control study in southern Italy. The American journal of clinical nutrition. 1999 ;69(1):120-6.

5. Leitzmann MF, Giovannucci EL, Rimm EB, Stampfer MJ, Spiegelman D, Wing AL, et al. The relation of physical activity to risk for symptomatic gallstone disease in men. Annals of internal medicine. 1998 ;128(6):417-25.

6. Leitzmann MF, Rimm EB, Willett WC, Spiegelman D, Grodstein F, Stampfer MJ, et al. Recreational physical activity and the risk of cholecystectomy in women. New England Journal of Medicine. 1999 ;341(11):777-84.

7. Greenberger NJ, Paumgartner G. Diseases of the gallbladder and bile ducts. In: Braunwald E., Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. (eds). Harrison's Principles of Internal Medicine, 15th Edn. New York: McGraw-Hill, 2001: 1776–1788.

8. Memon MA, Deeik RK, Maffi TR, Fitzgibbons Jr RJ. The outcome of unretrieved gallstones in the peritoneal cavity during laparoscopic cholecystectomy. Surgical endoscopy. 1999 ;13(9):848-57.

9. Walsh RM, Henderson JM, Vogt DP, Mayes JT, Grundfest-Broniatowski S, Gagner M, et al. Trends in bile duct injuries from laparoscopic cholecystectomy. Journal of Gastrointestinal Surgery. 1998 ;2(5):458-62.

10. Avicenna TbSA. Canon of Medicine (Qanun dar Tib). Soroosh Publisher, 1991(51 edition).

11. Cecil Essentials of Medicine the edituin. Ivor J. Benyamin, Robert C. Griygs, Edward J. wing, Grey Fite.

12. Moga MM. Alternative treatment of gallbladder disease. Medical hypotheses. 2003 ;60(1):143-7.

13. Breneman JC. Allergy elimination diet as the most effective gallbladder diet. Annals of Allergy. 1968 ;26(2):83-7.

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CASE REPORT

Not everything is what it seems

No todo es lo que parece

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Abstract

We report a case of a 36-year-old man, with previous medical history of marihuana consumption, high blood pressure and asthma. He came to the emergency room with a 4-month history of altered behaviour and a fall from his own height. After conducting complementary tests, diagnoses were acute renal failure secondary to rhabdomyolysis and brain space occupying lesions (SOLs) under study. Initial suspicion of brain metastasis radically changed with the results of brain magnetic resonance imaging and thoraco-abdomino-pelvic computed tomography. This lead us to focusing on inflammatory-granulomatous aetiology, with our first option being neurosarcoidosis, later confirmed by the histological results of an adenopathic biopsy performed by fiberoptic bronchoscopy.

Resumen

Se presenta el caso de un hombre de 36 años, con antecedentes de consumo de marihuana, hipertensión arterial y asma. Acudió a urgencias con una historia de 4 meses de alteración del comportamiento y una caída desde su propia altura. Tras la realización de pruebas complementarias, los diagnósticos fueron de insuficiencia renal aguda secundaria a rabdomiólisis y de lesiones cerebrales ocupantes de espacio (SOL) en estudio. La sospecha inicial de metástasis cerebral cambió radicalmente con los resultados de la resonancia magnética cerebral y la tomografía computarizada toraco-abdomino-pélvica. Esto nos llevó a centrarnos en la etiología inflamatoria-granulomatosa, siendo nuestra primera opción la neurosarcoidosis, posteriormente confirmada por los resultados histológicos de una biopsia adenopática realizada por broncoscopia de fibra óptica.

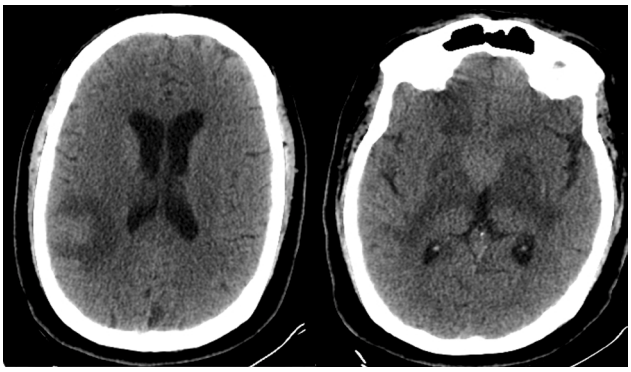
Case description

This is a 36-year-old man, a marijuana smoker (between 5-6 cigarettes a day), with a medical history of arterial hypertension treated with enalapril (unknown blood pressure controls) and bronchial asthma treated with salbutamol on demand.

The patient is brought to the emergency room by the emergency services after being unable to get up after a fall from his own height while at his home. During anamnesis, the patient and his relatives explained a 4 month history of blurry vision, behavioral alteration, difficulty walking and a 30 kg weight gain. He had been evaluated 72 hours previously by a psychiatrist in the emergency department, ruling out an eating disorder and recommending follow-up by Primary Care.

Upon initial assessment at the emergency department, the patient presented with a fever of 37,8ºC, with no clear signs of infection in the physical examination, displaying only spatial-temporal disorientation, verbhorrea, a cushingoid phenotype (full moon face, abdominal striate and buffalo hump), increased base of support and functional impotence in both shoulders due to pain. Blood tests showed acute renal failure with creatinine of 3.54 mg / dl in the context of rhabdomyolysis (creatine kinase of 3879 U / l). A brain computed tomography (CT) without contrast was requested, highlighting two intracranial lesions on the hypothalamic and right parietal level (**Figure 1**).

Figure 1: Simple head CT without contrast. In the image on the left, we can see a slightly hyperdense image of approximately 20x17mm at the right parietal level, isodendal with the brain parenchyma, with perilesional hypodensity suggestive of edema. On the right, a slightly hyperdense image of approximately 23x20x22mm is observed located at the hypothalamic level and extending towards the third ventricle, with perilesional hypodensity that extends to both internal capsules, suggestive of vasogenic edema.



With these results, the decision was made to admit the patient in the Internal Medicine department with initial diagnoses of acute renal failure secondary to rhabdomyolysis and brain lesions to be studied in a patient with a cushingoid phenotype.

Our main suspicion when faced with two brain lesions was a metastatic neoplastic aetiology, for which tumor markers, urinary cortisol, a full body CT with contrast and brain magnetic resonance imaging (MRI) were requested to better characterize the lesions. The first results showed negative tumor markers, normal urine cortisol and a CT scan that reported 5 pulmonary micro-nodules, inframillimetric mediastinal and retroperitoneal lymphadenopathies, without other notable alterations. Before obtaining the brain MRI results and due to the now low suspicion of a tumor, it was decided to expand the study at hormonal, infectious and autoimmune levels. It was decided to request quantiferon, serologies for HIV, toxoplasma, Treponema pallidum, HCV and HBV, which were negative. Likewise, an autoimmunity screen was requested (ANA, rheumatoid factor, C3, C4, CH 50, ECA and ANCA) which were also negative. Regarding the hormonal study, it showed hypogonadotropic hypogonadism and a prolactin of 92 ng / ml without macroprolactinemia. It was decided to extend the study of haematological neoplasia with a serum proteinogram, LDH and beta2-microglobulin, which were normal.

Finally, the brain MRI reported a main lesion in the hypothalamic region that cranially compressed the 3rd ventricle and fornices (**Figure 2** and **3**), infiltrated the bilateral retrochiasmatic optic pathway, sparing the hypothalamus. The imaging of the second lesion visualized on brain CT, was discussed with radiology, informing us that it was a small lesion with significant linear leptomeningeal hyper-enhancement at the parietal and temporal level.

Figure 2: T1 axial brain MRI. The left image shows a lesion in the bottom of the sulcus with vasogenic edema. In the image on the right, a lesion occupying the hypothalamic region can be seen which cranially compresses the 3rd ventricle and fornices.

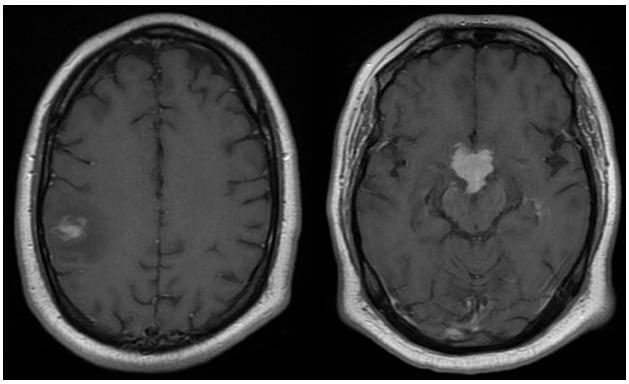
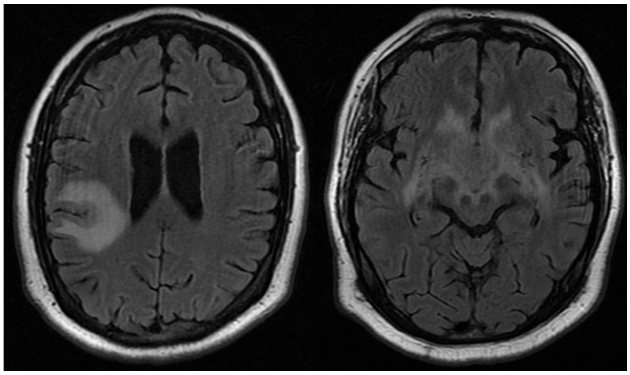


Figure 3: FLAIR T2 brain MRI. The image on the left shows thick linear leptomeningeal enhancement (we did not see a lesion at the bottom of the sulcus in this image). As for the image on the right, we appreciate a lesion in the hypothalamic area that compresses the 3rd ventricle and fornices cranially with significant edema.



Before requesting further diagnostic tests, the patient presented with an acute hypernatremia of 161 mEq/l, compatible with diabetes insipidus of central origin, showing good response to treatment with desmopressin.

Discussion

The importance of this clinical case lays not only in the correct differential diagnosis of brain SOLs, but also on the correct interpretation of the imaging tests requested. Initially, due to the performance of a brain CT without contrast in the context of acute renal failure, the diagnostic orientation was a possible neoplasm with paraneoplastic Cushing's syndrome and brain metastases. The results of the thoraco-abdomino-pelvic CT and brain MRI changed our view of the case completely.

A new differential diagnosis began, focusing on an inflammatory-granulomatous aetiology, with the most likely being neurosarcoidosis, Langerhans cell histiocytosis, and less likely granulomatosis with polyangiitis. Due to location, we also took into account primary neoplasia such as pituicytoma and suprasellar germinoma, with primary brain lymphoma being less likely.

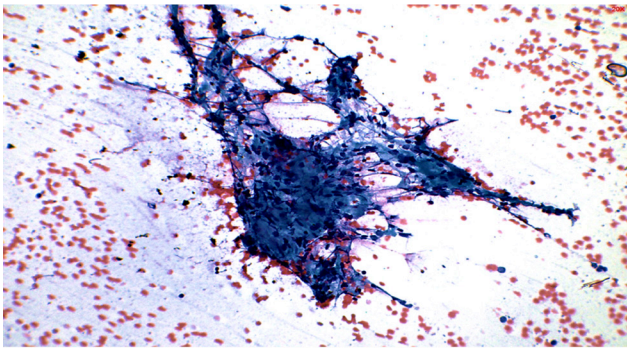
Our main suspicion focused on sarcoidosis with extra-pulmonary involvement, with between 5-10% presenting brain involvements. On the one hand, cerebral location and infiltration of the optic pathway is typical in neurosarcoidosis. This became our main diagnostic option due to its cerebral location and infiltration of the optic pathway. Likewise, due to hypothalamic inflammation, neuroendocrine alterations such as diabetes insipidus, appetite alteration and hypogonadotropic hypogonadism are also typical, as in the case of our patient. It is important to note that meningeal involvement can lead to confusion regarding infectious meningitis. Functional impotence in both shoulders also stood out upon physical examination, and is consistent with proximal myopathy that usually appears in cases of sarcoidosis.

Regarding the second option, Langerhans cell histiocytosis presents brain involvement in 6% of patients. In our clinical case, brain involvement aside, the typical picture of cystic pulmonary lesions did not match. In addition, the patient did not present osteolytic lesions (cranial being the most typical) or skin lesions such as eczematous rash or oral involvement.

Final clinical judgment

Pulmonary involvement and mediastinal lymphadenopathies visualized in the computed tomography lead us to request a fiberoptic bronchoscopy to perform a bronchoalveolar lavage and biopsy of the mediastinal inframillimetric adenopathy. While the CD4 / CD8 ratio of 1.60 with 10% of the lymphoid population obtained did not meet the criteria for sarcoidosis, pathological analysis non-caseating granulomas (**Figure 4**). Taking into account these histopathological results, the imaging tests performed and the patient's clinical history, the diagnosis of sarcoidosis with brain involvement was confirmed, beginning treatment with bolus of methylprednisolone 125mg every 24h for 3 days and subsequently rituximab 1g and mycophenolate mofetil 500mg every 12h. When the patient attended a check-up one month later, he presented a decrease in the size of the brain lesion and resolution of the myopathy.

Figure 4: Non-necrotizing granulomatous lymphadenitis. Aggregates of epithelioid-like histiocytes accompanied by lymphocytes and isolated plasma cells are observed in a hematic background. (20x Papanicolaou stain).



Conflict of interest

Authors do not have any conflict of interest to declare.

References

- Emile JF, Abla O, Fraitag S, Horne A, Haroche J, Donadieu J, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood 2016; 127:2672.

- Fritz D, Van de Beek D, Brouwer MC. Clinical features, treatment and outcome in neurosarcoidosis: systematic reviez and meta-analysis. BMC Neurol. 2016; 16(1):220.

- González de la Aleja P, García M, Sempere A, Menchi M, Sánchez R, Ramos J, et al. Linfadenitis granulomatosa, diferencias clínicas y en pruebas complementarias de los distintos diagnósticos finales. Rev Clin Esp. 2017; 217:1436.

- Ibitoye RT, Wilkins A, Scolding NJ. Neurosarcoidosis: a clinical approach to diagnosis and management. J Neurol. 2017; 264(5):1023-8.

- Rothman R, Weinreb J, Zucconi W, et al. Diagnostic Value of CT of Chest, Abdomen, and Pelvis in Patients With Solitary and Multiple Brain Lesions. Am J Roentgenol 2020; 214:636

- Voortman M, Drent M, Baughman RP. Management of neurosarcoidosis: a clinical challenge. Curr Opin Neurol. 2019; 32(3):475-83.

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CASE REPORT

Disfunción biventricular grave

Severe biventricular dysfunction

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Resumen

Varón de 81 años con shock cardiogénico rápidamente progresivo tras cirugía de revascularización coronaria.

Palabras clave: Amiloidosis, insuficiencia cardiaca, mieloma múltiple.

Abstract

An 81-year-old man with rapidly progressive cardiogenic shock after coronary artery bypass surgery.

Key words: Amyloidosis, heart failure, multiple myeloma.

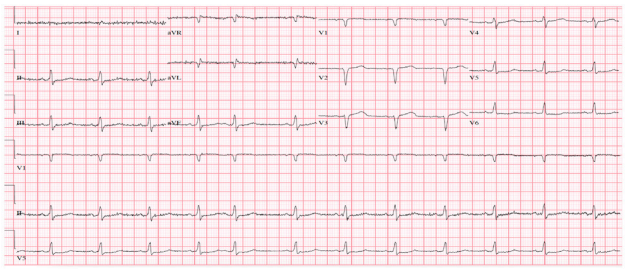
Presentación del caso

Se trata de un varón de 81 años, sin alergias medicamentosas conocidas ni hábitos tóxicos, independiente para las actividades básicas de la vida diaria y sin deterioro cognitivo conocido. Como antecedentes patológicos presenta dislipemia en tratamiento farmacológico y aterosclerosis carotidea leve.

Consulta en clínica privada por cuadro de una semana de evolución de angina, disnea y edemas en extremidades inferiores. Con la anamnesis y pruebas complementarias realizadas se orientó como enfermedad coronaria con afectación de tronco coronario izquierdo y tres vasos, sin movilización de biomarcadores. Se derivó al hospital público de referencia para tratamiento.

A su llegada, exploración física anodina, analíticamente destacaba discreta alteración de la función renal, GGT de 102 U/L, hemoglobina 12,2 g/dL y troponinas de 245,6ng/L. El electrocardiograma mostraba ritmo sinusal, QS en V1-V2, bajos voltajes y pobre progresión de R en precordiales (**Figura 1**). El ecocardiograma transtorácico (ETT) informó de FEVI 53%, anomalías de contracción segmentaria con hipocinesia inferior y disfunción diastólica moderada. Se decidió intervenir con realización de cuádruple bypass el tercer día de ingreso, sin complicaciones durante la intervención.

Figure 1: Electrocardiograma.



En el postoperatorio presentó evolución tórpida por disfunción biventricular severa objetivada por ETT con ventrículo izquierdo hipertrófico y rígido. A pesar de soporte vasoactivo el paciente persistía con inestabilidad hemodinámica, empeoramiento de la función renal y anasarca, requiriendo terapia de sustitución renal. Presentó varios episodios de taquicardia ventricular sostenida refractaria a tratamiento con amiodarona, presentando finalmente el día +18 de ingreso, parada cardiorespiratoria. Se procedió a la reesternotomía urgente, recuperando circulación espontánea tras masaje cardíaco interno. No se hallaron alteraciones macroscópicas evidentes por lo que se procedió a coronariografía emergente. Se objetivó estenosis de uno de los injertos, colocándose un stent farmacoactivo. A pesar de ello, el paciente presentó mala evolución siendo éxitus el día +20 de ingreso.

Discusión del caso

Desarrollaremos el diagnóstico diferencial entre las principales etiologías de shock cardiogénico postcardiotomía (**Figura 2**).

Figure 2: Etiologías del shock cardiogénico.

De entre las principales complicaciones postcirugía cardíaca (postCCA), podemos descartar –por los datos analíticos, clínicos, ecocardiográficos, datos intraoperatorios y de la monitorización invasiva– de forma relativamente sencilla: la pericarditis constrictiva, el taponamiento, el tromboembolismo pulmonar, el sangrado y la vasoplegía.

A continuación, discutiremos el resto de los diagnósticos diferenciales:

1. Infarto agudo de miocardio (IAM) tipo V, es decir, relacionado con el procedimiento.
Durante una cirugía de bypass se produce daño miocárdico que se traduce en una elevación de troponina ultrasensible (Tn-us). Este daño es secundario a diversos factores, como la calidad de la cardioprotección, la inflamación sistémica y miocárdica producidas por la intervención, el propio trauma directo sobre el miocardio, así como por un evento isquémico.

En ocasiones este puede ser lo suficientemente significativo como para producir un IAM secundario al procedimiento y con ello, una elevación Tn-us marcada. De hecho, se ha descrito que el grado de elevación de Tn-us en el postoperatorio temprano (<48 horas) se correlaciona con el hallazgo de realce tardío de gadolinio sugestivo de IAM en la resonancia cardíaca posterior[1].

De acuerdo a la 4ª definición de infarto, un IAM relacionado con la cirugía cardíaca se define como una elevación de Tn-us >10 veces por encima del límite superior de la normalidad durante las primeras 48h y algún otro criterio de los siguientes: cambios en ECG, obstrucción del bypass o arteria nativa y/o aparición de alteraciones segmentarias[2].

Por tanto, el paciente cumple criterios. Además, presenta inestabilidad eléctrica con taquicardias ventriculares (TV) que podrían ser consecuencia de un substrato isquémico. Sin embargo, el cateterismo mostró una lesión y no una oclusión del bypass, sin poder explicar esta por sí sola la disfunción biventricular severa encontrada. Igualmente, tampoco se objetivaron alteraciones segmentarias y, la elevación de Tn-us, no sería la esperable en un infarto extenso que ocasionara disfunción ventricular relevante. Por otra parte, si suponemos que esta es la causa, después de la revascularización debería haber mejorado en cierto grado, cosa que no ocurrió. Por todo ello, se plantea la duda razonable de que realmente esta lesión que vimos en el bypass no fuese la causa del cuadro clínico sino la consecuencia de la situación de bajo gasto y parada cardiorrespiratoria previa.

2. Miocarditis

Se trata de un paciente en shock cardiogénico sin etiología establecida, con TV, elevación de Tn-us y disfunción ventricular izquierda (VI) global. Por lo que, sí cumple criterios diagnósticos[3]. Aunque no tenemos apoyo de pruebas complementarias como la resonancia cardíaca, ni tampoco hemos excluido la enfermedad coronaria.

Dada la evolución, estaríamos hablando de una miocarditis fulminante, cuyas causas más probables en este caso serían una miocarditis linfocítica o de células gigantes. Especialmente la última, aunque la incidencia es mayor en gente de edad media, pues se suele presentar con insuficiencia cardíaca (IC) aguda, TV –siendo esto más frecuente que en otras etiologías–, presenta mal pronóstico con poca respuesta al tratamiento habitual y rápida evolución. Respecto a la miocarditis linfocítica, si bien el curso clínico es similar, esta suele cursar con fiebre y leucocitosis que no tiene nuestro paciente[4].

No hay ningún caso reportado en la literatura de miocarditis inmediata postCCA. Es posible que tuviese miocarditis previa a la intervención, de hecho, en la ecocardiografía inicial tenía derrame pericárdico ligero. Se ha descrito que niveles más bajos de Tn-us se asocian a peor pronóstico en el seno de una miocarditis aguda fulminante. Esto se debe a la presencia de anticuerpos antiTn-us que podrían interferir con la detección y, también con un diagnóstico e inicio de terapias adecuadas más tardío[5].

En contra de este diagnóstico, no disponemos de causa evidente, aunque esto ocurre en la mayoría de los casos, no hay elevación de reactantes de fase aguda ni tampoco se puede afirmar que la enfermedad coronaria detectada no fuera determinante.

3. Miocardiopatía de sepsis

En el contexto de una sepsis, el aumento de citoquinas inflamatorias puede producir un daño sobre los cardiomiocitos, pudiendo provocar lo que se conoce como miocardiopatía inducida por sepsis. Esta se define como dilatación y disfunción VI en contexto de sepsis. Se observa afectación de la contractilidad global sin segmentarismos típicos de otras afecciones. Confiere peor pronóstico al

cuadro infeccioso. Sin embargo, si el shock séptico se recupera, la disfunción mejora en unos 7-10 días[6].

Con respecto a nuestro paciente, no existe cuadro séptico por lo que se considera improbable.

4. Miocardiopatía de estrés o TakoTsubo

Se define como disfunción sistólica VI aguda y transitoria. Aparece tras desencadenantes como el estrés emocional o físico. Fisiopatológicamente se cree que se produce en contexto de hiperestimulación del sistema nervioso simpático. Ello conlleva liberación masiva de catecolaminas, que resulta tóxica produciendo vasoconstricción microvascular y pudiendo dar lugar a síntomas compatibles con IAM pero con arterias epicárdicas normales, así como disfunción VI con alteraciones segmentarias (típicamente acinesia apical y media e hipercontractilidad basal). Puede cursar con amplio espectro desde IC, inestabilidad eléctrica con taquiarritmias hasta shock cardiogénico[7].

En nuestro caso, existe un trigger claro (CCA) pero no tenemos alteraciones segmentarias típicas, tampoco evolución ECG típica, ni podemos afirmar que la enfermedad coronaria detectada no jugase un papel relevante ni hemos descartado miocarditis. Por lo tanto, se considera poco probable.

5. Miocardiopatía restrictiva (MCR).

El ETT previo al procedimiento describía hipertrofia de VI en un paciente no hipertenso y sin valvulopatías significativas, con disfunción diastólica avanzada y derrame pericárdico ligero. Esto añadido a que en el ETT postoperatorio se describe una disfunción diastólica grado 3 (es decir, patrón restrictivo) con VI hipertrófico y rigidez importante, nos lleva a pensar como posibilidad diagnóstica la MCR.

Respecto a la etiología, dado el contexto clínico, fundamentalmente contemplamos MCR idiopática y amiloidosis[8,9]. La MCR idiopática puede ser genética o esporádica y aparecer a cualquier edad (más del 15% de los pacientes son mayores de 80 años). Se debe a un aumento de la sensibilidad de los miofilamentos al calcio, aumento del depósito de colágeno y de desmina8. No hay ningún caso reportado de empeoramiento clínico abrupto con evolución a shock cardiogénico y es una entidad rara, poco probable.

En cuanto a la amiloidosis, es la miocardiopatía infiltrativa más frecuente, y continúa estando infradiagnosticada. Aparte de los hallazgos antes descritos, también nos apoyaría el diagnóstico el ECG. En él se observan bajos voltajes y patrón de pseudoinfarto en derivaciones precordiales derechas.

De entre los tipos de amiloidosis con afectación cardíaca, consideraríamos la senil, transtirretina o también llamada wild type y por cadenas ligeras o AL. La etiología senil sería más probable por la edad, sin embargo, el ETT suele ser más expresivo con más HVI, aurículas más dilatadas, etc. Además, no se han descritos casos de empeoramiento rápido postoperatorio. De hecho, hasta un 20% de todas las estenosis aórticas que se intervienen tienen amiloidosis senil y no se observan complicaciones. La amiloidosis AL, por su parte, se manifiesta con HVI más leve, incluso sin ella. Encajaría con nuestro paciente pues además tiene signos extracardíacos (anemia, enfermedad renal crónica). Se han descrito casos de empeoramiento brusco con taquiarritmias y bradiarritmias, disfunción ventricular severa de aparición en 5-10 días de diferencia con la última ETT previa, incluso hasta el punto de shock cardiogénico. Y esto sin necesidad de presentar ventrículos muy hipertróficos, pues las propias cadenas ligeras en sangre pueden provocar un efecto cardiotóxico sin que se hayan depositado en exceso sobre el miocardio[10]. Incluso hay casos descritos de mortalidad no esperada en el postoperatorio inmediato de CCA que han sido diagnosticados de amiloidosis AL en la necropsia[11].

Por todo ello, la amiloidosis se considera una causa probable del cuadro clínico del paciente.

Examen anatómico y patológico postmortem

En la necropsia, se inspeccionaron los injertos del cuádruple by-pass, sin encontrar dehiscencias ni otras alteraciones. El corazón pesó 700 g y al corte mostró hipertrofia de ventrículo izquierdo y áreas parduzcas en el miocardio. Se realizó la técnica de cloruro de trifeniltetrazolio, que mostró una tinción parcheada. En el estudio microscópico se observaron extensas áreas de fibrosis estrellada y depósitos en ambos ventrículos de material amorfo eosinófilo, tanto en el intersticio como alrededor de los vasos. Estos depósitos se tiñeron de rojo intenso con la técnica de rojo Congo, con viraje a verde bajo luz polarizada, lo que confirmó que se trataba de depósitos de amiloide (**Figuras 3** y **4**). No se vieron signos de infarto agudo.

Estos depósitos se vieron también en arterias de los espacios porta, en vasos del tejido adiposo alrededor de las glándulas suprarrenales, y en algunos vasos renales, aunque sin afectación glomerular.

Para tipificar los depósitos de amiloide, se realizaron técnicas de inmunohistoquímica para amiloide A, y cadenas ligeras kappa y lambda. De éstas, el amiloide A fue negativo, por lo que se descartó una amiloidosis secundaria (AA); la tinción para cadenas lambda también fue negativa, y la de kappa, positiva, por lo que se orientó como una amiloidosis sistémica tipo AL con depósito de cadenas ligeras kappa (**Figura 5**).

Figure 3: Miocardio. Estructura vascular e intersticio con depósitos de amiloide (Rojo Congo, x200).

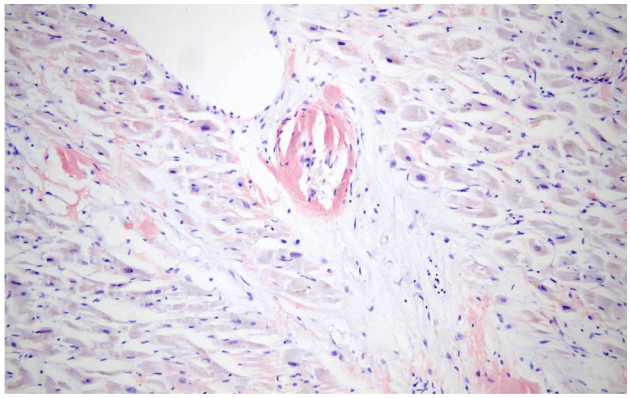


Figure 4: Misma área bajo luz polarizada.

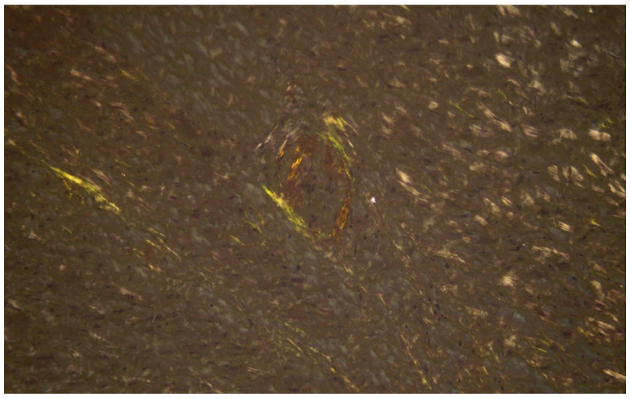
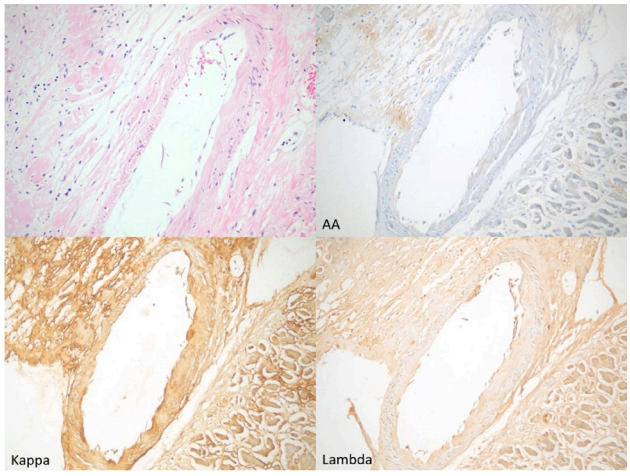


Figure 5: Vaso cardíaco con depósitos de amiloide. (Hematoxilina-eosina, inmunohistoquímicas AA, Kappa y Lambda, x200).



En el estudio de la médula ósea, se observó que esta mostraba marcada hipercelularidad a expensas de una proliferación de células plasmáticas, con positividad para CD38 y CD138, y que representaban más del 20% de la celularidad de la muestra de médula ósea. Mediante técnicas de hibridación in situ se confirmó la clonalidad de las células plasmáticas, que producían cadenas ligeras kappa. La técnica para detectar cadenas ligeras lambda fue estrictamente negativa (**Figuras 6** y **7**).

Figure 6: Médula ósea (hematoxilina-eosina, x400).

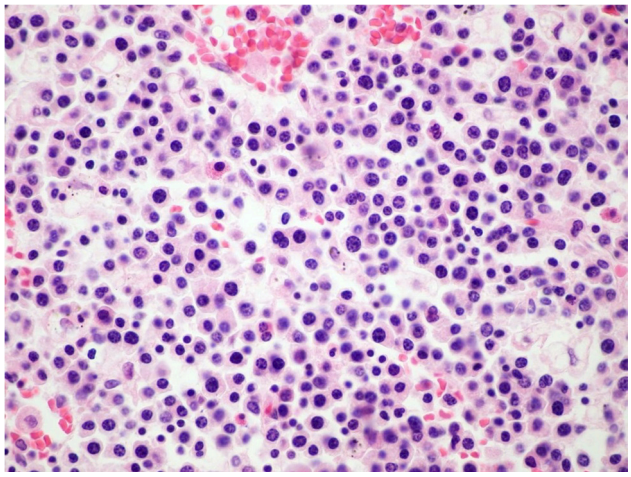
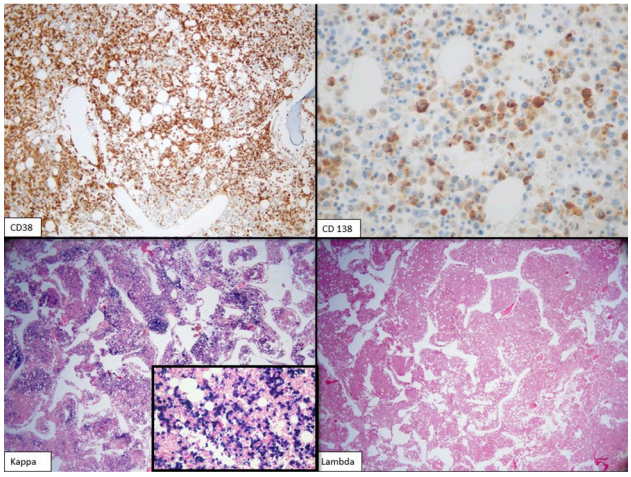


Figure 6: Médula ósea (Inmunohistoquímica para CD38 x100; CD138 x600; hibridación in situ kappa x20 y x400; hibridación in situ lambda x20).



En el resto de órganos se vieron signos de disfunción multiorgánica, con necrosis tubular renal, isquemia hepatocitaria centrolobulilar, congestión pulmonar y signos de hipoxia cerebral. Como hallazgos incidentales se identificaron un microtumor papilar de tiroides y un leiomioma en colon.

En conclusión, se trata de un paciente postquirúrgico al que se le encontró una amiloidosis sistémica AL con plasmocitosis medular compatible con mieloma múltiple, que murió de fallo cardíaco y la consecuente disfunción multiorgánica.

La amiloidosis es un conjunto de enfermedades producidas por el plegamiento anómalo de proteínas, las cuales se depositan en los tejidos y pueden llevar al fallo del órgano. Existen numerosos tipos, como el de este caso, que se produce por depósitos de cadenas ligeras que son producidas por células plasmáticas clonales. Los síntomas de la amiloidosis sistémica son poco específicos, por lo que es una enfermedad infradiagnosticada[12]. Existen algunos hallazgos específicos como la púrpura periorbitaria

o la macroglosia, pero sólo ocurren en el 15% de los pacientes[13]. En nuestro caso, no se observó ninguno de estos dos signos. La incidencia de la amiloidosis AL es de 12 casos por millón de personas al año[12]. Entre el 60-75% de los pacientes tendrán afectación cardíaca, entre el 50-70% renal, y en menor medida mostrarán afectación hepática (20%) o gastrointestinal (10%)[14].

Conflicto de intereses

Los autores declaran no tener ningún conflicto de interés.

References

1. Alam, S.R., Stirrat, C., Spath, N. et al. Myocardial inflammation, injury and infarction during on-pump coronary artery bypass graft surgery. J Cardiothorac Surg 12, 115 (2017). https://doi.org/10.1186/s13019-017-0681-6

2. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth Universal Definition of Myocardial Infarction (2018). J Am Coll Cardiol. 2018 Oct 30;72(18):2231-2264. doi: 10.1016/j.jacc.2018.08.1038. Epub 2018 Aug 25. PMID: 30153967.

3. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, Fu M, Heliö T, Heymans S, Jahns R, Klingel K, Linhart A, Maisch B, McKenna W, Mogensen J, Pinto YM, Ristic A, Schultheiss HP, Seggewiss H, Tavazzi L, Thiene G, Yilmaz A, Charron P, Elliott PM; European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2013 Sep;34(33):2636-48, 2648a-2648d. doi: 10.1093/eurheartj/eht210. Epub 2013 Jul 3. PMID: 23824828.

4. Cooper LT Jr. Myocarditis. N Engl J Med. 2009 Apr 9;360(15):1526-38. doi: 10.1056/NEJMra0800028. PMID: 19357408; PMCID: PMC5814110.

5. Freixa X, Sionis A, Castel A, Guasch E, Loma-Osorio P, Arzamendi D, Roig E, Perez-Villa F. Low troponin-I levels on admission are associated with worse prognosis in patients with fulminant myocarditis. Transplant Proc. 2009 Jul-Aug;41(6):2234-6. doi: 10.1016/j.transproceed.2009.06.012. PMID: 19715884.

6. Sato R, Nasu M. A review of sepsis-induced cardiomyopathy. J Intensive Care. 2015 Nov 11;3:48. doi: 10.1186/s40560-015-0112-5. PMID: 26566443; PMCID: PMC4642671.

7. Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, Cammann VL, Crea F, Galiuto L, Desmet W, Yoshida T, Manfredini R, Eitel I, Kosuge M, Nef HM, Deshmukh A, Lerman A, Bossone E, Citro R, Ueyama T, Corrado D, Kurisu S, Ruschitzka F, Winchester D, Lyon AR, Omerovic E, Bax JJ, Meimoun P, Tarantini G, Rihal C, Y-Hassan S, Migliore F, Horowitz JD, Shimokawa H, Lüscher TF, Templin C. International Expert Consensus Document on Takotsubo Syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology. Eur Heart J. 2018 Jun 7;39(22):2032-2046. doi: 10.1093/eurheartj/ehy076. PMID: 29850871; PMCID: PMC5991216.

8. Pereira NL, Grogan M, Dec GW. Spectrum of Restrictive and Infiltrative Cardiomyopathies: Part 1 of a 2-Part Series. J Am Coll Cardiol. 2018 Mar 13;71(10):1130-1148. doi: 10.1016/j.jacc.2018.01.016. PMID: 29519355.

9. Pereira NL, Grogan M, Dec GW. Spectrum of Restrictive and Infiltrative Cardiomyopathies: Part 2 of a 2-Part Series. J Am Coll Cardiol. 2018 Mar 13;71(10):1149-1166. doi: 10.1016/j.jacc.2018.01.017. PMID: 29519356.

10. Garcia-Pavia P, Rapezzi C, Adler Y, Arad M, Basso C, Brucato A, Burazor I, Caforio ALP, Damy T, Eriksson U, Fontana M, Gillmore JD, Gonzalez-Lopez E, Grogan M, Heymans S, Imazio M, Kindermann I, Kristen AV, Maurer MS, Merlini G, Pantazis A, Pankuweit S, Rigopoulos AG, Linhart A. Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2021 Apr 21;42(16):1554-1568. doi: 10.1093/eurheartj/ehab072. PMID: 33825853; PMCID: PMC8060056.

11. Fitzmaurice GJ, Wishart V, Graham AN. An unexpected mortality following cardiac surgery: a post-mortem diagnosis of cardiac amyloidosis. Gen Thorac Cardiovasc Surg. 2013 Jul;61(7):417-21. doi: 10.1007/s11748-012-0164-6. Epub 2012 Oct 21. PMID: 23086612.

12. Gertz MA, Dispenzieri A. Systemic Amyloidosis Recognition, Prognosis, and Therapy: A Systematic Review. *JAMA*. 2020;324(1):79-89. doi:10.1001/jama.2020.5493

13. Siddiqi OK, Ruberg FL. Cardiac amyloidosis: an update on pathophysiology, diagnosis, and treatment. Trends Cardiovasc Med. 2018;28(1):10-21. doi:10.1016/j.tcm.2017.07.004

14. Fotiou D, Dimopoulos MA, Kastritis E. Systemic AL Amyloidosis: Current Approaches to Diagnosis and Management. *Hemasphere*. 2020;4(4):e454. doi:10.1097/HS9.0000000000000454

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