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ORIGINAL

Universal access to sexual and reproductive health services among women affected by HIV in Morocco: What reality?

Acceso universal a los servicios de salud sexual y reproductiva entre las mujeres afectadas por el VIH en Marruecos: ¿Qué realidad?

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Abstract

Background: HIV remains a major global public health problem, resulting in 40.1 million deaths since the beginning of the epidemic. In 2021, 38.4 million people were living with HIV, 54% of who are women and girls. In Morocco, the number of people living with HIV (PLHIV) is 23,000 of which 63% of cases have been reported in three regions (Souss Massa, Casablanca and Marrakech). The objective of this study describe the barriers to access sexual and reproductive health for women living with HIV in Marrakech, Morocco.
Methods: This study is a mixed quantitative and qualitative descriptive study. The study population is composed of women living with HIV receiving health services in the prefecture of Marrakech. A questionnaire survey and interviews were conducted to gather descriptive data on this population, as well as to collect information on the accessibility of sexual and reproductive health care for this category of women.
Results: The average age of the women interviewed was 38.64 ± 8.58 (20 to 58 years). The majority of the women (89%) were from Marrakech with a clear predominance of urban areas (72%). The difficulties in accessing reproductive health services were reported by women surveyed, particularly for gynecological examinations (66.70%), family planning (33.30%) and psychosocial support (66.70%). The results of this study showed that HIV-positive women's access to reproductive health services depends on several barriers at different levels. Stigma and discrimination are still the main concerns of HIV-positive women in our context in addition to economic barriers.
Conclusion: Measures to improve access to and utilization of reproductive health services for women living with HIV must integrate all the biological, psychological and social (attributes) of these women with a change in provider behavior and a reorganization of services to ensure more integration and coordination of care between different levels of care.

Keywords: Women living with HIV, sexual and reproductive health, accessibility to care.

Resumen

Antecedentes: El VIH sigue siendo un grave problema de salud pública mundial, que ha causado 40,1 millones de muertes desde el inicio de la epidemia. En 2021, 38,4 millones de personas vivían con el VIH, de las cuales el 54% eran mujeres y niñas. En Marruecos, el número de personas que viven con el VIH (PVVS) es de 23.000, de las cuales el 63% de los casos se han registrado en tres regiones (Souss Massa, Casablanca y Marrakech). El objetivo de este estudio es describir las barreras de acceso a la salud sexual y reproductiva de las mujeres que viven con el VIH en Marrakech, Marruecos.
Métodos: Se realiza un estudio descriptivo mixto cuantitativo y cualitativo. La población de estudio está compuesta por mujeres que viven con el VIH y reciben servicios sanitarios en la prefectura de Marrakech. Se realizó una encuesta por cuestionario y entrevistas para recopilar datos descriptivos sobre esta población, así como para recoger información sobre la accesibilidad de la atención sanitaria sexual y reproductiva para esta categoría de mujeres.
Resultados: La edad media de las mujeres entrevistadas era de 38,64 ± 8,58 (20 a 58 años). La mayoría de las mujeres (89%) procedían de Marrakech, con un claro predominio de las zonas urbanas (72%). Las mujeres encuestadas señalaron las dificultades de acceso a los servicios de salud reproductiva, en particular para los exámenes ginecológicos (66,70%), la planificación familiar (33,30%) y el apoyo psicosocial (66,70%). Los resultados de este estudio mostraron que el acceso de las mujeres seropositivas a los servicios de salud reproductiva depende de varias barreras a distintos niveles. El estigma y la discriminación siguen siendo las principales preocupaciones de las mujeres seropositivas en nuestro contexto, además de las barreras económicas.
Conclusión: Las medidas para mejorar el acceso y la utilización de los servicios de salud reproductiva para las mujeres que viven con el VIH deben integrar todos los atributos biológicos, psicológicos y sociales de estas mujeres con un cambio en el comportamiento de los proveedores y una reorganización de los servicios para garantizar una mayor integración y coordinación de la atención entre los diferentes niveles de atención.

Palabras clave: Mujeres que viven con el VIH, salud sexual y reproductiva, accesibilidad a la atención.

Introduction

The number of people living with HIV worldwide at the end of 2021 is estimated to be 38.4 million, 54% of whom are women and girls aged 15 years and older, with approximately 4,900 young women aged 15-24 infected with HIV each week (UNAIDS, WHO 2022). In 2021, 650,000 people died of HIV-related causes and 1.5 million people were infected with HIV compared to three million in 1997 (WHO, 2022). The WHO African Region is the most affected region with more than 25.6 million people living with HIV in 2021 and nearly two-thirds of new HIV infections worldwide. In 2021, the percentage of new HIV infections in sub-Saharan Africa is 51%, women and girls accounted for 63% of all new HIV infections[1,2]. In Morocco, the number of people living with HIV (PLHIV) is 23,000 of which 63% of the cases have been notified in 3 Regions (Souss Massa, Casablanca and Marrakech). The number of AIDS-related deaths is estimated at 387 by the end of 2021. The incidence rate is 0.2 per 1000. According to the latest Spectrum estimates for 2020, women account for 43% of PLWHA (8,500), and fewer than 100 HIV infections will occur annually among children through mother-to-child transmission (PMTCT). The percentage of coverage of pregnant women with antiretroviral treatment to prevent mother-to-child transmission of HIV (PMTCT), meanwhile, has increased from 33% in 2011 to 62% in 2016[2,3].

The links between Sexual and Reproductive Health (SRH) and HIV are widely recognized, as HIV infections are most often sexually transmitted or associated with pregnancy, childbirth and breastfeeding, and the risk of HIV transmission and acquisition is increased in the existence of some Sexually Transmitted Infections (STI)[4]. In addition, sexual and reproductive health conditions have the same causes as HIV infections, including poverty, limited access to adequate information, gender inequality, cultural norms, and social marginalization of the most vulnerable populations[4]. Creating and organizing linkages between essential HIV services (prevention, treatment, care and support) and essential SRH services (family planning, maternal and newborn health, STI prevention and management, sexual health promotion, violence prevention and management, and unsafe abortion prevention) in national programs has important public health benefits[4,5].

That is the reason why several recommendations have been developed around the world to effectively link HIV and SRH actions. These include: the Glion Call to Action on Family Planning and HIV/AIDS in Women and Children (May 2004), the New York Call to Commit to Linking HIV/AIDS and Sexual and Reproductive Health (June 2004), the World Summit Outcome (September 2005), the Consensus Statement: Achieving Universal Access to Comprehensive Prevention of Mother-to-Child Transmission Services (November 2007), the UNAIDS "Fast-Track" three-ninety strategy, and the Global AIDS Strategy 2021-2026. Around 17.8 million women worldwide are living with HIV (UNAIDS, WHO 2016)[1,2]. These women require special treatment and care to meet their own health needs. However, violations of women's social, economic, and legal rights limit their ability to access treatment and protect their sexual and reproductive health rights6. Indeed, women face a "triple jeopardy" in the face of AIDS: as HIV-infected individuals, as mothers of infected children, and in their responsibility to care for their partners, family members, or orphans with AIDS[5,7,8]. In addition, HIV-positive women face stigma and judgmental attitudes from health care providers, economic barriers, and lack of decision-making power, which limit their access to information and choice of contraceptive methods[5,7,8]. Socially marginalized women, such as sex workers, immigrants, intravenous drug users and prisoners, face particular difficulties in accessing services because of the double discrimination they face due to their personal circumstances and their HIV status[7,9,10]. Women living with HIV infection therefore need particularly tailored access to HIV prevention services, access to accurate information, to reduce the risk of re-infection with another strain of HIV, to protect them from unwanted pregnancy, to monitor their pregnancies (ANC, PNC, etc.), and to have access to emergency obstetric care services to manage the mother and her newborn at the time of birth[11]. Several studies have explored the individual sexual and reproductive health needs of HIV-positive people and analyzed healthcare in relation to family planning, sexually transmitted infections, breast and uterine cancer, maternal protective services, and prevention of mother-to-child transmission[9,12]. So, organizing and strengthening existing linkages between SRH and HIV programs can provide important public health, socioeconomic and individual benefits[4], including: increased access to and utilization of SRH and HIV services, access to sexual and reproductive health services adapted to the needs of person living with HIV, reduced HIV-related stigma and discrimination, expanded care for key underserved and vulnerable populations, increased support for dual protection, improved quality of care, better understanding and protection of people's rights, and increased program effectiveness and efficiency.

In Morocco, we don't have enough information on the degree of integration of SRH and HIV/AIDS care and prevention services, and we have never explored HIV-positive women's perceptions of barriers to access and their needs and expectations regarding these SRH services (family planning, maternal and neonatal health, and breast and cervical cancer screening). Target 7 of the MDGs states that by 2030, there must be universal access to sexual and reproductive health services, including family planning, information and education, and the integration of reproductive health into national strategies and programs. To this end, we proposed to

conduct this study to identify barriers to accessing sexual and reproductive health services for HIV-positive women in areas of high HIV prevalence in Morocco.

Objective

The objectives of this study are to:

- Explore the needs and expectations of sexual and reproductive health services for women living with HIV regarding
- Describe the barriers and facilitators to accessing SRH services for women living with HIV

Method

Type of study
In order to achieve our objectives, we conducted a mixed qualitative and quantitative exploratory study. The proposed design is a single case study with multiple levels of analysis. The single case in our study is represented by the prefecture of Marrakech/Marrakech-Safi Region. Our study was conducted at the referral center of the city of Marrakech and the department of infectious diseases at the Mohammed VI University Hospital in Marrakech. The region of Marrakech is the second region most affected by HIV-AIDS in Morocco.

Study Population
The population of our study is composed of HIV-positive women attending the two services and health providers involved in the care of people affected by HIV and AIDS and SRH services (general practitioners, maternal and child health nurses, midwives, referral center staff, provincial, regional and central officials). We opted for a non-random accidental sampling for information on HIV-positive women during the nine-month data collection period. We recruited women who presented themselves at the referral center and at the infectious diseases department of the Marrakech University Hospital during the data collection period. The total number of women surveyed was 114. We conducted semi-structured interviews with health professionals, operational managers, key informants from non-governmental organizations, and managers from UN agencies involved in programs for the care of HIV-positive women of reproductive age until the information was saturated.

Data collection and analysis
The dimensions to be investigated in our study related to reproductive health services are institutional and organizational factors (accessibility, continuity of care, comprehensiveness, women-centered care, and coordination between levels), inter-relational factors (support from family and friends/community and peer support), individual factors (knowledge of the benefits and importance of accessing reproductive health services), and ethical factors (right to health and dignity of women affected by HIV/AIDS). A questionnaire administered to these 114 women provided us with information on their socio-demographic characteristics and their clinical follow-up related to a problem with reproductive health at the level of the health care services. The quantitative data were analyzed using SPSS 22.0 with a risk of error of less than 5%. First, a descriptive analysis of the socio-demographic characteristics and other variables to be studied of our population was performed.

Ethical Considerations
The research was carried out while respecting and ensuring all ethical considerations, namely, the acquisition of the agreement of the ethics committee, the authorization for data collection which was established by the supervising institution and presented to the persons concerned, the respect of anonymity and confidentiality concerning the information collected through the different data collection tools, as well as the obtaining of the free and informed written consents of the participants.

Results

We conducted 114 questionnaires face to face and 59 interviews with HIV-positive women at the study sites; the average duration of these interviews was 24.62 min. The average age of the women interviewed was 38.64 ± 8.58 (20 to 58 years). The majority of the women (89%) were from Marrakech with a clear predominance of urban areas (72%).

Socio-demographic characteristics
The majority of HIV positive women surveyed in our study are Moroccan (99.1%), and 0.9% are sub-Saharan. Women living in Marrakech represent 89% of our sample size followed by those from Safi (8%) while the cities of Essaouira, Youssoufia and El Kalaa represent only 1% each of our sample size. The urban area is the most represented with 72% of women. We found that 55% of PSF are married, 21% are divorced, 16% are widowed and 8% are single. Approximately 85% of the HPWs in our study have between one and three children. Women with primary and secondary education represent 64% of the women surveyed, while 29% of the latter have never attended school and 7% have a higher level of education. Housewives represent 75% of our sample size, while 25% of the HPWs in our series have different jobs. As for the average monthly income, it does not exceed 1500dh for 65% of the women in our study, and is between 1500 and 3000dh for 28% of them, while only 7% have a monthly income higher than 3000dh. About one third of the HPWs in our study have no medical coverage (27%) and 63% are beneficiaries of the medical assistance scheme offered to impoverished populations.

Medical characteristics

In our study, 58% of the women surveyed reported a medical history, while 10% reported having toxic habits. Women's HIV status has been increasingly discovered since 2000 until 2018, however 42% of this discovery is made incidentally or following screening campaigns organized by the Ministry of Health. In our study, 93% of the HPW are managed in a public institution and 7% in a private sector structure while 42% of the HPW are diagnosed with at least one symptom. The existence of another person affected by the virus in the family was reported by 54% of the women surveyed in our study, mainly the spouse (74% of cases) followed by the children (19% of cases).

Access to reproductive health services for HIV-positive women

The service needs reported by the women interviewed were psychosocial support (14.30%), the prevention of mother-to-child transmission (21.4%) and pregnancy and delivery follow-up (3.60% for ANC and 3.60% for PNC). The main services that the HPWs received were related to pregnancy and childbirth follow-up (14.9% in ANC and 15.80% in PNC) and family planning (14.90%). A difference between the services received and those needed by the HPWs in sexual and reproductive health. The difficulties in accessing reproductive health services were reported by women surveyed, particularly for gynecological examinations (66.70%), family planning (33.30%) and psychosocial support (66.70%). These difficulties were related to the non-availability or unawareness of the existence of the service or to inappropriate behavior of the health care personnel.

Table I: Services received versus services that HIV-positive women have difficulty accessing.

	Services received	Services that HIV-positive women have difficulty accessing
ANC	14.9% (17)	66.70% (76)
PNC	15.8% (18)	33.30% (38)
PMTCT	2.60% (3)	33.30% (38)
Gynecological problem	4.4% (5)	66.70% (76)
Family planning	14.90% (17)	33.30% (38)
Psycho-social support	15.80% (18)	66.70% (76)
Gender based violence	0.90% (1)	33.30% (38)

ANC: Ante-natal care
PNC, Post-natal care

Following the interviews conducted with the HPWs in our study, they expressed three types of needs that stem from the difficulties they have encountered and their previous experiences with the use of reproductive health services. The need most reported by these women is the need for a change in the behavior of health care providers in reproductive health facilities to ensure a good reception, a good listening ear, psychological support and respect for professional secrecy while fighting against stigmatization and discrimination.

Barriers and facilitators to accessing reproductive health services

Of the women surveyed, 27 responded that the quality of the reception, referral and listening services in reproductive health facilities was good to excellent. While six others were able to express their dissatisfaction with these services: «I have suffered at the level of health centers and for me the services they have are mediocre» Married 31 years old.

Regarding reproductive health services, 39 women surveyed expressed satisfaction with the health care provided by these services: «I am happy with my doctor's performance» Married 32 years old. While six others were dissatisfied with the lack of drugs and equipment as well as the inhumane behavior of the providers at these facilities «the health care offered by the reproductive health services is poor, they don't have enough drugs and equipment to take care of us» Married 43 years old. All 24 women in our series did not report their HIV status to the reproductive health service provider, of these women, nine did not know their HIV status at the time of using SRH «I was not aware of my illness» Married 31 years old. While 13 other women chose not to declare their seropositivity for fear of the reaction of those around them «for me it is a dangerous disease that society does not tolerate» Single, 38 years old. «…I was afraid of the reactions». Married 40 years old. The difficulties most reported by women who have already used a reproductive health service are related to expenses and the use of transportation (six women) «The difficulties I encounter are the distance from the center and the transportation expenses, especially with my son's illness». Married in rural areas 20 years old.

In addition to the high-waiting time (four women) and the fear of stigma and discrimination (four women) «I avoid going to the health center for fear of stigma» Married 27 years old. Exposure to stigma, discrimination and exclusion was reported by 13 women in different forms, either by delay or refusal to provide necessary care even when it is a therapeutic emergency «…The doctor let me wait two days before operating on me for appendicitis…» Married 32 years old, «…she refused to consult me on the grounds that she has no experience» Married 29 years old, «the nurse at the health center refused to treat me» Married 20 years old, or even by a behavior that does not respect the dignity of these women «…I am questioned in front of the patients without respect for professional secrecy» 31 years old married, «the doctor who consulted me sent me to another doctor and then she changed the blankets on which I was lying» 33 years old married, «…I was insulted and isolated I am depressed». Married 27 years old.

Discussion

Access to health care for HIV-positive women is a moral imperative, directly linked to human rights. The ultimate

goal is to ensure universal access to care for all patients. This study has shown that access to care can be affected by several factors, including HIV status. Perceived stigma in clinical settings discourages these women from accessing needed health care services. Good access to care is imperative to maintain the health, well-being and quality of life of people living with HIV/AIDS (PLWHA). The objective of this study was to explore the needs and expectations expressed by HIV-positive women regarding SRH and their experiences in accessing these services, including barriers and facilitating factors to access in the Marrakech Region Safi prefecture. We found that access to care was low among this population, with more than half of the women surveyed reporting difficulties accessing reproductive health care.

The services for which the women in our study report having the most difficulty in accessing are those related to reproductive health, in particular pregnancy monitoring, childbirth and vaccination, in addition to other surgical and stomatological services, even in the case of therapeutic emergencies, as well as the non-availability of several complementary check-ups in hospitals. These results are of particular importance because the lack of access or late access to care can lead to an alteration in the health of these women[13,14]. Social and financial conditions are not a major obstacle to accessing SRH as reported by our population, and it is mainly the stress and fear that precede their consultation that were most cited. Professional status and proximity to health facilities did not influence their access to reproductive health services. On the contrary, for some women, they prefer the hospital to be far away to limit the risk of disclosing their HIV status to their neighbours and relatives. About half of the sample reported perceived stigma from a health care provider. Few studies showed the factors and barriers that impede HIV-positive women's access to reproductive health care. In contrast, the majority of studies reviewed raised the relationship between access to care for HIV-positive women and stigma. According to these studies, it may be easier to reduce stigmatizing behaviours such as refusal to provide services than it is to reduce prejudicial attitudes such as those that reflect discomfort with HIV patients. The results of a systematic review that included 18 studies in 13 countries in Latin America and the Caribbean for a population of 5672 PLHIV, showed that the reproductive health needs of these women are not being met with greater exposure to institutional violence among PLHIV compared to non-HIV women. Stigma can be a significant barrier to health maintenance[14].

Interventions are needed to reduce perceived stigma in health care settings. Educational programs and modelling of non-stigmatizing behaviour can teach health care providers to provide humanistic care. Also, research is needed to improve our understanding of how health care providers' behaviours can negatively impact patients' experiences. The issues that emerged highlight the importance for Morocco to implement the good practice recommendations provided by the new guideline developed by WHO. These guidelines aim to create supportive environments for PLHIV with user-friendly health services that integrate SRH, providing sexual health counselling and support by trained and respectful health care providers.

Conclusion

Through this research, it seems obvious that the access of HIV positive women to reproductive health services depends on several factors at different levels; stigmatization and discrimination still constitute in our context the main concerns of HIV positive women in addition to the economic barriers with the expenses generated by HIV infection (additional check-ups, medication, travel expenses, absenteeism from work) and the social cost of the illness. Measures to improve access to and use of reproductive health services by these women must integrate all the biological, psychological and social features relating to these women with a change in the behavior of health care providers and a reorganization of services ensuring more integration and coordination of care between levels (PHC and hospital) and between specialties (infectious diseases, gynecology, pediatrics, biology).

Our study was conducted in the province of Marrakech, which is one of the regions most affected by HIV infection. However, our results cannot reflect the situation of the use of reproductive health services by HIV-positive women in other regions of the kingdom, so it would be relevant to conduct other studies in other regions, particularly those most affected by the HIV endemic.

Abréviations
HIV/AIDS (Human immunodeficiency virus infection and acquired immunodeficiency syndrome), PNC (Post-natal care), ANC (Ante-natal care), WHO (Word Health Organization), STI (Sexually transmissible disease), PMTCT (prevention of mother-to-child transmission), UNAIDS (United Nations Programme on HIV/AIDS), SRH (Sexual and reproductive health), SDGs (Sustainable Development Goals), UHC (University hospital center), NGO (non-governmental organization), SPSS (Statistical Package for the Social Sciences), HPW (HIV positive woman), MAD (Moroccan dirham).

Declarations

Ethics approval and consent to participate.
The research protocol was approved by the Ethics Committee for Biomedical Research. All study participants signed a consent form before the start of the study.

Competing interests

All authors declare no competing interest.

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Authors' contributions

Bouchra Assarag searched the literature, extracted data, and synthesized data and developed the first draft of the manuscript; Hanane HABABA carefully checked the manuscript, to provided essential methodological advice. The authors have read and approved the final manuscript.

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ORIGINAL

Relationship between self-perceived body image and excess weight among women in southern Morocco

Relación entre la imagen corporal autopercibida y el exceso de peso entre las mujeres del sur de Marruecos

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Abstract

Introduction and aim: The perception of obesity differs between societies. In developing countries, obesity was seen as a sign of high social status and a symbol of beauty and prosperity. In Western countries, obesity was viewed negatively and body control was seen as a mark of civilised society. The study, aims to describe perception womens in southern Morocco towards excess weight and the associated factors.

Methods: Study was conducted in health centres in the southern region of Morocco. Data were collected using a questionnaire. Weight and height were measured respectively by a mechanical/electronic scale and a tape measure graduated in centimetres. The perception was assessed using the Stunkard body shape assessment scale.

Results: Anthropometric data showed that 37.3% of women were normal weight, 33.9% (IC95% [30.03-37.77]) were overweight and 25.2% were obese (IC95% [21.65-28.75]). Results showed that over three quarters (76.04%; n=438) of the women were dissatisfied with their body image and 77% (n=443) of the participants considered overweight to be a disease. The study revealed that women who were satisfied with their body image (OR=0.235; CI95% [0.15-0.35]) and desire to lose weight had protective effects against developing overweight (OR=0.46; CI95% [0.30-0.70]). However, women with a positive representation of overweight women had a 1.60 risk of developing weight gain (OR=1.60; 95% CI [1.60-1.03]).

Conclusion: the study showed a change in the participants' perception of overweight. Reducing the magnitude of this public health problem requires strategies that consider this shift towards reducing the prevalence of weight gain, particularly among young women and students.

Keywords: Weight load, women, perception, overweight.

Resumen

Introducción y objetivos: La percepción de la obesidad difiere según las sociedades. En los países en desarrollo, la obesidad se consideraba un signo de alto estatus social y un símbolo de belleza y prosperidad. En los países occidentales, la obesidad se veía negativamente y el control corporal se consideraba una marca de sociedad civilizada. El estudio pretende describir la percepción que tienen las mujeres del sur de Marruecos del exceso de peso y los factores asociados.

Metodología: El estudio se realizó en centros de salud de la región sur de Marruecos. Los datos se recogieron mediante un cuestionario. El peso y la estatura se midieron respectivamente con una báscula mecánica/electrónica y una cinta métrica graduada en centímetros. La percepción se evaluó mediante la escala de evaluación de la forma corporal de Stunkard.

Resultados: Los datos antropométricos mostraron que el 37,3% de las mujeres tenían un peso normal, el 33,9% (IC95% [30,03-37,77]) tenían sobrepeso y el 25,2% eran obesas (IC95% [21,65-28,75]). Los resultados mostraron que más de tres cuartas partes (76,04%; n=438) de las mujeres estaban insatisfechas con su imagen corporal y el 77% (n=443) de las participantes consideraban que el sobrepeso era una enfermedad. El estudio reveló que las mujeres que estaban satisfechas con su imagen corporal (OR=0,235; IC95% [0,15-0,35]) y el deseo de perder peso tenían efectos protectores frente al desarrollo de sobrepeso (OR=0,46; IC95% [0,30-0,70]). Sin embargo, las mujeres con una representación positiva de las mujeres con sobrepeso tenían un riesgo de 1,60 de desarrollar un aumento de peso (OR=1,60; IC95% [1,60-1,03])

Conclusión: El estudio mostró un cambio en la percepción del sobrepeso por parte de las participantes. La reducción de la magnitud de este problema de salud pública requiere estrategias que consideren este cambio para reducir la prevalencia del aumento de peso, en particular entre las mujeres jóvenes y los estudiantes.

Palabras clave: Carga ponderal- mujeres- percepción- sobrepeso.

Introduction

Obesity is a multifactorial public health problem. Its perception differs from one society to another. In developing countries, it is considered a sign of high social status and is a cultural symbol of beauty, fertility and prosperity. In these countries, people tended to underestimate their weight. Indeed, a study in Tanzania found that both overweight and obese men and women did not perceive themselves as such[1]. In African cultures, weight is considered a sign of good health and weight loss is associated with acquired immunodeficiency syndrome (AIDS) and women are not motivated to engage in physical activity for fear of losing weight and being stigmatised as having AIDS[2]. Among South African women, thinness is not necessarily perceived as beauty; instead, being overweight is synonymous with beauty, health and higher social status. Furthermore, black African women associate being overweight with happiness, wealth and freedom from disease (such as HIV/AIDS)[3].

In contrast, a review of the literature conducted among African immigrants in Europe revealed wide variability in body image perception: African residents generally showed a preference for body weight over their immigrant counterparts, but differences in preferences emerged according to region of residence, ethnicity and social and cultural factors even within the same population. There is also evidence that subjects more aligned with Western values wanted to be thinner than those more aligned with African values[4].

In Arab society, fatness was traditionally considered a symbol of fertility and femininity[5].

In Morocco, a study found that the majority of women (90.4%) reported wanting to gain weight. To gain weight, Sahrawi women used a period of fattening through overeating, reduced physical activity and consumption of particular traditional meals. In addition, there was also the use of appetite stimulants, traditional suppositories and sometimes corticosteroids to accelerate weight gain[6].

In Western countries, obesity is a Western term, suggesting a lack of control by the individual over their own body. But such an assessment may not accurately represent the body image assessments of other cultures, or even of the Western world itself. In 19th century Europe, obesity was viewed negatively and body control was seen as a mark of civilised society. Thus, in most Western countries, people of high socio-economic status (SES) are thinner than those of low SES. In addition to lifestyle; smoking, physical activity and diet certainly have an influence on weight loss[7].

In European Union countries, 45% of individuals were dissatisfied with their weight. 40% considered it to be very high and 5% very low. Women were more dissatisfied (51%) than men (39%), although they were generally overweight or obese. The reason for dissatisfaction among women is that being overweight is a more serious problem than being underweight. For example, 46% of women in Europe thought their weight was too high, almost as many as those who were satisfied with their weight (49%). The subjective perception of being overweight is also observed in the USA, where 38% of 'normal' weight women consider themselves to be overweight[8].

On the other hand, adolescents and young adults are more interested in their body image due to the effect of the mass media, which emphasise the importance of having a normal body shape and that slim figures are symbols of beauty and good health.

Recent studies have shown that a large proportion of these young people tend to want to be thin. Indeed, a study conducted among students showed that 33.27% wanted to be thin[9]. This weight reduction is more desired in overweight subjects who are generally dissatisfied with their body image. Indeed, the study by Priya, D., et

al. showed that attempts to change weight depended on image perception and that all females who felt thin wanted to increase their weight; whereas females who felt overweight wanted to reduce their weight[10]. Thus, there is currently a change in the perception of obesity, especially among young adults and adolescents in Arab countries. Indeed, a growing proportion of Lebanese adolescents consider thinness as a sign of feminine beauty. Thinness is now valued by young urban women almost everywhere, largely due to the propagation of thin models by the media and fashion industries[11]. This is therefore an increasingly westernised view of the ideal body image, where thinness is now considered a beautiful characteristic of women[5,12].

In the light of these studies, there has been a shift in the perception of overweight and a tendency for young women in particular to become slim. In this perspective of changing perceptions, this study aimed to describe the perception of women in southern Morocco towards excess weight and the associated factors.

Materials and Methods

Study participants
This is a multicentre cross-sectional study conducted among adult women attending health centres in the provinces of the southern region of Morocco.

1 Inclusion and exclusion criteria
The participants in the study were non-pregnant women over 18 years of age who consulted health centres of the region. All women who satisfied the inclusion criteria and agreed to participate in the study were retained.

A number of 576 women consented to participate in this study, validated by the ethics committee of the Faculty of Medicine and Pharmacy of Rabat N°50/20 of 28/6/2020.

Data collection instrument
Epidemiological and socio-demographic data such as: age, sex, weight, height, ethnicity, marital status, socio-economic level was collected through a questionnaire. Weight and height were measured respectively by a mechanical/electronic scale of the SECA type and a tape measure graduated in centimetres. The body mass index (BMI) was calculated using the following formula BMI (kg/m^2) = weight (in kg)/height2 (in m^2). These measurements were made according to World Health Organization (WHO) recommendations[13]. In addition, Overweight is defined as a BMI equal to or greater than 25 kg/m^2 and obesity as a BMI equal to or greater than 30 kg/m^2 [14].

Measurement of perceived body image
Participants' perception of body image was measured by the Figure Rating Scale (Stunkard Figures)[15]. It consists of a series of nine figurines (or silhouettes) representing the face of the female body from the leanest to the fattest. Each woman is asked to indicate which one corresponds best to her (perceived body) and which one corresponds to what she would like to be (ideal body). Figures 1 and 2 represent a low weight. Figures 3 and 4 represent normal weight. Overweight is represented by Figures 5 to 7, while figures 8 and 9 represent obesity[16]. (**Figure 1**).

Figure 1: Stunkard figurines representing women from the slimmest to the heaviest.
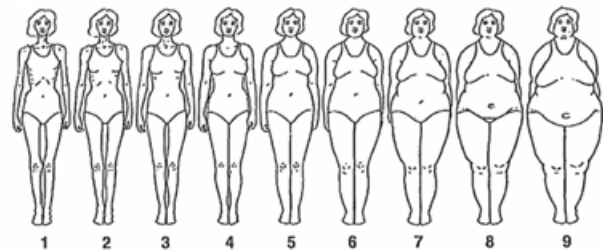
Measurement of body image satisfaction
Body image dissatisfaction was calculated as the difference between perceived weight and ideal weight (Feel minus Ideal Discrepancy (FID)). A score of 0 indicated satisfaction with body image and negative or positive scores indicated dissatisfaction with body image[17].

A body size satisfaction variable was created for each participant by subtracting the number of the silhouette selected as ideal body size from the number of the silhouette selected as personal body size. Four dummy variables were created for body size satisfaction based on the difference between personal body size and ideal body size: too small (ideal size - personal size < 1), satisfied (ideal size = personal), a little too large (ideal size - personal size = 1) and much too large (ideal size - personal size > 1)[16].

Statistical analyses
Data processing was done by SPSS version 13.0 statistical data processing software after coding. The qualitative variables were described in numbers and percentages and then compared by chi-square test. The quantitative variables were described as mean ± standard deviation. Factors associated with obesity/overweight were determined by binary logistic regression through the calculation of odds ratios (OR) and 95% confidence intervals (CI). In all analyses, a P ≤ 0.05 was considered statistically significant.

Results

Participant characteristics
A number of 576 women participated in the study. The mean age of the participants at the time of the study was 28.7 ±10.2 years with a range of 18 to 62 years.

Table I shows that more than three quarters (79%; n=454) of the women studied were 37 years of age or younger. As for ethnicity, the survey results showed that 49% (n=284) of the participants were of Arab ethnicity and 30% (n=170) were of Sahrawi Arab ethnicity.

The study of the racial groups of the participants showed that 82% (n=471) of the women surveyed were white and 13% (n=74) were mixed race.

The distribution of participants by marital status showed that more than half (n=309) were married. The proportion of single women at the time of the survey was 37% (n=213).

The data from the study concerning the occupation of the participants revealed that housewives represented 40.1% (n=231), the proportion of students was 34.4% (n=198) while those in paid employment reached 25.5% (n=147).

The study of the monthly family income of the women studied showed that about two thirds (n=362) reported an income of at least 555.92 United State Dollar (USD), while 25% (n=144) had an income between 556.03 and1111.95 USD and only 12% (n=70) of the participants had an income of more than 1112.06 USD. The data collected on education levels showed that 36.1% (n=208) of the women recruited had a higher level of education, and 26.6% (n=153) had no more than primary education, while 12.8% (n=74) had no education. (**Table I**).

Table I: Distribution of the population by socio-demographic characteristics.

Variables	Frequency	Percentage
Age		
[18-27]	293	50.9
[28-37]	161	28.0
[38-47]	89	15.5
[48-57]	26	04.5
Over 58 years	7	01.2
Ethnicity		
Sahrawi Arabic	170	29.5
Arabuc	284	49.3
Amazigh	122	21.2
Race		
White	471	81.8
Black	31	05.4
Metis	74	12.8
Marital status		
Married	309	53.6
Single	213	37.0
Divorced and widowed	54	09.4
Profession		
Housewife	231	40.1
Civil servant	97	16.8
Employee	50	8.7
Student	198	34.4
Monthly income (USD)		
Less than 278.02	174	30,2
[278.02-555.92]	188	32,6
[556.03-1111.95]	144	25
More than 1112.06	70	12,2
Education level		
Lliterate	74	12,85
Primary	153	26.56
Secondary	141	24.48
Higher	208	36.11

USD: United State Dollar

Weight status and perceived body image

The results of the survey (**Table II**) revealed that the average weight recorded in the study population was 70.84 ± 14.92 Kg and the average height was 1.63 ± 0.065 m. The mean body mass index (BMI) was 26.70 ± 5.36 Kg/m^2 with extremes ranging from 13.15 Kg/m^2 to 43.82 Kg/m^2.

Normal weight accounted for 37% (N=215) of the women studied, 34% (N=195) were overweight and 25% (N =145) were obese. Thus, 59% were overweight.

As for the participants' choice of image regarding their current weight, 4.34% (N=25) considered their weight to be low, 39.41% (N =227) considered their weight to be normal, 50% (N=288) considered themselves to be overweight and 6% (N=36) declared themselves to be obese.

The data collected showed that over three quarters (76.04%; N =438) of the women were dissatisfied with their body image. Only one hundred and thirty-eight women (23.96%; N=138) reported satisfaction with their body image.

The study of body size satisfaction showed that 52% (N=301) would have a small waist, 24% (N=138) would have a satisfactory waist, 15% (N =89) would have a large waist and 8%

(N=48) of the women had a much too large waist.

Concerning the representations of overweight, the results of the study showed that 77%

Table II: Distribution of women according to representations of overload.

Variables	Frequency	Percentage
Weight status		
Underweight	21	03.6
Normal weight	215	37.3
Overweight	195	33.8
Obese	145	25.2
Perception about the excess weight		
Illness	443	76.91
Sign of beauty	96	16.67
Sign of wealth	19	03.30
Sign of good health	18	03.13
Satisfaction with the body image		
Yes	138	23,96
No	438	76,04
Perception of body image		
Size little small	301	52,26
Satisfactory size	138	23,96
Size a little large	89	15,45
Size a little too large	48	8,33
Women's perceptions of excess weight		
Sick	271	47,05
Suffers from poor quality of life	172	29,86
Loved by men	79	13,72
Hated by people	21	3,65
Healthy life	33	5,73

(N=443) of the participants considered overweight to be a disease, while 17% (N=96) perceived fatness as a sign of beauty. For 3% of the women, being overweight is a sign of wealth and an indicator of good health.

Regarding the participants' representations of overweight women, the results of the study showed that 47% (N=271) of the participants think that these women are sick, and 30% (N=172) consider them to have a poor quality of life. A proportion of 14% (N=79) of the participants saw obese women as being preferred by men and only 4% felt that overweight women were disliked by men (**Table II**).

Binary regression analysis

Binary regression analysis between overweight and perceived body image revealed that women who were satisfied with their body image (OR=0.235; CI95% [0.15-0.35]) and desire to lose weight had protective effects against developing overweight (OR=0.46; CI95% [0.30-0.70]). However, women with a positive representation of overweight women had a 1.60 risk of developing weight gain (OR=1.60; 95% CI [1.60-1.03] (**Table III**).

Discussion

This study involved five hundred and seventy-six (576) women with a mean age of 28.7 ±10.2 years, almost half were of Arab ethnicity, 43% were married and more than a third had a higher level of education. Being a housewife or a student were the dominant occupations among the participants, almost two-thirds of whom had an income of less than 555.92 USD and more than two-thirds of whom had at least one child.

Anthropometric data showed that the average weight of the women was 70.84 ± 14.92 Kg and the average height recorded was 1.63 ± 0.065 m. Furthermore, the average body mass index (BMI) was 26.70 ± 5.36 Kg/m^2. Thus, 37% (n=215) were of normal weight, one in three women

(34%) were overweight and one in four women (25%) were obese. Therefore, 59% of the women suffered from excess weight. In general, these results confirm that this increase affects women more than men. Indeed, a study in Saudi Arabia showed an increase from 21% to 78% in women between 1992 and 2022[18]. Thus, the decrease in the prevalence of overweight among young women, compared to older women, may also reflect a shift in the perception of "obesity" from being a sign of beauty and prosperity among women (19,20); to a symbol of underdevelopment. This is especially true for younger, higher educated women who are more likely to adopt lower risk behaviours for obesity as a result of exposure to Western culture[21-23].

As for body image perception, 67% of dissatisfied women were overweight. Studies conducted in 2014, by El Ansari et al. and Garousi et al. affirmed these results[24,25].

As for the perception of the most attractive image for men according to the women studied, more than 61% of the participants had chosen images 3 and 4 that represented normal weight. These results were similar to other studies[4]. However, a study examining the interaction between weight status and perceived body image showed a preference for heavier women[26]. This difference in perception could be explained by the fact that an individual's body image may be more a response to cultural norms than to actual physical dimensions. The process of acculturation is a psychosocial change that occurs when an individual acquires the values and norms of other cultures. It is currently known that television, for example, emphasises an ideal image of thinness, which in turn can influence the perception of body image. Magazine images, such as photographs, stories and advertisements, may also encourage dissatisfaction with body image[27]. As a result, subjects' perceptions have shifted towards a preference for thinner body sizes as a symbol of female beauty over fat women. Thinness is now preferred by young women almost everywhere,

Table III: Binary regression analysis between overweight and perceived body image.

Variables	n	(%)	OR	IC$_{95\%}$	P
Desire to lose weight					
Yes	44	43	0.46	[0.30-0.70]	0.0004
No	296	62	1		
Satisfaction with body image					
Yes	43	32	0.23	[0.15-0.35]	< 0.0001
No	297	67	1		
Perception of excess weight as a diseas					
Yes	260	59	0.96	[0.65-1.43]	P = 0.86
No	80	60	1		
Positive representations of overweight women					
Yes	74	68	1.60	[1.03-2.48]	0.04
No	266	57	1		
Positive representations of overweight women					
Yes	74	68	1.60	[1.03-2.48]	0.04
No	266	57	1		

*IC: 95% confidence interval; OR : Odds Ratio.

largely due to the propagation of thin models by the global mass media, satellite channels and the propagation of top models. Women with positive representations of overweight were at risk of developing overweight, the choice of normal body images as the most attractive to men reflects the beginning of the shift from perceptions of overweight as a sign of beauty and prosperity to perceptions referring to illness and poor quality of life.

The survey results also highlighted that more than three quarters of the women considered obesity to be a disease and 21% had a positive view of it. However, the odds ratio was 1.6 times higher among these women, which put them at risk of being overweight. Although the results, in general, of body image perception are in favour of a shift towards normal or slim size preferences, culture and traditions still influence these choices.

Although this work has many advantages, it has some weaknesses: The main limitation of this study is its cross-sectional nature, which prevents a causal relationship between perceptions and overweight. In addition, there is the "social desirability bias", where participants would tend to give socially desirable answers. This is the case,

for example, when seeking to assess their perception of their body image and the perception of being overweight and the most attractive image for men.

Prospects

Conduct further prospective studies in other regions in both men and women
Conduct a similar study among university students

Conclusion

The risk factors are multiple and complex. The study showed a change in the participants' perception of overweight. Reducing the magnitude of this public health problem requires strategies that take into account this shift towards reducing the prevalence of weight gain, particularly among young women and students.

Conflicts of interest
The authors declare no conflict of interest.

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ORIGINAL

Workplace violence against nurses: Qualitative research

Violencia laboral contra enfermeras: Una investigación cualitativa

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Abstract

Background: Workplace violence against nurses is a serious problem identified in many countries around the world. This study aimed to identify the lived experiences of nurses working in the state of Rio de Janeiro, Brazil, concerning workplace violence and to provide recommendations to avoid such acts.

Methods: A qualitative and descriptive design was used. The snowball technique was used to reach the participants. Narratives (n=42) written by nurses were collected. A total of 42 nurses participated in the study. Data were interpreted through a manifest content analysis.

Results: The obtained data were presented in five themes: "acts of violence", "measures taken against acts of violence", "reasons for violence", "consequences of violence", and "recommendations to avoid violence". More security in health institutions, better working conditions, support from nursing councils and nurse managers, awareness of the population, and changing attitudes of nurses themselves may reduce workplace violence.

Conclusion: Violence in the workplace harms the health of nurses and reduces the quality of care since unhealthy nurses will not be able to perform their duties effectively and efficiently.

Keywords: Nursing, nurse administrators, occupational risks, workplace violence.

Resumen

Antecedentes: La violencia laboral contra las enfermeras es un problema grave identificado en muchos países del mundo. Este estudio tuvo como objetivo identificar las experiencias vividas por las enfermeras que actúan en el estado de Río de Janeiro, Brasil, en relación con la violencia en el trabajo y proporcionar recomendaciones para evitar tales actos.

Métodos: Se utilizó un diseño cualitativo y descriptivo. Se utilizó la técnica de la bola de nieve para llegar a los participantes. Se recogieron relatos escritos por enfermeros. Un total de 42 enfermeras participaron en el estudio. Los datos fueron interpretados a través de un análisis de contenido manifiesto.

Resultados: Los datos obtenidos se presentaron en cinco temáticas: "actos de violencia", "medidas tomadas frente a actos de violencia", "motivos de la violencia", "consecuencias de la violencia" y "recomendaciones para evitar la violencia". Más seguridad en las instituciones de salud, mejores condiciones de trabajo, el apoyo de los consejos de enfermería y de las enfermeras gestoras, la concientización de la población y el cambio de actitud de las propias enfermeras pueden reducir la violencia en el lugar de trabajo.

Conclusión: La violencia en el lugar de trabajo perjudica la salud de las enfermeras y reduce la calidad de la atención, ya que las enfermeras no saludables no podrán desempeñar sus funciones de manera eficaz y eficiente.

Palabras clave: Enfermería, enfermeras administradoras, riesgos laborales, violencia laboral.

Introduction

Violence in the workplace is a serious public health problem that is becoming increasingly common around the world[1]. Acts of workplace violence can be observed in several professional fields, but nursing is undoubtedly one of the professions most affected by such events[2-4]. The violence suffered by nurses can be related to the work process, relationships with patients and other health professionals, and also the work environment itself[5]. It is important to emphasize that with the emergence of Covid-19, acts of violence against nurses have relatively increased and are most often committed by patients or their relatives[6,7]. Among the professionals who make up the nursing team, nurses are the ones who suffer the most from violence, which can be physical, verbal, psychological, sexual, or institutional[3,4].

Violence is known as individual or collective human acts that lead to death, or that affect the integrity of individuals through physical, moral, mental, or spiritual damage[8]. Although physical violence (pushing, beating, torture, mutilation, among others) is the first type that comes to mind when the subject is discussed; violence is expressed in many different ways, which can be psychological, in face of threats and humiliation; verbal, through shouting and cursing; social, characterized by discrimination and intolerance; moral, when there are blackmail and defamation, among others[9,10]. Thus, not only physical aggressions are acts of violence, but any action that may cause psychological harm, inadequate development, or deprivation of any kind is also an act of violence[11].

Violence against nurses affects not only the individuals who were victims of the act, but the health institution in which they work for, the patients cared for by them, and also other health professionals, so it can be said that such events have a collective impact[12]. Nurses must be healthy to perform their duties with quality. Nurses who suffer from workplace violence have their physical-psycho-social health affected, thus reducing their quality of life, in addition to reducing the efficiency and effectiveness of the care provided by them[13-15].

Nursing has a very important role in health care institutions, so it is necessary to change the current scenario of workplace violence against these health professionals, not only in Brazil but also in several countries around the world[14-16]. It is necessary to give visibility to the phenomenon, as it is essential that nurses who have suffered from workplace violence participate in the development of measures to prevent such acts. Studies indicate that little is done to create measures to prevent acts of violence against nurses[17]. It is important to give voice to nurses and identify the acts of workplace violence of which these health professionals are victims, thus avoiding the trivialization of abuses of power, prejudice, harassment, and offenses[3], because acts of psychological and verbal abuse can be even more harmful than physical violence itself. Understanding the importance of the theme, this study aimed to identify the lived experiences of nurses working in the state of Rio de Janeiro concerning workplace violence and to provide recommendations to avoid such acts.

Method

Design
This is a descriptive study carried out with a qualitative approach. This design was chosen because it allows understanding of events experienced by individuals[18]. The Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist was used to guide the study[19].

Participants
The universe of the study was formed by nurses working in the state of Rio de Janeiro, Brazil. Emails and instant messages were sent through different social media to 11 nurses who 20 years ago graduated from the same nursing school as the researcher, the choice of these nurses was made due to the ease of access. The messages included the invitation to participate in the study, information about the study, the Free and Informed Consent Term, and the data collection tool. The snowball technique[20] was used to capture the other participants, so the first nurses indicated other nurses who met research inclusion criteria, thus ensuring maximum diversity through a small sample. A total of 42 written narratives of nurses who work in the state of Rio de Janeiro for at least one year, and who signed the informed consent form, were included in this study. Other members of the nursing team were not included.

Role of the researcher
The researcher is a female RN, Assistant Professor, who has a Ph.D. She took a course in qualitative research methods, and she has experience with qualitative studies. The author has a cultural background similar to the participants of this study.

Data collection
Although in most qualitative research face-to-face interviews or focus groups are used for data collection, telephone interviews or online approaches can also be used[21]. For this study data were collected in March 2022 using the online Google Forms as a research tool to ensure easy and quick access to participants. Google Forms has several benefits, such as agility in data collection, as it can be performed anywhere, anytime, and ease of use by the researcher and participant, being very useful in various academic activities[22]. The use of the online approach in qualitative studies is becoming more common, as it not only offers greater flexibility but also helps to achieve maximum variation sampling and to examine experiences from broader perspectives[23]. In addition, the method was

chosen to guarantee the privacy of participants, who could feel uncomfortable when reporting experienced situations related to workplace violence.

The first part of the data collection tool contains open questions related to the personal and professional characteristics of nurses, such as age, gender, educational level, position at work, unit of work, and years of working experience, among others. In the second part of the form, there are nine open questions related to nurses' experiences with workplace violence. The questions were developed by the researcher by scanning the literature[3,12,13,15,24-26]: (1) Have you ever suffered any type of physical violence at work? If yes, please explain. (2) Have you ever suffered any type of verbal violence at work? If yes, please explain. (3) Have you ever suffered any type of psychological violence at work? If yes, please explain. (4) Have you ever suffered any type of social violence at work? If yes, please explain. (5) Have you ever suffered any other type of violence at work? If yes, please explain. (6) Have you ever wanted to give up your profession due to some type of violence suffered? (7) If you have suffered any type of violence at work, what measures have you taken? (8) In your opinion, why do acts of violence against nurses occur? (9) What should be done to prevent acts of workplace violence against nurses? At the end of the form, there was a space in case the participant wanted to add further comments on the topic.

The questions were tested through two pilot interviews, after that, two questions were modified. The data of these two nurses were not included in the study. The questions were asked in Portuguese. The answers varied from a single word to a 14-line paragraph. At first, it was stipulated that a total of 20 nurses would be appropriate to reach the aim of the study, but even after reaching 27 participants, the need to collect more data was felt and invitations were sent again to some nurses asking them to resend messages to other nurses whose could be included in the study. Upon reaching 46 participants, data saturation was achieved[18]. However, two participants were excluded for not working in the state of Rio de Janeiro and two more for not being nurses. Thus, the total sample size was 42 nurses.

Table I: Characteristics of nurse participants.

Participant	Age	Gender	Educational Level	Marital Status	Position at Work	Type of Institution	Work Experience (years)
1	43	F	Postgraduate	Married	Epidemiological Surveillance Nurse	Municipal	20
2	43	F	Postgraduate	Single	Nurse	Private	20
3	46	F	Bachelor's degree	Single	Nurse Manager	Federal	22
4	37	F	Master's degree	Stable Union	Hospital Infec. Control Commission Nurse	Private/ Municipal	13
5	45	F	Doctorate	Divorced	Nurse	Federal	21
6	46	F	Bachelor's degree	Married	Nurse	Federal/ Municipal	19
7	40	F	Bachelor's degree	Stable Union	Nurse	Private	14
8	46	F	Postgraduate	Single	Nurse	State	20
9	45	F	Postgraduate	Married	Nurse	Municipal	20
10	66	F	Bachelor's degree	Divorced	Nurse	Federal	43
11	47	F	Bachelor's degree	Married	Nurse	Federal	24
12	48	F	Postgraduate	Married	Nurse	Municipal	22
13	44	F	Master's degree	Single	Nurse	Federal	21
14	57	F	Postgraduate	Divorced	Nurse	Municipal	36
15	46	F	Bachelor's degree	Married	Nurse	Private	7
16	38	F	Bachelor's degree	Single	Nurse	Private	10
17	41	F	Bachelor's degree	Divorced	Nurse	Federal	16
18	39	F	Master's degree	Divorced	Nurse	Federal	16
19	38	F	Postgraduate	Married	Preceptor Nurse	Municipal	3
20	41	F	Master's degree	Married	Nurse	Federal	17
21	36	F	Bachelor's degree	Married	Nursing Supervisor	Private	18
22	44	F	Master's degree	Married	Nurse	Federal	16
23	46	F	Bachelor's degree	Married	Nurse	Municipal	17
24	40	F	Postgraduate	Married	Nurse	Municipal	11
25	45	F	Bachelor's degree	Married	Informal Manager	Federal	23
26	43	F	Bachelor's degree	Married	Nurse	Municipal	19
27	42	F	Postgraduate	Divorced	Nurse	Municipal	2
28	44	F	Bachelor's degree	Single	Nurse	State	15
29	42	F	Bachelor's degree	Widow	Nurse	Municipal	15
30	49	F	Bachelor's degree	Single	Nursing Coordinator	Private	25
31	41	F	Postgraduate	Married	Nurse	Private/State	15
32	32	M	Postgraduate	Married	Nurse	Municipal	14
33	52	F	Bachelor's degree	Married	Nurse	Private	8
34	59	F	Bachelor's degree	Stable Union	Nursing Coordinator	State/ Municipal	41
35	41	F	Postgraduate	Married	Nurse	Private	16
36	40	F	Bachelor's degree	Divorced	Nurse	Municipal	14
37	42	F	Bachelor's degree	Married	Nurse	Private	16
38	43	F	Master's degree	Single	Research Assistant	Federal	19
39	25	F	Bachelor's degree	Single	Nursing Resident	State	1
40	43	F	Bachelor's degree	Married	Nurse	Municipal	19
41	38	F	Postgraduate	Married	Nurse	Federal	16
42	50	F	Bachelor's degree	Married	Nurse	Municipal	18

Data analysis

The description of the participants' characteristics was summarized (**Table I**). Data were evaluated with a manifest content analysis method[27]. The written words from the narratives of the 42 participants were read and re-read several times by the author and coded manually.

Rigor

The fact that the answers were provided in writing by the participants themselves facilitated data analysis and avoided possible influences of the researcher on the participants' answers. In addition, the anonymity of the participants is another factor that ensured the absence of bias. Data were read, reread, and grouped in codes by the author, who has experience in qualitative studies. Codes, subcategories, and categories have been checked several times by the author. Credibility, confirmability, dependability, and transferability, the four criteria indicated by Lincoln & Guba (1985)[28] to ensure the trustworthiness of qualitative studies were followed.

Ethical considerations

The ethical application was approved by the Research Ethics Committee of the Anna Nery School of Nursing- Sao Francisco de Assis School Hospital of the Federal University of Rio de Janeiro through the Brazil Platform (approval date: March 2, 2022; decision number: 5.268.912). All participants were informed of the purpose and the methods of the study and a Free and Informed Consent Term was signed by them. The anonymity of the participants was maintained in the transcriptions and the report.

Results

The average age of the participants was 33.64 years old, their average work experience was 17.66 years, and 97.61% of them were female. The characteristics of the participants are shown in **table I**. The forms of violence most reported by the participants of this study were verbal (73.8%) and psychological (66.7%). In addition, 35.7% of nurses reported having been victims of social violence, 11.9% of physical violence, and 35.7% of other types of violence such as institutional, economic, moral, and sexual. A total of 52.4% of the nurse participants emphasized having wanted to leave the profession due to violence. The obtained data were presented in five categories: "Acts of violence", "Measures taken against acts of violence", "Reasons for violence", "Consequences of violence", and "Recommendations to avoid violence" (**Table II**).

Table II: Results - Main themes, sub-themes, codes and examples of quotations obtained from participants.

Categories	Sub-categories	Codes	Examples of quotations
Acts of violence	1. Physical violence		The patient thought she was waiting too much for her appointment so she physically assaulted me, pushing me and ripping my badge (Participant 6).
	2. Verbal violence		Cursing and screaming from a child's family for not accepting the medical conduct, and for us, nurses, having to perform what was requested. We are the ones who always receive the greatest offenses (Participant 42).
			My immediate supervisor yelled at the nursing station, insulting me, saying I was a dirty person and that I did not know how to work. Honestly, I do not even remember the reason why she did it. The following week I found out that she did the same with two other nurses (Participant 41)
	3. Psychological violence		A director of a private hospital where I was a nurse manager said that I would never be able to pass an exam to work in a public hospital, so I would have to make do with this job. The reason for this was my complaint about my salary that was overdue for four months (Participant 34).
	4. Social violence	4.1. Racial discrimination	The supervisor said that the quota for black people in the sector was exhausted (Participant 1).
			Many years ago, a patient refused to talk to another nurse, the administrator, and me because we are black (Participant 34).
		4.2. Xenophobia	Preconception. Xenophobia. Mainly in Rio de Janeiro, nurses from the Northeast have to prove their competence twice. This is a fact! (Participant 15).
		4.3. Discrimination related to physical features	I suffer discrimination for being a person with a physical disability (Participant 17).
			A doctor complained to my supervisor that I was too overweight to work at a Day Hospital that performed plastic surgery (Participant 23).
		4.4.Gender discrimination	I took a leadership position and the wage of all my male nurse co-workers was increased but mine and other female nurse's did not... I requested to return to my old position after three years due to a lack of financial recognition (Participant 21).
		3.1. Prejudice against the profession	A patient did not accept to be attended by a nurse, because according to her a nurse is no good for anything (Participant 22).
	5. Other types of violence	5.1. Institutional	In the early days of the COVID pandemic, the area coordinator determined that even without Personal Protective Equipment (PPE) we should continue working. Another issue is the number of patients we assist daily. According to the service portfolio, we have to attend to all the patients who seek care at the unit. I got to care for 50 patients per shift. During the pandemic, we reached 390 patients a day (Participant 6).
		5.2. Economic	The salary was overdue and the institution's administrators said that we had to keep working as if nothing was wrong (Participant 34).
		5.3. Moral	A patient's relative wanted pillows and I said that I had wanted them from the responsible sector. After answering him, I was talking to the technician about money and the relative thought it was with him. So, he opened his wallet, took out a wad of money, and shouted that money was no problem! (Participant 2).
		5.4. Sexual	I suffered sexual violence; a doctor grabbed me (Participant 34).

Table II: Results - Main themes, sub-themes, codes and examples of quotations obtained from participants.

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Categories	Sub-categories	Codes	Examples of quotations
Measures taken against acts of violence	1. Seeking help from superiors		I always reported the case to my coordinator, except when the offender was the coordinator himself. Then I just ignored it with my silence while he was offending me. It was impossible to report the case to the general coordinator because they were close friends (Participant 23).
	2. Complaints at the police station		I reported the patient's relative to the police station (Participant 25).
	3. Not taking any action		The client is always right, that is why I gave up on fighting back against any kind of violence (Participant 12).
Reasons for violence	1. Seeing nursing as a subaltern profession		We are overloaded with tasks that are not our obligation, so we have a culture that thinks that nurses are the do-it-all. Thus, I believe that we have lost a little respect, as we are treated with a certain disregard by some people; it is like nursing is not so important (Participant 41).
	2. Lack of safety in the work environment		There is a lack of security in the workplace (Participant 9).
	3. Gender inequality		There is the issue of the female gender, which still brings great remnants of the need for submission to the opposite sex in the face of a sexist and patriarchal society (Participant 13).
	4. Being involved in care for long periods		Nurses are more exposed to violence because they provide patient care; nurses provide 24-hour assistance to the patient, whether performing direct care or dealing with bureaucratic issues (Participant 29).
	5. Being a link between multidisciplinary teams and patients		We are the ones who deal directly with the multidisciplinary team; nurses have to be problem-solving in all hospital areas (Participant 29).
	6. Accepting poor working conditions		As long as we accept low wages, excessive working hours, and devaluation, we will always be suffering from violence, we have to enforce our scientific studies and show that we are not frustrated doctors, but competent nurses (Participant 29).
Consequences of violence	1. Physical and mental damages		A patient called me names, and that day I felt bad with chest pain, like pressure in my chest. I went home in the middle of the day (Participant 23).
			I had to take a break from work because of burnout (Participant 38).
	2. Quitting jobs and changing sectors		I changed my attitude and quit my job (Participant 33).
			I did not give up the profession, but I changed the unit (Participant 11).
Recommendations to avoid violence	1. Better security system		There should be a security guard or a policeman in each clinic (Participant 12).
	2. Attitudes of nursing councils		It would be good to have nursing councils that effectively supervise and punish offenders (Participant 15).
	3. Improvement of working conditions		There needs to be professional valorization with decent wages and shorter working hours (Participant 34).
	4. Campaigns to inform the population about the nursing profession		It is necessary to make the patient and their relatives understand what the responsibility of the nursing team is in fact (Participant 7).
	5. Attitudes of nurses themselves		I believe that improving our posture through everyday situations, being better professionals, more prepared, educated, updated... Over time, we will have the respect and autonomy we deserve back (Participant 41).

Discussion

This study sought to identify the lived experiences of nurses working in the state of Rio de Janeiro concerning workplace violence and to provide recommendations to avoid such acts. Nurses reported being victims of various types of violence. However, verbal and psychological aggressions were the most addressed by the participants. When suffering from acts of violence, nurses turn to superiors and the police or prefer to remain silent and not take any action. Participants believe that nursing is considered a subordinate profession, without autonomy, with poor working conditions and that these facts favor acts of violence. In addition, according to nurse participants, lack of safety in the workplace, lack of support from nursing councils, and being in constant contact with patients facilitate violence. Violence affects the physical, emotional, mental, and professional health of nurses. More security in health institutions, better working conditions, support from nursing councils, awareness of the population, and changing attitudes of nurses themselves were pointed out as recommendations that may reduce acts of workplace violence.

As in the present survey, studies carried out previously in Brazil have reported various forms of violence against nursing professionals, such as physical, verbal[5,12,26,29], psychological, social, moral, institutional, and sexual

aggressions[5,29]. The most common form of violence is the verbal one, through shouting and calling names, most often by patients and their relatives who are dissatisfied with the health assistance[25,26]. Moral violence against health care workers, characterized by acts of discrimination and intolerance, is also quite common and was cited in a systematic literature review in which bullying and ethnic and racial harassment were reported by physicians and nurses[30]. Acts of violence against health professionals have become increasingly commonplace, and nurses are the most exposed, as they are in constant contact with the patient, being the most affected by workplace violence[25]. Studies carried out in several different countries showed similar results regarding the forms of violence, the aggressors, and their reasons for committing acts of violence against nurses[13,15,24,31]. Even in the presence of the Covid-19 pandemic where at first health care workers were considered heroes; violence, discrimination, and stigmatization against nurses were identified around the world[6,7,32].

In the relevant literature, it was discerned that in the face of violence, nurses seek support from co-workers, including supervisors and security staff[26,31,33]. There are cases in which complaints were made at the police station[12,33], but many nurses remain silent and do not take any action against the aggressor[3,12,26,33]. The act of remaining silent can trivialize violence as if it were part of nurses' routine[26]. One of the reasons for not taking action may be the lack of trust in the system, which does little to protect nurses[3,33].

The results of this survey are similar to those of other studies conducted on the subject concerning the reasons for aggression against nurses. Lack of security[31,34], poor working conditions, prejudice against health professionals, and exposure of nurses to being in contact with patients and their relatives for long periods[24] facilitate the emergence of acts of violence against them. The devaluation of nursing is related to the history of the profession, the lack of recognition of nurses' autonomy, and the disadvantageous working conditions, which make the population not recognize the real competencies of nurses, leading them to believe that nursing is a subaltern profession[35]. Moreover, nursing is a profession mostly performed by women, which can also be considered a factor that triggers acts of discrimination against nurses, since female-dominated professions are considered to be simpler, not requiring much knowledge[36,37].

Previous studies showed that workplace violence has physical, emotional, professional, and psychological consequences on nurses[38]. In studies conducted in different countries, nurses reported stress, insomnia[38], anger[31,38], fear, burnout[31], anxiety, and depression[24], due to acts of violence suffered in the workplace. In addition, violence can make nurses hate their profession[31], thus increasing turnover rates[39,40].

As in the present survey, related studies done in different countries addressed measures that must be taken so that acts of violence against nurses are avoided. Nurses need to feel safe in the workplace[40]. The working conditions of nurses need to be improved because low wages, overwork, and lack of equipment, as well as any other form of deprivation, are considered an act of violence[24,39]. The population needs to be better informed about the functions performed by nurses, and there should be aware so that nurses are more respected and valued[3,33]. Health managers should pay attention to situations that threaten the lives of nurses in the workplace, developing plans and strategies to better protect them[3,26,29,40]. Nurses' attitudes towards acts of aggression are also of paramount importance for the control of violence in the work environment, as such acts must be denounced and should not be seen as part of the work routine[3,26,40]. A practical reporting system where nurses can report the aggressions they have suffered can favor the control of workplace violence against these healthcare workers.

Limitations of the study
This study has many limitations, one of which is the fact that data were collected online through self-report questionnaires, which did not allow a deep approach to the topic. In addition, despite the author being an expert in qualitative research, the fact that the data were analyzed by only one researcher should be considered a weakness of the study. Another limitation is that, as the participants were anonymous it was not possible to provide feedback on the findings.

Conclusion

It was determined that nurses suffer aggressions that range from shoving, shouting, cursing, discrimination, low wages, overwork, and shortage of human resources to deprivations that prevent them from fighting for their right to life when PPE is lacking. Nurses seek support from their superiors when they are victims of acts of violence, this fact points to the importance of nursing councils and administrators of health institutions, including nursing managers, for the formulation and application of strategies aimed at protecting nurses against violence in the workplace.

Another important factor that must be observed is related to the reasons for the acts of violence. Nurses reported that being in direct contact with the patient and being a link between the other members of the multidisciplinary team is a facilitator for the emergence of acts of violence, which is a paradox, as the health professional who is constantly caring for patients and being a key point of the health team, should be valued, well treated and protected. In other words, having important functions in health institutions should not expose nurses to aggressive acts by patients, their relatives, and co-workers. Further studies using

different designs and data collection methods should be conducted to better explore the experiences of nurses regarding violence in the work environment.

Increasing safety in health institutions, creating channels where complaints can be made in a practical way, improving the working conditions of nurses, developing campaigns that inform and educate the population regarding the nursing profession, and increasing the representation of nursing councils are recommendations for reducing acts of violence against nurses. In addition, nurses should get more united as a professional group, they must develop themselves as professionals and fight for their rights; nurses should not remain silent and passive in the face of acts of violence. Thus, in-service training programs should address the issue of labor violence, providing knowledge for nurses to defend themselves against acts of violence.

Conflict of interest statement
The author declares that there is no conflict of interest with respect to research, authorship, and/or publication of this article.

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ORIGINAL

Comparison of pain intensity and disability in patients with and without metabolic syndrome undergoing spinal stenosis surgery

Comparación de la intensidad del dolor y la discapacidad en pacientes con y sin síndrome metabólico sometidos a cirugía de estenosis espinal

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Abstract

Objective: Lumbar spinal stenosis (LSS) refers to the narrowing of the canal to the extent that it causes pressure on the spinal cord or nerve roots. Considering the physical, mental and economic complications of LSS, the objective of the present study was to compare the treatment outcomes in patients with and without MetS.

Methods: The study population included LSS patients referred to Imam Khomeini Hospital in Ilam city for spinal stenosis surgery. The patients were assigned into case group (n=42) with MetS and control group (n=42) without MetS. Data collection instruments including demographic profile form, Quebec back pain disability scale (QBPDS) and Oswestry Disability Index (ODI). After dividing the patients into case and control groups, surgical procedures were performed on the patients and the pain and disability status of both groups were compared two months after surgery. Data analysis was carried out using SPSS software.

Result: Result showed, 88 patients with LSS were included in the study, of whom 44 were male and 44 were female. Also, the mean (SD) age of the patients was 48.23 (5.34) years and educational level of most of the patients was below high school diploma. The mean (SD) pain score of control and case groups was 49.88 (20.37) 63.14 (22.07), respectively, which shows a statistically significant difference (P=0.005) (**Table II**). Moreover, mean (SD) disability score of control and case groups was 44.21(22.78) and 55.29 (21.23), respectively, which shows a statistically significant difference (P=0.017).

Conclusion: Our study, like the review of the literature, shows a higher prevalence of pain and disability in LSS patients with MetS than in patients without MetS. For this reason, it is necessary to take necessary measures to control MetS in order to reduce the pain and disability in these patients.

Keywords: pain, disability, spinal stenosis surgery.

Resumen

Objetivo: La estenosis espinal lumbar (EEL) se refiere al estrechamiento del canal hasta el punto de causar presión sobre la médula espinal o las raíces nerviosas. Teniendo en cuenta las complicaciones físicas, mentales y económicas de la EEL, el objetivo del presente estudio fue comparar los resultados del tratamiento en pacientes con y sin MetS.

Métodos: La población del estudio incluyó pacientes con EEL remitidos al Hospital Imam Jomeini de la ciudad de Ilam para cirugía de estenosis espinal. Los pacientes fueron asignados a un grupo de casos (n=42) con SM y a un grupo de control (n=42) sin SM. Los instrumentos de recogida de datos incluían el formulario de perfil demográfico, la escala de discapacidad por dolor de espalda de Quebec (QBPDS) y el índice de discapacidad de Oswestry (ODI). Tras dividir a los pacientes en grupo de casos y grupo de control, se realizaron procedimientos quirúrgicos en los pacientes y se comparó el dolor y el estado de discapacidad de ambos grupos dos meses después de la cirugía. Los datos se analizaron con el programa SPSS.

Resultados: Se incluyeron en el estudio 88 pacientes con EEL, de los cuales 44 eran varones y 44 mujeres. Asimismo, la edad media (DE) de los pacientes era de 48,23 (5,34) años y el nivel educativo de la mayoría de los pacientes era inferior al bachillerato. La puntuación media (DE) de dolor de los grupos de control y de casos fue de 49,88 (20,37) 63,14 (22,07), respectivamente, lo que muestra una diferencia estadísticamente significativa (P=0,005) (**Tabla II**). Además, la puntuación media (DE) de discapacidad de los grupos de control y de casos fue de 44,21 (22,78) y 55,29 (21,23), respectivamente, lo que muestra una diferencia estadísticamente significativa (P=0,017).

Conclusiones: Nuestro estudio, al igual que la revisión de la literatura, muestra una mayor prevalencia de dolor y discapacidad en los pacientes con LSS con SM que en los pacientes sin SM. Por este motivo, es necesario tomar las medidas necesarias para controlar el SM con el fin de reducir el dolor y la discapacidad en estos pacientes.

Palabras clave: dolor, discapacidad, cirugía de la estenosis espinal.

Introduction

Lumbar spinal stenosis (LSS) refers to the narrowing of the canal to the extent that it causes pressure on the spinal cord or nerve roots. This narrowing occurs in different places, including the central canal of the spinal cord, intervertebral holes, or lateral recesses[1,2.] LSS can lead to pressure on the nerve roots in the lower back and cause symptoms such as significant neurologic deficits, back pain, or disability. Considering that a MRI or CT Scan on large scale is both expensive and time-consuming, the LSS prevalence has been investigated in epidemiological studies with a small sample size. On the other hand, the LSS prevalence has been different in various studies, which is probably due to the lack of standard diagnostic methods and criteria, which has in turn made it difficult to interpret and compare the results of relevant studies[3,4].

Patients with LSS experience various clinical symptoms such as numbness, fatigue, pain in the buttocks and legs. The most common reason for referral in these patients is pain in the lower limbs and pelvis, which begins after walking and activity and decreases by sitting and leaning forward[5-7]. There are various diagnostic criteria for LSS. Leg or buttock pain while walking, motor or sensory disorders while walking, lower extremity muscle weakness, bending forward to relieve symptoms and back pain are among the clinical manifestations of this disease[8,9]. On the other hand, MRI is used to evaluate the radiological symptoms of this disease and demonstrates information such as the extent of degenerative changes in the lumbar spine and spinal canal, which thus can help physicians achieve a correct and better diagnosis[10,11].

The treatment includes weight loss, rest, physiotherapy and other supportive care. The primary treatment is non-surgical treatment, but if non-surgical treatments fail to improve the symptoms, surgical treatments such as spinal stenosis surgery plus fusion or spinal stenosis surgery alone are recommended[12,13]. Surgical treatments can impose costs on the patient, the health system and cause complications. On the other hand, the LSS prevalence is high in the elderly, and they are among the high-risk patients due to being at risk for performing surgeries and taking anesthetics. For this reason, preventive procedures or supportive treatments to reduce the disease symptoms are a priority[14,15]. On the other hand, it is sometimes possible that a person has a comorbidity. For example, metabolic syndrome (MetS) has a significant global prevalence and can affect different people and lead to many complications[16,17].

Aim

Considering the high prevalence of stenosis in patients with metabolic syndrome and few data in the literature on the results of surgery and complications of LSS, the objective of the present study was to compare the treatment outcomes in patients with and without MetS.

Methods

The study population included LSS patients referred to Imam Khomeini Hospital in Ilam city for spinal stenosis surgery. The patients were assigned into case group (n=42) with MetS and control group (n=42) without MetS.

Data collection instruments including demographic profile form, Quebec back pain disability scale (QBPDS)[18] and Oswestry Disability Index (ODI)[19]. QBPDS is a 25-item instrument that is scored based on a five-point Likert scale ranging from 0 and 4. Scores 0-25, 26-50, 51-75, and 76 or higher indicate low, moderate, severe, and very severe and acute pain, respectively[18]. Also, ODI consists of 10 sections and 60 questions that measures level of function in activities of daily living. The disability level is rated using scores 0 (functioning without feeling pain) and 5 (inability to perform activities due to severe pain). Finally, the possible score range is 0-100 and scores 0-20, 21-40, 41-60, 61-80 and high scores demonstrate low, moderate, high, severe disability, and acute disability, respectively[19].

At baseline, the research objective was explained to the patients, and sampling began after obtaining the related permission from the University Research Ethics Committee. Patients were assigned into two groups, case (with MetS) and control (without MetS). MetS was diagnosed by an internal medicine specialist b based on the laboratory documentation, clinical and diagnostic examinations. After dividing the patients into case and control groups, surgical procedures were performed on the patients and the pain and disability status of both groups were compared two months after surgery.

In order to comply with ethics in the research, the objectives of the study were explained to all patients and informed written consent was obtained from all of them. Participation in this study was completely voluntary and patients participating in the study had the right to withdraw from the study at any time during the study. Data analysis was carried out using SPSS 16 software.

Result

According to the results, 88 patients with LSS were included in the study, of whom 44 were male and 44 were female. Also, the mean (SD) age of the patients was 48.23 (5.34) years and educational level of most of the patients was below high school diploma (**Table I**).

The mean (SD) pain score of control and case groups was 49.88 (20.37) 63.14 (22.07), respectively, which shows a statistically significant difference (P=0.005) (**Table II**). Moreover, mean (SD) disability score of control and case groups was 44.21(22.78) and 55.29 (21.23), respectively, which shows a statistically significant difference (P=0.017) (**Table III**).

Discussion

The prevalence of MetS in Iran and the world is high. For example, in the meta-analysis study by Maleki et al. on 60,635 patients in the age group of 3-90 years old, it was shown that the prevalence of MetS was 36% and its prevalence was reported to be higher in women than in men[20]. The present study was conducted with the aim of comparing the pain and disability of patients with and without MetS undergoing with spinal stenosis surgery.

According to the results, only a small number of patients reported low pain and most of them reported high pain. Different degrees of pain from mild to severe have been reported in patients suffering from various spinal problems. Patients with lumbar spinal stenosis (LSS) were enrolled into the study by Park et al. They reported that 24 (64.3%) of the patients had

Table I: Comparison of demographic variables in patients with and without MetS undergoing surgery with spinal canal stenosis.

Variable		Case	Control	P
Gender	Man Female	24 (54.5) 20 (45.5)	21 (47.7) 23 (52.3)	0.14
Marital status	Single Have a wife	10 (22.7) 34 (77.3)	12 (27.2) 32 (72.8)	0.41
Education	High school Diploma Master's degree and Bachelor's degree	18 (41) 17 (38.6) 9 (20.4)	17 (38.6) 16 (36.4) 11 (25)	0.13
Age	20-29 30-39 40-59 >65	2 (4.5) 9 (20.5) 19 (43.2) 14 (31.8)	0 (0) 16 (36.4) 16 (36.4) 12 (27.2)	0.22
Residence status	City Village	10 (22.7) 34 (77.3)	12 (27.3) 32 (72.7)	0.41

Table II: Comparison of pain intensity in patients with and without MetS undergoing surgery with spinal canal stenosis.

Variable	Low	Medium	High	Very High	M(SD)
Case Control	5 (11.9) 3 (7.1)	14 (33.3) 10 (23.8)	14 (33.3) 13 (31)	9 (21.4) 16 (38.1)	49.88 (20.37) 63.14 (22.07)
P F			0.005 0.77		

Table III: Comparison of disability status in patients with and without MetS undergoing surgery with spinal canal stenosis.

Variable	Low	Medium	High	Very High	Very very intense	M(SD)
Case Control	6 (14.3) 1 (2.4)	9 (21.4) 12 (28.6)	13 (31) 14 (33.3)	12 (28.6) 11 (26.2)	2 (4.8) 4 (9.5)	44.21 (22.78) 55.29 (21.23)
P F			0.017 0.20			

radicular pain[21]. Also, it was reported in the review study by Manzetti et al., that 3% to 90% of 2678 patients with spinal arthrodesis had pain[22].

Studies also showed that other patients with spinal cord injuries (SCIs) had pain. In this regard, Bresnahan et al. reported that 86% of SCI patients had neuropathic pain and 81% of these them had chronic pain[23]. Similarly, in a study of SCI patients, Rosner et al. reported that 11.3% of these patients had neuropathic pain[24]. In a meta-analysis study, Hunt et al. found that 68% of SCI patients had pain. In fact, chronic pain is one of the symptoms of SCIs, which can affect all physical and mental aspects of these patients and cause crises in their lives. These patients may experience one or several types of pain[25]. Various factors affect the pain experience of these patients, including the area of involvement and the type of SCI problems do that the prevalence of pain in LSS patients is reported to be significant[26,27].

According to the results of the present study, the prevalence of postoperative disability was reported to be high. Barker et al. reported disability in most of the SCI patients[28] and Silfverskiold et al. also reported disability in 84% of patients[29]. In a review study, Halicka et al. also demonstrated pain and disability in patients following spinal surgery[30], which is consistent with the results of the present study regarding the presence of disability in LSS patients. Regarding the level of disability in MetS patients, it was also shown that this group of patients suffer from high disability. In the study of MetS patients by Carriere et al., it was shown that the most of these patients had disability, which in turned led to impaired physical mobility[31], which is consistent with the results of the present study.

According to the results of previous studies, the prevalence of pain and disability in LSS patients who had MetS was higher than in patients without MetS. It has been shown in various studies that MetS reduces the quality of life and related variables. In this regard, it was shown in Rahimpour et al.'s study that MetS can lead to a decrease in the quality of life[32], which is consistent with the results of the present study. Due to the fact that the study was conducted in a limited population and one city (Ilam city), its results cannot be generalized to the whole country or the whole world.

In D'Agostino et al.'s study, which was conducted with the aim of relating MetS and Spinal epidural lipomatosis (SEL), it was shown that if SEL is detected in radiological examinations of the patient, such as MRI or CT scan, it can be used in the early diagnosis of MetS[33]. Also, in cohort study by Ono et al showed Having SEL can be effective in developing MetS. In fact, SEL is a risk factor for MetS and viceversa[34].

Conclusions

Our study, like the review of the literature, shows a higher prevalence of pain and disability in LSS patients with MetS than in patients without MetS. For this reason, it is necessary to take necessary measures to control MetS in order to reduce the pain and disability in these patients.

Conflict of interests
The authors declare that there is no conflict of interests.

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ORIGINAL

Evaluation of SLN status and its association with clinicopathological factors in patients with cutaneous melanoma: A retrospective study

Evaluación del estado del SLN y su asociación con factores clinicopatológicos en pacientes con melanoma cutáneo: un estudio retrospectivo

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Abstract

Objective: Cutaneous Melanoma (CM) is a cancer with rising prevalence worldwide. The most significant predictor of CM is regional lymph node metastasis. Sentinel Lymph Node (SLN) biopsy is a strong method used to stage CM and to identify lymphatic metastasis.
Aim: This research was aimed to study the SLN and its association with clinicopathological factors in the CM patients for the better surgical management of these patients.
Patients and Methods: The medical data of 80 CM patients who had gone through lymphatic mapping and SLN biopsy at Imam Khomeini Hospital in Tehran from 2011 to 2018 were collected. The clinical and histologic factors, including sex, age, tumor location, Breslow thickness, ulceration, angiolymphatic invasion, tumor mitotic rate (TMR), and Clark level, were analyzed in these patients. The categorical variables were analyzed by the chi-square (χ^2) test and the quantitative data were examined by the student t-test. The statistical significance was set at p<0.05.
Results: Fifty-six patients (70%) were found to have SLN, 19 patients (33.9%) were SLN-positive, and 37 patients (66.1%) were SLN-negative. Breslow thickness was the only variable that was significantly associated with the prediction of SLN. SLN was not correlated with other features such as ulceration, angiolymphatic invasion, and tumor mitotic rate. CLND was carried out in 18 out of 19 SLN-positive patients. Moreover, 5 patients (27.8%) were found to be non-SLN-positive out of 18 SLNB+CLND-positive patients. Furthermore, there was not any significant relationship between the clinicopathological features and the prediction of non-SLN.
Conclusion: Breslow thickness was significantly correlated with positive SLNB. Thus, it can be a strong predictor of positive SLN in the CM patients.

Keywords: Cutaneous Melanoma, Sentinel lymph node biopsy, Positive SLN status, Surgery, Clinicopathological features.

Resumen

Objetivo: El melanoma cutáneo (MC) es un cáncer con una prevalencia creciente en todo el mundo. El factor predictivo más importante del MC es la metástasis en los ganglios linfáticos regionales. La biopsia del ganglio linfático centinela (GLC) es un método muy utilizado para estadificar el MC e identificar metástasis linfáticas.
Objetivo: Esta investigación tuvo como objetivo estudiar el GLC y su asociación con factores clinicopatológicos en los pacientes con MC para el mejor manejo quirúrgico de estos pacientes.
Pacientes y métodos: Se recopilaron los datos médicos de 80 pacientes con MC que se habían sometido a mapeo linfático y biopsia de GLC en el Hospital Imam Jomeini de Teherán entre 2011 y 2018. En estos pacientes se analizaron los factores clínicos e histológicos, incluidos el sexo, la edad, la localización del tumor, el grosor de Breslow, la ulceración, la invasión angiolinfática, la tasa mitótica tumoral (TMR) y el nivel de Clark. Las variables categóricas se analizaron mediante la prueba de chi cuadrado (χ^2) y los datos cuantitativos se examinaron mediante la prueba t de student. La significación estadística se fijó en p<0,05.
Resultados: Cincuenta y seis pacientes (70%) tenían GLC, 19 pacientes (33,9%) tenían GLC positivo y 37 pacientes (66,1%) tenían GLC negativo. El grosor de Breslow fue la única variable que se asoció significativamente con la predicción de GLC. El GLC no se correlacionó con otras características como la ulceración, la invasión angiolinfática y la tasa mitótica tumoral. En 18 de las 19 pacientes con NGS positivo se realizó una DGLC. Además, 5 pacientes (27,8%) resultaron no GLC-positivos de los 18 pacientes GLCB+CLND-positivos. Además, no hubo ninguna relación significativa entre las características clinicopatológicas y la predicción de no GLC.
Conclusiones: El grosor de Breslow se correlacionó significativamente con la GLCB positiva. Por lo tanto, puede ser un fuerte predictor de GLC positivo en los pacientes con MC.

Palabras clave: Melanoma cutáneo, Biopsia del ganglio linfático centinela, Estado del GLC positivo, Cirugía, Características clinicopatológicas.

Introduction

Cutaneous Melanoma (CM) commonly is a tumor arising from the incidence of genetic mutations in melanocytes, the pigment generating cells, which can occur in different parts of the body such as skin, eye, inner ear, and leptomeninges. CM incidence has considerably been increasing around the world[1-4]. However, melanoma constitutes about 1% of all skin malignancies. CM is the most aggressive tumor with the highest mortality rate among skin cancers[5]. This prevalence probably yields a lifetime risk of 1 in 24 individuals for developing any type of CM. Among the registered cancers, CM is the fifth most common in males and the sixth most common in females. Further, men are at 40% more risk than women to develop invasive CM in their lifetime[6,7]. About 91,270 cases of CM have been identified in 2018 alone, leading to 9320 deaths[8]. Different risk factors for the development of CM consist of UV exposure, male sex, immunosuppression, age increase, genetic predisposition (skin phenotype), genetic mutations, inflammatory bowel disease, and phosphodiesterase-5 use[9-13]. According to the characteristics of the tumor (location, stage, and genetic profile), the therapeutic methods may be surgical resection, chemotherapy, radiotherapy, Photodynamic Therapy (PDT), immunotherapy, or targeted therapy. Currently, for patients with stage I–IIIB malignant CM, surgery is the mainstay of therapy[13-16]. The surgical management of regional Lymph Nodes (LNs) for all patients with CM has been controversial since 1892 when H. Snow first recommended Elective Lymph Node Dissection (ELND) as a method to prevent tumor progression regardless of the presence of clinical regional nodal metastases[17,18]. The main shortcoming of ELND is that only about 20% of patients with middle-thickness primary CM are evaluated to have metastases in the regional lymph nodes, whereas 80% of patients are exposed to the morbidity of lymphadenectomy without the real benefit (19). Moreover, several randomized trials have failed to show an overall survival (OS) benefit for ELND[20-23]. In recent decades with the introduction of sentinel lymph node biopsy (SLNB), ELND has mainly been replaced[24,25]. As metastases from CM significantly progress in LNs, SLNB has emerged as a major diagnostic tool for determining whether cancer has developed beyond the early tumor site to the LNs[26]. Therefore, SLNB with lymphatic mapping was developed as a minimally invasive surgical procedure and sensitive prognostic method to stage clinical regional LNs without the associated morbidity of ELND[18,19]. This is the surgical technique by which the sentinel LNs are removed and checked for the presence of cancer cells. SLNB was developed in order to determine early metastases in clinical regional LNs and to screen only patients with nodal metastases to candidate complete lymph node dissection (CLND) and to prevent this in patients without nodal metastases. The false-negative rate of SLNB ranges from 10 to 20%[27,29]. Most surgeons commonly advise the triple manner, which includes preoperative lymphoscintigraphy,

perioperative injection of blue dye (isosulfan blue or methylene blue), and intraoperative gamma probe identification. The accuracy of this procedure is approximately 99%[19]. Presently, several experts advocate SLNB for tumor stages Ib and II[30]. Recent research has shown that the overall occurrence of positive SLNs in patients undergoing SLNB is approximately 15 -20%. In addition, this range relies on the primary tumor thickness: 35-40% of T4 tumors and 5-7.8% of T1 lesions[31-33]. Further, several other predictive factors are correlated with increased risk of SLN involvement in patients with localized CM, including Breslow thickness, Clark level, ulceration state, angiolymphatic invasion, tumor location, high tumor mitotic rate (TMR), and young age[19,34-37]. Furthermore, the local, regional, systemic recurrence, and survival rates in CM are all strongly correlated with Breslow thickness[38]. The aims of this article were to evaluate the predictive factors of SLN positivity in CM and to provide a model to predict SLN status for the optimal surgical management of these patients.

Materials and method

Study Patients
In this retrospective randomized study, the data obtained from newly diagnosed CM patients (with histologically-confirmed diagnosis) who underwent SLN biopsy at the Cancer Institute of Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran from October 2011 to October 2018. This study was approved by the Committee of Research Ethics of Tehran University of Medical Sciences. Pathologic examination of the SLNs was performed at the hospital using standard methods that have already been reported (39-42). The patients were selected for the statistical analysis who met with the following inclusion criteria: the presence of clinical stage I or II, absence of distant metastases confirmed generally by physical examination, chest radiology and the abdominal cavity ultrasonography, and Breslow thickness equal to or above 0.75 mm. Furthermore, LN recurrence in the same basin after initially negative SLNB was calculated as false-negative. Also, local recurrence after tumor-positive SLN biopsy was determined as any nodal or non-nodal recurrence.

Clinical and Histologic Characteristics
Demographic and clinical features such as sex, age, and tumor location (head and neck, trunk, upper extremities, and lower extremities) were evaluated. Histologic characteristics including Breslow thickness, ulceration (presence, absence), angiolymphatic invasion (presence, absence), TMR, and Clark level were assessed.

Mapping Technique and SLNB
About 2 h prior to surgery, 0.1–0.2 ml of 10 mBq (0.5 mCi) ^{99m}Tc-labeled sulfur colloid (^{99m}Tc-SC) was prepared in 1 mL 0.9% normal saline and injected intradermally in equal

amounts in four quadrants around the primary tumor/scar at a distance of approximately 1-5 mm. Further, [99mTc]-SC was passed through a 0.22 µm filter before injection. Then, all patients underwent lymphoscintigraphy 2-4 hours postinjection. After lymphoscintigraphy, the patients were transported to the operating room where methylene blue dye (5 ml) was injected intradermally around the primary lesion 10-15 min prior to incision. Before the skin was incised, a handheld gamma probe confirmed higher radioactive counts within the SN and detected other SNs that were not stained blue. Finally, all SNs were excised and evaluated for metastases by intraoperative frozen section analysis and postoperative hematoxylin and eosin staining[43,44].

Statistical Analysis

At the first step of current research, variables were grouped in two divisions as categorical (sex, ulceration, tumor location, and angiolymphatic invasion) and quantitative (age, Breslow thickness, TMR, and Clark level) variables. All data were analyzed by SPSS software (version 18.0). Categorical data were presented with frequencies and percentages. Continuous data were expressed with medians. Chi-square (χ^2) test was applied to examine categorical variables and student t-test was used to analyze the quantitative data. $P < 0.05$ was considered statistically significant for all analyses.

Results

Analysis of the characteristics of the patients undergoing SLN biopsy

A total of 80 patients who underwent SLN biopsy were included in this study. SLN was identified in 56 patients (70%), of whom (50%) were female (28 women and 28 men). Positive SLN was observed in 19 patients (33.9%) and negative SLN was found in 37 patients (66.1%). Additionally, SLNs were positive for metastasis in 9 males (32.1%) and 10 females (35.7%) (P=0.77). The mean age was 53 years in patients with positive SLN and 57 years in patients with negative SLN (P=0.47). Results of the analysis of clinical and histologic features with the potential to predict SLN status are presented in **table I**. Of the variables associated with the prediction of SLN status, only Breslow thickness had a statistically significant relationship (P=0.04). The risk of SLN positivity was 1.24 for patients with Breslow thicknesses of 1-4 mm and 8.58 for Breslow thicknesses greater than 4.0 mm. By ignoring level 1, Clark levels 2 and 3 were associated with an increased rate of SLNB positivity. No significant association was found between the SLN status and other features, including the presence of ulceration, angiolymphatic invasion, and TMR. After SLNB, 37 patients were detected SLN-negative and 37 patients were detected SLN-negative. After further following, of these, 5 patients had developed clinically evident node

metastases in a nodal basin initially defined as SLN-negative. Regarding 5 nodal recurrences, the false-negative rate of the SLNB was 2.2%.

Table I: Clinicopathological features of study population based on SLN status.

Characteristics	No. of patients	Negative SLNB (N=37)	Positive SLNB (N=19)	P-value
Age (years) (mean)	56	57	53	0.41
Sex	56			0.77
Male	28	19 (67.9)	9 (32.1)	
Female	28	18 (64.3)	10 (35.7)	
Tumor location	56			0.19
H&N	12	10 (83.3)	2 (16.7)	
Upper E.	5	3 (60)	2 (40)	
Lower E.	35	23 (65.7)	12 (34.3)	
Trunk	4	1 (25)	3 (75)	
Ulceration	42			0.49
Yes	22	12 (54.5)	10 (45.5)	
No	20	13 (65)	7 (35)	
Angiolymphatic invasion	28			0.22
Yes	3	1 (33.3)	2 (66.7)	
No	25	19 (76)	6 (24)	
No of mitosis	28			0.2
< 1 / hpf	11	9 (81.8)	2 (18.2)	
>= 1 / hpf	17	10 (58.8)	7 (41.2)	
Breslow thickness, mm	47			0.04
0.75 < B < 1	1	1 (100)	0 (0)	
1 <= B <= 4	29	22 (75.9)	7 (24.1)	
>4	17	7 (41.2)	10 (58.8)	
Clark	52			0.16
1	2	1 (50)	1 (50)	
2	4	4 (100)	0 (0)	
3	11	9 (81.8)	2 (18.2)	
4	27	18 (66.7)	9 (33.3)	
5	8	3 (37.5)	5 (62.5)	

P value <0.05 was considered statistically significant. Continuous data were reported with medians. Categorical data were presented with frequencies and percentages. H&N: Head and Neck; Upper E: Upper extremity; Lower E: Lower extremity; hpf: high power field.

Analysis of the characteristics of the patients with non-SLN status

After the SLN biopsy, 19 cases detected SLN-positive. Of these, CLND was performed in 18 patients, of whom 10 (55.6%) were women. In 18 patients with positive SLNB+CLND, 5 patients (27.8%) were detected positive non-SLN, of whom 1 was female (P=0.06). The estimated median ages for non-SLN-negative and non-SLN-positive patients were 51 and 60 years, respectively (P=0.28). Correlations between clinicopathological features and non-SLN status are demonstrated in **table II**. According to the analysis, there was no statistically significant difference between the risk of non-SLN positivity and tumor location (P=0.529) and none of the non-SLNs were involved in the head, neck, and extremities. Furthermore, no significant association was observed between non-SLN status prediction and other features such as Breslow thickness, Clark level, angiolymphatic invasion, presence of ulceration, and TMR.

Table II: Clinicopathological features of study population based on non-SLN status.

Characteristics	No. of patients	Negative (N=13)	Positive (N=5)	*P*-value
Age (year) (mean)	18	51	60	0.28
Sex				0.06
Male	8	4 (50)	4 (50)	
Female	10	9 (90)	1 (10)	
Tumor location				0.53
H&N	1	1 (100)	0 (0)	
Upper E.	2	1 (50)	1 (50)	
Lower E.	12	8 (66.7)	4 (33.3)	
Trunk	3	3 (100)	0 (0)	
Ulceration	16			0.77
Yes	9	7 (77.8)	2 (22.2)	
No	7	5 (71.4)	2 (28.6)	
Angiolymphatic invasion	7			0.81
Yes	2	1 (50)	1 (50)	
No	5	3 (60)	2 (40)	
No. of mitosis	8			0.1
< 1 / hpf	2	0 (0)	2 (100)	
>= 1 / hpf	6	4 (66.7)	2 (33.3)	
Breslow thickness, mm	16			0.21
0.75 < B < 1	0	0 (0)	0 (0)	
1 <= B <= 4	6	3 (50)	3 (50)	
B >4	10	8 (80)	2 (20)	
Clark level	16			0.58
1	1	1 (100)	0 (0)	
2	0	0 (0)	0 (0)	
3	1	1 (100)	0 (0)	
4	9	5 (55.6)	4 (44.4)	
5	5	4 (80)	1 (20)	

P value <0.05 was considered statistically significant. Continuous data were reported with medians. Categorical data were presented with frequencies and percentages. H&N: Head and Neck; Upper E: Upper extremity; Lower E: Lower extremity; hpf: high power field.

Discussion

in our study, the overall positive rate of SLNB was 33.9%, which has been reported to be 13-30% in the majority of studies[45]. Currently, according to the AJCC system, SLN biopsy in patients with CM has been recommended from the stage (IB) onwards. Based on the standard treatment, if SLN is involved, CLND will be performed[46]. Morton et al.[47] showed that immediate screening after demonstrating SLN involvement against delayed screening (following clinical lymph node involvement) could improve the survival rate by up to 20% (72% versus 52% of 5-year overall survival). Given the ability to predict SLN metastasis in patients with melanoma, it improves the therapeutic interventions in these patients. Numerous studies have been performed to identify clinicopathological variables in these patients to estimate the likelihood of involvement of the lymphatic system and to benefit from these therapeutic effects[48,49]. One of the goals of our study was to find these predictors. In our study, there was only a statistically significant relationship between the primary tumor thickness (Breslow) and the probability of SLN involvement (P = 0.04). At a thickness of 1-4 mm, 24.1% involvement was observed and at a thickness of more than 4 mm, 58.8% involvement was

obtained, which is consistent with the results of previous studies[50]. An interesting finding in the present study was the 62% prevalence (35 out of 56 persons) of primary melanoma in the lower extremity. There was no significant relationship between tumor location and sentinel (P=0.19) or non-sentinel (P=0.53) lymph node involvement.

Of the primary tumor sites, tumors located in the trunk (75%) and upper extremities (40%) were most likely to have SLN involvement. However, previous reports have reported SLN metastasis to be more common in the trunk tumors. Another interesting finding was the frequency of 62% for the patients with a depth of Clark of 4-5, which led to a higher incidence of SLN involvement (40% for Clark levels 4-5 and 17% for Clark levels 1-2-3), which was not statistically significant (P=0.16). The false-negative rate of SLNB in our study was 2.2%, which is in line with the results of previous studies[51]. In addition, our study aimed to investigate the predictors of non-sentinel lymph node involvement after positive-SLN involvement.

Following the introduction of SLN biopsy into melanoma and subsequent scans, it was found that SLN involvement, with the exception of the SLN involved, is unlikely to affect other LNs of the same basin. Therefore, several studies have been designed to determine which patients with malignant tumors are less likely to develop other non-SLNs after sentinel lymph node involvement[52]. These studies have reported different results and found that this difference is due to differences in the sample size, population, and different histological protocols and measurements. The prevalence of non-SLN involvement in our study was 27.8%, which is in agreement with the figures obtained by other studies[53]. In our study, age, sex, tumor location, primary tumor ulceration, angiolymphatic invasion, TMR, tumor thickness (Breslow), and Clark level of the invasion were studied. None of the factors examined in our study had a significant relationship with non-SLN status. In a meta-analysis, however, Breslow thickness, Clark level, and primary tumor ulceration were significant predictors of non-SLN involvement[52]. It seems that our low sample size has not been able to prove this significance in our study. The primary tumor ulceration was not associated with non-SLN status (p = 0.77). This may be due to the difference in pathological and clinical definitions of the lesion. In most patients with primary tumor malignancies of Clarks 4 and 5 endpoints, Clark 5 had a lower risk of non-SLN status than Clark 4 (p=0.58), which may be due to differences in histological parameters among the pathologists. No relationship was found between the number of mitoses in the tumor and non-SLN status (p=0.1). As for the selection of the Cancer Institute of Imam Khomeini Hospital in Tehran for the treatment of patients in the current study, it is the only center in Iran to provide the latest guidelines and treatments (including NCCN) to patients. It should be noted that its results provide an overview of the patients with CM and the medical treatment for cases with lymphatic system

involvement in Iran. Based on the results obtained in this study, a long-term follow-up remains to be achieved for definitive results and consequently correct and effective management of treatment recommendations for these patients. The limitations of this study include low sample size, single-center study, retrospective study, and differences in histological measurements.

Conclusion

Our findings indicated that Breslow thickness was significantly associated with positive SLN biopsy. Thus, Breslow thickness appears to be a potent predictor of positive SLN status in CM cases. Further research, however, is required to validate these promising results.

Author's contributions
All authors contributed to the conceptualization and design of the paper, the acquisition, analysis and interpretation of data. They were drafting the study and revising the article critically for main intellectual content. At the end, all authors read and approved the final manuscript.

Availability of data and materials
Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This research was conducted in accordance with the amended Declaration of Helsinki. The study was approved by the Committee of Research Ethics of Tehran University of Medical Sciences.

Consent for publication
Not applicable.

Conflict of interest
There are no conflicts of interest.

ABBREVIATIONS
CM: Cutaneous Melanoma
SNs: Sentinel nodes
SLN: Sentinel lymph node
SLNB: Sentinel lymph node biopsy
LNs: Lymph nodes
TMR: tumor mitotic rate
UV: Ultraviolet
ELND: Elective lymph node dissection
OS: Overall survival
PDT: Photodynamic therapy
CLND: Complete lymph node dissection
H&N: Head and Neck
Upper E: Upper extremity
Lower E: Lower extremity
Hpf: High power field

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ORIGINAL

Liver abscesses in patients with coronavirus infection

Abscesos hepáticos en pacientes con infección por coronavirus

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Abstract

Background: Recent studies demonstrate that COVID-19 is associated with systemic infectious and inflammatory diseases. Various symptoms of liver and gastrointestinal damage are often diagnosed in patients with COVID-19 but there is limited data on liver abscesses.

Material and methods: The current analysis includes 11 patients who were treated at Botkin Hospital, Moscow in the period from September 2021 to May 2022 for liver abscesses and who previously suffered from COVID-19 infection.

Results: Surgical intervention has been performed in the volume of transcutaneous drainage of liver abscesses under ultrasound guidance. The complex therapy included antibacterial drugs (according to the results of a microbiological study with the determination of the sensitivity of the flora to antibacterial drugs), anti-inflammatory drugs, daily sanitation of the abscess cavity based on the proposed algorithm. Seven patients (63.6%) were discharged with drainage under the supervision of clinic doctors. Four patients (36.4%), who had significant regression of the abscess cavity had their drainage removed before discharge.

Conclusion: Patients with prior COVID-19 may develop liver abscesses. It is important to carry out thorough diagnostic evaluation in patients who complain of fever and/or abdominal pain after coronavirus infection and timely drainage of these abscesses. The current study demonstrates that percutaneous drainage, sanitation of the cavity combined with empirical antibiotic treatment is the optimal treatment modality for this group of patients.

Keywords: coronavirus infection; liver abscess; percutaneous drainage.

Resumen

Antecedentes. Estudios recientes demuestran que la COVID-19 está asociada a enfermedades infecciosas e inflamatorias sistémicas. En pacientes con COVID-19 suelen diagnosticarse diversos síntomas de daño hepático y gastrointestinal, pero existen pocos datos sobre abscesos hepáticos.

Material y métodos. El presente análisis incluye 11 pacientes que fueron tratados en el Hospital Botkin, Moscú, en el período comprendido entre septiembre de 2021 y mayo de 2022 por abscesos hepáticos y que previamente sufrieron infección por COVID-19.

Resultados. La intervención quirúrgica se ha realizado en el volumen de drenaje transcutáneo de abscesos hepáticos bajo guía ecográfica. La terapia compleja incluyó fármacos antibacterianos (de acuerdo con los resultados de un estudio microbiológico con la determinación de la sensibilidad de la flora a los fármacos antibacterianos), fármacos antiinflamatorios, saneamiento diario de la cavidad del absceso basado en el algoritmo propuesto. Siete pacientes (63,6%) fueron dados de alta con drenaje bajo la supervisión de médicos clínicos. A cuatro pacientes (36,4%), que presentaron una regresión significativa de la cavidad del absceso, se les retiró el drenaje antes del alta.

Conclusiones. Los pacientes con COVID-19 previa pueden desarrollar abscesos hepáticos. Es importante realizar una evaluación diagnóstica exhaustiva en los pacientes que se quejan de fiebre y/o dolor abdominal tras una infección por coronavirus y drenar a tiempo estos abscesos. El presente estudio demuestra que el drenaje percutáneo, el saneamiento de la cavidad combinado con un tratamiento antibiótico empírico es la modalidad de tratamiento óptima para este grupo de pacientes.

Palabras clave: infección por coronavirus; absceso hepático; drenaje percutáneo.

Introduction

The coronavirus infection (COVID-19) is an acute infection of the respiratory system, caused by severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV2) that has become a public health problem worldwide[1]. COVID-19 has causes significant global morbidity, mortality but also disruption to society and economies. However, the true incidence of COVID-19 is likely to have been underestimated, mostly due to individuals underreporting mild symptoms or inadequate testing strategies[2]. SARS-CoV2 belongs to the Coronaviridae family and is a single-stranded RNA virus. The main target of this virus is the angiotensin-converting enzyme 2 (ACE2) receptor. Therefore, it was initially considered that COVID-19 primarily affects the respiratory system[3].

In addition, ACE2 receptors are also present in the liver, gastrointestinal tract, heart, kidneys, pancreas, muscles, and nervous system. Therefore, the true nature of post-COVID-19 effects and changes in the body are yet to be discovered. According to recent data, COVID-19 is regarded as a systemic infectious and inflammatory disease[4,5].

There have been several studies of liver disease in patients who have had SARS-CoV2 infection. Elevated transaminases are seen in more than 50% of patients and are an indicator of liver damage and overall severity of the disease[6]. Studies have shown that coronavirus can bind to ACE2 receptors on cholangiocytes and lead to their dysfunction, which causes systemic inflammatory response and liver damage[7]. In addition, immune-mediated inflammation in severe forms of COVID-19 is accompanied by an increase in the level of C-reactive peptide (CRP), D-dimer, interleukin-6 and ferritin, which altogether contribute to liver damage[8].

Pyogenic liver abscess is an emerging healthcare problem with an increasing incidence worldwide[9,10]. The true incidence of this disease varies between countries and is hard to assess. The main reasons are increase in frequency of hepatobiliary interventions and organisms with multidrug resistance and comorbidities [9-11]. However, liver abscesses after COVID-19 infection is a new challenge. Some of the manifestations of infectious diseases may mask liver abscesses and therefore are a diagnostic challenge for physicians in patients with SARS-CoV2. Moreover, they may superimpose on already severe condition of the patient leading to increased morbidity and mortality.

Epidemiological studies have shown that half of the patients had impaired liver function, in particular an increase in the level of alanine aminotransferase (ALT) or aspartate aminotransferase (AST), and 1% of patients had severe liver damage, including liver abscess [12].

Nevertheless, there is limited data on liver dysfunction and infection in patients with COVID-19. We present an analysis of a group of patients who previously suffered from COVID-19 and developed liver abscesses during their recovery period.

Materials and methods

The work is based on the analysis of 11 patients who were treated at the surgical clinic of Botkin hospital from September 2021 to May 2022 for liver abscesses. The diagnosis of liver abscess was based on medical records, clinical picture, imaging studies, laboratory results, cytological and microbiological results. The study had a prospective design. The complete inpatient and outpatient medical records were extracted to collect the following clinical variables: age, sex, previous data on COVID-19 infection, BMI, comorbidities. The main characteristics of patients are presented in **table I**. The criteria of inclusion in the study were previous history of coronavirus infection (positive PCR test for SARS-CoV2) with previous vaccination. All patients underwent a systematic comprehensive preoperative examination and postoperative control. All patients underwent laboratory tests (white blood cell count, AST level, ALT, CRP, SARS-CoV2 IgM and IgG antibodies), abdominal ultrasound (USG), abdominal computer tomography (CT) with intravenous contrast, abdominal magnetic resonance imaging (MRI) with intravenous contrast, cytological and microbiological studies. Liver abscess was defined as a hepatic lesion on imagining (USG, CT, MRI) in patients with corresponding clinical picture, presence of pus in the aspirate, positive culture, response to antibiotic treatment and drainage. Percutaneous drainage was performed under local anesthesia (2% lidocaine solution) with USG guidance by two healthcare professionals ("free hand" technique): a surgeon and medical ultrasonography specialist. Aspirated pus was sent for gram stain and culture. The acquired quantitative variables were expressed as mean (M) with standard deviation (SD).

Results

Eleven patients with complaints of abdominal pain and hyperthermia were admitted to the surgical clinic of Botkin hospital. During ultrasound examination of the abdominal cavity, all patients had volumetric liquid formations in the liver (from 1 to 3), ranging in size from 20x18x14 mm to 185x150x135 mm. All patients showed changes in the laboratory values, namely leukocytosis, increased ALT, AST and CRP (**Tables I, II**).

All hospitalized patients had a history of coronavirus infection 4-6 months before the present hospitalization, without prior vaccination. Six patients (54.5%) had

Table I: Major clinical characteristics of the patients.

Parameters		
Age (M ± SD, min-max), years	61.2 ± 9.3 (38-74)	
Sex, n (%)	Males 6 (54.55%)	Females 5 (45.45%)
BMI (M ± SD, min-max), kg/m²	27.8 ± 2.9 (21.9-32.4)	
SARS-CoV-2 antibodies (M ± SD, min-max)	IgM 0.93 ± 1.03 (0.19-4.01)	IgG 163.17 ± 130.7 (7.96-358.17)

Table II: Laboratory values.

Parameters	Before	After
Leukocytes (M ± SD, min-max), 10^9/l	16.1 ± 4.19 (8.4-24.1)	7.7 ± 1.3 (5.6-13.6)
ALT (M ± SD, min-max), U/l	93.1 ± 56.8 (17.3-363)	19.9 ± 7.4 (5-30.1)
AST (M ± SD, min-max), U/l	90.3 ± 65.2 (21-282)	25.4 ± 8.6 (14-41)
CRP (M ± SD, min-max), mg/l	248.6 ± 41.6 (177.8-333.8)	103.8 ± 40.7 (3-175.2)

bilateral polysegmental pneumonia during the period of COVID-19 disease. In the remaining 5 patients (44.5%) there was no evidence of pneumonia. These patients underwent a blood test for antibodies to SARS-CoV-2 (IgM and IgG). All patients showed a significant increase in IgG antibody titer (**Table I**).

Further examination with CT of the abdominal cavity with intravenous contrast, in these patients, reveled multi-chamber hypodense formations in the liver parenchyma,

Figure 1: Multispiral CT. Liver abscess (arrow). A. Frontal section. B. Axial section. Multiloculated hypodens mass in the liver parenchyma with uneven fuzzy contours (arrow).
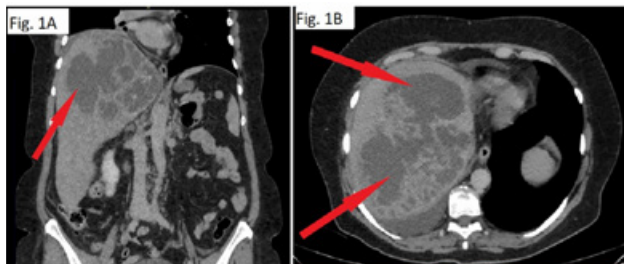
Figure 2: Magnetic resonance imaging. Liver abscess (arrow). Axial section.
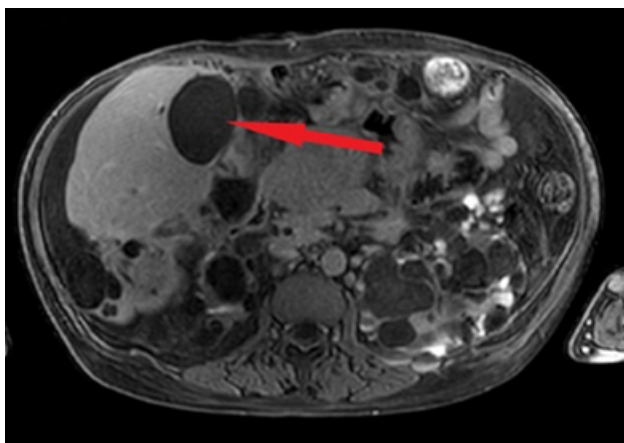
uneven fuzzy contours, actively accumulating contrast agent along the periphery (**Figure 1**).

Moreover, these patients underwent MRI of the abdominal cavity with intravenous contrast, in which the above formations are described as cystic, with signs of limited diffusion and sedimentation, poorly accumulating the contrast drug in its wall (**Figure 2**).

Blood test for antibodies to parasitic liver diseases (Echinococcus) and tumor markers (AFP) were negative in all cases.

After a comprehensive examination, all patients underwent percutaneous drainage of liver abscess under ultrasound guidance. Thick creamy pus was obtained in all cases. The contents of the abscess cavity were subjected to cytological and microbiological studies. In all of the cytological studies there were half-decayed neutrophilic leukocytes in large numbers and macrophages. Microbiological analysis revealed Klebsiella pneumonia in all patients in various titers and additionally, in 2 cases Escherichia coli. The sensitivity of the obtained microflora to antibacterial drugs was determined in order to guide the treatment process, however none of the patients required change of their initial regiment. The analysis of antibiotic resistance pattern demonstrated that Klebsiella pneumonia was sensible in all cases to amoxicillin/clavulanic acid, ampicillin/sulbactam, piperacillin/tazobactam, gentamicin, amikacin, imipenem, ertapenem, meropenem, levofloxacin, ciprofloxacin, trimethoprim/sulfamethoxazole, cefazolin, cefepime, ceftazidime, ceftriaxone, ceftolosan/tazobactam, cefuroxime and vancomycin. It was resistant to ampicillin and fosfomycin in all cases.

All patients underwent complex treatment, including appropriate antibacterial therapy based on the results of microbiological resistance, anti-inflammatory therapy, daily sanitation of abscess cavities with antiseptic solutions. All patients received i/v antibiotic treatment (cefoperazone with sulbactam 2 g every 12 hours). The medium duration of treatment was 12 days (minimum 8 days and maximum 18 days). There was an improvement in the general condition, regression of fever, a significant decrease in the flow rate of discharge through the drainage, and in some cases, its complete absence.

During control laboratory studies, normalization of all indicators was noted, including leukocytes, transaminases and CRP. The dynamics of laboratory parameters is shown in **table II**.

During control instrumental studies (including fistulography), there was a significant decrease in abscess cavities, and in 4 cases, complete regression of the cavity till the size of the drainage tube (**Figure 3**). There was no communication with the bile ducts in any cases.

Figure 3: Multispiral CT. Liver abscess after drainage. A. Frontal section. B. Axial section. The drainage tube can visualized (arrow) and the abscess cavity has decreased after therapy.
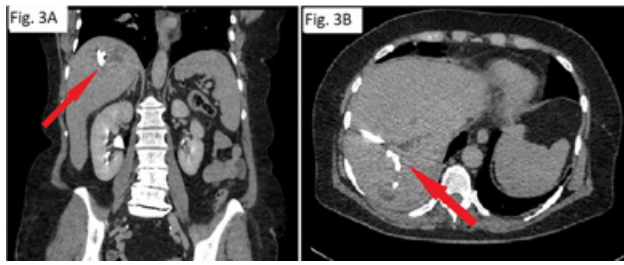
In one case (9.09%) the patient had thrombosis of the portal vein, which gradually resolved after treatment. Six patients had comorbid conditions. Two patients had diabetes mellitus type 2 (18.18%), two patients had end stage chronic kidney disease (18.18%) and another 2 had endophthalmitits (18.18%).

Figure 4: Multispiral CT. A. Portal vein thrombus (arrow). B. Decrease of the portal vein thrombus after 11 days of treatment (arrow).
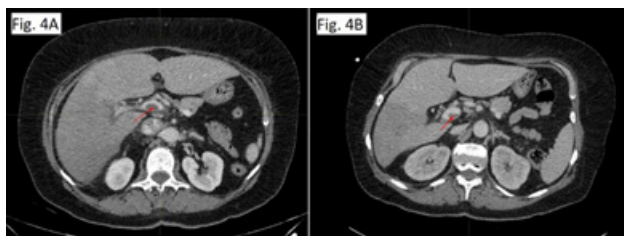
All patients were discharged to the outpatient follow-up stage in a stable satisfactory condition. Seven patients (63.6%) were discharged with drainage under the supervision of polyclinic doctors. Four patients (36.4%) who had regression of the abscess cavity had their drainage removed before discharge. There were no cases of lethal outcomes in our study group.

Discussion

There is limited data on liver abscesses in patients who had a coronavirus infection, and is mostly reflected in a few publications of clinical cases. We present an analysis of case histories of 11 patients. There is a wide range of biochemical alterations that are seen in patients with COVID-19[2]. COVID-19 associated hepatic injury is defined as ALT or AST exceeding 3 times the upper limit of the normal value; ALP, GGT or total bilirubin exceeding 2 times the upper limit of the normal values and pathogenetically can be classified into hepatocellular, cholestatic and mixed type[13]. Signs and symptoms of gastrointestinal disease are common in patients who had COVID-19. A study by Weng et al. showed that 52 (44%) of 117 patients had gastrointestinal complications after a coronavirus infection, including anorexia, nausea, diarrhea, bloating, belching, vomiting, abdominal pain, and bloody stools[14]. In comparison, in all of our patients the prevailing complaints were abdominal pain and hyperthermia. Abnormal liver function tests and liver injury can develop during the next two weeks of hospitalization in up to 76.3-93% of patients[15,16]. However, in our group of patients liver transaminases were typically 2 times the upper limit of normal value.

The easiest imaging modality to diagnose liver abscess is USG due to its wide accessibility, low cost and time-efficiency. However, the sensitivity of USG is 85% compared to 97% of CT[17]. This depends on several factors including experience of the personnel, size of the lesion and technical parameters of the device. In our study group all abscesses were visible during USG, CT and MRI examination. However, the minimal size of the abscess in our study group was 2 cm.

Treatment of patients with liver abscesses includes antimicrobial therapy together with mini-invasive procedures such as percutaneous drainage/aspiration or in some cases surgery[18,19]. USG-guided drainage is the optimal treatment strategy with empirical antibiotic therapy followed by correction of antibiotic therapy in case of inefficiency or results of culture and other modalities. All of our patients undergone percutaneous drainage under USG guidance. The proposed method should be the golden standard since surgical procedures should be reserved for individual cases. As we demonstrate in our study percutaneous drainage is mini-invasive, allows to obtain material for culture and provides time for rational antibiotic therapy. In the current study patients were assessed based on their clinical picture, laboratory results followed by USG and another imaging technique (CT and/or MRI). Drainage was possible in all cases, patients received empirical antibiotic therapy and the abscess was sanitized using antiseptic solutions daily. However, there is limited evidence-based guidelines on liver abscesses in the literature[20]. Moreover, COVID-19-related liver abscess are described in the literature mostly as case reports. Sharma and coworkers report that in their group of patients with pyogenic liver abscess (before COVID-19 period) percutaneous aspiration was required in 27.8% of cases, percutaneous catheter drainage in 43.1% and surgery in 15.5% of cases[11]. Surgery is often considered a risky procedure especially in the settings of a pandemic[21]. The main indications for drainage are: left lobe abscess, thin rim (less than 10 mm) of hepatic parenchyma, multiple abscesses, rupture, nonresponse to medical therapy after 3-5 days[20]. Antibiotic therapy should be initiated after drainage (or blood culture is septic patients)[22]. Initial antibiotic therapy usually includes a third-generation cephalosporin and metronidazole or piperacillin/tazobactam. The selection of therapy should be based on in vitro antimicrobial resistance testing and clinical response[22]. The current standard of treatment in the institution was based on empirical treatment with cefoperazon with sulbactam. None of the patients required additional treatment and the results of antimicrobial studies corresponded to the treatment. Patients who develop liver abscesses typically have predisposing factors such

as diabetes mellitus, immunosuppression, malnutrition, advances age or alcohol consumption[20]. Other risk factors may include current malignancy, liver-transplant, end-stage renal disease, and cirrhosis[9]. Glycated hemoglobin level more than 7% and systemic problems assessed by Charlson Comorbidity index are predictors of severe course of the disease and poor outcome[23]. An important point in this study is that none of the patients had any diagnosed comorbid conditions, therefore, were considered healthy at admission. This underlines an important pathogenic mechanism of immune suppression in patients with COVID-19[24]. There is severely decreased expression of adaptive immunity-related genes that may lead to secondary infections[25]. The current study brings to light clinical evidence that patients are susceptible to infection after their COVID-19 recovery period.

Ferry et al. in 2020 presented a clinical case of a patient with a purulent liver abscess who recovered from COVID-19. Liver abscess is an extremely rare disease with an annual incidence of 2.3 cases per 100,000. The authors believe that all medical professionals, in particular surgeons, should be aware not only of the typical respiratory symptoms of COVID-19, but also of possible extrapulmonary manifestations of this disease[26].

Liemarto et al. published a clinical case report of a liver abscess with necrosis in a patient with a history of SARS-CoV-2. The team of authors state that the pathophysiological causes of liver injury after COVID-19 are: direct cytotoxicity of SARS-CoV-2; immune-mediated injury due to Systemic Inflammatory Response Syndrome (SIRS); hypoxemia and vascular changes due to coagulopathy, endotheliitis or congestion due to right ventricular failure and drug-induced liver injury[19]. It is important to mention that the prevalence of chronic liver disease in patients with COVID-19 is 2-11% and can be overlooked[16,27,28]. However, all of our patients had screening for infectious disease of the liver, which were negative in all cases. Some comorbidities that are common in the population are also frequently seen in COVID-19 and are associated with liver damage such as diabetes, hypertension, obesity and cardiovascular disease[29]. Interestingly besides the commonly known risk factors such as diabetes mellitus and end stage chronic kidney disease two of our patients had endophthalmitis. Endophthalmitis is considered a rare complication, however, it has increased during COVID-19 epidemic[30]. One of the major risk factors in eye surgery, especially vitrectomy and the predominant infectious agent is Streptococcus spp. It is important to assess the patient comprehensively taking into account all the systems[31].

Portal vein thrombosis is a rare but serious complication, which is more commonly seen in underlying disease such as cirrhosis, malignancies, pancreatitis, systemic autoimmune disease, and hypercoagulable states. The diagnosis of this complication and any accompanying reason is challengeable, while rapid diagnosis and

treatment are essential[32]. One of our patients had portal vein thrombosis which resolved during the treatment period with anticoagulant therapy. The true nature of this event is hard to assess as the patient had no other comorbid conditions, but had a large multilocular abscess. Therefore, a combination of the proinflammatory state together with infection from the liver abscess and COVID-19 induced hypercoagulable state may be the explanation.

Patients with severe COVID-19 may develop Hypoxic-Ischemic Liver Injury. A study by Zhong et al. showed that liver ischemia-reperfusion can activate Kupffer cells, neutrophils and platelets, causing cellular destructive reactions that lead to inflammation and damage to the liver. Violation of microcirculation due to damage to the sinusoidal cells of the liver endothelium will also exacerbate liver ischemia and oxygen deficiency[33].

Hypoxia and inflammation are common in patients with severe COVID-19, which play an important role in the regulation of hepatocellular ACE2 expression. This explains the cause for the extrapulmonary dissemination of SARS-CoV2 in patients with acute respiratory distress syndrome (ARDS) and hypoxia. Hypercoagulability in patients with COVID-19 also contributes to liver damage with the occurrence of pulmonary thrombotic complications, which exacerbates acute right ventricular failure caused by high pulmonary vascular resistance in ARDS and leads to liver congestion[34]. Overall, it seems that liver injury during SARS-CoV-2 infection is most likely multifactorial, including direct cytopathic effect of the virus, systemic immune response, vascular damage and coagulopathy and drug-induced liver injury[6,35].

A variety of pathogenic organisms can be isolated from liver abscesses of patients with COVID-19 such as: Pseudomonas aeruginosa, Escherichia coli, Fusobacterium nucleatum, Entamoeba histolytica, Actinomyces israelii and other[18,19,36-38]. In our study all patients had Klebsiella pneumonia liver abscess and additionally in two cases Escherichia coli. The pattern of antibacterial resistance suggests that overall the bacteria were sensible to most of the available antibiotic therapy. None of the patients required step up therapy for their treatment regimen.

Autopsy studies demonstrate that patients who died of COVID-19 had histologic findings of macrovesicular steatosis and acute hepatitis combined with mild portal inflammation[39]. Most likely, the combination of the above factors and pathophysiological processes led to the formation of liver abscesses in our group of patients. However, despite the small number of scientific papers and insufficient understanding of all the morphological changes that occur in patients after COVID-19 the true nature of these cases is difficult to assess. There were no lethal outcomes in patients diagnosed with liver

abscesses. All 11 patients presented were discharged in a stable condition. The analysis of the available data and experience with this group of patients lead to the development of a clinical algorithm (**Table III**).

The main limitation of the current study is small number of cases. However, the present study represents a single center experience and one of the first attempts to analyze a group of patients with liver abscesses after COVID-19 infection from a clinical, radiological and surgical perspective.

Table III: Treatment algorithm of patient with SARS-CoV2-induced liver abscesses.

Obligatory steps	Possible complementation	Comments
COVID-19 test (PCR, IgM, IgG) History of liver disease Clinical picture of liver damage	---	Evaluation of COVID-19 status, past infections and past history of liver disease
USG of the liver	CT and/or MRI with contrast enhancement	CT with intravenous contrast enhancement should be performed for differential diagnosis and in complex abscesses MRI should be performed in cases when the biliary tract is suspected to be involved
Laboratory markers of liver function (ALT; AST; total, direct, indirect bilirubin, ALP) Laboratory marker of inflammation (CRP, leukocytes)	Oncological markers (AFP) Parasites (Echinococcus and other epidemiologically significant agents)	Other conditions which mimic liver abscess should be excluded
Drainage/aspiration of the abscess Assessment of antimicrobial resistance	Cytological evaluation	Cytological evaluation should be performed in cases when malignant conditions are suspected
Multidisciplinary approach	Telemedicine	Since this group of patients often have different comorbidities it is important to correct any metabolic, cardiovascular, kidney or other derangements

Conclusions

Patients with COVID-19 may develop liver abscesses, most likely due to direct damage to cholangiocytes, by binding of coronavirus to angiotensin-converting enzyme 2 receptors. Another important factor is a change in the immune status against the background of a systemic infectious and inflammatory disease in these patients. Moreover, patients with severe COVID-19 may develop hypoxic-ischemic liver disease. It is important to perform thorough diagnostic evaluation of the liver in patients who present with fever and/or abdominal pain after coronavirus infection. The patients should undergo complex evaluation due to comorbidities (metabolic and renal diseases). Further prospective studies are needed, including morphological evaluation of liver changes especially during autopsy. The current study demonstrates that percutaneous drainage, sanitation of the cavity combined with empirical antibiotic treatment is the optimal treatment modality for this group of patients.

Institutional Review Board Statement
The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board at Botkin Hospital, Moscow.

Informed Consent Statement
Informed consent was obtained from all subjects involved in the study.

Acknowledgments
None

Conflicts of Interest
None

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ORIGINAL

Complications of Total Joint Arthroplasty: An Epidemiological and Clinical Observations Outcomes Data

*Complicaciones de la artroplastia articular total:
una observación epidemiológica y clínica de los datos*

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Abstract

Introduction: Nowadays, total hip replacement is a highly effective surgical procedure in healthcare systems. Even though this procedure provides very effective outcomes, complications in many times are inevitable.

Methods: This observational study focused on the collection of data regarding the complications that occurred in patients who underwent Total Joint Arthroplasty for a period of 5 years. The data are collected from the arthroplasty registry in the University Trauma Center Hospital. All the major and minor procedure complication findings are analyzed by SPSS software 20.0. The logistic regression was used to identify some of the risk factors for complications A p-value of <5% was statistically significant.

Results: Overall of 812 patients, over 50 years old, who underwent total hip arthroplasty, about 62.9% were women, and the most predominant age 71-80 years old was. Women were more likely to be older and to have hypertension, anemia, and kidney disease compared to men (P < 0.02). The rate of major and minor complication procedures was reported at 2.4% and 5.5% respectively. A significant association was seen between risk factors such as BMI, syndrome metabolic, and previous THA. The most predominant complications were dislocations 1.8%, infections 2.5%, leg length discrepancy 1%, nerve damage 0.2% and muscle weakness 5.5%. Readmission as a consequence of postoperative complications was reported only in 1.2% of patients.

Conclusion: The findings of this study, suggest a minor rate of postoperative complication procedures among patients who underwent the intervention for total joint arthroplasty. Furthermore, studies are recommended to clarify the risk factors that influence postoperative complication procedures in total joint arthroplasty patients.

Keywords: replacement of total joint arthroplasty, complication, procedure.

Resumen

Introducción: Hoy en día, la artroplastia total de cadera es un procedimiento quirúrgico muy eficaz en los sistemas sanitarios. Aunque este procedimiento proporciona resultados muy eficaces, en muchas ocasiones las complicaciones son inevitables.

Métodos: Este estudio observacional se centró en la recogida de datos relativos a las complicaciones ocurridas en pacientes sometidos a artroplastia total de articulación durante un periodo de 5 años. Los datos proceden del registro de artroplastias del Hospital Universitario Trauma Center. Todos los resultados de las complicaciones mayores y menores del procedimiento se analizan mediante el programa SPSS 20.0. Se utilizó la regresión logística para identificar algunos de los factores de riesgo de complicaciones Un valor p de <5% fue estadísticamente significativo.

Resultados: En total de 812 pacientes, mayores de 50 años, que se sometieron a artroplastia total de cadera, alrededor del 62,9% eran mujeres, y la edad más predominante era 71-80 años. Las mujeres tenían más probabilidades de ser mayores y de padecer hipertensión, anemia y enfermedad renal en comparación con los hombres (p < 0,02). La tasa de procedimientos con complicaciones mayores y menores fue del 2,4% y el 5,5% respectivamente. Se observó una asociación significativa entre factores de riesgo como el IMC, el síndrome metabólico y la ATC previa. Las complicaciones más predominantes fueron las luxaciones (1,8%), las infecciones (2,5%), la discrepancia en la longitud de las piernas (1%), las lesiones nerviosas (0,2%) y la debilidad muscular (5,5%). El reingreso como consecuencia de complicaciones postoperatorias sólo se registró en el 1,2% de los pacientes.

Conclusiones: Los resultados de este estudio, sugieren una tasa menor de procedimientos de complicaciones postoperatorias entre los pacientes que se sometieron a la intervención para la artroplastia total de la articulación. Además, se recomiendan estudios para aclarar los factores de riesgo que influyen en los procedimientos de complicaciones postoperatorias en pacientes con artroplastia articular total.

Palabras clave: sustitución de artroplastia articular total, complicación, procedimiento.

Introduction

Total joint replacement surgery is a widely performed procedure in orthopedics with a high success rate and cost-effectiveness. This intervention is undertaken for patients suffering from an advanced level of degenerative hip osteoarthritis or traumatic arthritis, Rheumatoid arthritis, malignancy, etc. The main outcomes of total joint replacement are to relieve pain and improve the function and quality of life of the patients (1,2). Unfortunately, total arthroplasty surgery may be accompanied by certain complications. Patient health status affects the level of risk that might be faced. According to statistical data, the percentage of complications in adults undergoing hip replacement surgery is only 4% (3).

Some of the complications are not specific to this type of procedure and they may occur with any surgery. Patients may present complications such as respiratory problems after surgery; heart attack or stroke during or after surgery; lung, urinary tract, or joint infections. Bleeding from operatory wounds is also a concern. Fatality cases are strongly associated with lower respiratory tract infection and renal failure (4-6).

Some major complications that can be encountered after total joint arthroplasty replacement include clots in the legs known as Deep Vein Thrombosis or in the lungs known as Pulmonary Emboly. About 1% of people can face this complication. Other concerns related to prosthesis are postoperative dislocation, fracture, and aseptic loosening. Less than 2% of people are subject to dislocation. Breakage of implants can happen in less than 0.5% of patients (7). Heterotopic ossification can be observed by imagery as early as 3 weeks after surgery and patients complain of pain and stiffness (8). Rarely during the surgery, the blood vessels (0.1%), or the nerves (1%) may get damaged. and if these problems will not resolve they would bring about the death of the patient (9). Being aware of perioperative and postoperative complications should help to focus on reducing the risk of total joint arthroplasty. The purpose of this paper aims to shed light on the frequency of complications in order to adverse outcomes and to have better results from procedures.

Methods

All the major and minor procedure complication findings are analyzed by SPSS software 20.0. The logistic regression was used to identify some of the risk factors for complications A p-value of <5% was statistically significant.

Methods

Study design
This is an observational study focused on the collection of data regarding total joint arthroplasty replacement (total hip THA and total knee arthroplasties TKA). The data are collected from the arthroplasty registry in the University Trauma Center Hospital for a period of 5 years.

Study population
The inclusion criteria were all patients over 50 years old admitted to the Trauma Hospital center during the periods January 2013 to December 2018, and undergoing total joint arthroplasty replacement. The exclusion criteria were all patients admitted to the hospital under 50 years. We have prepared a questionnaire, which is completed for each patient. We analyzed the sociodemographic data (such as age, gender, place of residence, co-morbidities according to the ASA score (American Society of Anesthesiologists score), mobility, and type of injury), as well as clinical data and those operators and post-operator (such as data related to the process, the type of prosthesis used, the result obtained after the intervention, days of hospital stay, and complications encountered, mobility in 120 days and mortality).

Outcomes Complications were collected in two categories. In the first category, we have classified the 'major' complications, and in the second one, we have classified 'minor' complications. Major complications we have defined as those requiring complex medical intervention, meanwhile in minor all other complications.

Statical data
The obtained data were analyzed with the statistical program SPSS (Inc, Chicago, Illinois), version 23.0. Data were presented in frequency, percentage, mean, and standard deviation. Continuous variables of socio-demographic characteristics of patients were analyzed using descriptive statistics followed by independent Student's t-tests, and the chi-squared (χ^2) test, while Fisher's exact test was used to analyze categorical variables comparing the changes of the variables and the results obtained from the intervention. To compare the data obtained where gender was taken as an independent variable, we used an in-depth analysis of logistic regression. Odds ratios (OR) and intervals were evaluated 95% confidence level (95% CI), and a p-value of <0.05 was considered statistically significant.

Results

Overall of 812 patients, over 50 years old, who underwent total hip arthroplasty, about 511 (62.9%) were women, and 301 (37.1%). In this study, the mean age resulted in 71.15±4.09 With a minimum age of 53 and as well as a maximum age of 91, the study's mean age was 71.15.40. If we quickly compare the ages of the patients, we see that there are, respectively, 62 (7.6%) and 99 (12.2%) fewer patients in the extreme age groups who need a full joint arthroplasty replacement. However, the largest percentages were found among 297 (36.6%)

people aged between 60 and 70 and 354 (43.6%) those aged between 71 and 80. Regarding residency, there were more patients among those residing in urban regions 559 (68.8%), compared to those in rural regions 253 (31.2%). Furthermore, more than half of patients undergoing TJA, were from Tirana's capital city 438 (53.9%), and 374 (46.1%) are from other cities such as Elbasan, Durres, Vlore, Fier, etc.

Based on the married status, we classified patients into two categories which are no-married and married. In the no-married category, we included all patients who were referred as single, widow, or divorced, while in the second category we included all patients who were referred that were married at the time undergoing TJA. More than ¾ of patients 630 (77.6%) resulted married, and 182 (22.4%) were single/widows/divorced. Out of 182 patients classified as no married category, 124 (68.1%) were widows, 36 (19.8%) were divorced, and 20 (11%) were single.

Patients with body mass index (BMI) classified in the category overweight and /or obese are seen as a negative predictor for many diseases included here and problems with the joints. More than half of the patients 464 (57.1%) resulted with BMI of overweight and /or obese, while 348 (42.9%) were underweight/normal weight. We have also evaluated the patient's living habits.

Based on statistical analysis data collected by each patient, about 219 (27%) had been or were alcohol users, 305 (37.6%) were smoking users and 490 (60.3%) used drugs. **Table I** shows the epidemiological baseline characteristics of patients who underwent total joint arthroplasty.

Before the intervention, all patients were assessed for pre-anesthesia medical co-morbidities based on the ASA score (The Physical Status Classification System). Approximately 142 (17.5%) patients were assessed in the first category of ASA score, 441 (54.3%) in the second and third categories, and 229 (28.2%) in the fourth category. Regarding the comorbidities of patients, nearly 348 (42.9%) are treated for hypertension, 215 (26.5%) have CVD, 184 (22.7%) have DM, and anemia was present in 52 (6.4%). Moreover, 67 (8.2%) have kidney diseases, 237 (29.2%) have osteoarthritis or degenerative joint disease, 290 (35.7%) have connective tissue-rheumatoid arthritis and other rheumatic diseases, and 49 (6%) have chronic pulmonary disease. To others 102 (12.6%) we have included dyslipidemia, hypothyroidism, etc.

In this stud, we have evaluated the WOMAC score based on three subscales such as pain with 5 questions, stiffness with 2 questions, and physical function with 17 questions. The mean Womac score evaluation among our patients resulted in 78.50 ±5.18.

Related to the procedure type of 812 patients undergoing total joint arthroplasty replacement, 376 (46.3%) underwent THA while 436 (53.7%) underwent TKA. Despite the procedure typically used in the replacement, contralateral articulation which is included but is not operated results in 241 (29.7%) patients, contralateral articulation included and operated results in 164 (20.2%) of patients, and not contralateral articulation included results in 407 (50.1%). Cemented-type prostheses were applied in 168 (20.7%) of the patients who underwent total joint replacements while most of them 644 (79.3%) applied cementless-type prostheses. **Table II** shows the clinical pre-operative conditions, comorbidities, and procedures used in total joint replacements of patients.

Table I: The epidemiological baseline characteristics of patients who underwent TJA.

Variables	Total number
Mean age (St.D)	71.15±4.09
Age groups 50-60 years old 61-70 years old 71-80 years old ≥ 81	62 (7.6%) 297 (36.6%) 354 (43.6%) 99 (12.2%)
Gender Female Male	511 (62.9%) 301 (37.1%)
Residence regions Rural Urban	253 (31.2%) 559 (68.8%)
City Tirana Other Cities	438 (53.9%) 374 (46.1%)
Marital status Singel/Widow/Divorced Married	182 (22.4%) 630 (77.6%)
Body mass index (BMI) Underweight/normal weight Overweight and /or obese	348 (42.9%) 464 (57.1%)
Living habits Alcohol use Smoking Use of drugs	219 (27%) 305 (37.6%) 490 (60.3%)

Table II: Clinical conditions, comorbidities of patients, and procedures used in replacement.

Variables	Total number
ASA score First category Second & third categories Fourth category	142 (17.5%) 441 (54.3%) 229 (28.2%)
Comorbidities Hypertension Cardio Vascular Diseases (CVD) Diabetes Mellitus (DM) Anemia Kidney diseases Osteoarthritis or degenerative joint disease Connective tissue- Rheumatoid arthritis and other rheumatic diseases Chronic pulmonary disease Other comorbidities	348 (42.9%) 215 (26.5%) 184 (22.7%) 52 (6.4%) 67 (8.2%) 237 (29.2%) 290 (35.7%) 49 (6%) 102 (12.6%)
Procedure Type Total hip arthroplasty (THA) or Total knee arthroplasty (TKA) Womac score evaluation (mean ± StD)	376 (46.3%) 436 (53.7%) 78.50 ±5.18
Contralateral articulation Included but not operated Included and operated Not included	241 (29.7%) 164 (20.2%) 407 (50.1%)
Type of prostheses Commented prostheses Cementless prostheses	250 (30.8%) 562 (69.2%)

The rate of major and minor complication procedures was reported at 0.25% and 5.5% respectively. We have separated the complications into major and minor. Major complications included reoperation, dislocation, deep vein thrombosis, and pulmonary embolism. Minor complications include bladder, infection, joint stiffness, unexpected pain, nerve damage, leg length discrepancy, muscle weakness, and readmission. In THA, the percentage of complications was 1.35% bladder, 2.6% infections, 1% leg length discrepancy, 3% unexpected pain, 0.25% nerve damage, 5.54% muscle weakness, and 1.5% joint stiffness. Readmission as a consequence of postoperative complications was reported only in 2.46% of patients. While in TKA, 1.1% böadder, 2.2% infections, 0.73% leg length discrepancy, 2.2% unexpected pain, 0.1% nerve damage, 3.80% muscle weakness, 0.90% joint stiffness, and 0.61%. **Figure 1** shows the minor complications of THA and TKA replacement arthroplasty. There is found a significant association between minor complications between TKA and THA, χ^2=14, 95% CI [5.3-21.7], p-value=0.001.

Major complications in THA replacements resulted in 0.5% reoperation, 1.85% dislocation, 0.6% deep vein thrombosis, and 0.37% pulmonary embolism. TKA major complications resulted in 0.36 reoperation, 2% dislocation, 0.73% deep vein thrombosis, and 0.25% pulmonary embolism. There is found a significant association between major complications between TKA and THA, χ^2=5.2, 95% CI [1.9-11.6], p-value=0.02 (**Figure 2**).

Table III shows the logistic regression between THA and TKA. A significant association was seen between some of the risk factors such as age, gender, marital status, living habits, BMI, comorbidities including syndrome metabolic, and minor and major complications for THA. P-value resulted <0.05 in these risk factors, while for Asa score, contralateral articulation, and type of prostheses there was not found a significant association in patients undergoing THA replacements.

In contrast with THA, in patients undergoing TKA, a significant association was found for gender, marital status, living habits, BMI, comorbidities, contralateral articulation, and minor and major complications. There was no found significant association only for age and type of prostheses with p-value>0.05.

Figure 1: The minor complication of THA and TKA replacement arthroplasty.
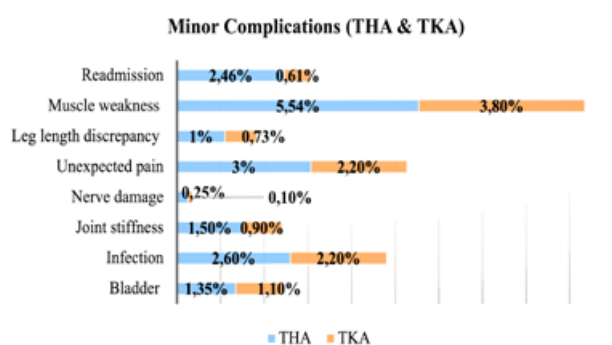
Figure 2: The major complication of THA and TKA replacement arthroplasty.
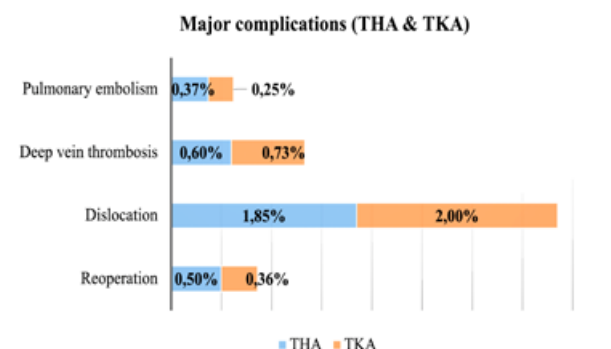
Table III: Logistic regression THA versus TKA.

Variables (risk factors)	Reference -1	THA Odds ratio 95% CI	p-value	TKA Odds ratio 95% CI	p-value
Age	Per 10 years each age group	1.2 [0.4-4.6]	0.04	1.08 [0.5-3.8]	0.051
Gender, female	Male	1.8 [1.1-5.2]	0.02	2.1 [1.4-4.7]	0.01
Marital status, no married	Married	2.4 [1.3-7.5]	0.002	1.7 [1.02-5.1]	0.03
Living habits, Yes	No	1.6 [0.9-4.1]	0.03	1.4 [0.5-3.9]	0.04
BMI, overweight, obese	Underweight, normal weight	2.1 [1.4-6.3]	0.004	2.3 [1.7-5.9]	0.008
Asa score II-IV category	I category	0.9 [0.1-2.07]	0.8	1.6 [0.8-4.05]	0.04
Comorbidities Yes	No	3.5 [1.3-11.6]	<0.0001	2.8 [1.7-6.4]	0.009
Contralateral articulation included	No included	0.5 [0.02-2.05]	0.6	1.02 [0.4-3.4]	0.048
Type of prostheses, Cementless prostheses	Commented prostheses	0.7 [0.2-3.3]	0.8	0.5 [0.09-2.5]	0.09
Minor complications Yes	No	11.8 [6.4-19.9]	0.001	9.4 [2.5-15.7]	0.005
Major complications, Yes	No	6.03 [1.3-13.5]	0.01	4.03 [1.2-8.4]	0.03

Discussion

Total joint arthroplasty is a treatment that helps patients for relieving pain and restore function in these patients when medical therapy fails[10]. In this study, we have analyzed data from 812 patients who underwent arthroplasty over 5 years. The prevalence of total hip arthroplasty among patients resulted in 46.3% while total knee arthroplasty replacements resulted in 53.7%.

Even though many studies have highlighted the predominance of females who underwent total joint arthroplasty replacements compared to males[11-14], other researchers reported that no existing difference related to gender and total joint replacements. In general, females often postponed opting to undergo total joint replacement and require help only when there have substantial pain and functional limitations of the joints. In our study, we found a predominance of females in 62.9% compared to males in 37.1%. There is found a significant association between gender and total joint arthroplasty χ^2= 2.4 95% CI [0.7-5.3], p-value =0.03. These findings are similar to other studies[15-18].

The application of arthroplasty replacements in patients with joint problems has improved their vital function, reduced pain, and most importantly improved quality of life for these patients[19,20]. In the next 10-20 years, joint arthroplasty replacement rates will substantially increase based on previsions. This will happen in two ways. The first way, the increased rate will come as the aging population consequence, and the other way increasing use in patients younger than age 60 years, who currently represent 15% of the entire population undergoing surgery. This will increase the rate of joint arthroplasty replacement necessity in the future for people under 60 years old[19,21]. Milanovic et al and Van der Willik et al, highlight in their study that the age-related decline in physical function is commonly experienced in older people. They further continue to say that the impact of joint arthroplasty replacement on functional outcomes needs to be considered exactly in elderly people[22,23]. In this study, the largest percentages were found among 297 (36.6%) people aged between 60 and 70 and 354 (43.6%) those aged between 71 and 80.

Many studies have reported more than one comorbidity among patients undergoing total joint arthroplasty replacements[24-26]. According to the comorbidities of our patients, 42.9% have hypertension, 26.5% have CVD, 22.7% have DM, 6.4% have anemia 29.2% have osteoarthritis or degenerative joint disease, 35.7% have connective tissue-rheumatoid arthritis and other rheumatic diseases. Women were more likely to be older and to have hypertension, anemia, osteoarthritis, rheumatoid arthritis, and other rheumatic diseases compared to men, p-value <0.02. Piano et al. in a study reported a high percentage of hypertensive patients submitted to HTA, 45.9% were hypertensive. This finding was almost similar to our study[27]. Moreover, the previous study conducted by Woo-Yong et al reported a high rate of osteoarthritis and rheumatoid arthritis among patients Undergoing Total Hip Arthroplasty in Korea, which was almost the same as our findings[26].

Related to the complications that happened as a consequence of joint arthroplasty replacements, we have recorded a low rate with a range from 0.25% to 5.5%. In many studies, factors such as gender, elderly people, BMI, comorbidities, Bleeding disorders, and anemia play a critical predictors role in post-operative complications overall in both THA and TKA patients[28-33]. Based on logistic regression between complications that happened during THA and TKA replacements and some of the risk factors, we found a significant association was seen between age, gender, marital status, living habits, BMI, and comorbidities, with a p-value <0.05. Approximately 20% of patients used the cemented prosthesis, belonging to the age of over 65 years. Total arthroplasty significantly improves function and quality of life and reduces pain in 89.2% of patients.

Conclusion

The findings of this study, suggest a minor rate of postoperative complication procedures among patients who underwent the intervention for total joint arthroplasty. Furthermore, studies are recommended to clarify the risk factors that influence postoperative complication procedures in total joint arthroplasty patients.

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Conflict of interest

The authors declare that there is no financial or non-financial conflict of interest. All the data presented in this paper have been collected on my part and the participant's anonymity is preserved.

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ORIGINAL

Diagnostic and Prognostic Role of Delta Neutrophil Index (DNI), With Emphasis on Gastrointestinal Disorders

Función diagnóstica y pronóstica del índice de neutrófilos delta (DNI), con énfasis en los trastornos gastrointestinales

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Abstract

Background: A brand-new biomarker for diagnosis and prognosis for a variety of inflammatory or infectious conditions is the delta neutrophil index (DNI). DNI is a laboratory index that is determined by dividing the total number of peripheral blood neutrophils by the number of immature granulocytes. However, there are few studies that have examined the potential use of DNI as a prognostic biomarker in gastrointestinal disorders and their associated infections. The purpose of this study was to explore the role of delta neutrophil index (DNI) as a biomarker to determine the prognosis of infectious conditions, especially in gastrointestinal diseases.
Methods: The research is a bibliographic review. To review the articles, from the databases PubMed, Science Direct, Scopus, Google Scholar, etc., and based on the inclusion criteria, case reports, cohorts and numerous clinical studies used in a period of mostly 4 years (2019-2023) were selected. The final sample used in this review included 120 articles.
Results and conclusion: The results showed that DNI may be considered as a primary and reliable biomarker for diagnosis, prognosis, initial triage, surgical outcomes, various infections, as well as predicting the severity of pediatric and gynecological conditions and cardiopulmonary or gastrointestinal disorders and etc.

Keywords: Delta Neutrophil Index (DNI), Prognosis, Infectious Conditions, Gastrointestinal Disorders.

Resumen

Antecedentes: El índice delta de neutrófilos (DNI) es un nuevo biomarcador para el diagnóstico y el pronóstico de diversas enfermedades inflamatorias o infecciosas. El DNI es un índice de laboratorio que se determina dividiendo el número total de neutrófilos de sangre periférica por el número de granulocitos inmaduros. Sin embargo, hay pocos estudios que hayan examinado el uso potencial del DNI como biomarcador pronóstico en los trastornos gastrointestinales y sus infecciones asociadas. El propósito de este estudio fue explorar el papel del índice delta de neutrófilos (DNI) como biomarcador para determinar el pronóstico de afecciones infecciosas, especialmente en enfermedades gastrointestinales.
Métodos: La investigación es una revisión bibliográfica. Para la revisión de los artículos, a partir de las bases de datos PubMed, Science Direct, Scopus, Google Scholar, etc, y en base a los criterios de inclusión, se seleccionaron informes de casos, cohortes y numerosos estudios clínicos utilizados en un periodo mayoritariamente de 4 años (2019-2023). La muestra final utilizada en esta revisión incluyó 120 artículos.
Resultados y conclusiones: Los resultados mostraron que el DNI puede considerarse como un biomarcador primario y confiable para el diagnóstico, pronóstico, triaje inicial, resultados quirúrgicos, diversas infecciones, así como para predecir la gravedad de afecciones pediátricas y ginecológicas y trastornos cardiopulmonares o gastrointestinales y etc.

Palabras clave: Índice de neutrófilos delta (DNI), pronóstico, afecciones infecciosas, trastornos gastrointestinales.

Introduction

Excessive production of cytokines and chemokines in the early stages of infection or inflammation limits the migration of neutrophils to the target organ, and therefore fewer mature neutrophils enter the blood circulation to compensate for the lack of active neutrophils. This modification process is referred to as "left shift". By using the DNI index, which actually indicates the ratio of immature granulocytes to the total number of neutrophils, myeloperoxidase channels and nuclear lobularity can be indirectly measured. This technique makes it possible to predict the prognosis in various infectious or inflammatory conditions, and in this way, the number of immature granulocytes in the blood circulation can be shown . This is how DNI is a biomarker that indicates the number of immature neutrophils in the peripheral circulation and is calculated by subtracting the fraction of mature polymorphonuclear leukocytes from the total cells that react to myeloperoxidase[1].

A change in the DNI index occurs before a change in the number of neutrophils or white blood cells. In inflammatory and infectious conditions, this change is primarily the result of the formation of immature granulocytes, which differentiate into granular leukocytes[2]. Various reports have confirmed the role of DNI as an important indicator in determining the prognosis of infection or inflammation[3].

The diagnostic ability of the combined use of DNI and procalcitonin may improve the prediction of sepsis severity and survival[4,5]. showed also that DNI against ESR, CRP and procalcitonin was significantly associated with predicting sepsis and septic shock.

The findings of Park et al. (2020) also showed that the area under the curve (AUC) for peak DNI 24 hours after admission to the emergency department for predicting the development of sepsis was significantly superior to other parameters such as CRP, ESR, procalcitonin and WBC count (**Figure 1**).

Kim et al. on emergency department admissions also showed that comparing ROC curves for predicting acute kidney injury (AKI) the area under the ROC (AUROC) for DNI was significantly higher and more effective than other markers such as CRP, WBC, and neutrophil levels. The AUROC also showed that Time-12 was significantly more reliable than procalcitonin for DNI as well. In addition, the value of DNI during admission to the emergency department was not significantly lower than the values of lactate and procalcitonin, and at Time-12, the value of DNI was not lower than lactate (**Figure 2**). Totally, by comparing C-statistics regarding DNI levels and other markers, this index was superior to CRP, WBC, procalcitonin, and neutrophils in predicting 30-day mortality at Time-12. In predicting 30-day mortality, DNI levels at Time-12 were similar to lactate[2].

This study aimed to investigate the role of delta neutrophil index (DNI) as a biomarker to determine the prognosis of infectious conditions in the context of various diseases, especially in gastrointestinal diseases.

Methods

We searched PubMed, Science Direct, MEDLINE, EMBASE, and other reliable medical indexing websites to identify studies evaluating DNI as a predictive or prognostic factor in infectious conditions, particularly for gastrointestinal diseases.

Figure 1: ROC curves for the predictability of DNI and inflammatory biomarkers at 24 hours after emergency department (ED) admission to predict sepsis in acutely poisoned patients[5].
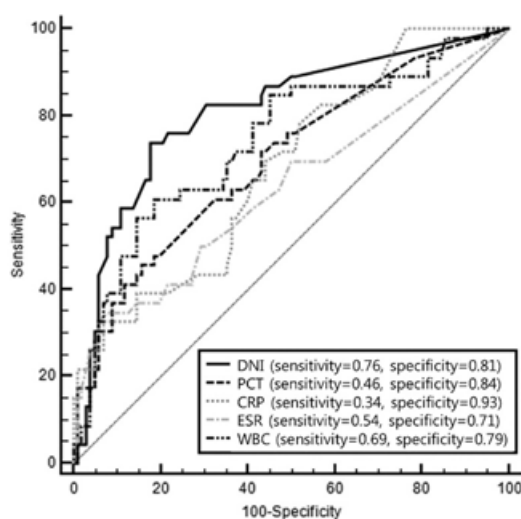
Figure 2: Comparative area under the curve (AUC) for DNI to predict the development of severe acute kidney injury (AKI)[2].
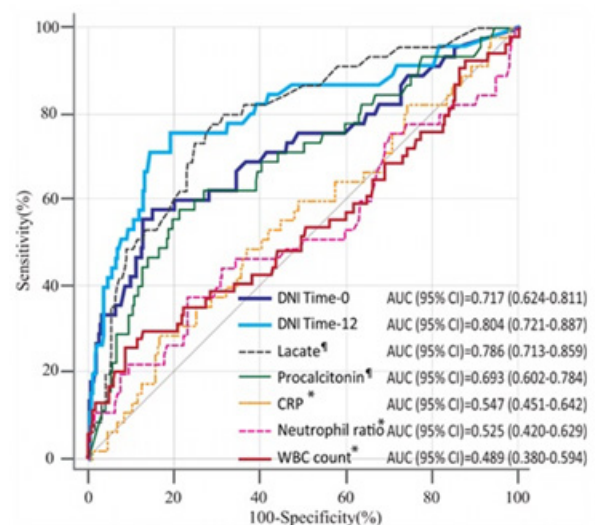
DNI and Non-Gastrointestinal Disorders

Evaluations have shown that increased DNI levels can be a predictive marker in determining the prognosis of chronic obstructive pulmonary disease (COPD)6. An increase in DNI level can be considered as a prognostic marker in cases of cardiac arrest[7].

A systematic review shows that, in general, DNI can play an important diagnostic role in patients with infectious diseases and be used more widely. The DNI index is now a new biomarker that It can be used in diagnosing and determining the prognosis of death in patients with infections, it has been confirmed. Also, it has been determined that high levels of DNI, together with C-reactive protein (CRP), the absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet count, are predictive factors for the diagnosis of Multisystem Inflammatory Syndrome in Children (MIS-C)[8].

DNI can also be used as a new biomarker to differentiate bacterial infections from candidemia in patients with systemic inflammatory response syndrome (SIRS). Predicting the severity of sepsis and determining the prognosis of 14-day mortality in patients with candidemia is also possible by determining DNI levels[9].

Since the septic status of patients admitted to the emergency department is an important factor for predicting their prognosis and mortality, suitable biomarkers that indicate its severity are of particular importance. Several studies have used the DNI value in evaluating patients with sepsis and bacteremia have been reported[10].

Hence, along with other inflammatory markers such as WBC, CRP and procalcitonin, DNI can also be considered as a diagnostic tool to predict mortality in patients with sepsis, disseminated intravascular coagulation (DIC) and bacteremia[11]. On the other hand, high DNI values can be used to quickly diagnose the severity of sepsis, predict acute kidney injury (AKI) and subsequent 30-day mortality, as well as design treatment strategies. DNI can be also considered as an independent factor of mortality in septic acute kidney injury patients with continuous renal replacement therapy (CRRT)[12].

One study used cluster analysis to determine strong predictors of sepsis that could screen potentially overlooked patients with possible sepsis (eg, sepsis patients without elevated WBC count). The results have shown that although WBC is considered a well-known parameter for sepsis, it had little relationship with sepsis status in elderly clusters. Instead, neutrophil-to-lymphocyte ratio (NLR) and DNI were strong predictors in all subjects[13].

Although delta neutrophil index (DNI) is a marker that has been reported to predict the diagnosis, prognosis, and severity of bacteremia and sepsis, the results of a study of febrile pediatric patients in the emergency department

(ED) suggest that DNI in the absence Bacteremia will not be useful in differentiating bacterial infection without bacteremia (BIWB) from viral infections[14].

In cases of severe infection or inflammation in patients with chronic rhinosinusitis (CRS), evaluation of DNI levels reflects the severity of the disease. Therefore, DNI values may be a useful predictor to determine the need for surgical intervention in these patients[15].

The DNI value as an indicator of infection can be useful in predicting acute pyelonephritis (APN) in patients with urinary tract infection (UTI) suffering from ureteral stones. DNI can be checked together with a complete blood count and the result can be obtained quickly and without incurring additional costs. Hence, Careful management should be considered if DNI levels are >1.3% in patients admitted to the emergency department or outpatient urology clinic for ureteral stones with suspected APN[16].

There is little study on the role of determination of delta neutrophil index (DNI) levels in determining the severity of multiple organ dysfunction (MODS) and short-term mortality. A study investigated the use of automatically calculated DNI as a marker in the prognostic assessment of severity in trauma patients admitted to the intensive care unit (ICU). The results indicated that DNI is useful for rapid and simple estimation of the severity of traumatic injury using an analyzer. Automated hematology is convenient, with no additional cost or time[17].

An interesting association has also been shown between DNI levels and gestational diabetes as a novel inflammatory marker. In such a way that this biomarker is more in women with gestational diabetes than in women with normal pregnancy[18]. Several studies also have reported that DNI levels are increased in certain pathological conditions such as preeclampsia[19].

Postpartum hemorrhage (PPH) is one of the most dangerous complications related to maternal mortality. It is difficult to accurately estimate the amount of bleeding by sight. Using delta neutrophil index (DNI) as a predictive biomarker can also be useful in this regard. The results showed that the relationship between DNI levels and shock index (SI) can be routinely measured in the emergency department (ED) and used as a suitable tool to classify the initial risk level in patients with primary PPH[20].

DNI and Gastrointestinal Disorders

The increase in DNI values can be related to the occurrence of mortality in acute upper gastrointestinal bleeding (UGIB) conditions. It can also help to differentiate between perforated and non-perforated appendicitis[21].

Since predicting severe acute pancreatitis (SAP) in the early stages of clinical evidence is very important to reduce complications and mortality, delta neutrophil index
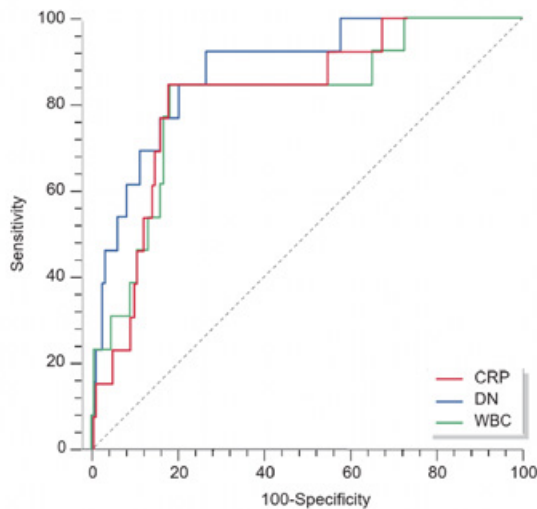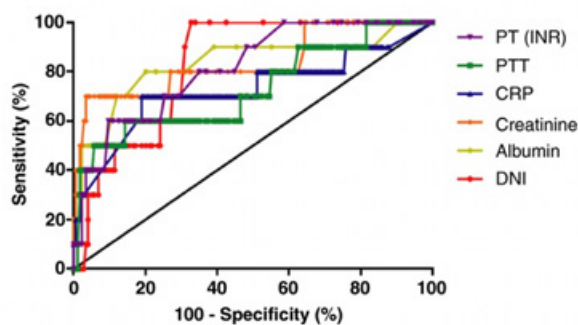
(DNI) is used to diagnose infection and inflammation. However, few studies have evaluated the usefulness of DNI as a predictor of disease progression to severe acute pancreatitis (SAP) (**Figure 3**).

The DNI measured in the emergency department (ED) is a potentially useful auxiliary marker for predicting SAP. This review suggests that intensive care should be considered for patients with severe acute pancreatitis, with a DNI value greater than 1.8% when presenting to the ED[2].

Esophagectomy is a complex and invasive procedure and shows a high incidence of complications. Hence, early detection of complications is important. The results have shown that the evaluation of DNI levels after esophagectomy can be useful as an early predictive biomarker of postoperative complications[22].

Gallbladder disorders, including complicated cholecystitis, can be associated with increased mortality and complications. A study aimed at evaluating the predictive value of the number of immature granulocytes and delta neutrophil index (DNI) showed that IG count and DNI level determination are two new and valuable parameters for the early diagnosis of complicated acute cholecystitis[23].

In patients with acute peritonitis, DNI values can predict 30-day mortality. The results showed that high DNI values can indicate high severity and more disappointing prognosis in acute abdomen. The use of DNI can be also considered as an efficient predictive marker in determining the prognosis of patients who need urgent abdominal surgery. The high levels of DNI can be considered as an efficient predictive marker in determining the prognosis of patients who need urgent abdominal surgery. **Figure 4** compares the functions of PT, PTT, CRP, creatinine, albumin, and DNI with respect to 30-day mortality in such patients. In patients with more underlying diseases, the practical value of DNI as a prognostic indicator for Intra-abdominal infection (IAI) was more valuable. In trauma

patients who have undergone abdominal surgery, delta neutrophil index (DNI) can be a predictor of complications and mortality during emergency surgical interventions[24].

Regarding the prediction for emergency surgical intervention in acute diverticulitis, it can be useful to evaluate DNI levels along with CT. The treatment protocol recommends that if DNI values are more than 0.7% and CT complications suggest the possibility of acute diverticulitis, immediate surgical intervention may be needed[25].

The results show that in mesenteric ischemia, determining the number of immature granulocytes and DNI may be used to evaluate intestinal necrosis. Interpretation of the results of these indices are more reliable than conventional parameters such as WBC, CRP and LDH[26].

Early detection of intestinal strangulation in the emergency department (ED) showed that the initial DNI levels in the strangulation group (SG) were significantly higher than the non-strangulation group (NSG). Initial assessment of DNI along with CT can be an additional useful parameter to improve the diagnostic accuracy of strangulated mechanical bowel obstruction in the emergency department (**Figure 5**)[27].

The results of using delta neutrophil index (DNI) to determine the prognosis of 30-day mortality in patients with spontaneous bacterial peritonitis (SBP) due to advanced cirrhosis were completely satisfactory[28].

Conclusion

This narrative review study showed that DNI is a simple but efficient test that can be quantitatively measured in routine complete blood counts. In diseases such as sepsis, meningitis, pediatric diseases and conditions, urinary infections, some cardiovascular disorders, gynecological conditions, and especially the gastrointestinal system disorders. it has a diagnostic value and can even be a very important biomarker in determining prognosis. Considering the sensitivity, specificity, and area under the curve (AUC), the evaluation of DNI levels can be used to predict severity, surgical outcomes, or mortality, and as a triage tool during the initial admission to the emergency department in patients with gastrointestinal diseases[29].

Finally, a meta-analysis of patients with infectious diseases has shown that the evaluation of DNI levels can serve as a reliable parameter and a potentially useful diagnostic and prognostic tool in the diagnosis of infection and prediction of mortality[30].

As a result, the measurement of DNI levels can also be considered a reliable early biomarker for triage as well as prediction of severity, results of surgical procedures, and mortality rate in gastrointestinal diseases.

Conflicts of Interest
None

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ORIGINAL

Relationship between sociodemographic variables and tobacco consumption with vascular age values using the Framinghan model in 336,450 spanish workers

Relación entre variables sociodemográficas y consumo de tabaco con los valores de edad vascular con el modelo de Framinghan en 336.450 Trabajadores españoles

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Abstract

Introduction: Traditionally, risk scales have been used to assess the probability of presenting a cardiovascular event in a given period. In recent years, tools have been developed to assess cardiovascular risk by estimating the age of the vascular tree.
Material and methods: Descriptive, cross-sectional study of 336450 Spanish workers in which vascular age was calculated using the Framingham model and the number of years lost (ALLY). The relationship of ALLY of vascular age with different sociodemographic variables (age, sex and social class) and tobacco consumption was also determined.
Results: In our study, the cut-off points for considering ALLY of vascular age with the Framingham model as moderate at 10 years and high at 18 years were established. Both the mean values and the prevalence of high vascular-age ALLY values increased in men, with increasing age, in people from the most disadvantaged social classes, and in those who smoked. The multivariate analysis showed that the sociodemographic variables analyzed and smoking increased the risk of presenting moderate or high ALLY, of which the one that increased the risk the most was age followed by smoking.
Conclusions: The cut-off points for moderate and high ALLY are 10 and 18 years respectively. Male sex, age, belonging to lower social classes and smoking increase the ALLY values for vascular age with the Framingham model.

Keywords: Vascular age, sociodemographic variables, cut-off, cardiovascular risk, Framingham.

Resumen

Introducción: Tradicionalmente se han empleado escalas de riesgo para valorar la probabilidad de presentar un evento cardiovascular en un periodo determinado. En los últimos años se han desarrollado herramientas que valoran ese riesgo cardiovascular estimando la edad del arbol vascular.
Material y métodos: Estudio descriptivo y transversal en 336450 trabajadores españoles en los que se calcula la edad vascular con el modelo Framingham y el número de años perdidos (ALLY). Se determina igualmente la relación de ALLY de edad vascular con diferentes variables sociodemográficas (edad, sexo y clase social) y consumo de tabaco.
Resultados: En nuestro estudio se establecen como puntos de corte para considerar ALLY de edad vascular con el modelo Framingham como moderada en 10 años y como alta en 18 años. Tanto los valores medios como la prevalencia de valores elevados de ALLY de edad vascular se ven incrementados en los varones, a medida que aumenta la edad, en personas de las clases sociales más desfavorecidas y en los que fuman. En el análisis multivariante se aprecia que las variables sociodemográficas analizadas y el tabaco incrementan el riesgo de presentar ALLY moderado o alto, de todas ellas la que más incrementa el riesgo es la edad seguida del consume de tabaco.
Conclusiones: Los puntos de corte para ALLY moderado y alto son de 10 y 18 años respectivamente. El sexo masculino, la edad, pertenecer a clases sociales más baja y fumar elevan los valores de ALLY de edad vascular con el modelo Framingham.

Palabras clave: Edad vascular, variables sociodemográficas, puntos de corte, riesgo cardiovascular, Framingham.

Introduction

Tobacco consumption has been responsible for the death of more than 100 million people during the 20th century, a figure that exceeds those caused jointly by the first and second world wars. According to figures from the World Health Organization (WHO), in the first years of this century some 5 million people over 30 years of age have died annually as a direct consequence of smoking[1]. According to the same organization, tobacco was responsible for one out of every eight adult deaths at the beginning of the century, with Europe and the Americas being the regions with the highest mortality rates[2].

Many studies have linked tobacco consumption to a higher prevalence of different diseases such as cardiac pathologies, including heart attacks, various types of cancer, such as lung cancer and chronic obstructive disease, among others. It has also been observed that the life expectancy of smokers is much lower than that of non-smokers[3-4].

It has been known for years that the prevalence of cardiovascular disease is lower in women mainly due to the protection afforded by estrogens[5]. It has also been observed that the presence of cardiovascular pathologies increases over the years[6].

Many studies have linked cardiovascular disease and socioeconomic level, with most of them concluding that there is a higher prevalence of cardiovascular disease in people with lower incomes6. Among the possible causes, we could highlight poorer diet and less access to health care[7].

Cardiovascular risk has traditionally been estimated using scales that assess the probability of presenting a cerebrovascular event, fatal or non-fatal, in a given period of time, generally 10 years. These scales give a false sense of security because, although the person presents various risk factors, their values are not very high. For this reason, different tools have been developed that, based on the traditional risk scales, determine the aging of the vascular tree, known as vascular age scales, in which the percentage risk is replaced by a number that represents the age of the vessels and which different studies have shown to be more easily understood[8].

The aim of this study is to assess the relationship between various sociodemographic variables and tobacco consumption and the vascular age values determined with the Framingham model. The cut-off points for considering moderate and high vascular ageing will also be established.

Methods

A prospective study was conducted in 390181 Spanish workers in companies of different productive sectors, mainly hospitality, construction, commerce, health, public administration, education, industry and cleaning between the years 2019-2022.

The flowchart of the participants is presented in **figure 1**.

Figure 1: flowchart of the participants.

390.181 people start the study

51.024 are under 30 years of age

2.298 lack some parameter for calculating the scales

409 did not agree to participate

336.450 finally entered the study
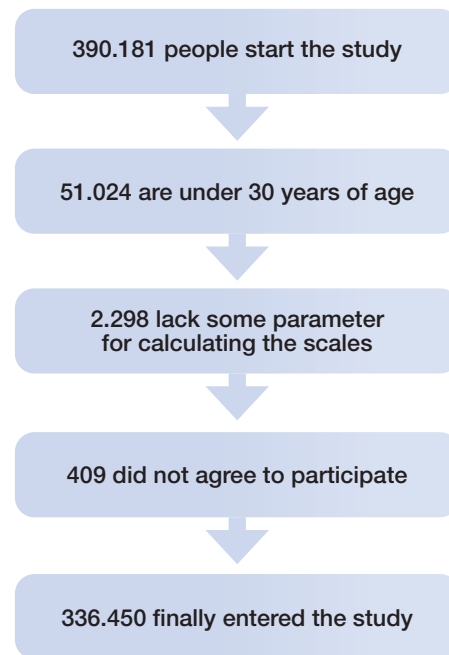
Inclusion criteria
- Age between 30 and 69 years.
- To have completed the occupational medical examination.
- Belonging to one of the companies collaborating in the study.
- To agree to participate in the study and to cede the data for epidemiological studies.

Different anthropometric, clinical and analytical variables were determined by the personnel of the different occupational health units participating in the study.

To measure weight, expressed in kilograms, and height, expressed in cm, a SECA 700 model scale with a capacity of 200 kg and 50 g divisions was used, with a SECA 220 telescopic measuring rod with millimetric division and a range of 60 to 200 cm.

Waist circumference was measured with a tape measure while the person was standing upright with feet together and trunk erect, abdomen relaxed and upper limbs hanging on both sides of the body. The tape measure was placed parallel to the ground at the level of the last floating rib.

Blood pressure was obtained with the person seated and after a resting period of 10 minutes, three determinations were made at one-minute intervals and the mean of the three measurements was obtained. The analytical determinations were performed after a fasting period of no less than 12 hours in reference laboratories. Automated enzymatic methods were used to measure blood glucose, total cholesterol and triglycerides. HDL was determined by precipitation with dextran sulfate Cl2Mg. LDL was calculated with the Friedewald formula (provided triglycerides were less than 400 mg/dL). All values are expressed in mg/dL.

Friedewald formula: LDL = total cholesterol – HDL – triglycerides/5

A person was considered a smoker when he or she had consumed at least 1 cigarette per day in the last 30 days or if he or she had quit smoking less than 12 months before.

The 2011 National Classification of Occupations (CNO-11) was used, according to the proposal of the social determinants group of the Spanish Society of Epidemiology to establish the social class was classified into three categories based on the 2011 national classification of occupations (CNAE) and applying the criteria of the Spanish Society of Epidemiology[9]: class I (directors/managers, university professionals, athletes and artists); II (intermediate occupations and self-employed workers without salaried workers); and III (unskilled workers).

Vascular age with the Framingham model was calculated by applying tables[10] using different variables: sex, age, HDL, total cholesterol, systolic and diastolic blood pressure, tobacco use, diabetes, and antihypertensive treatment.

Avoidable lost life years (ALLY) was defined as the difference between chronological age (CA) and vascular age (VA)[11]. ALLY = VA - CA. As the significance of the value of ALLY is different according to the CA, we defined' the ratio of ALLY to CA as ratio of avoidable lost life years (RALLY = ALLY/CA).

Statistical analysis
Categorical variables were described by frequency and percentage, and quantitative variables by mean and standard deviation (SD). To evaluate the association between the different variables, the chi-square test was used (with Fisher's test if necessary) and Student's t test when the samples were independent. Multivariate analysis was performed using the multinomial logistic regression test, calculating the odds ratio and 95% confidence intervals. The Hosmer-Lemeshow goodness-of-fit test was also performed.

Cut-off points to determine moderate and high values of vascular age were calculated using ROC curves and determining sensitivity, specificity and Youden index.

Statistical calculations were performed with the SPSS 28.0 package, establishing a statistical significance level of p < 0.05

Ethical Considerations and Aspects
The study was approved by the Clinical Research Ethics Committee of the Balearic Islands Health Service (Approval Code: IB 4383/20). All procedures were performed in accordance with the ethical standards of the institutional research committee and the 2013 Declaration of Helsinki. All participants signed written informed consent documents before participating in the study.

Results

Study participants and participant characteristics
Table I shows the sociodemographic, clinical and analytical characteristics of the 336450 workers included in the study. The mean age of the participants was 43.4 years in women and 44.3 years in men, with the majority group being between 30 and 49 years of age. The percentage of smokers was similar in both sexes, approximately one third. Most of the workers belonged to social class III. All analytical and clinical parameters showed worse values in men.

Table II shows the ALLY and RALLY values according to the different sociodemographic variables and tobacco consumption. ALLY and RALLY values are much higher in men. The values of ALLY and RALLY increase with age and as we descend in social class. The values of both parameters are significantly lower among non-smokers. In all cases the differences obtained are statistically significant.

In the areas under the ROC curve, values of 0.913 (95% CI 0.909-0.916) for moderate ALLY and 0.970 (95% CI 0.967-0.973) are observed. The cut-off point established for moderate ALLY is 10 years (sensitivity 0.833, specificity 0.830 and Youden index 0.664) and for high ALLY is 18 years (sensitivity 0.973, specificity 0.876 and Youden index 0.849).

Figure 2: ROC curve of ALLY moderate and high.

ALLY moderate · ALLY high
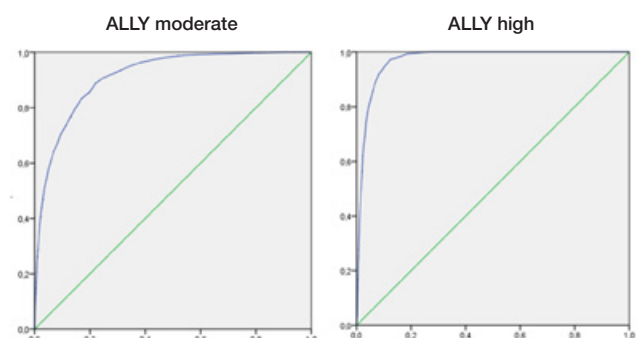
Table I: Characteristics of the population.

	Men n=199829	Women n=136621	
	Mean (SD)	Mean (SD)	p-value
Age (years)	44.3 (8.7)	43.4 (8.6)	<0.0001
Height (cm)	174.3 (7.0)	161.5 (6.5)	<0.0001
Weight (kg)	82.4 (14.5)	67.0 (13.9)	<0.0001
Body mass index (kg/m²)	27.1 (4.4)	25.7 (5.1)	<0.0001
Waist circumference (cm)	86.7 (10.9)	75.0 (10.6)	<0.0001
Systolic blood pressure (mmHg)	129.2 (15.8)	118.6 (16.2)	<0.0001
Diastolic blood pressure (mmHg)	79.2 (10.8)	73.6 (10.5)	<0.0001
Total cholesterol (mg/dl)	198.8 (37.7)	195.5 (35.5)	<0.0001
HDL-c (mg/dl)	49.6 (8.5)	56.1 (8.7)	<0.0001
LDL-c (mg/dl)	123.8 (35.6)	121.1 (34.3)	<0.0001
Triglycerides (mg/dl)	130.7 (90.3)	91.5 (47.6)	<0.0001
Glycaemia (mg/dl)	94.9 (22.3)	88.8 (15.6)	<0.0001
	%	%	p-value
30-39 years	33.9	37.4	<0.0001
40-49 years	37.0	37.3	
50-59 years	24.3	21.2	
60-69 years	4.8	4.1	
Social class I	5.2	6.7	<0.0001
Social class II	15.9	24.4	
Social class III	78.9	68.9	
Non smokers	67.1	67.5	0.002
Smokers	32.9	32.5	

Table II: Mean values of ALLY and RALLY vascular age with Framingham model according sociodemographic variables and tobacco consumption.

		ALLY VA Framingham		RALLY VA Framingham	
	n	Mean (SD)	p-value	Mean (SD)	p-value
Women	136621	0.9 (11.9)	<0.0001	0.14 (0.22)	<0.0001
Men	199829	6.7 (10.5)		0.001 (0.26)	
30-39 years	118852	-0.5 (7.4)	<0.0001	-0.01 (0.21)	<0.0001
40-49 years	124952	3.6 (10.8)		0.08 (0.24)	
50-59 years	77473	10.9 (13.0)		0.20 (0.24)	
60-69 years	15173	14.4 (12.2)		0.23 (0.20)	
Social class I	19545	1.8 (10.6)	<0.0001	0.03 (0.23)	<0.0001
Social class II	65150	2.4 (11.6)		0.04 (0.24)	
Social class III	251755	5.0 (11.6)		0.10 (0.25)	
Non smokers	226310	1.0 (9.8)	<0.0001	0.01 (0.21)	<0.0001
Smokers	110140	11.3 (11.4)		0.24 (0.24)	

Table III: Prevalence of moderate and high values of ALLY vascular age with Framingham model according sociodemographic variables and tobacco consumption.

		ALLY VA moderate		ALLY VA high	
	n	%	p-value	%	p-value
Women	136621	8.5	<0.0001	11.2	<0.0001
Men	199829	17.2		15.9	
30-39 years	118852	7.4	<0.0001	2.0	<0.0001
40-49 years	124952	15.7		10.7	
50-59 years	77473	18.8		31.3	
60-69 years	15173	18.8		46.9	
Social class I	19545	11.2	<0.0001	9.5	<0.0001
Social class II	65150	11.9		10.5	
Social class III	251755	14.3		15.3	
Non smokers	226310	9.1	<0.0001	7.3	<0.0001
Smokers	110140	22.9		27.8	

Table III shows the prevalence of moderate and high ALLY values according to the values of the sociodemographic variables and tobacco consumption. The same trend is observed as with the mean values, i.e. higher prevalence in men, as age increases and social class decreases, and in smokers. In all cases the differences observed are also statistically significant.

Tables IV and **V** present the results of the multinomial logistic regression analyses. In both cases, an increase in the risk of presenting moderate or high ALLY values is observed in males, more disadvantaged social classes and smokers. The greatest increase in risk is observed with age.

Table IV: Multinomial logistic regression.

	ALLY VA moderate-high	
	OR (95% CI)	p-value
Women Men	1 2.36 (2.31-2.41)	<0.0001
30-39 years 40-49 years 50-59 years 60-69 years	1 2.27 (2.19-2.37) 8.54 (8.20-8.89) 38.76 (37.09-40.51)	<0.0001
Social class I Social class II Social class III	1 1.33 (1.30-1.36) 1.55 (1.48-1.61)	<0.0001
Non smokers Smokers	1 9.06 (8.88-9.25)	<0.0001

Table V: Multinomial logistic regression.

	ALLY VA high	
	OR (95% CI)	p-value
Women Men	1 1.48 (1.44-1.51)	<0.0001
30-39 years 40-49 years 50-59 years 60-69 years	1 2.36 (2.27-2.45) 11.38 (10.92-11.87) 74.81 (70.75-79.10)	<0.0001
Social class I Social class II Social class III	1 1.43 (1.38-1.47) 1.65 (1.56-1.74)	<0.0001
Non smokers Smokers	1 7.55 (7.37-7.73)	<0.0001

Discussion

Our work establishes 10 years as the cut-off point for moderate ALLY and 18 years for high ALLY. We have not found in the literature consulted, including the authors of the tool, any reference to cut-off points, for this reason we cannot compare our results with those obtained by other authors. We have found similar determinations to ours in a Spanish study in which the cut-off points for the age of the heart were assessed[12].

Our study shows a clear influence of age, male sex, lower social class, and tobacco consumption on the mean values and prevalence of elevated ALLY and RALLY values, and these data are consistent with those obtained in the aforementioned study[12].

We have not found research that assesses the effects of sociodemographic variables (age, sex or social class) or tobacco consumption on vascular age values; however, there is a study that relates these variables to heart age[8], and this study shows results similar to those found by us.

It is interesting to know that the scales that assess vascular aging have a good relationship with various scales that assess[13].

Tobacco consumption is one of the factors that in the present study had the greatest influence on the appearance of moderate and high ALLY with ORs of 9.06 and 7.55, respectively. This negative influence of tobacco consumption was also seen in the RICARTO study[14] and in an Indian study where the odds ratio was 15.23, that is, somewhat higher than that obtained here[15].

Two studies evaluated the influence of tobacco consumption and vascular age determined by carotid artery measurement, one was performed in 121 Croatian nationals[16] and the other in 501 Spanish subjects[17], in both cases it was concluded that tobacco had a negative influence on vascular age values. A previously cited review study that assessed arterial stiffness showed the negative effect of tobacco consumption on arterial stiffness[18].

An American study concluded that the social determinants of health, which encompass the economic, social, environmental and psychosocial factors that influence health, play an important role in the development of risk factors for cardiovascular disease and morbidity and mortality[19]. Another North American article on 168,969 people expressed the same view[20].

One of the strengths of this study is that it is the first to establish the cut-off points for moderate and high vascular age using the Framingham model. Another aspect to highlight is the large sample size, more than 336,000 persons.

The limitations of this study include the fact that it was carried out in the working population, so it is not known whether the results can be extrapolated to the general population. population, so it is not known whether the results can be extrapolated to the general population. population and also correspond to a specific country, Spain, so the data may not coincide with those found by other researchers in their own countries. data may not coincide with those found by other researchers in their own countries.

Conclusions

The cut-off points for considering moderate ALLY Framingham vascular age are set at 10 years and for high ALLY at 18 years.

Male sex, social class III, tobacco use and especially age are the variables that most affect ALLY Framingham vascular age values.

Conflicts of Interest
None

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Relationship between sociodemographic variables and tobacco consumption with vascular age values using the Framinghan model in 336,450 spanish workers.

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ORIGINAL

Spontaneous Bacterial Peritonitis in Decompensated Liver Cirrhosis. A Retrospective Study

Peritonitis bacteriana espontánea en la cirrosis hepática descompensada. Un estudio retrospectivo.

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Abstract

Background: Spontaneous bacterial peritonitis (SBP) is a frequent and severe complication in patients with liver cirrhosis, which is associated with high mortality. Various studies have shown that the prevalence of SBP varies from 20-40% in patients with cirrhosis and ascites. Not in all cases it is accompanied by obvious symptoms, which makes early diagnosis difficult.

Aim: The aims of this study were to determine several clinical and laboratory features and risk factors in bacterial spontan peritonitis.

Methodology: In this study, are included 137 patients diagnosed with decompensated cirrhosis, divided into three groups 83 cases with SBP and alcoholic cirrhosis, 22 cases with SBP and viral cirrhosis, and 32 cases with cirrhosis without SBP. All patients included in this study were over 18 years old. This is a retrospective study, where are analyzed clinical and laboratory characteristics of patients with SPB and liver cirrhosis, admitted to the Service of Gastro-Hepatology, University Hospital Center, Tirana, Albania during 2018-2022. Diagnosis of SBP is based on the European Association for the Study of Liver (EASL) guidelines. The degree of liver function damage is evaluated by the Child-Pough score and MELD score, clinical and laboratory indicators, and complications associated with cirrhosis with PBS, and ascitic fluid analyses. All categorical variables were analyzed by using SPSS version 25, and t-tests were used for continuous data.

Results: The average age of the 137 participants in the study was 54.15±12.5 years, 132 males (96.4%) and 5 females (3.6%), where 105 patients were with SBP. According to the evaluation of MELD, it was seen to be higher in the group with PBS than those without PBS ($p<0.05$). From the laboratory data, in this study seen the level of platelets ($p<0.015$) , serum creatinine level ($p<0.001$), serum bilirubin level ($p<0.002$), INR ($p<0.049$), and prothrombin level ($p<0.002$) were seen as predictive factors. The most frequent complications accompanying SBP were Encephalopathy ($p<0.004$), hepatorenal syndrome ($p<0.002$) , and gastrointestinal hemorrhage ($p<0.002$).

Conclusions: The most probable predictive factors in the case of PBS in liver decompensated cirrhosis were found the low level of platelets, prolonged levels of INR and prothrombin, increased levels of creatinine, increased levels of bilirubin, and low ascetic protein. While the most frequent associated complications were hepatic encephalopathy, HRS, G\I hemorrhage, and jaundice.

Keywords: SBP, cirrhosis, complications, predictive, alcohol.

Resumen

Antecedentes: La peritonitis bacteriana espontánea (PBE) es una complicación frecuente y grave en pacientes con cirrosis hepática, que se asocia a una elevada mortalidad. Diversos estudios han demostrado que la prevalencia de la PBE oscila entre el 20-40% en pacientes con cirrosis y ascitis. No en todos los casos se acompaña de síntomas evidentes, lo que dificulta el diagnóstico precoz.

Objetivo: Los objetivos de este estudio fueron determinar diversas características clínicas y de laboratorio y factores de riesgo en la peritonitis espontánea bacteriana.

Metodología: En este estudio, se incluyen 137 pacientes diagnosticados de cirrosis descompensada, divididos en tres grupos 83 casos con PAS y cirrosis alcohólica, 22 casos con PAS y cirrosis vírica, y 32 casos con cirrosis sin PAS. Todos los pacientes incluidos en este estudio tenían más de 18 años. Se trata de un estudio retrospectivo, donde se analizan las características clínicas y de laboratorio de los pacientes con SBP y cirrosis hepática, ingresados en el Servicio de Gastro-Hepatología, Centro Hospitalario Universitario, Tirana, Albania durante 2018-2022. El diagnóstico de SPB se basa en las directrices de la Asociación Europea para el Estudio del Hígado (EASL). El grado de daño de la función hepática se evalúa mediante la puntuación Child-Pough y la puntuación MELD, indicadores clínicos y de laboratorio, y complicaciones asociadas a la cirrosis con PBS, y análisis de líquido ascítico. Todas las variables categóricas se analizaron mediante el programa SPSS versión 25, y para los datos continuos se utilizaron pruebas t.

Resultados: La edad media de los 137 participantes en el estudio fue de 54,15±12,5 años, 132 varones (96,4%) y 5 mujeres (3,6%) , donde 105 pacientes presentaban PBE. Según la evaluación del MELD, se observó que era mayor en el grupo con SBP que en los que no tenían SBP (p<0,05). De los datos de laboratorio, en este estudio se observaron como factores predictivos el nivel de plaquetas (p<0,015) , el nivel de creatinina sérica (p<0,001) , el nivel de bilirrubina sérica (p<0,002), el INR (p<0,049) y el nivel de protrombina (p<0,002). Las complicaciones más frecuentes que acompañaron al SBP fueron la encefalopatía (p<0,004), el síndrome hepatorrenal (p<0,002) y la hemorragia gastrointestinal (p<0,002).

Conclusiones: Los factores predictivos más probables en el caso de TBP en la cirrosis hepática descompensada se encontraron el bajo nivel de plaquetas, los niveles prolongados de INR y protrombina, el aumento de los niveles de creatinina, el aumento de los niveles de bilirrubina y la baja proteína ascítica. Mientras que las complicaciones asociadas más frecuentes fueron la encefalopatía hepática, el SHR, la hemorragia G\I y la ictericia.

Palabras clave: PAS, cirrosis, complicaciones, predictivo, alcohol.

Introduction

Spontaneous Bacterial Peritonitis (SBP) is defined as the infection of ascitic fluid in patients with decompensated liver cirrhosis with ascites from various bacteria, without previous intra- abdominal surgical history[1,2]. SBP is one the most common and important complications in cirrhotic patients with ascites because of significant morbidity and mortality[3,4]. The reason of SBP in liver cirrhosis is multifactorial and is associated with a defective immune system, gut dysmotility, alterations in microbiome, increased intestinal permeability, and bacterial translocation[5,6]. During or after an episode of spontaneous bacterial peritonitis, patients often present with signs of decompensation such as the development or progressive worsening of ascites or hepatic encephalopathy (HE), gastrointestinal bleeding (GI), and another organ compromise such as acute kidney injury (AKI), with or without hepatorenal syndrome (HRS)[7,8]. In fact, the most frequent cause of death in patients with PBS is the development of acute hepatic failure over a chronic injury characterized by a high mortality rate as a result of multiorgan failure[9,10]. In daily practice, the diagnosis of PBS and other infections can be complicated by the fact that typical signs and symptoms such as temperature and leukocytosis are often absent in cirrhotic patients, and the liquid culture in most cases up to 60% results negative. However, early suspicion is very important for the diagnosis and treatment of PBS without delay in order to achieve the best possible treatment results, since being treated and continuing antibiotic prophylaxis has reduced the mortality rate by up to 20% per year after the first episode of SBP[11,12,13,14]. All patients with cirrhosis and ascites are at risk of developing PBS, and it has been seen that the prevalence of PBS in outpatient's ranges from 1.5-3.5%, while in hospitalized patients up to 10% of cases. PBS in some patients could be present from the beginning of admission to the hospital, while other patients are discovered during the staying in the hospital[5,14]. Risk factors associated with SBP development include ascitic fluid total protein less than 1gr\dL, total serum bilirubin greater than 2.5 mg\dL, variceal hemorrhage and a previous episode of SBP[7,15]. Therefore, we conducted a retrospective study in cirrhotic patients with ascites fulfilling the diagnosis of SBP. Our aim was to study the epidemiological, clinical, laboratory and risk factors in SBP.

Patients and methods

This is a retrospective study to all patients diagnosed with PBS in our hospital during 2018-2022 at Service of Gastro-Hepatology, University Hospital Center "Mother Teresa" Tirana, Albania. In this study, are included 137 patients diagnosed with decompensated cirrhosis, divided in three groups 83 cases with SBP and alcoholic cirrhosis, 22 cases with SBP and viral cirrhosis and 32

cases with cirrhosis without SBP. All patients included in this study were over 18 years old. Data recorded included patient demographics, clinical information including presenting symptoms, medical comorbidities, cirrhosis etiology, time from decompensation to SBP development, gastrointestinal bleeding and MELD score, laboratory work-up (ascitic fluid neutrophils, albumin and culture, serum creatinine, albumin). Detailed data on chronic administration of b-blockers, proton pump inhibitors (PPIs) and antibiotic prophylaxis for SBP were also recorded. On admission, all patients are analyzed for biochemical evaluation, liver imaging (ultrasound or computed tomography) to exclude malignancy or other source of infection. SBP was diagnosed as an infection of ascetic fluid without any intra-abdominal surgically treatable source of infection, and was based on a neutrophil count >250/mm3 in ascetic fluid, as determined by microscopy or positive culture of the ascetic fluid according to the guidelines of the European Association for the Study of the Liver (EASL)[1].

For statistical analysis, use the package SPSS (Statistical Package for Social Sciences, version 25) and t-test were used for continuous date. For all the data, the mean ± standard deviation (SD) was calculated. P values ≤ 0.05 were considered statistically significant (negligible).

Results

The average age of the 137 participants in the study was 54.15±12.5 years, 132 males (96.4%) and 5 females (3.6%), where 105 patients were with SBP. According to the distribution according to the age group in years, it was observed that the largest number of patients with decompensated cirrhosis was after the age of 40 (44.6%). The leading etiology of cirrhosis was alcohol-related 115 (80.5%), followed by viral 22 (16%). Most of cases were first episode of SBP, only 13 cases were another episode. Before the first episode 92 (80%) cases were on PPI treatment (**Table I**). Most of patients were Child-Pough C (66.4%).

The most of patients were MELD-score > 19 (**Figure 1**).

Table I: Baseline characteristics (n 137).

Carachteristics		N 137 (%)
Age (years)	54.15 ± 12.5 years	
Gender	Male	132 (96.4%)
Etiology of cirrhosis	Alcohol	115 (80.5%),
	Viral hepatitis	22 (16%).
PPI	With SBP	90 (85%)
First episode of SBP		92 (87%)
MELD score	With SBP	19 ± 9.2
	Without SBP	16 ± 4.86
Child-Pough score	A	9 (6.6%)
	B	37(27%)
	C	91 (66.4%)

Figure 1: Cirrhosis according to MELD-score.
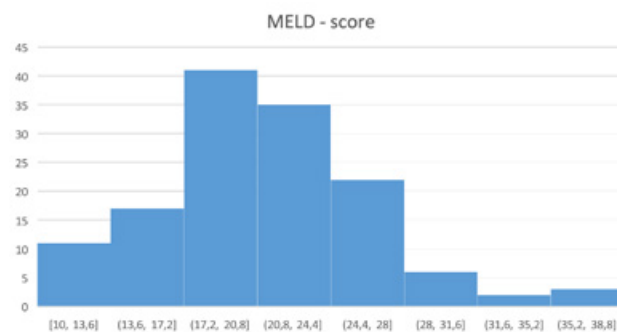
In this study it was seen that the main complaint was adynamic (84%), abdominal distention 68%, and diffuse abdominal pain 54% (48.2%) and fever 36%.

Figure 2: Complaints in patients with SBP at the first moment of admitted to the hospital.
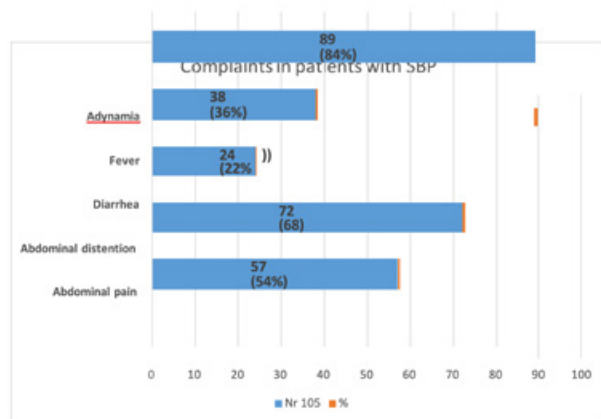
There was no significant difference between the two groups with SBP and without SBP about the age (55.12±9.7, vs 54.68±12.1, p=0.8). The most frequent in the group with SBP were EH (41.9% vs 16.6%, p < 0.04), HRS (29% vs 13.1%, p < 0.002), hemorrhage g/i (37.3% vs 11.6%, p<0.002) jaundice (92.8% vs 77%, p<0.002) (**Table II**).

Table II: Evaluation of complications in patients with SBP.

Data	With SBP	Without SBP	p
Age (mean ± SD)	55.12 ± 9.7	54.68 ± 12.1	0.872
Jaundice (%)	92.8 %	77 %	**0.002**
Fever (%)	36%	29.74%	0.701
Hemorrhage (%)	37.3%	11.6%	**0.002**
Encephalopathy (%)	41.96%	16.6%	**0.004**
HRS (%)	29 %	13.1%	**0.002**

P<0.05 for comparison between two groups.

Laboratory data in the group with SBP and without SBP (**Table III**), it was observed that INR had a significant difference in patients with SBP (p<0.049). Also, patients with SBP had a lower level of platelets compared to those without SBP (p<0.015), serum creatinine level was higher in the group with SBP (p<0.001). Significant difference between the group with PBS and without PBS

was also seen in the level of prothrombin (p<0.002). No significant difference was seen on level of ascitic albumin in both groups.

Comparison of SBP in cirrhosis of two groups, with alcoholic and viral etiology are seen no significant changes in relation to age, MELD–score, and other complications such EH, HRS, and G\I hemorrhage and laboratory data, except transaminases (**Table IV**). Regarding the laboratory data in the SBP of the two groups, in alcoholic cirrhosis the AST level was higher than ALT level (89.7 ± 64 vs 83.4 ± 52 U\L).

Regarding the laboratory data in the SBP of the two groups, in alcoholic cirrhosis the AST level was higher than ALT level (89.7 ± 64 vs 83.4 ± 52 U\L) (**Figure 3**).

The culture of the liquid, which was carried out only in 45 cases with SBP, and only 10 patients (22%) resulted in a positive culture, 7 patients with *E. coli* and 3 patients with *staphylococcus aureus*.

Figure 3: Level of transaminases ALT and AST in patients with SBP in two groups of cirrhosis (alcoholic and viral).
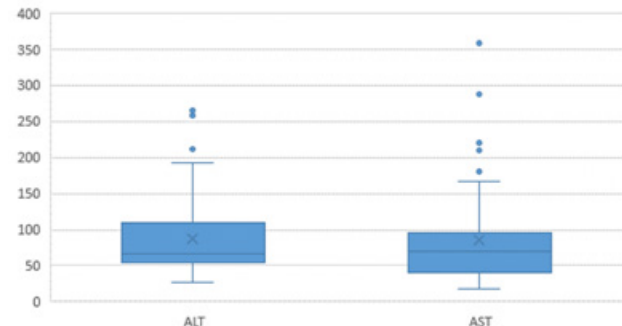
Table III: Biochemical data in patients with SBP.

Variable	With PBS	Without PBS	p
Leukocytes (mean ± SD)	6054.22 ± 2985.59	4371.25 ± 1750	0.316
Platelets (mean ± SD)	127698 ± 6161.54	14215.25 ± 94054.58	0.015
Hemoglobin (mean ± SD)	10.471 ± 2.076	10.613 ± 2.041	0.691
Creatinine (mean ± SD)	1.470 ± 0.918	0.745 ± 0.427	0.001
AST (mean ± SD)	86.78 ± 64.84	66.63 ± 41.175	0.950
ALT (mean ± SD)	73.45 ± 62.98	71.93 ± 23.302	0.192
Ascites albumin (mean ±SD)	0.76 ± 0.46	0.706 ± 0.524	0.750
INR (mean ± SD)	2.0216 ± 0.67	1.7784 ± 0.609	0.049
Prothrombin (mean±SD)	38.056 ± 11.08	47.3506 ± 19.503	0.002
Natremia (mean ± SD)	128.97 ± 6.210	130.68 ± 4.145	0.515

Table IV: Comparison between alcoholic cirrhosis wth SBP and viral cirrhosis with SBP.

Variable	Alcoholic with SBP	Viral with SBP	p
Leukocyte (mean ± SD)	9154.22 ± 5985.599	6295.45 ± 4315.020	0.034
Thrombocyte (mean ± SD)	157698.80 ± 50612.54	100909.09 ± 49097.482	0.103
Hemoglobin (mean± SD)	10.481± 2.086	10.80 ± 2.082	0.525
Creatinine (mean ± SD)	1.370 ± 0.8172	1.066 ± 0.5431	0.103
AST (mean ± SD)	89.78 ± 64.845	50.37 ± 35.253	0.025
ALT (mean ± SD)	73.46 ± 52.988	75.67 ± 18.475	0.103
Albumin ascites (mean ±SD)	0.676 ± 0.4695	0.532 ± 0.3908	0.190
INR (mean ± SD)	2.0227± 0.8033	2.0314 ± 0.43023	0.948
Prothrombin (mean ±SD)	39.0622 ± 12.09659	40.5773 ± 10.94083	0.596
Natremia (mean ± SD)	129.98 ± 5.310	130.77 ± 4.730	0.006

Discussion

Spontaneous bacterial peritonitis (SBP) is a frequent and severe complications in patients with liver cirrhosis. Various studies have shown that the prevalence of SBP varies from 20-40% in patients with cirrhosis and ascites. Not in all cases it is accompanied by obvious symptoms, which makes early diagnosis difficult[1,2,15]. An appropriate diagnosis and correct treatment are the first option in SBP management as untreated patients' mortality is much higher and approaches 50%[1,16]. Our study investigated adherence to the guidelines for diagnosis, and predictive factors in patients with SBP in decompensated cirrhosis. The average age of the 137 participants in this study was 54.15 ± 12.5 years, 132 males (96.4%) and 5 females (3.6%), where 105 patients were with SBP. Most of patients were male because of alcoholic cirrhosis, where it is known that men drink more alcohol in our Country. Age according to the distribution in years, most were over 40 years old, this is explained by the fact that before cirrhosis develops, it goes through several stages of disease, steatosis of the liver, alcoholic hepatitis which is associated with signs of necroinflammation of the liver, and finally cirrhosis[14]. The main age of presentation of cirrhosis is 40-50 years old, and this happens when they systematically consume 30-40 grams of alcohol a day in a systematic manner[15,16]. The mean age of our patients was 54.15 ± 12.5 years

and most of them were > 40 years old. At the moment of hospitalization, most of patients with SBP had jaundice (92.8%), encephalopathy (41.9%), upper gastrointestinal bleeding (37%), fever (36%), HRS (29%). The data of the study are similar to those of *Sort et al*, which demonstrates that renal function impairment occurs in about 30-40% of patients with PBS and is considered a predictive factor of deaths in PBS[20]. This study show that abdominal pain was encountered in 54%, abdominal distention in 68%, similar to other studies[21]. The classification according to MELD score in this study resulted > 19 points in the majority of patients with SBP, which was slightly higher than the group without SBP[20]. In our study, it was seen that the group of patients with SBP had lower number of platelets (p < 0.015), higher creatinine level (p < 0.002), prolonged level of INR (p < 0.049), lower prothrombin level (0.002). Regarding the laboratory data in the SBP of the two groups, in alcoholic cirrhosis the AST level was higher than ALT level (89.7 ± 64 vs 83.4 ± 52 U\L).

The level of albumin in ascites did not have any significant difference between the group with SBP and without SBP, but low levels of albumin in ascites is a known risk factor for SBP (<1.5 g) , especially when associated with any of the following characteristics Child-Pough score > 9, bilirubin level > 3 mg/dl, creatinine 1.2 mg/dl, uremia > 25 mg/dl, or hyponatremia[22,23]. A study by *Filik et al* from the analysis of all factors in patients with chronic liver diseases such as fatigue, hepatitis, encephalopathy, leukocytosis, impairment of renal function (creatinemia >2 mg/dl), coagulopathy (PTI >2.5 INR) and the level of decreased protein levels (< 1 mg/dl) were statistically associated with poor prognosis (p< 0.005)[21].

The culture of the liquid, which was carried out only in 45 cases with SBP, and only 10 patients (22%) resulted in a positive culture, 7 patients with *E. coli* and 3 patients with *staphylococcus aureus*. *Piroth et al*.[22] in a retrospective study conducted in France in five different hospitals during the year 2006-2007 in 114 cases observed that the most frequent pathogens were Staphylococcus and *E. coli*. While in a study by *Ardolino et al*.[23] conducted in the United States of America during 2005-2015 in 160 cases with PBS, it was seen that the main cause was *E. coli*. While gram-positives in this study such as *Enterococci, Streptococci* and *Staphylococci* were found in up to 37.5% of cases. The role of proton pump inhibitors as a risk factor for spontaneous bacterial peritonitis is controversial, so that its use should be restricted to those with a clear indication[1]. Our study has limitations, including being a single - center retrospective study, and not represented other hospitals. Some patients had a lack of data in their documentation.

Conclusions

The most probable predictive factors in the case of SBP in liver decompensated cirrhosis were found the increased level of creatinine, increased level of bilirubin, low level of platelets, prolonged level of INR and low level of prothrombin. While the most frequent associated complications were hepatic encephalopathy, HRS, G\I hemorrhage, and jaundice. As a result of this study, we can say that patients with alcoholic cirrhosis and SBP had not difference with viral cirrhosis with SBP, about the predictive factors. The MELD score was higher in the SBP group, but is considered independent factor. It is very important to emphasize the fact that early diagnosis and treatment, even in cases where they are asymptomatic, will lead to an increase in the quality and survival of patients.

Conflicts of Interest
None

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ORIGINAL

Evaluating the anticancer activity of protein crude extract from *Californicus Conus*

Evaluación de la actividad anticancerígena del extracto crudo proteico de Californicus Conus

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Abstract

Aim and methods: In this study, venom proteins of cone snail (Californicus Conus) were isolated by protein precipitation. This acquired crude extract was assessed by SDS-PAGE. Biological activities (cell toxicity and gene expression) was evaluated on normal (HEK) and cancerous (HT-29) cell lines.

Results: Electrophoresis evaluation showed that the weight range of proteins was <3kDa->10kDa. Thus, this extract contain peptides and large proteins. The extract showed a dose-dependent anticancer and cell toxicity activities against HT-29 cancerous and HEK normal cell lines. However, the anticancer activity was higher than normal cell toxicity. The extract had no toxicity on normal cells in concentrations of 0.5, 1, 2, and 4 µg/ml.

Conclusions: Based on results, venom proteins of cone snail contains a suitable anticancer agents. Therefore, further study of this protein isolate is suggested in future studies.

Keywords: Californicus Conus, Anticancer, Toxicity, Venom, Extract.

Resumen

Objetivo y metodología. En este estudio, las proteínas del veneno del caracol cono (Californicus Conus) se aislaron por precipitación de proteínas. El extracto crudo obtenido se evaluó mediante SDS-PAGE. Se evaluaron las actividades biológicas (toxicidad celular y expresión génica) en líneas celulares normales (HEK) y cancerosas (HT-29).

Resultados. La evaluación por electroforesis mostró que el rango de peso de las proteínas era <3kDa->10kDa. Así pues, este extracto contiene péptidos y proteínas de gran tamaño. El extracto mostró una actividad anticancerígena y de toxicidad celular dependiente de la dosis contra las líneas celulares HT-29 cancerosas y HEK normales. Sin embargo, la actividad anticancerígena fue superior a la toxicidad de las células normales. El extracto no tuvo toxicidad sobre las células normales en concentraciones de 0,5, 1, 2 y 4 µg/ml.

Conclusiones. Según los resultados, las proteínas del veneno del caracol cono contienen agentes anticancerígenos adecuados. Por lo tanto, se sugiere seguir estudiando este aislado proteico en estudios futuros.

Palabras clave: Californicus Conus, Anticancerígeno, Toxicidad, Veneno, Extracto.

Introduction

The marine gastropods known as cone snails (*Conus*) constitute an unusually species-rich group of venomous predators, one of the largest single genera (~700 species) of living marine invertebrates. They are usually classified into three groups depending on their feeding habits: worm hunters (vermivorous), mollusk hunters (molluscivorous), and fish hunters (piscivorous)[1,2]. The venom of marine gastropods belonging to the genus Conus has yielded numerous structurally and functionally diverse peptidic components. The increase variety of bioactive agents identified in cone snail venoms is the product of the variety of molecular adaptations taken by Conus species in evolving neuroactive molecules to suit their diverse biological purposes[3]. These compounds, called conotoxins, are synthesized in the venom gland of the snails[4,5]. The other aspect of cone snails that has attracted human interest is that they can be deadly to humans like *C. geographus*[6,7], which has caused more than thirty human fatalities[8]. It has been estimated that approximately 100,000 different agents can potentially be expressed in the venoms of the entire current *Conus genus*[9,10]. To date, several conotoxins have already demonstrated potential therapeutic effects in preclinical or clinical trials[11-15]. An early focus of conotoxin discovery has been to identify and characterize novel pain modulators, which was the logical first step considering that conotoxins often target ion channels involved in pain signaling. Having said that, in recent years scientists are characterizing these conotoxins for other therapeutic properties —including antioxidant (xx), cytotoxicity (xx) and anticancer properties— which are promising agents in pharmacology. Only few studies have reported the anticancer effects of these conotoxins (xxx). In addition, many *Conus* species which have therapeutic potential are unknown, for example, *Conus. Pennaceus*. This species is one of the rare species in the world that live in the harsh ecosystem of Persian Gulf. Thus, the aim of present study was to Evaluating the anticancer activity of protein crude extract from *Californicus Conus*.

Materials and Methods

Collection of Specimen
Live specimens of *C.penneus* were collected from the Persian Gulf, Qeshm Island, Iran. Samples then were frozen at -20ºC. Then transported to the laboratory within the liquid Nitrogen container.

Venom Extraction
Frozen cone snails were smashed with hammer and the venomous apparatuses (venom bulbs and venom ducts) separated from the specimens immediately. Venom ducts cut into smaller pieces (fragmented) and mixed with cold homogenization solution (40% ACN+60% PBS+0.1%TFA) and centrifuged for 20 min at 12000 rpm (2 times). The supernatants were collected and preserved at -80 0C for further studies.

Bicinchoninic Acid (BCA) Assay
BCA assay was used for protein determinations using the Pierce BCA Protein Assay Kit (ThermoFisher) in 96-well-plate format. The assay mixture contained 200 µL of the reagent (solution A + B) and 10 µL of sample containing either fractionated conopeptides or BSA standard as well as different potential interfering reagents. Absorbance was read at 562 nm using 9 nm bandwidth using a Biotech plate reader.

SDS-PAGE
The chromatographic fractions were analyzed by 15% polyacrylamide non-reducing SDS-PAGE gel with 29:1 of acrylamide:bisacrylamide ratio . Each sample (10 µL) was mixed with an equal volume of Laemmli SDS-sample buffer (62.5 mM Tris-HCl pH 6.8, 2.0% SDS, 10% glycerol, 0.005% bromophenol blue) and boiled for 5 min using a digital dry bath (Labnet, USA), and then cooled on ice. The 15% separation or resolving gel was prepared with a acrylamide:bisacrylamide solution at a ratio of 29:1 in 250 mM Tris-HCl, pH 8.8, 5% glycerol, and 5% stacking gel in 189 mM Tris-HCl, pH 8.8. Both gel components contained 0.1% SDS. The wells were rinsed with Tricine running buffer (25 mM Tricine, 400 mM glycine, 0.1% SDS) using a syringe with a 24G 1 inch needle (Terumo, Tokyo, Japan) before loading. Electrophoresis was carried out at 30 V per gel for 3 h until the dye had run to the edge of the gel. Protein profile was visualized by silver staining.

Cytotoxicity Assay
Human colone cancer cells (HT-29) and humane embryoinic kidney (HEK-293) were obtained from the Pasteur Institue, Tehran, Iran . Mentioned cells were cultured in DMEM supplemented with 10% fetal bovine serum (FBS), penicillin-streptomycin at 370C in 5 % CO2 and 95% air. In vitro experiments were done at ~70% cell confluence. Cells were subcultivated using trypsin-EDTA (0.05% trypsin) in 96-well plates (Corning, USA) at a density of 30000 cells/well in 100 µL complete medium. The toxicity of venom peptides isolated from C. Penneceus was evaluated against HT-29 and HEK-239 as normal cell line using an MTT assay. The assay was carried out using 96 microtiter plates with various concentrations (0.5, 1, 2, 4, 8, 16, 32, 64 µg/µl) of each conopeptide fractions with three replicate wells. The MTT staining method was performed. After incubation period (24h), the absorbance of the formazan was read at the wavelength of 570 nm using a Biotek Microplate reader.

Results

The electrophoresis pattern of acquired extract was shown in **figure 1**. According to this figure, there are

various peptides and proteins in this extract with the weight range of <3kDa to >10kDa.

Figure 1: Electrophoretic pattern of crude extract obtained from cone snail (*Californicus Conus*).
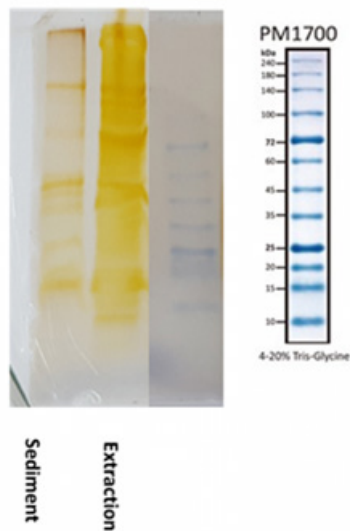
Based on BCA assay, the acquired crud extract had 54.31 mg/ml of proteins. After treatment of cancerous and normal cells with different concentrations of extract (0.5, 1, 2, 4, 8, 16, 32, and 64 µg/ml), the highest toxicity belonged to concentration of 64 µg/ml (**Figure 2**). Figure 2 showed that the extract had no toxicity on normal cells in concentrations of 0.5, 1, 2, and 4 µg/ml. On the other hand, all concentrations showed highest toxicity on cancerous cells than normal cells.

Figure 2: Comparison of the toxicity effect of protein extracts from cone snail (*Californicus Conus*) on cancer and normal cells.
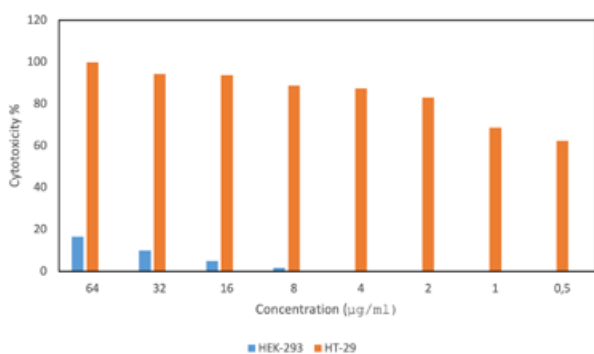
Discussion

Colon cancer is the main cause of cancer-related deaths worldwide and is one of the most common malignant tumors[16]. This cancer accounts for one third of all malignant tumors in the world and is the fourth most common cause of death. This disease occurs due to the uncontrolled growth of cells that can invade other body tissues (metastasis) or multiply in those tissues[17]. Despite major advances in current treatment strategies, the survival rate is still not satisfactory[18]. Therefore, it is necessary to

develop new therapeutic methods for cancer treatment. Nature has always been an attractive source for drug design research[19]. Natural sources have the potential to help discover new promising anticancer agents with low side effects[20]. Proteins and peptides may be interesting anticancer agents because they act specifically against their targets to induce apoptosis[21,22]. Different marine species are known as a potential source of compounds with different biological effects[23]. Proteins and peptides of marine origin are one of the most important of these compounds[24]. These compounds have shown various beneficial effects, including their anti-cancer effect[25]. One of the animals with potential biological agents is the cone snail of the genus Conus. Cone snails are a family of marine mollusks with approximately 700 species. It is estimated that there are more than 50,000 compounds in the venom of cone snails, but less than 0.1% have been functionally characterized. Many of these compounds target different types of ion channels[26]. However, there are only a few reports that have studied the cytotoxic effects of Conus cone snail venom on eukaryotic cells[27,28]. We examined the anticancer activity of protein crude extract from *Californicus Conus*. According to results, this extracts has potent anticancer activity on Human colone cancer cells (HT-29). Our data showed that protein crude extract from *Californicus Conus* can be considered as potent anticancer agent for treatment of colon cancer. Damsio et al. showed that the compound isolated from snake venom (*Bothrops Jararacussa*) has a lethal effect on HT-29 colon cancer cells and causes apoptosis in cancer cells through increased expression of caspase 8, BAX and other related proteins to apoptosis[29]. Fezai et al. indicated that the crude venom of lesser weaver fish causes cell cycle arrest and activation of apoptosis in HCT116 clone cancer cells[30]. Abdel-Rahman et al showed that *C. vexillum* cone venom has cytotoxic potential in EAC tumor cells by inducing oxidative stress-mediated mechanisms[31]. Magdy et al. showed thta the cytotoxic activity of Conus flavidus crude venom was confirmed through apoptotic cell death in HepG2 liver cancer cells[32]. Salimi et al showed that crude textile cone venom is selectively cytotoxic to U87MG human glioma cells, causing activation of caspase-3 and induction of cell apoptosis through mitochondrial signaling[33]. So, anticancer activity of our extract can also be related to the mentioned reasons.

Conclusion

Based on results, venom proteins of cone snail contains a suitable anticancer agents. Therefore, further study of this protein isolate is suggested in future studies.

Competing interests
All authors declare no competing interest.

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Investigation of the prognostic significance of c-kit and c-erb-b2 expression in osteosarcoma, ewing sarcoma, and rhabdomyosarcoma and comparison with clinical parameters

Investigación de la importancia pronóstica de la expresión de c-kit y c-erb-b2 en osteosarcoma, sarcoma de ewing y rabdomiosarcoma y comparación con parámetros clínicos

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Abstract

Objective: In the present study, the prognostic and treatment-guiding roles of the c-erb-B2 oncoprotein and tyrosine kinase receptor c-kit in osteosarcoma (OS), Ewing sarcoma (ES), and rhabdomyosarcoma (RMS) were evaluated.

Materials and methods: With 25 cases from each group, c-kit and c-erb-B2 expression were investigated immunohistochemically in a total of 75 cases.

Results: Staining for c-kit was found to be positive in 15 (60%) of the RMS, 11 of the OS (44%), and 11 of the ES cases (44%). C-erbB-2 staining was positive in 7 RMS cases (8%) and negative in all cases of OS and ES.The SISH method was applied to six c-erb-B2 positive RMS cases, and amplification of the HER2 gene (encoding c-erb-B2) was detected in one case. It was determined that c-kit expression in OS was significantly associated with survival (p<0.05) and could be considered as a poor prognostic parameter. In contrast,c-kit expression had no prognostic significance in ES and RMS. In the RMS group, there was no relationship between c-erb-B2 positivity and prognosis.

Conclusion: It was concluded that c-kit expression can be used as a poor prognostic parameter for OS and therapy targeting c-kit may be an alternative treatment option.

Keywords: Osteosarcoma, Ewing Sarcoma, Rhabdomyosarcoma, C-Kit, c-erb-B2.

Resumen

Objetivo: En el presente estudio, se evaluaron las funciones de guía de tratamiento y pronóstico de la oncoproteína c-erb-B2 y el receptor de tirosina quinasa c-kit en osteosarcoma (OS), sarcoma de Ewing (ES) y rabdomiosarcoma (RMS).

Materiales y métodos: Con 25 casos de cada grupo, se investigó inmunohistoquímicamente la expresión de c-kit y c-erb-B2 en un total de 75 casos.

Resultados: Se encontró que tinción para c-kit fue positiva en 15(60%) de RMS, 11 de casos de OS (44%) y 11 de los casos de ES (44%). La tinción de C-erbB-2 fue positiva en 7 casos de RMS (8%) y negativa en todos los casos de OS y ES. Se aplicó el método SISH a seis casos de RMS positivos para c-erb-B2, la amplificación del gen HER2 (que codifica c-erb-B2) se detectó en caso. Se determinó que expresión de c-kit en OS se asoció significativamente con supervivencia (p<0,05), podría considerarse como un parámetro de mal pronóstico.

Conclusión: se concluyó que la expresión de c-kit se puede utilizar como un parámetro de mal pronóstico para OS y que la terapia dirigida a c-kit puede ser una opción de tratamiento alternativa.

Palabras clave: Osteosarcoma, sarcoma de Ewing, rabdomiosarcoma, C-Kit, c-erb-B2.

Introduction

Bone and soft tissue sarcomas constitute a large group of malignancies diagnosedin childhood and young adulthood. Osteosarcoma (OS) is the most commonly observed primary malignant bone tumor in this group; while it accounts for approximately 20% of primary malignant bone tumors, it comprises 56% of childhood malignant bone tumors[1-3]. The second-most common malignant bone tumor after OS is Ewing sarcoma (ES)[4,5]. Rhabdomyosarcoma (RMS), on the other hand, accounts for 19% of soft tissue sarcomas diagnosed in adolescents and young adults[6].

Despite advances in treatment methods forbone and soft tissue sarcomas, the desired improvements in survival rates have not been achieved, especially in metastatic and recurrent cases. In recent years, biological inhibitors targeting proteinsthat play a role in oncogenesis have been introduced into treatment regimens and positive results have been obtained[7,8].

C-kit (CD117) is a proto-oncogene encoding the transmembrane cell surface receptor kit. It is a member of the same subclass of genes as platelet-derived growth factor and colony-stimulating growth factor. Functional mutations inc-kit have been associated with the pathogenesis of a number of malignancies expressing c-kit, including gastrointestinal stromal tumors, mast cell disease, and acute leukemia[9].

The c-erb-B2 receptor (encoded by the *HER2* gene) belongs to the epidermal growth factor receptor family and plays a crucial role in the activation of the subcellular signal transduction pathways that control the growth and differentiation of epithelial cells. Monoclonal antibody therapy directed against the extracellular region of c-erb-B2 has long been used to treat breast and stomach carcinomas[10-13].

Our research aims to investigate c-kit and c-erb-B2 protein expression in OS, ES, and RMS cases; to determine their relationships with clinical parameters, and to determine their effect on prognosis.

Materials and Methods

A total of 75 patients diagnosed with OS, ES, or RMS (25 from each group)in the authors' institution were randomly selected. The patients' clinical and macroscopic information, such as age, gender, resection type, and survival time, were obtained by reviewing the archived reports and reports from oncology clinic follow-ups. The archived slides were re-evaluated histopathologically, and histological classification was performed for the OS and RMS cases.

Immunohistochemistry

A total of four new 4 µm sections were prepared from the selected paraffin blocks, including one for H&E examination, two for immunohistochemical (IHC) examinations, and one as a backup. In this study, c-erb-B2 (monoclonal, mouse anti-human, Code: NCL-L-CBE-356, Clone: 10A7, 1:100, 60 min, Lot no: L 135613, Novocastra, Newcastle, UK)and c-kit/CD117 (Polyclonal, rabbit anti-human, Code: RB-9038-P1, 1:100, 60 min, Lot no: 9038P412F, NeoMarkers, Fremont, CA, USA) antibodies were used to evaluate the expression of their respective targets using the standard avidin-biotin-peroxidase complex technique. Gastrointestinal stromal tumors and breast carcinoma were used as positive controls for c-kit and c-erb-B2, respectively.

Immunohistochemical evaluation

In the IHC evaluation using the c-kit antibody, the percentage of positive cells was categorized into three groups as follows: staining in 0%–10% of tumor cells, in 10%–50% of tumor cells, or in >50% of tumor cells. In addition, the staining intensity was categorized as weak (1+), moderate (2+), or strong (3+). Results were accepted to be negative if staining was observed in 0%–10% of tumor cells and the staining intensity was (1+), positive if 0%–10% of tumor cells were stained and the staining intensity was (2+) or (3+), and positive if staining was observed in 10%–50% or>50% of tumor cells and the staining intensity was (1+), (2+), or (3+).

In the IHC evaluation using the c-erb-B2 antibody, the percentage of stained cells was categorized into two groups: staining of 0%–10% of tumor cells or >10% of tumor cells. In addition, the staining intensity was classified as weak, moderate, or strong, with staining visible with the x2 or x4 microscope objective considered strong, with the x10 or x20 objective considered moderate, and with the x40 objective considered weak. The localization of staining in the cells was indicated as membranous or cytoplasmic-membranous. The results were considered negative if <10% of tumor cells had staining (regardless of staining intensity) and negative (1+) if more than 10% of tumor cells had staining, but the staining was weak. The results were considered positive (2+) if >10% of tumor cells were stained and the staining intensity was moderate and positive (3+) if >10% of tumor cells had strong staining[12,14].

Silver in situ hybridization

For silver in situ hybridization (SISH), the inform HER2 DNA probe kit (VENTANA) was used with the VENTANA Benchmark LT instrument. Microscopic examination was performed on the slides treated with c-erb-B2 and chromosome 17 DNA probes.

Evaluation of the silver in situ hybridizationmethod

Nuclear signals of a total of 40 cells were counted in

at least two fields that met the scoring criteria and the average number of signals per nucleus was determined. If the average number of signals for c-erb-B2 (*HER2*) divided by the average number of signals for chromosome 17 was >2.2, it was considered significant.

Statistical evaluation
For cross-sectional variables, Chi-square, Fisher's exact, Kaplan–Meier, andlog-rank tests were performed for statistical evaluation. p<0.05 was considered significant. Statistical analyseswere performedusing SPSS 8.0 software.

Results

Clinicopathological results
The peak incidence of disease in the OS group, which consisted of 25 cases, was in the second decade. The distribution of histological types according toage and gender is presented in **table I**. The most common location was the extremities (15 cases; 60%). Of those, nine (36%) were in the femur and six (24%) were in the tibia. Other locations were the mandible in three (12%) and the pelvis in two (8%) of the cases. It was determined that the patients had an average follow-up period of 25.4 months. Thirteen of the patients had died due to disease-related causes, one patient had local recurrence, and one patient had metastasis. The remaining nine patients are alive and healthy, with no symptoms of disease.

The patients were divided into two age groups (under 18 years of age and 18 years of age and older), and the correlation with gender, localization, histological type, and survival was investigated. There was no statistically significant difference between the two age groups. In addition, no difference in correlation was observed between the age groups with regard to histological type, tumor location, and survival. Necrosis rates, which were divided into two groups (below 90% and above 90%), were found not to be correlated with histological type orsurvival.

The age and gender distributions of the 25 ES cases are shown in **table II**. The peak incidence was determined to be the second decade. The most common site of involvement in ES cases wasthe lower extremities (52%), while the other locations were the trunk (20%), upper extremity (12%), head-neck (12%), and 4% lymph nodes (4%).

Clinical follow-up data were obtained for15 of the 25 cases. The mean follow-up period was 23.2 months. Eight of the patientshave died due to disease-related causes, and metastasis was detected in four of the patients. The remaining three patients are alive and healthy, with no symptoms of disease.

In the statistical analysis, it was determined that gender was not correlated with survival. There was no significant difference ingender, tumor location,orsurvival according to age group (cases were divided into two groups, <18 years old and ≥18 years).

The association of age and gender with histological type in RMS cases is shown in **table III**. The distribution of the tumor locations was head-neck (36%), trunk (24%), urogenital region (16%), upper extremity (12%), lower extremity (8%), and lymph nodes (4%).

In the 14 (out of 25) cases whose clinical follow-up records were accessed, the follow-up period ranged between14 and 51 months, with an average of 27.6 months. Two patients have died due to disease-related causes, one patient had local recurrence, and four patients had metastasis. The remaining seven patients are alive and healthy, with no symptoms of disease.

There was no statistically significant difference between male and female patients with RMS in terms of mean age and survival. Gender, localization, histological type, and survival rates were found to be similar between the two age groups (under 18 years and over 18 years old). Histological types, localization, and survival were found not to be correlated with age group.

Immunohistochemistry results

C-kit
Cytoplasmic positivity was detected in 11 (44%) of the OS cases (**Figure 1A**). In some cases, cytoplasmic staining was accompanied by a weak membranous staining. Of the positive cases, two (8%) had diffuse-strong, six (24%) had diffuse-moderate, and the remaining three (12%) had focal, weak-moderate staining. Weak staining was observed below 10% in 3of the 14 cases evaluated as negative. Cytoplasmic positivity was observed in osteoblastic and osteoclastic cells in one of the negative cases. The association between c-kit expression leveland overall survival is shown in **Graphic 1**. A statistically significant correlation was found between c-kit positivity andoverall survival (p<0.05) (**Table IV**, **Graphic 1**). In addition,a result at the limit of statistical significance was obtainedbetween the intensity of c-kit expression and survival (p>0.05). However, there was no difference between the c-kit expression groups in terms ofclinicopathological characteristics, including age, gender, localization, histological type, and response to neoadjuvant chemotherapy.

Similar to OS,c-kit expression was positive in 11 (44%) patients with ES (**Figure 1B**). No staining was observed in 14 cases (56%). In eight of these cases, weak staining was detected in below 10% of tumor cells, which was evaluated as negative. Staining was diffuse-strong in

two positive cases (8%), diffuse and weak-moderate in four cases (16%), and focal and weak-moderate in the remaining five cases (20%). Mean survival was 13 months in cases with c-kit expression and 41 months in c-kit–negative cases; however, no significant correlation was found between c-kit immunoreactivity, overall survival, age, gender, ortumor location.

Positive cytoplasmic staining was found in 15 (60%) of the 25 RMS cases (**Figure 1C**). Diffuse and strong staining was detected in 3 cases (12%), diffuse and weak-moderate staining was observed in 6 cases (24%), and focal and weak-moderate staining was observed in the remaining 6 positive cases (24%). In 4 of the 10 (40%) negative cases, weak staining in less than 10% of tumor cells was observed.

The association of c-kit expression with overall survival and histological type is presented in **table V**. The mean survival was determined to be35 months in cases with c-kit expression and 43 months in cases with no c-kit expression. There was no statistically significant correlation between c-kit immunoreactivity and survival, age, gender, tumor location, or histological type (p>0.05).

C-erb-B2

No staining was detected with thec-erbB-2 antibody in OS and ES cases, whereas positive staining was observed in 7 (28%) of the RMS cases (**Figure 1D**). Of these cases, 4 (16%) were '2+' and 3 (12%) were '3+'. A membranous-cytoplasmic staining pattern was observed in all postive cases (28%). It was noted that rhabdomyoblastic differentiation was distinct in positive cases. C-erbB-2 expression was not found to be correlated with overall survival (p>0.05).

Silver in situ hybridization

The SISH test was performed in6 of the 7 RMS cases that stained positive with c-erb-B2(1 case could not be studied due to the absence of tissue in the paraffin block) to detect *HER2* gene amplification. HER2 gene amplification was detected in one patient (**Figure 1E**).

Table I: Gender and age distribution of osteosarcoma cases according to histological types.

Histological Type	Number of Cases (%)					
	Total	Female	Male	Age Distribution	Mean±SS	Median
Osteoblastic	11	8 (73)	3 (27)	14-29	19.82±5.07	17.00
Chondroblastic	11	4 (37)	7 (63)	11-52	23.36±11.89	18.00
Fibroblastic	2	2 (100)	-	21-34	27.5±9.19	27.5
Telangiectatic	1	-	1 (100)	39	39.00±0.00	39
Total	25	14 (56)	11 (44)	11-52	22.76±9.49	19

Table II: Gender and age distribution in Ewing sarcoma cases.

Gender	Number of cases	Average Age	Standard Deviation	Age Distribution
Male	16	27.50	19.58	10-80
Female	9	20.56	11.62	3-35
Total	25	25.00	17.21	3-80

Table III: Gender and age distribution of rhabdomyosarcoma cases according to histological types.

	Number of Cases (%)					
	Total	Female	Male	Age Distribution	Mean	Standard Deviation
Alveolar	12	6 (50)	6 (50)	1-35	14.8	11.76
Embryonal	9	6 (67)	3 (33)	2-74	16.9	23.06
Spindle Cell	2	1 (50)	1 (50)	14-17	15.5	5.19
Pleomorphic	1	-	1 (100)	6	6	0.00
Botryoid	1	1 (100)	-	25	25	0.00
Total	25 (100)	14 (56)	11 (44)	1-74	15.7 (1-74)	15.79

Table IV: Distribution of C-kit immunoreactivity according to histological type and survival in osteosarcoma cases.

		Number of Cases (%)	C-kit Positive (%)	C-kit Negative (%)
Histological Type	Osteoblastic	11 (44)	4 (37)	7 (50)
	Chondroblastic	11 (44)	5 (45)	6 (43)
	Fibroblastic	2 (8)	2 (18)	-
	Telangiectatic	1 (4)	-	1 (7)
	Total	25 (100)	11 (100)	14 (100)
Survival	Live	11 (46)	3 (30)	8 (57)
	Dead	13 (54)	7 (70)	6 (43)
	Total	24 (100)	10 (100)	14 (100)

Table V: Distribution of C-kit immunoreactivity according to histological type and survival in rhabdomyosarcoma cases.

		Number of Cases (%)	C-kit Pozitive (%)	C-kit Negative (%)
Histological Type	Alveoler	12 (48)	6 (40)	6 (60)
	Embryonal	9 (36)	7 (46.6)	2 (20)
	Spindle Cell	2 (8)	1 (6.7)	1 (10)
	Pleomorphic	1 (4)	1 (6.7)	-
	Botryoid	1 (4)	-	1 (10)
	Total	**25 (100)**	**15 (100)**	**10 (100)**
Survival	Live	12 (86)	8 (89)	4 (80)
	Dead	2 (14)	1 (11)	1 (20)
	Total	**14 (100)**	**9 (100)**	**5 (100)**

Figure 1A: Cytoplasmic c-kit positivity in osteosarcoma (x200).
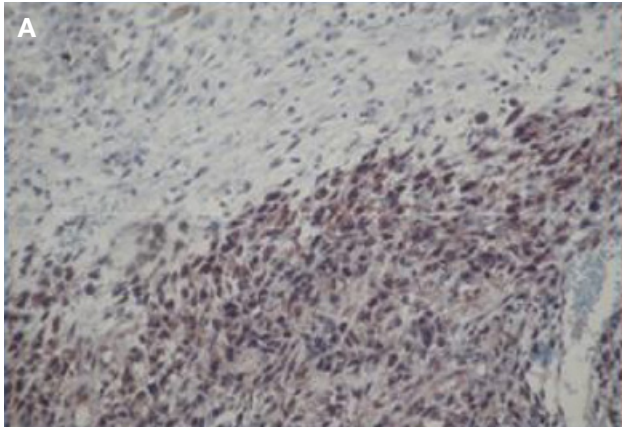
Figure 1D: Strong cytoplasmic-membranous c-kit positivity in rhabdomyosarcoma (x200).
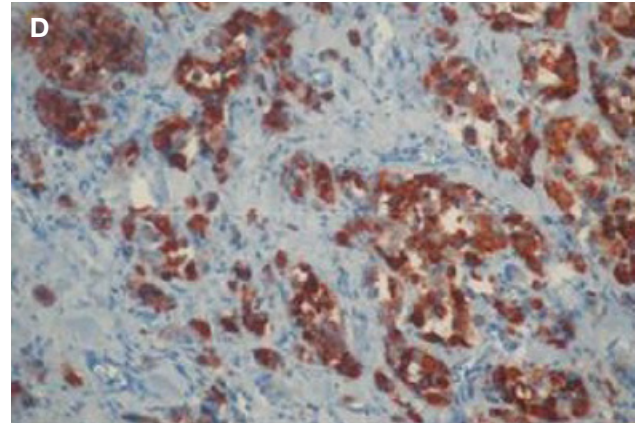
Figure 1B: Cytoplasmic c-kit positivity in Ewing sarcoma (x200).
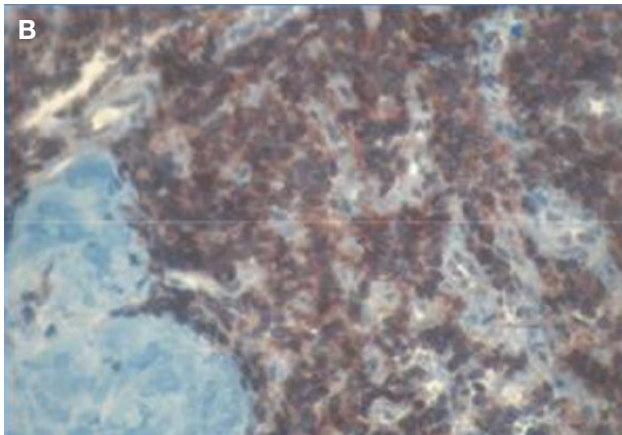
Figure 1E: Increased number of signals in c-erb-B2 gene by SISH method in rhabdomyosarcoma (x400).
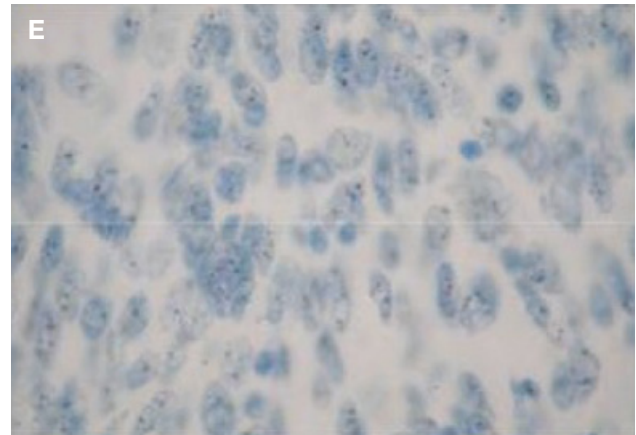
Figure 1C: Strong positivity of cytoplasmic-membranous c-kit in rhabdomyosarcoma (x400).
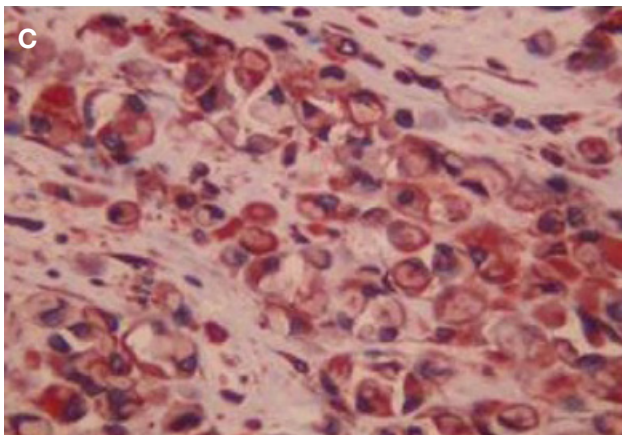
Discussion

With the demonstration of the roles of c-kit and c-erb-B2 in the etiopathogenesis of some epithelial and stromal tumors, and the successful results of treatments targeting these receptors in recent years, the expression of c-kit and c-erb-B2 has been investigated in many different tumors.

Mutations inc-kit have been identified in tumor pathogenesis for more than 20 years, and nearly 500 different mutations have been revealed over the years. More than 80% of small cell carcinoma of the lung, malignant melanoma, colorectal cancer, and gastrointestinal stroma are among these tumors[15].

Although c-kit is a transmembrane receptor protein, its expression is usually cytoplasmic by immunohistochemistry in sarcomas. In a study by Sabah et al., it was explained that the distinction between cytoplasmic and membranous staining was difficult in tumors with a high nucleocytoplasmic ratio. Therefore, both membranous-cytoplasmic and membranous staining were considered positive[16,17]. In studies investigating c-kit expression in OS, the positivity rate obtained by Entz-Werle et al.[7] was 57%, by Miiji et al.[18] was 46%, and by Saeter et al.[19] was 62.5%, whereas we obtained a positivity rate of 44% in our study. In our study, it was determined that the overall survival was lower in cases with c-kit expression, and this finding was statistically significant (p=0.04). While the 5-year survival was 100% in negative cases in a study by Werle et al.[7] and 85% in positive cases, it was reported that c-kit expression could be a poor prognostic parameter, which is consistent with our study. In a series of 100 cases reported by Sulzbacher et al.[20], 20% c-kit positivity was detected, and there was no correlation with overall survival. It has been suggested that c-kit expression can be observed in OS, but that it has no effect on prognosis[21].

Studies on c-kit expression in soft tissue sarcomas have reported different results in the literature. C-kit expression was detected in between 38% and 71% of tumors in the ES tumor family[22]. In our study, positive staining was detected in 44% of the ES cases. The mean survival was 13 months in patients with c-kit expression and 41 months in patients without c-kit expression; however, remarkably, no statistically significant correlation was found between c-kit positivity and overall survival (p>0.05). Since no relationship could be established with survival in ES cases with c-kit expression, other clinicopathological parameters were thought to be more determinative of survival.

In different series investigating c-kit expression in RMS cases, expression rates were found to be quite low in the literature. Landuzzi et al. reported that c-kit expression is negligible in RMS, but stem cell factor production is quite high[23]. In another study, c-kit was found to be positive in 6% of 105 RMS cases. In contrast to the literature, we found c-kit positivity in 60% of the cases in the RMS group. The average survival time was 35 months in positive cases and 43 months in negative cases. However, there was no statistically significant relationship between c-kit staining and survival (p>0.05)[24].

Overexpression of c-erb-B2 protein due to the amplification of the *HER2* gene has been identified in many tumors originating from breast, ovary, lung, pancreas, stomach, colon, salivary gland, bladder, and kidney. C-erbB2 expression has been considered to promote increased tumorigenesis and metastatic potential, as well as resistance to chemotherapeutic agents[11,25,26].

In a case series by Onda et al.[25] in which 26 cases of OS were examined, c-erb-B2 expression was detected at a rate of 42%, while gene amplification and mutation were not observed. Another similar study[27] suggested a statistically significant correlation of c-erb-B2 expression with multiple metastases and recurrences in a series of 115 OS cases, including primary tumor biopsies and resections for metachronous lung cancers. In our study, staining with c-erb-B2 was not observed in any of the 25 OS cases; only nonspecific cytoplasmic staining was detected in the muscle tissue adjacent to the tumor in four cases. It is thought that the conflicting results of studies on c-erb-B2 expression in OS may be due to the use of different fixation and decalcification methods, antibody clones, antigen retrieval methods, and evaluation scores[15].

In studies investigating c-erb-B2 expression in ES, cytoplasmic c-erb-B2 staining was found at a rate of 16% by Scotlandi et al. and 27% by Thomas et al.[26,27], but no correlation with clinical parameters was found. In our ES study group consisting of 25 cases, c-erb-B2 protein expression was not observed.

In studies investigating c-erb-B2 expression in RMS cases, there are series that show 9%–33% positivity, as well as series in which all of the cases were negative. However, no correlation was found between clinical parameters and c-erb-B2 expression in cases with positive staining[24,28]. In our study, positive staining with the anti-c-erb-B2 antibody was found in 7 (28%) of RMS cases, similar to the rates in some studies in the literature, but *HER2* gene amplification was found in only 1 of these cases—a remarkable finding. It is known that expression of c-erb-B2 protein in tumors by IHC does not imply a specific alteration in the *HER2* gene in all cases, so we believe that the results should be supported by molecular tests. Notably, there was no statistically significant correlation between c-erb-B2 immunoreactivity and survival (p>0.05).

In our series in which cases of common bone and soft tissue tumors were evaluated, we concluded that c-kit and c-erb-B2 expression did not have prognostic significance in ES and RMS, but c-kit expression in OS is a poor prognostic parameter. The different results observed in studies on c-kit and c-erb-B2 expression may be due to antibody clones used, IHC methods used, and evaluation criteria. By using standardized IHC methods such as those used for breast cancer, stomach cancer, and gastrointestinal stromal tumors in studies, as well as investigating gene mutations using molecular methods and comparing and sharing the results along with follow-ups in long-term and large patient series, it will be possible to accurately determine the contexts in which molecular therapies targeting these receptors could be used and achieve meaningful results for patients.

Competing interests

All authors declare no competing interest.

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ORIGINAL

Prevalence, Types and Risk factors of Glaucoma Among Patients Attending Department of Ophthalmology in a Tertiary Care Hospital: A Descriptive Cross-sectional Study

Prevalencia, tipos y factores de riesgo del glaucoma entre los pacientes que acuden al servicio de oftalmología de un hospital terciario: Un estudio descriptivo transversal

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Abstract

Background: Glaucoma is one of the leading causes of visual impairment, and blindness worldwide. Early detection of glaucoma can prevent sight threatening complications. The study was designed to find out the prevalence, and types of glaucoma among patients attending the Department of Ophthalmology in a tertiary hospital of Nepal.

Methods: A hospital-based cross-sectional study was conducted in the Department of Ophthalmology after receiving ethical approval from the institutional review board The study was conducted from 10 September 2022 to 10 March 2023. Convenience sampling was done to reach the sample size. Relevant data was entered in a proforma specified for the study. Data analysis was done using Statistical Package for the Social Sciences version 26, point estimate at 95% Confidence Interval (CI) was calculated along with frequency and proportion for binary data.

Results: Among 1140 participants, 25 (2.19%) (1.49-3.22 at 95% Confidence Interval) study subjects had glaucoma at least in one eye. Primary open angle glaucoma was much more common 10 (0.87%), followed by primary narrow angle glaucoma 9 (0.78%), and secondary glaucoma 6 (0.53%) in the study population. Primary narrow angle glaucoma was much more common in female gender. Within the diagnosed glaucoma cases 9 (36%) subjects had a positive family history.

Conclusion: The prevalence of glaucoma was higher than the recent national estimates in the current study. Primary open angle glaucoma remains the commonest type of glaucoma. First degree relative of a diagnosed case of glaucoma should be subjected for glaucoma screening.

Keywords: first degree relative, glaucoma, intraocular pressure, malignant glaucoma, optical coherence tomography.

Resumen

Antecedentes: El glaucoma es una de las principales causas de discapacidad visual y ceguera en todo el mundo. La detección precoz del glaucoma puede evitar complicaciones que pongan en peligro la visión. El estudio se diseñó para averiguar la prevalencia y los tipos de glaucoma entre los pacientes que acuden al Departamento de Oftalmología de un hospital terciario de Nepal.

Métodos: Se realizó un estudio transversal hospitalario en el Departamento de Oftalmología tras recibir la aprobación ética de la junta de revisión institucional El estudio se llevó a cabo del 10 de septiembre de 2022 al 10 de marzo de 2023. Se realizó un muestreo de conveniencia para alcanzar el tamaño de la muestra. Los datos pertinentes se introdujeron en un formulario específico para el estudio. Los datos se analizaron con el paquete estadístico SPSS 26. y se calculó la estimación puntual con un intervalo de confianza (IC) del 95%, así como la frecuencia y la proporción de los datos binarios.

Resultados: Entre los 1140 participantes, 25 (2,19%) (1,49-3,22 en el Intervalo de Confianza del 95%) sujetos de estudio tenían glaucoma al menos en un ojo. El glaucoma primario de ángulo abierto era mucho más frecuente 10 (0,87%), seguido del glaucoma primario de ángulo estrecho 9 (0,78%) y el glaucoma secundario 6 (0,53%) en la población del estudio. El glaucoma primario de ángulo estrecho era mucho más frecuente en el sexo femenino. Dentro de los casos de glaucoma diagnosticados, 9 (36%) de los sujetos tenían antecedentes familiares positivos.

Conclusiones: La prevalencia del glaucoma fue superior a las estimaciones nacionales recientes en el estudio actual. El glaucoma primario de ángulo abierto sigue siendo el tipo de glaucoma más frecuente. Los familiares de primer grado de un caso diagnosticado de glaucoma deberían someterse a un cribado de glaucoma.

Palabras clave: familiar de primer grado, glaucoma, presión intraocular, glaucoma maligno, tomografía de coherencia óptica.

Introduction

Glaucoma is one of the leading causes of irreversible blindness worldwide, and is associ¬ated with a reduced quality of life[1]. Various notable risk factors of glaucoma have been identified which include age, gender, genetics, family history, smoking, race, systemic hypotension and hypertension, vasospasm, use of systemic or topical steroids, obstructive sleep apnea and most significantly raised intraocular pressure (IOP)[2-4].

An estimated global prevalence of glaucoma is 3.54%, with the highest prevalence in Africa. The number of people with glaucoma worldwide (aged 40-80 years) is expected to rise from 64.3 million in 2013 to 111.8 million in 2040, more frequent in populations residing in Asia and Africa[5].

There are studies on glaucoma from various parts of Nepal; however; the data is limited and varies. This study aimed to determine the prevalence and types of glaucoma among patients attending the Department of Ophthalmology in a tertiary care hospital of central Nepal.

Methods

This hospital based descriptive, cross-sectional study was conducted in the outpatient Department (OPD) of Ophthalmology of Chitwan Medical College (CMC) Teaching Hospital, from 10 September 2022 to 25 February 2023. Ethical approval was obtained from the Institutional Review Committee (**Ref: CMC-IRC/079/080-053**). An informed consent was obtained from the study subjects. A convenient sampling was done to enroll the participants during the study.

The sample size was calculated using the formula as given in the following table.

n = (Z² × p × q) / e²
= (1.96² × 0.019 × 0.981) / 0.025²
= 115
Where,
n = required sample size,
Z = 1.96 at 95% Confidence Interval (CI),
p = prevalence of glaucoma reported by a similar study from Nepal, 1.90%[4]
q = 1-p
e = margin of error, 2.5%

Required sample size	115

As convenience sampling was done, the sample size was doubled to 230. Considering the non-respondent rate of 10%, the total sample size becomes 253. However, our study included 1140 study participants during the study period. All study subjects who are more than 30 years of age, glaucoma suspect study participants were enrolled in the study. Patients over 85 years of age, study

subjects not providing informed consent, patients with systemic chronic debilitating illnesses were excluded from the study.

All the study participants underwent a thorough ocular examination including visual acuity testing, refraction when needed, slit lamp biomicroscopy including detailed anterior segment examination and posterior segment examination. A detailed retina evaluation, including the optic disc examination was carried out in study participants with clear media. If a mydriasis was needed to complete the examination, Tropicamide 0,8 or 1 % and Phenylephrine 2,5 % were used

Patients needing further examinations and tests were subjected for intraocular pressure measurement using Schiotz tonometry, and pulsair tonometer, Goldman applanation tonometer was used to confirm the intraocular pressure besides visual field examination, fundus photography, gonioscopy, and Optical coherence tomography (OCT) when and where required. In addition, phasing and water drinking tests were performed in cases to help confirm the diagnosis of normal tension glaucoma (NTG). This test was performed following a quick baseline IOP measurement a litre of sterile water was given to the patient early morning and IOP was measured every 15 minutes till the IOP starts declining. The highest IOP recorded was taken as the IOP for that study subjects. A glaucoma specialist, and a retina specialist examined the suspected study subjects to confirm the diagnosis of glaucoma and further management. Data was collected using a form designed for the study. Statistical analysis was done in SPSS version 26. Interobserver agreement of Kappa was taken as a reliability tool, and to validate the findings, a Kappa value more than 0.8 was considered complete agreement between the examiners. The statistical methods used were frequencies, percentages, mean, and standard deviation. Any p value less than 0.05 was considered significant when applicable.

Results

Among 1140 participants, of the 2280 eyes examined, 25 (2.19%) (1.49-3.22 at 95% Confidence Interval) study subjects had glaucoma at least in one eye. Primary open angle glaucoma was the commonest 10 (0.87%), followed by primary narrow angle glaucoma in nine (0.78%), and secondary glaucoma in six (0.53%) study participants of all the study subjects (**Table I**).

Nine (36%) study subjects in the study population were overweight or obese, 10 (40%) subjects consumed alcohol, 11 (44%) used tobacco, only four (16%) study subjects were aware about glaucoma, whereas nine (36%) study subjects gave a positive family history of glaucoma. Only four (16%) study subjects experienced Raynaud's phenomenon, 21 (84%) study subjects were either diabetic or a hypertensive as summarized in **table II**.

Table I: Prevalence and types of glaucoma in the study subjects (n=25).

Types of glaucoma in the study population		n	%
Primary open angle glaucoma	Primary open angle glaucoma	04	16.00
	Normal tension glaucoma	01	4.00
	End stage open angle glaucoma	02	8.00
	Chronic open angle glaucoma	03	12.00
Primary narrow angle glaucomas	Primary angle closure glaucoma	06	24.00
	Acute congestive glaucoma	03	12.00
Secondary glaucomas	Steroid induced glaucoma	02	8.00
	Neovascular glaucoma	02	8.00
	Malignant glaucoma	01	4.00)
	Other types of glaucoma	01	4.00)
Total		**25**	**100**

Table II: Patient related clinical characteristics (n=25).

Variables	n	%
Body mass index (BMI) of the study subjects with glaucoma		
Overweight study subjects	08	32.00
Obese study subject	01	4.00
Alcohol consumption status of the study subjects		
Social	06	24.00
Regular	03	12.00
Alcohol addiction	01	4.00
Tobacco use by the study subjects		
Study subjects who use tobacco	11	44.00
Awareness on glaucoma		
Aware about glaucoma	04	16.00
Unaware about glaucoma	21	84.00
Family history of glaucoma		
First degree relative with glaucoma	09	36.00
First degree relatives not yet diagnosed as glaucoma patients	16	64.00
Chronic problems in the study subjects		
Diabetes mellitus	07	28.00
Hypertension	14	56.00
Myopia	04	16.00
Pseudophakia	13	52.00
Raynaud's phenomenon	04	16.00
Total	**25**	**100**

Table III: Clinical and investigative findings in the study subjects (n=25).

Variables	n	%
Impaired visual acuity at presentation	12	48.00
Presence of corneal edema	06	24.00
Rubeosis iridis (iris neovascularization)	03	12.00
Vertically oval fixed pupil	05	20.00
Relative afferent pupillary defect/afferent pupillary defect	06	24.00
Raised intraocular pressure	20	80.00
Optic disc changes/findings in the study subjects with glaucoma (n=25)		
Optic disc notch (Inferotemporal)	01	4.00
Glaucomatous optic disc cupping	06	24.00
Hyperemic optic disc	08	32.00
Crowded small optic disc	01	4.00
Splinter hemorrhage	01	4.00
Peripapillary changes	01	4.00
Glaucomatous optic disc atrophy	05	20.00
Optic disc could not be visualized	02	8.00
Total	**25**	**100**
Gonioscopy findings in the study subjects (n=25)		
Open angle	16	64.00
Occludable or closed angle	09	36.00
Visual fields finding in the study subjects (n=25)		
Borderline visual field defects	07	28.00
Glaucomatous visual field defects	07	28.00
Could not be assessed	06	24.00
Normal visual field findings	05	20.00
OCT findings suggestive of glaucoma in the study subjects	12	48.00
Total	**25**	**100**

Table IV: Demographic profile of the study subjects (n=25).

Age group of the study subjects	n	%
Study subjects less than fifty years of age	04	16.00
Study subjects more than fifty years of age	21	84.00
Gender distribution of the study subjects		
Male	12	48.00
Female	13	52.00
Geographical representation by the study subjects		
Urban Nepal	20	80.00
Rural areas	05	20.00
Occupation of the study subjects		
Agriculture	05	20.00
Retired	10	40.00
Other occupation	10	40.00
Educational background of the study subjects		
Literate	18	72.00
Illiterate	07	28.00
Total	**25**	**100**

Impaired visual acuity 12 (48%) was a significant presenting complaint in the study subjects, corneal edema was present in six (24%), neovascularization in the iris in three (12%), pupillary defect in 11 (44%), hyperemic optic disc in eight (32%), and 16 (64%) study subjects had open angle while doing a gonioscopy procedure (**Table III**).

Mean age of presentation of the study subjects was 61.64±12.78 years. Twenty-one (84%) of the study subjects with glaucoma were above 50 years of age group. Females just outnumbered the males 13 (52%), and 12 (48%) respectively, however Females outnumbered the males by more than three times in primary angle closure glaucoma group seven (28%), and two (8%) respectively. Majority of the study subjects 20 (80%) represented urban geographic area. Occupation wise retired, and other occupation was common 10 (40%) each among the study subjects with glaucoma. Majority of the study subjects 18 (72%) were literate (**Table IV**).

Discussion

Among 1140 study participants in 2280 eyes examined the overall prevalence of glaucoma was 2.19% in the present study. The prevalence of primary open-angle glaucoma was higher (0.87%) than that of primary narrow-angle glaucoma (0.78%) or secondary glaucoma (0.53%) in the current study.

In different studies from Nepal and elsewhere, the overall prevalence of glaucoma were 1.90%, 0.93%, and 1.92%[3,4,6] in our study the overall prevalence of glaucoma was higher. The global prevalence of glaucoma is estimated at 3.54%[5] which is much higher than our study estimates.

The drop in the prevalence of glaucoma in Nepal is due to the efforts of the eye care sector of Nepal to reduce the preventable and treatable causes of blindness for the last four decades. The higher prevalence of glaucoma in the current study when compared to recent national estimates[4,6] could be attributed to this study being done in a tertiary care hospital where mostly the needy patients visit, improved hospital-seeking behavior of the patients, skilled human resources, infrastructure to detect glaucoma early, and a proper referral channel to establish a diagnosis and management. Primary open-angle glaucoma is the most common kind of glaucoma in the current study, followed by primary angle closure, and secondary glaucoma in concordance with other studies from Nepal, and elsewhere[3,4,7].

Various known patient-related risk factors were explored and observed in the present study. The 84% of study subjects with chronic systemic problems, like diabetes or hypertension, 84% of glaucoma patients over the age of 50 years of age, 16% of study subjects with a history of Raynaud's phenomenon, 40% study subjects consuming alcohol and only 44% study subjects consuming tobacco is also in accordance with findings across the globe[8-12].

In the present study obesity were explored as a risk factor, the as a potential risk to developing glaucoma, in our findings 36% of the study subjects were overweight or obese. This high rate, as in other studies,13 allows us to warn of the potential increased risk of open-angle glaucoma in young adults in the future.

In the current study, only four (16%) study subjects were aware of glaucoma, which was slightly higher than in a study from Nepal[14]. This could be attributed to the type of study population, and their level of education. Nine (36%) study subjects' first-degree relatives had been diagnosed with glaucoma in the family this finding of the study did not correlate with a study finding from Nepal. Nevertheless, this finding emphasized the importance of screening for glaucoma in first-degree relatives of a glaucoma patient.

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The causes of visual acuity in the study subjects were, 12 (48%), corneal edema in six (24%), neovascularization in the iris in three (12%), pupillary defect in 11 (44%), raised intraocular pressure in 20 (80%), hyperemic optic disc in eight (32%) which are in accordance with other studies[4-8].

In the current study the mean age of diagnosis for glaucoma was above 50 years of age 61.64±12 this finding was comparable to many studies from Nepal and elsewhere further reemphasizing that the prevalence of glaucoma rises with increasing age, especially after the age of 50 years[4-6,11-14]. In the present study, females outnumbered the males by more than three times in primary angle closure glaucoma group seven (28%), and two (8%) in agreement with a study from Nepal and elsewhere establishing that narrow angle glaucomas are more common in females[4].

In the current study majority of the study subjects 20 (80%) represented urban geographic area this could be contributed to the fact the study hospital itself lies in an urban location. In the current study majority of the study subjects 18 (72%) were literate but only four (16%) of them were aware about glaucoma this was an interesting finding in the study which also highlighted the need of health education regarding glaucoma and eye care in all levels eye health care in Nepal.

Conclusions

The prevalence of primary open-angle glaucoma is higher (0.87%) than that of primary narrow-angle glaucoma (0.78%) or secondary glaucoma (0.53%), and primary open angle glaucoma is the most common kind of glaucoma. The drop in the prevalence of glaucoma in Nepal is due to the efforts of the eye care sector of Nepal to reduce the preventable and treatable causes of blindness for the last four decades. The known patient related risk factors like age, gender, systemic chronic illnesses, alcohol consumption, and tobacco use, Raynaud's phenomenon remain the same. Obesity can be a confounding risk to develop primary open-angle glaucoma in young adults, and can be explored further. Awareness regarding glaucoma (16%) remains still very low despite increasing literacy levels (72%). Visual impairment, and blindness in glaucoma subjects is attributed to various causes.

Conflict of interest
None.

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ORIGINAL

Estimación del nivel de riesgo cardiometabolico relacionado con obesidad en trabajadores sanitarios españoles

Cardiometabolic level risk estimation and obesity in health workers

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Resumen

Introducción: La obesidad abdominal es el componente observado con mayor frecuencia en el síndrome metabólico y se relaciona con doble riesgo de desarrollar enfermedad coronaria y cerebrovascular. Es objetivo de este trabajo estimar el nivel de riesgo cardiometabólico asociado a la obesidad en profesionales sanitarios para poder actuar en su prevención, control y seguimiento coordinado desde salud laboral.

Metodología: Estudio descriptivo transversal en 2.591 trabajadores del sector sanitario de la Comunidad Autónoma de Illes Balears. El nivel de riesgo cardiometabólico (NR) se calculó valorando la presencia o no de: síndrome metabólico (MetS), RCV con score elevado y dos o más indicadores de adiposidad alterados (IA). Estos valores se relacionaron de forma independiente con el valor del Índice de Masa corporal (IMC).

Resultados: El nivel de riesgo cardiometabólico asociado a obesidad en profesionales sanitarios es mayor en hombres, aumenta con la edad y se incrementa según lo hace el IMC (p<0,0001). La presencia de ≥2 IA alterados es mayoritaria en el NR1 en ambos sexos; en el NR2, en las mujeres destaca la presencia de MetS y en los hombres es el RCV por encima del MetS (p<0,0001).

Conclusiones: Para poder implementar acciones en prevención cardiometabólica y en promoción de la salud en ámbito laboral es de utilidad estimar el nivel de riesgo incluyendo los tres parámetros incluidos en la valoración: presencia de riesgo cardiovascular, síndrome metabólico e indicadores de adiposidad alterados, junto con el IMC.

Palabras clave: obesidad; riesgo cardiovascular; síndrome metabólico; trabajadores sanitarios; salud laboral.

Abstract

Introduction: Abdominal obesity is the most frequently observed component of the metabolic syndrome and is associated with a double risk of developing coronary heart disease and cerebrovascular disease. The aim of this study is to estimate the level of cardiometabolic risk associated with obesity in healthcare professionals in order to be able to act in its prevention, control and coordinated follow-up from occupational health.

Method: Cross-sectional descriptive study in 2,591 Balearic Islands health sector workers. The level of cardiometabolic risk (CR) was calculated by assessing the presence or absence of: metabolic syndrome (MetS), CVR with an elevated score and two or more altered adiposity indicators (AI). These values were independently related to the Body Mass Index (BMI) value.

Results: The level of cardiometabolic risk associated with obesity in healthcare professionals is higher in men, increases with age and increases with BMI (p<0.0001). The presence of ≥2 altered AI is higher in NR1 in both sexes; in NR2, in women the presence of MetS stands out and in men it is the CVR above MetS (p<0.0001).

Conclusions: In order to implement actions in cardiometabolic prevention and health promotion in the workplace, it is useful to estimate the level of risk by including the three parameters included in the assessment: presence of cardiovascular risk, metabolic syndrome and altered adiposity indicators, together with BMI.

Keywords: obesity; cardiovascular risk; metabolic syndrome; healthcare workers; occupational health.

Introducción

Tradicionalmente, el concepto de obesidad va unido al índice de masa corporal (IMC) y se considera que una persona es obesa a partir de un IMC>30 kg/m². En las últimas décadas, la prevalencia mundial de obesidad ha aumentado un 27,5% para adultos y un 47,1% para niños, y es un factor de riesgo para el desarrollo de condiciones comórbidas con repercusión en los costes sanitarios y sociales de ella derivados[1].

El aumento de obesidad en la población afecta tanto a todos los países, independientemente de su renta per cápita. La evidencia epidemiológica relaciona la obesidad con una variedad de condiciones de salud física y psicosocial, que la convierten en un problema de salud pública que afecta gravemente a la salud y a la calidad de vida de las personas, pero que además influye considerablemente en los presupuestos nacionales de salud[2].

Es considerada una enfermedad en cuanto que se trata de una disfunción fisiológica del organismo humano con etiologías ambientales, genéticas y endocrinológicas, con sus propias características incapacitantes, fisiopatologías y repercusiones sistémicas[3].

Independientemente del IMC, la adiposidad total y la acumulación de grasa subcutánea troncal se asocian de forma positiva e independiente con la aterosclerosis y la acumulación central de grasa corporal con la resistencia a la insulina. La obesidad abdominal es el componente observado con mayor frecuencia en el síndrome metabólico y se relaciona con un aumento del doble del riesgo de desarrollar enfermedad coronaria y enfermedad cerebrovascular y un incremento de 1,5 veces en el riesgo de mortalidad por todas las causas[4].

En el medio laboral, a medida que aumenta la prevalencia de la obesidad lo hacen sus consecuencias económicas por absentismo, discapacidad, lesiones y reclamaciones, convirtiéndose en un factor importante de costos en el lugar de trabajo[5]. Estrictamente hablando, la obesidad no es una enfermedad laboral, pero su epidemia global plantea importantes desafíos actuales para los profesionales de la salud ocupacional[6].

El sector sanitario se caracteriza por turnos cambiantes y prolongados, nocturnidad y elevado nivel de estrés; todo ello puede repercutir en la salud y ocasionar alteraciones metabólicas en los profesionales con aumento de riesgo cardiovascular.

Es objetivo de este estudio estimar el nivel de riesgo cardiometabólico asociado a obesidad en profesionales sanitarios para poder actuar en prevención primaria, control y seguimiento coordinado desde las unidades básicas de salud de los servicios de prevención de las empresas. Se valora para ello la presencia de riesgo cardiovascular, síndrome metabólico e indicadores de adiposidad, junto con el índice de masa corporal.

Metodología

Estudio descriptivo transversal en población laboral española del sector sanitario (médicos, enfermeros, auxiliares de clínica, administrativos, celadores y técnicos) de la Comunidad Autónoma de Illes Balears, con muestra de 2.591 trabajadores (615 hombres y 1.976 mujeres), de edades entre 18-66 años. Los datos se recogieron durante los reconocimientos periódicos de vigilancia de la salud de las empresas participantes desde enero 2020 hasta diciembre 2022, con participación voluntaria y consentimiento informado para el uso epidemiológico de los resultados, tal y como recoge la legislación española[7,8].

El estudio fue aprobado por el Comité Ético de Investigación Clínica del Área de Salud de Baleares (IB 4383/20).

El peso y la altura se midieron con báscula SECA 700 y tallímetro SECA 220. El IMC se calculó como el peso en kg dividido por el cuadrado de la altura en metros. Se utilizaron los rangos para IMC considerados por la OMS: Normopeso, si el IMC es de 18,5-24,9; Sobrepeso (no obeso), si el IMC es de 25 a 29,9; Obesidad grado 1 (de bajo riesgo), si el IMC es de 30 a 34,9; Obesidad grado 2 (riesgo moderado), si el IMC es de 35 a 39,9; Obesidad grado 3 (de alto riesgo, obesidad mórbida), si el IMC es igual o mayor a 40; Obesidad grado 4 (obesidad extrema), si el IMC es igual o mayor a 50[5].

El perímetro de cadera y el perímetro de cintura fueron determinados con cinta métrica modelo SECA 20.

La composición corporal se determinó con el analizador TANITABC-420MA, estimando el porcentaje de grasa corporal y grasa visceral.

Como indicadores de adiposidad (IA) se calcularon los siguientes: Perímetro de cintura (PCI): normal en el hombre un valor <94 cm y en la mujer <80 cm. Índice cintura/cadera (ICC): normal en hombres si es <0,94 y en mujeres si es <0,84. Índice cintura/altura (ICA): normal si es <0,5, tanto para hombres como para mujeres. El porcentaje de grasa corporal (GC): normal en hombre si es <10 y en la mujer si es <20. La grasa visceral (GV): normal si es <10 para ambos, hombres y mujeres.

Las variables sociales y laborales incluidas en el estudio han sido:
Edad- rangos: 18-39 años; 40-50 años; 51-66 años. Género: mujer u hombre. Clase social y tipo de trabajo: a partir de la Clasificación Nacional de Ocupaciones

del año 2011 (CNO-11), según propuesta del grupo de determinantes sociales de la Sociedad Española de Epidemiologia[9]. Para el tratamiento estadístico de nuestros datos se ha utilizado la clasificación reducida a tres categorías: Clase I. Directores/gerentes, profesionales universitarios, deportistas y artistas. Clase II. Ocupaciones intermedias y trabajadores por cuenta propia sin asalariados. Clase III. Trabajadores/as no cualificados/as. El tipo de trabajo, según la simplificación de estos mismos autores, se distingue en manual (blue collar) y no-manual (white collar).

Se consideraron pacientes con RCV elevado a los que obtuvieron un riesgo de muerte cardiovascular ≥ 5% en las tablas del método Systematic Coronary Risk Evaluation (SCORE). En este trabajo se ha utilizado la versión aplicable para países de bajo riesgo, que es la recomendada para España (Sanz, Fitzgeral, Royo et al, 2007). Se estima el riesgo a 10 años de que ocurra un evento aterosclerótico mortal (coronario y no coronario). Los puntos de corte que se recomiendan en la literatura científica son (Buitrago, Cañón-Barroso, Díaz-Herrera et al, 2007): *Riesgo bajo:* SCORE < 3%. *Riesgo moderado:* SCORE 4-5%. *Riesgo alto:* SCORE > 5%.

El síndrome metabólico (MetS) se calculó atendiendo a los criterios NCEP-ATP III (Adult Treatment Panel III) del NCEP (National Cholesterol Educational Program)[10], considerando que existe síndrome metabólico cuando están presentes tres o más de los siguientes factores de riesgo: perímetro de cintura >102 cm en hombres o >88 cm en mujeres, triglicéridos séricos ≥150 mg/dL, o estar en tratamiento específico para esta anormalidad lipídica, presión arterial ≥ 130/85 mm Hg o estar recibiendo tratamiento específico con fármacos antihipertensivos, cHDL <40 mg/dL en hombres o <50 mg/dl en mujeres o en tratamiento específico para esta anormalidad lipídica y glucemia en ayunas > 100 mg/dL o estar en tratamiento específico con fármacos antidiabéticos.

El Nivel de Riesgo Cardiometabólico (NR) se calculó valorando la presencia o no de: MetS, RCV elevado y valores anómalos en 2 o más de los indicadores de adiposidad (IA). Estos valores se relacionaron de forma independiente con el valor del IMC clasificado por la OMS con los parámetros anteriormente referidos[11]. La clasificación del NR y las actuaciones preventivas propuestas se muestran en la **tabla I**.

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 y para las cualitativas el porcentaje. Se realizó un análisis de asociación bivariante mediante el test de 2 (con una corrección con el test estadístico exacto de Fisher cuando las condiciones lo requerían) y una prueba t de Student para muestras independientes. El análisis estadístico se realizó con el programa SPSS 27.0, considerando valor $p < 0,05$ estadísticamente significativo.

Resultados

Muestra poblacional de 2.591 sanitarios con mayoría de mujeres (76,3%) y edad media 41 años en ambos sexos. Tanto hombres como mujeres pertenecen mayoritariamente a la clase social I y con trabajo no manual. El IMC en niveles de sobrepeso o de obesidad, grasa visceral, índices cintura/altura y cintura cadera son

Tabla I: Estimación del Nivel de Riesgo Cardiometabólico y Recomendaciones Preventivas en Salud Laboral.

Síndrome Metabólico	Sí No	Puntear la opción correcta	
Riesgo Cardiovascular	Sí No	Puntear la opción correcta	
Indicadores de Adiposidad (>2)	Sí No	Puntear la opción correcta	
Nivel de Riesgo estimado y recomendación preventiva	NR0	No se detecta ninguno de los 3 parámetros valorados (MetS, RCV, >2IA)	Actitud médico laboral: control y seguimiento preventivo
	NR1	Se detecta 1 de los 3 parámetros valorados	Actitud médico laboral: intervención sanitaria asistencial, control y seguimiento. Valorar derivación especializada
	NR2	Se detectan 2 de los 3 parámetros valorados	Actitud médico laboral: intervención sanitaria asistencial, desde medicina del trabajo. Derivación especializada y control y seguimiento coordinado
	NR3	Se detectan los 3 parámetros valorados	Actitud médico laboral: intervención sanitaria asistencial desde medicina del trabajo. Derivación especializada y control y seguimiento coordinado.

Ref: Nivel de Riesgo Cardiometabólico estimado (NR) Modificado de Vicente-Herrero MT et al, 2022.

más elevados en los hombres, mientras que la grasa corporal es más elevada en mujeres. Presión arterial, valores lipídicos y de glucemia más elevados en los hombres (**Tabla II**).

La estimación del NR muestra relación significativa con la edad, aumentando el NR con la edad; y con el sexo, siendo mayor el porcentaje de hombres con NR 2 y 3 que el de las mujeres (p<0,0001) (**Tabla III**).

Tabla II: Características de la muestra. Comparativa Hombres-Mujeres.

Variables analizadas-valores medios		Hombres n 615 Media (dt)	Mujeres n 1.976 Media (dt)	P
Variables antropométricas y de adiposidad (medias)	Edad	41,40 (10,66)	41,02 (10,58)	0,445
	Peso (Kg)	81,22 (14,47)	63,84 (13,40)	<0,0001
	Altura (cm)	175,78 (7,23)	162,47 (6,04)	<0,0001
	IMC	26,27 (4,25)	24,19 (4,95)	<0,0001
	Cintura (cm)	89,68 (12,48)	77,34 (22,29)	<0,0001
	Cintura/altura	0,51 (0,07)	0,48 (0,14)	<0,0001
	Cadera (cm)	101,69 (8,65)	99,38 (10,73)	<0,0001
	Cintura/cadera	0,88 (0,07)	0,78 (0,18)	<0,0001
	Grasa corporal	25,02 (6,40)	33,83 (6,87)	<0,0001
	Grasa visceral	7,45 (2,87)	4,48 (1,95)	<0,0001
Presión arterial	Sistólica (mmHG)	128,32 (13,16)	116,39 (14,15)	<0,0001
	Diastólica (mmHG)	79,91 (10,32)	75,35 (18,14)	<0,0001
Variables analíticas	Colesterol total (mg/dL)	191,88 (36,14)	188,57 (34,74)	0,041
	C-HDL (mg/dL)	48,84 (11,31)	59,18 (12,72)	<0,0001
	C-LDL (mg/dL)	124,52 (57,33)	113,44 (30,62)	<0,0001
	Triglicéridos(mg/dL)	110,14 (71,55)	82,02 (46,36)	<0,0001
	Glucemia(mg/dL)	93,36 (18,32)	88,88 (12,55)	<0,0001
Variables analizadas-valores porcentuales		Hombres %	Mujeres %	P
Clasificación IMC (porcentajes)	Normopeso	45,04	66,35	<0,0001
	Sobrepeso	39,19	23,08	
	Obesidad	15,77	10,57	
Variables sociales y laborales (porcentajes)	Clase social Clase I	63,57	57,64	<0,0001
	Clase II	12,20	13,97	
	Clase III	24,23	28,39	
	Tipo de trabajo Trabajo no manual	75,77	71,61	<0,0001
	Trabajo manual	24,23	28,39	

dt= desviación típica. Se considera significativo p<0,05

Tabla III: Relación porcentual del Nivel Riesgo Cardiometabólico estimado con variables sociodemográficas: edad, sexo, clase social, tipo de trabajo y nivel cultural.

		NR 0	NR1	NR2	NR3	p
Edad	18-39	54,26	38,76	6,98	0,00	<0,0001
	40-50	25,19	55,18	15,93	3,70	
	51-66	51-66	37,03	33,65	14,66	
Sexo	hombre	20,58	39,09	28,48	11,85	<0,0001
	mujer	29,94	49,40	16,47	4,19	
Clase social	I	20,83	58,33	12,50	8,33	0,483
	II	22,52	40,55	26,58	10,36	
	III	25,31	43,76	22,85	8,08	
Tipo de trabajo	manual	25,31	43,76	22,85	8,08	0,582
	no manual	22,36	42,28	25,20	10,16	
Nivel cultural	bajo	19,41	43,35	25,80	11,44	0,015
	medio	27,27	43,27	22,91	6,55	
	alto	31,10	43,29	19,51	6,10	

Nivel de Riesgo Cardiometabólico estimado (NR) Se considera significativo p<0,05

El nivel de riesgo estimado se incrementa según lo hace el IMC, siendo predominante el NR0 en trabajadores con normopeso, el NR1 en relación con sobrepeso y los NR2 y NR3 en obesidad, con relación estadísticamente significativa (p<0,0001). (**Figura 1**).

La distribución porcentual de los parámetros incluidos en la estimación del NR muestra diferencias por sexo, siendo destacable la elevada presencia de 2 o más IA alterados en ambos sexos. En los hombres, encontramos

también mayor porcentaje de RCV elevado. En todos los casos, los valores de los hombres son superiores a los de las mujeres con diferencias significativas (p<0.0001 en MetS y RCV y p=0,001 en IA). (**Figura 2**)

En los parámetros utilizados para la estimación del NR, el primero que muestra valores elevados ya en el NR1 y en ambos sexos es la presencia de ≥2 IA alterados; en el NR2, en las mujeres destaca la presencia de MetS junto con los IA alterados, mientras que en los hombres es el

RCV el predominante después de los IA, por encima del MetS (p<0,0001). (**Figura 3**).

Figura 1: Simulación de los Niveles de Riesgo Cardiometabólico estimados con el Índice de Masa Corporal (IMC).

Clasificación de la obesidad según criterios de la OMS. Nivel de riesgo cardiometabólico estimado (NR) (en base a Vicente-Herrero MT et al, 2022). P<0,0001. Se considera significativo un valor de p<0,05.

Figura 2: Distribución porcentual de los Parámetros incluidos en la valoración del Nivel de Riesgo Cardiometabólico estimado. Diferencias por sexo.
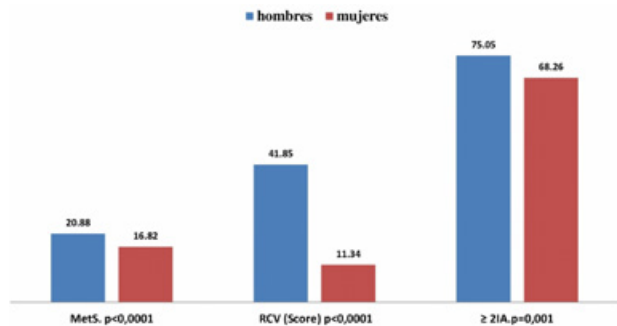
Nivel de riesgo estimado (NR) (en base a Vicente-Herrero MT et al, 2022); MetS=Síndrome Metabólico; RCV=Riesgo Cardiovascular; Parámetros de Obesidad/Indicadores Adiposidad (IA) (Grasa Corporal, Grasa Visceral, Perímetro de Cintura, Índice Cintura/Altura, Índice Cintura/Cadera.) Se considera significativo un valor de p<0,05.

Discusión

En nuestro estudio se aborda la obesidad como una enfermedad con repercusión multiorgánica y multisistema en la que la actuación precoz desde el ámbito laboral puede impedir su aparición o limitar sus consecuencias.

Esta actitud preventiva, basada en la promoción de la salud laboral, ya ha sido recogida en estudios previos sustentados en la repercusión laboral que suponen los cambios crecientes en formas de trabajo cada vez más sedentarias y con poca actividad física, junto con la influencia de los factores psicosociales y de los turnos de trabajo[12]. A esto se une el hecho de que las exposiciones en el lugar de trabajo pueden modificar los efectos de otros factores de riesgo de la obesidad[13]. En todos los casos, en el mundo del trabajo la obesidad implica un incremento estimado en riesgo de lesiones de hasta un 25 % y repercusiones laborales por absentismo, incapacidad o discapacidad en hasta un 50%[14].

Lograr avances desde salud laboral supone partir de actuaciones en promoción de la salud que vayan más allá de las individuales y para las que no hay una actuación de consenso ni una solución fácil, siendo imprescindible ahondar en actividades de investigación desde el lugar de trabajo[15].

Este ha sido el objetivo de nuestro estudio, poniendo el foco en personal sanitario, donde encontramos diferencias en parámetros de obesidad por sexo y edad, con mayor prevalencia de obesidad entre los hombres y con incremento de la obesidad a medida que aumenta la edad. En estudios previos realizados también entre profesionales de la salud, solo el 43% de los sujetos tenía un IMC normal, mientras que el 33,1% se categorizó con sobrepeso y el 21,1% con obesidad.

Figura 3: Relación porcentual del NR estimado con los 3 factores incluidos en la valoración. Diferencias por sexo.
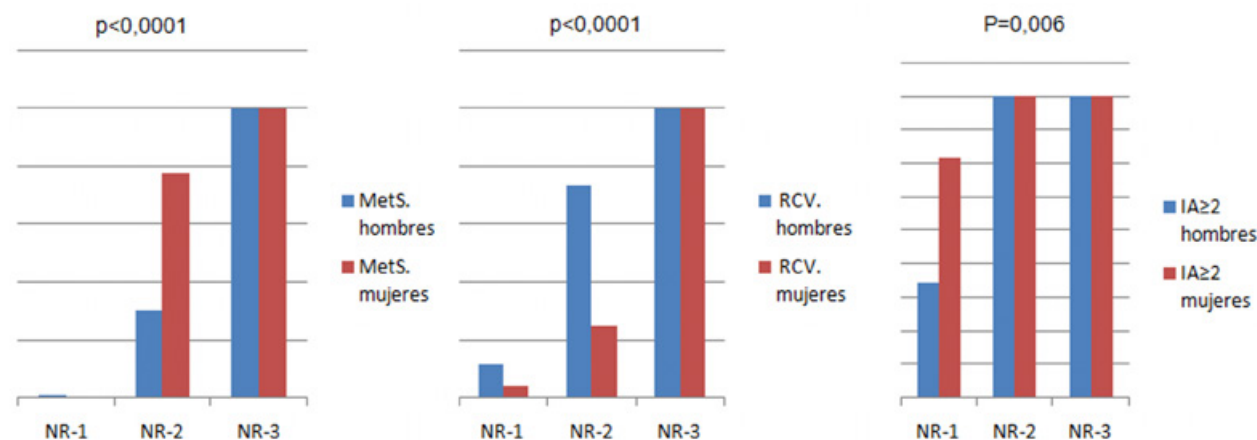
MetS=Síndrome Metabólico; RCV=Riesgo Cardiovascular (Score): Parámetros de Obesidad/Indicadores Adiposidad (IA) (Grasa Corporal, Grasa Visceral, Perímetro de Cintura, Índice Cintura/Altura, Índice Cintura/Cadera.) Nivel de Riesgo estimado (en base a Vicente-Herrero MT etal, 2022). Se considera significativo un valor de p<0,05.

Diferentes categorías de trabajadores de la salud estaban significativamente asociadas con obesidad, y las enfermeras aparentemente tenían un mayor riesgo de ser obesas[16].

En nuestro estudio hemos clasificado a las personas partiendo de la clasificación nacional de ocupación (CNO) y son las incluidas en la clase I y los trabajadores no manuales los que presentan los peores valores: médicos, enfermeros y técnicos. En un estudio realizado en población latina se confirma esta diferencia dentro del sector sanitario, con mayor prevalencia de obesidad entre los hombres: Odds Ratio significativamente mayor (OR 1,56, IC del 95 %: 1,02-2,37) de tener sobrepeso u obesidad[17].

Lo mismo ocurre con los factores de riesgo cardiovascular y metabólico, donde destacan los resultados negativos de los hombres frente a las mujeres y la importancia de las medidas de obesidad central: perímetro de cintura, índice cintura altura, índice cintura cadera, grasa visceral y grasa corporal. Esta valoración del riesgo de obesidad ya ha sido remarcada en el colectivo sanitario y también en población general. En un reciente estudio en población latinoamericana en trabajadores de la salud, la obesidad y la obesidad central estuvieron presentes en el 32,4% y el 58,5% de los participantes, respectivamente. La presión arterial era normal-alta en el 11,8% y se encontró hipertensión de grado 1 en el 7,2%. El 19% de los trabajadores estudiados tenía nivel de RCV distinto de cero (bajo/ moderado o alto); y el 53,9% registró ≥ 3 factores de riesgo. La edad ≥ 38 años y el sexo masculino supusieron riesgo incrementado[18], al igual que hemos obtenido en nuestro trabajo.

Las actuaciones preventivas son importantes en salud laboral para anticiparse al daño o minimizar sus consecuencias y esta es la base del cálculo de nivel de riesgo cardiometabólico asociado a la obesidad. El NR estimado en población sanitaria aumenta según lo hace la obesidad coincidiendo con el cálculo realizado con este mismo método en otros sectores profesionales y muestra su relación con su repercusión sistémica, como ocurre con el riesgo de desarrollar hígado graso no alcohólico[19].

Más que el peso corporal total, la distribución de grasa es un determinante clave en el riesgo de enfermedades cardiovasculares, ya que los factores secretados por el tejido adiposo y el aumento de la inflamación sistémica que se producen en la obesidad impactan perjudicialmente en la salud cardiovascular y metabólica[20]. En nuestro estudio la alteración de los indicadores de adiposidad estudiados es lo más prevalente y de más precoz aparición en ambos sexos (NR1), con diferencias significativas respecto al resto y entre sexos y, por ello sería lo primero que permitiría predecir un aumento del riesgo de complicaciones de cara a iniciar actuaciones

en prevención y promoción de la salud dentro del marco de la salud laboral. Cuando se presentan más factores de riesgo (Nivel de Riesgo 2), destacan, junto con los indicadores de adiposidad, en la mujer la presencia de MetS y en el hombre el RCV elevado.

Aunque se acepta que la presencia de síndrome metabólico por sí sola no puede predecir el riesgo global de enfermedad cardiovascular, la obesidad abdominal, que es la manifestación más prevalente del síndrome metabólico, es un marcador de tejido adiposo disfuncional de gran importancia en el manejo clínico por su relación con trastornos de los lípidos en sangre, inflamación, resistencia a la insulina o diabetes y con un mayor riesgo de desarrollar enfermedades cardiovasculares. Por ello, la comunidad científica busca mejores algoritmos de evaluación de riesgos para cuantificar el riesgo sistémico relacionado con la obesidad y adiposidad[21]. Esta es la intención buscada con este trabajo mediante la estimación del nivel de riesgo cardiometabólico.

Son fortalezas de este estudio el tamaño muestral y las variables recogidas en el estudio que aportan información para la estimación del nivel de riesgo cardiometabólico. Es una debilidad el sesgo de edad en el cálculo de riesgo cardiovascular con SCORE que supone excluir a los menores de 40 años, no poder establecer un comparativo entre los distintos puestos de trabajo y categorías profesionales del sector sanitario y no poder extrapolar los resultados obtenidos.

En un tema como el que aquí se aborda de una enfermedad prevalente y con repercusiones multisistémicas, son necesarias actividades preventivas y correctivas para disminuir los eventos cardiovasculares y las repercusiones metabólicas ligadas a la adiposidad y obesidad en unos profesionales, como los sanitarios, que son clave en la atención a la población y personal de referencia en salud pública. Actualmente, la formación, la práctica profesional y la investigación en salud ocupacional evolucionan hacia un modelo de salud más holístico y orientado a la salud pública. Esto requerirá la participación de una amplia red de partes interesadas con alineación en investigación y capacitación con las realidades actuales del trabajo y la salud preparando a los profesionales para la variedad cambiante de desafíos en salud ocupacional[22].

En países de nuestro entorno, como el Reino Unido, una revisión encargada por el Departamento de Salud sobre intervenciones para conseguir un entorno laboral saludable para el personal sanitario se apoyaron en las reseñas de Boorman, recomendando cinco cambios en el sistema: identificación y respuesta a las necesidades, compromiso del personal en todos los niveles, participación, liderazgo visible desde y hacia arriba, apoyo a la salud y al bienestar de las personas por el personal directivo y un enfoque de

gestión competente con capacidad para mejorar tanto la salud como el bienestar de las personas que trabajan cuidando a otros[23].

Consideramos, por ello, que la mejor medida de cuidar es evitar el daño, si es posible anticipándonos a él. Esta estimación del Nivel de Riesgo por obesidad y basado en la adiposidad puede ser de ayuda y serán los estudios prospectivos futuros los que lo reafirmen o complementen si es necesario.

Conclusiones

El nivel de riesgo cardiometabólico asociado a la obesidad en profesionales sanitarios guarda relación directa con el índice de masa corporal, es más elevado en los hombres y aumenta con la edad en ambos sexos. Los indicadores de adiposidad son los factores que más influyen en la estimación del riesgo y los que se alteran más precozmente. El síndrome metabólico es de aparición más temprana en mujeres y el riesgo cardiovascular en hombres.

Para poder actuar en prevención, control y seguimiento coordinado de la obesidad y sus repercusiones en ámbito laboral es de utilidad estimar el nivel de riesgo cardiometabólico incluyendo los tres parámetros valorados en este trabajo: presencia de riesgo cardiovascular, síndrome metabólico e indicadores de adiposidad alterados, junto con el índice de masa corporal.

Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses.

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ORIGINAL

Análisis de los ingresos procedentes de una Unidad de Diagnóstico Rápido en un hospital de segundo nivel

Analysis of hospitalization from a quick diagnosis unit in a second-level hospital

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Resumen

Objetivo: Definir las características de los pacientes en evaluación activa en una Unidad de Diagnóstico Rápido (UDR) que son ingresados en planta, sus diferencias con el resto de pacientes que continúan de forma ambulatoria hasta completarse el proceso diagnóstico, e intentar establecer factores predictores de ingreso.

Métodos: Estudio retrospectivo de los pacientes atendidos en la UDR de Palencia entre 2008 y 2020, centrado en los que requirieron ingreso hospitalario durante el cual se completó el proceso diagnóstico.

Resultados: De 9090 pacientes, 393 (4.3%) ingresaron; de éstos, el 34.4% lo hizo desde la UDR y el 65.6% desde urgencias. Los ingresos decrecieron con el tiempo. El 18.1% falleció. Ingresaron más los varones (61.3%), los derivados desde Atención Primaria (57.3%) y aquellos con diagnóstico final de neoplasia (47.1%; sólo el 17.1% en los no ingresados). Las principales causas de ingreso fueron: dolor (16.8%), disnea (14%), realización de pruebas (13%) y alteraciones analíticas graves (10.7%). Únicamente 214 pacientes (54.4%) ingresados no necesitaron oxigenoterapia, cirugía, UVI ni fallecieron.

Conclusiones: Aunque mayoritariamente son procedentes, la tasa de hospitalizaciones evitables puede reducirse reescribiendo los criterios de derivación para adecuarlos a las necesidades de cada hospital, fortaleciendo canales de comunicación con urgencias y atención primaria, implicando a otros servicios en la reducción de demoras excesivas en las pruebas diagnósticas, creando hospitales de día asociados, y atendiendo más estrechamente a los varones de edad avanzada con pérdida de peso, astenia o ictericia, y paliando de forma intensiva algunos síntomas para poder mantener el estudio ambulatorio.

Palabras clave: Unidad de diagnóstico rápido, ingreso evitable, alternativa a ingreso hospitalario.

Abstract

Objective: To define the characteristics of patients under active evaluation in a Quick Diagnostic Unit (QDU) who are admitted to the hospital, their differences with the rest of the patients who continue as outpatients until the diagnostic process is completed, and to try to establish predictors of admission.

Methods: Retrospective study of patients seen in the QDU of Palencia between 2008 and 2020, focusing on those who required hospital admission during which the diagnostic process was completed.

Results: Out of 9090 patients, 393 (4.3%) were admitted; of these, 34.4% were admitted from the QDU and 65.6% from the Emergency Department. Admissions decreased over time. 18.1% died. Admission was more frequent in males (61.3%), those referred from Primary Care (57.3%) and those with a final diagnosis of neoplasia (47.1%; only 17.1% in those not admitted). The main causes of admission were: pain (16.8%), dyspnea (14%), tests (13%) and serious analytical alterations (10.7%). Only 214 patients (54.4%) admitted did not require oxygen therapy, surgery, ICU or death.

Conclusions: Although the majority of these hospitalizations are appropriate, the rate of avoidable hospitalizations can be reduced by rewriting referral criteria to suit the needs of each hospital, strengthening communication channels with Emergency Department and Primary Care, involving other services in reducing excessive delays in diagnostic tests, creating associated day centers, and attending more closely to elderly men with weight loss, asthenia or jaundice, and intensively palliating some symptoms in order to maintain the outpatient study.

Keywords: Quick diagnosis unit; Avoidable hospital admission; Hospital admission alternative.

Introducción

En los años 90 del pasado siglo en varios países europeos se evidenció una alarmante carencia de camas de hospitalización para pacientes agudos, en gran medida causada por una necesaria limitación en los recursos económicos destinados a financiar los sistemas sanitarios públicos. Esto llevó a la búsqueda de diversas alternativas a la hospitalización convencional, entre las que se incluyeron los hospitales de día, las unidades de corta estancia, la hospitalización a domicilio y las unidades de diagnóstico rápido (UDR)[1]. Las bases para el desarrollo de las UDR se establecieron en el Queen Elisabeth Hospital, de Birmingham (Reino Unido), donde se definió el concepto "Quick and early diagnosis"[2].

Varios hospitales en Cataluña tomaron el relevo muy poco después, creando las primeras UDR a cargo de un servicio de Medicina Interna (MI)[3-5]. El modelo, aunque ha sido adaptado a cada centro en el que se ha implantado, se fundamenta en unas premisas comunes: unos criterios pre-definidos de derivación, la posibilidad física y socio-familiar para que el proceso sea ambulatorio, la aceptación del paciente y su familia, inmediatez entre la derivación y la primera visita a la UDR, el acceso preferente a las pruebas diagnósticas complementarias, y la restricción de la atención a los pacientes con sospecha de enfermedad severa[6]. El objetivo de las UDR es el de lograr el diagnóstico de estos pacientes en el menor tiempo posible, contribuyendo en gran medida a un menor impacto emocional, a una reducción en la iatrogenia propia de la hospitalización, y a un mayor acercamiento entre atención primaria y especializada[7]. Además, contribuye a liberar camas de hospitalización de agudos, con costes por proceso muy inferiores a los de la hospitalización, y manteniendo un grado de satisfacción muy elevado en el paciente; de hecho, la mayoría de los usuarios de una UDR, en caso de precisar otro proceso diagnóstico, elegirían este sistema antes que el ingreso[3,5,8].

En noviembre de 2008 se instituyó la UDR del Complejo Asistencial Universitario de Palencia (CAUPA). Desde su inicio ha atendido a más de 9000 pacientes. Sin embargo, no en todos los casos el comienzo del estudio en la UDR ha conseguido evitar la hospitalización antes de completarse. Esta observación se constata de forma similar en todas las series publicadas[3,4,9]. Aunque estos ingresos suponen un teórico fracaso en el propósito primordial de las UDR, su análisis puede aportar conocimiento para optimizar el funcionamiento de las mismas. El objetivo fundamental de nuestro estudio es el de definir las características de los pacientes en evaluación activa en la UDR del CAUPA que son ingresados en planta (PI), sus diferencias con el resto de pacientes que continúan de forma ambulatoria hasta completarse el proceso diagnóstico (PA), e intentar establecer factores predictores de ingreso. El análisis de los ingresos potencialmente evitables y de los obligados por una inadecuada derivación a la UDR, nos permitirá proponer un plan de mejora redefiniendo los criterios de derivación, y adecuando los canales de comunicación al servicio de urgencias hospitalarias y a los centros de salud de Atención Primaria.

Material y métodos

Estudio

Estudio retrospectivo de los pacientes atendidos en la UDR del CAUPA desde el inicio de su funcionamiento en noviembre de 2008 hasta el 31 de diciembre de 2020, centrado en los que requirieron ingreso hospitalario durante el cual se completó el proceso diagnóstico. El CAUPA, con 495 camas, atiende a la totalidad de la población de la provincia de Palencia, de unos 160.000 habitantes en el año 2020, y la UDR está habilitada para todos los mayores de 13 años. Los datos se obtuvieron a partir de la base de datos que se cumplimenta prospectivamente, en la que se registran características demográficas y clínicas de todos los pacientes estudiados. En los casos necesarios, se rellenaron los datos incompletos a partir de las historias clínicas. El estudio fue aprobado por el Comité de Ética de la Investigación del Área de Salud de Palencia, y respeta la legislación vigente para estudios observacionales.

Variables

Para cada paciente se registraron de forma prospectiva las siguientes variables: edad, sexo, origen de la derivación, vía de petición (telefónica, correo electrónico, verbal, fax), motivo de consulta, fecha de la 1ª consulta, intervalo hasta la 1ª consulta, intervalo diagnóstico, diagnósticos principal y secundarios, adecuación a la unidad, destino final y necesidad de ingreso durante el proceso diagnóstico. Se consideró intervalo hasta la 1ª consulta el existente desde la comunicación a la UDR de la solicitud de cita por parte del servicio peticionario hasta que ésta tuvo lugar (en días naturales). Se consideró intervalo diagnóstico el existente entre la 1ª consulta y la obtención del diagnóstico definitivo y la indicación de la conducta a seguir (alta en la Unidad y seguimiento por el médico de atención primaria, citación en la consulta de la especialidad correspondiente, ingreso hospitalario, etc)[10]. Se consideró una derivación adecuada si ésta se ceñía a uno de los criterios de derivación previamente definidos, el paciente estaba en condiciones físicas, psicológicas y de apoyo socio-familiar para poder realizar un estudio ambulatorio, y la gravedad del estado del paciente ni obligaba a su hospitalización inmediata, ni era lo suficientemente leve como para permitir un estudio por medio de otros recursos convencionales.

Además, en los PI se registraron las siguientes variables: localidad de residencia, institucionalización previa a la 1ª cita en la UDR, consultas previas en Psiquiatría, cifras

de hemoglobina, de filtrado glomerular y de proteína C reactiva en la 1ª visita en la UDR, fecha de ingreso y de alta en el hospital, procedencia del ingreso (urgencias/ UDR), servicio de ingreso y de alta, causa principal del ingreso, necesidad de oxigenoterapia, de cirugía y de cuidados intensivos durante el ingreso, fallecimiento en el ingreso y Grupo Relacionado por el Diagnóstico (GRD) al alta hospitalaria.

No se consideró ingreso la estancia de menos de 12 horas en un hospital de día o similar para la realización de determinadas pruebas intervencionistas.

Análisis estadístico

Para comparar variables categóricas se empleó el test Chi-cuadrado o el test exacto de Fisher en caso necesario, y los resultados se expresaron en frecuencias absolutas (%). Para las variables cuantitativas se calcularon la media y desviación standard (DE), o bien la mediana y percentiles 25% y 75% (RIC) si no cumplían la asunción de normalidad según la prueba de Kolmogorov-Smirnov; y la comparación de medias se realizó mediante la T de Student para muestras independientes en caso de distribución normal, o mediante la prueba no paramétrica de U de Mann-Whitney en caso de distribución no normal. Se estableció un nivel de significación estadística de $p=0.05$. Así mismo, se empleó el coeficiente de correlación de Spearman para estudiar la asociación entre dos variables cuantitativas no paramétricas. Para el análisis estadístico se utilizó el paquete SPSS 22.0.0.0

Resultados

Fueron atendidos 9090 pacientes, de los que 393 (4.3%) debieron ingresar antes de completar el estudio, ocasionando un total de 5275 días de estancia hospitalaria [mediana por paciente 10 (6-17) días]. De ellos, 388 (98.7%) ingresaron en el CAUPA y 5 (1.3%) en otras provincias. La **figura 1** recoge la evolución anual de los ingresos. Del total de hospitalizaciones, 220 (56%) se realizaron en el servicio de MI, 68 (17.3%) en Digestivo, 33 (8.4%) en Neumología, 22 (5.6%) en Cirugía general, 16 (4.1%) en Neurología y los 34 (8.6%) restantes en otros servicios.

En la **tabla I** se detallan las diferencias entre los PA y los PI. Los principales motivos de derivación a la UDR en ambos grupos (ambulatorio / ingresado) fueron: afectación intensa del estado general (20.6% / 36.1%), anemia (10.4% / 7.9%), abdominalgia (8% / 7.1%), adenopatías persistentes (7.6% / 1.3%), ictericia e hipertransaminasemia (5.2% / 6.9%) y fiebre prolongada sin foco (5% / 4.8%). Dentro del grupo PA, los tumores más frecuentemente diagnosticados fueron los de colon (21.3% de todas las neoplasias de este grupo), los de riñón y vías urinarias (15.3%), los hematológicos (12.8%), los de pulmón (11.4%), los de esófago y estómago (8.5%) y los de páncreas (6.9).

Figura 1: Evolución anual de los pacientes atendidos en la UDR y de los ingresos procedentes de la misma.
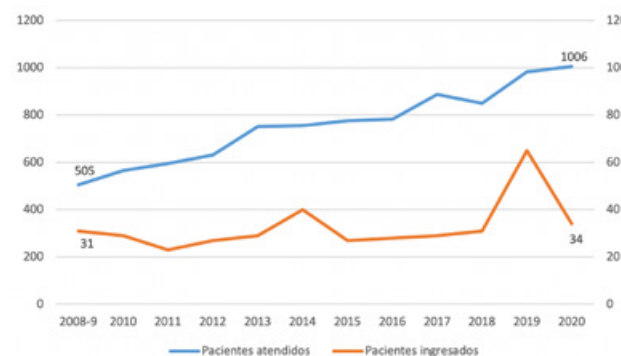
Tabla I

	PA	PI	p
Pacientes	8697 (95.7%)	393 (4.3%)	
Edad (años)[a]	64 (48-77)	74 (63-82)	<0.05

Sexo:
  H
  M
	
	4266 (49.1%)
	4431 (50.9%)
		
		241 (61.3%)
		152 (38.7%)
			<0.05

Origen de derivación:
  Atención Primaria
  Atención Especializada
  Urgencias
  Otros
	
	4622 (53.1%)
	2053 (23.6%)
	1967 (22.6%)
	55 (0.6%)
		
		226 (57.5%)
		56 (14.2%)
		109 (27.7%)
		2 (0.5%)
			<0.05

Vía petición:
  Teléfono
  Correo electrónico
  Interconsulta escrita
  Verbal
	
	5655 (65%)
	1182 (13.6%)
	932 (10.7%)
	928 (10.7%)
		
		274 (69.7%)
		70 (17.8%)
		27 (6.9%)
		22 (5.6%)
			<0.05

Demora 1ª visita (días)[a]	1 (1-3)	1 (1-3)	0.13
Demora diagnóstica (días)[a]	14 (6-27)	11 (5-20)	<0.05
Correcta adecuación en la derivación	6686 (76.9%)	332 (84.5%)	<0.05
Neoplasia	1487 (17.1%)	185 (47.1%)	<0.05

[a]Mediana (RIC). PA: Pacientes que continuaron el estudio de forma ambulatoria hasta el final. PI: Pacientes que debieron ingresar antes de finalizar el estudio.

Tabla II

	Total PI	Ingresos desde UDR	Ingresos desde urgencias	p
Nº de pacientes	393	135 (34.4%)	258 (65.6%)	
Edad (años)[a]	74 (63-82)	73 (60-81)	76 (65-82)	0.53

Sexo
  H
  M
	
	241 (61.3%)
	152 (38.7%)
		
		83 (61.5%)
		52 (38.5%)
			
			158 (61.2%)
			100 (38.8%)
				0.96

Demora 1ª visita[a]	1 (1-3)	1 (1-2)	1 (1-3)	0.57

Origen de la 1ª consulta:
  Atención Primaria
  Urgencias
  Atención Especializada
  Otros
	
	226 (57.5%)
	109 (27.7%)
	56 (14.2%)
	2 (0.5)
		
		72 (53.3%)
		40 (29.6%)
		22 (16.3%)
		1 (0.7%)
			
			154 (59.7%)
			69 (26.7%)
			34 (13.2%)
			1 (0.4%)
				0.63

Vía de petición de la consulta:
  Teléfono
  Correo electrónico
  Consulta escrita
  Verbal
	
	274 (69.7%)
	70 (17.8%)
	27 (6.9%)
	22 (5.6%)
		
		91 (67.4%)
		24 (17.8%)
		11 (8.1%)
		9 (6.7%)
			
			183 (70.9%)
			46 (17.8%)
			16 (6.2%)
			13 (5%)
				0.78

Correcta adecuación en la derivación	332 (84.5%)	102 (76.3%)	229 (88.8%)	<0.05
Demora diagnóstica[a]	11 (5-20)	8 (3-18)	13 (6-21)	<0.05
Días entre la 1ª visita y el ingreso[a]	6 (2-13.5)	4 (0-12)	7 (3.75-14)	<0.05
Días de ingreso[a]	10 (6-17)	11 (7-17)	10 (5-17)	0.33
Neoplasia	185 (47.1%)	62 (45.9%)	123 (47.7%)	0.74
O_2 durante el ingreso[b]	118 (30%)	31 (23%)	87 (33.7%)	0.05
Cirugía durante el ingreso	62 (15.8%)	22 (16.3%)	40 (15.5%)	0.83
UCI durante el ingreso[c]	24 (6.1%)	3 (2.2%)	21 (8.1%)	0.05
Exitus durante el ingreso	71 (18.1%)	10 (7.4%)	61 (23.6%)	0.05

Tipo de población:
  Rural
  Semiurbana
  Urbana
	
	141 (35.9%)
	87 (22.1%)
	165 (42%)
		
		54 (40%)
		24 (17.8%)
		57 (42.2%)
			
			87 (33.7%)
			63 (24.4%)
			108 (41.9%)
				0.25

Distancia domicilio-hospital[a,d]	12 (0-50)	14 (0-50)	11 (0-50)	0.74
Institucionalizado al ingreso	34 (8.7%)	9 (6.7%)	25 (9.7%)	0.31
Consulta previa en psiquiatría	55 (14%)	20 (14.8%)	35 (13.6%)	0.73
Hemoglobina 1ª visita[a,e]	13.1 (11.2-14.5)	13.1 (11.1-14.5)	13.1 (11.2-14.3)	0.82
Filtrado glomerular 1ª visita[a,f]	60 (53-86)	65 (55-90)	60 (51-83.7)	0.11
PCR 1ª visita[a,g]	53 (5-128)	61.5 (7-130)	47 (4-126)	0.88
La causa de ingreso existía en la 1ª visita	246 (62.6%)	117 (86.7%)	129 (50%)	<0.05

PI: Pacientes que debieron ingresar antes de finalizar el estudio. [a]Mediana (RIC). [b]2 valores perdidos. [c]1 valor perdido. [d]En kilómetros. [e]En gramos/decilitro. [f]En mililitro/minuto /1,73m². [g]Proteína C Reactiva; en miligramos/litro.

Tabla III

	Total PI	Ingresos desde UDR	Ingresos desde urgencias	La causa existía en la 1ª visita	Mortalidad
Dolor	66 (16.8%)	15 (11.1%)	51 (19.8%)	80.3%	13.6%
Disnea	55 (14%)	14 (10.4%)	41 (15.9%)	43.6%	25.5%
Realización de pruebas	51 (13%)	47 (34.8%)	4 (1.6%)		3.9%
AAPM[a]	42 (10.7%)	21 (15.6%)	21 (8.1%)	59.5%	26.2%[a]
Fiebre	38 (9.7%)	7 (5.2%)	31 (12%)	52.6%	7.9%
Cansancio	32 (8.1%)	11 (8.1%)	21 (8.1%)	93.8%	34.4%
Vómitos o disfagia	25 (6.4%)	3 (2.2%)	22 (8.5%)	64%	20%
Diarrea	13 (3.3%)	4 (3%)	9 (3.5%)	76.9%	15.4%
Otros	71 (18.1%)	13 (9.6%)	58 (22.5%)		

PI: Pacientes que debieron ingresar antes de finalizar el estudio. [a]Alteraciones analíticas potencialmente mortales.

Sin embargo, dentro del grupo PI los más frecuentes fueron los de pulmón (18.3%), los de esófago y estomago (13.5%), los hematológicos (12.9%), los de colon (10.8%), los de riñón y vías urinarias (10.2%) y las carcinomatosis de origen desconocido (10.2%).

La **tabla II** describe las características fundamentales de los pacientes que debieron ingresar y las diferencias observadas entre los pacientes ingresados por indicación de la UDR y los ingresados desde Urgencias o desde otras especialidades. En la **tabla III** se cuantifican los

motivos de ingreso. De los hospitalizados cuya causa de ingreso ya estaba presente en la primera visita, el 13% (32 pacientes) fallecieron, frente al 26.5% (39 pacientes) entre aquellos cuya causa de ingreso apareció con posterioridad. La mortalidad también fue mayor en varones respecto a mujeres (19.9% / 15.1%), aunque en este caso las diferencias no fueron estadísticamente significativas. La edad de los fallecidos fue de 80 (72-84) años, y la de los supervivientes de 72.5 (60.7-81) años (p<0.05). Cabe destacar que únicamente 214 pacientes (54.4%) ingresados no necesitaron oxigenoterapia, cirugía, UVI ni fallecieron.

La mediana desde la 1ª visita hasta el ingreso fue de 6 (2-13.5) días, aunque esta cifra fue de sólo 3 (0-9) días en los casos de inadecuación en la derivación, y de 5 (1-11) días en los casos en los que la causa del ingreso ya estaba presente en la 1ª visita; sin embargo, ascendió a 10 (5.75-25) en caso de pacientes institucionalizados. La mediana de días de ingreso fue de 10 (6-17), llegando hasta los 18 (9.75-28.25) días en los casos de necesidad de cirugía. No se demostró correlación significativa entre los días desde la 1ª visita hasta el ingreso por una parte y el tiempo de ingreso (r-0.037), la distancia desde la población de residencia del paciente y el hospital (r 0.121) ni la edad (r-0.035) por otra. Tampoco entre la estancia hospitalaria por una parte y la edad (r 0.024) ni la distancia desde la residencia al hospital (r-0.038) por otra.

Entre los motivos de derivación de los pacientes de ambos subgrupos (ingresados desde la UDR / desde Urgencias), los más frecuentes fueron la afectación importante del estado general (36.3% de los ingresos en este grupo / 36%), la anemia (5.9% / 8.9%), la abdominalgia (5.9% / 7.8%), y la ictericia e hipertransaminasemia (5.2% / 7.8%). Desde la UDR los pacientes ingresaron más frecuentemente en MI (60.7%), Neumología (14.1%) y Digestivo (9.6%); y desde urgencias, en MI (53.5%), Digestivo (21.3%) y Cirugía general (7.8%). Además, destacamos que en el grupo de pacientes ingresados directamente desde la UDR el 63.7% no precisaron oxigenoterapia, cirugía, cuidados intensivos ni fallecieron; este porcentaje descendió al 49.6% en el grupo de pacientes ingresados desde urgencias.

Discusión

Uno de los problemas que dificultan la comparación de la actividad entre las diferentes UDR es la ausencia de una concepción estandarizada de la variable "ingreso". En algunos estudios se cuantifican los ingresos únicamente como las hospitalizaciones tras la finalización del proceso diagnóstico, mientras que otros se limitan a considerar los ocasionados en un servicio determinado, por una patología concreta o en un grupo seleccionado de pacientes; y habitualmente no se registra la causa ni origen del ingreso[3,4,9]. Teniendo en cuenta la finalidad

de la UDR, hemos considerado como ingreso aquel que sustituye a la misma, es decir, el que tiene lugar antes de que termine el proceso diagnostico ambulatorio, y durante el cual se completa este.

Si bien el porcentaje de ingresos es similar al descrito por otras UDR, a lo largo de los años hemos evidenciado una reducción en el mismo. Este hecho ya había sido constatado con anterioridad, y se explica esencialmente por el cambio en la concepción de la función de la hospitalización[9,11]. La existencia de este recurso permite evitar los ingresos para adelantar o realizar pruebas, lo que había considerado como la principal causa de una hospitalización inadecuada[12-14]. Sin embargo, el cambio en la tendencia suele ser gradual, y precisa de una confianza progresiva en esta alternativa ambulatoria por parte de usuarios y facultativos de los distintos niveles asistenciales. Nuestra experiencia demuestra que con el tiempo incluso se consigue revertir la predisposición a la hospitalización para el diagnóstico de pacientes con pobre calidad de vida, y de los ancianos con incapacidad funcional o con comorbilidades severas, dos grupos poblacionales en los que el estudio ambulatorio se limitaba notablemente. Tampoco la distancia desde el domicilio hasta el centro hospitalario ha obstaculizado la atención de los pacientes en la UDR. La especial geografía del área de salud de Palencia, con localidades separadas más de 120 kilómetros del CAUPA, nunca ha sido impedimento para el desplazamiento de los usuarios.

Comprobamos en nuestro estudio una mayor probabilidad de ingreso entre los pacientes derivados por alteración del estado general, hecho también señalado por otros autores[9]. Síntomas o signos más precisos, a excepción de la ictericia e hipertransaminasemia, habitualmente permiten el estudio ambulatorio. También ingresan más los pacientes de mayor edad, varones, derivados desde Atención Primaria y urgencias y aquellos con diagnóstico final de neoplasia, sobre todo de pulmón y aparato digestivo superior, probablemente porque sus síntomas evolucionan más rápidamente y limitan más la calidad de vida. Uno de los escasos trabajos que han analizado los factores asociados al ingreso en los pacientes procedentes de la UDR acreditó entre los mismos la edad avanzada, un alto índice de comorbilidad y el hecho de ser soltero y vivir sólo[15]. Este exhaustivo trabajo, aunque circunscrito a los pacientes con anemia, pretende ayudar en la selección y orientar desde el inicio hacia un estudio ambulatorio u hospitalizado, y propone que el conocimiento de los factores asociados al ingreso podría ayudar a definir más precisamente la sistematización y manejo de estos pacientes en urgencias.

Queremos destacar dos evidencias referentes al origen de las derivaciones. Las realizadas a la UDR desde Atención Especializada, que habitualmente requieren comunicación verbal directa y una aceptación previa, conllevan un bajo riesgo de ingreso. Sin embargo, un

gran porcentaje de pacientes ingresados desde la UDR habían sido remitidos a la misma desde Urgencias; en estos casos las citas se aceptan de forma automática tras el envío de un correo electrónico, y en ellas se comprueba una elevada tasa de incorrecta adecuación a la UDR, y de presencia de la causa de ingreso ya en la primera visita, por lo que deben ingresar precozmente. En nuestra opinión, la comunicación previa puede evitar riesgos para el paciente, demoras diagnósticas y estancias duplicadas en los servicios de urgencias.

Por otra parte, los ingresos para la realización de pruebas fueron más frecuentes desde la UDR que desde urgencias, aunque con una tendencia descendente a lo largo de los años, durante los cuales se habilitaron opciones alternativas como un hospital de día para estancias breves tras la ejecución de biopsias profundas o para realizar paracetesis, toracocentesis o punciones lumbares, por ejemplo.

Otro dato reseñable que diferencia los ingresos desde la UDR y desde urgencias es que en estos últimos la necesidad de estancia en UCI y de oxigenoterapia, y la mortalidad, fueron mayores, así como el porcentaje de ingresos por causas no presentes en la 1ª consulta. Estos datos confirman observaciones previas que afirman que muchos pacientes en estudio en la UDR se inestabilizan durante el mismo y finalmente son hospitalizados[11]. No debemos olvidar que la UDR es una alternativa a la hospitalización convencional, y no una consulta tradicional. De hecho, la mortalidad global de los ingresos procedentes de la UDR es muy superior a la del resto de pacientes hospitalizados en el servicio de MI del CAUPA.

Por tanto, queremos concluir que en nuestra experiencia la UDR evita una gran cantidad de ingresos, y aquellos que finalmente se realizan no pueden considerarse como fracasos de la unidad. Aunque mayoritariamente son procedentes, la tasa de hospitalizaciones evitables puede reducirse aún más con la implementación de varias medidas. Por una parte, reescribiendo los criterios de derivación para adecuarlos a las necesidades particulares de cada hospital, y fortaleciendo los canales de comunicación con los servicios de urgencias y con atención primaria, evitando así derivaciones inadecuadas que ocasionan ingresos directos desde la UDR. Por otra, implicando a otros servicios e incluso a la dirección del centro en la búsqueda de soluciones para las demoras excesivas en la realización de pruebas diagnósticas, que aumentan el riesgo de inestabilizaciones e ingresos desde urgencias. Además, proveyendo de mecanismos como los hospitales de día asociados, para evitar estancias hospitalarias para la realización de técnicas diagnósticas. Y finalmente, atendiendo más estrechamente a los varones de edad avanzada con pérdida de peso, astenia o ictericia, y paliando de forma intensiva el dolor o la anemia para poder mantener el estudio ambulatorio.

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Could the percutaneous intracorporeal ring suturing method be the primary surgical option for the treatment of Morgagni hernia in children?

¿Podría el método de sutura intracorpórea percutánea en anillo ser la primera opción quirúrgica para el tratamiento de la hernia de Morgagni en niños?

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Abstract

Objective: This study presents our clinic's experience with using the percutaneous internal ring suturing (PIRS) technique during laparoscopic Morgagni hernia repair.

Materials and methods: The files of 23 cases operated in our clinic between 2012-2021 were evaluated retrospectively.

Results: Ages of 23 patients ranged from 1 month to 60 months (median 36 months). Nine were female and 14 were male. All cases were prediagnosed by chest X-ray, and at least one of the contrast-enhanced passage X-rays and abdominal tomography were taken before the surgery decision. Six cases were asymptomatic, 6 cases had intestinal obstruction, 11 cases had pulmonary symptoms. There were right hernias in 13 cases, left hernias in 5 cases, and bilateral hernias in 5 cases. All cases were operated on with the laparoscopic PIRS method. The diameters of the hernia defect ranged from 5 to 16 cm. The sac was completely removed in all cases. Median discharge was 4 days. The median follow-up period was 13 months. There was no mortality, morbidity, or conversion to open surgery. Late recurrence was not observed.

Conclusions: Laparoscopic PIRS method is an easily applicable, effective, and safe alternative surgical method for Morgagni hernia repair in children.

Keywords: Children, Morgagni Hernia, Laparoscopy.

Resumen

Objetivo: Este estudio presenta la experiencia de nuestra clínica con uso de técnica de sutura percutánea en anillo interno (PIRS) durante la reparación laparoscópica de la hernia de Morgagni.

Materiales y métodos: Se evaluaron retrospectivamente los expedientes de 23 casos operados en nuestra clínica entre 2012-2021.

Resultados: Edades de 23 pacientes oscilaron entre 1 mes-60 meses. Nueve eran mujeres y 14 eran hombres. Todos los casos fueron prediagnosticados mediante radiografía de tórax, y al menos una de las radiografías de pasaje con contraste y tomografía abdominal se tomaron antes de la decisión quirúrgica. Seis casos estaban asintomáticos, 6 casos tenían obstrucción intestinal, 11 casos tenían síntomas pulmonares. Hubo hernias derechas en 13 casos, hernias izquierdas en 5 casos y hernias bilaterales en 5 casos. Todos los casos fueron operados con el método laparoscópico PIRS. Diámetros del defecto herniario oscilaron entre 5-16 cm. Saco se eliminó por completo en todos los casos. Mediana de alta fue de 4 días. Mediana del período de seguimiento fue de 13 meses. No hubo mortalidad, morbilidad ni conversión a cirugía abierta.

Conclusiones: Método laparoscópico PIRS es un método quirúrgico alternativo de fácil aplicación, efectivo y seguro para reparación de la hernia de Morgagni en niños.

Palabras clave: Niños, Hernia de Morgagni, Laparoscopia.

Introduction

Morgagni hernia (MH) is an anterior retrosternal diaphragmatic hernia originally identified by Morgagni in 1769. The estimated incidence is 1/2000-5000 births. However, the true incidence rate remains unknown[1]. A Morgagni hernia is located posterolaterally to the sternum and is caused by a failure of the pars tendinalis part of the costochondral arches to fuse with the pars sternalis[2-4]. Failure of fusion on the right side is a Morgagni hernia, while a failure of fusion on the left is often called a Larrey hernia. Although left-sided and bilateral hernias occur, 90% of Morgagni hernias occur on the right side due to the pericardial attachments to the diaphragm that provide protection and support to the left side[5,6]. The defects originally are small, with over 90% of defects having a hernia sac, however, can grow over time due to increases in intra-abdominal pressure, causing weakness of the diaphragm. While open surgery is still considered the traditional approach for treatment, laparoscopic methods have become increasingly popular in recent years. Although the laparoscopic PIRS method is traditionally defined as an inguinal hernia repair technique in children, it has started to be used in Morgagni hernia repair. In this study, the experience of repair with PIRS method, which is a laparoscopic method in the repair of Morgagni hernia, is presented.

Materials and methods

The case files of 23 cases operated in our clinic between 2012-2021 were evaluated retrospectively. Age, gender, symptoms, diagnostic methods, additional anomalies, surgical findings, and postoperative follow-up information of the patients were evaluated (**Table I**). All cases were operated by the same surgeon. The findings were analyzed using the descriptive statistical method.

All cases were prediagnosed by chest X-ray (**Figure 1**), and at least one of the contrast-enhanced passage X-rays and abdominal tomography (**Figure 2**) were taken before the surgery decision.

Surgical technique: Under general anesthesia, while the patient was in the supine position with proper covering, the abdomen was inflated by insufflation from the umbilicus with the Hasson technique through a 10 mm trocar (10 mm pressure, flow rate at 0.5 lt/min). Two working trocars of 5mm were inserted from

Figura 1: Preoperative computed tomography view.
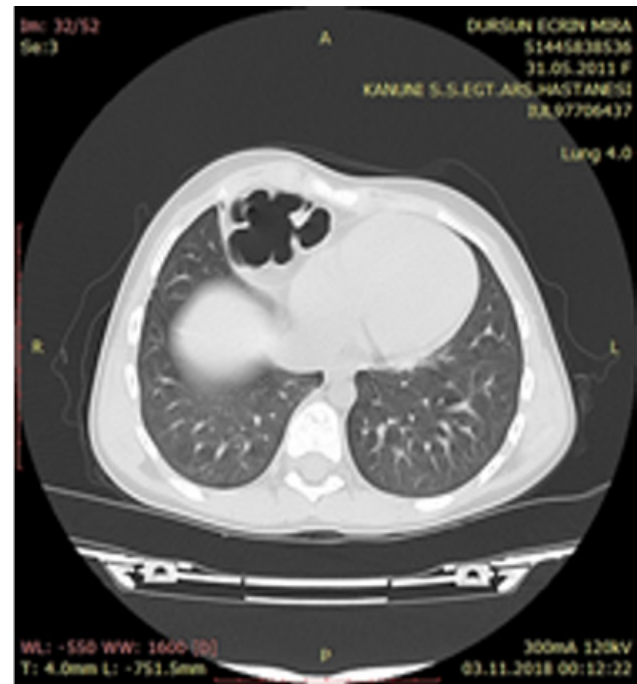
Figura 2: Preoperative view of the chest X-ray.

Tabla I: General findings.

Gender	9 cases female – 14 cases Male
Morgagni Hernia Side	13 case Right – 5 case Left - 5 case Bilateral
Symptoms	6 cases asymptomatic - 6 cases intestinal obstruction - 11 cases pulmonary symptoms
Additional Anomalies	3 cases down syndrome - 1 case Ehler Danlos – 1 case William Bauren Syndrome

Figura 3: Intraoperative view -1.   **Figura 4:** Intraoperative view-2.   **Figura 5:** Intraoperative view-3.
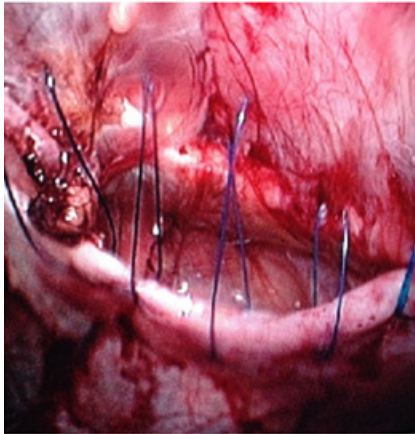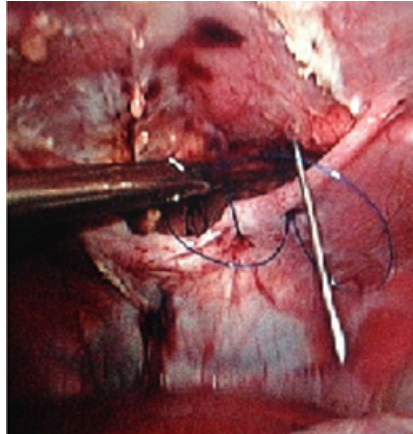
the right and left lower quadrants. In bilateral cases, the falciform ligament was cut for proper vision. The hernia sac was identified and its contents were reduced into the abdomen, and the sac was partially or completely excised. Three or six incisions of 3 mm were made under the xiphoid depending on the size of the sac. A non-absorbable suture (2-0 prolene) was passed through the fascia and the edges of the hernia sac with an 18-gauge gray branule, leaving the ends out, and inserting it into a ring and the needle was removed. Then, another suture of the same kind was passed through the needle and this time it was entered through a different fascia point without forming a ring, and passed directly through the ring and the needle was removed. The ring was pulled out and the other suture was taken out and suspended. In this way, 4-5 sutures were placed along the edges of the hernia sac and were individually tied, leaving the knots subcutaneously. (**Figures 3, 4 and 5**).

Results

Of all 23 cases, 9 were female and 14 were male. Their ages ranged from 1 month to 60 months (with a median of 36 months). Chest X-rays were taken in all cases and the diagnosis study was started. At least one of the contrast-enhanced passage X-rays and abdominal tomography were taken preoperatively. Six cases were asymptomatic, 6 cases had vomiting, and 11 cases had pulmonary symptoms.

Thirteen patients had right hernia, 5 patients had left hernia, and 5 patients had bilateral hernia. Of the 23 cases, 16 had colon organs in the sac and 7 patients had organs including the small intestine, liver and stomach.

Three patients had Down, 1 case had Ehler Danlos syndrome, 1 case had William-Bauren syndrome. The diameters of the hernia defect ranged from 5 to 16 cm. All cases were operated with the laparoscopic PIRS method.

The hernia sac was partially or completely removed in all cases. Discharge time ranged between 3-6 days (median 4). Late follow-up was 10-16 (median 13) months. There was no mortality, morbidity or transition to open surgery. There was no recurrence in late follow-up.

Discussion

Morgagni hernia (MH) is caused by a deficiency in diaphragm fusion or muscle development. This leads to a triangular retrosternal hernia between pars sternalis and pars costalis during diaphragm development. Usually, the diagnosis is made radiologically and includes anterior-posterior and lateral chest radiography first[7] Lateral radiographs show a retrosternal radiolucent paracardiac shadow with intestinal herniation[8] Chest radiography alone, usually when the bowel is seen in the chest, can make a diagnosis about 71% of the time[9] To confirm the diagnosis, chest computed tomography (CT) scan, oral contrast radiography can be used. Because CT scan has an accurate identification rate of up to 100%, it is often the next step in diagnosis[10]. We made a preliminary diagnosis with anterior-posterior and lateral chest X-ray in our entire case series. However, we preferred one of the contrast-enhanced passage radiography or CT methods before the operation.

If a herniated bowel loop is seen throughout the defect on chest radiograph, differential diagnosis may include a pericardial cyst, localized pneumothorax or hiatal hernia. Similar conditions in which chest radiography is seen as a solid structure; if the omentum or part of the liver has herniated into the defect, atelectasis, pneumonia, perikardiyal fat pad, intrathoracic lipoma, bronchial carcinoma, mesothelioma or an atypical mediastinal tumor are included in the differential diagnosis[11]. Further imaging scans should be able to confirm a Morgagni defect.

Approximately 91% of MH cases are on the right, 5% on the left, and 4% on the bilateral sides. In our series,

there were 13 cases with a right-side hernia (56%), 5 cases with a left-side hernia (22%), and 5 cases with bilateral hernias (22%). Clinical symptoms may be asymptomatic and discovered incidentally or there may be vague gastrointestinal or recurrent chest infections with respiratory symptoms[12]. In our series, four cases were asymptomatic, five cases had vomiting, and eight cases had pulmonary symptoms.

Morgagni hernias, especially when detected in infancy or early childhood, are known to be associated with other congenital anomalies with an incidence ranging from 34% to 50%[7]. The most common anomalies include heart defects (25% to 60%) and trisomy 21 (15% to 71%), as well as malrotation, anorectal malformations, omphalocele, skeletal anomalies, and pentalogy. Additionally, Cantrell was associated with Morgagni hernia. The association with trisomy 21 is thought to be due to defective dorsoventral migration of rhabdomyoblasts caused by increased cellular adhesion seen in trisomy 21 patients and it may also be why people with Down syndrome are more likely to relapse after repair . In our series, 3 cases were diagnosed with Down syndrome (17%), 1 case with Ehler danlos syndrome, 1 case with William-Bauren syndrome.

Unlike patients with Bochdalek hernia, Morgagni's hernia is asymptomatic in up to 50% of patients when diagnosed. Patients under two years of age are more likely to be symptomatic at the time of diagnosis[13]. In our case series, 6 cases were asymptomatic and under 2 years of age.

It is recommended that all Morgagni hernias be surgically repaired due to the risk of strangulation, however, the repair approach and the type of repair are still being discussed. It can be approached surgically through an abdominal approach or a thoracic incision. In the thoracic approach, posterolateral right thoracotomy is performed. However, we did not apply a thoracic approach in our cases. Because the disadvantages of this approach include the risk of bilateral defect leakage due to the inability to see the left side and the risk of chest wall deformity[14].

The abdominal approach can be performed with an open laparotomy incision or with minimally invasive laparoscopic techniques[15]. The advantages of the abdominal approach include the ability to evaluate and repair other intra-abdominal pathologies, such as malrotation. Open laparotomy can most often be performed in emergency cases, in patients who cannot tolerate laparoscopy, in those with severe scoliosis or extensive adhesions, if large bowel resection is require.

The hernia primarily contains the large intestine (between 54% and 72%) or the omentum (65%), but it can also contain the small intestine, stomach, and liver[16]. In our series, there were organs including the colon, small intestine, liver, and stomach in 23 cases in the sac.

There is controversy over whether the hernial sac should be excised or included in sutures; there are those who recommend placing supplementary material for all hernias larger than 20 to 30 cm[15]. The defect is repaired in the style of a mattress with nonabsorbable sutures, including costal margins[17-19]. The open laparotomy approach has been shown to have shorter operative times compared to laparoscopy, but the minimally invasive approach provides more space for dissection and better visualization while providing a shorter recovery time and faster return to normal activities[17,20,21]. In our series, all the defects were under 20 cm (ranging from 5-16 cm), so we did not use any reinforcement material.

In 1997, Georgacopulo was the first person to report the successful laparoscopic repair of Morgagni hernia in children[17] The laparoscopic approach involves positioning the patient in reverse Trendelenburg on the operating table with their feet up. The camera port is inserted through the umbilicus and two working ports are positioned on the right and left upper quadrants along the midclavicular line. Depending on the size of the defect, the falciform ligament may need to be cut for sufficient expulsion[18]. The contents of the hernia are drained; if the pouch is to be excised, it is done at this time. The defect can be closed by bringing stitches from the abdominal wall, which can be non-absorbable stitches since the defect is generally wider transversely than anteroposteriorly. For larger defects (bigger than 20 cm), placement of the mesh is performed by first suturing the mesh to the posterior edge of the hernia defect. The mesh is then combined with non-absorbable sutures running full thickness along the anterior abdominal wall and connected to the subcutaneous tissue. The closure is achieved similarly by placing cross-abdominal, staying sutures that encompass the hernia sac, include the rear edge of the diaphragm defect, and take in the incoming "U" shaped stitches, without the need for mesh placement in the case of smaller defects. Nodes are hidden in subcutaneous tissue. This type of repair is useful in patients without anterior diaphragmatic edges and is easier to perform than intracorporeal sutures. Recovery is often smooth and most patients are discharged within three days after surgery. In our surgeries, we followed the general laparoscopic rules but placed the transfasial U sutures using the PIRS method. We preferred 2/0 prolene as a suture. We performed a sac excision in all cases.

It is recommended that even asymptomatic patients be referred for surgical correction due to the concern for intestinal obstruction, choking, volvulus, and/or necrosis, which can occur in up to 10% of cases. Complications observed after surgical correction are common complications that can occur after any surgical procedure and include low-grade wound infections, incisional or port-site hernias, suture abscesses, and the incidence of intestinal obstruction. Recurrence rates

have been reported to range from 2% to 42%, but in many studies, no recurrence has been reported up to 10 years after the repair, with follow-up periods. The risk factors for recurrence are the closure of the defect under tension without the use of a mesh, leaving the sac in place without resection, use of absorbable sutures for repair, and history of Down syndrome in the patient.

In conclusion, the laparoscopic PIRS method, which involves the removal of the hernia sac through laparoscopy and the secure attachment of the lower rim of the sac to the abdominal fascia with extra-abdominal, subcutaneous, non-absorbable ring sutures, is a simple, safe, and cosmetically pleasing approach for the surgical treatment of Morgagni hernias. From this perspective, it may be a widely used surgical technique that can be the first option in treatment.

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ORIGINAL

Impacto personal y académico de la pandemia por COVID-19 en los estudiantes de enfermería en España (EsE-COVID)

Personal and academic impact of the COVID-19 pandemic on nursing students in Spain (EsE-COVID)

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Resumen

Fundamentos: La pandemia por COVID-19 y las medidas de aislamiento social forzaron la docencia virtual en los estudios universitarios.

Objetivo: Determinar el impacto de la pandemia en el bienestar de los estudiantes de enfermería, así como analizar la valoración de los nuevos modelos de docencia y las repercusiones académicas percibidas por los estudiantes de enfermería durante el curso 2020-2021.

Métodos: Estudio transversal con estudiantes de enfermería de 15 universidades españolas. Se utilizó un cuestionario anónimo en línea que incluía datos sociodemográficos, modalidad docente (en línea, mixta o presencial), opiniones y actitudes relacionadas con el aprendizaje en línea, competencias tecnológicas y recursos electrónicos, y repercusiones físicas, mentales y sociales de la pandemia en los estudiantes.

Resultados: Participaron un total de 1.276 estudiantes de enfermería (86,8% mujeres con una media de edad de 22,9±6,1 años). El 63,8% de los estudiantes consideraban que era posible aplicar la educación a distancia pero que no podía sustituir a la presencial. El 68,1% de los estudiantes consideraron que la pandemia afectó a su aprendizaje, concretamente en la adquisición de competencias profesionales. Además, manifestaron que la pandemia afectó a su bienestar social (86,7%), salud mental (82,1%), bienestar intelectual (65,5%) y bienestar físico (60,5%).

Conclusiones: Los estudiantes consideran que la docencia en línea en el contexto de pandemia tuvo repercusiones negativas a nivel personal y académico. En las crisis sanitarias es importante amortiguar el impacto en la docencia y asegurar la continuidad de la formación de las futuras enfermeras para garantizar la salud de la población.

Palabras clave: Infecciones por coronavirus, síndrome respiratorio agudo grave, estudiantes de enfermería, educación a distancia, educación estándar, rol de la enfermera, salud mental.

Abstract

Background: The COVID-19 pandemic and social isolation measures forced virtual teaching in high education.

Objective: To determine the impact of the pandemic on the well-being of nursing students, as well as to analyze the assessment of the new teaching models and the academic repercussions perceived by nursing students during the 2020-2021 academic year.

Methods: Cross-sectional study with nursing students from 15 Spanish universities. An anonymous online questionnaire was used, including sociodemographic data, teaching modality (online, mixed or face-to-face), opinions and attitudes related to online learning, technological skills and electronic resources, and physical, mental and social repercussions of the pandemic on students.

Results: A total of 1,276 nursing students participated (86.8% women with a mean age of 22.9±6.1 years). Sixty-three percent of the students considered that it was possible to apply distance education but that it could not replace face-to-face education. 68.1% of the students considered that the pandemic affected their learning, specifically in the acquisition of professional skills. In addition, they stated that the pandemic affected their social well-being (86.7%), mental health (82.1%), intellectual well-being (65.5%) and physical well-being (60.5%).

Conclusions: The students consider that online teaching in the context of the pandemic had negative repercussions at a personal and academic level. In health crises, it is important to palliate the impact on teaching and ensure the continuity of the training of future nurses to guarantee the health of the population.

Keywords: coronavirus infections, severe acute respiratory syndrome, nursing students, distance education, standard education, nurse's role, mental health.

Introducción

La pandemia por COVID-19[1], provocó que en España se decretara el estado de alarma y un confinamiento estricto de toda la población desde marzo hasta mayo del 2020[2], derivando en el cierre inmediato de todos los centros educativos. Las medidas de prevención y seguridad para reducir la transmisión del SARS-CoV-2 provocaron cambios en las metodologías docentes[3], predominando la enseñanza virtual[4,5] y requiriendo adaptaciones tanto por parte de los docentes como de los estudiantes[6,7]. La metodología más utilizada durante la pandemia fue la videoconferencia sincrónica a través de plataformas educativas[8]. Hasta entonces, nunca se había experimentado una situación que obligase a someter a todo el alumnado a cambiar radicalmente la metodología de enseñanza, generando muchas dudas sobre el impacto que este cambio brusco podía tener sobre ellos.

Antes de la pandemia, la eficacia y la adecuación de la docencia a distancia ya generaba controversia –incluso en escenarios de aplicación más controlados y programados–, problemática que se incrementó por la situación inesperada y de incertidumbre que supuso la declaración del estado de alarma. Este tipo de metodologías podrían repercutir de forma negativa en las futuras competencias profesionales de los estudiantes[9,10]. Además, una revisión sistemática indica que la enseñanza a distancia podría mejorar los conocimientos y la satisfacción del alumnado respecto a modelos de enseñanza tradicionales o presenciales[10].

Igualmente, los estudios realizados durante la pandemia sobre el efecto de las metodologías en línea en la educación han obtenido resultados contradictorios[11,12]. En este sentido, una revisión sistemática indica que la situación de crisis sanitaria alteró significativamente el proceso de aprendizaje de los estudiantes de ciencias de la salud, poniendo en riesgo su adquisición de conocimientos clínicos, teóricos y prácticos[11]. En cambio, un estudio realizado en Jordania concluía que el modelo en línea resultaba satisfactorio para la adquisición de conocimientos, aunque no resultó eficaz para la adquisición de habilidades clínicas y técnicas[12].

Además de los efectos sobre las competencias adquiridas por parte del alumnado, es reseñable el impacto que la pandemia ha tenido sobre su salud mental. Un estudio realizado en diferentes universidades libanesas indica que la enseñanza en línea durante la pandemia causó sintomatología de depresión y ansiedad entre los estudiantes[13], existiendo una relación inversa entre su satisfacción con el aprendizaje en línea y la prevalencia de depresión, ansiedad y estrés[13]. Una revisión sistemática concluyó que los principales problemas de salud mental de los estudiantes de enfermería eran el miedo, la ansiedad, el estrés y las alteraciones del sueño[14] y un estudio realizado en Europa mostró que los estudiantes españoles refirieron más síntomas de depresión que el resto de estudiantes europeos[15].

El agravamiento de las desigualdades sociales ante una crisis como la producida por la pandemia por COVID-19 es incuestionable, de forma que la pandemia ha contribuido a ampliar la brecha digital[16]. En España, se evidencia que, en la enseñanza primaria, los determinantes sociales han aumentado las desigualdades en la adquisición de competencias en función de los hogares y la capacidad de adaptabilidad a la realización de clases desde el domicilio[17]. Sin embargo, no existen estudios que analicen este tema en estudiantes universitarios[18].

En España, las facultades de enfermería suspendieron sus clases y/o prácticas presenciales durante el confinamiento. A partir del curso 2020-2021, la presencialidad se fue recuperando de forma irregular en las diferentes comunidades autónomas, predominando la enseñanza virtual. Además, la implantación de la metodología a distancia de forma repentina pudo provocar una exclusión de los estudiantes más vulnerables, tanto tecnológica como económicamente, impactando en ellos a distintos niveles: educativo, personal y social. Comprender el impacto de la docencia virtual en el aprendizaje de los estudiantes de enfermería, sobre todo en lo que concierne a las habilidades prácticas, nos proporcionará información relevante que nos permitirá incorporar nuevos métodos de aprendizaje en la enseñanza en situaciones de futuras pandemias o crisis sanitarias.

El objetivo principal del estudio fue determinar el impacto de la pandemia en el bienestar de los estudiantes de enfermería, así como analizar la valoración de los nuevos modelos docentes y las repercusiones académicas percibidas por los estudiantes de enfermería en España durante el curso 2020-2021.

Sujetos y método

Se realizó un estudio transversal a través de una encuesta a los estudiantes de enfermería de diferentes universidades de España entre marzo y junio del 2021. Se contactó con todas las universidades donde se impartía el grado de enfermería gracias a la colaboración de la Conferencia Nacional de Decanos y Decanas de Enfermería. Finalmente participaron 15 facultades de enfermería tanto públicas como privadas. Las universidades divulgaron el cuestionario anónimo en línea del estudio mediante Google Forms a través del correo electrónico interno de la universidad.

El cuestionario recogió: a) datos sociodemográficos como: sexo, edad, curso académico, vía de acceso a la universidad, estudios universitarios previos, situación

laboral y tipo de convivencia; b) información sobre la realización de pruebas diagnósticas de SARS-CoV-2, realización de aislamientos y/o cuarentenas; c) modalidad de las actividades docentes realizadas (en línea, mixta o presencial) durante el curso 2020-2021; d) actitudes respecto a la educación a distancia en línea, opiniones y experiencias en el acceso y utilización de las nuevas tecnologías, recursos electrónicos, viabilidad del aprendizaje en línea en su universidad, cambios en los intereses profesionales tras la pandemia y preferencias sobre los diferentes modelos docentes; e) afectación y repercusiones a nivel físico, mental y social en los estudiantes durante la pandemia y su satisfacción respecto a la gestión institucional (universidad, gobierno autonómico y gobierno estatal) de la pandemia.

Se realizó un análisis descriptivo para evaluar las características sociodemográficas de los estudiantes encuestados (frecuencias y porcentajes). Las variables numéricas, con una distribución normal, se describieron según medidas de tendencia central y dispersión (media y desviación estándar). Para la comparación de variables cualitativas se realizó mediante el test de Chi-cuadrado con un nivel de significación estadística $p < 0,05$. Todos los análisis estadísticos de los datos se realizaron con el software estadístico SPSS versión 21.0.

El diseño y el desarrollo del estudio siguió las recomendaciones recogidas en la Declaración de Helsinki y la Ley Orgánica de Protección de Datos (LOPD 3/2018). El proyecto fue evaluado favorablemente por el Comité de Ética de la Investigación de la Universitat de les Illes Balears (Referencia: 199CER21).

En el cuestionario en línea, se introdujo un texto introductorio en el que se informaba a los estudiantes del carácter voluntario de la cumplimentación del mismo, y que su cumplimentación no tendría ningún tipo de compensación ni perjuicio a nivel académico. Los estudiantes disponían de una dirección electrónica de contacto en caso de que necesitaran más información.

Tabla I: Características sociodemográficas de la población del estudio (n=1.276).

Variables	Total (%) n=1.276	Femenino (%) n= 1.108	Masculino (%) n= 168	p-valor
Edad (media ±DE)	22,9 ± 6,1	22,8 ± 6,1	23,5 ± 6,5	0,029
Curso				0,946
Primero	371 (29,1)	324 (29,2)	47 (28,0)	
Segundo	381 (29,9)	329 (29,7)	52 (31,0)	
Tercero	307 (24,0)	265 (23,9)	42 (25,0)	
Cuarto	217 (17,0)	190 (17,1)	27 (16,0)	
Vía de acceso				0,697
Bachillerato	846 (66,3)	737 (66,5)	109 (64,9)	
Cambio de estudios	16 (1,3)	14 (1,3)	2 (1,2)	
Grado Superior de Formación Profesional	302 (23,7)	264 (23,8)	38 (22,6)	
Acceso >25 años	41 (3,2)	33 (3,0)	8 (4,8)	
Acceso >40 años	23 (1,8)	18 (1,6)	5 (3,0)	
Otros títulos	48 (3,8)	42 (3,8)	6 (3,6)	
Estudios previos				0,889
Sí	87 (6,8)	76 (6,9)	11 (6,5)	
No	1.189 (93,2)	1.038 (93,1)	157 (93,5)	
Convivencia				0,469
Familia de origen	764 (59,9)	671 (60,6)	93 (55,4)	
Pareja con hijos	55 (4,3)	45 (4,1)	10 (6,0)	
Pareja sin hijos	88 (6,9)	77 (6,9)	11 (6,5)	
Con hijos sin pareja	13 (1,0)	13 (1,2)	0 (0)	
En residencia de estudiantes	37 (2,7)	30 (2,7)	5 (3,0)	
Piso compartido	262 (20,5)	223 (20,1)	39 (23,2)	
Solo	33 (2,6)	26 (2,3)	7 (4,2)	
Otras situaciones	26 (2,0)	23 (2,1)	3 (1,8)	
Estatus laboral				0,055
Parado	954 (74,8)	834 (75,3)	120 (71,4)	
Activo (parcial)	198 (15,5)	174 (15,7)	24 (14,3)	
Activo (completo)	124 (9,7)	100 (9,0)	24 (14,3)	
Trabajo en el ámbito sanitario (n=321)				0,073
Sí	177 (44,9)	124 (45,4)	28 (58,3)	
No	144 (55,1)	149 (54,6)	20 (41,7)	
Test COVID-19				0,978
Test realizado y negativo	820 (64,3)	712 (64,3)	108 (64,3)	
Test realizado, positivo con sintomatología	142 (11,1)	122 (11)	20 (11,9)	
Test realizado, positivo sin sintomatología	50 (3,9)	44 (3,9)	6 (3,6)	
No realización de la prueba	264 (20,7)	230 (20,8)	34 (20,2)	
Realización de cuarentena y/o aislamiento				0,705
No	747 (58,5)	650 (58,7)	97 (57,7)	
Sí	529 (41,5)	458 (41,3)	71 (42,3)	

Resultados

Participaron en el estudio 1.276 estudiantes de enfermería, lo que representa del 8,5% de los alumnos matriculados (14.916). La media de edad fue de 22,9±6,14 años, un total de 1.108 (86,8) fueron mujeres, el 39,1% cursaban primer curso, el 29,9% segundo, el 24% tercero y el 17% cuarto. El 59,9% de los participantes vivía con su familia de origen y el 20,5% compartían piso. El 15,2% trabajaban a media jornada y el 9,7% a jornada completa (41,6% en el sector sanitario y/o sociosanitario).

En cuanto al contacto con la COVID-19 en el momento de la encuesta, el 79,2% de los estudiantes declaró haberse realizado alguna prueba diagnóstica de detección del SARS-CoV-2. Entre los positivos, el 11,1% habían presentado sintomatología, mientras que el 3,9% no presentaron síntomas. Por otro lado, el 41,1% del total de los estudiantes habían realizado cuarentenas y/o aislamientos durante el período escolar.

Las variables sociodemográficas se presentan por sexos (**Tabla I**). Se encontraron diferencias estadísticamente significativas en relación con la situación laboral (trabajaban el 24,0% de las mujeres vs el 28,6% de los hombres) y en edad (media en mujeres 22,8 ± 6,1 vs hombres 23,5 ± 6,5).

Evaluación de disponibilidad y usabilidad de la tecnología

El 42,4% de los estudiantes de enfermería valoraron sus competencias tecnológicas como "muy buenas/excelentes" y el 54,5% como "aceptables/buenas", a pesar de que el 42,9% manifestó haber tenido en algún momento problemas de conexión. El 38,0% de los estudiantes utilizaron únicamente el ordenador como herramienta principal de estudio, mientras que el 39,8% combinó el uso de ordenador y tableta. Por el contrario, únicamente el 0,5% de los estudiantes utilizaron exclusivamente la tableta y el 0,2% sólo el teléfono para su formación. En general, en el 95% se trataba de dispositivos propios.

El 86,6% de los estudiantes disponía de un espacio adecuado para realizar las clases en línea. A un 30,7% de los estudiantes les supuso un gasto adicional el cambio de modelo de enseñanza (**Tabla II**).

Tabla II: Acceso y utilización de las nuevas tecnologías (n=1.276).

Variables	Frecuencia n (%)
Competencias TICs	
Muy bueno/Excelente	541 (42,4)
Aceptable/Bueno	696 (54,5)
Insuficiente/escaso	39 (3,1)
Conexión a Internet	
Conexión adecuada	601 (47,1)
Problemas de conexión:	
Ocasional	564 (44,2)
A menudo	106 (8,3)
Siempre	5 (0,4)
Dispositivos utilizados	
Ordenador	484 (37,9)
Tableta	6 (0,5)
Teléfono	2 (0,2)
Ordenador, tableta, teléfono	168 (13,2)
Ordenador, tableta	97 (7,6)
Ordenador, teléfono	508 (39,8)
Tableta, teléfono	11 (0,9)
Dispositivos propios	
No dispongo de dispositivos	4 (0,3)
Sí, compartido	53 (4,2)
Sí, propio	1.219 (95,5)
Espacio para docencia en línea	
Sí	1.106 (86,6)
No	171 (13,4)
Coste económico adicional docencia en línea	
No	885 (69,3)
Sí, dispositivos electrónicos	114 (8,9)
Sí, otros gastos	79 (6,2)
Préstamo de ordenador en la universidad	4 (0,3)
Sí, mejorar la conexión a internet	104 (8,1)
Más de dos gastos adicionales	91 (7,2)

Tabla III: Modalidades de actividades curso 2020-2021 (n=1.276).

Variables	Frecuencia n (%)
Clases magistrales	
Modalidad mixta	677 (53,1)
Modalidad en línea	359 (28,1)
Modalidad presencial	240 (18,8)
Seminarios	
Modalidad mixta	485 (38,0)
Modalidad en línea	168 (13,2)
Modalidad presencial	623 (48,8)
Teórico-Prácticas de laboratorio	
Modalidad en línea /simulación	104 (8,2)
Modalidad presencial	881 (69,0)
No tengo	291 (22,8)
Prácticas Clínicas	
No tengo programadas	367 (28,8)
Se han mantenido	744 (58,3)
Se han suspendido	165 (12,9)
Realización de prácticas	
No programadas/realizadas	563 (44,1)
Sí	714 (55,9)
Prácticas en unidad COVID (N=712)	
No	464 (65,2)
Sí	248 (34,8)
Afectación personal de los cambios de cronograma (N=712)	
No he sufrido cambios en el cronograma	190 (26,7)
No me ha afectado	195 (27,4)
Sí me ha afectado	327 (45,9)
Consecuencias de la experiencia en las prácticas (N=662)	
Cambio de estudios dentro de la salud	6 (0,9)
Cambio de estudios fuero de la salud	14 (2,1)
Seguir con enfermería	642 (97,0)
Carga de trabajo curso 2020-2021	
No ha afectado	319 (25,0)
Sí, la carga de trabajo ha aumentado	920 (72,1)
Sí, la carga de trabajo ha disminuido	37 (2,9)

Modalidad de enseñanza y preocupación de los estudiantes por su aprendizaje

Durante el curso 2020-2021, el 18,8% de los estudiantes siguieron recibiendo las clases magistrales en formato presencial, el 53,1% realizaron un modelo mixto (presencial y en línea), mientras que para el 28,1% la docencia de clases magistrales fue totalmente en línea. Respecto a los seminarios y las teórico-prácticas, un 48,8% de los estudiantes y un 69,1%, respectivamente, manifestaron haber seguido cursándolos de forma presencial. El 72,2% de los estudiantes encuestados consideraron que la docencia en línea les supuso un aumento en la carga de trabajo.

Respecto al impacto de la pandemia sobre las prácticas clínicas, el 13% de los estudiantes sufrieron la suspensión de sus prácticas clínicas programadas durante el curso académico 2020-2021. Estos cambios en el cronograma de prácticas afectaron a la vida diaria del 42,7% de los estudiantes. El 55,9% pudieron realizar prácticas clínicas, de los cuales un 34,8% las realizaron en unidades COVID (**Tabla III**).

Se observó una asociación estadísticamente significativa entre la metodología docente utilizada y la preocupación de los estudiantes por la repercusión en su aprendizaje (**Tabla IV**). Los estudiantes que realizaron las clases magistrales en línea mostraron más preocupación por su progreso educativo y por la adquisición de competencias que los estudiantes con una metodología presencial (71,6% vs 54,2% para progreso educativo; 71,6% vs 60,0% para adquisición de competencias; $p<0,05$ en ambos casos). Por otro lado, los estudiantes a los que se les suspendió sus prácticas clínicas fueron los que mostraron más preocupación por su progreso educativo (81,9% vs 65,2%; $p<0,001$), su adquisición de competencias (85,5% vs 67,5%; $p<0,001$) y su futuro profesional (79,9% vs 66,4%; $p<0,001$).

Tabla IV: Asociación entre la metodología docente utilizada durante la pandemia y la preocupación de los estudiantes por la repercusión en su aprendizaje (n=1.276).

	Repercusión en el progreso educativo			p-valor
	De acuerdo N (%)	Neutral N (%)	En desacuerdo N (%)	
Metodología de las clases magistrales				<0,001
En línea	254 (70,8)	65 (18,1)	40 (23,0)	
Mixta	458 (67,6)	120 (17,7)	100 (14,7)	
Presencial	130 (54,2)	76 (31,7)	34 (14,2)	
Metodología de los seminarios				0,08
En línea	116 (68,6)	30 (17,8)	23 (13,6)	
Mixta	332 (68,5)	83 (17,1)	70 (14,4)	
Presencial	394 (63,2)	148 (23,8)	81 (13,0)	
Prácticas clínicas				<0,001
No tengo programadas	221 (60,2)	81 (22,1)	65 (17,7)	
Se han mantenido	485 (65,2)	159 (21,4)	100 (13,4)	
Se han suspendido	136 (81,9)	21 (12,7)	9 (5,4)	
	Repercusión en la adquisición de competencias			
	De acuerdo	Neutral	En desacuerdo	
Metodología de las clases magistrales				0,022
En línea	257 (71,6)	63 (17,5)	39 (10,9)	
Mixta	469 (69,2)	129 (19,0)	80 (11,8)	
Presencial	144 (60,0)	66 (27,5)	30 (12,5)	
Metodología de los seminarios				0,013
En línea	127 (75,1)	19 (11,2)	23 (13,6)	
Mixta	331 (68,2)	94 (19,4)	60 (12,4)	
Presencial	412 (66,1)	145 (23,3)	66 (10,6)	
Prácticas clínicas				<0,001
No tengo programadas	226 (61,6)	89 (24,3)	52 (14,2)	
Se han mantenido	502 (67,5)	153 (20,6)	89 (12,0)	
Se han suspendido	142 (85,5)	16 (9,6)	8 (4,8)	
	Afectación en la futura carrera profesional			
	De acuerdo	Neutral	En desacuerdo	
Metodología de las clases magistrales				0,669
En línea	244 (68,0)	61 (17,0)	54 (15,0)	
Mixta	458 (67,6)	118 (17,4)	102 (15,0)	
Presencial	157 (65,4)	51 (21,3)	32 (13,3)	
Metodología de los seminarios				0,109
En línea	128 (68,8)	24 (12,9)	34 (18,3)	
Mixta	361 (68,2)	89 (16,8)	79 (14,9)	
Presencial	421 (66,5)	128 (20,2)	84 (13,3)	
Prácticas clínicas				<0,001
No tengo programadas	250 (64,1)	85 (21,8)	55 (14,1)	
Se han mantenido	517 (66,4)	137 (17,6)	125 (16,0)	
Se han suspendido	143 (79,9)	19 (10,6)	17 (9,5)	

Afectación de la pandemia a nivel personal

La mayoría de los estudiantes de enfermería manifestaron su preocupación respecto a la exposición a la COVID-19 en los siguientes ámbitos de las actividades de la vida diaria (**Tabla V**): en el transporte público (73,2%), en la comunidad (68,1%), en las prácticas o tareas profesionales (57,3%) y en el aula (55,1%).

Los estudiantes consideraron que la COVID-19 les he afectado a nivel personal. Concretamente, el 82,1% de

Tabla V: Afectación de la pandemia de la COVID-19 en las diferentes áreas personales (n=1.276).

Variables	Frecuencia n (%)
Preocupación de la exposición en la comunidad (N=1.276) De acuerdo Neutral En desacuerdo	868 (68,0) 275 (21,6) 133 (10,4)
Preocupación de la exposición en el transporte público (N=1.163) De acuerdo Neutral En desacuerdo	851 (73,2) 212 (15,2) 100 (11,6)
Preocupación de la exposición en el aula (N=1.276) De acuerdo Neutral En desacuerdo	703 (55,1) 354 (27,7) 219 (17,2)
Preocupación de la exposición en las prácticas (N=1.276) De acuerdo Neutral En desacuerdo	732 (57,4) 326 (25,5) 218 (17,1)
Afectación para encontrar espacio para el aprendizaje De acuerdo Neutral En desacuerdo	624 (48,9) 306 (24,0) 346 (27,1)
Afectación del bienestar intelectual De acuerdo Neutral En desacuerdo	835 (65,5) 234 (18,3) 207 (16,2)
Afectación del bienestar social De acuerdo Neutral En desacuerdo	1.106 (86,7) 106 (8,3) 64 (5,0)
Afectación de la salud mental y estado de ánimo De acuerdo Neutral En desacuerdo	1.047 (82,1) 140 (11,0) 89 (7,0)
Afectación del bienestar físico De acuerdo Neutral En desacuerdo	771 (60,4) 273 (21,4) 232 (18,2)
Afectación del progreso educativo De acuerdo Neutral En desacuerdo	841 (65,9) 261 (20,5) 174 (13,6)
Afectación en la adquisición de competencias profesionales De acuerdo Neutral En desacuerdo	869 (68,1) 258 (20,2) 149 (11,7)
Afectación en la futura carrera profesional De acuerdo Neutral En desacuerdo	858 (67,3) 230 (18,0) 188 (14,7)

los estudiantes (1.047) afirma que su salud mental y su estado de ánimo se habían visto afectados. También consideraron que afectó a su bienestar intelectual (65,5%), social (86,7%) y físico (60,5%). En relación con su formación académica, consideraron que la pandemia les había afectado tanto en el progreso educativo (65,9%), como en la adquisición de competencias profesionales (68,1%) y en su futura carrera profesional (67,3%).

Evaluación de los intereses profesionales y educativos tras la pandemia

Con relación a los diferentes modelos de docencia, el 60,8% de los estudiantes de enfermería, prefirieron el modelo totalmente presencial. Respecto a la metodología en línea, el 81,5% de los estudiantes prefirieron una docencia en línea en directo y con publicación de la grabación para su posterior consulta. Por tanto, la mayoría se decantaron por un modelo mixto de actividades sincrónicas y diacrónicas (**Tabla VI**).

El 63,8% de los estudiantes consideraron que la educación a distancia es aplicable en su universidad. Sin embargo, el 58,5% rechazaron que se pueda sustituir la educación presencial por la educación en línea. Los estudiantes descartaron que la modalidad en línea permita una interacción similar a la presencial, tanto entre estudiantes (77,2%) como con el profesorado (73,8%). El 50,4% de los estudiantes consideraron que el fraude o plagio es mayor en la evaluación en línea que en las evaluaciones presenciales (**Tabla VI**). Además, los estudiantes consideraron que los profesores se habían esforzado durante la pandemia para mantener el nivel educativo (59%).

Tras la pandemia de la COVID-19, los estudiantes mostraron un mayor interés por los cuidados intensivos (46,0%) y la atención al final de la vida (27,8%). Por otro lado, el 81% de los estudiantes consideraron que no había disminuido el interés en ningún área de conocimiento específica (**Tabla VI**).

Discusión

Las medidas de confinamiento y la distancia social adoptadas por el gobierno para hacer frente a la pandemia por la COVID-19 afectaron profundamente a los estudiantes de enfermería en aspectos académicos, pero también a nivel personal y de salud. Nuestros resultados indican que, aunque la mayoría del alumnado tenía un elevado nivel de competencias digitales, en general se mostraron preocupados sobre su adecuado progreso educativo, su aprendizaje y su futuro profesional como enfermeras. Los estudiantes que asistieron a clases en línea y aquellos a los que se les suspendieron las prácticas clínicas fueron los que manifestaron una mayor preocupación. Además, 8 de cada 10 participantes consideraron que la pandemia había afectado a su salud mental.

Tabla VI: Preferencias e intereses educativos y profesionales tras la pandemia COVID-19 (n=1.276).

Variables	Frecuencia n (%)
Modelo docencia	
Mixto	436 (34,2)
En línea	65 (5,1)
Presencial	775 (60,7)
En línea	
En directo	166 (13)
Directo y publicación de grabación	1.040 (81,5)
En diferido	70 (5,5)
Aplicabilidad de la educación a distancia en la universidad	
De acuerdo	815 (63,9)
Neutral	243 (19)
En desacuerdo	218 (17,1)
La educación a distancia es un sustituto adecuado de la educación presencial teórica	
De acuerdo	306 (24)
Neutral	224 (17,5)
En desacuerdo	746 (58,5)
Comparación de la comunicación entre la educación presencial y en línea entre los estudiantes	
De acuerdo	163 (12,8)
Neutral	128 (10)
En desacuerdo	985 (77,2)
Comparación de la comunicación entre la educación presencial y en línea entre el docente y el estudiante	
De acuerdo	198 (15,5)
Neutral	137(10,7)
En desacuerdo	941 (73,8)
Comparación de la comunicación entre la educación presencial y en línea en las tutorías	
De acuerdo	552 (43,2)
Neutral	393 (30,8)
En desacuerdo	331 (26)
Comparación de la comunicación entre la educación presencial y en línea entre en las evaluaciones	
De acuerdo	234 (18,3)
Neutral	280 (21,9)
En desacuerdo	762 (59,7)
Comparación de la evaluación entre la educación presencial y en línea en el Fraude y/o plagio en exámenes	
De acuerdo	643 (50,4)
Neutral	355 (27,8)
En desacuerdo	278 (21,8)
Intereses tras la pandemia de la COVID-19 han aumentado	
Atención al final de la vida	373 (27,8)
Atención primaria/comunitaria	359 (26,7)
Cuidados intensivos	619 (46)
Epidemiología y salud pública	373 (27,7)
Geriatría	157 (11,7)
Otras áreas	155 (11,5)
No ha afectado	371 (27,6)
Intereses tras la pandemia de la COVID-19 han disminuido	
Atención al final de la vida	32 (2,4)
Atención primaria/comunitaria	58 (4,4)
Cuidados intensivos	36 (2,7)
Epidemiología y salud pública	107 (8,1)
Geriatría	73 (5,6)
Otras áreas	42 (3,2)
No ha afectado	1.064 (81)

La transformación repentina de la metodología docente provocó cierta preocupación sobre las dificultades de acceso a la formación a distancia entre el alumnado de clase social menos favorecida. A pesar de que estas dificultades sí se han producido en otros contextos[19] o ámbitos educativos[17], no ha sido así entre los estudiantes de enfermería, posiblemente esto sea debido a que los estudiantes universitarios ya utilizaban de manera cotidiana dispositivos electrónicos para su formación académica previamente a la pandemia[20,21].

Según nuestros resultados y coincidiendo con estudios previos[22,23], más de la mitad de los estudiantes de enfermería percibieron que su progreso educativo y su adquisición de competencias profesionales se vieron afectados por la pandemia y la crisis sanitaria. Aunque la mayoría de los participantes pensaba que la educación a distancia era aplicable en el grado de enfermería y disponían de una buena conexión a internet, se mostraron en desacuerdo con la posibilidad de sustituir el modelo presencial por un modelo de enseñanza a distancia. Estos resultados podrían estar relacionados con la percepción del aumento de la carga de trabajo frente a los modelos tradicionales[24]. La mayoría de los estudiantes prefirieron un modelo completamente presencial y una proporción minoritaria de ellos estudiantes elegiría un modelo docente totalmente en línea, modalidad que no existe en dichos estudios.

Algunos de los argumentos a favor de la metodología presencial que se extraen del presente estudio son las diferencias encontradas en la preocupación de los estudiantes sobre la repercusión de la metodología utilizada en su aprendizaje. Así, aquellos que recibieron formación presencial o mixta, mostraron una menor preocupación respecto a su formación, que los que la recibieron exclusivamente a distancia. En este sentido, también se observa que los estudiantes a los que se les cancelaron las prácticas clínicas mostraron una mayor preocupación por su aprendizaje. Este resultado es especialmente relevante teniendo en cuenta que la pandemia sobrecargó el sistema sanitario y, por tanto, afectó a la capacidad de los profesionales sanitarios para tutorizar de forma óptima a los estudiantes durante sus estancias clínicas[25].

En línea con estudios previos[26-28], nuestros resultados muestran que los estudiantes vieron afectado su bienestar físico y emocional durante la pandemia. En concreto, en estudiantes de medicina se observó una elevada prevalencia de depresión y síntomas de ansiedad por el impacto de la pandemia[28]. Y declararon sentirse significativamente más estresados en sus vidas privadas debido a la COVID-19[29]. Entre las posibles causas del incremento del malestar emocional se encuentra el confinamiento y el distanciamiento social. A nivel social, los estudiantes estaban preocupados por la exposición a la COVID-19. Concretamente, a nivel comunitario, los estudiantes tenían miedo a contagiarse en los medios de transporte, en las aulas y durante la realización de las prácticas clínicas. Además, en determinadas comunidades autónomas de nuestro país, los estudiantes de último curso de enfermería y medicina se vieron obligados a incorporarse laboralmente mediante los contratos generados ad hoc de auxilio sanitario, exponiéndoles además a nivel profesional a la COVID-19.

Sin embargo, y pese a las dificultades experimentadas por los estudiantes durante la pandemia de COVID-19, la mayoría tenían intención de continuar con sus estudios e incrementaron su interés por las áreas de cuidados intensivos y de atención al final de la vida.

Finalmente, los estudiantes estuvieron satisfechos con el esfuerzo realizado por parte del profesorado, sin embargo, su satisfacción fue menor respecto a la gestión de las comunidades autónomas y el gobierno estatal

Una de las fortalezas de este estudio es que participaron distintas universidades, tanto públicas como privadas, siendo una muestra considerable tanto de Facultades como de estudiantes de enfermería a nivel nacional. Por otro lado, el cuestionario que se utilizó contemplaba múltiples aspectos (bienestar social, físico, mental, etc.) que han permitido valorar el impacto de la pandemia en los estudiantes. Por otro lado, una de las principales limitaciones podría ser el sesgo de participación diferencial, dado que la encuesta se realizó únicamente por vía telemática. Por este motivo, es posible que haya habido una mayor representación de los estudiantes con menor dificultad de acceso a las nuevas tecnologías. Otra limitación podría ser la baja participación que se obtuvo en la cumplimentación de las encuestas, aunque es muy habitual en este tipo de estudios[30,31].

A modo de conclusión, la pandemia tuvo un importante impacto sobre el bienestar físico y emocional, así como en la formación de los estudiantes de enfermería en España. La adaptación del modelo educativo a la situación generada por la pandemia ha sido heterogénea entre las diferentes Facultades españolas. Así, podemos concluir que aquellas que optaron por mantener la realización de prácticas clínicas y la presencialidad tuvieron un menor impacto en el progreso educativo percibido por los estudiantes. La pandemia ha puesto de manifiesto que el grado de enfermería ha podido adaptarse a una situación de crisis integrando la metodología a distancia y manteniendo el interés del alumnado por los estudios.

La crisis por COVID-19 ha puesto de manifiesto la necesidad de disponer de planes de contingencia que aseguren la continuidad y la calidad de la formación de las enfermeras para poder preservar la salud de la población. Además, son necesarias estrategias motivacionales y de apoyo emocional para disminuir el impacto de estas situaciones en el alumnado.

Conflicto de intereses
Los autores declaran no tener conflicto de intereses.

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ORIGINAL

A Simplified Approach to Covid-19 Pneumonia Classification

Un enfoque simplificado para la clasificación de neumonía por Covid-19

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Abstract

Introduction: The outbreak of Covid-19 has triggered a worldwide problem, especially in Asia and America. The World Health Organization (WHO) declared the sickness a pandemic on March 20, 2020. It arrived in waves, and most countries around the world have now experienced two waves and are on the approach of experiencing the third. The goal of this study is to build up and certify a Computer-Aided Diagnosis (CADx) system for distinguishing between COVID-19 positive patients and Non-Covid Patients people.
Methods: Chest X-ray (CXR) images are used to accomplish Covid-19 Pneumonia Classification. From public datasets GitHub 2295 CXR images were obtained which include 712 COVID-19 positive and 1583 normal cases. The proposed CADx system utilized a Conventional Neural Network (CNN) model for data argumentation and CNN is built, compiled and trained with help of Tensor flow and Keras. For the sake of appraisal, the dataset is estranged into three categories: Train, Test and Validation.
Results: The three sets accuracy was evaluated and the results for Training, Validation and Test were observed as 97.77%, 97.81% and 97.72%, respectively.
Conclusion: The presented study can create a precise Computer-Aided Diagnosis system for the two categories of classification.

Keywords: Computer-Aided Diagnosis (CADx), Conventional Neural Network (CNN), Keras and Tensorflow, Chest X-ray (CXR).

Resumen

Introducción: El brote de Covid-19 ha desencadenado un problema mundial, especialmente en Asia y América. La Organización Mundial de la Salud (OMS) declaró la enfermedad pandémica el 20 de marzo de 2020. Llegó en oleadas, y la mayoría de los países del mundo ya han experimentado dos oleadas y están a punto de experimentar la tercera. El objetivo de este estudio es construir y certificar un sistema de Diagnóstico Asistido por Ordenador (CADx) para distinguir entre pacientes COVID-19 positivos y personas No-Covid.
Métodos: Se utilizan imágenes de radiografía de tórax (CXR) para realizar la clasificación de la neumonía Covid-19. De los conjuntos de datos públicos GitHub se obtuvieron 2295 imágenes CXR que incluyen 712 COVID-19 positivos y 1583 casos normales. El sistema CADx propuesto utiliza un modelo de Red Neuronal Convencional (CNN) para la argumentación de datos y la CNN se construye, compila y entrena con la ayuda de Tensor flow y Keras. Para la evaluación, el conjunto de datos se divide en tres categorías: Entrenamiento, Prueba y Validación.
Resultados: Se evaluó la precisión de los tres conjuntos y los resultados de Entrenamiento, Validación y Prueba fueron del 97,77%, 97,81% y 97,72%, respectivamente.
Conclusiones: El estudio presentado puede crear un sistema preciso de Diagnóstico Asistido por Ordenador para las dos categorías de clasificación.

Palabras clave: Diagnóstico asistido por ordenador (CADx), Red neuronal convencional (CNN), Keras y Tensorflow, Radiografía de tórax (CXR).

Introduction

Pneumonia is a pervasive ailment caused by viruses, microorganisms, and fungus, among other microbes. The term "pneumonia" is derived from the Greek word "pneumon", which means "lung." As a result, the word pneumonia is linked to lung disease[14]. Pneumonia arises when a bacterial or viral contagion in the lungs produces noteworthy harm and irritation. The coronavirus is responsible for the damage to the lungs in COVID pneumonia[2]. When COVID pneumonia builds up, it causes extra signs, such as:

- Shortness of breath
- Increased heart rate
- Low blood pressure

AI-based computer-aided diagnostic tools are used to detect and treat different types of cancer, such as breast cancer and brain tumors. These tools are commonly referred to as deep learning (DL). Deep learning (DL) is a subset of machine learning (ML) stimulated as a result of the structure of the human brain. This is a subfield of machine learning that uses neural networks to interpret data related to the biology of a being's brain[3]. CNNs are the most widely used of these tools because they can analyze and interpret complex data. The Objectives of this research are:

- Have a model that is going accelerate prediction processes and to assist medical professionals.
- Create a CADx which will give an accurate classification between Covid-19 patients and Normal patients using CXR image.
- Make it easy even for leman to be able to check whether he/she is Covid-19 positive or negative, by just uploading the CXR image onto the CADx.

Related work

The use of deep learning (DL) in the healthcare sector and other image related tasks has increased exponentially over the last decade[12]. DL models have been shown to help classify Computed Tomography (CT) scans of pneumonia and Tuberculosis (TB), malignant cancer pictures, diabetic retinopathy, microbiological slide images, and many pattern/object recognition problems in various studies8,10. Pathologists, computer scientists, and radiologists work together in the field of pathology to diagnose diseases such as cancer, pneumonia, and tuberculosis using computer-assisted diagnostics.

Recent developments in a number of medical image-processing tasks involved algorithms that have outperformed using deep learning models and on enormous datasets. Some examples include the Classification of skin cancer5, the detection of diabetic

retinopathy[15], etc. Automatic diagnosis is gaining popularity through chest radiography[7]. These algorithms are increasingly being used to detect pulmonary nodules and classify pulmonary tuberculosis. Using the published Open dataset, researchers have discovered that the same deep convolutional network design does not work for all anomalies; ensemble models outperform single models in classification accuracy, and deep learning improves classification accuracy dramatically. A method presented in is superior to the rule-based methods[13]. Many other applications also used training-based system for recognition[8,9] and classification purpose with the help of machine learning algorithms like artificial neural network (ANN)[6], convolution neural network (CNN). The CNN are used for optimizing the performance to enhance the models by changing hyperparameters and hidden layers. The problem of dealing with overfitting and model normalization during model training are generally done using dropout and batch normalization respectively[10,11].

Materials and methods

The results of extensive tests and assessments carried out to determine the viability of the suggested approach are reported in this study. To design and train the Convolutional Neural Network Model, we have used Keras, a deep learning framework that is open-source with a Tensor Flow API. All experiments are performed on a typical personal computer (Windows 10, 64-bit, CPU) equipped with graphics processing unit (GPU) and a Google Colab Notebook.

Datasets

The COVID-19 chest X-ray dataset[4] containing 2295 images is used in the study[1]. The original dataset is divided into two main folders (training and testing) and two subfolders containing Covid-19 Positive and Non-Covid chest X-ray images, respectively 2295 CXR images were obtained which included 712 COVID-19 positive and 1583 normal. For experimental purposes, images are split as 80% for training and 20% for validation. Each of the training set validation set and the testing set contains the subdirectories as COVID-19 and normal. The COVID-19 folder contains the COVID X-ray images, while the normal directory contains the negative X-ray images.

Pre-processing and Augmentations

To ensure that the datasets grew in size and quality, we used a variety of data augmentation techniques. This helped in reducing overfitting tribulations and enhances our model's overview aptitude while training. **Table I** presents the configurations used for image augmentation.

Firstly, well rescale of the data is done by a factor of 1/255. That will help us to do the normalization. We then divided our training into 20% of the validation set. In order to do that, we used the validation split constraint.

Parameter	Value
Rescale	1/255
Validation_split	0.2
Zoom Range	0.2
Horizontal Flip	True

The Model

Input Image
The accumulated input image is set for pre-processing to make the model's execution effective. To maximize the datasets, data augmentation techniques are used. Physical data collection is complex due to the COVID19 global pandemic[6]. The augmented data is sent to the preceding convolution to retrieve essential elements.

Convolution steps
Convolutions extract local aspects from large input data sets and multiply the resulting NxN matrices. Conv2D uses filters, kernel size, input shapes and activation functions for image classification1. In this study domain, the values of the variables are already stated in **table I**.

Max Pooling Layer
In advanced learning algorithms, max-pooling reduces dimensionality and extracts maximum features. The pooling layer reduces the number of variables and regularizes overfitting by finding the average of the provided elements[6].

Fully Connected Layer
It plots pooling layers, flattened and fed into the subsequent layer. The fully connected layer is essential for classification in CNN. The following classification outcome is performed with the aid of the activation function (sigmoid, Dense). The summary of layers of the proposed network architecture (CNN model) is shown in **Figure 1**.

For the mining of features from the input image, we used a modus operandi identified as convolution. The input is fed to the conv 2d block, after which ReLU (Rectified Linear Unit) is applied, followed by MaxPooling and lastly the dropout regularization. After this, the convolution is repeated but with more filters i.e., flattening them using the final layer into a one-dimensional array, which is heading to a fully connected layer.

Finally, an opaque (dense) layer with a sigmoid activation utility is deployed. So, in short, we feed the image into the conv2d for feature extraction. And lastly, that information is fed to the tightly connected artificial neural network. Supply forward neural architecture's output is presented in **figure 2**.

Figure 2: Training of the model.

Figure 1: The architecture of the proposed CNN.
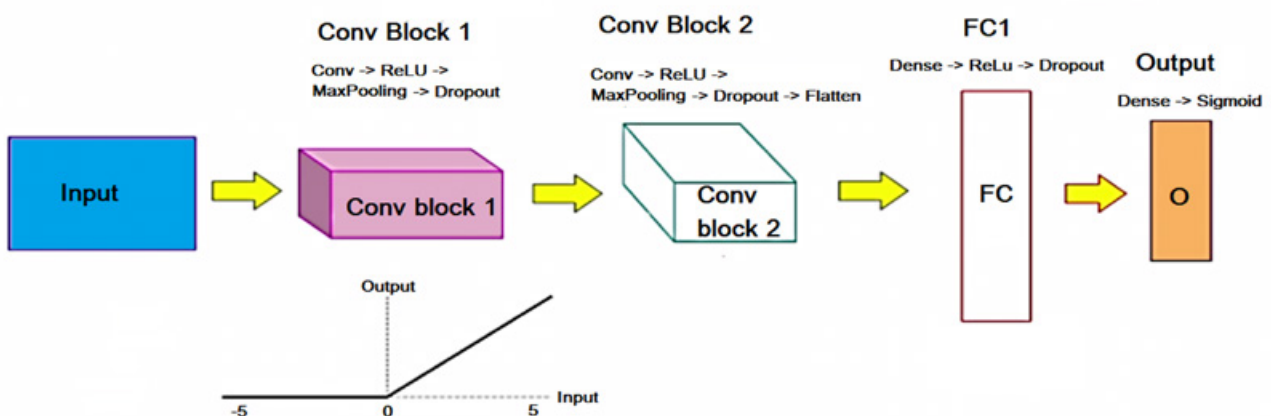
Results

For the compilation of the model, we used Adam Optimizer with learning at a pace of 0.001. After that, we had to train our model for 30 epochs on all of the training images that we had. So, when we trained the model, four values per epoch were lost. The precision and loss of training data are very useful in assessing the effectiveness of training.

Figure 3: Training and validation loss.
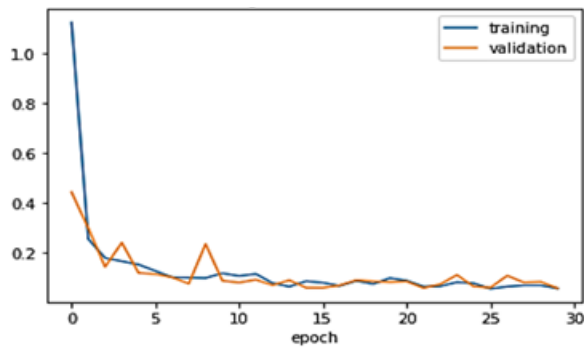
Figure 4: Training and validation accuracy.
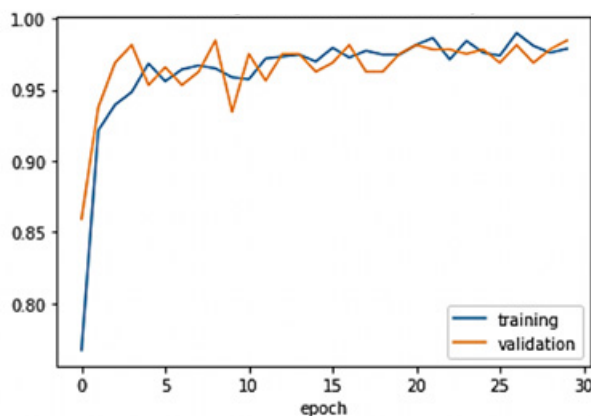
Figure 5: Test accuracy and test loss.
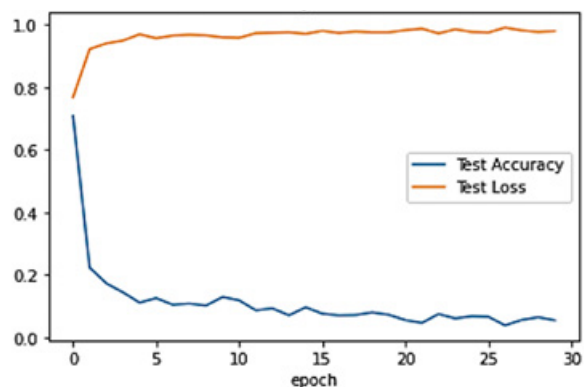
The accuracy, on the other hand, is the percentage of right guesses, and the validation accuracy is the measurement using data that has not been used in training. After training, we need to know how the model performed during the training phase. We plotted two graphs, one for loss, and the other one for accuracy (as shown in **figures 3, 4** and **5**). The accuracy of our final training observed was 97%. The validation accuracy was around 98%, while the training loss was only 0.0677%. And the validation was 0.0372. Therefore, a good accuracy of the test of roughly 97% was achieved and the test loss was around 0.7071%.

Discussion

From the chest X-ray pictures acquired from front views, we build a model to detect and categorize pneumonia for Covid-19. This technique starts by shrinking the chest X-ray pictures to a fraction of their original size. The photos are then enhanced by a convolutional neural network framework, which extracts and classifies characteristics from the images. When compared to other approaches, our model's validation accuracy was marginally greater.

We had to redo the model's training process numerous times before getting the same results each time. This will benefit developing countries with a doctor shortage, such as the majority of African countries. Significant improvements could be made if we had access to patient and non-patient statistics from around the world; however, our system is constrained because of short of information.

Conclusion

From a series of X-ray scans, the study demonstrated how to distinguish between positive and negative Covid-19 patients. The proposed model is implemented from the ground up, which distinguishes it from existing systems that heavily rely on transfer learning. The model is light CNN as it uses less number of layers and resulting faster training over any graphics processing unit (GPU). The accuracy of model is also very good to predict the classification accurately. The presented research is going to be expanded in the near future to perceive and classify X-ray images of Retinal Image Analysis, Skin Cancer Detection and more like Brain analysis.

Interests Conflict
The authors declare no conflict of interest.

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ORIGINAL

Comparison of dialysis practice and medication prescription pattern in chronic kidney disease patients undergoing hemodialysis at tertiary care and private hospital, Pune, India

Comparación de la práctica de diálisis y el patrón de prescripción de medicamentos en pacientes con enfermedad renal crónica sometidos a hemodiálisis en un hospital de atención terciaria y uno privado, Pune, India

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Abstract

Background: Chronic kidney disease (CKD) is a worldwide public health problem associated with various complications. CKD patients undergoing hemodialysis have associated comorbidities and prescribing drugs rationally in these patients is a difficult task.
Objective: To evaluate the prescription pattern of chronic kidney disease patients undergoing hemodialysis in both hospitals.
Methodology: the study was carried out in a tertiary care and a private hospital for a period of nine months. Chronic kidney disease patients on maintenance hemodialysis for at least one month were included. Details like sociodemographic and clinical characteristics, past medication history, comorbidities, and current medications were noted in self-pre-designed Patient Proforma. Mean ± standard deviation and percentages and relevant statistical tests likethe Chi-square test was used.
Result: The majority of the patients belongedthe to middle socio-economic class in private hospital and the lower-middle classa in tertiary hospital. Maximum were unemployed (50.60%, 36%), married (90.36%, 88,%) and had high school qualification (62.65%, 45.33%). About 78 (93.97%) patients were covered with insurance/health scheme in tertiary hospital and 39 (52%) in private hospital. Hypertension was found to be the leading cause in tertiary and private hospital. Calcium channel blockers (77.10%, 53.30%) were highly prescribed in both hospitals. Erythropoietin (69.80%), calcium acetate (21.70%) an,d anti-diabetics (Insulin 10.84%) in tera tiary hospital, whereas newer and costlier drugs like Darbepoetin, Iron preparations, and Lanthanum carbonate were prescribed ina private hospital.
Conclusion: Socioeconomic status led to variation in prescription patterns among both hospitals as newer and costlier drugs like Lanthanum carbonate, Sevelamer, and Darbepoetin were prescribed only in private hospital.

Keywords: Chronic kidney disease, Hemodialysis, Polypharmacy, Prescription pattern, Socioeconomic status.

Resumen

Antecedentes: La enfermedad renal crónica (ERC) es un problema de salud pública mundial asociado a diversas complicaciones. Los pacientes con ERC sometidos a hemodiálisis presentan comorbilidades asociadas y la prescripción racional de fármacos en estos pacientes es una tarea difícil.
Objetivo: Evaluar el patrón de prescripción de los pacientes con enfermedad renal crónica sometidos a hemodiálisis en varios hospitales.
Metodología: el estudio se llevó a cabo en un hospital de atención terciaria y otro privado durante un periodo de nueve meses. Se incluyeron pacientes con enfermedad renal crónica en hemodiálisis de mantenimiento durante al menos un mes. Se anotaron detalles como las características sociodemográficas y clínicas, los antecedentes de medicación, las comorbilidades y la medicación actual en un formulario de paciente de diseño propio. Se utilizaron la media ± desviación estándar y los porcentajes, así como pruebas estadísticas pertinentes como la prueba de Chi-cuadrado.
Resultados: La mayoría de los pacientes pertenecían a la clase socioeconómica media en el hospital privado y a la clase media-baja en el hospital terciario. La mayoría estaban desempleados (50,60%, 36%), casados (90,36%, 88,%) y tenían estudios secundarios (62,65%, 45,33%). Alrededor de 78 (93,97%) pacientes estaban cubiertos por un seguro o plan de salud en un hospital terciario y 39 (52%) en un hospital privado. Se observó que la hipertensión era la causa principal en los hospitales terciarios y privados. Los antagonistas del calcio (77,10%, 53,30%) se prescribieron con mayor frecuencia en ambos hospitales. La eritropoyetina (69,80%), el acetato cálcico (21,70%) y los antidiabéticos (insulina, 10,84%) se prescribieron en el hospital terciario, mientras que los fármacos más nuevos y costosos, como la darbepoetina, los preparados de hierro y el carbonato de lantano, se prescribieron en el hospital privado.
Conclusiones: El nivel socioeconómico provocó variaciones en los patrones de prescripción de ambos hospitales, ya que los fármacos más nuevos y costosos, como el carbonato de lantano, el sevelamer y la darbepoetina, sólo se prescribieron en el hospital privado.

Palabras clave: Enfermedad renal crónica, Hemodiálisis, Polifarmacia, Patrón de prescripción, Nivel socioeconómico.

Introduction

Worldwide there has been an upward trend in the incidence and prevalence of chronic kidney disease (CKD) prompting increased cost of treatment with poor outcomes[1]. CKD patients going through maintenance hemodialysis have associated comorbidities like hypertension, diabetes mellitus, anemia, acid-base balance, and electrolyte disturbances etc[2]. The primary Objectives in CKD patients on maintenance hemodialysis are treatment of the complications and avoidance of morbidity and mortality[3]. The patients of CKD have one of the greatest daily pill burden[4]. Inappropriate utilization of medications can increment adverse drug effects and cause excessive length of emergency clinic stays, medical care use, and costs. Chronic Kidney Disease (CKD) is currently recognized as a significant medical problem worldwide[5].

The Global Burden of Disease (GBD) concentrate on 2015 positioned chronic kidney disease as seventeenth among the reason for passings globally (Age-standardized yearly demise pace of 19.2 passings per 100,000 population)[6]. Albeit the exact incidence and prevalence rates are not accessible, it is assessed that one out of 10,000 people suffer from CKD in India and around 100 thousand new patients foster End Stage Renal Disease (ESRD) in India annually[7]. Chronic hemodialysis patients have various complications, for example, liquid maintenance, expansion in potassium levels, low hemoglobin levels, frail bones requiring pharmacologic therapy. Multiple medications are basically expected to control comorbid conditions like hypertension, diabetes mellitus and cardiovascular diseases. It can build the cost of treatment and likewise represent a challenge for the treatment of patients with CKD. Rebelliousness with drug regimens might expand the gamble of extreme complications and addresses an expected problem in hemodialysis patients who are on multiple medications. There are a few known indicators for multiple medications, i.e., age, female gender, low educational status[8]. Lower socioeconomic status is connected to bring down health education[9]. The distinction in the socioeconomic status might prompt variability in the prescription pattern among CKD patients. Thus, the purpose of this study was to obtain information about the prescription pattern in CKD patients undergoing hemodialysis and observe the variations among both the hospitals.

Methods

It was a prospective, observational study conducted on patients admitted to tertiary hospital and a private hospital, who are on antihypertensive and antidiabetic drugs. for nine months from September 2017 to May 2018. Patients having CKD and on maintenance hemodialysis for a minimum of 1 month were included in our study. Exclusion criteria included pregnant women on dialysis, age less than 18 years, patients who are being dialyzed for Acute Kidney Injury and patients who are being evaluated for renal transplantation. Ethical approval was obtained for the study from the institutional ethics committee. The details like sociodemographic and clinical characteristics, past medication history, comorbidities and current medications (Number of medications, dose regimen and frequency) were noted in the self-pre-designed Patient Proforma. Mean ± standard deviation and percentages was used for summarizing the data. Other relevant statistical tests Chi-square test was used for quantitative data and comparison of proportions. The P value < 0.05 was considered as statistically significant.

Results

Ethical approval was obtained for the study from the ethics committee of Bharati Medical College. patients having CKD who were undergoing hemodialysis for greater than one month were enrolled in this study. Patients informed consent was taken for the study. Mean ± standard deviation and percentages was used for summarizing the data, other relevant statistical tests Chi-square test was used for quantitative data and comparison of proportions. The P value < 0.05 was considered as statistically significance.

A total of 158 patients were included, from two hospitals in Pune of which 83 and 75 were from a tertiary and private hospital respectively, which satisfied the inclusion criteria. Majority of the patients in the private hospital were front the middle socio-economic class (80%) whereas, in the tertiary hospital subjects belong to lower-middle socio-economic class (100%) which was found to be statistically significant (/>-< 0,001). Highest number of patients were unemployed (50.60%, 36%). Married (90.36%, 88%). Higher school education qualification (62.65%, 45.33%), was found to be statistically significant (P = <0.001). About 78 (93.97%) patients were covered with insurance / health scheme in the tertiary hospital and only 39 (52%) were insured in the private hospital (P = < 0.001) (**Table I**).

Tabla I: Socio-demographic characteristics of CKD patient undergoing hemodialysis.

Characteristics	Number of patients (%)		Total
	Tertiary Hospital (n=83)	Private Hospital (n=75)	(n=158)
Gender			
Male	61 (73.49)	45 (60)	106 (67.09)
Female	22 (26.51)	30 (40)	52 (32.91)
Age (year)			
18-31	11 (13.25)	7(9.33)	18(11.39)
32-45	22 (26.51)	18(24)	40 (25.32)
46-59	25 (30.12)	24 (32)	49 (31.01)
≥60	25(30.12)	26 (34.67)	51(32.28)

The highest number of patients undergoing hemodialysis in the both the hospitals were found to be males (73.49%, 60%). The mean age in the patients undergoing hemodialysis in both the hospitals was 49.53 ± 15.09 years and 51.52 ± 14.53 years. Majority of the patients in the private hospital were from the middle socio-economic class (80%) whereas, in tertiary hospital subjects belonged to lower-middle socioeconomic class (100%) which was found to be statistically significant (P= < 0.001). The mean duration of dialysis was 2.71 ± 2.36 in tertiary and 3.21 ± 2.85 in private hospital. The frequency of twice weekly dialysis was highest in tertiary hospital whereas thrice weekly in private hospital (**Table I**). Hypertension (100%, 89.06%) was the commonest comorbidity followed by diabetes plus hypertension (35%, 31.25%) in both the hospitals (**Table II**). The total number of medications prescribed in 158 patients was 1262 out of which 623 were from tertiary hospital and 639 from private hospital. The average numbers of drugs per prescription from tertiary and private hospital were 7.51± 2.09 and 8.52 ± 1.35 respectively. Polypharmacy (use of ≥5 medications) was observed in 86.75% patients in tertiary hospital and 97.33% patients in private hospital. Anti-coagulants were given to all patients during hemodialysis.

Table III showed that in tertiary hospital 78.31% of the patients were undergoing twice weekly hemodialysis, whereas in the private hospital there were equal number of patients undergoing twice (48.00%) and thrice (50.67%) weekly hemodialysis. The average duration of hemodialysis in both the centers was 4 hours. About 51.81% of patients in the tertiary and 58.67% in the private hospital were undergoing hemodialysis for 1-5 years. Nearly all the Patients were vaccinated for Hepatitis B virus (HBV). Out of the anti-hypertensive drugs, calcium channel blockers were highly prescribed for the treatment of hypertension in both the hospitals (77.10%, 53.30%) (**Figure 1**).

Tabla II: Comorbidities of CKD Patients Undergoing Hemodialysis.

Characteristics	Number of patients		Total (n=144)	
	Tertiary hospital (n=83)	Private hospital (n=75)		
Co-morbid condition			Chi-square value	P-value
Present	80	64	0	0.34
Absent	3	6		
Hypertension	46(57.5)	35 (54.69)	81(56.25)	
Diabetes + Hypertension	28(35)	20(31.25)	4S (33.33)	
Diabetes Mellitus	0(0)	5(7.81)	5 (3.47)	
Hypothyroidism/ Hyperthyroidism m	0(0)	2(3.13)	2(1.39)	
Hypertension + Hypothyroidism	3 (3,75)	0(0)	3 (2,08)	
Hypertension + Diabetes+ coronary artery disease+ Hypothyroidism	1(1.25)	0(0>	1 (0.69)	
Hypotension + Diabetes+ coronary artery disease	I (1.25)	0(0)	1 (0.69)	
Hypertension + coronary artery disease	1(105)	I (1.56)	2(1.39)	
Hypertension + Diabetes + COPD	0(0)	1 (1.56)	1 (0.69)	

Chi-square test. * P < 0.05 is considered to be statistically significant.

Tabla III: Dialysis related characteristics of CKD patient undergoing hemodialysis.

	Number of patients				
Characteristics	Tertiary hospital (n=83)	Private hospital (n=75)	Total (n=158)	Chi-square value	P-value
Duration of dialysis per session (hrs.)	4 (hrs.)	4 (hrs.)			
Frequency of dialysis session per week Once Twice Thrice	6 (7.23) 65 (78.31) 12(14.46)	1 (1.33) 36 (48) 38 (50.67)	7 (4.43) 101 (63.92) 50(31.65)	25.07	<0.001*
Duration on Dialysis Less than 1 year 1 -5 years 6-10 years More than 10 years	30(36.14) 43 (51.81) 8 (9.64) 2(2.41)	19 (25.33) 44 (58.67) 11 (14.67) 1 (1.33)	49 (31.01) 87 (55.06) 19(12.03) 3(1.90)	2.89	0.408
Interdialytic Weight Gain Less than 1kg 1-2 kg 2-3 kg 3-4 kg >4 kg Nil	12(14.46) 18(21.69) 25 (30.12) 15(18.07) 5 (6.02) 8 (9.64)	8(10.67) 19(25.33) 25 (33.33) 18(24) 5 (6.67) 0(0)	20(12.66) 37 (23.42) 50(31.65) 33 (20.89) 10(6.33) 8 (5.06)	1.1	0.894
Mean Ultrafiltration volume (ml)	2405.31 ± 1268.85	2964.48 ± 982.85			

Chi-square test. * P < 0.05 is considered to be statistically significant.

Figure 1: Anti-hypertensive Drugs Prescribed in CKD Patients Undergoing Hemodialysis.
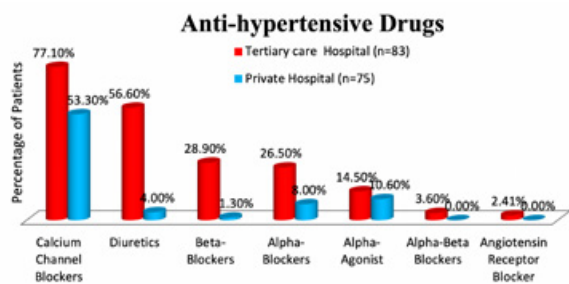
Figure 2: Anti-Diabetic Drugs Prescribed in CKD Patients Undergoing Hemodialysis.
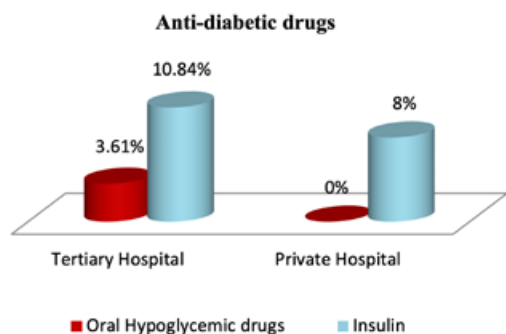
Figure 3: Phosphate Binders Prescribed in CKD Patients Undergoing Hemodialysis.
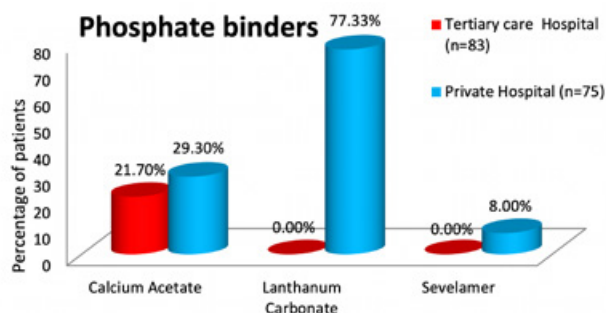
The most prescribed drugs in tertiary hospital were anti-hypertensive drugs (93.97%), hematopoietic agents (72.28%), Vitamins and mineral supplements (65.06%) and the least prescribed were anti-arrhythmic drugs (1.21%) and anti-thyroid drugs (1.21%). In private hospital, hematopoietic agents (97.33%), Vitamins and mineral supplements (94.66%) and phosphate binders (93.33%) were highly prescribed and least prescribed drugs were statins (2.66%).

Out of the anti-hypertensive drugs, calcium channel blockers were highly prescribed for the treatment of hypertension in both the hospitals (77.10%, 53.30%) (**Figure 2**). Among the Calcium Channel Blockers (CCBs), Amlodipine was most commonly prescribed both in tertiary (65.60%) and in private (92.50%) hospital. Other CCBs prescribed were Nifedipine, Cilnidipine and Barnidipine. Metoprolol was the commonest beta blocker prescribed for hypertension in tertiary

and private hospital (91.6% and 100% respectively). Hematopoietic agents used in tertiary and private hospital were Erythropoietin/Epoetin alfa (69.87% and 68.00%) and iron preparations (49.40% and 92.00%) respectively in parenteral forms. Iron preparations in tertiary hospital included iron sucrose 48.19% (Parenteral), ferrous sulphate 1.20% (Parenteral) and ferric citrate 1.20% (Oral) whereas in private hospital iron preparations include iron sucrose 92.00% (Parenteral) and ferric carboxylates 2.66% (Parenteral). The oral hypoglycemic drugs prescribed were 3.61% and 8% patients in tertiary and private hospital respectively (**Figure 2**). Insulin was slightly prescribed more in tertiary hospital 10.84% (n=9) than private hospital 8.00% (n=6). Among anti-secretory drugs, Proton Pump Inhibitors (PPIs) were more widely used than H2 blockers and antiemetics in both hospitals. The most commonly used PPIs were pantoprazole 84.60% (n=11) in tertiary and 95.20% (n=20) in private hospital. Phosphate binders were prescribed in the form of calcium and calcium free agents. Calcium Acetate was maximally prescribed in private hospital 22 (29.33%) than in a tertiary setting 18 (21.68%) (**Figure 3**). Lanthanum carbonate 58 (77.33%) and Sevelamer 6 (8.00%) was only prescribed in private hospital.

Discussion

The majority of the patients undergoing hemodialysis were males which showed a consistent pattern when contrasted with Sanjay K. Agarwal et al.[10] Manfred Hecking et al.[11] and Lakshminarayan et al.[12] who detailed similar results. Males showed higher risk factors like overweightness, having greater waist circumference and a raised circulatory strain which makes them more helpless against foster chronic kidney disease over a time of time[13]. On the contrary Lori L. Pounds et al. and Idan Goldberg et al. in their report expressed that the prevalence of CKD will in general be higher in women, while the movement of disease is more severe in men[13,14]. The mean age detailed in tertiary care hospital and confidential hospital were viewed as similar. Bernard Canaud et al. in his review expressed that elderly patients account for an increased fraction of patients on renal replacement treatment worldwide because of aging and underlying comorbidities (25%-30%)[14] hence justifying the higher number of our review subject belonging to the age group of 60 years and above (30.12%, 34.67%). In India hemodialysis is more preferred and is largely influenced by socioeconomic status and restricted insurance schemes[15]. In this review patients in confidential hospital were on threefold weekly hemodialysis, while in the tertiary care hospital they were on twice weekly hemodialysis significantly considering that a greater number of them had a place with the lower-center socioeconomic class, were jobless and economically depended on their family or insurance coverage for dialysis and medication use.

Length of dialysis was similar in both the hospitals. Similar results were published by Brian Bieber et al. which manifested higher number of patients reliant upon twice weekly hemodialysis[16].

Hypertension can be a reason or a consequence of chronic kidney disease and has been accounted for to occur in 85% to 95% of patients with chronic kidney disease (Stages 3-5) in the Unified States[17]. In present study, the medications were prescribed in light of the comorbid conditions and complications involved during the patient treatment. Numerous medications are an unavoidable predicament looked during the management of CKD patients because of the prevalence of co-existing illnesses. In present study, polypharmacy (utilization of ≥5 medications) was seen in 86.74% patients in tertiary hospital and 97.33% patients in confidential hospital. In a study by Chiu Y et al. the daily pill burden in the patients were extremely high and almost one-half of the patients were prescribed to take more than 20 pills daily[18]. The average number of medications prescribed in the present study was almost similar in both the hospitals. Enemies of coagulants were given during hemodialysis to all patients to prevent coagulation of blood during hemodialysis.

Hypertension is the most common comorbidity associated with chronic kidney disease (CKD) followed by diabetes. In this study, the counter hypertensive medications were significantly prescribed in tertiary hospital though hematopoietic agents were maximally prescribed in confidential hospital. The most commonly involved drugs for the treatment of hypertension were calcium channel blockers, followed by diuretics, beta blockers and alpha blockers in tertiary hospital while calcium channel blockers followed by alpha agonist, alpha blocker and diuretics were utilized in confidential hospital. All the antihypertensive medications were prescribed in oral dosage structure. Similar results were found in examinations conducted by Al Ramahi et al. Devi DP et al. and Bailie GR et al.[19-21] Among the Calcium Channel Blockers (CCBs), Amlodipine was most commonly prescribed to diminish blood tension for dialysis patients. Other CCBs prescribed were Nifedipine, Cilnidipine and Barnidipine in tertiary hospital though just Cilnidipine and Nifedipine were given in confidential hospital. Metoprolol was the commonest beta blocker prescribed for hypertension in both tertiary and confidential hospital in this study. Different medications utilized from this class included Nebivolol.

Diuretics were utilized commonly in about over half of the patients especially loop diuretics like Furosemide (74.5%) in tertiary hospital which is consistent with the examinations conducted by Al Ramahi et al. Ahlawat R et al.[19-22] Different classes of cardiovascular drugs prescribed were cardiac glycosides, anti-anginals, cholesterol lowering agents, antiarrhythmics. Cholesterol lowering agents like statins namely atorvastatin was prescribed more in tertiary than private hospital. In a study by AlRamahi et al.[19] around 47% of the patients were using serum lipid reducing agents mostly Lovastatin.

Anemia is the most common complication due to decreased erythropoietin secretion. In this study, hematopoietic agents utilized in tertiary and private hospital were Erythropoietin/epoetin alfa (EPO) and iron preparations separately which were viewed as higher than a study conducted by Ahlawat R et al.[22] and in a study by Al Ramahi et al.[19] where erythropoietin was under prescribed and higher frequency of blood transfusion were compounded. Iron preparations were exceptionally prescribed in private hospital than in tertiary hospital. Darbepoetin (DPO) was mostly prescribed in private hospital than tertiary hospital. As the maximum number of patients in tertiary hospital belonged to either lower/middle socioeconomic class, Erythropoietin was maximally given in both the hospitals. Notwithstanding, Santra S et al. and others, in their study revealed that hematopoietic agents like Erythropoietin and Darbepoetin were underused due to low patient compliance and high cost[23]. The prescription of water-soluble vitamin supplements is a regular practice in many dialysis units. Vitamins and minerals were prescribed maximally in private hospital. Folic acid was just utilized in private hospital (54.7%). Vitamin B complex was prescribed in both the hospitals. A new meta-analysis by Wang L et al. included observational and randomized investigations of vitamin D supplementation and concluded that on the basis of restricted proof, vitamin D supplements when given at moderate to high portions may lessen cardiovascular risk[24]. Vitamin D analogs namely calcitriol and alfacalcidol were maximally prescribed in private hospital and minimally prescribed in tertiary hospital. Combination of calcium carbonate with vitamin D 3 and vitamin B complex with iron was given exclusively in tertiary hospital. It was found that very few could afford the higher cost of vitamin D analogs, so a combination therapy with calcium was given to patients in tertiary hospital.

Hyperphosphatemia is a habitually seen complication in patients with End Stage Renal Disease (ESRD). Phosphate binders are prescribed to CKD patients in the type of calcium and calcium free agents. In the present study, calcium acetate was maximally prescribed as a phosphate binder in both the hospitals. One research also stated that calcium acetate ought to be considered the calcium-based binder of decision in the management of uremic hyperphosphatemia. A study by Galani V et al. proposed that calcium acetate can be utilized for patients of lower socioeconomic status with hyperphosphatemia and hypocalcemia similar to present study[25]. The significant expense of treatment of Sevelamer hydrochloride and Lanthanum carbonate makes it more expensive for a decent extent of the Indian population. Calcium supplements are more affordable because of

minimal expense when compared to Sevelamer. In the present study, Lanthanum carbonate and Sevelamer were just prescribed in private hospital. The significant expense of Sevelamer hydrochloride can restrict its utilization for the poor socioeconomic population in this manner just prescribed in private hospital. Hyperglycemia is a fundamental cause of vascular target organ complications, including Diabetic Kidney Disease (DKD) and there is a greater requirement for stricter glycemic control in diabetic patients undergoing dialysis to prevent hypoglycemic episodes. Insulin was prescribed more in the two hospitals as compared to oral hypoglycemic drugs which was consistent with a study carried out by Zaman Huri H. et al. where in excess of a half of diabetic patients with CKD were prescribed with insulin for their glycemic control[26]. In this study, Meglitinides and DDP-4 inhibitors were the class of drugs preferred in tertiary hospital rather than a study where no monotherapy involving DPP-4 inhibitors were seen in the study population by which they were prescribed other anti-diabetic combinations. Regular insulin and Isophane insulin were equally prescribed in both the hospitals whereas combinations of Insulin Neutral Protamine Hagedorn (NPH) (half) + Insulin Regular (half) and Human Insulin (30%) + Human Isophane Insulin (70%) were preferred in tertiary hospital.

Among anti-secretory drugs, Proton Pump Inhibitors (PPIs) were more widely used than H2 blockers and antiemetics in both hospitals. The most commonly used PPIs were Pantoprazole 84.6% (n=11) in tertiary and 95.2% (n=20) in private hospital. Apart from Pantoprazole, Rabeprazole was prescribed in tertiary hospital whereas Esomeprazole was prescribed in private hospital. In the tertiary hospital, majority of the patients belonged to lower middle socioeconomic class and were covered under insurance/ health scheme. Hypertension was the most common cause of CKD and also the highest co-morbidity reported. Presence of multiple comorbidities led to polypharmacy in both the hospitals. Newer and costlier drugs like Lanthanum carbonate, Sevelamer and Darbepoetin were more prescribed in private hospital than tertiary hospital where Calcium acetate and Erythropoietin was prescribed. Hematopoietic agents, vitamin and mineral supplements were majorly prescribed in both the hospitals, which were followed by prescription of anti-hypertensives in tertiary hospital and phosphate binders in the private hospital. Prescribing pattern of private hospital, where newer and costlier drugs were prescribed, varied from tertiary hospital based on the socioeconomic status of the patients.

Conclusion

In the tertiary hospital, majority of the patients belonged to lower middle socioeconomic class and were covered under insurance/ health scheme. Hypertension was the most common cause of CKD and also the highest co-morbidity reported. Presence of multiple comorbidities led to polypharmacy in both the hospitals. Newer and costlier drugs like Lanthanum carbonate, Sevelamer and Darbepoetin were more prescribed in private hospital than tertiary hospital where Calcium acetate and Erythropoietin was prescribed. Hematopoietic agents, vitamin and mineral supplements were majorly prescribed in both the hospitals, which were followed by prescription of anti-hypertensives in tertiary hospital and phosphate binders in the private hospital. Prescribing pattern of private hospital, where newer and costlier drugs were prescribed, varied from tertiary hospital based on the socioeconomic status of the patients.

Consent for publication
Not applicable.

Availability of data and materials
The data that support the findings of this study are available within the article.

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Conflict of interest
The authors declare no conflict of interest, financial or otherwise.

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Comparison of dialysis practice and medication prescription pattern in chronic kidney disease patients undergoing hemodialysis at tertiary care and private hospital, Pune, India

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ORIGINAL

Estudio cualitativo a través de grupos focales sobre la factibilidad de una intervención en automanejo de la Hipertensión Arterial

Qualitative study through focus groups on the feasibility of an intervention in self-management of Arterial Hypertension

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Resumen

Introducción: La Hipertensión Arterial (HTA) es uno de los principales factores de riesgo cardiovascular (FRCV), siendo un problema de salud relevante. El grado de control deficitario, podría mejorarse mediante mayor implicación de los pacientes a través del autocontrol y automanejo.
Objetivos: Valorar la factibilidad del automanejo de la HTA por los pacientes.
Métodos: Técnica de 2 grupos focales (GF), uno de profesionales sanitarios y otro de pacientes.
Resultados: Existe margen de mejora en las expectativas de educación en HTA entre profesionales y pacientes. Ambos coinciden en utilización de medidas no farmacológicas además de medicación pautada. La aceptación del automanejo es generalizada por ambas partes siendo necesarias medidas de cambio organizativo y elementos de soporte.
Conclusiones: Aceptación generalizada sobre la viabilidad del automanejo si bien las necesidades detectadas entre profesionales y pacientes son diferentes. Ambos grupos manifiestan la necesidad de reforzar e intensificar la educación sanitaria a los pacientes.

Palabras clave: Hipertensión arterial, automanejo, adherencia.

Abstract

Introduction: Hypertension Blood Pressure (HBP) is one of the main cardiovascular risk factors (CVR), being a very relevant health problem. The degree of deficient control could be improved through greater involvement of patients through self-control and self-management.
Objectives: To assess the feasibility of self-management of HBP by patients.
Methods: Technique of 2 focus groups (FG), one of health professionals and another of patients.
Results: There is room for improvement in expectations regarding education on HBP among professionals and patients. Both agree on the use of non-pharmacological measures in addition to the prescribed medication. The acceptance of self-management is widespread by both parties, although organizational change measures and support elements are necessary.
Conclusions: There is widespread acceptance of the feasibility of self-management, although the needs detected between professionals and patients are different. Both groups express the need to reinforce and intensify health education on HBP for patients.

Key words: Hypertension blood pressure, self-management, adherence.

Introducción

La hipertensión arterial (HTA) es un factor de riesgo tratable responsable en gran proporción de la morbimortalidad cardiovascular. En España 58% de varones y 61% de mujeres no la controlan[1]. La mortalidad atribuible se ha duplicado en la última década[2].

Los factores que perpetúan su mal control son inercia terapéutica, estilos de vida no saludables y fármacos que la elevan. La falta de adherencia es un factor clave[3]. La atención a las enfermedades crónicas que se centra en el paciente y la autogestión se ha demostrado efectiva[4]. Los pacientes deben adoptar un estilo de vida saludable y tomar su tratamiento para ser agentes activos en su cuidado. Los profesionales sanitarios deben motivar, supervisar y corregir este proceso[5,6].

La automonitorización y automanejo de la tensión arterial (TA) pueden ser los siguientes pasos efectivos[7]. Un ensayo aleatorizado demostró efectividad de la autogestión combinada con telemonitorización[8]. Nuestro estudio tiene como objetivo explorar las opiniones, barreras y facilitadores para su implementación.

Material y métodos

Utilizamos la técnica de grupos focales (GF) para explorar las opiniones y detectar barreras y facilitadores para la implementación del autocontrol y automanejo de la TA mediante grupo de pacientes y grupo de profesionales siguiendo el modelo recopilado de distintos autores por Escobar y Bonilla-Jiménez[9].

Objetivos:
- Grupo profesionales:
  Valorar factibilidad de un programa de automanejo de la HTA.
  Conocer dificultades para profesionales y pacientes.
  Explorar opinión sobre propuesta del estudio y oportunidades de mejora.

- Grupo pacientes:
  Valorar factibilidad de un programa de automanejo de la HTA.
  Conocer experiencias previas de automanejo.
  Explorar beneficios que les implicaría.
  Explorar opinión sobre propuesta del estudio y oportunidades de mejora.

Selección participantes:
Profesionales: seis médicos y enfermeras, expertos en HTA o enfermedades cardiovasculares, o interesados en participación de pacientes y toma de decisiones compartida. **Pacientes:** seis pacientes con HTA, enfermedades cardiovasculares, con diabetes, o "pacientes expertos" en patologías crónicas.

Desarrollo:
2 GF de 1h y 45 minutos de duración cada uno con guion estructurado de acuerdo con los objetivos del estudio. GF de profesionales: 1) conocimientos de los pacientes, 2) realización del tratamiento y, 3) viabilidad del automanejo. GF de pacientes: 1) conocimientos generales, 2) tratamiento, 3) toma de TA y 4) automanejo. Sesiones grabadas con consentimiento verbal de los asistentes.

Análisis:
Transcripción del contenido, identificación por pares de los verbatims representativos, puesta en común y clasificación por categorías.

Resultados

Características GF:
Pacientes: 6 hombres, 4 jubilados y 2 en activo. Edad entre 55 y 85 años, estudios medios (uno universitario). **Profesionales:** 6 participantes, 3 médicas, 2 enfermeras y 1 enfermero. Edad entre 33 y 65 años.

A. GF PACIENTES

1. Conocimientos sobre HTA

1.1 Conocimientos generales
Relacionaron buen control con estilos de vida saludable (incluida actividad laboral), actitud proactiva ante la enfermedad y ejercicio. Uno restaba importancia a la enfermedad mostrando actitud pasiva. Identificaron un componente hereditario en la HTA.

1.2 Parámetros normales
Tres desconocían los parámetros normales y tres referían cifras aproximadas a las de normalidad.

1.3 Síntomas relacionados
Relacionaron Mareos, vértigos y cefalea con aumento y sensación de debilidad con descenso.

1.4. Cifras de alarma
Mostraron Preocupación por cifras iguales o superiores a 180 mmHg.

2. Tratamiento

2.1 Tratamiento antihipertensivo
Conocían su medicación, la preparaban y se la administraban. Algunos habían detectado efectos secundarios.

2.2 Otros fármacos e interacciones
Dos refirieron interacciones con antiinflamatorios con

elevación de la TA. Uno mencionó su tratamiento inmunosupresor (trasplantado renal) como más importante que el antihipertensivo.

2.3 Tratamiento no farmacológico
Dieta sin sal y ejercicio para el control. Medidas "naturales", el limón y ajo crudo. Estrés como factor de aumento tensional y relajación como ayuda al control.

3. Toma de TA

No dificultades para la autotoma que realizan todos excepto uno (se la toma su hija, sanitaria). Toma sentados o tumbados, brazo apoyado. Frecuencia: desde varias veces al día, al mes o al año. Usan tensiómetro de brazo.

4. Del automanejo

4.1 Automanejo no reglado
Algunos disminuyen dosis en verano por síntomas experimentados (debilidad), otros consultan a su médico.

4.2 Viabilidad del automanejo reglado
Algunos lo ven viable con indicaciones claras, apoyo y seguimiento, otros lo consideran función del médico. Demandan un sistema de comunicación rápida (línea telefónica) para dudas.

La edad avanzada, medicación compleja o personas que vivan solas, suponen barreras.
Todos con disposición a incorporarse al estudio.

A. GF PROFESIONALES

1. Sobre conocimientos de la HTA

1.1 Conocimientos generales
La capacidad intelectual, nivel cultural, edad, autorresponsabilidad y tiempo de evolución de la enfermedad pueden incidir en el conocimiento de la enfermedad. Poco conocimiento sobre cifras de normalidad.

1.2 Importancia de la enfermedad y factores de riesgo cardiovascular (FRCV)
Frecuente banalización de la enfermedad y desconocimiento o poca conciencia de FRCV. Ser asintomática favorece que se le reste importancia.

1.3 Oportunidades de mejora
Destacaron la importancia de la consulta individual y de grupos sobre HTA. Necesidad de reflexión sobre formas de trabajo y relación sanitario-paciente. Uno mencionó la iniciativa del "paciente experto".

2. Tratamiento

2.1. Farmacológico
La mayoría de pacientes salvo excepciones (gente mayor), se preparan y administran los fármacos. Dificultades: polimedicación y falta de conciencia del riesgo. Repasan medicación con sus pacientes, la falta de tiempo puede dificultarlo. Efectos secundarios más referidos tos y edemas.

2.2 No farmacológico
Los pacientes dan más importancia a la medicación que a las medidas no farmacológicas y mayor importancia a la dieta hiposódica que al ejercicio y cambios en estilos de vida (reducción del estrés y horarios de descanso). Los pacientes comentan medidas "naturales" y no farmacológicas que aplican.

3. Automanejo

3.1 Percepción actual del automanejo
Pocos modifican su medicación por iniciativa propia. Dificultades para la automonitorización de la TA por parte del sanitario (requiere tiempo) y del paciente. Duda de la mayoría sobre calibración de tensiómetros.

3.2 Viabilidad del automanejo
Consideraron viable el automanejo con excepciones (edad avanzada, deterioro cognitivo y situación económica precaria). Necesidad de poder pedir ayuda, y de cambios en la organización de atención primaria. Riesgo de disminución de la adherencia por desmotivación. Demostrando la eficiencia del automanejo se extenderá su práctica.

Discusión

Diferencias en las expectativas sobre educación y apoyo ante la enfermedad, los profesionales demandan educación grupal mientras que los pacientes se decantan por una línea telefónica para dudas tras formarse en consulta individual.

Los profesionales opinan que los pacientes dan mayor importancia a la dieta hiposódica que al ejercicio y cambios en los estilos de vida; en cambio, los pacientes resaltaron el ejercicio, los estilos de vida como medidas para controlarla y destacaron el estrés laboral como dificultad en el control.

Actualmente pocos pacientes ajustan el tratamiento según síntomas.

Satisfacción del grupo de pacientes por haberles convocado a la reunión y solicitud de reuniones periódicas.

Se detecta buena aceptación, con apoyo, por parte de pacientes y profesionales al igual que Zamanillo et al en diabetes mellitus[10,11]. Nuevas herramientas tecnológicas de comunicación podrían facilitar este automanejo[8].

Se identifican dificultades y necesidad de cambios organizativos en el sistema sanitario como en el estudio de Magueo et al[12].

Conclusiones

Aceptación generalizada sobre la viabilidad del automanejo si bien las necesidades detectadas entre profesionales y pacientes son diferentes.

Ambos grupos manifiestan la necesidad de reforzar e intensificar la educación sanitaria a los pacientes.

Conflicto de intereses
Los autores declaran no tener conflicto de intereses.

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ANEXO

VERBATIMS GRUPO FOCAL DE PROFESIONALES

1. Sobre la HTA

1.1 Conocimientos generales
- Creo que dependerá del conocimiento que tenga el enfermo, también de su nivel de entendimiento (**Capacidad intelectual**).
- El conocimiento varía algo si es un enfermo que hace muy poco que ha sido diagnosticado o es un enfermo reciente, y también puede variar en función de las otras patologías que pueda tener (**Tiempo de enfermedad**).
- Sobre todo, de los que llevan muchos años con el diagnóstico, estos si les pidiéramos ahora ¿qué es esto? ¿O qué significa esto? No sé si sabrían que quiere decir. Alguno te diría que puedo tener una embolia, pero poco más (**Tiempo de evolución de la enfermedad**).
- Depende mucho de la edad, del paciente, del nivel cultural que tiene, y también quiero decir, tienes sorpresas (Edad y nivel cultural)
- Está a 13 y 8 y todavía no saben si esto es normal o no lo es (**Poco conocimiento sobre cifras de normalidad**).
- Te llevas sorpresas, no todos saben lo que deben saber, ni hacen lo que deben hacer, pero bueno, aquí también está que la salud es del paciente. Quiero decir, que se banaliza un poco el tema de los controles de tensión arterial y puede ser, se toma como un juego (**Autoresponsabilidad del paciente**).

1.2 Importancia de la enfermedad y factores de riesgo cardiovascular (FRCV)
- Ah, el vecino tiene hipertensión, el primo, el tío, el hermano, la abuela, y se resta importancia a lo que es la patología crónica que puede llevar a unas consecuencias graves al largo del tiempo si no se controla bien (**Frecuente banalización**).
- Porque si un día tú tienes una consulta tranquila, pues le explicas: mire, usted es hipertenso tiene un tanto por ciento de riesgo para hacer un problema cardiovascular, si no lo fuera, sería ese otro tanto por ciento (**Desconocimiento de FRCV**).
- Pero claro, si haces un diagnóstico con 40 años, está trabajando, no nos coinciden los horarios, tengo cosas mejores que hacer, esto no duele, no pica, me ha dado la pastilla (**Poca conciencia de FRCV**).
- No produce ninguna sintomatología, no produce dolor (**Enfermedad asintomática**).

1.3 Oportunidades de mejora
- Hacer sesiones formativas sobre patologías para los pacientes hipertensos, como grupos, pero de formación y de práctica de mirarse la tensión y de conocimientos con el tensiómetro…todo esto, coges 15 o 20 pacientes hipertensos, la enfermera, el médico, le dan una charla y esto va penetrando. Lo haces periódicamente, cada mes una charla de hipertensión y el paciente podría ir, volver a repetirla, quiero decir que es mucho más eficiente que en cada consulta tener que dar toda la información. (**Educación sanitaria individual y en grupos**).
- Y al paciente le cuesta, es verdad, cuando tú le cambias poquito el chip de "venga cada mes", pero después de mucho trabajarlo , se dan cuenta y luego te dicen "vale, ya nos vemos dentro de tres meses, si tengo cualquier cosa antes, ¡ya vendré a verla! (**Consulta individual y relación sanitario-paciente**).
- Hemos llevado una inercia, unas formas de actuar, hemos pasado de esta medicina más del médico… paternalista, de que el paciente va allí y "hágame usted" y debemos cambiar un poco el chip, una medicina más centrada en los pacientes, más enfocada en la educación, más eficiente, y dejar de hacer cosas, porque se pueden hacer otras (**Necesidad de reflexión sobre formas de trabajo**).
- Tiene que haber un feedback (**relación sanitario-paciente**).
- Pues lo mismo, cursos de formación de cuatro patologías, con EPOC, existe también paciente experto, que se pudiera incluir dentro de una de estas sesiones, que fuera el propio paciente quien dé un poco de charla también, que les gusta mucho a los demás (**Paciente experto**).

2. Tratamiento

2.1 Farmacológico
- En la gente de mayor edad probablemente habrá un tanto por ciento mayor que les prepara la farmacia, pero la otra parte de la gente sí. (**Edad avanzada**).
- Si tomas muchos medicamentos, complica más las cosas. (**Polimedicación**).
- ¡Con la hipertensión están más contentos de que les des una pastillita, así la tensión ya la tengo controlada y "ancha es Castilla!" (**Falta de conciencia del riesgo**).
- Tos (IECAS), edemas (Amlodipinio): "lo que te comentan ellos tos y se me hinchan los pies" (**Efectos secundarios**).
- Habitualmente si, dificultades por tiempo: tú revisas y dices "¡tú esto lo tienes caducado de hace 6 meses!" No, pero yo lo voy a comprar. (**Repasan la medicación con los pacientes, la falta de tiempo puede dificultarlo**).

2.2 No farmacológico
- Farmacológico con el control de la hipertensión (**Mayor importancia a la medicación**).
- Es verdad que vinculan mucho ya la dieta hiposódica

con el control de la hipertensión, porque supongo que ha habido mucho mensaje hace muchos de años, pero en cambio no entienden el ejercicio físico (**Consideran más efectiva la dieta hiposódica, que el ejercicio y los cambios en el estilo de vida**).

- Limón, olivo. "Yo todas las mañanas me bebo medio vaso de agua con limón" "Olivo" (**Comentan o piden sobre medidas "naturales" y no farmacológicas que aplican**).

3. Automanejo

3.1 Percepción actual del automanejo

- Hay alguno, poquitos, que empiezan a afinar algo. A lo mejor, porque ha tenido otras patologías y en un momento determinado se han aumentado varios fármacos, además se ha añadido y después ha bajado un poco y vuelve a incorporar otros hábitos y va viendo que tiene unas tensiones muy bajas y se marea... y luego he quitado esa media pastilla y viene y te lo cuentan. Es verdad que hay pocos todavía de éstos, son los buenos" (**Pocos modifican su medicación por iniciativa propia**).
- Dificultades por el paciente, por el sanitario: "Si lo hacen bien, da igual si es joven o viejo, a mí lo que me crea una duda siempre es si calibran o no sus aparatos de tensión, si van a algún sitio o yo se lo tengo que recomendar, porque claro, si tú lo dices, lo siguiente es ¿dónde lo hago? Y ¿qué hago? yo no lo sé, pero ¡si lo tienen allí de hace no sé cuántos años! ..." (**Dudas sobre calibración de los tensiómetros**).
- Tipos de paciente, tiempo, organización: Has de tener algo de tiempo y explicarlo. (**Dificultades para indicar AMPA**).
- Si se lo explicas no, hay que tomarla dos o tres veces... ah vale, pues ellos se quedan como tranquilos, ah, pues mira la verdad que la última estaba mejor (**Técnica de la toma**).
- A mí lo que me crea una duda siempre es si se calibran o no sus aparatos de tensión o si van a algún sitio o yo se lo tengo que recomendar (**Dudas sobre calibración de los tensiómetros**).
- Tenemos que saber qué aparato, en principio somos los profesionales los que tenemos que saber para poder recomendar el tipo de aparato (**Tipo de aparato**).

3.2 Viabilidad del automanejo

- Sí. Si tú te autocontrolas, te sabes autogestionar y sabes cuándo pedir ayuda, sabes cuándo ir a hacerte el control, lógicamente todo esto mejora. Mejoran ellos, mejoramos nosotros. (**Viabilidad del automanejo y necesidad de poder pedir ayuda**).
- Cambiar la estrategia por otra, con dinámica de funcionamiento dentro de los equipos de Atención Primaria. Dejar de hacer coses "tontas" para hacer cosas más...Se tiene que cambiar la organización,

puede que no sea necesario cambiar la organización de todo el centro a la vez (**Cambios en la organización de Atención Primaria**).

- Si es una persona muy mayor y tiene deterioro cognitivo o no lo entiende...esta persona ya no la podemos incluir en este grupo. La barrera económica ... (**Excepciones para el automanejo: edad avanzada, deterioro cognitivo y situación económica precaria**).
- El paciente no puede avanzar si nosotros no avanzamos (**Cambios en la organización de Atención Primaria**).
- Lo suyo es demostrar que esto es eficiente y una vez está demostrado, pues claro, ya vendes un poco la historia como que es más eficiente (**Demostrando la eficiencia del automanejo se extenderá su práctica**).
- Y también hay que entender que un paciente crónico es eso, un crónico. Llega a cansar y es verdad que se les hace cuesta arriba, y que en un momento dado necesitan una motivación. Sí, porque me la he mirado esta mañana y la tenía bien, no me he tomado la pastilla (**Riesgo de disminución de la adherencia por desmotivación**).

VERBATIMS GRUPO FOCAL PACIENTES

1. Conocimientos sobre HTA

1.1 Conocimientos generales

- Porque yo estoy trabajando, trabajo de noche o sea que llevo el horario cambiado. Y pienso que ha influido bastante con la tensión, quiero decir, el cambiar lo que es el propio sistema de vida, por mucho que te acostumbres, el cuerpo es el cuerpo, quiero decir las horas de descanso de la noche no son iguales que de día, todo esto creo que también me ha influido bastante en lo que tengo (**Estilos de vida incluida actividad laboral**).
- Debemos estar activos, no podemos ser pacientes pasivos y el decir "yo esto no lo haré porque...", ¡no, no, al revés! Pienso así (**Actitud proactiva y ejercicio**).
- Porque al final todos los que sufrimos la enfermedad somos quienes podemos ayudar a arreglarlo (**Actitud proactiva del paciente**).
- Sí, perdona, yo también estoy totalmente de acuerdo con esto, que hay que hacer algún deporte, andar... (**Ejercicio**).
- Porque no debemos perder de vista que una subida de tensión nos puede llevar al otro lado... (**Importancia de la enfermedad**).
- Bien, yo soy un perfecto ignorante con todo esto, nunca he detectado una subida de presión, estoy medicado, soy diabético, entonces si tengo una bajada de azúcar, sí me doy cuenta, pero una subida o una altura de presión nunca, ni me he tomado la

presión, tengo un "aparato" je je…está allá…y la verdad, entre un estudio que me hacen en la farmacia cada año y me dicen "¡va bien, fantástico!" y el optimismo que uno se apunta, pues ignorante total en cuanto a la presión, tomo sal, tomo de todo…y no je, je no lo detecto…así como el azúcar cuánto era a lo mejor más joven, sí me daba cuenta de que sudaba, un sudor….con la tensión yo no me he enterado de nada. (**Poca importancia de la enfermedad o actitud más pasiva del paciente**).

- Bueno Bueno pues, mi experiencia es que, bueno, de parte de la familia de mi madre, la madrina y eso, sabéis que dicen que vienen de antepasados ¿no?… (**Componente hereditario en la HTA**).

1.2 Parámetros normales

- No tengo ni idea (**Desconocen cifras de normalidad**).
- Mi normal era 14-7 (**Cifras aproximadas a las de normalidad**).
- Entonces, ¿cuál es un estándar de la presión correcto? Es que no tengo ni idea (**Desconocen cifras de normalidad**).
- 12-8 la última vez que recordaba, no sé si me dijeron que era baja…que 8 era bajo… (**Desconocen cifras de normalidad**).
- Sí, yo tengo bastante controlado el tema. La tensión cuando la tengo baja, baja son 11-6 y entonces estás de esa manera…bueno, ¡hoy no haré nada! Porque no tienes ganas de hacer nada. Y alta, yo he tenido desde 19-9 hasta 10. Sé los límites, dónde estoy en peligro hacia arriba y peligro hacia abajo (**Cifras aproximadas a las de normalidad**).
- Pero yo no sé ni qué… ¿qué es alto y es bajo? ¿Cuál es la tensión ideal? Yo no, no lo sé, yo he oído uno que te dice… pero no hay tampoco, ni los médicos lo dicen muy claro (**Desconocen cifras de normalidad**).

1.3 Síntomas relacionados

- Sí, pero tengo como mareo… ¡también tengo una especie de vértigo! (**Mareo y vértigo**).
- Respecto a los efectos de cuando uno tiene una subida de tensión o no, yo sí noto y lo noto con dolor de cabeza, de acuerdo, yo noto una presión en la cabeza diferente, un dolor de cabeza diferente al normal que uno suele tener cuando tiene dolor de cabeza. (**Dolor de cabeza**).
- Y bajadas también, notas…buff que dices y ahora que debemos hacer, que no tienes ganas de hacer nada y tal (**Debilidad**).

1.4 Cifras de alarma

- Es conveniente mirárselo básicamente para tener un control, porque si uno no tiene síntomas pues igual tiene la tensión a 19 y… a punto de un infarto y no lo sabe.(**Preocupación por cifras iguales o superiores a 180mm Hg**).

- Cómo me llegó a pasar en aquel tiempo, que aquello fue terrorífico, no sabía de dónde salía, yo soy jugador de billar y tenía un campeonato y estaba haciendo la final y me cogió un mareo que subió a 18 la presión, bueno, pasó, paró y seguí. (**Preocupación por cifras iguales o superiores a 180mm Hg**).
- Yo hasta los 50 años bien, pero de cumplir los 50 años fue… ¡buuu! Una subida de éstas fuertes. De ésas que, 22 y no sé qué, 10 y 22. Bien, a partir de ahí me puse a tomar ya una pastilla y, desde entonces no lo he abandonado. (**Preocupación por cifras iguales o superiores a 180mm Hg**).

2. Tratamiento

2.1 Tratamiento antihipertensivo

- ¡Sí, sí, sí! Tomo los medicamentos recetados por el Dr. Pou cambiados recientemente (**Conocen la medicación, la preparan y administran**).
- Tanto antes como ahora la tensión sí que me tiene, me tiene… quiero decir, no preocupado porque está controlada, pero sí tomo cuatro fármacos por el tema de la hipertensión (**Conocen la medicación, la preparan y administran**).
- ¡Venga, hoy no me he tomado las pastillas, normalmente no me pasa! Es decir, lo que hacía pam pam… me he tomado el medicamento (**Responsabilidad de tomar la medicación**).
- Yo también me la controlo, yo tengo el tenderete en casa hace muchos años y lo he llegado a controlar a diario (Conocen la medicación, la preparan y administran)
- El único medicamento que suelo tomar se llama "april" por la mañana y después por la noche (**Conocen la medicación, la preparan y administran**).
- No recuerdo el nombre de uno… que me bloqueaba las pulsaciones; ¿qué pasaba?, que yendo en bicicleta con este medicamento hacía unas medias de 104-105 y otras de 135 ni me cansaba y hacía kilómetros y kilómetros... el último año y medio aparte de haberme adelgazado 12 kg, me cambiaron este medicamento, me recetaron otro y he pasado de ir de pulsaciones ya de media 130-140. (**Reconocimiento de un efecto secundario de la medicación y pérdida de peso**).
- Sí que al principio tuve bastantes, bastantes que me hacían una reacción de mucho dolor de cabeza, eh… me acuerdo, creo que los probé todos eh…y en el trabajo…sí que me afectaba porque no podía de dolor de cabeza y eran unos efectos secundarios de estos medicamentos. (**Reconocimiento de un efecto secundario de la medicación**).

2.2 Otros fármacos e interacciones

- Me están vigilando porque he tenido una descompensación debido a un antiinflamatorio y me subió a 18 y 10 (**Interacciones con otros

medicamentos).

- A ver, es que también depende del antiinflamatorio, enantyum, ibuprofeno... Yo fue "arcoxia" que por lo visto es más fuerte. Y eso, pues me descontroló. (**Interacciones con otros medicamentos**).
- Yo estoy también medicado por depresión con ansiolíticos y tomo también "alsatin" de 1.5, y por la noche también tomo se "almodipino" y unas gotas por los ojos (**Toma de otros medicamentos**).
- Yo soy diabético, tomo insulina lenta por la mañana y por la noche, 30-20, la mañana tomo Adiro y después ya no tomo más que una "atovastatina" por la tarde (**Toma de otros medicamentos**).
- Bien, yo tengo también otro tipo de patología, tengo un trasplante renal y tomo varios tipos de medicamentos, tomo estos 4 por hipertensión cardipino eh...cardiuneo, carvedirol y más que no me acuerdo ahora. Yo tomo inmunosupresores por tema del rechazo, los más importantes son los del rechazo, evidentemente porque me garantizan la vida (**Inmunosupresores**).

2.3 Tratamiento no farmacológico

- Que es importante también el tema de poder controlarlo, controlarlo a través de lo que es, eh, el deporte dijéramos, a través de hacer bicicleta, bicicleta estática, con el programa de "Viajar" y vas por todo, pero no te mueves de sitio (**Ejercicio**).
- Ahora intento mirar cómo puedo hacer, bajar en un momento dado si tengo la tensión algo alta, lo que charlábamos de la sal, o según qué alimentos también ayudan e intentar controlar de esta manera. (**Dieta sin sal y otros alimentos a tener en cuenta**).
- Yo lo he notado muchísimo, es decir, el tema de la sal, también llevo 20 años sin utilizarlo, utilizo el mínimo, el mínimo, el mínimo... no utilizamos ya en nuestra casa (**Dieta sin sal**).
- El utilizar remedios naturales como es el zumo de limón, que baja la tensión, hacer deporte y tal, pero bueno, creo que debería, deberíamos poder compensar un poco la medicación y tomar cosas más naturales en todo... (**Remedios naturales que ayudan a controlar la TA**).
- ¡Un diente de ajo pisado y un vaso de agua detrás, en ayunas! (**Remedios naturales que ayudan a controlar la TA**).
- Cosas, así como por ejemplo hacer relajación o meditación, o algo así, técnicas orientales, eh... lo de... eh respirar (**Otras medidas, relajación**).
- La verdad que hay dos épocas en la tensión, hasta que hice trabajo, y la otra, la situación de ahora que cada día, o día sí día no, hago deporte, y los demás voy a mi pueblo, yo estoy en María de la Salud y estoy muy bien (**Estrés laboral**).
- Yo lo hice una época y el estrés del trabajo me implicaba: ahora clientes, comidas, fiestas, beber, dedicación. Mi profesión me ha gustado toda la vida

hacerla, la vivía día y noche, porque era, era la fuente de ingresos de la casa y era lo que me gustaba hacer. Claro, ahora que he podido comprobar que llevando otro tipo de vida me ha estado bajando mucho, mucho las tensiones (**Estrés laboral**).
- Yo soy hipertenso de hace 2 años, prácticamente hace poco, hace 2 años que yo lo sé, o sea a lo mejor lo era y no me enteraba. Lo que estábamos charlando antes, por motivos de trabajo, trabajo, trabajo, iba a casa, dormía y hacía trabajo, o sea diga un ritmo.... Trabajo y dormir, dormir y trabajo... y no me enteraba, hasta que en una revisión de su trabajo me dijeron "tiene la tensión un poco alta, debería ir al médico a que la mirarán" (**Estrés laboral**).

3. Toma de TA

- "Sí, es muy sencillo, no hay complicaciones" (**los demás asienten**)   (**No dificultades para la toma de TA**).
- Yo en casa tengo una hija que es enfermera, y me la suele tomar (**Toma de TA por parte de la hija**).
- Yo me la tomo siempre igual, como en esta mesa, siempre el brazo izquierdo, siempre sentado en la misma silla (**Técnica de la toma**).
- Yo siempre el brazo derecho (**Técnica de la toma**).
- Tumbado en la cama y en el brazo izquierdo, siempre el izquierdo. (**Técnica de la toma**).
- Pequeñas correcciones como poner bien el brazo, no estar en una postura algo forzada, cuatro cositas como estas, de indicaciones siempre son buenas (**Técnica de la toma**).
- Yo tengo el brazo estirado, normalmente lo tengo apoyado sobre la pierna si estoy en el sofá o si estoy en la cocina sobre la mesa, pero siempre intentando relajarme. (**Técnica de la toma**).
- ¿Con la camisa puesta? Nooo... (**Técnica de la toma**).
- No, no... me la tomo un día que voy en el médico "Ah, ¿cómo tienes la tensión? Venga..." (**Frecuencia de toma de TA**).
- Yo tengo un aparato que me compré para entrar en el club de los hipertensos (risas, ¡jeje, sí! También hay clubes de eso). Y la verdad, no lo utilizo (**Frecuencia de toma de TA**).
- Yo me la miro, tengo un aparatito de hace mucho tiempo, me la miro 2-3 veces al mes (**Frecuencia de toma de TA**).
- No lo sé, esto es por los médicos, pero me miro la tensión, pues una vez que vas al centro de salud. Cuatro veces al año, ¡no más! Ahora a lo mejor, mañana cuando llegue me la tomaré (**Frecuencia de toma de TA**).
- Pero es cierto que cuando yo me encontraba bien, lo tenía controlado, si no venía a ver a Amparo, que es la enfermera de la Doctora Lucía, pues a lo mejor una vez al mes cuando iba a la farmacia a comprar los

medicamentos aprovechaba y ya pedía: ¿me pueden mirar la tensión? (**Frecuencia de toma de TA**).

- Ahora como he dicho antes, me la estoy tomando por la mañana y tarde por este motivo (**Frecuencia de toma de TA**).
- 3 veces por la mañana y a veces también, cuando tengo mala época, al mediodía y por la noche (**Frecuencia de toma de TA**).
- Me miro la tensión siempre a las 8 de la mañana (**Frecuencia de toma de TA**).
- Yo particularmente los de brazo (**Tipo de tensiómetro**).
- Yo me fío de los de brazo, hace muchos años que lo tengo (**Tipo de tensiómetro**).
- Yo utilizo el del brazo (**Tipo de tensiómetro**).

4. Del automanejo

4.1. Automanejo no reglado

- Sí, sobre todo en verano. En verano puedes estar bien a 11-6 y si me tomo la pastilla, quedo tirado por el suelo (**Automanejo a partir de síntomas**).
- Yo si me da alguna molestia prefiero comentarlo al médico y que el médico me diga, lo subamos o lo bajamos (**No automanejo**).
- A veces, no me acuerdo si la he tomado o no, pero no me la vuelvo a tomar (**Automanejo**).
- El hecho de que, con la subida de tensión, me la tome o no, es por regulación del médico, no es por voluntad propia, me dijo: regúlatela tu (**No automanejo**).

4.2 Viabilidad del automanejo reglado

- Lo veo viable, veo viable, siempre que me den la indicación (**Lo ve viable**).
- No, yo creo que es un problema médico. Si te comparas con insulina (**No lo viene viable**).
- Saber a quién llamar si necesitas (**Línea telefónica para dudas**).
- Sería más conveniente, poder tomar el teléfono y consultar directo allí (**línea telefónica para dudas**).
- Yo creo que nosotros no tenemos capacidad de dominarnos a nosotros mismos, debemos dar la confianza al médico (**Complejidad de la enfermedad y el tratamiento**).
- Es que es un tema bastante complicado (**Complejidad de la enfermedad y el tratamiento**).
- Es que es muy difícil (**complejidad de la enfermedad y el tratamiento**).
- Las personas que viven solas, mayores… (**Edad avanzada y soledad como barreras**).
- Yo sí (**Posibilidad de incorporarse al estudio**).
- Yo sí (**Posibilidad de incorporarse al estudio**).
- Yo sí (**Posibilidad de incorporarse al estudio**).
- Sí, está bien (**Posibilidad de incorporarse al estudio**).
- Sí, yo digo que sí (**Posibilidad de incorporarse al estudio**).
- Yo pregunto, ¿necesito esto? ¿Necesito esto que dices? (**Posibilidad de incorporarse al estudio**).

ORIGINAL

Relationship between nonalcoholic fatty liver disease and liver fibrosis risk scales and various cardiometabolic risk scales in 219.477 Spanish workers

Relación entre escalas de riesgo de higado graso no alcohólico y fibrosis hepática con diversas escalas de riesgo cardiometabólico en 219.477 Trabajadores españoles

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Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the main cause of chronic liver disease in the West, and in late stages it can lead to cirrhosis, which is expected to become the most frequent indication for liver transplantation in the next decade.

Material and methods: Descriptive and cross-sectional study in 219.477 Spanish workers in which the risk of presenting NASH and liver fibrosis was determined with 7 different scales and the cardiometabolic risk established from atherogenic indices, metabolic syndrome, atherogenic dyslipidemia, lipid triad and risk of prediabetes applying the PRISQ scale.

Results: There was an increase in the mean values and in the prevalence of high-risk values of all the NASH and liver fibrosis scales in persons at high cardiometabolic risk compared to those at lower risk.

Conclusions: There is a good relationship between the NASH and liver fibrosis risk scales and the cardiometabolic risk scales analyzed.

Keywords: non-alcoholic fatty liver disease (NAFLD), cardiometabolic disease, metabolic syndrome, atherogenic dyslipidemia, atherogenic indices, prediabetes.

Resumen

Introducción: La enfermedad del hígado graso no alcohólico (EHGNA) es la principal causa de hepatopatía crónica en occidente, pudiendo cursar en estadios tardíos con cirrosis por lo que se prevé que se convierta en la indicación más frecuente para el trasplante de hígado para la próxima década.

Material y métodos: Estudio descriptivo y transversal en 219.477 trabajadores españoles en los que se determina el riesgo de presentar EHGNA y fibrosis hepática con 7 escalas diferentes y el riesgo cardiometabólico establecido a partir de los índices aterogénicos, síndrome metabólico, dislipemia aterogénica, triada lipídica y riesgo de prediabetes aplicando la escala PRISQ.

Resultados: Se aprecia un incremento en los valores medios y en la prevalencia de valores de alto riesgo de todas las escalas de EHGNA y fibrosis hepática en las personas con alto riesgo cardiometabólico frente a las personas con menor riesgo.

Conclusiones: Existe una buena relación entre las escalas de riesgo de EHGNA y fibrosis hepática y las escalas de riesgo cardiometabólico analizadas.

Palabras clave: Enfermedad del hígado graso no alcohólico (EHGNA), enfermedad cardiometabólica, síndrome metabólico, dislipemia aterogénica, índices aterogénicos, prediabetes.

Introduction

Cardiometabolic diseases are highly prevalent in all countries of the world and not only in developed countries[1] and are responsible for high morbidity and mortality rates[2].

2 Non-alcoholic fatty liver disease (NAFLD) is a pathological entity that is also very common throughout the world today and its prevalence is increasing[3]. Its histological basis is an excessive accumulation of fat in the hepatocytes[4] which, left to its natural evolution, can develop into a picture of steatohepatitis[5] and even liver cirrhosis[6]. In contrast to other histologically similar pathological pictures very frequent in heavy alcohol consumers, NASH is observed in people who do not consume any or only small amounts of alcohol.

NASH can be considered a cardiometabolic disease and for this reason the aim of this study was to assess the relationship between different risk scales for NASH and liver fibrosis and other cardiometabolic risk scales.

Methods

A descriptive and cross-sectional study was performed on 219,477 Spanish workers belonging to different labor groups and Spanish regions. The workers were selected from those who attended occupational medical examinations between January 2017 and December 2019. See flow diagram in **Figure 1**.

Figure 1: Flow chart of participants in the study.

221,218 workers start the study

419 are under 18 or over 69 years old

326 do not agree to participate

996 lack any variable to calculate scales

219,477 (2125,403 men and 94,074 women) finally entered the study
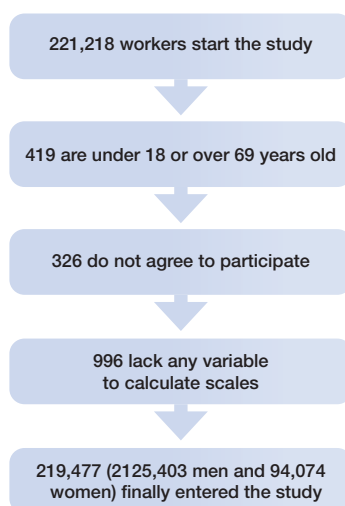
Inclusion criteria:
- Age between 18 and 69 years.
- Acceptance to participate in the study.
- Authorization to use the data obtained for epidemiological purposes.

- Belonging to one of the companies included in the study and not being on temporary disability at the time of the study.

The anthropometric variables (height, weight and waist circumference), analytical and clinical, were carried out by the occupational health professionals of the participating companies after standardization of the processes to avoid interobserver bias.

Weight and height were obtained with a SECA 700 model scale-measuring scale. Waist circumference was measured with a tape measure placed parallel to the floor at the level of the last floating rib and with the person standing, abdomen relaxed, upper limbs hanging down and feet together.

The anthropometric variables (height, weight and waist circumference), analytical and clinical, were carried out by the occupational health professionals of the participating companies after standardization of the processes to avoid interobserver bias.

Weight and height were obtained with a SECA 700 model scale-measuring scale. Waist circumference was measured with a tape measure placed parallel to the floor at the level of the last floating rib and with the person standing, abdomen relaxed, upper limbs hanging down and feet together.

Blood pressure was obtained with the person seated and after 10 minutes of rest. Three measurements were obtained one minute apart and the mean was calculated.

Blood analysis was performed after at least 12 hours. Enzymatic techniques were used to determine cholesterol, triglycerides and glycemia, and precipitation techniques were used for HDL. LDL was calculated indirectly with the Friedewald formula (total cholesterol -HDL-c- triglycerides/5), which is only applicable for triglycerides up to 400.

Seven risk scales for nonalcoholic fatty liver disease and liver fibrosis were determined:

- Fatty liver index (FLI)[7].

$$FLI = (e^{0.953*\log_e (triglycerides) + 0.139*BMI + 0.718*\log_e (GGT) + 0.053*waist\ circumference - 15.745}) / (1 + e^{0.953*\log_e (triglycerides) + 0.139*BMI + 0.718*\log_e (GGT) + 0.053*waist\ circumference - 15.745}) \times 100$$

High risk is considered to be 60 or more.

- Hepatic steatosis index (HSI)[8]
HSI = 8 × GOT/GPT + BMI + 2 if diabetes, + 2 if female. Risk is high from 36.

- Zhejian University index (ZJU index)[9]
ZJU = BMI + Glycemia (mmol L) + Triglycerides (mmol L) +3 GOT/GPT +2 if female.
The cut-off point to consider high risk is 38.

- Fatty liver disease index (FLD)[10]
FLD = BMI+Triglycerides+3 × (GOT/GPT) +2 × Hyperglycemia (present=1; absent=0).
Values above 37 is high risk.

- Framingham Steatosis Index (FSI)[11]
FSI = -7.981 + 0.011 x age - 0.146 x sex (female =1, male = 0) + 0.173 x BMI + 0.007 x triglycerides + 0.593 x hypertension (yes = 1, no =0) + 0.789 x diabetes (yes = 1, no =0) + 1.1 x GOT/GPT ratio ≥1.33 (yes = 1, no =0) There are no cut-off points.

- Lipid accumulation product (LAP)[12]
    Men: (waist (cm) - 65) x (triglycerides (mMol)).
    Women: (waist (cm) - 58) x (triglycerides (mMol)).
The risk is high from 42.7.

- BARD score[13] This is a risk scale for liver fibrosis.

BMI from 28 (1 point), GOT/GPT from 0.8 (2 points), diabetes mellitus (2 points). Values between 2-4 points indicate high risk.

- Different cardiometabolic risk scales are calculated:
    - Atherogenic indices present different cut-off points[14]: Total cholesterol/HDL-c ratio: low risk: < 5 in men and < 4.5 in women; moderate risk: between 5 and 9 in men and between 4.5 and 7 in women; and high risk: > 9 in men and > 7 in women. LDL-c/HDL-c ratio: low risk: < 3 and high risk ≥ 3. The triglyceride/HDL-c ratio is considered high risk as from 3%.
    - The metabolic syndrome is determined by applying three criteria[15]: (a) NCEP ATP III (National Cholesterol Educational Program Adult Treatment Panel III). Metabolic syndrome is considered to exist when at least three of the following factors are present: waist circumference > 88 cm in women and > 102 cm in men, triglycerides greater than 150 mg/dL or specific treatment for this lipid disorder, blood pressure greater than 130/85 mm Hg, HDL less than 50 mg/dL in women or less than 40 mg/dL in men or specific treatment, and fasting blood glucose greater than 100 mg/dL or specific treatment for blood glucose. b) International Diabetes Federation (IDF) Requires the presence of central obesity (waist circumference greater than 80 cm in women and 94 cm in men), in addition to two of the other factors mentioned above for ATP III (triglycerides, HDL, blood pressure and blood glucose). c) The JIS model[16] uses the same criteria as the NCEP ATPIII but with waist circumference cut-off points starting at 80 cm in women and 94 cm in men.
    - Prediabetes risk score Qatar (PRISQ)[16] is a scale that assesses the risk of prediabetes. It is considered low risk (0-16 points), moderate risk (17-27 points) and high risk (>27 points).
    - Deuremberg fat mass index[17]. It is obtained by applying the formula: fat mass %= 1.2 x (BMI) + 0.23 x (Age) - 10.8 x (sex) - 5.4 Women are given a value of 0 and men a value of 1. Obesity is considered to be 25% or more in men and 32% in women.

- Relative fat mass (RFM)[18] is obtained by applying these formulas: women: 76 - (20 × (height/waist)) and men: 64 - (20 × (height/waist)).

- We considered atherogenic dyslipidemia[19] if: triglycerides ≥ 150 mg/dL, HDL < 40 mg/dL in men and <45 mg/dL in women and normal LDL. If LDL levels were > 160 mg/dL, it was considered LT.

A smoker is a person who has smoked at least one cigarette (or its equivalent in another type of consumption) in the last month or has quit less than 12 months ago.

To obtain the social class, we used the proposal of the Spanish Society of Epidemiology based on the 2011 National Classification of Occupations[20]. Three groups were established: class I (executives, managers and university professionals), class II (intermediate occupations and self-employed workers) and class III (manual workers).

Statistical analysis
A descriptive analysis of the categorical variables was performed, calculating the frequency and distribution of the responses for each of them. For quantitative variables, the mean and standard deviation were calculated following a normal distribution.

Bivariate association analysis was performed using the chi2 test (corrected by Fisher's exact statistic when conditions required it) and Student's t test for independent samples (for comparison of means). Multivariate techniques were used to establish the most significant variables associated with the risk factors. Logistic regression was used for multivariate analysis, with calculation of the odds ratio and the Hosmer-Lemeshow goodness-of-fit test. Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 28.0 (IBM Company, New York, NY, USA) for Windows, with an accepted statistical significance level of 0.05.

Ethical considerations and/or aspects
The research team undertook at all times to follow the ethical principles of health sciences research established nationally and internationally (Declaration of

Helsinki), paying special attention to the anonymity of the participants and the confidentiality of the data collected. Approval was requested from the Ethics and Research Committee of the Balearic Islands (CEI-IB), which was obtained with indicator IB 4383/20. Participation in the study was voluntary, so the participants gave their written and oral consent to participate in the study after receiving sufficient information about the nature of the study. For this purpose, they were given an informed consent form, as well as an information sheet explaining the objective of the study.

The data collected for the study were identified by a code and only the person responsible for the study can relate these data to the participants. The identity of the participants will not be disclosed in any report of this study. The investigators will not disseminate any information that could identify them. In any case, the research team is committed to strict compliance with the Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, guaranteeing the participant in this study that they may exercise their rights of access, rectification, cancellation and opposition of the data collected.

Results

The average age of the sample is over 40 years (41.8 years in men and 39.9 years in women), the largest group being 30-49 years. All the variables analyzed show more unfavorable values in men. The most prevalent social class is III. One third of the workers smoke. The data are presented in **table I**.

Tables 2a and **2b** show how all the NASH and liver fibrosis risk scales increase their mean values in parallel to the increases in the different cardiometabolic scales analyzed. In all cases these mean values are higher in men.

Table IV shows the results of the multivariate analysis using multinomial logistic regression. The risk of presenting elevated values for all the nonalcoholic fatty liver disease and liver fibrosis risk scales increased in parallel to the increase in the values of the different cardiometabolic risk scales. The greatest increases are seen with the obesity scales (Deuremberg and RFM).

Table I: Characteristics of the population.

	Men n=125,403 Mean (SD)	Women n=94,074 Mean (SD)	p
Age	41.8 (10.5)	39.9 (10.5)	<0.0001
Height	175.2 (6.8)	162.3 (6.3)	<0.0001
Weight	82.6 (15.0)	68.0 (14.7)	<0.0001
SBP	126.1 (15.6)	115.4 (15.5)	<0.0001
DBP	77.3 (11.1)	72.3 (10.5)	<0.0001
Cholesterol	195.6 (37.9)	192.1 (35.5)	<0.001
HDL-c	52.1 (9.8)	57.2 (10.3)	<0.0001
LDL-c	118.4 (35.1)	116.3 (33.5)	<0.001
Tryglicerides	125.7 (76.0)	93.1 (45.6)	<0.0001
Glycaemia	93.4 (21.5)	88.3 (16.0)	<0.0001
AST	29.0 (17.5)	18.7 (11.6)	<0.0001
ALT	24.4 (13.3)	18.2 (7.9)	<0.0001
GGT	32.7 (31.8)	18.8 (16.3)	<0.0001
Creatinine	0.86 (0.17)	0.68 (0.14)	<0.0001
	%	%	p
18-29 years	14.4	19.4	<0.0001
30-39 years	26.6	28.9	
40-49 years	33.6	32.0	
50-59 years	21.5	16.8	
60-69 years	3.9	2.9	
Social class I	6.1	7.5	<0.0001
Social class II	14.5	20.5	
Social class III	79.4	72.0	
Non smokers	67.5	66.7	<0.001
Smokers	32.5	33.3	

SBP systolic blood pressure. DBP diastolic blood pressure. HDL High density lipoprotein. LDL Low density lipoprotein. AST aspartate transaminase. **ALT** alanine transaminase. **GGT** gamma-glutamyl transferase.

Table IIa: Mean values of NASH and liver fibrosis risk scales according to values of cardiometabolic risk scales in men.

		FLI	HSI	ZJU	FLD	FSI	LAP	BARD
Men	n	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
CT/HDL low	107718	36.4 (25.5)	36.3 (6.6)	36.6 (5.4)	31.5 (5.1)	0.2 (0.2)	29.8 (23.8)	1.0 (1.0)
CT/HDL moderate	17544	59.7 (25.4)	39.8 (7.0)	40.7 (5.9)	35.3 (5.5)	0.3 (0.2)	57.1 (43.3)	1.9 (1.1)
CT/HDL high	141	70.3 (25.6)	40.4 (6.7)	44.2 (7.3)	36.7 (5.2)	0.5 (0.2)	90.8 (47.4)	2.1 (1.1)
TG/HDL normal	92151	31.5 (22.9)	35.7 (6.3)	35.8 (5.0)	30.8 (4.8)	0.1 (0.1)	23.2 (14.0)	0.8 (0.8)
TG/HDL high	33252	62.4 (23.4)	39.8 (7.0)	40.8 (5.7)	35.5 (5.4)	0.4 (0.2)	62.6 (38.7)	2.1 (1.0)
LDL/HDL normal	97914	36.2 (25.7)	36.2 (6.6)	36.5 (5.4)	31.4 (5.2)	0.2 (0.2)	29.9 (23.5)	1.0 (1.0)
LDL/HDL high	27489	52.1 (26.9)	38.8 (6.9)	39.5 (5.9)	34.2 (5.5)	0.3 (0.2)	46.9 (40.7)	1.6 (1.1)
PRISQ low	52974	22.8 (18.1)	33.4 (5.4)	33.7 (3.9)	28.8 (3.8)	0.1 (0.1)	21.3 (17.0)	0.5 (0.7)
PRISQ moderate	53811	46.2 (22.9)	38.1 (5.9)	38.4 (4.5)	33.2 (4.3)	0.2 (0.2)	37.4 (27.0)	1.4 (1.0)
PRISQ high	18618	68.8 (24.4)	42.7 (7.1)	43.3 (6.2)	37.7 (5.8)	0.4 (0.2)	58.0 (41.0)	2.21 (0.9)
Normalweight Deuremberg	22125	12.4 (8.5)	30.5 (4.1)	31.0 (2.6)	26.1 (2.4)	0.06 (0.05)	14.9 (10.8)	0.3 (0.5)
Overweight Deuremberg	38502	26.1 (15.6)	34.3 (4.6)	34.6 (2.8)	29.6 (2.6)	0.12 (0.09)	23.7 (16.8)	0.6 (0.7)
Obesity Deuremberg	64776	57.1 (23.5)	40.4 (6.3)	40.8 (5.0)	35.5 (4.7)	0.31 (0.20)	46.0 (33.1)	1.8 (1.0)
No obesity RFM	116964	36.3 (24.3)	36.0 (6.1)	36.4 (4.8)	31.3 (4.6)	0.2 (0.2)	30.6 (24.9)	1.1 (1.0)
Yes obesity RFM	8439	86.3 (11.9)	47.6 (6.4)	47.8 (5.5)	42.3 (5.1)	0.5 (0.2)	75.5 (45.3)	2.2 (0.9)
No atherogenic dyslipidemia	117276	37.6 (25.8)	36.4 (6.6)	36.7 (5.4)	31.7 (5.2)	0.2 (0.2)	30.7 (25.0)	1.0 (1.0)
Yes atherogenic dyslipidemia	8127	70.3 (22.0)	41.8 (7.0)	43.0 (6.0)	37.4 (5.5)	0.4 (0.2)	76.2 (45.4)	2.5 (0.9)
No lipid triad	123519	39.2 (26.5)	36.7 (6.7)	37.0 (5.6)	31.9 (5.3)	0.2 (0.2)	32.7 (26.9)	1.1 (1.0)
Yes lipid triad	1884	74.3 (20.6)	41.5 (6.8)	43.8 (6.3)	38.0 (5.7)	0.5 (0.3)	96.1 (67.7)	2.6 (0.8)
No MS NCEP ATPIII	105330	33.9 (23.4)	35.7 (6.1)	35.9 (4.7)	31.0 (4.6)	0.2 (0.1)	27.4 (20.0)	0.9 (0.9)
Yes MS NCEP ATPIII	20073	70.0 (22.6)	42.4 (7.1)	43.4 (6.0)	37.6 (5.7)	0.4 (0.2)	66.8 (43.2)	2.3 (0.9)
No MS IDF	108318	33.6 (22.8)	35.6 (6.0)	35.9 (4.7)	30.9 (4.5)	0.2 (0.1)	27.3 (19.6)	1.0 (0.9)
Yes MS IDF	17085	78.3 (15.6)	44.2 (6.7)	44.8 (5.5)	39.1 (5.1)	0.5 (0.2)	74.3 (42.9)	2.3 (0.9)
No MS JIS	93204	30.5 (21.4)	35.1 (5.8)	35.3 (4.4)	30.4 (4.3)	0.1 (0.1)	24.5 (16.8)	0.8 (0.8)
Yes MS JIS	32199	66.2 (22.8)	41.6 (7.0)	42.4 (5.7)	36.7 (5.4)	0.4 (0.2)	60.1 (39.1)	2.1 (1.0)

FLI Fatty liver index. HSI hepatic steatosis index. ZJU Zhejianng University index. FLD Fatty liver disease index. FSI Framingham steatosis index. LAP Lipid accumulation producto. CT Total colesterol. HDL High density lipoprotein. LDL Low density lipoprotein. PRISQ Prediabetes score Qatar. RFM Relative fat mass. MS ATPIII. Metabolic syndrome Adult Treatment Panel III. MS IDF Metabolic syndrome International Diabetes Federation.   Metabolic syndrome Joint Interim Statement

Table IIa: Mean values of NASH and liver fibrosis risk scales according to values of cardiometabolic risk scales in women.

		FLI	HSI	ZJU	FLD	FSI	LAP	BARD
Women	n	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
CT/HDL low	84117	17.7 (21.2)	35.9 (6.7)	36.5 (5.9)	29.7 (5.7)	0.1 (0.1)	17.7 (15.9)	0.6 (0.8)
CT/HDL moderate	9825	33.9 (27.4)	36.3 (6.9)	40.5 (6.5)	33.3 (6.2)	0.2 (0.2)	32.5 (27.8)	1.3 (1.0)
CT/HDL high	132	51.9 (29.4)	40.6 (8.9)	43.1 (8.7)	35.8 (8.4)	0.4 (0.3)	60.0 (54.5)	1.7 (1.0)
TG/HDL normal	86841	17.2 (20.4)	35.9 (6.7)	36.4 (5.8)	29.6 (5.6)	0.1 (0.1)	16.6 (13.1)	0.5 (0.7)
TG/HDL high	7233	47.0 (27.9)	41.2 (7.6)	42.8 (6.8)	35.5 (6.5)	0.4 (0.2)	51.9 (33.4)	2.0 (0.9)
LDL/HDL normal	83238	18.1 (21.5)	36.0 (6.8)	36.5 (6.0)	29.7 (5.8)	0.1 (0.2)	18.1 (16.4)	0.6 (0.8)
LDL/HDL high	10836	30.2 (26.6)	38.8 (7.2)	39.7 (6.5)	32.6 (6.2)	0.2 (0.2)	28.5 (26.8)	1.1 (0.9)
PRISQ low	65310	11.8 (15.3)	34.2 (5.8)	34.8 (4.8)	28.1 (4.7)	0.1 (0.1)	14.0 (12.9)	0.3 (0.6)
PRISQ moderate	22764	32.8 (24.3)	40.2 (6.5)	40.8 (5.8)	33.7 (5.6)	0.2 (0.2)	28.8 (20.6)	1.2 (0.8)
PRISQ high	6000	51.6 (28.4)	44.0 (7.5)	44.7 (6.9)	37.3 (6.6)	0.4 (0.2)	40.9 (26.3)	1.9 (0.8)
Normalweight Deuremberg	5373	2.9 (1.9)	28.2 (3.1)	29.0 (1.9)	22.4 (1.7)	0.03 (0.02)	7.1 (6.0)	0.1 (0.3)
Overweight Deuremberg	20754	4.7 (3.0)	31.1 (3.4)	31.8 (2.1)	25.1 (2.0)	0.05 (0.03)	9.2 (6.3)	0.1 (0.3)
ObeYesdad Deuremberg	67947	25.3 (24.0)	38.5 (6.6)	39.1 (5.7)	32.2 (5.5)	0.18 (0.17)	23.3 (19.7)	0.9 (0.9)
No obeYesdad RFM	85293	14.4 (15.6)	35.1 (5.7)	35.7 (4.8)	28.9 (4.6)	0.1 (0.1)	16.1 (13.6)	0.5 (0.8)
Yes obeYesdad RFM	8781	68.7 (19.1)	48.1 (5.9)	48.7 (5.1)	41.5 (4.9)	0.5 (0.2)	50.5 (26.2)	1.6 (0.7)
No atherogenic dyslipidemia	90057	18.0 (21.1)	36.0 (6.7)	36.6 (5.9)	29.8 (5.7)	0.1 (0.1)	17.6 (14.8)	0.6 (0.7)
Yes atherogenic dyslipidemia	4017	51.6 (28.0)	42.0 (7.4)	43.8 (6.9)	36.4 (6.5)	0.4 (0.2)	57.8 (36.6)	2.2 (0.8)
No lipid triad	93060	19.1 (22.2)	36.2 (6.9)	36.8 (6.1)	30.0 (5.9)	0.1 (0.2)	18.8 (17.1)	0.6 (0.8)
Yes lipid triad	1014	50.0 (27.1)	41.1 (6.9)	43.5 (6.6)	35.9 (6.1)	0.4 (0.3)	62.7 (47.9)	1.2 (0.8)
No MS NCEP ATPIII	85026	15.5 (17.9)	35.4 (6.2)	35.9 (5.3)	29.2 (5.1)	0.1 (0.1)	16.1 (12.9)	0.5 (0.7)
Yes MS NCEP ATPIII	9048	57.0 (26.4)	44.9 (7.1)	46.0 (6.4)	38.4 (6.2)	0.4 (0.2)	49.3 (30.0)	1.9 (0.9)
No MS IDF	84996	15.1 (17.6)	35.3 (6.1)	35.9 (5.2)	29.1 (5.1)	0.1 (0.1)	15.9 (12.7)	0.5 (0.7)
Yes MS IDF	9078	59.8 (23.1)	45.7 (6.7)	46.5 (5.8)	39.0 (5.5)	0.4 (0.2)	51.2 (28.5)	1.8 (0.9)
No MS JIS	83280	15.1 (17.9)	35.3 (6.2)	35.8 (5.3)	29.1 (5.1)	0.1 (0.1)	15.8 (12.7)	0.5 (0.7)
Yes MS JIS	10794	53.2 (25.8)	44.2 (7.0)	45.2 (6.2)	37.7 (5.9)	0.4 (0.2)	46.5 (28.7)	1.8 (0.9)

FLI Fatty liver index. HSI hepatic steatosis index. ZJU Zhejianng University index. FLD Fatty liver disease index. FSI Framingham steatosis index. LAP Lipid accumulation producto. CT Total colesterol. HDL High density lipoprotein. LDL Low density lipoprotein. PRISQ Prediabetes score Qatar. RFM Relative fat mass. MS ATPIII. Metabolic syndrome Adult Treatment Panel III. MS IDF Metabolic syndrome International Diabetes Federation.   Metabolic syndrome Joint Interim Statement

Table IIIa: Prevalence of high values of the NASH and liver fibrosis risk scales according to values of the cardiometabolic risk scales in men.

		FLI high	HSI high	ZJU high	LAP high	BARD high
Men	n	%	%	%	%	%
CT/HDL low	107718	20.8	46.2	33.7	36.1	28.7
CT/HDL moderate	17544	52.5	69.3	65.9	73.1	64.8
CT/HDL high	141	74.5	72.3	78.7	91.5	74.5
TG/HDL normal	92151	14,0	42.2	27.8	25.4	19.9
TG/HDL high	33252	56.8	69.6	67.3	85.4	72.2
LDL/HDL normal	97914	20.8	45.7	33.4	36.2	28.5
LDL/HDL high	27489	41.2	62.9	55.6	59.5	52.5
PRISQ low	52974	5.9	25.3	12.5	19.2	10.9
PRISQ moderate	53811	29,0	61.3	48.5	50.4	41.6
PRISQ high	18618	69.9	84.3	82.1	78,0	76.3
Normalweight Deuremberg	22125	0.2	7.7	0.7	6.2	2.4
Overweight Deuremberg	38502	14.2	28.2	9.4	23.7	11.1
Obesity Deuremberg	64776	46.5	76.4	68.2	63.8	57.9
No obesity RFM	116964	20.2	45.9	33.9	37.4	30.7
Yes obesity RFM	8439	95.3	98.9	98.6	95.3	76.1
No atherogenic dyslipidemia	117276	22.2	47.4	35.4	37.8	30.1
Yes atherogenic dyslipidemia	8127	70.1	80,0	80.5	91.9	86,0
No lipid triad	123519	24.5	49.1	37.6	40.5	32.9
Yes lipid triad	1884	77.1	79,0	83.3	93,0	89.2
No MS NCEP ATPIII	105330	16.9	43.1	29.7	32.9	24.5
Yes MS NCEP ATPIII	20073	69.7	82.9	83,0	85.7	82.3
No MS IDF	108318	15.7	42.6	29.7	33,0	26.1
Yes MS IDF	17085	86.3	93.4	92.8	93.9	82.1
No MS JIS	93204	39.9	38.8	24.4	27.3	19.6
Yes MS JIS	32199	64.1	80.4	78.5	81.9	74.7

FLI Fatty liver index. HSI hepatic steatosis index. ZJU Zhejianng University index. FLD Fatty liver disease index. FSI Framingham steatosis index. LAP Lipid accumulation producto. CT Total colesterol. HDL High density lipoprotein. LDL Low density lipoprotein. PRISQ Prediabetes score Qatar. RFM Relative fat mass. MS ATPIII. Metabolic syndrome Adult Treatment Panel III. MS IDF Metabolic syndrome International Diabetes Federation.   Metabolic syndrome Joint Interim Statement

Table IIIa: Prevalence of high values of the NASH and liver fibrosis risk scales according to values of the cardiometabolic risk scales in women.

		FLI high	HSI high	ZJU high	LAP high	BARD high
Women	n	%	%	%	%	%
CT/HDL low	84117	20.8	46.2	33.7	36.1	28.7
CT/HDL moderate	9825	52.5	69.3	65.9	73.1	64.8
CT/HDL high	132	74.5	72.3	78.7	91.5	74.5
TG/HDL normal	86841	14,0	42.2	27.8	25.4	19.9
TG/HDL high	7233	56.8	69.6	67.3	85.4	72.2
LDL/HDL normal	83238	20.8	45.7	33.4	36.2	28.5
LDL/HDL high	10836	41.2	62.9	55.6	59.5	52.5
PRISQ low	65310	5.9	25.3	12.5	19.2	10.9
PRISQ moderate	22764	29,0	61.3	48.5	50.4	41.6
PRISQ high	6000	69.9	84.3	82.1	78,0	76.3
Normalweight Deuremberg	5373	0.2	7.7	0.7	6.2	2.4
Overweight Deuremberg	20754	14.2	28.2	9.4	23.7	11.1
ObeYesdad Deuremberg	67947	46.5	76.4	68.2	63.8	57.9
No obeYesdad RFM	85293	20.2	45.9	33.9	37.4	30.7
Yes obeYesdad RFM	8781	95.3	98.9	98.6	95.3	76.1
No atherogenic dyslipidemia	90057	22.2	47.4	35.4	37.8	30.1
Yes atherogenic dyslipidemia	4017	70.1	80,0	80.5	91.9	86,0
No lipid triad	93060	24.5	49.1	37.6	40.5	32.9
Yes lipid triad	1014	77.1	79,0	83.3	93,0	89.2
No MS NCEP ATPIII	85026	16.9	43.1	29.7	32.9	24.5
Yes MS NCEP ATPIII	9048	69.7	82.9	83,0	85.7	82.3
No MS IDF	84996	15.7	42.6	29.7	33,0	26.1
Yes MS IDF	9078	86.3	93.4	92.8	93.9	82.1
No MS JIS	83280	39.9	38.8	24.4	27.3	19.6
Yes MS JIS	10794	64.1	80.4	78.5	81.9	74.7

FLI Fatty liver index. HSI hepatic steatosis index. ZJU Zhejianng University index. FLD Fatty liver disease index. FSI Framingham steatosis index. LAP Lipid accumulation producto. CT Total colesterol. HDL High density lipoprotein. LDL Low density lipoprotein. PRISQ Prediabetes score Qatar. RFM Relative fat mass. MS ATPIII. Metabolic syndrome Adult Treatment Panel III. MS IDF Metabolic syndrome International Diabetes Federation.   Metabolic syndrome Joint Interim Statement

Table IV: Multinomial logistic regression.

	FLI high OR (95% CI)	HSI high OR (95% CI)	ZJU high OR (95% CI)	LAP high OR (95% CI)	BARD high OR (95% CI)
CT/HDL low	1	1	1	1	1
CT/HDL moderate	1.15 (1.09-1.22)	1.32 (1.19-1.45)	1.07 (1.03-1.11)	1.23 (1.16-1.30)	1.35 (1.28-1.42)
CT/HDL high	1.28 (1.10-1.47)	1.47 (1.26-1.62)	1.22 (1.14-1.30)	1.50 (1.44-1.56)	1.69 (1.63-1.75)
TG/HDL normal	1	1	1	1	1
TG/HDL high	7.83 (7.52-8.15)	1.46 (1.41-1.51)	2.52 (2.43-2.62)	14.85 (14.26-15.46)	8.31 (8.01-8.62)
LDL/HDL normal	1	1	1	1	1
LDL/HDL high	1.22 (1.16-1.29)	1.05 (1.01-1.10)	1.08 (1.04-1.13)	1.26 (1.26-1.30)	1.11 (1.05-1.16)
PRISQ low	1	1	1	1	1
PRISQ moderate	2.27 (2.17-2.37)	1.10 (1.06-1.15)	1.36 (1.30-1.42)	1.21 (1.16-1.26)	3.04 (2.93-3.16)
PRISQ high	5.45 (5.17-5.74)	2.00 (1.91-2.09)	2.46 (2.35-2.58)	2.77 (2.64-2.90)	9.52 (9.10-9.96)
Normalweight Deuremberg	1	1	1	1	1
Overweight Deuremberg	4.35 (4.10-4.60)	4.36 (4.25-4.47)	11.05 (10.65-11.48)	2.54 (2.47-2.63)	3.82 (3.67-3.97)
Obesity Deuremberg	40.59 (30.22-54.52)	13.76 (13.08-14.48)	88.72 (76.11-103.42)	6.84 (6.43-7.27)	8.80 (8.02-9.65)
No obesity RFM	1	1	1	1	1
Yes obesity RFM	16.20 (15.42-17.03)	52.98 (44.11-63.63)	77.48 (65.47-91.71)	17.72 (16.53-19.00)	1.13 (1.08-1.18)
No atherogenic dyslipidemia	1	1	1	1	1
Yes atherogenic dyslipidemia	1.15 (1.08-1.20)	1.22 (1.13-1.31)	1.23 (1.13-1.33)	1.24 (1.13-1.35)	2.12 (1.97-2.29)
No lipid triad	1	1	1	1	1
Yes lipid triad	1.20 (1.07-1.34)	1.20 (1.09-1.29)	1.29 (1.17-1.41)	1.22 (1.16-1.28)	1.17 (1.01-1.35)
No MS NCEP ATPIII	1	1	1	1	1
Yes MS NCEP ATPIII	1.18 (1.14-1.23)	1.10 (1.03-1.17)	1.34 (1.26-1.43)	1.18 (1.14-1.23)	1.11 (1.06-1.17)
No MS IDF	1	1	1	1	1
Yes MS IDF	3.76 (3.56-3.95)	4.50 (4.22-4.81)	5.29 (4.94-5.66)	7.15 (6.69-7.64)	1.18 (1.12-1.24)
No MS JIS	1	1	1	1	1
Yes MS JIS	1.57 (1.49-1.66)	1.32 (1.26-1.40)	1.47 (1.39-1.56)	1.32 (1.24-1.39)	2.13 (2.03-2.24)

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Discussion

Our results show that the mean values and the prevalence of high-risk values of all the NASH and liver fibrosis scales analyzed increased in parallel with the cardiometabolic risk scales.

Multivariate analysis showed that the variable that most increased the risk of presenting high values of the different NASH and liver fibrosis risk scales were the scales that assessed obesity (RFM and Deuremberg).

Many authors consider obesity and dyslipidemia to be the main risk factors for NAFLD, and it is known that they increase cardiometabolic diseases, which are the main cause of death in these patients. A study by Tutunchi et al[21] in 256 individuals concluded that the severity of hepatic steatosis and fibrosis correlated very well with the atherogenic lipid profile. The Raine study[22] in adolescents also found similar results indicating that the presence of atherogenic lipoproteins increased the risk of NASH in adulthood. A study by Katsiki et al[23] showed that NASH was associated with various risk factors, including dyslipidemia.

The association that we have found between NAFLD and metabolic syndrome has also been described by other authors, and Sheka et al[24] concluded that there is a strong relationship between the two entities. Other authors such as Yki-Järvinen[25] and Wainwright[26] expressed the same opinion, although in the latter case the relationship was bidirectional.

The same relationship that we have found between NAFLD and risk of prediabetes has been observed by some authors. Insulin resistance, which is common to both pathologies, seems to be involved in the genesis of this association27. A study of more than 2000 individuals with a 10-year follow-up showed that increased risk of NAFLD assessed with the FLI was associated with increased risk of prediabetes and diabetes mellitus.

Strengths and limitations

The strengths of the study include the large sample size, more than 200,000 individuals, and the large number of NASH and liver fibrosis risk and cardiovascular risk scales used. The main limitation is that no objective diagnostic techniques for NAFLD or liver fibrosis other than the risk scales were used.

Conclusions

Taking into account the results obtained in our study, we can conclude that in our population there is a direct relationship between the values of the different NASH and liver fibrosis risk scales and the values of the cardiometabolic risk scales analyzed.

Conflict of Interest

The authors declare that no competing interests exist.

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Substance use among university students and affecting factors in Central Morocco: a cross-sectional Study

Uso de sustancias entre estudiantes universitarias y factores que afectan en el centro de Marruecos: un estudio transversal

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Summary

Introduction: University is a period characterized by an absence of parental supervision and independence. Few research has been conducted in Morocco among this particular population, the aim of this study is to assess the prevalence to substance use among student, to develop knowledge of how and why substances are used and or abused.

Subjects and methods: This is a cross-sectional study, there were 1054 participants, divided into university student group (n=444) and non-student group (n=610) using a random sampling process for the university student group, and multistage stratified probability procedure for the other group. Data were collected using structured questionnaire from subjects.

Results: The current study revealed that tobacco use was found the most prevalent substance used among university student representing 65,1%. While the prevalence of cannabis use was 29,1%, and psychotropic drugs was 2,5%. university female were two times more likely to report substance use than non-university'(OR 2,09 p<.001); occasional or regular physical activity were less likely to use substance compared to the other group (OR 0,26, p<.001). those who had an alcoholic parent were eight times more likely to report substance use than non-user (OR 8,71,p<.001).cannabis, pipe and more than 3 substances were more likely to be reported among non-university students than students (OR 2,51;p<.001), (OR 3,44,31; p<.001) and (OR 2,90; p<.001) respectively

Conclusion: This study has demonstrated a high prevalence of substance use among young educated adults who should be role models for their community, fighting substance use rather than using it.

Key words: Substance use, university students, substance-related disorders, illicit drugs.

Resumen

Introducción: La etapa universitaria se caracteriza por una ausencia de supervisión parental y una mayor independencia. A pesar de esto, existen pocos estudios realizados en Marruecos que se hayan centrado en esta población. El objetivo de este estudio es evaluar la prevalencia del consumo de sustancias entre los estudiantes, así como desarrollar el conocimiento sobre cómo y por qué se utilizan o abusan de ellas.

Sujetos y métodos: Se llevó a cabo un estudio transversal con 1054 participantes, divididos en un grupo de estudiantes universitarios (n = 444) y un grupo no universitario (n = 610). El grupo de estudiantes universitarios fue seleccionado mediante un proceso de muestreo aleatorio, mientras que el otro grupo se seleccionó mediante un procedimiento de probabilidad estratificado por múltiples etapas. Se recopilaron los datos a través de un cuestionario estructurado.

Resultados: El estudio actual ha revelado que el tabaco es la sustancia más utilizada entre los estudiantes universitarios, representando un 65,1% del consumo. Mientras tanto, la prevalencia del consumo de cannabis fue del 29,1%, y la de drogas psicotrópicas del 2,5%. Las mujeres universitarias fueron dos veces más propensas a informar el consumo de sustancias que las no universitarias (OR 2,09 p <.001), y aquellos que llevaban a cabo actividad física ocasional o regular eran menos propensos a consumir sustancias en comparación con el otro grupo (OR 0,26, p <.001). Aquellos que tenían un padre alcohólico tenían ocho veces más probabilidades de informar el consumo de sustancias que aquellos que no lo tenían (OR 8,71, p <.001). Además, el consumo de cannabis, la pipa y más de 3 sustancias fue más probable que se informara entre los estudiantes no universitarios que entre los universitarios (OR 2,51; p <.001), (OR 3,44,31; p <.001) y (OR 2,90; p <.001), respectivamente.

Conclusión: Este estudio ha demostrado una alta prevalencia de consumo de sustancias entre adultos jóvenes educados que deberían servir como modelos a seguir para su comunidad, combatiendo el consumo de sustancias en lugar de perpetuarlo.

Palabras clave: Consumo de sustancias, estudiantes universitarios, trastornos relacionados con sustancias, drogas ilícitas.

Introduction

Substance use and abuse is a major public health problem worldwide. According to the United Nations Office on Drugs and Crime (UNODC) report some 271 million people, or 5,5 percent of the world's population aged 15 - 64 have used either one or more of these substances- cannabis, cocaine, ecstasy, alcohol, tobacco, at least once in the last 12 months, and 35 million people worldwide suffer from substance use disorders[1].

University is a period characterized by a lack of parental supervision and newfound independence. At this special age, students try many new things. The initial factor that appears to influence adolescent substance use experiments is curiosity, social pressure and peer group influence, those are reported to be primary reasons for substance use, as well as to feel better, to lower stress, or to feel mature[2].

Although substance use is widely considered to be a normative part of the university experience, university students seems to be at a greater risk of substance use than other people of similar age[2]. But they are less likely to develop substance use disorders than their non–university-attending peers, the consequences of substance use are significant[3].

Substance use is becoming a major global public health and socioeconomic problem, widespread among high school and college students. These problems are emerging as one of the most threatening and challenging social and public health problems today[1]. Especially in developing countries, it is a serious problem in its own right and has so far been an aggravating factor in the economic crisis, leading to under development[4].

Adolescence is a sensitive period of development, characterized by brain changes and high levels of emotion, motivation, and risk-taking. The early exposure to substance uses often predicts future substance use and other psychiatric disorders[5]. Rohde and colleagues demonstrated that adolescent substance use disorder is associated with numerous functioning difficulties at age 30, some of which appears to be related to recurrent substance use disorder, co-morbid adolescent disorders, or functioning problems already evident in adolescence[6].

Little research has been conducted in Morocco among this particular population, the aim of this study is to assess the prevalence to substance use among student and affecting factors, to develop knowledge that increases our understanding of how and why substances are (ab)used.

Subjects and methods

Study design and setting

The study was conducted at Cadi Ayyad University Marrakech city, Morocco, from February -July 2021. The university hosts students from central and south regions of Morocco country, from 07 region out of 12, representing 32,03% from the national general population7. In order to evaluate the difference, the second group consists of non-student (n=610), aged 17 to 30 years. These subjects come from different socio-economic strata, native or residents in Central Morocco.

Sample size determination and sampling technique

In total, there were 1054 participants, divided into student group (n=444) and non-student group (n=610), in order to have a representative sample to the entire target population. And to generalize the results[8]:

With an assumption of: P=15 (prevalence of Drug use) CI=95%, Marginal error=5%. Then the sample sizes become:

$$ n = \frac{Z^2 \times P \times Q}{d^2} = \frac{(1,96)^2 \times (0,15) \times (100-0,15)}{5^2} = 185 $$

Then 10% non-response rate and 1.5 design effects was considered, However, we decided to recruit a higher total sample of 500 students in order to be able to make meaningful analyses. The random sampling process for the university student group was adopted, where interviewer was near the central covid 19 vaccination centers placed by the university. It is based on the principle of random selection which considers that all target individuals have the same probability of being in the sample and that the results of the study are representative of the entire target population.

For the non-student group, a multistage stratified probability procedure was used, stage 1 the selection of particular geographic areas based on urban rural and preurban, stage 2 especially urban cities, stratified districts were chosen, and stage 3 randomly vaccine center was chosen.

Inclusion and exclusion criteria

Group students who were enrolled at the university during 2020-2021 at the specified faculties and consented to participate in the study were eligible and included in the present study. Antecedent of use of any psycho active substance during lifetime was considered an inclusion criterion for both groups. Those who refused or hesitated to participate in the study and those who submitted incomplete questionnaire were excluded from the present study.

Data collection method

The questionnaire created for this study consists of four parts: socio-demographic part, antecedent, family history of substance use and matters related to participant's substance use. the last section included the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) was used in order to diagnose psycho active substance addiction, when the patient has a score: <2: No addiction, 2-3 Low addiction, 4-5 moderate addiction, >6 severe addiction[9].

The Alcohol Use Disorders Identification Test (AUDIT) was developed by the World Health Organization, to easily detect alcohol-related problems in the last 12 months prior to the survey. a score of 7 or less denotes abstinence or low risk, scores of 7-12 indicates an alcohol misuse, and a score higher than 13 denote alcohol dependence[10]. One-on-one in-person interview was conducted in an isolated place using a self-designed structured questionnaire. During the survey, necessary clarification or instruction was provided promptly when needed.

Data Analysis

Data collected were encrypted, filtered and put into Excel software and exported to SPSS version 25 computer software for final analysis. Descriptive data was presented using tables. In order to identify associations between the dependent and independent variables a binary logistic regression was performed. Multivariable logistic regression to identify factors associated with substance use and to minimize confounders between variables at p-value of <0.02 were transported. The association between variables were measured using adjusted odds ratio with 95% confidence interval at significance level of <0.05.

Results

Among all participants (N=1054), the participation rate was 88,2% among students (500 participants and 444 was retained), and 87% among non-student (700 while 610 was retained). The mean age of university student was 22,15±2,79 ranged from 17-30 years, majority of university students were male (87,12%) from urban residency (80,4%). The major part of student group, were single during the study period (96,2%), Almost the majority of students doesn't have an income (79,1%), while out of those who exercised a remunerated activity, 10,6% had a salary less than the Moroccan minimum wage (**Table I**).

The univariate logistic regression revealed an association between substance use and gender, where university female were two times more likely to report substance use than non-university'(OR 2,09[95% CI 1.37 to 3.20]; p=0,001). Also, urban residency was more associated with student than others (OR 1,72 [95% CI 1.28 to 2.30]; p<.001). Students living away from their parents were almost two times more likely to report substance use than the other group (OR 2,03 [95% CI 1.28 to 2.30]; p<.001).

An association between physical activity and use, where university student who practiced occasional or regular physical activity were less likely to use substance compared to the other group (OR 0,26 [95% CI 0,18 to 0.39]; p<.001) and (OR 0,27 [95% CI 0.20 to 0.36]; p<.001), also collective sports were less likely to be associated with substance (OR 0,18 [95% CI 0.12 to 0.25]; p<.001).

Table I: Students and non-students Socio demographic status.

Modality	Variable	Students (n=444) n (%)	Non Students (n=610) n (%)	P Value	χ^2	Unajusted Odds ratio (CI 95%)	P Value
Age		22,15 (17-30) ±2,79	26,24 (17-30) ±3,51	NS			
Sexe	Male female	387 (87,12%) 57 (12,8%)	570 (93,4%) 40 (6,6%)	<.001***	12,13	2,09 (1,37-3,20) 1	0,001***
living	urban	357 (80,4%)	429 (70,3%)	<.001***	34,16	1,72 (1,28-2,30)	<.001***
Education level	illiterate primary secondary university	- - - 444 (100%)	79 (13%) 95 (15,6%) 270 (44,3%) 156 (25,6%)	<.001***	565,576	124,10 (30,19-510,057) 133,97 (32,63-550) - 1	<.001*** <.001***
Marital status	single married Divorced/widowed	427 (96,2%) 15 (3,4%) 2 (0,4%)	412 (67,5%) 178 (29,2%) 20 (3,3%)	<.001***	130,97	1 12,29 (7,13-21,19) 9,84 (2,27-42,53)	<.001*** 0,002**
Number of children	0 1-feb More than 3	439 (98,9%) 3 (0,7%) 2 (0,5%)	457 (74,9%) 94 (15,4%) 59 (9,6%)	<.001***	115,77	1 30,09 (9,46-95,72) 23,53 (5,68-97,36)	<.001*** <.001***
Living	alone colocation	313 (70,49%) 131 (29,5%)	507 (83,11%) 103 (16,9%)	<.001***	22,92	1 2,03 (1,51-2,73)	<.001***
Income	none Minimum Wage low Medium High	351 (79,1%) 47 (10,6%) 21 (4,7%) - 25 (5,6%)	145 (23,8%) 222 (36,4%) 193 (31,6%) 38 (6,2%) 12 (2,0%)	<.001***	363,09	0,08 (0,06-0,12) 1 1,94 (1,12-3,37) ns 0,10 (0,04-0,21)	<.001*** 0,01** - <.001***

NS non signifiant *p < .05; **p < .01; ***p < .001.

The type of substance used by parents was also associated with use among participants, for those who had an alcoholic parent were eight times more likely to report substance use than non-user (OR 8,71 [95% CI 3.70 to 20.47]; p<.001). On the other hand, place of substance use by parents was associated with substance use, whom their parents used at home were at greater risk for substance use than others (OR 1,78 [95% CI 1.31 to 2.41]; p<.001) (**Table III**).

The univariate logistic regression revealed a negative correlation, where students were less likely than non-students to use substance at a lower age: (OR 0,46[95% CI 0.33 to 0.63]; p<.001) (**Table IV**).

The first substance used among university group was tobacco (65,1%), followed by Cannabis (15,5%) and alcohol (14,18%), while among non-university group,

tobacco was the most used (70%), followed by alcohol (15,57%) and cannabis (9,8).

Even tough tobacco still the main current substance used by the two group (60,1%), the prevalence of cannabis has increased between first and current substance used, representing 29,1% among university student, and 22,8% among non-university student, while the opposite was observed in alcohol where it decreased, to be 8,3% and 5,6% out of university and non-university respectively. The use of cocaine as a principal substance was used among only 3 students (0,7%) while none of the other group had reported that use. on the other hand, psychotropic drugs, mainly clonazepam, were used by 4 students (0,9%) and 65 of non-students (10,7%). these latter are statistically different, as shown by the univariate logistic regression (OR 11,99 [95% CI 4.31 to 33.33]; p<.001).

Table II: Students and non-students physical activity and alimentation.

Modality	Variable	Students (n=444)	Non Students (n=610)	P Value	χ^2	Unajusted Odds ratio (CI 95%)	P Value
Physical activity	no Occasional Regular	99(22,3%) 92(20,7%) 253(57%)	314(51,5%) 78(12,8%) 218(35,7%)	<.001***	91,81	1 0,26(0,183-0,39) 0,27(0,2-0,363)	<.001*** <.001***
Type of sport	No individual collective	99(22,3%) 151(34,0%) 188(42,3%)	314(51,5%) 206(33,7%) 90(14,8%)	<.001***	63,51	1 0,34(0,25-0,46) 0,18(0,127-0,25)	<.001*** <.001***
Nutrition	No Yes	101(22,7%) 252(77,25%)	50(8,2%) 560(91,8%)	<.001***	22,51	3,29(2,29-4,74) 1	<.001***

NS non signifiant *p < .05; **p < .01; ***p < .001.

Table III: Students and non-students parent' substance use status.

Modality	Variable	Students (n=444)	Non Students (n=610)	P Value	χ^2	Unajusted Odds ratio (CI 95%)	P Value
Parent' education	Illiterate	108 (24,3%)	205 (33,6%)	0,001***	19,2	1,65 (1,15-2,37)	0,007**
Parent' working status	No Yes	33 (7,4%) 411 (92,56%)	147 (24,1%) 263 (43,11%)	<.001***	125,66	3,91 (2,41-6,344) 1	<.001*** -
Parent' substance use	Yes No	157 (35,4%) 287 (64,6%)	286 (46,9%) 324 (53,1%)	<.001***	14	1,61 (1,25-2,07) 1	<.001***
Parent' substance use	tobacco Cannabis Alcool Non user	115 (25,9%) 36 (2,9%) 42 (1,4%) 287 (64,6%)	198 (32,5%) 27 (4,42%) 88 (14,42%) 324 (53,3%)	<.001***	50,73	1,57 (1,19-2,07) 0,56 (0,32-0,97) 8,71 (3,70-20,47) 1	0,001*** 0,04* <.001***
Place of use	House outside Non user	44 (10%) 76 (17,1%) 287 (64,6%)	166 (27,2%) 120 (19,6%) 324 (53,1%)	<.001***	56,27	1,78 (1,31-2,41) 1,41 (1,01-1,97) 1	<.001*** 0,04*

NS non signifiant *p < .05; **p < .01; ***p < .001.

Table V: Students and non-students DSM, and AUDIT scores.

Modality	Variable	Students (n=444)	Non Students (n=610)	P Value	χ^2	Unajusted Odds ratio (CI 95%)	P Value
DSM 5	No addiction <2 low addiction 2-3 Moderate addiction 4-5 Severe addiction >6 DSM Score	148 (33,3%) 37 (8,3%) 78 (17,6%) 181 (40,8%) 4,09 (0-17) ±3,38	10 (1,6%) 24 (3,9%) 69 (11,3%) 507 (83,1%) 7,58 (0-11) ±2,41	<.001*** <.001***	1313,84 ANOVA F 382,35	1 9,60 (4,22-21,81) 13,09 (6,38-26,83) 41,45 (21,37-80,41)	 <.001*** <.001*** <.001***
AUDIT	Low risk <7 Mis use 7-12 Alcohol dependance >13 AUDIT score	393 (88,5%) 21 (4,7%) 30 (6,8%) 1,79 (0-32) ±5,23	471 (77,2%) 34 (5,6%) 104 (17%) 4,23 (0-34) ±8,24	<.001*** <.001***	26,73 ANOVA F30,12	1 NS 2,08 (1,05-4,09)	 0,03*
Monthly expense (USD)		70,3 (10,-35,)±56	84,8 (10-500) ± 59	<.001***	ANOVA F 12,63		

NS non signifiant *p < .05; **p < .01; ***p < .001.

Table IV: Students and non-students substance use.

Modality	Variable	Students (n=444)	Non Students (n=610)	P Value	Chi Square	Unajusted Odds ratio (CI 95%)	P Value
Age at first use	<15 y/o 15-18 >18	109 (24,54%) 194 (43,7%) 141 (31,75%)	243 (39,83%) 222 (36,4%) 145 (23,77%)	0,000***	27,49	1 0,51 (0,38-0,69) 0,46 (0,33-0,63)	 0,000*** 0,000***
First use	Curiosity Relax Forget problems Be with friends Euphoria	205 (46,2%) 26 (5,9%) 60 (13,5%) 109 (24,5%) 44 (9,9%)	407 (66,7%) 10 (1,6%) 59 (9,7%) 114 (18,7%) 20 (3,3%)	0,000***	58,2	4,36 (2,50-7,60) 2,16 (1,14-4,09) 2,30 (1,27-4,15) NS 1	
Current use	Stop Relax Forget problems Be with friends "Addiction"	129 (29,05%) 86 (19,36%) 55 (12,4%) 108 (24,3%) 66 (14,9%)	09 (1,4%) 235 (38,52%) 193 (31,6%) 102 (16,7%) 71 (11,6%)	0,000***	229,13	1 35,78 (17,96-71,31) 45,61 (22,43-92,74) 12,27 (6,11-24,67) 13,98 (6,77-28,88)	 0,000*** 0,000*** 0,000*** 0,000***
1st substance used	Tobacco Cannabis Alcohol Psychotropic Mdma Cocaine Inhalants	289 (65,1%) 69 (15,5%) 63 (14,18%) 5 (1,1%) 2 (0,5%) 15 (3,4%) 1 (0,2%)	427 (70%) 60 (9,8%) 95 (15,57%) 8 (1,3%) 1 (0,2%) 7 (1,1%) 12 (2,0%)	0,002**	21,33	1 0,58 (0,40-0,85) Ns Ns Ns 0,31 (0,12-0,78) 8,12 (1,05-62,80)	 0,006** 0,01** 0,04*
Principal substance	Tobacco Cannabis Alcohol Psychotropic Cocaine-heroine Inhalants	271 (61,0%) 129 (29,1%) 37 (8,3%) 4 (0,9%) 3 (0,7%) 0 (0%)	367 (60,2%) 139 (22,8%) 34 (5,6%) 65 (10,7%) 0 (0%) 5 (0,8%)	0,000***	52,01	NS NS NS 11,99 (4,31-33,33) NS NS	 0,000***
Frequency	Daily Weekly Monthly	331 (74,5%) 97 (21,8%) 16 (3,6%)	565 (92,6%) 44 (7,2%) 1 (0,2%)	0,000***	69,85	27,31 (3,60-206,87) NS 1	0,000***
Associated substance	No	273 (61,5%)	277 (45,4%)	0,000***	67,75	1	

NS non signifiant *p < .05; **p < .01; ***p < .001.

The use of multiple substances was reported by more than half of participants, among university students' alcohol remain the most associated substance (18,2%), followed by cannabis (8,1%), while more than tree substances was reported among (4,1%), on the other hand among non-university students' cannabis was the most associated substance (15,1%), followed by alcohol (12%) and pipe (11,5%), while more than tree substances was used by 8,7% (**Table IV**, Supplementary material).

The univariate logistic regression showed that cannabis, pipe and more than 3 substances were more likely to be reported among non-university students than students (OR 2,51 [95% CI 1.65 to 3.83]; p<.001), (OR 3,44,31 [95% CI 1.65 to 5.08]; p<.001) and (OR 2,90 [95% CI 1.65 to 5.08]; p<.001) respectively. The frequency use of substance was significant among the studied group, where daily use represented 2,7% among university student, and 20,5% among non-university group (P value <.001, χ^2= 90,87). Daily use was strongly associated with non-student group (OR 10,26[95% CI 5.54 to 18.99]; p<.001).

According to DSM 5 score, among university student no addiction to substance use was observed in 33,3%, low in 8,3%, moderate in 17,6% and severe addiction among 40,8%, on the other hand, among non-university group, only 1,6% hadn't addiction, while almost the majority presented a severe addiction status (83,1%), while the rest was divided between low and moderate addiction by 3,9% and 11,3% respectively, a statically significant difference was noted between the two groups (P value <.001, χ^2= 1313,84). The mean score of DSM 5 was 4,09 ±3,38 ranged from 0-17, among student group while it was 7,58±2,41 ranged from 0-11, this difference was also significant (ANOVA F=382,35) (**Table V**).

Overall, the mean monthly expenses among university student was 70,3 ±5,60 ranged from 10-350 United states Dollar (USD), while among non-university student the mean was 84,8 ±59,3 ranged from 10-500 USD, this difference is statistically significant (P value <.001, F= 12,63) (**Table V**).

Discussion

The current study revealed that tobacco use was found to be the most prevalent form as a first and principal substance use among university student representing 65,1% and 60,1% respectively, this use remain doubled compared to a study conducted among Moroccan

student (Fes), where tobacco was used by 29,5% of students[11], while in Casablanca,37,4% university students had reported tobacco use[12], cigarettes are cheaper and more accessible for students with little financial resources, this could explain this high prevalence.

But the cannabis use was higher (37,9%), among Casablanca', followed by Marrakech'(current study) and Fes' student representing 29,1% and 16,1% respectively. Alcohol use was quite similar between our study (8,3%), and Zarrouq end collaborators finding (7,4%), on the other hand it remained very high among Soubhi end collaborators, where it was reported by 35,2% university students[11,12].

The current lifetime prevalence of smoking remains high, compared to others, a study conducted among Ethiopian student was 22%[13], and a study in Saudi university students was 14%[14], but quite lower than a study conducted among Kenyan university student where the prevalence was 69,1%[15].

However, the prevalence of lifetime substance use among female university student was high compared to non-university student 12,8% versus 6,6% respectively, as this topic is considered taboo in conservative communities. Still substance use among male is higher, probably due to the high level of substance exposure.

According to DSM 5, two in every five student had a severe addiction, those results are consistent with a study conducted in the US among university and non-university student where it was 39,6%, but on the other hand, the non-student group of this current study had much higher sever addiction compared to non-university student among US representing 83,1% against 44,5% respectively[9], the World Health Organization World Mental health surreys that conducted in 21 low and middle income countries, found that substance disorders was 58% among male, and 24,9% among female[16].

Alcohol dependance was diagnosed among 6,8% of students according to AUDIT, this rate remained very low compared to other findings, Naguib et al (2021) found that alcohol was the only and most substance abused among students (50%) it could be explained by the physical and psychological tolerance of alcohol abuse[17]. Early use of alcohol may be the consequence of this current dependence, a study conducted in Morocco among adolescents found that, the rate of alcohol consumption is positively associated with age: among students aged 12 to 14 years old and 15 to 18 years old were respectively 1.6% and 9.7%, while among students aged over 18 years old, the prevalence of consumption was 15.6%[18].

In our sample the prevalence of psychotropic drugs was 2,5% of all time, mainly benzodiazepine, this finding is consistent with another study conducted in Nepal, where 3,5% medical student had reported its use[19].

The prevalence of life time cocaine use among student was 5,7%, this rate remain higher than the findings of university students in Nigeria where it was 2,1%[20], and also among US students where it was 4,8%[3].

There was a high prevalence of multiple substance use among respondent, with 38,5% reported using more than one type of substance, these finding are in line with those of Egyptian (41,3%)[17], Turkish (31,2%)[21]. Multiple drug use has been associated with higher rates of complications such as rule-breaking behavior[22], sexual and physical abuse[23], and some psychiatric disorders[24]. While this present study did not assess the link s between drug use and those risky behaviors, a high prevalence of multiple drug use may be an indication that this population is a high-risk group for complications of drug abuse.

Substance use initiation age was also significant in this current study where out of 3 students, 2 had used a substance before age of 18 years, which is consistent with other studies[15,20]. The development of cognitive, emotional, and social abilities in children and adolescents get affected by substance use may compromise later functioning in important adult domains such as marriage, parenting, and gainful employment[20].

In this study, most respondents indicated that curiosity was the mean reason of first initiation to substance use, subsequently being with friends and to relax become the main reasons. Similar finding has been reported in other studies, a survey among medical student in the US found similar reasons, including to relax, to have a good time, to feel good and even to experiment[25].

Student drug use is influenced by various features associated with youth development, including living away from the control of parents, maintaining contact with same age peer groups, opportunities for obtaining and using drugs, and freedom from the responsibilities associated with employment, that was found in the current study and it has been argued in the literature[26,27].

Having a parent who used substances had a statistically significant effect of their offspring, such findings confirm similar results reported among Saudi university students, UAE and Bahrain too, indicating that having a substance user in family was an important predictor[14,28].

Those who were living in urban area were associated to substance use among student compared to non-student, the same finding was reported in a study conducted among Egyptian university student, where they two times more risk for use[17].

The marital status was found to be statistically significant predictor of substance use, those students who were ever married was likely to use substance than never married, same finding was found by among Ethiopian university

students[13]. Married university students may suffer the effect of marital condition and own family departure on their day-to-day campus life that may lead them to use substances more than single students who were relatively at a low stress level.

Physical activity provides numerous benefits, besides improving cardiovascular endurance, and the prevention of obesity it is considered to an encouraging mechanism for pro-social behavior[29], in consequence the current study showed that university students who practiced physical activity were less likely to report substance use (OR 0,27 [95% CI 0,20 to 0,36]; p<.001), the same finding was found among Kenyan students, hence physical health represent a protective factor[15].

Having a higher monthly income, and bad nourishment are factors associated with substance use, this results in consistent with another study conducted among another group of Ethiopian university student[30].

Conclusion

This study has demonstrated a high prevalence of substance use among university and non-university students in a low-income country, among young educated adults who should be role models for their community, fighting substance use rather than using it. Substance use are affected by complex factors at individual, family, school social and environmental factors, and the risk of substance dependance, mental and physical problems is elevated in this population.

Strategies and interventions are recommended to alleviate this issue, starting with families and peers where they should be role models to their children by keeping away from substance use, school/university health policies should be adjusted to include programs toward substance use education and prevention, providing on-campus special services which could assist users efficiently quit this addictive habit, interventions focusing on reducing access to substance should be implemented at different levels.

Competing interests
All authors declare that there are no conflicts of interest.

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SPECIAL ARTICLE

Inequidades en salud, One Health y lucha contra el cambio climático: retos en salud pública

Health inequities, One Health and the fight against climate change: challenges in public health

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Resumen

Las condiciones de vida son las responsables de las inequidades en salud y que son sistemáticas, injustas y evitables entre grupos sociales, económicos, demográficos y geográficos de la población. Así, los grupos con peor salud son aquellos que se encuentran más desfavorecidos socialmente. Su abordaje se plantea mediante políticas públicas centradas en los ejes de inequidad.

Por otra parte, la pandemia de la Covid, ha puesto de manifiesto la íntima y frágil relación entre la salud humana, los animales y el medio ambiente. Actualmente enfermedades transmisibles emergentes y reemergentes afectan a los seres humanos en gran magnitud y con consecuencias diversas y, aunque este hecho se deba a un proceso multifactorial, el cambio climático es sin duda uno de los factores que más influyen.

Palabras clave: Inequidades en salud, cambio climático, salud pública.

Summary

Living conditions are responsible for health inequities that are systematic, unfair and avoidable between social, economic, demographic and geographic groups of the population. Thus, the groups with the worst health are those that are most socially disadvantaged. They are addressed through public policies focused on the axes of inequity.

Moreover, the Covid pandemic has highlighted the intimate and fragile relationship between human health, animals and the environment. Emerging and re-emerging communicable diseases are currently affecting humans on a large scale and with diverse consequences, and although this is due to a multifactorial process, climate change is undoubtedly one of the most influential factors.

Key words: Health inequities, climate change, public health.

Inequidades en salud

El concepto de salud sido explicado por muchos investigadores a través de la historia desde diferentes perspectivas. El de tipo ecológico de los años 90 desarrolló modelos para explicar los determinantes de la salud (entramado de factores sociales, políticos, económicos, ambientales y culturales[1] que configuraban la salud individual y de la comunidad. Así, el modelo del "Policy Rainbow"[2] de Dahlgren y Whitehead -ilustrado como un arco iris de capas concéntricas- divide los determinantes de la salud en cinco: los macroestructurales y situados en la capa más externa, se componen por las condiciones socioeconómicas, culturales y medioambientales de un lugar y vienen marcados por la influencia política y condiciona todos los demás que están por debajo; le siguen en una capa inferior las condiciones de producción alimentarias, la educación, el ambiente laboral, el paro, el agua y servicios sanitarios, y la vivienda; por debajo, se encuentran las redes familiares, sociales y comunitarias de ayuda y soporte mutuo; posteriormente se sitúan los estilos de vida y, por último, en la capa más interna, los factores no modificables como la edad, el sexo y los factores hereditarios.

Sin embargo, este modelo resulta insuficiente para explicar las interrelaciones entre los determinantes. Así, surge el modelo de Determinantes sociales de las inequidades en salud[1] definiendo:

a) Los determinantes estructurales o determinantes sociales de las inequidades en salud, a aquellos que generan mecanismos de contexto político, social y económico que conducen a una estratificación y posición social;

b) Los determinantes intermedios, llamados específicamente como factores sociales intermedios o determinantes sociales de la salud, son aquellos que se sitúan en una posición intermedia entre los determinantes sociales de las inequidades en salud –que los anteceden– y el resultado o impacto en la equidad en la salud y el bienestar. Así, el hecho de que los determinantes estructurales estratifiquen socialmente a las comunidades, provoca diferencias en la exposición a condiciones que afectan a la salud, siendo más vulnerables –o no- a padecer problemas de salud[3] (**Figura 1**). Estos son: las condiciones materiales de la vida (aquellos determinantes que se relacionan con el medio ambiente físico como la vivienda, el barrio o municipio; el medio laboral con determinadas condiciones de trabajo y empleo, la alimentación, el gasto para la compra de ropa, etc. Probablemente, este determinante sea uno de los factores intermediarios más importantes de la salud y que, además, puede estudiarse desde varias perspectivas a través de los llamados índices de privación material. Estos adoptan una naturaleza de privación multidimensional como los ingresos, educación y el tipo de casa, las circunstancias psicosociales o el entorno social, los factores biológicos y conductuales y, por último, el mismo sistema sanitario[3].

c) A su vez, los factores que se sitúan en un nivel más individual y próximos a la persona, se señalan como los determinantes de salud intermediarios[4].

Figure 1: Determinantes sociales de las inequidades en salud.
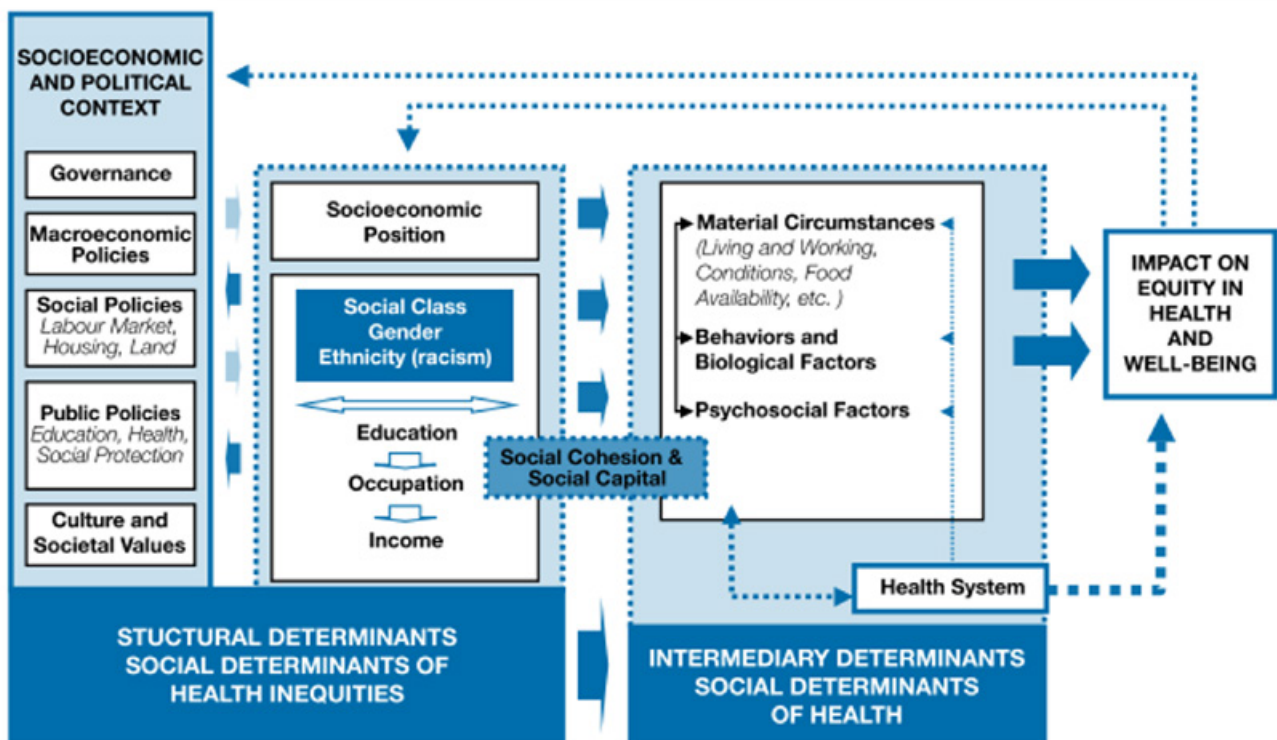
Fuente: Solar y Irwin (2010)

De manera general, se ha definido que los determinantes estructurales y las condiciones de vida (determinantes intermediarios) constituyen los determinantes sociales de la salud y son los responsables de la mayor parte de las inequidades en salud dentro y entre los países. Las inequidades sociales en salud son aquellas "desigualdades en salud sistemáticas, injustas y evitables entre grupos sociales, económicos, demográficos y geográficos de la población". Son el resultado de la distribución desigual de acuerdo con la estructura social del género, la clase social, etnia, territorio etc. De esta manera, los grupos con peor salud son aquellos que se encuentran más desfavorecidos socialmente[5] y, por norma, se posicionan en forma de gradiente[6]; cuanto más deprimidas son las comunidades peor es su condición de salud. Y esa tendencia sucede en todos los países cualquiera que sea su nivel de desarrollo[7].

Las inequidades se objetivan con cualquier indicador de salud. A nivel local de la ciudad de Palma, el estudio MEDEA pone en evidencia que en áreas geográficas altamente privadas socioeconómicamente, entre los hombres, se destaca una alta mortalidad por el cáncer de pulmón, el SIDA, la enfermedad del hígado y la cirrosis, el cáncer de estómago, el de vejiga, la EPOC, el suicidio y las lesiones por accidentes de tráfico. En cambio, entre las mujeres, en las zonas con un alto grado de privación socioeconómica hay un exceso de la mortalidad por cáncer de estómago, diabetes, la enfermedad hepática y cirrosis y la isquémica del corazón.

Con toda la evidencia científica existente, para alcanzar el máximo potencial en salud se deberían desarrollar políticas teniendo en cuenta los ejes de las inequidades; evaluar los procesos de gobernanza, políticas macroeconómicas, sociales, públicas, la prestación de servicios públicos a pequeña y gran escala; recurrir a la mirada de la "Salud en todas las políticas" integrando la perspectiva multisectorial y por último se propone la teoría salutogénica como una intervención con evidencia que reporta resultados satisfactorios.

One Health

Entre los retos esenciales de la Salud Pública actual y del futuro cobran una importancia destacada todos aquellos que resultan de la interacción entre la salud humana, la salud animal y la del medio ambiente, tal y como ha demostrado claramente la reciente pandemia de COVID de modo que, para prevenir situaciones similares en el futuro, deben considerarse dichos elementos desde una perspectiva holística, multidisciplinar y coordinada entre todos los agentes y profesionales implicados[8] .

Y para ello, surge el concepto One Health/Una salud que engloba los tres ámbitos mencionados. Realmente no es algo completamente nuevo ya que diversas enfermedades, como la rabia animal, la hidatidosis o la brucelosis, se han conseguido controlar desde la colaboración de la salud humana y la salud animal. Pero la incorporación de la perspectiva ambiental ha sido fundamental por su clara incidencia en las anteriores y, recientemente, se ha incluido la salud de las plantas como un nuevo elemento diferenciador y necesario[9].

Múltiples ámbitos de la salud pública pueden ser abordados desde el enfoque One Health, pero esencialmente debe centrarse en aquellos en los que la vida animal incide directamente en la salud humana, a través de microrganismos transmisibles.

Fuente:
DC (https://www.cdc.gov/onehealth/resource-library/one-health-graphics.html)

Las enfermedades zoonóticas son aquellas que pueden ser transmitidas a las personas desde el mundo animal (o viceversa). Es importante destacar que el 60% de los agentes patógenos humanos son de origen animal, porcentaje que se incrementa al 75% si consideramos a los emergentes y reemergentes, es decir, los que ocasionan nuevas enfermedades o los que, siendo responsables de otras ya conocidas en una zona geográfica, ven modificada su incidencia, virulencia o transmisibilidad[10]. Además, se estima que el 77% de enfermedades animales pueden afectar a varias especies demostrando que el salto entre especies es habitual en la naturaleza y el 39% incluye a la especie humana entre sus hospedadores potenciales[11].

Los factores asociados con la emergencia y reemergencia de estas enfermedades son variados, se interrelacionan entre sí y evolucionan continuamente. De forma esquemática podemos agruparlos en las siguientes categorías:

• Los importantes cambios demográficos acaecidos el último medio siglo, encabezados por el incremento de la población mundial y todas las consecuencias derivadas de éste: envejecimiento de la población (y por tanto, mayor vulnerabilidad inmunológica); y la necesidad de una mayor ocupación de espacios habitables, con el incremento de la densidad de población y la tendencia a la agrupación urbana,

con el crecimiento de las ciudades, muchas veces descontrolado, que deriva en condiciones precarias de habitabilidad, de saneamiento y de accesibilidad a la asistencia sanitaria.

- La mejora del bienestar de la población que ha impulsado cambios en los hábitos de consumo y una mayor demanda de bienes e, íntimamente relacionado con el anterior, el fenómeno de la globalización con el incremento del número y la rapidez de los desplazamientos de bienes y personas a escala mundial, favoreciendo la difusión global de microorganismos patógenos, de vectores de enfermedad y de reservorios en un corto espacio de tiempo. La llegada del *Aedes albopictus* (mosquito tigre) a la Europa mediterránea y su posterior colonización es un claro ejemplo de lo expuesto, hecho que ha permitido que el Dengue sea una enfermedad endémica en el sur de Francia en la actualidad[12].

- El incremento de la producción alimentaria, tanto en volumen (dirigido a satisfacer la mayor demanda) como en la introducción de nuevos alimentos (productos veganos, insectos, etc.) que han incidido en una mayor intensificación (agrícola y ganadera), en el uso de productos para mejorar el rendimiento (fertilizantes, pesticidas, etc.) y en la implementación de procesos tecnológicos novedosos. Todos estos hechos están asociados a la posibilidad de aparición de nuevos riesgos, tanto por nuevos microorganismos patógenos como por favorecer las condiciones para la difusión de los ya conocidos.

- Finalmente, el impacto sobre la salud del medio ambiente de actividades humanas como la deforestación (dirigida tanto a la obtención de más tierras productivas como residenciales), la contaminación ambiental y, muy especialmente, el cambio climático debido al calentamiento global, favorecen el incremento de la interacción de agentes patógenos, reservorios y vectores con otras especies, y entre ellas, la humana.

Por tanto, es evidente que la enorme complejidad de las causas que motivan la aparición y difusión de un agente patógeno zoonótico transmisible, nuevo o conocido, no permite abordar con éxito estos problemas de salud desde la orientación actual. Y precisamente, para conseguirlo es imprescindible la puesta en práctica inmediata del enfoque One Health en todos los niveles y muy especialmente, en la vigilancia epidemiológica, incorporando a los registros de salud humana los correspondientes a la salud animal, la salud ambiental, la seguridad alimentaria y, sin duda alguna, la vigilancia de la resistencia antimicrobiana.

Así parecen haberlo entendido las autoridades sanitarias, tanto en Europa como en España, donde ha sido claramente incluido en la Declaración de Zaragoza de Vigilancia de Salud Pública[13] y en el Plan Estratégico de

Salud y Medio Ambiente[14] aprobado hace unos meses. Ahora es necesario que todo el sistema sanitario y sus profesionales también lo incorporen a su práctica diaria.

Un camino de doble sentido: Salud Pública y la lucha contra el Cambio Climático

El cambio climático derivado de la emisión de gases de efecto invernadero es una realidad que ya es tangible. De ello se derivan consecuencias meteorológicas y ambientales evidentes, con claros efectos para la salud pública[16]. Hablamos de desastres naturales, de la modificación de patrones epidemiológicos, o de la disrupción de las cadenas de producción y suministro alimentario, entre otros ejemplos.

La especie humana se enfrenta así a una crisis sin precedentes en su historia, con un impacto indudable en la salud pública. La literatura científica es contundente en lo referente a la necesidad creciente de enfocar las políticas de salud pública en la mitigación de los efectos de esta crisis climática[17]. Cuanto más extremos sean los efectos, más dramáticas deberán ser dichas medidas.

El aumento de desastres naturales en los últimos años en países como los Estados Unidos, por ejemplo, se corresponde con un aumento en las consecuencias adversas tanto a nivel de salud física como mental entre sus ciudadanos. Existe además una correlación evidente entre la condición socioeconómica de la ciudadanía y su vulnerabilidad ante estos eventos[18]. De igual manera, la relación entre el cambio climático y la existencia de problemas en el suministro alimentario ha sido puesta de manifiesto en investigaciones recientes. Aunque esta conexión en los países más desarrollados requiere de estudios más extensivos, el riesgo para la salud pública derivado de disrupciones en la cadena de suministro alimentario es también indudable[19].

Adicionalmente, el cambio climático está provocando una modificación en los mapas epidemiológicos del planeta[20]. Enfermedades reservadas a zonas ecuatoriales o tropicales están comenzando a extenderse de manera decisiva por Europa o Norteamérica. Ejemplos son el Zica, el Chikunguña o el virus del Nilo Oriental. El reto que supone este nuevo escenario es especialmente complejo, ya que la degradación climática se ve complementada con los procesos migratorios modernos. Esta conjunción hace que la transmisión de patógenos desde zonas endémicas a nuevos territorios sea sencillamente inevitable.

Un ejemplo claro de esta realidad es la vigilancia epidemiológica que deben realizar los bancos de sangre en el hemisferio norte. Son varios los virus que hasta ahora carecían de la capacidad para transmitirse dados

los climas y los vectores biológicos tradicionales de Europa, por ejemplo[21]. Dicha transmisibilidad es posible ahora, hecho que reduce las potenciales donaciones de sangre en estos territorios. Se llega al extremo de que, en bancos de sangre, como el de las Illes Balears, se aplican exclusiones territoriales por estos virus no sólo a las personas originarias o que han visitado los países tradicionalmente endémicos, sino también a las que han pernoctado en zonas de Europa donde ya existe transmisión comunitaria de estos patógenos.

Así, se insiste una vez más en que las políticas de salud pública se centrarán cada vez más en mitigar los efectos del cambio climático sobre la salud física y mental de las personas. Sin embargo, también puede ponderarse lo siguiente: ¿podrían ser las políticas de salud pública instrumentos o enfoques válidos en la lucha contra el propio cambio climático? Se trataría de una suerte de política preventiva, siguiendo otras de éxito histórico dentro de la salud pública como son la lucha contra el tabaquismo o la promoción de la vacunación.

Y es que desde las instituciones responsables de la salud pública pueden ponerse en marcha medidas tanto de prevención como de mitigación de los efectos del cambio climático, incluso proponiendo mecanismos de adaptación para reducir el peso sanitario derivado de esta crisis climática. La mitigación puede centrarse en aspectos tan diversos como la promoción de energías renovables, transporte sostenible o sistemas de edificación de impacto ambiental cero, mientras que la adaptación puede focalizarse en la previsión y la planificación de cambios quizás ya inevitables, como la transmisión de patógenos antes mencionada[22].

En realidad, se trataría de observar las causas que originan el cambio climático de la misma manera que se ha hecho con el tabaquismo, por ejemplo, proponiendo consecuentemente medidas de salud pública de igual magnitud[23].

Lo más sorprende es quizás reflexionar sobre un hecho muy sencillo: la salud pública forma parte indisoluble de los sistemas públicos de salud, sistemas generalmente insostenibles desde un punto de vista ambiental16. Si bien es cierto que el marco de investigación no es todo lo sólido que debería ser, no es osado afirmar que son pocos los hospitales, o los sistemas de salud en general, con políticas de sostenibilidad ambiental de carácter estructural. Ello se debe principalmente a la priorización de objetivos por parte de estas instituciones, sobre todo en aquellos casos en los que las instituciones son públicas. El prisma principal es y debe ser la salud de las personas. Sin embargo, ejemplos como el Banco de Sangre y Tejidos de las Illes Balears, con un Plan de Sostenibilidad integral en desarrollo y ejecución, sirven para mostrar que la sostenibilidad puede formar parte de los objetivos estratégicos de las instituciones sanitarias,

ya que de la lucha contra el cambio climático dependen las propias donaciones de sangre.

La conclusión es simple: el cambio climático es una fuente de disrupción de la salud pública. Por ello, la respuesta reactiva a las consecuencias es no sólo necesaria sino inevitable. Sin embargo, un planteamiento bidireccional o proactivo es posible: tratar la lucha contra el cambio climático como una política más de salud pública.

Conclusiones

No cabe duda de que los sistemas mundiales de salud pública han sido puestos a prueba de manera intensa desde marzo de 2020. A pesar de las desgraciadas pérdidas humanas que ha comportado la pandemia por SARS-COV-2 en todo el planeta, nuestra civilización ha dado muestra de una resiliencia nunca vista hasta ahora. Y ello, contando con un modelo productivo y demográfico de fortísima interrelación global, supone un acelerador en la propagación de todas las amenazas a nivel de salud pública que se conocen hasta la fecha.

Es por ello necesario abordar las políticas de salud pública desde una perspectiva integral y proactiva. Se ha podido comprobar que la necesidad de considerar la "big picture" anglosajona, es absolutamente indispensable para dar una respuesta adecuada a las amenazas que persisten en esta materia; o que aparecerán a corto, medio y largo plazo. Además, serán instrumentos como la planificación, el análisis de riesgo o los planes estratégicos, los que evitarán esas políticas reactivas tan poco efectivas en este campo.

Las lecciones aprendidas son muchas. De su correcto análisis y del desarrollo de nuevas y mejores políticas de salud pública depende que el sistema esté preparado para los siguientes retos a afrontar.

Conflicto de intereses
Ninguno.

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CASE REPORT

Fiberglass materials in the extreme reconstruction of a second maxillary premolar with apical periodontitis

Materiales de fibra de vidrio en la reconstrucción extrema de un segundo premolar maxilar con periodontitis apical

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Abstract

Introduction and aim: Dental reconstruction of endodontic teeth represents a great clinical challenge in restorative dentistry. The biomechanical factors of the tooth to be restored, the position of the tooth in the arch, and the habits and parafunctions of the patient play an important role in the longevity and fractures of endodontic tooth reconstructions. When there are a ferrule allows us to perform adhesive techniques with guaranteed isolation of the operative field, dental restoration should be considered a reliable and long-lasting therapeutic option, even when the loss of tooth structure is severe. The aim of this manuscript is to expose the conservative treatment in a second maxillary premolar with extreme lost structure and apical periodontitis.

Clinical case: A 47-year -old woman was referred for the evaluation of extraction of second upper right premolar with extreme coronal destruction and periapical lesion. Conservative treatment was recommended because the destruction of the coronal tissue was supragingival and it was believed that the apical lesion could be resolved with endodontic treatment. Endodontic treatment and adhesive dental reconstruction with elastic fiberglass post (FRC), short fiber-reinforced composite (SFRC) as dentine-replacing material and microhybrid composite was done.

Results: In the six-year follow-up, the healing of the periapical lesion is observed, and the dental reconstruction is maintained functionally and esthetically.

Conclusion: With the limitations of this clinical case, we can conclude that this type of reconstruction is a therapeutic option to consider in the extreme rehabilitation of endodontic teeth.

Key words: fiberglass materials, extreme reconstruction, apical periodontitis, endodontically treated teeth, case report.

Resumen

Introducción y objetivos: La reconstrucción de dientes endodonciados representa un gran reto clínico en odontología restauradora. Los factores biomecánicos del diente a restaurar, la posición del diente en la arcada y los hábitos y parafunciones del paciente juegan un papel importante en la longevidad y fracturas de las reconstrucciones dentales endodónticas. Cuando existe una férula que nos permite realizar técnicas adhesivas con garantía de aislamiento del campo operatorio, la restauración dental debe considerarse una opción terapéutica fiable y duradera, incluso cuando la pérdida de estructura dental es grave. El objetivo de este manuscrito es exponer el tratamiento conservador en un segundo premolar maxilar con pérdida extrema de estructura y periodontitis apical.

Caso clínico: Una mujer de 47 años fue remitida para valoración de extracción de segundo premolar superior derecho con destrucción coronal extrema y lesión periapical. Se recomendó tratamiento conservador porque la destrucción del tejido coronal era supragingival y se creía que la lesión apical podría resolverse con tratamiento endodóntico. Se realizó tratamiento endodóncico y reconstrucción dental adhesiva con poste elástico de fibra de vidrio (FRC), composite reforzado con fibra corta (SFRC) como material de sustitución de la dentina y composite microhíbrido.

Resultados: En el seguimiento a seis años se observa la curación de la lesión periapical y la reconstrucción dental se mantiene funcional y estéticamente.

Conclusiones: Con las limitaciones de este caso clínico, podemos concluir que este tipo de reconstrucción es una opción terapéutica a considerar en la rehabilitación extrema de dientes endodonciados.

Palabras clave: materiales de fibra de vidrio, reconstrucción extrema, periodontitis apical, dientes tratados endodónticamente, reporte de caso.

Introduction

Dental reconstruction of endodontic teeth represents a great clinical challenge in restorative dentistry[1]. We always begin with teeth with severe tissue destruction, a consequence of etiologies as diverse as caries, destructive dental processes or fractures, which implies that there will be many factors that hinder the success of the restoration, since they are teeth with minimal remaining structures that will be subjected to significant occlusal forces, particularly in patients with parafunctions.

Very often the loss of tooth structure is located below the soft tissues and the periodontium that surrounds the tooth, which prevents us from having an adequate ferrule for reconstruction. In such cases, the clinical importance of the tooth must be weighed carefully and the possibilities of crown lengthening or abandoning the dental reconstruction and all restorative possibilities must be examined.

However, when we have a ferrule that can ensure the subsequent rehabilitation with a fixed prosthesis of the restored piece and that allows us to perform adhesive techniques with guaranteed isolation of the operative field, dental restoration should be considered a reliable and long-lasting therapeutic option, even when the loss of tooth structure is extreme[2]. Naumann et al.[3] consider that the most important factor in the survival of the restored endodontic tooth is the presence of a ferrule and the retention of some of the cavity walls. Rodriguez et al.[4] conclude that if the presence of the ferrule is uniform throughout the perimeter of the neck of the tooth, it is the best way to obtain the strongest resistance to fracture of the endodontic tooth.

The intraradicular post is a necessary complement to maintain the restoration in cases of severe destruction of dental tissue. Despite doubts about the benefits of the post in endodontic reconstruction, the selection of clinical cases, the type of post and the appropriate clinical technique lead to high success rates[5,6]. Different types of prefabricated posts or individual posts can be used for each root canal.

Precast post materials and designs range from metallic to carbon fiber, quartz, or glass posts. The shape can be conical, cylindrical or cylindrical-conical. Research has found no significant differences in resistance to fracture among the different post types[7]. They have a circular section, which makes it difficult to adapt the post to oval canals, with the cement occupying all the free space left by the post with the walls of the canal. We can solve this with individualized posts.

We can make individualized posts with fiberglass covered with unpolymerized composite (FRC) called elastic fiberglass posts[8]. Post preparation requires time and is not without some clinical difficulty, which has meant that it is not considered a practical therapeutic option in everyday dentistry. However, studies have given this type of post good results, obtaining more resistance to fracture in wide or oval canals and suffering a type of fracture with an increased possibility of repair than conventional prefabricated posts[9].

When we have narrow ducts, prefabricated posts yield better results; however, in wide ducts where we can introduce a significant number of fiberglass types and composites, the results vary.

We present a clinical case of extreme dental reconstruction. The extraction and subsequent prosthetic replacement of the tooth was assessed, but conservative treatment was opted for considering that we had favorable factors for clinical success. Treatment included an individually manufactured elastic post with FRC EverStick posts and a SFRC as dentine-replacing material.

Clinical case

This investigation complies with the Helsinki Declaration, and the patient signed an informed consent form.

A 47-year -old woman attended for an extraction of second upper right premolar[15]. After taking the medical history, in which there were no data of interest that could condition dental treatment, the dental clinical examination was performed.

The severe loss of tooth structure was noted as a consequence of a coronal caries process, which had damaged the pulp tissue (**Figure 1-A**). In soft tissues, no fistulous tract was detected. The tooth was not mobile, but there was painful percussion. The vitality test was negative. The radiographic examination revealed a radiolucent periapical image of approximately 4mm (**Figure 1-C**). Conservative treatment was recommended because the destruction of the coronal tissue was supragingival and it was believed that the apical lesion could be resolved with endodontic treatment.

The endodontic treatment was carried out in one session on November 25th, 2014. The tooth presented a single oval root canal, in the vestibule-palatal direction, which made cleaning with instrumentation difficult. A constant chemical cleaning of the canal was performed and after combined manual-mechanical instrumentation (K3™ Kerr Dental Files), the filling was performed with Sealapex™ cement (Kerr Dental), gutta-percha cone number 35, and lateral condensation with accessory tips (**Figure 1-D**). The provisional filling was carried out (**Figure 1-C**) and in the second appointment the dental reconstruction treatment was performed.

Due to the great coronal destruction of the tooth, the decision was made to perform reconstruction with an

intraradicular post. Given the oval shape of the canal, an individual post was made, adapted to its shape. For this, FRC everStick Post® GC 1.2mm and a SFRC as dentine-replacing, GC everX Posterior ® GC, was used to increase the retention of the restoration and reinforce the resistance to fracture of the tooth.

A week later (December 2nd, 2014), in a second appointment dental reconstruction was performed. After removing the provisional filling and cleaning the cavities (**Figure 2-A**), 13-14-15 and 16 were isolated (**Figure 2-B**). The gutta-percha was removed from the coronal and middle third of the root, preserving the sealing of the apical third. The 1.2mm glass tape post was selected; two posts were used. The fibers were grouped ovally in the root part and fanned out in the coronal part. This was adjusted to the shape of the canal (**Figure 2-C**). Once the post had the proper shape (oval shape in the root area and fan in the coronal area), it was cured for 3 seconds with Demi™ Plus curing light (Kerr Dental) to keep the shape of the post stable and to be able to proceed to cement without deforming. The post was impregnated with Stick-resin® GC resin for 3 minutes before cementing it, protecting it from light (**Figure 2-D**) to ensure correct adhesion. Cementation was performed with the GC Grandia CORE® GC dual polymerization and self-etching technique, applying the adhesive and cement inside the canal with microtips and endodontic dispensing tip (**Figure 2-E** and **2-F**). Next, the post was placed in the canal, applying light but firm pressure and polymerizing for 20 seconds (**Figure 2-G** and **2-H**).

The MetaFix™ matrix ((Kerr Dental) **Figure 3-A**) was then placed and reconstruction proceeded. A light-curing self-etching adhesive G-ænial Bond® GC (**Figure 3-B**) was used, which was applied with a tip throughout the cavity and in the coronal portion of the post. After polymerization, GC everX Posterior® (**Figure 3-C**) was placed in the entire cavity floor, performing a 20-second polymerization cycle. Then, G-aenial Posterior® GC color A-3 composite was applied (**Figure 3-D**). Polymerization was carried out in each of the clinical steps with a Demi™ Plus lamp (Kerr Dental) at 1100 mW/cm² for 20 seconds. The matrix and the isolation were then removed, modeling
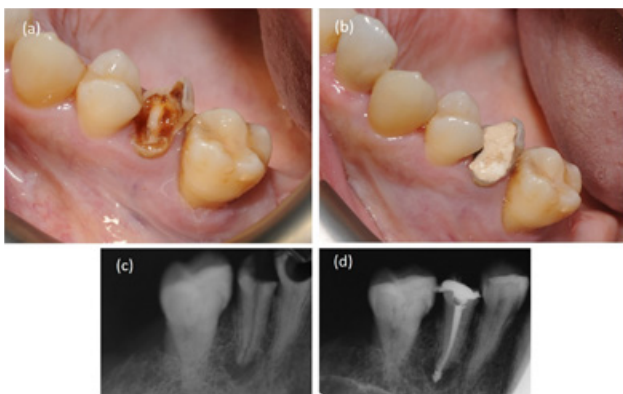
and polishing the restoration. Radiographic control was performed (**Figure 3-E** and **3-F**).
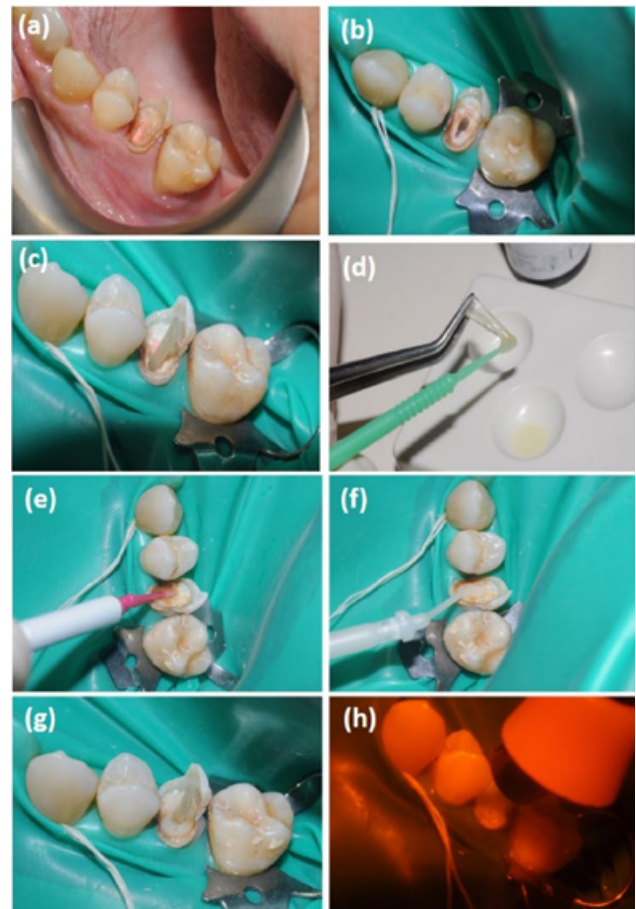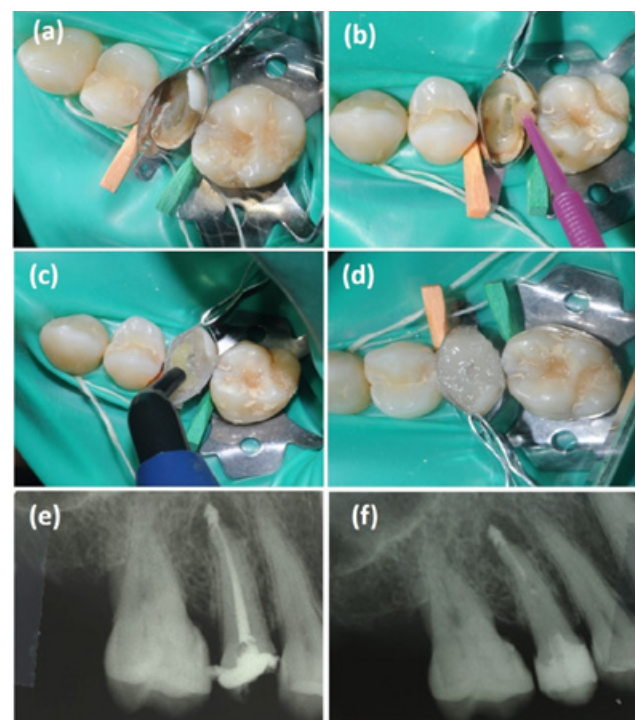
Figure 2:

Figure 3:

Figure 1:

Once the treatment was finished, a clinical and radiographic image was taken (**Figure 4-A** and **4-E**) and the patient was scheduled for follow-up visits to monitor the evolution of the apical lesion and reconstruction. Check-ups demonstrated the favorable evolution of the clinical case, with the resolution of the apical lesion and the maintenance of the reconstruction from both the functional and esthetic point of view. In **figure 4** the clinical and radiographic images are shown one year after treatment (**Figure 4-B** and **4-F**) and six years after treatment (**Figure 4-C** and **4-G**). In the last control, the patient had a caries lesion on the distal side of tooth 14, that was resolved in the same session by filling with Black's class II cavity preparation (**Figure 4-D** and **4-H**).

Figure 4:
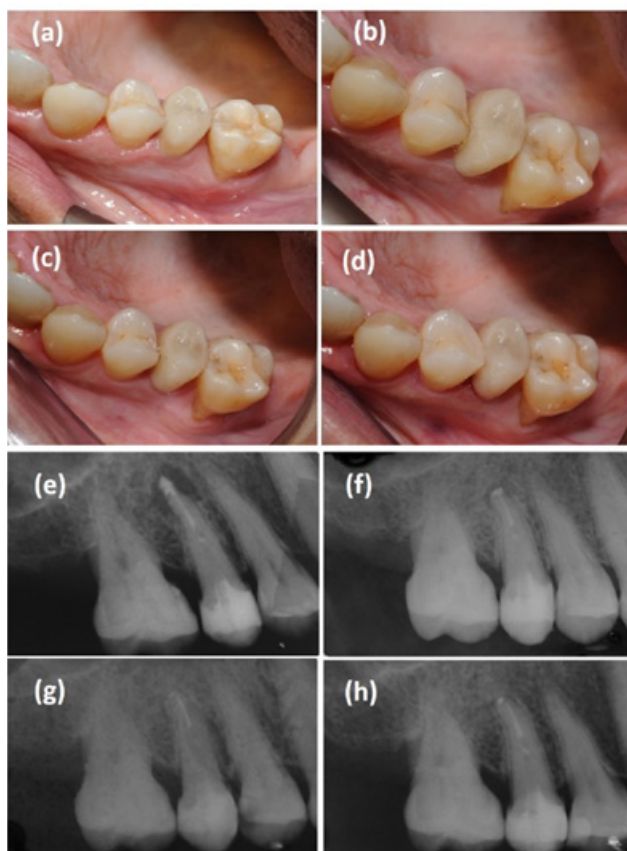
Discussion

The biomechanical factors of the tooth to be restored, the position of the tooth in the arch, and the habits and parafunctions of the patient play an important role in the longevity and fractures of endodontic tooth reconstructions[10]. The recently published meta-analysis by Garcia, PP. et al.[11] concluded that the failure rates in anterior and posterior teeth with post and core restorations were similar in the short- and medium-term follow-up. They recommend the need for better designed clinical trials comparing survival and failure rates with

longer follow-up times. This means that the clinician with extreme restorations does not have sufficient scientific support to make decisions, leaving them largely to their own experience and skill.

The scientific bibliography shows us different dental reconstruction techniques in endodontic teeth. The recent publication by Rodrigues, MP. et al. concluded that endodontic treatment followed by direct composite resin restoration is an effective method to restore the biomechanical performance of teeth. Reconstruction should not take long after endodontic treatment[12]. The use of SFRC as dentin and fiberglass posts can strengthen the dental structure and reduce the risk of fracture, especially in severely weakened teeth[13,14]. In the case we present, the dental reconstruction was carried out following these recommendations.

In cases of severe loss of tooth structure in which we indicate the placement of a post, the selection of the post, the adhesive technique and the cement are essential to the success of dental reconstruction. It is very important that we have good adhesion between the intra-root dentin, the adhesive, the cement and the post. For this we need to use compatible materials and ensure a good polymerization in the most apical area, the most critical point, especially when using non-self-curing cements. The goal is to have sufficient bonding between the materials and the dental structure so as to achieve a monoblock effect that can be more resistant to possible subsequent fractures.

There are different commercial brands of FRC with which we can make intraradicular posts. The study by Kivanc et al.[15], which compared Luminex, Dentatus, Ribbond and everStick posts, found no significant differences between the results of the different types of CRF.

To obtain a good bond between the fiberglass post and the cement, the surface of the post must be treated by applying different products (silane, H_2O_2, etc.) or by creating macroretention on the surface[16]. In the studies by Weingartner, Machado et al.[17], silanizing the post and using an adhesive that adheres the silanized post to the cement is the option with the best results in terms of retentive strength of the precast post. In the case of posts made with fiberglass reinforced with non-polymerized composites, the activation of the adhesion is required by impregnating the post with bonding. In the case we present, the post was impregnated with Stick-resin® GC to activate the adhesion of the semi-interpenetrating polymer network (semi-IPN), a non-polymerized organic matrix, a mixture of polymethylmethacrylate and Bis-GMA, which creates a network that can be dissolved by fresh monomers of adhesive resin, creating the so-called secondary IPN and increasing the potential for adhesion to other resins and to the tooth structure.

In addition, cleaning the dentin walls of the post bed with the complete removal of the smear layer is essential to obtain a correct interface between the dentin and the cementum. The use of laser-activated irrigation techniques on the dentin combined with the application of 17% EDTA has been shown to have a significant cleaning effect on the smear layer according to the studies by Kırmalı Ö, et al.[18]. Photodynamic therapy has also been evaluated in the preparation of the dentin walls for post cementation, showing negative effects on the bond strength on the dentin in the cervical third after cementation with Relyx ARC and on the dentin penetrability of the post, adhesive system of total etching in the prosthetic space of the cervical and apical third[19]. For all this, despite the popularization of adhesive cements in the fixation of fiberglass posts, long-term predictable bonding may be compromised due to procedures related to endodontic treatment and/or the sensitivity of the adhesive cementation protocols. The phenomena of microfiltration and degradation of the adhesive interface can jeopardize adhesion[20], causing decementation. The use of fiberglass posts also improves the transmission of the polymerization light along the canal, helping the polymerization of the cement in the most apical part.

Several studies have concluded that the use of SFRC as dentine-replacing materials offers significant improvement in the resistance to fracture of restored teeth[21,22], having good results in combination with conventional composites[23,24], as we have done in this clinical case, where the everX Posterior® GC and the G-aenial Posterior® GC color A-3 composite were used. This is particularly advisable in reconstructions with large cavities, as the bibliographic review published by Garoushi S, et al. concluded[25].

Whit the limitation of this report we could concluyed that that Endodontic success is linked to restorative success. The use of materials that help improve the resistance to tooth fracture and the meticulous clinical application of adhesive techniques can lead to restorative success even in teeth with severe destruction and loss of structures.

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CASE REPORT

An unexpected cause of delirium: severe hypercalcemia due to primary hyperparathyroidism. A case report

Una causa inesperada de delirio: hipercalcemia grave debida a hiperparatiroidismo primario. Informe de un caso

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Abstract

Acute confusional syndrome (ACS) or delirium is a frequent reason for emergency department consultation in elderly people. Moderate-severe hypercalcemia secondary to primary hyperparathyroidism is not a typical or frequent presentation of ACS. Serum calcium levels would be proportional to the severity of neuropsychiatric symptomatology. Normalization of calcium levels should lead to the reversibility of the symptomatology. However, case series of primary hyperparathyroidism report a high prevalence of neuropsychiatric symptoms in these patients, and it is hypothesized that these symptoms may be underreported in the scientific literature. We present the case of a 79-year-old woman with a diagnosis of ACS as a result of severe hypercalcemia secondary to primary hyperparathyroidism due to parathyroid adenoma.

Key words: delirium, hypercalcemia, hyperparathyroidism, parathyroid adenoma.

Resumen

El síndrome confusional agudo (SCA) o delirium es un motivo frecuente de consulta en urgencias en ancianos. La hipercalcemia moderada-grave secundaria a hiperparatiroidismo primario no es una presentación típica o frecuente de SCA. Los niveles séricos de calcio serían proporcionales a la gravedad de la sintomatología neuropsiquiátrica. La normalización de los niveles de calcio debería conducir a la reversibilidad de la sintomatología. Sin embargo, las series de casos de hiperparatiroidismo primario informan de una alta prevalencia de síntomas neuropsiquiátricos en estos pacientes, y se plantea la hipótesis de que estos síntomas pueden estar infradeclarados en la literatura científica. Presentamos el caso de una mujer de 79 años con diagnóstico de SCA como consecuencia de hipercalcemia grave secundaria a hiperparatiroidismo primario por adenoma paratiroideo.

Palabras clave: delirio, hipercalcemia, hiperparatiroidismo, adenoma paratiroideo.

Introduction

ACS or delirium is defined as an acute change in alertness, attention, and cognition, and it is caused by a medical condition excluding the pre-existence of a previous neurocognitive disorder[1]. There are predisposing factors for the onset of the condition, principally advanced age, as well as acute or triggering factors. Among the latter, infections, drug intoxication, glucose metabolism alterations, and ionic alterations are the most frequent causes[2]. Fifty percent of the causes of delirium are reversible.

Calcium plays a role in the metabolism of monoamines at the cerebral level, which explains how calcium alterations can produce psychological/psychiatric symptomatology[3]. Primary hyperparathyroidism is the most frequent cause of hypercalcemia. However, in most cases, this entity is asymptomatic[4]. In fact, in 1964, Agras et al.[5] postulated that only 4.6% of primary hyperparathyroidism cases caused delirium. Although there are published cases of ACS caused by moderate-severe hypercalcemia secondary to primary hyperparathyroidism, this is not a typical nor frequent presentation[5]. Serum calcium levels would be proportional to the severity of neurological symptoms[5].

There is a strong probability that the normalization of calcium levels resolves the acute clinical situation, but psychiatric symptoms such as depression, apathy, and irritability may persist even with calcium levels between 10-14 mg/dL[5]. Psychiatric symptoms are not included in the surgical criteria for primary hyperparathyroidism, despite the fact that some studies show significant improvements after a surgical approach is followed with respect to these patients[6-9].

In this report, we describe a clinical case where ACS was the initial presentation for a diagnosis of primary hyperparathyroidism.

Case report

A 79-year-old Caucasian woman with a relevant history of arterial hypertension, dyslipidemia, anxious depressive syndrome receiving treatment regularly with lercanidipine 20mg/day, chlorthalidone 50mg/day, tramadol/paracetamol 75mg/650mg and escitalopram 15mg/day was brought to the emergency department by her daughter, after two days of bradypsychia, disorientation, and significant functional impairments. She had been leading an active life up to this point, with neither cognitive nor physical limitations. No other clinical signs by apparatus or systems were reported. On physical examination, the palpation of a nodule of homogeneous consistency in the anterior-cervical region, at the inferior level of the left thyroid lobe, stood out. The rest of the physical examination showed results within the normal range.

However, in the analysis in the emergency room, severe hypercalcemia 15.80 mg/dL (8.80-10.20mg/dL), mild hypophosphatemia 2.10 mg/dL (2.30 - 4.70mg/dL), and mild hypomagnesemia 1.30 mg/dL (1.60-2.60 mg/dL) were observed. Renal function, together with the rest of the laboratory tests resulted normal. An electrocardiographic study was performed and chest and lumbar radiographs were anodyne.

Intensive fluid therapy with saline, calcitonin, and a dose of zoledronic acid was administered. During her stay in the hospital, the case was studied and the ionic disbalances were corrected. Complementary tests were requested and the patient's previous medical history was reviewed.

- Laboratory tests on admission: severe hypercalcemia 15.80 mg/dL (8.80-10.20 mg/dL), mild hypophosphatemia 2.10 mg/dL (2.30-4.70 mg/dL), and mild hypomagnesemia 1.30 mg/dL (1.60-2.60 mg/dL) secondary to hyperparathyroidism. Parathyroid hormone levels were 470.70 pg./mL (15-68 pg./mL) with slightly decreased vitamin D levels 19.90 ng/mL (30-50 ng/mL).
- Daily ionic control: serum calcium levels are monitored with the pertinent therapeutic adjustment (see **table I**).
- Ultrasound of the abdomen showed non-obstructive lithiasis in both kidneys. Cholecystectomy (see **image 1**).
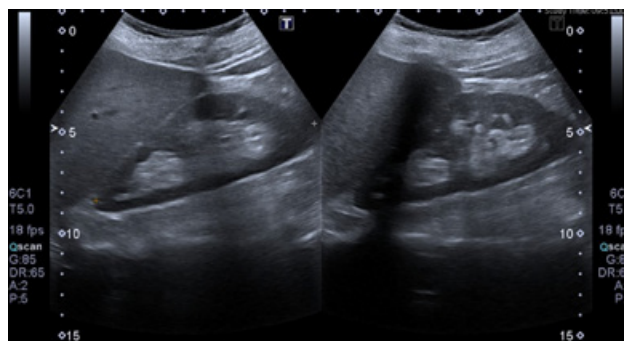
Image 1: Abdominal ultrasound.

Table I: daily ionic monitoring evolution.

|	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Calcium (8.80-10.20 mg/dL)	15.80	13.70	12.10	11.0	10.20	9.80	9.40
Phopspahte (2.30-4.70 mg/dL)	2.10	1.30	1.10	1.40	1.60	2.40	2.60
Magnesium (1.60-2.60 mg/dL)	1.20	1.35	1.80	1.94	2.10	2.30	2.41
Sodium (136-145 mmol/L)	141.3	143.2	137.0	139.1	138.3	137.7	138.1
Potassium (3.6-5.3 mmol/L)	3.12	3.05	3.30	3.53	3.80	3.83	4.65

- 24-hour urine: Correct urine collection with a calculated glomerular filtration rate of 85 mL/min, calcium 145.20 mg/24h (100-300 mg/24h), phosphate 488.40 mg/24h (400-1200mg/24h), magnesium 130.68 mg/24h (73-122mg/24h), sodium 231mg/24h (40-220mg/24h) and potassium 58mg/24h (25-125mg/24h).
- Thyroid ultrasound: Thyroid of normal size, morphology, and echogenicity, with no evidence of nodular images. No images suggestive of pathology were identified in the parathyroid areas. No latero-cervical adenopathies of any significant size are observed (see **image 2**).

Image 2: Thyroid ultrasound.
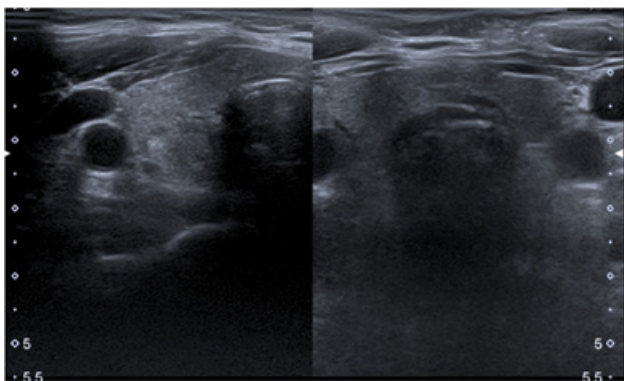
- 99mTc-sestamibi scintigraphy (administered dose of 20,0 mCi): Overactive nodular lesion of 13x10mm located at posterior and superior region of the right thyroid lobule (see **image 3**).

Image 3: 99mTc-sestamibi scintigraphy showing an overactive nodule at posterior and superior region of the right thyroid lobule.
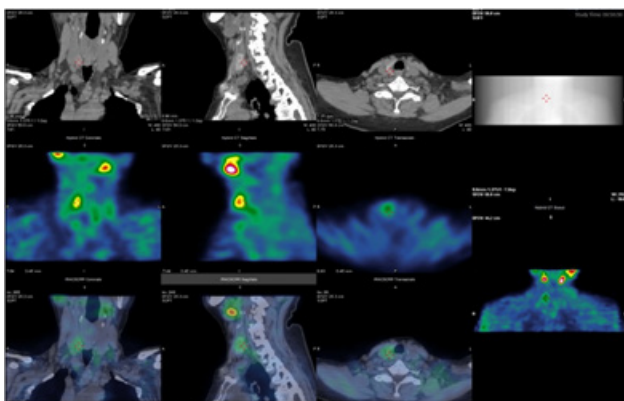
- Medical history review: The previous blood test prior to admission was 14 months before and showed normal levels of calcium in the blood. An ultrasound of the abdomen 12 years prior to admission showed renal lithiasis.

The case was diagnosed as an acute confusional syndrome, resulting from severe hypercalcemia, secondary to primary hyperparathyroidism due to parathyroid adenoma.

Along with the gradual improvement of blood calcium levels and the previously mentioned diagnosis, calcimimetics (cinacalcet) were introduced, achieving not only normalization of calcemia, but also a clear and sustained improvement of the acute confusional syndrome with which she was admitted. Gradually, the patient recovered orientation and higher functions prior to baseline according to herself and her daughter (her main caregiver). She was discharged with stable blood calcium levels, adjusted treatment, interconsultation for preferential surgery, and follow-up at Endocrinology and Nutrition outpatient clinics. The first appointment was made a week later in our offices with stable calcemia at 8.90mg/dL (8.80-10.20 mg/dL), stable with cinacalcet at a dose of 60mg every 24 hours.

Discussion

We describe a case of acute confusional syndrome as the first manifestation of severe hypercalcemia, secondary to primary hyperparathyroidism due to parathyroid adenoma. By means of pharmacological treatment, calcium levels were reduced with a clear improvement in neuropsychiatric symptoms. The patient meets the criteria for surgical management (non-urgent) for removal of the parathyroid adenoma[10].

Cases of acute confusional syndrome due to primary hyperparathyroidism have been reported in the literature for more than 50 years[11]. Park et al[5] attribute the severity of neuropsychiatric symptoms to plasma calcium levels. In fact, moderate hypercalcemia (10-14mg/dL) is associated with depression, apathy, and irritability. Severe hypercalcemia (>15mg/dL), as in the presented case, could therefore cause acute confusional syndrome with or without psychotic symptoms, catatonia, and even lethargy[5]. Normalization of calcium levels would lead to the reversibility of the symptomatology. Many of the cases described in the literature make use of an urgent surgical approach for the management of these patients and report good results[6-9].

Rao et al[12] performed a randomized clinical trial in asymptomatic primary hyperparathyroidism patients with normal or slightly elevated calcemia (10.1 to 11.5 mg/dL), with PTH higher than 20pg/mL, normal renal function, and absence of complications and relevant symptoms. Patients were divided into two groups: one group was managed conservatively, and the other group underwent total parathyroidectomy. People who underwent total parathyroidectomy showed a decrease in suicidal ideation from 22% to 10.7%, a decrease in anxiety from 49% to

22.4%, and a decrease in depression from 16.6% to 6.6%[12]. This is not the only study reporting these results. Weber et al (9) et al 2007 performed a case-control trial on neuropsychological symptoms in patients with primary hyperparathyroidism who were going to undergo total parathyroidectomy. 66 patients were evaluated both pre- and post-surgery using validated tests (HADS, PHQ-9 and SF-12). Preoperative depressive symptoms were present in 23.4% of patients and 15.6% had anxiety symptoms. The surgical approach achieved a significant reduction in prevalence: 7.8% and 15.7%, respectively. It should be noted that the prevalence of depression before surgery was higher in subjects with calcium levels above 11.2mg/dL.

In fact, some authors claim that neuropsychiatric symptomatology in patients with primary hyperparathyroidism could be underreported, especially in the older population[5,13]. Neuropsychiatric symptomatology in some series of patients undergoing parathyroidectomy would have a prevalence of 43.1% to 53% for anxiety, 33-62.1% for depression, 22% for suicidal ideation, 51.9% for irritability, 5% to 20% for hallucinations and 37.3% to 46.5% for cognitive impairment[5,6,14,15].

In the scientific literature, we have not found data comparing pharmacological management to surgical management in neuropsychiatric symptomatology caused by hypercalcemia secondary to primary hyperparathyroidism.

Conclusions

- Alterations in calcium metabolism can be associated with neuropsychiatric symptoms, the severity of which is potentially proportional to the severity of the ionic alteration.
- Neuropsychiatric symptomatology may be underreported in the scientific literature in patients with primary hyperparathyroidism.
- The high prevalence of these symptoms and the clear improvement reported by the surgical approach could support the inclusion of neuropsychiatric symptomatology within the surgical criteria for primary hyperparathyroidism.

Conflict of interest

The authors declare no conflict of interest.

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CASE REPORT

Ectopic renal insulinoma: case report

Insulinoma renal ectópico: informe de un caso

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Abstract

Insulinoma, the most common cause of hypoglycemia related to endogenous hyperinsulinism, is a rare neuroendocrine tumor. Its diagnosis is often delayed due to difficulties in identifying and localizing the functioning tumor. We report a case of a woman who suffered from an ectopic insulinoma, where the source of hormonal excess was not the pancreas as one might think, but the left renal mass. A 45-year-old female was admitted for evaluation of recurrent hypoglycaemic episodes she does not have diabetes mellitus. She referred a several-week history of symptoms :palpitations, tremors, sweating altered behavior, and anxiety (CT) scan of the chest and abdomen for localization of insulinoma with dimensions of 12x12 mm. In the left kidney, where a hypodense cortical lesion was observed in the middle part, well-limited, with necrotic areas inside, with dimensions of 62x81 mm which enhances after contrast After renal tissue pathology showed characteristics of a neuroendocrine tumor.

Key words: Insulinoma, Hypoglycemia, Whipple's triad Neuroendocrine tumor, renal mass.

Resumen

El insulinoma, la causa más frecuente de hipoglucemia relacionada con el hiperinsulinismo endógeno, es un tumor neuroendocrino raro. Su diagnóstico suele retrasarse debido a las dificultades para identificar y localizar el tumor funcionante. Presentamos el caso de una mujer que padecía un insulinoma ectópico, donde el origen del exceso hormonal no era el páncreas como podría pensarse, sino la masa renal izquierda. Una mujer de 45 años ingresó para evaluación de episodios hipoglucémicos recurrentes, no tiene diabetes mellitus. Refería cuadro de sintomatología de varias semanas de evolución: palpitaciones, temblores, alteración de la sudoración y ansiedad (TC) de tórax y abdomen para localización de insulinoma de 12x12 mm. En el riñón izquierdo, donde se observó una lesión cortical hipodensa en la parte media, bien delimitada, con áreas necróticas en su interior, con unas dimensiones de 62x81 mm que realza tras el contraste. Posterior a la patología del tejido renal, presenta características de tumor neuroendocrino.

Palabras clave: insulinoma, hipoglucemia, tríada de Whipple, tumor neuroendocrino, masa renal.

Background

Insulinoma, the most common cause of hypoglycemia-related to endogenous hyperinsulinism, is a rare neuroendocrine tumor with an annual incidence of 1-4 per million population per year[1]. Its diagnosis is often delayed due to difficulties in identifying and localizing the functioning tumor. We report a case of a young lady who suffered from an ectopic insulinoma, where the source of hormonal excess was not the pancreas as one might think, but the left renal mass.

Case presentation

A 45-year-old female was admitted for evaluation of recurrent hypoglycemic episodes in a person who does not have diabetes mellitus. She referred to suffering from a several-week history of symptoms that included: palpitations, tremors, hunger, sweating, altered behavior, and anxiety. Most of her symptoms occurred early in the morning (usually between 3-6 a.m.) and these symptoms improved spontaneously in 15 minutes or after intake of simple carbohydrates. Her clinical manifestations were consistent with Whipple's triad. The patient was admitted to the hospital and was subjected to a series of examinations.

The baseline blood results, including hemoglobin, white cell count, platelets, and renal and liver profiles were all within normal ranges. HbA1c was 4.5%. Laboratory test results showed an increase in C-reactive protein (CRP) levels to 9.06 mg/dL.

In conditions of an episode of hypoglycemia (venous glycemia-55 mg/dl), insulinemia, C-Peptide, and anti-insulin antibodies were obtained. The results were suggestive of insulinoma, with insulinemia 35.66 mcIU/mL (2.6-24.9) and C-Peptide 8.176 ng/ml(0.3-3.73). During another symptomatic episode of hypoglycemia, she had plasma glucose of 45 mg/dl while her plasma insulin and C-peptide were 42 mcIU/mL and 12 ng/ml (respectively) confirming the diagnosis of endogenous hyperinsulinemic hypoglycemia. The anti-insulin antibody test result was negative.

In terms of multiple endocrine neoplasia type 1(MEN-1) screening, anterior pituitary function, including levels of prolactin, thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), sex hormones, growth hormone(GH) and cortisol, all these were within normal range. The patient's PTH level was normal. As a result, there was no evidence for a diagnosis of MEN-1.

Later on, she underwent Computed tomography (CT) scan of the chest and abdomen for localization of insulinoma. It showed a small, isointense signal lesion at the level of the head of the pancreas that tends to be hyperattenuating on the arterial phase, with dimensions of 12x12 mm. Another finding was in the left kidney, where a hypodense cortical lesion was observed in the middle part, with mainly pararenal extension, well-limited, with necrotic areas inside, with dimensions of 62x81 mm, which enhances after contrast. There were no complaints of haematuria, frequent or burning micturition, or lumbar tenderness.

She underwent open surgical abdominal exploration. Pancreatic nodule enucleation and left nephrectomy were performed. Immediately after surgical treatment, the glucose level increased to the normal range. She became euglycemic without the need for dextrose infusion.

At first, we considered the diagnosis of incidentally detected left renal cell carcinoma in a patient with insulinoma. The histopathological findings disproved this idea. Microscopically, the pancreatic tumor was composed of a conglomerate of cysts lined by simple cuboidal epithelium. The nuclei were small, round to oval with dense, homogenous chromatin, thus suggesting the diagnosis of a Solid Serous Adenoma.

On the other hand, renal tissue pathology showed characteristics of a neuroendocrine tumor. Immunohistochemical staining revealed intense staining for pancytokeratin, insulin, chromogranin A, and neuron-specific enolase (NSE), confirming the left-sided renal mass to be the source of ectopic insulin secretion.

Discussion, Conclusions

Clinical hypoglycemia is, by definition, a plasma glucose concentration low enough to cause symptoms or signs, including impairment of brain function. Hypoglycemia is most convincingly documented by the Whipple triad. Documentation of the Whipple triad is particularly important when hypoglycemia is suspected in a person who does not have diabetes mellitus because hypoglycemic disorders are rare[2].

Insulinomas, the most common cause of hypoglycemia-related to endogenous hyperinsulinism, occur in 1-4 people per million of the general population[1]. Common autonomic symptoms of insulinoma include diaphoresis, tremor, and palpitations, whereas neuroglycopenenic symptoms include confusion, behavioral changes, personality changes, visual disturbances, seizures, and coma[3]. More than 90% of insulinomas are benign and usually small, well-encapsulated, solitary tumors[4].

Diagnosis of insulinomas can be challenging. The classical diagnosis of insulinoma depends on satisfying the criteria of Whipple's triad, which remains the cornerstone of the screening process: 1) hypoglycemia (plasma glucose < 50 mg/dL); 2) neuroglycopenic symptoms; and 3)

prompt relief of symptoms following the administration of glucose. In adults with symptoms of neuroglycopenia or documented low blood glucose levels, the gold standard for biochemical diagnosis remains measurement of plasma glucose, insulin, C-peptide, and proinsulin during a 72-h fast. This prolonged fasting test can detect up to 99% of insulinomas[2].

Ectopic insulin-secreting tumours are rare, comprising only 1% to 2% of all insulinomas, and are commonly located in the peripancreatic or periduodenal region where most heterotopic pancreatic tissue is located[5]. Ectopic insulin-producing tumours located away from pancreatic beds are infrequently reported in the literature[6,7].

Also its seems that like rare tumours Ectopic insulinoma to have a lower incidence four cases in million potion in years. Are diagnosis case ectopic insulinomas in the pelvis secondary to rectum[8], also in jejunum[9] and liver from metastasic pancreas.

Our patient had presented with a pancreatic lesion and a left renal mass lesion in imaging examinations and in the laboratory panel as hyperinsulinemic hypoglycemia. We initially considered the possibility of incidentally detected left renal cell carcinoma in a patient with insulinoma. The neuroendocrine and insulin-secreting nature of the renal tumor was confirmed by histopathological examination and immunohistochemistry, rejecting our initial hypothesis of pancreatic insulinoma.

Our case emphasizes the difficulty of the preoperative diagnosis of insulinoma. The localization diagnosis is the key to the success of surgical treatment. In general, the sensitivity of the noninvasive examinations commonly used in the diagnosis is approximately 56-70% for CT and 63-86% for MRI[10]. The imaging findings cannot determine the relationship between the lesion and hypoglycemia. Lesions found solely on CT or MRI can only be identified as insulinomas that cause hypoglycemia by postoperative pathology and the glycemic response. Nuclear medicine examinations including somatostatin receptor imaging and ^{68}Ga-NOTA-Exendin-4 PET/CT have greater advantages in determining the types and function of tumors[11]. However, the sensitivity rate of somatostatin receptor imaging is very low; the rate reported in the literature is only 19.5-50%. ^{68}Ga-NOTA-Exendin-4 PET/CT is currently the most sensitive noninvasive test, with a sensitivity rate of 97.7%, and is of great value for the diagnosis of ectopic insulinoma[12]. Surgical removal of the lesion is the main treatment and long-term close follow-up is needed for the malignant behavior of these ectopic lesions[13].

Conclusions

Ectopic insulinoma is a rare entity that is difficult to diagnose before surgery. This case emphasizes some of the challenges posed in the detection and management of insulinoma.

Conflict of interest
The authors declare no conflict of interest.

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ORIGINAL

Exploring biomedical waste management and disposal practices among hospitals in Port Harcourt, Rivers State

Exploración de las prácticas de gestión y eliminación de residuos biomédicos en los hospitales de Port Harcourt, Estado de Rivers

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Abstract

Background: Globally, disposal of biomedical waste is an environmental concern, as most medical wastes are infectious and could potentially lead to the spread of infectious diseases. The aim of this study was to assess the biomedical waste management and disposal practices among hospitals in Port Harcourt, Rivers State.

Method: A hospital based cross sectional design was adopted for this study on the biomedical waste management and disposal practices among hospitals in Port Harcourt, Rivers state. Statistical package for Social Sciences (SPSS) version 22.0 was used for the analysis of the study and chi square to determine association between variables (P=0.05). A structured questionnaire was used for data collection and a stratified and simple random sampling technique was used to draw out a total of 202 respondents who participated for the study.

Results: The study revealed that 35% (70) of the respondents were between 35-44 years of age. Overall knowledge of biomedical waste management among the health workers was 80.2%. From the study, age (p=0.00923), Level of Education (p= 0.0025) and Length of experience (p= 0.0457) were all associated with the level of knowledge of biomedical waste management.

Conclusion: A significant number of hospital workers are aware of biomedical waste generation, management and disposal practices. Although, attitude to biomedical waste management and disposal practices among health workers is average therefore a challenge. Sensitization of hospital staff by the public health personnel to improve biological waste disposal among the inexperienced is recommended. Also the government and policy makers should design laws that would facilitate the reduction and susceptibility of improper hospital waste disposal.

Key words: Waste Management, biomedical waste, knowledge, Attitude, Waste Disposal, Hospitals.

Resumen

Antecedentes: En todo el mundo, la eliminación de los desechos biomédicos es una preocupación ambiental, ya que la mayoría de los desechos médicos son infecciosos y podrían conducir a la propagación de enfermedades infecciosas. El objetivo de este estudio era evaluar las prácticas de gestión y eliminación de residuos biomédicos en los hospitales de Port Harcourt, estado de Rivers.

Método: Se realizó un diseño transversal sobre las prácticas de gestión y eliminación de residuos biomédicos en los hospitales de Port Harcourt, estado de Rivers. Se utilizó el paquete estadístico para las ciencias sociales (SPSS) versión 22.0 para el análisis del estudio y el chi cuadrado para determinar la asociación entre las variables (P=0.05). Se utilizó un cuestionario estructurado para la recogida de datos y una técnica de muestreo aleatorio estratificado y simple para extraer un total de 202 encuestados que participaron en el estudio.

Resultados: El estudio reveló que el 35% (70) de los encuestados tenía entre 35 y 44 años de edad. El conocimiento general de la gestión de residuos biomédicos entre los trabajadores sanitarios era del 80,2%. Del estudio se desprende que la edad (p=0,00923), el nivel de estudios (p= 0,0025) y la antigüedad (p= 0,0457) están asociados al nivel de conocimientos sobre la gestión de residuos biomédicos.

Conclusiones: Un número significativo de trabajadores hospitalarios conoce las prácticas de generación, gestión y eliminación de residuos biomédicos. Sin embargo, la actitud hacia las prácticas de gestión y eliminación de residuos biomédicos entre los trabajadores sanitarios es media, por lo que constituye un reto. Se recomienda la sensibilización del personal hospitalario por parte del personal de salud pública para mejorar la eliminación de residuos biológicos entre los inexpertos. Asimismo, el gobierno y los responsables políticos deberían diseñar leyes que faciliten la reducción y la susceptibilidad de la eliminación inadecuada de residuos hospitalarios.

Palabras clave: Gestión de residuos, residuos biomédicos, conocimientos, actitud, eliminación de residuos, hospitales.

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