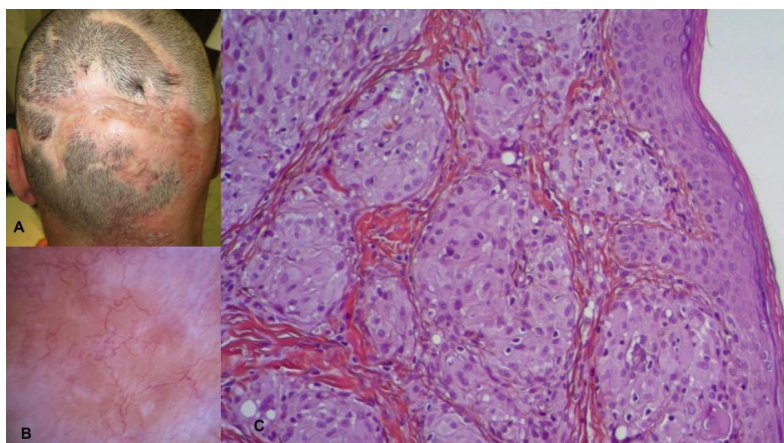


ACADEMIC JOURNAL OF HEALTH SCIENCES

MEDICINA BALEAR



Violencia de género, salud y trabajo

La relación entre los profesionales sanitarios y los pacientes en tiempo de Covid-19

Determination of scales related to cardiovascular risk and fatty liver in 5.370 spanish farmers

Reduction of the average length of stay in internal medicine: difficult, but not impossible

Evaluation of the prevalence of hearing loss and associated patterns in hemodialysis patients: A cross-sectional study in Iran

Influence of tobacco consumption, age and sex on cardiovascular risk levels

Nigella sativa extract attenuates benzene induced oxidative DNA damage and abnormality in hematological parameters in rats

Identifying the Factors Affecting Integrated Care of the Elderly in Iran

Relationship between alcohol consumption and obesity determined with different scales

The effectiveness of nutrition care training program to nurses of Intensive Care Unit on patient's nutritional consequences

The anti-tumor molecular mechanisms of mentioned fruits in the holy Quran; a systematic review

Investigating the relationship between job stress and coronary mental health (Covid Virus 19) in Iranian companies and families

The cryonic medical application from the perspective of Islamic jurisprudence and ethics; a review of theories

Extra-articular manifestations in rheumatoid arthritis and its relationship with serology markers in Saudi patients

La colisión de dos pandemias: retos y oportunidades

TSUNAMI COVID-19. Reflexions d'entitats de l'entorn de les Cures Pal·liatives

Anemia ferropénica refractaria en la infancia ¿Y si la causa no es tan frecuente?

Manifestaciones cutáneas con implicación pronóstica

Traumatic retroclival epidural hematoma in a child

Fracture resistance of teeth with simulated cervical root resorptions restored by various materials

ACADEMIC JOURNAL OF HEALTH SCIENCES

www.medicinabalear.org

Academic Journal of Health Sciences Medicina Balear is the organ of the **Royal Academy of Medicine of the Balearic Island**. It was created in 1986 with the aim of following up the scientific concerns and promoting the research spirit of health professionals in the Balearic Islands and with the additional objective of projecting health issues of interest to society.

Currently **Academic Journal of Health Sciences Medicina Balear** publishes in English, Spanish or Catalan original papers, review articles, letters to the editor and other writings of interest related to health sciences. The journal submits the originals to the anonymous review of at least two external experts (peer review).



The scientific material published in **AJHS Medicina Balear** is protected by copyright. **AJHS Medicina Balear** is not responsible for the information and opinions of the authors.

This work-unless otherwise indicated in the text, photographs, or other illustrations-is licensed under the Creative Commons NonCommercial-NoDerivativeWorks 3.0 Spain license.

Creative Commons; <http://creativecommons.org/licenses/by-nc-nd/3.0/es/>. In addition, the general public is authorized to reproduce, distribute and communicate the work provided that the authorship and the publishing entity are acknowledged and that no commercial use or derivative work is made.

Medicina Balear is included in the Digital Library of the Balearic Islands, of the University of the Balearic Islands, and is included in the following databases: Emerging Sources Citation Index (ESCI), Sherpa Romeo, Dulcinea, Latindex (catàleg), Dialnet, Índice Médico Español, DOAJ, Imbiomed, REDIB i Google Scholar.



Biblioteca digital de les
Illes Balears



Universitat
de les Illes Balears



SHERPA
ROMEO



DULCINEA
CONDICIONES DE AUTO-ARCHIVO DE
LAS REVISTAS CIENTÍFICAS ESPAÑOLAS

latindex

Dialnet



CSIC

IME

Índice
Médico
Español

DOAJ
DIRECTORY OF
OPEN ACCESS
JOURNALS

IMBIOMED

REDIB Red Iberoamericana
de Investigación y Conocimiento Científico

Google Scholar

EDIT

Royal Academy of Medicine of the Balearic Islands



www.ramib.org

Campaner, 4, baixos. 07003 Palma de Mallorca Tel. 971 72 12 30 Email: info@ramib.org
Pàgina web: <http://www.ramib.org>

Dipòsit Legal: PM 486 - 95

eISSN: 2255 - 0569

Design and layout

Inteligencia Publicitat - www.intelagencia.es - intelagencia@intelagencia.es

ACADEMIC JOURNAL OF HEALTH SCIENCES

Three-monthly journal of the Royal Academic of Medicine
of the Balearic Island

Editor A. Arturo López González, *RAMIB*,
Reial Acadèmia de Medicina de les Illes Balears (*RAMIB*)

EDITORIAL COUNCIL

Assistant manager	Joan March Noguera, <i>RAMIB</i>
Scientific editor	Marta Couce Matovelle, <i>Case Western Reserve University</i>
Editorials consultings	José A. Guijarro Pastor, <i>AEMET</i> · Jaume Rosselló Mir, <i>UIB</i>
Editor-in -chief	J. L. Olea Vallejo, <i>RAMIB</i>
Vowels	Antoni Aguiló Pons, <i>Universitat de les Illes Balears</i> · Antonia Barceló Bennassar, <i>Hospital Son Espases</i> · Bartolomé Burguera González, <i>Cleveland Clinic (Ohio)</i> · Amador Calafat Far, <i>Socidrogalcohol</i> · Carlos Campillo Artero, <i>Universitat Pompeu Fabra</i> · Valentín Esteban Buedo, <i>Conselleria de Sanitat, Generalitat Valenciana</i> · Carmen González Bosch, <i>Universitat de València</i> · Miguel A. Limon Pons, <i>Institut Menorquí d'Estudis</i> · Jordi Martínez Serra, <i>Hospital Son Espases</i> · Virgili Páez Cervi, <i>Bibliosalut</i> · Lucio Pallarés Ferreres, <i>Hospital Son Espases</i> · Ignacio Ricci Cabello, <i>University of Oxford</i> · Guillermo Sáez Tormo, <i>Universitat de València</i> · M ^a Teófila Vicente Herrero, <i>IUNICS</i>

SCIENTIFIC COUNCIL

M^a José Anadón Baselga (*Universidad Complutense de Madrid*), Miquel Capó Martí (*Universidad Complutense de Madrid*), Antonio Coca Payeras (*Universitat de Barcelona*), James Drane (*Edinboro University*), Leopoldo Forner Navarro (*Universitat de València*), Alexandre García-Mas, (*Universitat de les Illes Balears*), Antoni Gelabert Mas (*Universitat Autònoma de Barcelona*), Joan Grimalt Obrador (*Consell Superior d'Investigacions Científiques, CSIC*), Federico Hawkins Carranza (*Universidad Complutense de Madrid*), Joan Carles March Cerdà (*Escuela Andaluza de Salud Pública, EASP*), Gabriel Martí Amengual (*Universitat de Barcelona*), Jasone Monasterio Aspiri (*Universitat Autònoma de Barcelona*) Rosa Pulgar Encinas (*Universidad de Granada*), Ciril Rozman (*Universitat de Barcelona*), Joan Benejam Gual (*Hospital de Manacor*), Joan Llobera Cànaves (*Atenció Primària - Mallorca*), José Reyes Moreno (*Hospital de Inca*), José María Vicens Colom (*Cercle d'Economia de Mallorca*), Carmen Tomás-Valiente Lanuza (*UIB*), Antonio Pareja Bezares (*Conselleria de Salut*), Farhad Safarpour Dehkordi (*Tehran University*), Anton Erkoreka Barrena (*Director del Museo Vasco de Historia de la Medicina y de la Ciencia*), José Ignacio Ramírez Manent (*Atención Primaria de Mallorca-Facultad de Medicina UIB*), Colwyn M. Jones (*European Association of Dental Public Health*), Pål Barkvoll (*Universitetet i Oslo*), Teresa Szupiany-Janeczek (*Jagiellonian University Medical College Krakow*), Yarmukhamedov Bekhzod (*Tashkent University*).

With the collaboration



G CONSELLERIA
O PRESIDÈNCIA,
I CULTURA I IGUALTAT
B
/

Fundació
Patronat Científic



Col·legi de Metges
Illes Balears



PREMIOS Y BECAS 2021

PREMIOS DE INVESTIGACIÓN

La **Fundació Patronat Científic** convoca los Premios de Investigación **Mateu Orfila**, **Damià Carbó** y **Metge Matas** con la finalidad de **premiar la trayectoria de la investigación en Ciencias de la Salud** en nuestra comunidad.

<http://www.comib.com/wp-content/uploads/2021/02/01-Convocatoria-Premios-investigacio0n-2021-web.pdf>

PREMIO FUNDACIÓ MUTUAL MÈDICA AL MEJOR PROYECTO DE TESIS DOCTORAL

El premio tiene como finalidad **facilitar a los médicos colegiados** en las Illes Balears la **obtención del título de Doctor**. Con el patrocinio de la **Fundació Mutual Mèdica**.

<http://www.comib.com/wp-content/uploads/2021/02/04-Convocatoria-mejor-proyecto-de-tesis-doctoral-2021-web.pdf>

BECAS FUNDACIÓ BANCO SABADELL DE ROTACIÓ EXTERNA PARA MÉDICOS RESIDENTES

Facilitar a los médicos que realicen la residencia en hospitales de Balears la **formación**, al menos durante un mes, en **centros hospitalarios nacionales y extranjeros**, en los dos últimos años de la residencia o al terminar la misma. Con la colaboración de la **Fundació Banc Sabadell**.

<http://www.comib.com/wp-content/uploads/2021/02/02-Convocatoria-Becas-Fundaci0-Banc-Sabadell-web-.pdf>

BECAS DE INNOVACIÓN

Tienen como objetivo facilitar a los médicos colegiados en las Illes Balears, excepto MIR, la **formación**, durante al menos un mes, en **centros sanitarios nacionales y extranjeros en técnicas diagnósticas o terapéuticas**.

<http://www.comib.com/wp-content/uploads/2021/02/03-Convocatoria-Becas-de-Innovacion-2021-web.pdf>

CERTAMEN DE CASOS CLÍNICOS PARA MÉDICOS RESIDENTES

Premios a los mejores casos clínicos presentados por médicos residentes colegiados en Illes Balears de cualquier **especialidad médica o quirúrgica**.

<http://www.comib.com/wp-content/uploads/2021/02/05-Convocatoria-Certamen-de-casos-clinicos-2021-web.pdf>

PREMIO CAMILO JOSÉ CELA DE HUMANIDADES MÉDICAS

Premio literario de ámbito nacional destinado a **honrar la especial relación que tuvo el Nobel con los médicos** a lo largo de su vida.

<http://www.comib.com/wp-content/uploads/2021/02/06-Convocatoria-Premio-Camilo-Jose3-Cela-2021web.pdf>

EDITORIAL

- NRT, a safe and effective smoking treatment** 9-10
Miguel C. Aguiló Juanola

ORIGINALS ARTICLES

- Gender violence, health and work** 11-22
Lucila Chust-Morató, Lucila Morató Moscardó, Ignacio Torres-Alberich, M^a Victoria Ramírez-Iñiguez de la Torre, Luisa Capdevila García, M^a Teófila Vicente-Herrero
- The relationship between health professionals and patients in time of the Covid-19** 23-25
Carlos Fernández Juliá, Joana María Juliá-Móra, Sebastian Roig Noguera
- Determination of scales related to cardiovascular risk and fatty liver in 5.370 spanish farmers** 26-33
Vahid Mohebbi, Andrés Aramayo, Jorge Morales
- Reduction of the average length of stay in internal medicine: difficult, but not impossible** 34-38
Daniel Nan, Marta Fernández-Ayala, Gonzalo Martínez de las Cuevas, Eloísa Canga, José Manuel Olmos, José Luis Hernandez
- Evaluation of the prevalence of hearing loss and associated patterns in hemodialysis patients: A cross-sectional study in Iran** 39-43
Gholam-Ali Dashti Khavidaki, Reza Gharibi
- Influence of tobacco consumption, age and sex on cardiovascular risk levels** 44-50
Kristýna Mudrychová, Jitka Mudrychová, Martina Houšková Beránková, Bárbara Altisench Jané, María Albaladejo Blanco, José Ignacio Ramírez Manent
- Nigella sativa* extract attenuates benzene induced oxidative DNA damage and abnormality in hematological parameters in rats** 51-56
Mohamed M. El-Khawanky, Basel A. Abdel-Wahab, Metwally E. Abdalla, Abdulmohsen M. Alruwetei
- Identifying the Factors Affecting Integrated Care of the Elderly in Iran** 57-63
Mansoor Khojani, Fatemeh Dabbaghi, Ghahraman Mahmoodi
- Relationship between alcohol consumption and obesity determined with different scales** 64-69
Yarianne Inalvis Rivero Ledo, Dorey Arderí Guerra, Yamileris Patchana, María Ladisa, Onel Valdes Garcia, Hilda González San Miguel, Maria del Mar Rigo Vives
- The effectiveness of nutrition care training program to nurses of Intensive Care Unit on patient's nutritional consequences** 70-75
Fakhrudin Faizi, Ali Bahrāmifār, Masoud Sirati Nir, Hamid Soleymanzadeh, Abolfazl Rahimi
- The anti-tumor molecular mechanisms of mentioned fruits in the holy Quran; a systematic review** 76-83
Atefeh Ashtari, Firoozeh Niazvand, Narges Chamkouri
- Investigating the relationship between job stress and coronary mental health (Covid Virus 19) in Iranian companies and families** 84-97
Hanieh Sadat Safavi Homami
- The cryonic medical application from the perspective of Islamic jurisprudence and ethics; a review of theories** 98-105
Laila Fakher, Rajab Akbarzadeh, Mohammad Reza Zamiri, Ahmad Hossain Fallahi, Sayed Morteza Mosavi, Sayed Mohammad Saeid Mohamadi
- Extra-articular manifestations in rheumatoid arthritis and its relationship with serology markers in Saudi patients** 106-110
Fehaid Ghali Alanazi

SPECIAL ARTICLES

- The collision of two pandemics: challenges and opportunities** 111-121
Luis Masmiquel Comas
- COVID-19 TSUNAMI. Palliative Care environment entity reflections** 122-126
Joana María Juliá Mora, Mercè Llagostera Pagés, Carmen Moreno Hoyos, Javier Cortés Bordoy, Catalina Rosselló Forteza, Susana Jordá Martí, Jorge Calvin Gil-Mascarell, Bárbara Massó Pomés

CASE REPORT

- Iron deficiency anemia in children. What if the etiology is not that common?** 127-128
Unai Díaz-Moreno, Margarita Cañellas-Fuster, Georgina Sanchis-Blanco, Susana Fuertes-Blas, Carmen Vidal-Palacios, Claudia Marhuenda
- Cutaneous manifestations with prognostic implication** 129-131
Amador Solá Truyols
- Traumatic retroclival epidural hematoma in a child** 132-135
Aidin Shakeri, Rezvan Rahimifār, Shima Zargar, Alireza Kamali
- Fracture resistance of teeth with simulated cervical rootresorptions restored by various materials** 136-141
Fateme Mohammadian, Seyyed Sina Hazinehei, Sedighe Sadat Hashemikamangar, Fatemeh Dibaji, Mohammad Javad Kharrazifard



¿Qué profesional puede tener 45 años de edad y 90 de experiencia?

La respuesta es Banca March

La experiencia de un profesional no está únicamente en su edad, sino también en la edad de la firma para la que trabaja.

Y 90 años de experiencia es lo que ofrecen los profesionales de Banca March.

90 años gestionando patrimonios y demostrando entre otras cosas, que la prudencia no está reñida con la rentabilidad.

 **BancaMarch**

EDITORIAL

- La TSN, un tratamiento del tabaquismo seguro y efectivo** 9-10
Miguel C. Aguiló Juanola

ORIGINALES

- Violencia de género, salud y trabajo** 11-22
Lucila Chust-Morató, Lucila Morató Moscardó, Ignacio Torres-Alberich, M^a Victoria Ramírez-Iñiguez de la Torre, Luisa Capdevila García, M^a Teófila Vicente-Herrero
- La relación entre los profesionales sanitarios y los pacientes en tiempo de Covid-19** 23-25
Carlos Fernández Juliá, Joana María Juliá-Móra, Sebastian Roig Noguera
- Determinación de escalas relacionadas con el riesgo cardiovascular y el hígado graso en 5.370 agricultores españoles** 26-33
Vahid Mohebbi, Andrés Aramayo, Jorge Morales
- Disminución de la estancia media en medicina interna: difícil, pero no imposible** 34-38
Daniel Nan, Marta Fernández-Ayala, Gonzalo Martínez de las Cuevas, Eloisa Canga, José Manuel Olmos, José Luis Hernandez
- Evaluación de la prevalencia de hipoacusia y patrones asociados en pacientes en hemodiálisis: un estudio transversal en Irán** 39-43
Gholam-Ali Dashti Khavidaki, Reza Gharibi
- Influencia del consumo de tabaco, la edad y el sexo en los niveles de riesgo cardiovascular** 44-50
Kristýna Mudrychová, Jitka Mudrychová, Martina Houšková Beránková, Bárbara Altisench Jané, María Albaladejo Blanco, José Ignacio Ramírez Manent
- El extracto de *Nigella sativa* atenúa el daño oxidativo del ADN inducido por el benceno y la anomalía en los parámetros hematológicos en ratas** 51-56
Mohamed M. El-Khawanky, Basel A. Abdel-Wahab, Metwally E. Abdalla, Abdulmohsen M. Alruwetei
- Identificación de los factores que afectan la atención integral de las personas mayores en Irán** 57-63
Mansoor Khojamli, Fatemeh Dabbaghi, Ghahraman Mahmoodi
- Relación entre el consumo de alcohol y la obesidad determinada con diferentes escalas** 64-69
Yrienne Inalvis Rivero Ledo, Dorey Arderi Guerra, Yamileris Patchana, María Ladisa, Onel Valdes Garcia, Hilda González San Miguel, María del Mar Rigo Vives
- La efectividad del programa de capacitación en atención nutricional para enfermeras de la unidad de cuidados intensivos sobre las consecuencias nutricionales del paciente** 70-75
Fakhruddin Faizi, Ali Bahramifar, Masoud Sirati Nir, Hamid Soleymanzadeh, Abolfazl Rahimi
- Los mecanismos moleculares antitumorales de las frutas mencionadas en el sagrado Corán; una revisión sistemática** 76-83
Atefeh Ashtari, Firoozeh Niazvand, Narges Chamkouri
- Investigación de la relación entre el estrés laboral y la salud mental coronaria (virus Covid 19) en empresas y familias iraníes** 84-97
Hanieh Sadat Safavi Homami
- La aplicación médica crónica desde la perspectiva de la jurisprudencia y la ética islámicas; una revisión de teorías** 98-105
Laila Fakher, Rajab Akbarzadeh, Mohammad Reza Zamiri, Ahmad Hossain Fallahi, Sayed Morteza Mosavi, Sayed Mohammad Saeid Mohamadi
- Identificación de los factores que afectan la atención integral de las personas mayores en Irán** 106-110
Fehaid Ghali Alanazi

ARTICULOS ESPECIALES

- La colisión de dos pandemias: retos y oportunidades** 111-121
Luis Masmiquel Comas
- TSUNAMI COVID-19. Reflexions d'entitats de l'entorn de les Cures Pal·liatives** 122-126
Joana Maria Juliá Mora, Mercè Lagostera Pagés, Carmen Moreno Hoyos, Javier Cortés Bordoy, Catalina Rosselló Forteza, Susana Jordá Martí, Jorge Calvín Gil-Masarell, Bárbara Massó Pomés

ESTUDIO DE CASOS

- Anemia ferropénica refractaria en la infancia ¿Y si la causa no es tan frecuente?** 127-128
Unai Díaz-Moreno, Margarita Cañellas-Fuster, Georgina Sanchis-Blanco, Susana Fuertes-Blas, Carmen Vidal-Palacios, Claudia Marhuenda
- Manifestaciones cutáneas con implicación pronóstica** 129-131
Amador Solá Truyols
- Hematoma epidural retroclival traumático en un niño** 132-135
Aidin Shakeri, Rezvan Rahimifar, Shima Zargar, Alireza Kamali
- Resistencia a la fractura dental con reabsorciones radiculares cervicales simuladas y restauradas con diversos materiales** 136-141
Fateme Mohammadian, Seyyed Sina Hazinehei, Sedighe Sadat Hashemikamangar, Fatemeh Dibaji, Mohammad Javad Kharrazifard

Haz algo grande por tu salud



#Duerme 1HoraMás

En Asisa somos expertos en salud y sabemos que el sueño es vital para el buen funcionamiento de tu corazón, tu cerebro y todo tu organismo.

Los especialistas determinan que **una persona adulta necesita entre 7 y 9 horas diarias de sueño** para estar bien.

Sin embargo, se estima que el 80% de los españoles duermen menos de este tiempo,

exponiéndose a **sufrir hipertensión, taquicardia, depresión, pérdida de memoria, sobrepeso y diabetes**, entre otros problemas. Y como sabes, **en Asisa solo nos preocupa tu salud. Por eso invertimos todos nuestros recursos en cuidarte**, incluido este anuncio en el que te aconsejamos que duermas una hora más todos los días.

Empresa Colaboradora:

TR 200 AÑOS

Asisa Palma de Mallorca.
C/ Pere Dezcallar i Net, 10
asisa.es 901 10 10 10

*Nada más que tu salud
Nada menos que tu salud*

asisa

NRT, a safe and effective smoking treatment

La TSN, un tratamiento del tabaquismo seguro y efectivo

Miguel C. Aguiló Juanola 

Community Pharmacist in Palma

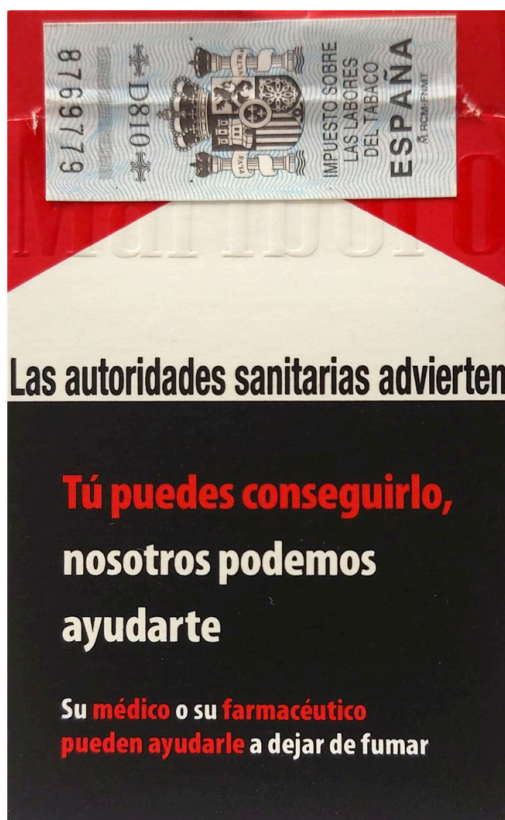
Smoking is an addictive and chronic disease and, therefore, requires prevention and treatment, with the greatest effectiveness being achieved by combining pharmacological and cognitive-behavioral treatment.

The drugs considered first-line are varenicline, bupropion and nicotine replacement therapy (NRT). However, as these include drugs that are not subject to medical prescription, they are not usually well known and, therefore, underutilized in all their possibilities by smoking therapists.

To optimize its use and provide the latest strategies regarding its use, the Spanish Society of Clinical, Family and Community Pharmacy (SEFAC) has just published a Guide¹ on NRT, aimed at community pharmacists in general, whether or not they are experts in smoking, but which can be useful for all healthcare professionals working in this field.

It covers from the most general aspects, such as the approach to different types of smokers, and the management of NRT as a single forms, to more specific aspects such as Combined NRT (patches with oral forms) or with other drugs (bupropion or varenicline), use in pregnancy or in special situations, alternative strategies to the usual pharmacological treatment, or tobacco-drug interactions, a little known aspect, sometimes of notable clinical significance, which was already reviewed in this same publication².

NRT, in addition to presenting proven data on safety and effectiveness, has the versatility of being able to use different pharmaceutical forms in different dosages, and can be adapted to the patient's smoking pattern, which favors the effectiveness of the therapy. Combined NRT



and varenicline are considered the two options of choice in the pharmacological treatment of smoking³. On the other hand, a recent Cochrane review, based on 63 studies with more than 41,000 participants, concludes that Combined NRT is as effective as varenicline, between 15 and 36% more effective than single NRT, in its different forms, and that the safety of using high-dose regimens, such as 25 mg with 16-hour patches, has been proven in highly dependent smokers⁴.

Alternative therapeutic strategies described in the document:

- “Cutting Down before to Quit”, used for some years now, which makes it possible to broaden the range of intervention by being able to address patients who are poorly motivated or who do not want to stop abruptly. The use of oral forms of NRT in this

strategy clearly increases its effectiveness⁵.

- “Pre-loading”, which is carried out by administering progressive doses of the drug before D-day (the day of cessation) in motivated smokers who are not planning to cut down, increases the smoker's confidence in the treatment and reduces subsequent episodes of craving. Varenicline can be used, which has a recent convincing study⁶ and NRT, which, for the moment, has only one study, conducted with patches, with moderate evidence⁷.

- The “Flexible Quit Dates”, making it possible to extend total cessation for up to one month, is effective and useful with varenicline⁸, but not adequate with NRT.

- The combination with the other first-line drugs, bupropion or varenicline, with greater evidence of efficacy, so far, with the first of the two aforementioned drugs⁹.

The Guide is completed with a reference to cognitive-behavioral treatment, also a key element in the approach to the smoking patient, considering that different levels of various types of dependence must be addressed: physical, psychological, gestural, behavioral and social.

The effectiveness of the tobacco industry to enter the world of young people, its current main objective, through electronic nicotine delivery systems, heated

tobacco products, and the most recent synthetic nicotine products, supported to a large extent by interventions in social networks, and even by those of some health professionals prone to their use, located in key positions, mean that we must make even more effort and work in coordination all health professionals from the different scientific societies and institutions that have the common goal of achieving a world without tobacco.

References

1. Aguiló Juanola MC, Serantes García L. Guía de actuación farmacéutica. La terapia sustitutiva con nicotina (TSN). Madrid: IMC-SEFAC; 2021.
2. Aguiló Juanola MC. Actualización en el abordaje del tabaquismo. Interacciones del tabaco con los tratamientos farmacológicos. *Medicina Balear*. 2018;33(3):35-40.
3. Jiménez CA, Granda JI, Cicero A, Perera L, Mayayo M, Cristóbal M, et al. Combinación de fármacos para el tratamiento del tabaquismo. *Rev Patol Respir*. 2014;17(3):87-9.
4. Lindson N, Chepkin SC, Ye W, Fanshawe TR, Bullen C, Hartmann-Boyce J. Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2019;(4):CD013308.
5. Díaz-Maroto JL, Jiménez-Ruiz CA. Tratamiento farmacológico del tabaquismo. *Inf Ter Sist Nac Salud*. 2008;32:71-82.
6. Bohadana A, Freier-Drorb Y, Pelesa V, Babaib P, Izbickia G. Extending varenicline preloading to 6 weeks facilitates smoking cessation: A single-site, randomised controlled trial. *EClinicalMedicine*. 2020;19:100228.
7. Aveyard P. Effects on abstinence of nicotine patch treatment before quitting smoking: parallel, two arm, pragmatic randomised trial. *BMJ*. 2018;361:k2164.
8. Rennard S, Hughes J, Cinciripini, PM, Kralikova E, Raupach T, Arteaga C, et al. A Randomized Placebo Controlled Trial of Varenicline for Smoking Cessation Allowing Flexible Quit Dates Nicotine & Tobacco Research. 2012;14(3):343-50.
9. Stead LF, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2012;(11):CD000146.

ORIGINAL

Violencia de género, salud y trabajo

Gender violence, health and work

**Lucila Chust-Morató¹, Lucila Morató Moscardó², Ignacio Torres-Alberich³,
M^a Victoria Ramírez-Iñiguez de la Torre⁴ , Luisa Capdevila García⁵ ,
M^a Teófila Vicente-Herrero⁶ **

1. Psicóloga sanitaria Equipo Base Servicios Sociales. Valencia 2. Médico del Trabajo. Valencia

3. Abogado Ilustre Colegio de Abogados de Valencia 4. Médico del Trabajo. Servicio de Prevención de Riesgos Laborales Grupo Correos. Albacete 5. Médico del trabajo Servicio de Prevención Mancomunado MAPFRE. Valencia 6. Médico del Trabajo. Servicio de Prevención de Riesgos Laborales Grupo Correos. Valencia.

Correspondencia

M^a Teófila Vicente Herrero

Servicio Medicina del Trabajo. Grupo Correos

Plaza del Ayuntamiento nº 24. 46002 Valencia

E-mail: vicenteherreromt@gmail.com/grupo.gimt@gmail.com

Recibido: 9 - I - 2021

Aceptado: 2 - III - 2021

doi: 10.3306/AJHS.2021.36.02.11

Resumen

La violencia de género en la pareja afecta a casi una de cada tres mujeres en el mundo. En los últimos años se ha convertido en un fenómeno social difícil de gestionar. En España la normativa es amplia siendo abordada esta problemática de forma total o parcial por distintas Leyes y Reglamentos.

Las diferentes formas de violencia, simbólica, estructural e interpersonal, no son excluyentes, sino que se interrelacionan y repercuten en la salud. Son objeto de investigación las repercusiones derivadas: psicológicas, biológicas, neurológicas, conductuales y fisiológicas.

Las consecuencias psicológicas son, en ocasiones, más graves que sus efectos físicos ya que la merma de autoestima de las mujeres aumenta el riesgo de problemas de salud. Los psicólogos actúan en coordinación con el personal sanitario para minimizar el daño derivado de la violencia y facilitar la integración social y laboral de la mujer.

En España, cuando la mujer retorna al trabajo después de un proceso de Incapacidad Temporal es valorada por el médico del trabajo del servicio de prevención de riesgos laborales de la empresa, a efectos de garantizar su seguridad y lograr la mejor adaptabilidad en esta etapa.

La psicología es una de las especialidades de los servicios de prevención, presentes en la propia empresa o concertados externamente, y su actuación coordinada con los profesionales sanitarios puede facilitar un retorno sin riesgo actuando conjuntamente con los responsables de la gestión empresarial y, de forma especial con los responsables de los recursos humanos.

Palabras clave: Violencia de género, intervención psicológica, salud laboral.

Abstract

Gender violence in the couple affects one in three women in the world. It is currently a difficult social phenomenon to manage, although there is a generous legal support regulation.

The different forms of violence are not exclusive, but are interrelated and have an impact on health with consequences: psychological, biological, neurological, behavioural and physiological.

The psychological consequences are, occasionally, more serious than the physical ones. Therefore, psychologists and health workers must act in coordination to minimize the damage and facilitate the recovery and socio-labour integration of the affected woman.

In Spain, preventive legislation contemplates psychosociology as a specialty, incorporated into the company, or external agreements. The psychologist and the health prevention service workers working together will facilitate the return to work without risk, requiring the collaboration of business managers and human resources managers to adopt the required preventive-adaptive measures.

Key words: Intimate partner violence, Psychological intervention, occupational health.

Nota: En este documento, no se discrimina a nadie por razón de sexo. A lo largo de todo este documento se utilizará el género gramatical masculino para referirse a colectivos mixtos, como aplicación de la ley lingüística de la economía expresiva. Tan solo cuando la oposición de sexos sea un factor relevante en el contexto se explicitarán ambos géneros.

Introducción

El concepto de violencia viene definido en la Real Academia de la Lengua (RAE)¹ como: *cualidad de violento, acción y efecto de violentar o violentarse, acción violenta o contra el natural modo de proceder*. De forma complementaria, el diccionario del español jurídico define la violencia como: *fuerza física que aplica una persona sobre otra y que constituye el medio de comisión propio de algunos delitos, como el robo o los delitos contra la libertad sexual, entre otros (JRAE)².*

No es un fenómeno exclusivo de hombres o de mujeres, pudiendo afectar a ambos, pero en los últimos tiempos la violencia sufrida por las mujeres ha adquirido proporciones que la convierten en un fenómeno social, de compleja gestión.

La violencia de pareja íntima afecta a casi una de cada tres mujeres en todo el mundo durante su vida. Su distribución es muy desigual, con una prevalencia de menos del 4% en muchos países de altos ingresos, mientras llega al 40% en algunos entornos de bajos ingresos.

Poco se sabe sobre los factores que impulsan la distribución geográfica de la violencia de pareja o cómo los macrofactores podrían combinarse con factores individuales para determinar estas cifras. Los resultados de una encuesta llevada a término en 44 países, a 481.205 mujeres, entre el 1 de enero de 2000 y el 17 de abril de 2013 muestran que, junto con el estatus de las mujeres y otros factores relacionados con el género, podrían incluirse otros factores presentes en el entorno. La educación de las niñas está fuertemente asociada con un menor riesgo de violencia de pareja en países donde el abuso de la esposa está normalizado.

Del mismo modo, la violencia de pareja es menos frecuente en países con una alta proporción de mujeres incorporadas al mundo del trabajo, pero trabajar por dinero en efectivo aumenta el riesgo de una mujer en países donde trabajan pocas mujeres. Los resultados de este trabajo sugieren que los formuladores de políticas podrían reducir la violencia al eliminar el sesgo de género en los derechos de propiedad y abordar las normas que justifican la violencia a la pareja y el control masculino del comportamiento femenino. Se propone poner mayor énfasis en las reformas de políticas a nivel macroeconómico y tener en cuenta los efectos a nivel transversal al diseñar las intervenciones (Heise LL, Kotsadam A, 2015)³.

Sin embargo la violencia está presente en todas las sociedades. En diversos grados, mujeres y niñas son víctimas de violencia física, sexual y psicológica que trasciende diferencias en renta, clase y cultura. Así lo destacó la Organización de Naciones Unidas (ONU) en 2015, afirmando que *esta violencia es reconocida como una violación de los derechos humanos y una forma de discriminación contra*

la mujer, que refleja el desequilibrio generalizado del poder entre mujeres y hombres. Dicha violencia puede conducir a problemas de salud a largo plazo a nivel físico, mental y emocional (The World's Women 2015)⁴.

La violencia de género como problema social

La violencia sobre la mujer en cualquiera de sus tipos está extendida en todos los países del mundo y afecta a todos los estratos sociales. Los estudios apuntan a diferencias en función de las distintas concepciones sociales. Un aspecto que cobra importancia creciente es el incremento de comportamientos violentos entre adolescentes y donde la labor educativa es fundamental. Se destaca la urgencia e importancia de implementar acciones preventivas tempranas en las escuelas, involucrando a las familias y la comunidad y centradas en la deconstrucción de los patrones culturales de género actuales, en función de su origen histórico, a fin de apoyar enfoques pedagógicos emancipadores y liberadores (Taquette SR, Monteiro DLM, 2019)⁵.

Casi un tercio (30%) de todas las mujeres que han tenido una relación ha sufrido violencia física o sexual por parte de su pareja. Las estimaciones de prevalencia de la violencia de pareja oscilan entre el 23,2% en los países de ingresos altos y el 24,6% en la región del Pacífico Occidental, al 37% en la región del Mediterráneo Oriental y el 37,7% en la región de Asia Sudoriental (OMS violence-against-women)⁶.

Datos de nuestro país (de julio de 2019) procedentes de la Delegación del Gobierno para la Violencia de Género del Ministerio de la Presidencia, Relaciones con las Cortes e Igualdad (estadísticas violencia género-igualdad)^{7,8} estiman un total de casos recogidos de 557.101. El concepto de "caso de violencia de género" es muy similar al de "víctima de violencia de género", aunque no es idéntico. Un caso contiene toda la información que relaciona a una víctima con único agresor. De esta manera, si una mujer, a lo largo del tiempo, es víctima de violencia de género con más de un agresor, hablaremos de un caso distinto por cada uno de los diferentes agresores.

Aunque conocer y comprender la prevalencia y las consecuencias de la violencia hacia las mujeres es complejo, no se puede ignorar cómo los patrones de violencia están conectados con los sistemas sociales y las instituciones sociales. En algunos trabajos los autores han examinado cómo la violencia estructural y simbólica contribuye a la violencia interpersonal contra las mujeres; y cómo interactúan los determinantes sociales de la salud y la violencia interpersonal contra las mujeres. Las diferentes formas de violencia, simbólica, estructural e interpersonal, no son mutuamente excluyentes, sino que se relacionan entre sí. La violencia estructural está marcada por un

acceso profundamente desigual a los determinantes de la salud (vivienda, atención médica de calidad y desempleo), que luego crean condiciones en las que puede ocurrir violencia interpersonal y que configuran formas de violencia de género para las mujeres en posiciones sociales vulnerables. Los factores estructurales pueden tener impactos negativos en los determinantes sociales de la salud y aumenta el riesgo de violencia interpersonal entre las mujeres. Los autores proponen respuestas de las políticas de salud pública a la violencia contra las mujeres yendo más allá de los enfoques de violencia a nivel individual, para considerar cómo la violencia a nivel estructural e interpersonal y las relaciones de poder configuran las 'experiencias vividas' de violencia para las mujeres (Montesanti SR, Thurston WE, 2015)⁹.

Un estudio realizado en Nigeria destaca la asociación positiva entre el trabajo en efectivo y la violencia de pareja íntima (IPV) de tipo físico, que fue significativamente mayor para las mujeres que residían en localidades donde se contaba con una mayor aprobación social en el uso de la violencia del hombre contra la mujer y donde la toma de decisiones dominada por el esposo era más común. Esta brecha educativa conyugal favorecía a la IPV sexual y frente a ello se proponen programas integrados de prevención de IPV y empoderamiento económico que consideren las normas de género y las creencias de rol de género adaptadas a cada entorno y localidad, a fin de promover entornos sociales en los que las mujeres puedan beneficiarse de su empoderamiento económico (Gage AJ, Thomas NJ, 2017)¹⁰.

En Panamá un estudio, realizado entre marzo de 2014 y marzo de 2015, trató de visibilizar las desigualdades de género, violencia y su relación con el proceso salud-enfermedad en trabajadoras de instituciones públicas (civiles, policías militares y oficiales de prisiones). Los resultados revelaron los dilemas a los que están sometidas estas mujeres en el campo de la seguridad pública, la exposición a la violencia, principalmente institucional y de género, y su impacto en la salud; las relaciones de poder, marcadas por las jerarquías de las corporaciones y las asimetrías de género entre hombres y mujeres en entornos profesionales. Recomienda promover la visibilidad de las mujeres que trabajan en instituciones de seguridad pública, considerando el impacto de la violencia y las desigualdades de género en sus vidas personales y profesionales, incluida la resistencia y los reordenamientos promovidos por estas mujeres en las instituciones en respuesta a su presencia en un ambiente hegemónico y tradicionalmente masculino (Schneider D, Signorelli MC, Pereira PPG, 2017)¹¹.

Las mujeres inmigrantes y refugiadas corren un alto riesgo de IPV y homicidio de pareja íntima (IPH). Países como EE.UU, con un elevado y creciente número de inmigrantes y refugiados, muestran especial preocupación por este tema con el objetivo de identificar

las percepciones de los sobrevivientes y agresores y poner en marcha factores de protección y riesgo comunes y culturalmente específicos para IPV e IPH para mujeres inmigrantes y refugiadas, priorizar áreas de intervenciones de planificación de seguridad para sobrevivientes que están en riesgo de violencia severa o letal por parte de una pareja íntima. El trabajo se realiza con inmigrantes adultos y refugiados sobrevivientes de IPV: asiáticos, latinos y africanos. Los resultados revelaron factores de riesgo y protección multinivel para IPV / IPH a nivel social (Normas culturales patriarcales), a nivel de relación (Comportamientos abusivos de la pareja) y a nivel individual (Aculturación en los EE. UU.). Los autores sugieren priorizar las intervenciones de evaluación de riesgos y planificación de seguridad culturalmente receptivas en entornos legales, de servicios sociales y de atención médica (Sabri B et al, 2018)¹².

Páez Cuba concluye su trabajo *Génesis y evolución histórica de la violencia de género, afirmando que la violencia de género es uno de los efectos colaterales del sistema patriarcal y androcéntrico en el que hemos nacido mujeres y hombres. Los rasgos esenciales de la violencia de género son su carácter sociocultural, multifacético, pluricausal, cíclico, asimétrico y antijurídico; debiendo ser necesariamente tratada desde un enfoque multidisciplinario. Debemos sistematizar el tratamiento del fenómeno violencia de género desde el estudio multidisciplinario: psicológico, sociológico, antropológico, sociocultural, pedagógico, entre otros* (Páez Cuba LD, 2011)¹³.

Normativa

En 1993, la Asamblea General de las Naciones Unidas *Reconociendo la urgente necesidad de una aplicación universal a la mujer de los derechos y principios relativos a la igualdad, seguridad, libertad, integridad y dignidad de todos los seres humanos... Proclama solemnemente la siguiente Declaración sobre la eliminación de la violencia contra la mujer e insta a que se hagan todos los esfuerzos posibles para que sea universalmente conocida y respetada*. Se aprueba así una declaración sobre la eliminación de la violencia contra las mujeres (United Nations General Assembly. Declaration on the elimination of violence against women, 1993)¹⁴. En 1996 Enterada con gran preocupación del dramático aumento en todo el mundo de la incidencia de lesiones intencionales que afectan a personas de todas las edades y de ambos sexos, pero especialmente a mujeres y niños, la OMS lo declaró prioridad en salud pública (WHA. Prevention of violence: a public health priority, 1996)¹⁵.

En España la normativa al respecto es amplia, siendo abordada esta problemática de forma total o parcial por distintas Leyes y Reglamentos y con especial incidencia en la violencia de género como forma específica que afecta a la mujer (**Tabla I**).

Tabla I: Normativa internacional y española de especial referencia en violencia de género.

<p>NORMATIVA EUROPEA</p> <ul style="list-style-type: none"> • Carta de los Derechos Fundamentales de la Unión Europea (2000). • Web de EU JUSTICE- Legislación de la Unión Europea sobre Violencia de Género. • Convenio del Consejo de Europa para prevenir y combatir la violencia contra la mujer y la violencia doméstica de 2011 (Convenio de Estambul). 	<ul style="list-style-type: none"> • Carta de los Derechos Fundamentales de la Unión Europea (2000). • Web de EU JUSTICE- Legislación de la Unión Europea sobre Violencia de Género. • Convenio del Consejo de Europa para prevenir y combatir la violencia contra la mujer y la violencia doméstica de 2011 (Convenio de Estambul).
<p>NORMATIVA INTERNACIONAL</p> <ul style="list-style-type: none"> • Declaración universal de los Derechos Humanos. • Convención sobre la eliminación de todas las formas de discriminación contra las mujeres (CEDAW). 	<ul style="list-style-type: none"> • Declaración universal de los Derechos Humanos. • Convención sobre la eliminación de todas las formas de discriminación contra las mujeres (CEDAW).
<p>NORMATIVA EN ESPAÑA</p> <p>I.- CÓDIGO DE VIOLENCIA DE GÉNERO Y DOMÉSTICA</p> <p>II.- CONVENIOS Convenio sobre prevención y lucha contra la violencia contra la mujer y la violencia doméstica. Instrumento de ratificación del Convenio del Consejo de Europa sobre prevención y lucha contra la violencia contra la mujer y la violencia doméstica, hecho en Estambul el 11 de mayo de 2011.</p> <p>III.- CONSTITUCIÓN ESPAÑOLA Constitución Española (parcial).</p> <p>IV.- NORMATIVA ESTATAL SOBRE VIOLENCIA DE GÉNERO Ley Orgánica de Medidas de Protección Integral contra la Violencia de Género (parcial). Ley Orgánica para la igualdad efectiva de mujeres y hombres. Medidas urgentes para el desarrollo del Pacto de Estado contra la violencia de género.</p> <p>IV.1.- MEDIDAS COMPLEMENTARIAS</p> <p>IV.1.1.- ORDEN DE PROTECCIÓN Ley reguladora de la Orden de protección de las víctimas de la violencia doméstica. Ley de reconocimiento mutuo de resoluciones penales en la Unión Europea. Sistema de registros administrativos de apoyo a la Administración de Justicia. Modelos de remisión al Registro Central para la Protección de las Víctimas.</p> <p>IV.1.2.- ASISTENCIA JURÍDICA Ley de asistencia jurídica gratuita (parcial). Reglamento de asistencia jurídica gratuita (parcial).</p> <p>IV.1.3.- ÁMBITO PENAL Ley Orgánica del Código Penal (parcial). Medidas concretas en materia de violencia doméstica. De medidas concretas en materia de seguridad ciudadana, violencia doméstica e integración social de los extranjeros. Ley del Estatuto de la víctima del delito. Desarrolla la Ley 4/2015, de 27 de abril, del Estatuto de la víctima del delito, y se regulan las Oficinas de Asistencia a las Víctimas del Delito. Ley de Enjuiciamiento Criminal (parcial) Circunstancias de ejecución de las penas de trabajo en beneficio de la comunidad. Se establecen las circunstancias de ejecución de las penas de trabajo en beneficio de la comunidad y de localización permanente en centro penitenciario, de determinadas medidas de seguridad, así como de la suspensión de la ejecución de las penas privativas de libertad y sustitución de penas.</p> <p>IV.1.4.- ÁMBITO CIVIL Código Civil (parcial). Ley de Enjuiciamiento Civil (parcial). Ley reguladora de la rectificación registral de la mención relativa al sexo de las personas.</p> <p>IV.1.5 ÁMBITO SOCIAL, LABORAL Y SEGURIDAD SOCIAL Texto refundido de la Ley del Estatuto de los Trabajadores (parcial). Ley del Estatuto del trabajo autónomo (parcial). Texto refundido de la Ley del Estatuto Básico del Empleado Público (parcial). Se aprueba el Reglamento General de Ingreso del Personal al servicio de la Administración general del Estado y de Provisión de Puestos de Trabajo y Promoción Profesional de los Funcionarios Civiles de la Administración general del Estado. Reglamento General de Ingreso del Personal al servicio de la AGE (parcial). Se establece el procedimiento de movilidad de las empleadas públicas víctimas de violencia de género. Procedimiento de movilidad de las empleadas públicas víctimas de violencia de género. Se aprueba el Acuerdo para favorecer la movilidad interadministrativa de las empleadas públicas víctimas de violencia de género. Movilidad interadministrativa de las empleadas públicas víctimas de violencia de género. Programa de inserción sociolaboral para mujeres víctimas de violencia de género. Renta activa de inserción para desempleados con especiales necesidades económicas.</p>	<p>BOE 12 de agosto de 2019</p> <p>BOE núm. 137, de 06/06/2014</p> <p>BOE núm. 311, de 29/12/1978</p> <p>BOE núm. 313, de 29/12/2004</p> <p>BOE núm. 71, de 23/03/2007 BOE núm. 188, de 04/08/2018</p> <p>BOE núm. 183, de 01/08/2003</p> <p>BOE núm. 282, de 21/11/2014 BOE núm. 33, de 07/02/2009</p> <p>BOE núm. 39, de 14/02/2009</p> <p>BOE núm. 11, de 12/01/1996 BOE núm. 188, de 07/08/2003</p> <p>BOE núm. 281, de 24/11/1995 BOE núm. 234, de 30/09/2003</p> <p>BOE núm. 101, de 28/04/2015 BOE núm. 312, de 30/12/2015</p> <p>BOE núm. 260, de 17/09/1882 BOE núm. 145, de 18/06/2011</p> <p>Gaceta de Madrid núm. 206, de 25/07/1889 BOE núm. 7, de 08/01/2000 BOE núm. 65, de 16/03/2007</p> <p>BOE núm. 255, de 24/10/2015 BOE núm. 166, de 12/07/2007 BOE núm. 261, de 31/10/2015</p> <p>BOE núm. 295, de 10/12/2015</p> <p>BOE núm. 278, de 17/11/2018</p> <p>BOE núm. 278, de 17/11/2018</p> <p>BOE núm. 297, de 10/12/2008 BOE núm. 290, de 05/12/2006</p>



Se regula el programa de renta activa de inserción para desempleados con especiales necesidades económicas y dificultad para encontrar empleo.

Ley para la mejora del crecimiento y del empleo (parcial)
 Texto refundido de la Ley General de la Seguridad Social (parcial)

IV.1.6 EXTRANJERÍA E INMIGRACIÓN

Ley Orgánica sobre derechos y libertades de los extranjeros en España (parcial).
 Reglamento Ley Orgánica sobre derechos y libertades de los extranjeros en España (parcial).
 Entrada, libre circulación y residencia en España de ciudadanos de la Unión Europea (parcial).

IV.1.7 MENORES

Ley Orgánica de Protección Jurídica del Menor
 Derivación entre centros de acogida para las mujeres víctimas de violencia de género.
 Protocolo de derivación entre centros de acogida para las mujeres víctimas de violencia de género y sus hijos e hijas.

IV.2- JUZGADOS SOBRE LA VIOLENCIA SOBRE LA MUJER

Ley de Demarcación y de Planta Judicial (parcial).
 Ley Orgánica del Poder Judicial (parcial).

IV.3- ORGANIZACIÓN

Estructura orgánica Ministerio de Presidencia, Relaciones con las Cortes e Igualdad (parcial).
 Estructura orgánica básica del Ministerio del Interior.
 Observatorio Estatal de Violencia sobre la Mujer y se modifica el Real Decreto 1600/2004, de 2 de julio, por el que se desarrolla la estructura orgánica básica del Ministerio de Trabajo y Asuntos Sociales.
 Desarrolla la estructura orgánica y funciones Dirección General de la Policía.

IV.4 - OTRAS NORMAS RELACIONADAS

Ayuda económica Ley Orgánica de medidas de protección integral contra la violencia de género.
 Fondo de Garantía del Pago de Alimentos.
 Protección a los deudores hipotecarios (parcial).
 Plan Estatal de Vivienda 2018-2021 (parcial).

V. NORMATIVA AUTONÓMICA SOBRE VIOLENCIA DE GÉNERO

ANDALUCÍA

Ley de medidas de prevención y protección integral contra la violencia de género.

ARAGÓN

Ley de Prevención y Protección Integral a las Mujeres Víctimas de Violencia.
 Instituto Aragonés de la Mujer.
 Servicios de asesoramiento y orientación jurídicos gratuitos de Aragón.

CANARIAS

Ley de Prevención y Protección Integral de las Mujeres contra la Violencia de Género.

CANTABRIA

Ley Integral para la Prevención de la Violencia Contra las Mujeres.

CASTILLA-LA MANCHA

Ley para una Sociedad Libre de Violencia de Género en Castilla-La Mancha.

CASTILLA Y LEÓN

Ley contra la violencia de género en Castilla y León.

CATALUÑA

Ley del derecho de las mujeres a erradicar la violencia machista.

COMUNIDAD DE MADRID

Ley integral contra la violencia de género de la Comunidad de Madrid.

COMUNIDAD FORAL DE NAVARRA

Ley Foral para actuar contra la violencia hacia las mujeres.

COMUNIDAD VALENCIANA

Ley integral contra la violencia sobre la mujer en el ámbito de la Com. Valenciana.

EXTREMADURA

Ley de Igualdad entre mujeres y hombres y contra la violencia de género.

GALICIA

Ley para la prevención y el tratamiento integral de la violencia de género.

ILLES BALEARS

Ley de igualdad de mujeres y hombres

LA RIOJA

Ley de prevención, protección y coordinación institucional en materia de violencia.

PAÍS VASCO

Ley para la Igualdad de Mujeres y Hombres.

PRINCIPADO DE ASTURIAS

Ley para la igualdad de mujeres y hombres y la erradicación de la violencia de género.

REGIÓN DE MURCIA

Ley Igualdad entre Mujeres y Hombres y de Protección contra la Violencia de Género.

BOE núm. 312, de 30/12/2006
 BOE núm. 261, de 31/10/2015

BOE núm. 10, de 12/01/2000
 BOE núm. 103, de 30/04/2011

BOE núm. 51, de 28/02/2007

BOE núm. 15, de 17/01/1996
 BOE núm. 161, de 07/07/2015

BOE núm. 313, de 30/12/1988
 BOE núm. 157, de 02/07/1985

BOE núm. 164, de 07/07/2018

BOE núm. 183, de 30/07/2018
 BOE núm. 62, de 14/03/2006

BOE núm. 21, de 24/01/2013

BOE núm. 301, de 17/12/2005

BOE núm. 299, de 14/12/2007
 BOE núm. 116, de 15/05/2013
 BOE núm. 61, de 10/03/2018

BOJA núm. 247, de 18/12/2007, BOE núm. 38, de 13/02/2008

BOA núm. 41, de 09/04/2007, BOE núm. 141, de 13/06/2007
 BOA núm. 24, de 01/03/1993, BOE núm. 71, de 24/03/1993
 BOA núm. 209, de 31/10/2017, BOE núm. 310, de 22/12/2017

BOC núm. 86, de 07/05/2003, BOE núm. 162, de 08/07/2003

BOCT núm. 70, de 12/04/2004, BOE núm. 101, de 26/04/2004

DOCM núm. 201, de 15/10/2018, BOE núm. 301, de 14/12/2018

BOCL núm. 243, de 20/12/2010, BOE núm. 317, de 30/12/2010

DOGC núm. 5123, de 08/05/2008, BOE núm. 131, de 30/05/2008

BOCM núm. 310, de 29/12/2005, BOE núm. 52, de 02/03/2006

BON núm. 71, de 15/04/2015, BOE núm. 107, de 05/05/2015

DOGV núm. 6912, de 28/11/2012, BOE núm. 297, de 11/12/2012

DOE núm. 59, de 25/03/2011, BOE núm. 88, de 13/04/2011

DOG núm. 152, de 07/08/2007, BOE núm. 226, de 20/09/2007

BOIB núm. 99, de 04/08/2016, BOE núm. 202, de 22/08/2016

BOR núm. 31, de 07/03/2011, BOE núm. 66, de 18/03/2011

BOPV núm. 42, de 02/03/2005, BOE núm. 274, de 14/11/2011

BOPA núm. 64, de 18/03/2011, BOE núm. 106, de 04/05/2011

BORM núm. 91, de 21/04/2007, BOE núm. 176, de 22/07/2008

Nota: revisión no extensa actualizada a fecha julio 2019.

Violencia de género y repercusión en salud

El concepto de violencia incluye la física, la sexual y la psicológica y representa un problema de salud pública mundial. Se ha documentado una asociación clara entre violencia de pareja (IPV) y un mayor riesgo de desarrollar trastorno de estrés postraumático (TEPT). En algunos estudios se ha correlacionado el TEPT y cada tipo diferente de IPV. De hecho, el componente psicológico de la violencia dentro de la pareja fue el predictor más fuerte del TEPT, y señala la importancia de separar los efectos de los diferentes tipos de abuso de pareja íntima cuando se tienen en cuenta sus efectos sobre la salud mental de las mujeres (Pico-Alfonso MA, 2005)¹⁶.

La alta prevalencia de resultados adversos para la salud relacionados con la IPV está bien documentada, pero sin embargo, se sabe poco sobre las vías que conducen a resultados adversos para la salud. La investigación sobre las alteraciones psicológicas, biológicas, neurológicas, conductuales y fisiológicas después de la exposición al IPV, muchas de las cuales están asociadas con el TEPT, requiere de nuevas tecnologías y esfuerzos de colaboración interdisciplinarios para integrar diversas metodologías y aplicar nuevos hallazgos con el fin de minimizar su impacto en salud y bienestar de las personas afectadas. Son aspectos a destacar la carga sociosanitaria por el impacto adverso en salud, especialmente en salud mental, y lo que implica de innovación metodológica integrada, interdisciplinaria, biopsicosocial y bioconductual (Dutton MA et al, 2006)¹⁷.

El suicidio es una de estas consecuencias en salud mental. Un estudio realizado entre 2005 y 2015 en Kentucky revela que hay evidencia de apoyo que muestra que la violencia subyacente y directa en las relaciones íntimas está exacerbando el riesgo de suicidio en las personas afectadas (Brown S, Seals J, 2019)¹⁸. En 2015, aproximadamente 62.000 personas murieron en los Estados Unidos como resultado de lesiones relacionadas con la violencia. Datos del Sistema Nacional de Denuncia de Muerte Violenta (NVDRS) de 27 estados de EE.UU proporcionan información por sexo, grupo de edad, raza/etnia, ubicación de la lesión, método de la lesión, circunstancias de la lesión y otras características seleccionadas. Los resultados ponen de manifiesto que las muertes violentas afectan con mayor frecuencia a hombres, a ciertos grupos de edad y poblaciones minoritarias. Los problemas de salud mental, los problemas de la pareja íntima, los conflictos interpersonales y los factores estresantes de la vida en general fueron los principales eventos precipitantes de múltiples tipos de muertes violentas, incluidos los suicidios. Este tipo de estudios son esenciales para los esfuerzos de salud pública para reducir las muertes por violencia (Jack SPD, et al, 2015)¹⁹.

Excluyendo las consecuencias fatales de la violencia, se muestran en la tabla algunas de las patologías relacionadas con la repercusión en la salud por la violencia sufrida (Tabla II).

Tabla II: Consecuencias no fatales de la violencia en la salud.

Salud física	<ul style="list-style-type: none"> • Lesiones • Deterioro funcional • Síntomas físicos inespecíficos • Peor salud subjetiva • Incapacidad permanente • Obesidad
Condiciones crónicas	<ul style="list-style-type: none"> • Dolor crónico • Síndrome del intestino irritable • Trastornos gastrointestinales • Quejas somáticas • Fibromialgia
Salud mental	<ul style="list-style-type: none"> • Estrés postraumático • Depresión • Ansiedad • Trastorno de pánico • Trastornos alimenticios • Disfunciones sexuales • Baja autoestima • Abuso de sustancias
Conducta negativa de salud	<ul style="list-style-type: none"> • Hábito de tabaco • Alcohol y abuso de drogas • Conductas sexuales de riesgo • Inactividad física
Salud reproductiva	<ul style="list-style-type: none"> • Embarazo no deseado • VIH/ETS • Trastornos ginecológicos • Aborto no deseado • Complicación en el embarazo • Hijos de bajo peso • Inflamación pélvica

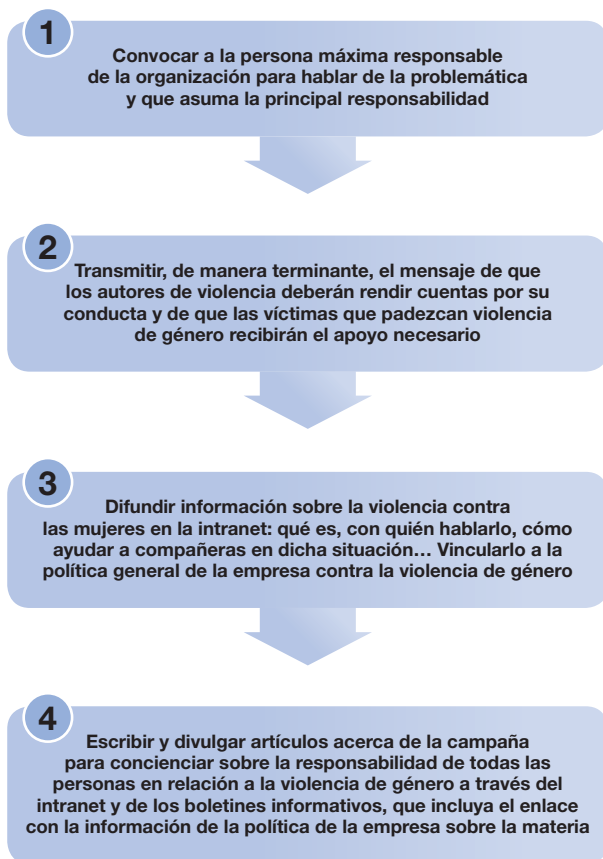
Fuente: Isabel Ruíz Pérez. Escuela Andaluza de Salud Pública. Programa de Formación de Formadores/as en Perspectiva de Género en Salud. Disponible en: http://www.msccbs.gob.es/organizacion/sns/planCalidadSNS/pdf/equidad/04modulo_03.pdf.

Abordaje de la violencia de género desde salud laboral

Si bien la violencia contra las mujeres, y de forma concreta la IPV, es un concepto complejo donde intervienen múltiples factores, algunas investigaciones destacan que, con frecuencia, se asocia con inestabilidad laboral y con el bajo nivel económico y cultural, analizando los efectos específicos de la violencia física, la violencia psicológica y los síntomas del TEPT como predictores de desempleo, sin que los resultados sean concluyentes (Kimerling R et al, 2009)²⁰.

Un colectivo sobre el que tiene especial impacto es el de trabajadores migrantes. A nivel mundial, hay más de 150 millones de trabajadores migrantes internacionales, trabajando fuera de su país de origen y un número considerable de ellos en entornos peligrosos y de explotación, donde pueden correr un riesgo considerable de lesiones y problemas de salud. Sin embargo, existen pocos datos sobre salud laboral entre los trabajadores migrantes para permitir la formulación de políticas globales y la prestación de servicios de salud (Hargreaves S et al, 2019)²¹.

Gráfico 1:
Toma de conciencia de la violencia de género en los centros de trabajo.

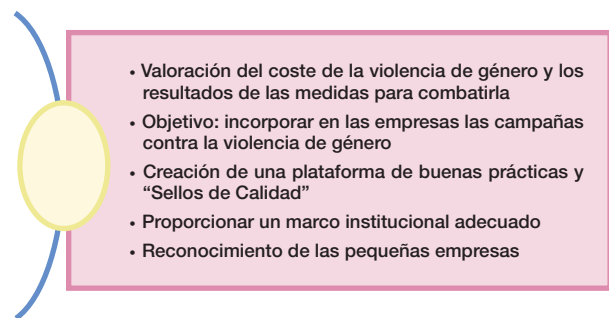


Fuente: Modificado de CARVE (companies againsts gender violence). Disponible en: <https://asceps.org/makingprojects/carve-daphne/wp-content/resources/CARVEguideCAST.pdf>

El abordaje de la violencia de género en ámbito laboral incluye actuaciones individuales y actuaciones protocolizadas y estandarizadas en la gestión empresarial. Existen referencias de proyectos en diversas empresas que pueden servir de orientación.

Partiendo de la anteriormente comentada legislación española sobre la implantación obligatoria de planes de igualdad en las empresas (Ley Orgánica 3/2007, de 22 de marzo, para la igualdad efectiva de mujeres y hombres y Real Decreto Legislativo 2/2015, de 23 de octubre, por el que se aprueba el texto refundido de la Ley del Estatuto de los Trabajadores), destacamos aquí la propuesta de CARVE (companies againsts gender violence) que resulta particularmente interesante por dar una visión global desde y para las empresas en torno a este tema especialmente sensible (**Tabla III**) (**Gráficos 1 y 2**).

Gráfico 2:
La implicación de las empresas para mitigar la violencia contra las mujeres. Recomendaciones de políticas específicas.



Fuente: Modificado de CARVE (companies againsts gender violence). Disponible en: <https://asceps.org/makingprojects/carve-daphne/wp-content/resources/CARVEguideCAST.pdf>

Tabla III: buenas prácticas empresariales y recomendaciones para prevenir y abordar la violencia contra las mujeres.

Desarrollo e implementación de políticas laborales relativas a la violencia contra las mujeres	<ul style="list-style-type: none"> Planificación Implicación Compromiso firme Establecimiento de mecanismos de reclamación internos
Detección y abordaje de la problemática en los centros de trabajo	<ul style="list-style-type: none"> Informar y formar al personal y a la dirección Generar confianza Disponer de un protocolo estándar incorporado a la política de contratación de personal Proporcionar apoyo o ayuda a través de remisiones a los servicios de apoyo y asistencia a las víctimas
Interacción con las trabajadoras víctimas en los centros de trabajo	<ul style="list-style-type: none"> Escuchar Informar y explicar
Apoyo a las mujeres víctimas de violencia	<ul style="list-style-type: none"> Disponer permisos de baja laboral especiales y reincorporación laboral Apoyo en la superación del aislamiento Opción de flexibilidad laboral Posibilidad de oferta de nuevos puestos de trabajo
Garantizar la seguridad y protección de los empleados y las víctimas en el trabajo	<ul style="list-style-type: none"> Condiciones de trabajo seguras Confidencialidad Seguridad
Colaboración con las partes interesadas en relación a la violencia de género	<ul style="list-style-type: none"> Colaboración con las partes interesadas especializadas (ONG, ayuntamientos fundaciones organizaciones sindicales...) Coordinación entre las instituciones (gubernamentales o privadas) Participación de representantes sindicales en las sesiones formativas y las campañas de sensibilización

Fuente: CARVE (companies againsts gender violence) Disponible en: <https://asceps.org/makingprojects/carve-daphne/wp-content/resources/CARVEguideCAST.pdf>

La terapia psicológica como intervención en mujeres víctimas de violencia de género

Las consecuencias psicológicas de la violencia en las mujeres son en ocasiones más graves que sus efectos físicos ya que la agresión, física o psicológica, merma la autoestima de las mujeres y aumenta el riesgo de desarrollo de múltiples problemas de salud (Tabla IV).

Tabla IV: Consecuencias psicopatológicas más frecuentes de la violencia psicológica.

• Trastorno por estrés postraumático (TEPT)
• Depresión
• Trastornos de ansiedad (ansiedad generalizada, ataques de pánico, agorafobia, etc.)
• Trastornos de la alimentación
• Alteraciones del sueño
• Abuso y dependencia de sustancias
• Problemas psicósomáticos
• Baja autoestima
• Problemas crónicos de salud
• Inadaptación. Aislamiento.
• Problemas de relación social/familiar/laboral
• Suicidio

Fuente: Asensi Pérez LF. La prueba pericial psicológica en asuntos de violencia de género. Revista Intermata de Práctica Jurídica, n.º 21, enero-junio del 2008, pp. 15-29 (www.uv.es).

La violencia psicológica es considerada un subtipo y la forma más común de violencia de pareja, cuyas consecuencias en salud mental son severas (Dokkedahl S et al, 2019)²². Los psicólogos participan activamente en programas para prevenir la violencia desde la enseñanza en las escuelas promoviendo conductas en igualdad de género, en trabajo como voluntarios en ONG y asociaciones contra la violencia, orientando, formando y asesorando individualmente o en grupos de autoayuda, si bien las competencias profesionales recaen sobre los técnicos de igualdad de servicios sociales (Ley Orgánica 3/2007, de 22 de marzo, para la igualdad efectiva de mujeres y hombres y Real Decreto Legislativo 2/2015, de 23 de octubre, por el que se aprueba el texto refundido de la Ley del Estatuto de los Trabajadores) y también en las unidades de emergencia, grupos terapéuticos o grupos de intervención psicológica, recursos de vivienda de emergencia social y otros servicios de apoyo de los que se dispone en muchos países europeos, y que tienen un papel central en los procedimientos judiciales.

Los psicólogos actúan en coordinación y colaborando con el personal sanitario en cualquier ámbito donde exista una situación que suponga daño por violencia a la mujer. Existen iniciativas auspiciadas por colegios profesionales y expertos en psicoterapia para estas situaciones concretas (García MÁ et al, 2016)²³, (Bosch Fiol et al, 2005)²⁴, (Matud MP et al, 2016)²⁵ y en esta línea la Federación Europea de Asociaciones de Psicólogos (EFPA-*European Federation of Psychologists Association*), de forma conjunta con la Asociación Europea de Psicología Comunitaria (*European Association*

of Community Psychology) y el Comité Permanente de Psicología Comunitaria subrayan la necesidad de realizar las siguientes actuaciones (INFOCOP 2018)²⁶:

1. Promover la conciencia social y profesional sobre la violencia de género contra las mujeres, entre los psicólogos y todos los profesionales sociales y de la salud.
2. Establecer pautas de género específicas en los Departamentos de Emergencia y en todos los servicios públicos y privados (asociaciones contra la violencia, asesoría legal y expertos en apoyo, policía, servicios sociales, tribunales ordinarios y especiales), para crear unas directrices orientadas a las distintas consecuencias de la violencia.
3. Desarrollar programas de formación dirigidos a mejorar las actitudes y el conocimiento del personal sobre las mujeres maltratadas y a desarrollar protocolos médicos y psicológicos integrados, promoviendo, a su vez, la concienciación de la comunidad y las estrategias para abordar estas situaciones.

Las actuaciones deben adaptarse a la situación de la mujer en cada una de las fases por las que pasa tras el episodio de violencia de género.

En el proceso de recuperación

La violencia de género es una problemática con causas múltiples, como se refleja anteriormente, sin embargo, en su base se encuentra siempre la asimetría y desigualdad entre hombres y mujeres (Goodman Lisa A et al, 1993)²⁷. Este concepto es necesario para comprender la aparición, desarrollo y consecuencias de la violencia de género y, por tanto, el contenido y el proceso terapéutico de recuperación para las mujeres que la han sufrido.

El tratamiento psicoterapéutico, tanto en formato individual como grupal, supone la herramienta básica para la recuperación integral de la mujer y la prevención de repetición de relaciones basadas en el abuso. No es posible entender el proceso terapéutico únicamente desde el enfoque psicológico individualista, basado en la modificación de parámetros cognitivos y conductuales, sin un análisis de contenido sociológico y cultural, desde un modelo explicativo comprensivo que permita una adecuada valoración y conocimiento de todos los factores individuales, sociales y del contexto que explican la violencia contra la mujer. Los estereotipos asociados al género, la asimetría en las relaciones y la desigualdad en entornos tanto privados como públicos han relegado a la mujer a una posición de inferioridad.

La primera meta en el abordaje terapéutico es la evaluación, siguiendo la propuesta de Mary Ann Dutton(28), donde se destacan las principales cuestiones a analizar: tipo y patrón de violencia, abuso y control ejercido por el agresor; efectos psicológicos de ese abuso; estrategias

de afrontamiento (activas o pasivas) que ha utilizado y factores mediadores (institucionales, creencias previas, recursos materiales y apoyo social...)

En España el grupo de Matud establece una batería de instrumentos de evaluación para su programa de intervención en mujeres maltratadas por su pareja: Entrevista semiestructurada de historia y tipo de maltrato (Matud, 1999); Escala de gravedad de síntomas del trastorno de estrés postraumático (Echeburúa, Corral, Amor, Zubizarreta y Sarasúa, 1997); Inventario para la ansiedad de Beck (BAI; Beck y Steer, 1990); Inventario para la depresión de Beck-Segunda Edición (BDI-II; Beck, Steer y Brown, 1996); Inventario de autoestima (SEQ-MR) Versión reducida y validada con mujeres maltratadas del Self-esteem Inventory de Rector y Roger (1993); Inventario de Apoyo Social (Matud, 1999); Inventario de evaluación del maltrato a la mujer por su pareja (APCM, Matud, 2004b).

Existen propuestas terapéuticas basadas en el modelo clásico cognitivo-conductual, de demostrada eficacia en multitud de trastornos psicológicos, incluido el trastorno por estrés postraumático (TEPT) con una orientación individual basada en el tratamiento del trauma, como la realizada por F. Labrador (Labrador F J, 2004)²⁹ o las llevadas a cabo desde instituciones como el Colegio de Psicología de Guipúzcoa de la mano de M. García et al. Por su parte, el modelo de psicoterapia de orientación feminista de Bosch, Ferrer y Alzamora propone una terapia (Tabla V).

Teniendo en cuenta todo lo mencionado, consideramos imprescindible resaltar la importante coordinación de la intervención psicológica con la terapia social,

encaminada a la completa recuperación de la mujer de un entorno sociofamiliar y laboral; sin detrimento de la labor sanitaria y la orientación y acompañamiento judicial, necesarios en múltiples ocasiones para lograr el objetivo último del empoderamiento y el establecimiento de relaciones saludables, equitativas y equilibradas alejadas de cualquier forma de violencia. En el siguiente gráfico mostramos el proceso terapéutico en sus diferentes fases, establecidas en orden cronológico pero no estricto, es decir: tanto la evaluación como el establecimiento de objetivos están en constante desarrollo a lo largo del proceso terapéutico, pudiendo revisar y reevaluar las metas o estrategias establecidas en función del desarrollo de la paciente (Tabla VI).

En el retorno al trabajo

A efectos de garantizar la seguridad de la trabajadora y de su entorno y lograr la mejor adaptación en esta etapa, cuando se produce el retorno al trabajo después de un proceso de Incapacidad temporal por daños físicos o psíquicos derivados de violencia contra la mujer, es necesaria una valoración global del puesto y de la situación clínica de la mujer por el médico del trabajo del servicio de prevención de riesgos laborales.

Los Servicios de Prevención de Riesgos laborales constan de cuatro especialidades: tres técnicas (Higiene, Seguridad y Ergonomía y Psicología aplicada) y una sanitaria (la Unidad Básica de Salud constituida por Medicina y Enfermería del trabajo).

Las empresas pueden tener un Servicio de Prevención propio con todas las especialidades, o al menos dos de ellas, pudiendo concertar externamente las no incluidas

Tabla V: Programa de Intervención Terapéutica.

Objetivos generales	
<ul style="list-style-type: none"> • Toma de conciencia de la situación vivida, comprensión de los hechos delictivos, desmontar mitos sobre el amor romántico • Reducción de la sintomatología y recuperación de la autoestima • Autonomía e independencia frente a la figura masculina • Analizar las relaciones familiares y con los hijos • Interiorización de los roles igualitarios y deshacer mitos y estereotipos • Reconstrucción de la vida social de la mujer • Empoderamiento como objetivo final y paso hacia una nueva vida de mecanismos de reclamación internos 	
Objetivos de la intervención	Objetivos terapéuticos
Valoración del riesgo: medidas de autoprotección	Establecer estilos de afrontamiento, potenciar sus recursos personales
Percepción del maltrato: reconocimiento del ciclo de violencia, reconocimiento de indicadores, reconocimiento de la tipología de violencia sufrida y reconocimiento del impacto en los hijos.	Devolución de información (exposición del modelo explicativo y propuestas de tratamiento), psicoeducación en TEPT (información sobre las respuestas traumáticas normales), psicoeducación sobre el ciclo de la violencia, nombrar el abuso (validar sus experiencias del maltrato), psicoeducación sobre el impacto de la violencia en los hijos.
Empoderamiento: modificación de mitos y creencias, autoafirmación, asertividad, regulación emocional, toma de decisiones, potenciar la autonomía y las relaciones igualitarias y de buen trato.	Revisión de creencias, revisión de problemas, atención a los sentimientos de culpa y de vergüenza, valoración de cosas positivas-inventario de sí misma, trabajo intrapsíquico (resignificación del hecho traumático), psicoeducación sobre asertividad, reelaboración afectiva a través del vínculo.
Sintomatología clínica.	Control de la respiración, ejercicio físico, relajación, elaboración del duelo (ruptura de la relación).
Cambios en la realidad social: entrenamiento, desarrollo de actividades sociales y red de apoyo social, afrontamiento del área de lo laboral.	Programación de actividades y tareas agradables, entrenamiento afectivo (expresar, recibir), entrenamiento social (iniciar y mantener contactos).

Fuente: Extraído de García, M. Á., Alías, A. M. S., & Ballester, P. B. (2016). Manual de atención psicológica a víctimas de maltrato machista. Colegio Oficial de Psicología de Guipúzcoa (España).

en la empresa; o bien dispondrá de Servicio de Prevención Ajeno, con todas las especialidades externalizadas.

En todos los casos la psicología es una parte de estos servicios, bien en la propia empresa o concertado externamente en los casos en que sea necesario.

Cuando una mujer víctima de violencia de género retorna al trabajo después de un periodo de incapacidad temporal, o sigue trabajando sin recurrir a la baja laboral, debe ser apoyada por los especialistas del servicio de prevención en colaboración con los asistenciales, a nivel sanitario, psicológico y técnico, para facilitar su recuperación y adaptación del puesto, en caso necesario, con la información requerida de los responsables de la gestión empresarial y, de forma especial, en coordinación con los responsables de recursos humanos.

Sin embargo, hay dos principios básicos que rigen esta actuación profesional:

1. Respeto escrupulosos a la intimidad personal.
2. Riguroso cumplimiento de la protección de datos y de la confidencialidad, requerida siempre, pero de forma muy escrupulosa en estas situaciones de extrema sensibilidad y riesgo personal.

A efectos de agilizar los procedimientos y evitar duplicidades en la recogida de información se recomienda actuar conjuntamente, aunque el riguroso cumplimiento de la Ley Orgánica de Protección de Datos (LOPD, última actualización de 2018)³⁰ hace necesaria la colaboración de la mujer, que será quien transmita, si lo considera oportuno, la información de los distintos agentes implicados en aras de agilizar los trámites y mejorar su

situación personal y laboral.

La RAE define protocolo como:

- *Secuencia detallada de un proceso de actuación científica, técnica, médica, etc.*

O también como:

- *Conjunto de reglas que se establecen en el proceso de comunicación entre dos sistemas.*

Proponemos seguidamente un procedimiento protocolizado y coordinado para facilitar la atención e incorporación laboral de la mujer víctima de violencia (Gráfico 3).

Conclusiones

La violencia de género es un problema mundial de creciente prevalencia y difícil de gestionar.

Los distintos tipos de violencia se interrelacionan entre sí y repercuten en la salud de la mujer que la ha sufrido. La repercusión psicológica es un aspecto a destacar y la intervención coordinada de psicólogos y sanitarios supone una atención más completa y facilita el proceso de recuperación y reintegración socio-laboral.

El retorno al trabajo de la mujer que ha sufrido violencia de género requiere una actuación conjunta de todos los implicados en la gestión preventiva de la empresa, destacando la labor del personal Médico y de Enfermería del Trabajo, la del profesional de psicología de empresa y la labor facilitadora de los responsables de Recursos Humanos.

Tabla VI: Proceso de recuperación. Intervención psicológica en mujeres que han sufrido violencia de género.

Fase I: EVALUACIÓN	Fase II: ESTABLECIMIENTO DE OBJETIVOS	Fase III: INTERVENCIÓN PSICOLÓGICA
Entrevista semiestructurada e instrumentos de evaluación estructurados.	Devolución de los resultados de evaluación y establecimiento de metas en conjunto con la paciente.	Trabajo desde la perspectiva cognitivo conductual para la reducción de síntomas y el desarrollo de habilidades.
<ul style="list-style-type: none"> • Elaboración de un diagnóstico a nivel psicopatológico, si corresponde • Exploración de las distintas áreas relacionadas con el proceso terapéutico: habilidades de afrontamiento, rasgos de personalidad, ansiedad rasgo-estado, habilidades sociales... • Análisis de la historia de violencia y relacional • Exploración de la existencia o no de red de apoyo social y familiar • Recogida de datos sociodemográficos y de coordinación con otras áreas (sanitaria, laboral...) 	<p>Como norma general:</p> <ul style="list-style-type: none"> • Autoestima • Regulación emocional • Trabajo del trauma • Identificación y comprensión de la violencia de género • Asertividad, establecimiento de límites, comunicación y pautas de relación • Análisis desde la perspectiva de género de mitos relativos a las relaciones, el amor romántico y los roles asociados a la mujer • Sexualidad y relaciones de pareja saludables • Habilidades sociales, establecimiento o fortalecimiento de red de apoyo social-familiar 	<ul style="list-style-type: none"> • Identidad, género, autoestima y empoderamiento • Sexualidad, maternidad, relaciones interpersonales y de pareja desde un análisis de género • Proceso de cambio y prevención de recaídas: círculo de la violencia machista • Género y violencia • Regulación emocional: identificación, gestión y afrontamiento de las emociones, establecimiento de límites, culpa y responsabilidad, vínculo y apego. • Trabajo cognitivo: Discusión de pensamientos irracionales, "debería", roles de género interiorizados, indefensión aprendida, normalización de la violencia... • Motivación y toma de decisiones

Gráfico 3: Atención coordinada socio-sanitario-laboral a la mujer víctima de Violencia de género.



Bibliografía

1. Real Academia Española (2018). *Diccionario de la lengua española*. Edición del tricentenario. Recuperado de <https://dle.rae.es>.
2. Real Academia Española y Consejo General del Poder Judicial (2017). *Diccionario panhispánico del español jurídico*. Madrid: Santillana. Recuperado de <https://www.rae.es/obras-academicas/diccionarios/diccionario-panhispanico-del-espanol-juridico>.
3. Heise, L.L. & Kotsadam, A. (2015). *Cross-national and multilevel correlates of partner violence: an analysis of data from population-based surveys*. *Lancet Glob Health*, 3(6):e332-40.
4. United Nations (2015). Capítulo 6: *Violence against women*. En *The World's Women 2015: Trends and Statistics*. New York: United Nations, Department of Economic and Social Affairs, Statistics Division. Sales No. E.15.XVII.8
5. Taquette, S.R. & Monteiro, D.L.M. (2019). Causes and consequences of adolescent dating violence: a systematic review. *J Inj Violence Res*, 11(2):137-47.
6. Organización Mundial de la Salud (2017). *Violencia contra la mujer*. Recuperado de <https://www.who.int/es/news-room/fact-sheets/detail/violence-against-women>.

7. Delegación del Gobierno para la Violencia de Género (s.f.). *Portal Estadístico violencia de Género*. Gobierno de España. Ministerio de la Presidencia, Relaciones con las Cortes e Igualdad. Recuperado de <http://estadisticasviolenciagero.igualdad.mpr.gob.es/>.
8. Secretaría de Estado y Seguridad (2019). Gabinete de Coordinación y Estudios. *Sistema de seguimiento integral en los casos de Violencia de Género (Sistema VioGén)*. Gobierno de España. Ministerio del Interior. Recuperado de <http://www.interior.gob.es/documents/642012/9896454/dartos+estad%C3%ADticos+julio/e291c740-792e-4b79-84ac-6baf9dc757d1>.
9. Montesanti, S.R. & Thurston, W.E. (2015). *Mapping the role of structural and interpersonal violence in the lives of women: implications for public health interventions and policy*. BMC Womens Health, 15:100.
10. Gage, A.J. & Thomas, N.J. (2017). *Women's Work, Gender Roles, and Intimate Partner Violence in Nigeria*. Arch Sex Behav, 46(7):1923-38.
11. Schneider, D., Signorelli, M.C. & Pereira, P.P.G. (2017). *Public security female workers at the coast of Paraná, Brazil: intersections of gender, work, violence(s), and health*. Cien Saude Colet, 22(9):3003-11.
12. Sabri, B., Nnawulezi, N., Njie-Carr, V.P.S., Messing, J., Ward-Lasher, A., Alvarez, C., & al. (2018). *Multilevel Risk and Protective Factors for Intimate Partner Violence Among African, Asian, and Latina Immigrant and Refugee Women: Perceptions of Effective Safety Planning Interventions*. Race Soc Probl, 10(4):348-65.
13. Páez Cuba, L.D. (2011). *Génesis y evolución histórica de la violencia de género*. Contribuciones a las Ciencias. Recuperado de www.eumed.net/rev/cccss/11/.
14. United Nations General Assembly (1993). *Declaration on the elimination of violence against women*. Proceedings of the 85th Plenary Meeting. Recuperado de <https://www.ohchr.org/sp/professionalinterest/pages/violenceagainstwomen.aspx>.
15. World Health Assembly (1996). *Prevention of violence: a public health priority (handbook of resolution)*. WHA, (Sixth plenary meeting, Committee B fourth report. 3rd ed). Recuperado de https://apps.who.int/iris/bitstream/handle/10665/203914/WHA49_B-Conf.Paper-;jsessionid=5D15007CF854E766B04859D4E086B384?sequence=1.
16. Pico-Alfonso, M.A. (2005). *Psychological intimate partner violence: the major predictor of posttraumatic stress disorder in abused women*. Neurosci Biobehav Rev, 29(1):181-93.
17. Dutton, M.A., Green, B.L., Kaltman, S.I., Roesch, D.M., Zeffiro, T.A. & Krause, E.D. (2006). *Intimate partner violence, PTSD, and adverse health outcomes*. J Interpers Violence, 21(7):955-68.
18. Brown, S. & Seals, J (2019). *Intimate partner problems and suicide: are we missing the violence?* J Inj Violence Res, 11(1):53-64.
19. Jack, S.P.D., Petrosky, E., Lyons, B.H., Blair, J.M., Ertl, A.M., Sheats, K.J. & a.l (2018). *Surveillance for Violent Deaths - National Violent Death Reporting System, 27 States*. MMWR Surveill Summ, 67(11):1-32.
20. Kimerling, R., Alvarez, J., Pavao, J., Mack, K.P., Smith, M.W. & Baumrind, N. (2009). *Unemployment among women: examining the relationship of physical and psychological intimate partner violence and posttraumatic stress disorder*. J Interpers Violence, 24(3):450-63.
21. Hargreaves, S., Rustage, K., Nellums, L.B., McAlpine, A., Pocock, N., Devakumar, D., & al (2019). *Occupational health outcomes among international migrant workers: a systematic review and meta-analysis*. Lancet Glob Health, 7(7):e872-e882.
22. Dokkedahl, S., Kok, R.N., Murphy, S., Kristensen, T.R., Bech-Hansen, D., Elkitt, A. (2019). *The psychological subtype of intimate partner violence and its effect on mental health: protocol for a systematic review and meta-analysis*. Syst Rev, 8(1):198.
23. García, M.A., Alías, A.M.S. & Ballester, P.B. (2016). *Manual de atención psicológica a víctimas de maltrato machista*. Colegio Oficial de la Psicología de Gipuzkoa.
24. Bosch Fiol, E., Ferrer Pérez, V.A. & Alzamora Mir, A. (2005). *Algunas claves para una psicoterapia de orientación feminista en mujeres que han padecido violencia de género*. Feminismo/s, 6:121-36.
25. Matud, M.P., Padilla, V., Medina, L. & Fortes, D. (2016). *Eficacia de un programa de intervención para mujeres maltratadas por su pareja*. Ter psicol. 2016;34(3): 199-208.
26. Consejo general de la Psicología de España (2018). *Los psicólogos desempeñan un papel importante en el abordaje de la violencia contra la mujer*. Infocop Online. Recuperado de http://www.infocop.es/view_article.asp?id=7810.
27. Goodman, L.A., Koss, M.P., Fitzgerald, L.F., Russo, N.F. & Keita, G.R. (1993). *Male violence against women. Current research and future directions*. American Psychologist, 48:(10):1054-8.
28. Dutton M.A. (1992). *Empowering and healing the battered woman: a model of assessment an intervention*. New York, Springer.
29. Matud Aznar, M.P.(2004). *Impacto de la violencia doméstica en la salud de la mujer maltratada*. Psicothema, 6(3):397-401.
30. Matud, M.P. (1999). *Impacto psicológico del maltrato a la mujer: un análisis empírico*. Informe del proyecto de investigación. Instituto Canario de la Mujer
31. Echeburúa, E., Corral, P. Amor, P.J., Sarasua, B. & Zubizarreta, I. (1997a). *Repercusiones psicopatológicas de la violencia doméstica en la mujer: un estudio descriptivo*. Revista de Psicopatología y Psicología Clínica, 2, 7-19.
32. Echeburúa, E., Corral, P., Amor, P.J., Zubizarreta, I. & Sarasua, B. (1997b). *Escala de Gravedad de Síntomas del Trastorno de Estrés Postraumático: propiedades psicométricas*. Análisis y Modificación de Conducta, 23, 503-26
33. Beck, A.T. & Steer, R.A. (1990) *Manual for the beck anxiety inventory*. The Psychological Corporation, San Antonio.
34. Beck, A.T., Steer, R.A., Ball, R. & Ranieri, W (1996). *Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatient*. J Pers Assess, 67(3):588-97.
35. Rector, N. A., & Roger, D. (1993). *Self-concept and emotion-control*. Presentado en el 3rd Annual Meeting of the European Congress of Psychology. Helsinki, Finland.
36. Matud, M. P. (1998). *Social Support Scale [Database record]*. Retrieved from PsycTESTS. doi: 10.1037/t12441-000.
37. Matud, M. P. (2004). *Diseño y validación de un programa de intervención psicológica con mujeres víctimas de maltrato por parte de su pareja*. Informe de investigación. Madrid, Instituto de la Mujer.
38. Labrador F.J., De Luis P.P. & Fernández R (2004). *Mujeres víctimas de la violencia doméstica. Programa de actuación*. Madrid, Pirámide.
39. Jefatura de Estado. *Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales*. España. Boletín Oficial de Estado, núm. 294, de 06 del 12 de 2018.

ORIGINAL

La relación entre los profesionales sanitarios y los pacientes en tiempo de Covid-19

The relationship between health professionals and patients in time of the Covid-19

Carlos Fernández Juliá¹⁻⁴ , Joana Maria Julià-Móra²⁻⁴ , Sebastian Roig Noguera³⁻⁴ 

1. Médico del Servicio de Urgencias. Hospital Manacor. 2. Enfermera del Equipo de Soporte Hospitalario de Atención Paliativa.
3. Médico de la Unidad de Cuidados Intensivos. Hospital Manacor. 4. Comité de Ética Asistencial del Hospital Manacor.

Correspondencia

Carlos Fernández Juliá
Servicio de Urgencias. Hospital Manacor
Ctra. Manacor-Alcudia s/n. Manacor
E-mail: cfernandez@hmanacor.org

Recibido: 22 - I - 2021

Aceptado: 22 - III - 2021

doi: 10.3306/AJHS.2021.36.02.23

Resumen

La situación de pandemia por la COVID-19 ha supuesto una revolución organizativa en todas las estructuras estatales afectando a pequeña escala a los más íntimos aspectos de las relaciones personales. Es nuestro deber plantear una serie de reflexiones y conflictos éticos que están apareciendo en esta situación excepcional. La accesibilidad a los centros de salud, hospitales y residencias geriátricas han sido restringidas, afectando a las personas más vulnerables, con mensajes confusos para la población ocasionando situaciones de desamparo en algunos casos. Los profesionales de la salud ante esta situación de crisis sanitaria, nos hacemos una serie de preguntas que desde la ética no siempre tienen una clara y única respuesta, pero sí nos ayudan a una reflexión crítica con el fin de promover cambios que favorezcan la atención centrada en la persona. Tal vez sea el momento de adaptarse a una realidad distinta en nuestra práctica clínica habitual pero que esta no nos conduzca al distanciamiento y al miedo.

Palabras clave: COVID-19, Bioética, Comunicación en salud.

Abstract

The Pandemic situation due to COVID-19 has meant an organizational revolution in all state structures affecting on a small scale the most intimate aspects of personal relationships. It is our duty to propose a series of reflections and ethical conflicts that are appearing in this exceptional situation. Accessibility to health centers, hospitals and geriatric residences have also been restricted, affecting the most vulnerable people, with confusing messages for the population causing situations of abandonment in some cases. Health professionals in this situation of health crisis ask ourselves a series of questions that, from ethics, do not always have a clear and unique answer, but they do help us to critical reflection with the aim to promote changes that favour care focused on the person. Perhaps it is time to adapt to a different reality in our usual clinical practice, but this do not lead us to distance and fear.

Key words: COVID-19, Bioethics, Health Communication.

“...som molt conscient que la situació era molt complicada i perillosa, però la proximitat, el consol, el transmetre tranquil·litat i l’empatia van més enllà dels protocols...”

“...perquè, anem al metge cercant remei i consol, no distància i por...”

Frases extraídas de la carta de un hijo por la muerte de su padre en esta situación de pandemia remitida al Hospital de Manacor.

¿Ha enfrentado y/o vulnerado la pandemia los derechos individuales de los pacientes?

Esta situación de pandemia ha supuesto una revolución organizativa en todas las estructuras estatales afectando a pequeña escala a los más íntimos aspectos de las relaciones personales, así como la propia asistencia sanitaria, generando conflictos éticos que precisan una profunda valoración, reflexión y deliberación¹.

Después de 9 meses desde el inicio de la pandemia provocada por el Coronavirus² (SARS-CoV-2) y aún siendo conscientes del esfuerzo personal realizado por los profesionales sanitarios en todos los niveles asistenciales, le corresponde al Comité de Ética Asistencial del Hospital de Manacor (CEA-HM) velar y alertar de la vulneración de ciertos derechos y obligaciones, fruto de las tensiones en el propio Sistema de Salud y que podrían suponer un conflicto ético entre valores individuales como, la relación entre los profesionales de la salud y el paciente, y los valores generales que procura la Salud Pública.

Es nuestro deber plantear una serie de reflexiones y conflictos éticos que están apareciendo en esta situación excepcional de pandemia por la COVID-19.

En Atención Primaria (AP) y hospitalaria se adoptaron unas medidas para atender a los pacientes en circuitos bien diferenciados según sintomatología sugestiva de COVID-19 o no y se recomendó evitar la consulta presencial, lo que ha contribuido al infradiagnóstico e inclusive a diagnósticos erróneos en algún caso, como han declarado diversas sociedades científicas, que reportan retrasos diagnósticos, así como el aumento de la mortalidad en patologías comunes³.

Las visitas domiciliarias de los médicos de AP se limitaron con la intención de disminuir el riesgo de contagio de los profesionales, que contaban con unas medidas de protección insuficientes durante los primeros meses de la pandemia⁴.

La accesibilidad a los centros de salud, hospitales y residencias geriátricas también han sido restringidas, afectando a las personas más vulnerables⁵, con mensajes confusos para la población ocasionando situaciones de desamparo en algunos casos.

Es cierto que a través de la telemedicina se ha intentado paliar parte del problema con una anamnesis y autoexploración dirigida, pero también parece claro que es una herramienta no desarrollada, no estandarizada, no universal y sin un perfil de paciente claro⁶. Tenemos mucho que aprender y mejorar con esta práctica clínica, donde nos dejamos por el camino la empatía y cercanía en la relación con el paciente⁷.

El Sistema Sanitario asume una buena parte de la responsabilidad del servicio que presta a los usuarios y no parece estar muy claro que los asuma con la suficiente corrección ética, que siempre debe acompañar a la corrección técnica, es por ello que los profesionales debemos velar por la equidad y la accesibilidad en la asistencia sanitaria para evitar la discriminación entre pacientes; el compromiso con la persona más que con un determinado tipo de enfermedad; la atención centrada en la persona y su entorno socio/familiar; el protagonismo de la relación entre los profesionales y el paciente; la prevención y la promoción de la salud. Principios que debemos promover y conciliar en esta situación de pandemia sin enfrentarnos con el utilitarismo⁸ de, "el máximo beneficio para el mayor número de personas", que marcan la dinámica en Salud Pública.

Frecuentemente los profesionales de la salud ante esta situación de crisis sanitaria, nos hacemos una serie de preguntas (**Tabla I**) que desde la ética no siempre tienen una clara y única respuesta, pero sí nos ayudan a una reflexión crítica con el fin de promover cambios que favorezcan la atención centrada en la persona especialmente en tiempo de pandemia.

Tabla I: Proceso de recuperación. Intervención psicológica en mujeres que han sufrido violencia de género.

PREGUNTAS ÉTICAS FRECUENTES EN LA PRÁCTICA CLÍNICA

- ¿Se ha respetado durante la pandemia la confianza y el compromiso ético con el paciente y la familia?
- ¿Son éticamente asumibles las medidas que se han puesto en marcha en nombre del bien común y el utilitarismo en esta situación de pandemia?
- ¿Cómo se ha visto afectada la calidad ético-asistencial en la atención a los pacientes en los centros de salud y en los hospitales en esta situación de pandemia?
- ¿Ha habido un criterio uniforme con la información aportada al paciente en los distintos niveles asistenciales?
- ¿Ha predominado el paternalismo profesional en detrimento de la autonomía del paciente?
- ¿Priorizamos los valores de Salud Pública, básicamente utilitaristas, frente a valores individuales del paciente?

Comentarios

La relación con el paciente, que va más allá de la entrevista clínica estructurada y pasa a convertirse en una relación de confianza donde la comunicación y la empatía constituyen una parte fundamental del compromiso ético profesional, se ve amenazada en esta situación de pandemia.

Es cierto también, que debemos aprender a manejarnos con otras herramientas que también generen confianza: la consulta no presencial a través del teléfono, la videoconferencia etc. pero este tipo de relación con el paciente debe mejorarse, aprender a usarla mejor y

sobretudo ser aceptada tanto por el médico como por el paciente.

Tal vez sea el momento de adaptarse a una realidad distinta en nuestra práctica clínica habitual pero que esta no nos conduzca al distanciamiento y al miedo.

La relevancia de la Salud Pública en este marco de pandemia debe tenerse en cuenta y sus principios utilitaristas tenerse en consideración, pero no puede hacernos olvidar el compromiso con la persona enferma y sus familiares.

Bibliografía

1. Bertran J, Sánchez I, Ibañez JJ. Conflictos éticos relacionados con la enfermedad por Coronavirus Covid-19. *Bioética & Debat*. 2020;26(87)
2. World Health Organization. WHO Emergencies Coronavirus Emergency Committee Second Meeting. En 2020. p. 1-7. Disponible en: https://www.who.int/docs/default-source/coronaviruse/transcripts/ihr-emergency-committee-for-pneumonia-due-to-the-novel-coronavirus-2019-ncov-press-briefing-transcript-30012020.pdf?sfvrsn=c9463ac1_2
3. Cardo Miota A, Valls Pérez B, Lara Morales PA, Alguacil Martínez C, Serrano Ivars L, Ferrer Amengual V, et al. Respuesta de un centro de salud ante la pandemia COVID-19: percepciones de la plantilla médica. *Comunidad*. 2020;22(3):1-8.
4. Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A, et al. Fair Allocation of Scarce Medical Resources in the Time of Covid-19. *N Engl J Med*. 2020;382(21):2049-55.
5. Amblàs-Novellas J, Martínez-Gómez R, Blasco-Rovira M. La atención paliativa en las residencias durante la pandemia COVID-19 (o cuando el coronavirus llamó a la puerta del ámbito más vulnerable del sistema). *Med Paliativa*. 2020;27(3):234-41.
6. Comisión central Deontológica OMC. La Telemedicina en el acto médico [Internet]. 2020. Disponible en: https://www.cgcom.es/sites/default/files//u183/informe_e-consulta_ccd_10_06_2020.pdf
7. Boceta-Osuna J, García-Llana H, Altisent R. Reflexiones éticas desde la experiencia práctica de la crisis COVID-19. *Med Paliativa*. 2020;27(3):255-62.
8. Montero Delgado F, Morlans Molina M. Las escuelas clásicas de la filosofía moral. En: *Fundació Doctor Robert*, editor. *Para deliberar en los comités de ética*. Barcelona: Sanofi aventis; 2009. p. 79

Determination of scales related to cardiovascular risk and fatty liver in 5.370 spanish farmers

Determinación de escalas relacionadas con el riesgo cardiovascular y el hígado graso en 5.370 agricultores españoles

Vahid Mohebbi¹ , Andrés Aramayo² , Jorge Morales³ 

1. Especialista en Medicina de Trabajo. Supervisor de Salud Ocupacional en Minera San Cristóbal S.A. Potosí. Bolivia.

2. Magister en Salud Pública. Supervisor de Programas y Servicios en Minera San Cristóbal S.A. Potosí. Bolivia.

3. Especialista en Cirugía General, Hospital San Juan de Dios. Potosí. Bolivia.

Correspondencia

Vahid Mohebbi
Supervisor de Salud Ocupacional
Minera San Cristóbal. Potosí. Bolivia.

Recibido: 1 - III - 2021

Aceptado: 26 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.26

Abstract

Introduction: Cardiovascular diseases are one of the main causes of morbidity and mortality worldwide. Although these pathologies mainly affect the elderly, they also affect younger people.

Material and methods: Descriptive and cross-sectional study carried out in 5.370 Spanish farmers (3.695 men and 1.675 women) with a mean age of approximately 41 years. Different indexes of overweight and obesity, fatty liver, atherogenic indices, cardiovascular risk scores, metabolic syndrome and other indicators related to cardiovascular risk were analyzed.

Results: Approximately 20% of our workers presented obesity, hypertension and hypertriglyceridemia. Around 40% had hypercholesterolemia. We found a high prevalence of metabolic syndrome, fatty liver and high values of REGICOR and SCORE cardiovascular risk scores.

Conclusions: Despite the low mean age of our farmers, the prevalence of altered values of the different scores related to cardiovascular risk can be considered high.

Keywords: metabolic syndrome, fatty liver, hypertension, dyslipidemia, farmers.

Resumen

Introducción: Las enfermedades cardiovasculares son una de las principales causas de morbimortalidad a nivel mundial. Estas patologías aunque afectan principalmente a personas de edad avanzada, también están presentes en personas más jóvenes.

Material y métodos: Estudio descriptivo y transversal realizado en 5.370 granjeros españoles (3.695 hombres y 1.675 mujeres) con una edad media de aproximadamente 41 años. Se analizan diferentes escalas de sobrepeso y obesidad, escalas de hígado graso, índices aterogénicos, escalas de riesgo cardiovascular, síndrome metabólico y otros indicadores relacionados con riesgo cardiovascular.

Resultados: Aproximadamente un 20% de nuestros trabajadores presentan obesidad, hipertensión e hipertrigliceridemia. Un 40% hipercolesterolemia. Hemos encontrado altas prevalencias de síndrome metabólico, hígado graso y de valores elevados de las escalas de riesgo cardiovascular REGICOR y SCORE.

Conclusiones: Pese a la baja edad media de nuestros granjeros, la prevalencia de valores alterados de las diferentes escalas relacionadas con el riesgo cardiovascular se pueden considerar elevadas.

Palabras clave: Síndrome metabólico, hígado graso, hipertensión, dislipemias, agricultores.

Introduction

Among the tasks of occupational physicians we can highlight the preventive one, Considered as the set of activities aimed at reducing or eliminating occupational risks by individual or collective interventions, although in recent years, comprehensive health promotion has gained special importance, defined by the WHO in the Ottawa letter (WHO, 1986)¹ as the process that allows people to exercise control over the determinants of health, thus improving their health, and which encompasses actions to improve the health and well-being of workers.

Within the preventive activities we find a continuous Health Surveillance, which allows the occupational health personnel to have information about health problems, health indicators or unhealthy life habits of workers that may contribute to the development of diseases.

Various institutions (Public Health or Occupational Health) have begun to take action to prevent cardiovascular diseases by studying the factors related to greater cardiovascular risk and by implementing measures aimed at reducing the incidence and consequences of these diseases among the working population.

CVD is the leading cause of disability and premature death worldwide², with significant health care costs. In Europe they are also the leading cause of death in men and women, although preventive measures to control cardiovascular risk factors and treatments have increased the overall survival³.

Despite the fact that Spain is the second country in the European Union with the lowest mortality rates due to cardiovascular diseases, in 2015 diseases of the circulatory system continued to be the leading cause of death in our country, with ischemic coronary heart disease standing out as the pathology responsible for the greatest number of deaths⁴.

In addition to the classic factors related to cardiovascular risk (diabetes, obesity, smoking and hypertension, among others), there are others, especially sociodemographic and occupational factors, that influence the risk of the population that has not yet developed clinical signs of cardiovascular pathology and therefore, on which primary prevention can be carried out to avoid the onset of CVD, The work environment is an ideal place to put it into practice, especially in the context of health surveillance, where action is taken on active healthy workers, and where, in addition to the classic risk factors, different sociodemographic and occupational variables have to be taken into consideration, such as age, gender, level of education, social class and type of work performed.

The different professions can have a positive or negative influence on the levels of cardiovascular risk, so it is

interesting to know what this level is in each of the occupational groups.

In this study, we set out to determine the level of cardiovascular risk in an occupational group that has been little studied in Spain, namely farmers.

Methods

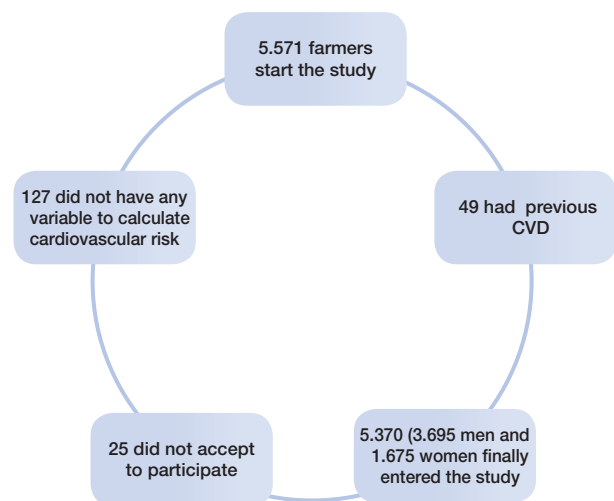
A retrospective and cross-sectional study was carried out in 5.571 farmers from different Spanish geographical areas between January 2019 and September 2020. The farmers were selected on the basis of their attendance at periodic occupational health checkups.

Inclusion criteria:

- Belongs to one of the participating companies.
- Accepts participating in the study.
- Not having suffered a serious cardiovascular disease event in the past (myocardial infarction, cerebrovascular disease...)

5.571 farmers began the study, 127 were excluded because data were not available for all the variables needed to calculate the cardiovascular risk indicators; 49 had a history of cardiovascular disease and 25 did not agree to participate in the study. The final number of workers included in the study was 5.370 farmers. See flow chart in **figure 1**.

Figure 1: Participant flow chart.



All anthropometric, clinical and analytical measurements were performed by health personnel from the occupational health units that participated in the study, after standardizing the measurement techniques. The following parameters related to cardiovascular risk were included in the assessment:

Weight, expressed in kilograms, and height in cm, were determined with a SECA 700 scale equipped with a SECA 220 telescopic height bar.

Waist circumference (in cm): was measured with a SECA model 200 tape measure. The individual stood with feet together, trunk straight and upper limbs hanging on both sides of the body. The tape measure was placed parallel to the ground at the height of the last floating rib.

Blood pressure was measured with a calibrated OMRON M3 automatic sphygmomanometer and after 10 minutes rest. Three determinations were made at one-minute intervals, obtaining the mean of the three. Hypertension was considered when the values were equal to or greater than 140 mm Hg systolic or 90 mm Hg diastolic blood pressure.

Glycemia, total cholesterol and triglycerides: These were determined by automated enzymatic methods and HDL by precipitation with dextran sulfate C12Mg. LDL was calculated using the Friedewald formula (provided that triglycerides were less than 400 mg/dl). All the above values are expressed in mg/dl.

Friedewald's formula: $LDL = \text{total cholesterol} - HDL - \text{triglycerides} / 5$

Glycemia was classified according to the recommendations of the American Diabetes Association⁵, considering hyperglycemia >125 mg/dL. Cholesterol values >239 mg/dL, LDL >159 mg/dL and triglycerides >200 mg/dL were considered high.

The cut-off points for the atherogenic indexes were⁶: Cholesterol/HDL (considered as high values >5 in men and >4.5 in women), LDL/HDL and Triglycerides/HDL (high values >3).

Three models of metabolic syndrome were determined:

- NCEP ATP III (National Cholesterol Educational Program Adult Treatment Panel III), at least three of the following factors are required: waist circumference >88 cm in women and 102 cm in men; triglycerides >150 mg/dL or under treatment; blood pressure >130/85 mm Hg or under treatment; HDL <40 mg/dL in women or <50 mg/dL in men or under treatment, and fasting blood glucose >100 mg/dL or under treatment.
- The International Diabetes Federation (IDF)⁷ requires central obesity, waist circumference >80 cm in women and >94 cm in men, and in addition two or more of the other factors cited above for ATP III.
- JIS⁸ criteria the same as NCEP ATP III, except waist, which is the same as the IDF model.

Hypertriglyceridemic waist⁹: waist circumference greater than 94 cm in men and greater than 80 cm in women and triglycerides greater than 150 mg/dl or treatment.

REGICOR is the Framingham scale adapted to the Spanish population¹⁰ and is applied between 35 and 74 years of age. We speak of moderate risk >5% and high risk >10%¹¹. The SCORE scale is the version recommended for Spain¹²⁻¹³ It can be determined between 40 and 65 years of age and we speak of moderate risk >4% and high risk >5%.

Framingham vascular age is determined using calibrated tables¹⁴ and assesses arterial aging. It can be calculated from the age of 30 years. Vascular age with the SCORE model¹⁵ is also calculated using tables and in persons between 40 and 65 years of age. A concept that applies to both vascular ages is avoidable years of life lost (ALLY)¹⁶, which can be defined as the difference between biological age and vascular age.

$$ALLY = \text{vascular age} - \text{biological age}.$$

Other different indicators are calculated using the following formulas:

Visceral adiposity index¹⁷ (VAI)

Male:

$$VAI = \left(\frac{WC}{39,68 + (1,88 \times BMI)} \right) \times \left(\frac{TG}{1,03} \right) \times \left(\frac{1,31}{HDL} \right)$$

Female:

$$VAI = \left(\frac{WC}{39,58 + (1,89 \times BMI)} \right) \times \left(\frac{TG}{0,81} \right) \times \left(\frac{1,52}{HDL} \right)$$

Waist triglyceride index¹⁸

Waist circumference (cm) x triglycerides (mmol).

Body shape index (ABSI)¹⁹.

$$ABSI = \frac{WC}{BMI^{2/3} \times \text{height}^{1/2}}$$

Normalized weight-adjusted index (NWA)²⁰

$[(\text{weight}/10) - (10 \times \text{height}) + 10]$ with weight measured in kg and height in m.

Conicity index²¹

$$\frac{\text{waist circumference (in metres)}}{0,109} \times 1 / \sqrt{\frac{\text{weight (in kilogram)}}{\text{height (in metres)}}}$$

Cardiometabolic index²²

Waist-to-height ratio x atherogenic index triglycerides / HDL-c.

Triglyceride glucose index²³ = $LN(\text{triglycerides [mg/dl]} \times \text{glycaemia [mg/dl]}/2)$.

Triglyceride glucose index-BMI, Triglyceride glucose index-waist²⁴

$$\begin{aligned} \text{TyGindex-BMI} &= \text{TyGindex} \times \text{BMI} \\ \text{TyGindex-waist} &= \text{TyGindex} \times \text{waist} \end{aligned}$$

Atherogenic dyslipidemia is defined by triglycerides >150 mg/dL, HDL<40 mg/dL in men and <50 mg/dL in women and normal LDL. If LDL is > 130 mg/dL we speak of lipid triad²⁵.

The overweight and obesity index analyzed include:

- Body mass index (BMI) was calculated by dividing weight by height in squared meters. Obesity was considered over 30kg/m².
- The waist-to-height ratio was considered risky over 0.5026.
- The body surface index²⁷ (BSA) is calculated from the body surface area (BSA) where w represents weight in kg and h height in cm

$$\text{BSA} = w^{0,425} * h^{0,725} * 0,007184$$

$$\text{BSI} = \frac{\text{WEIGHT}}{\sqrt{\text{BSA}}}$$

Formulas to estimate the percentage of body fat:

- Relative fat mass²⁸ 76- (20 x (height/p waist)) Height and waist circumference are expressed in meters.
- CUN BAE²⁹ (University of Navarra Body Adiposity Estimator Clinic)
-44.988 + (0.503 x age) + (10.689 x sex) + (3.172 x BMI) - (0.026 x BMI²) + (0.181 x BMI x sex) - (0.02 x BMI x age) - (0.005 x BMI² x sex) + (0.00021 x BMI² x age)
- ECORE-BF (Equation COrdoba Estimator Body Fat)³⁰
-97.102 + 0.123 (age) + 11.9 (gender) + 35.959 (LnBMI)

In CUN BAE and ECORE-BF male is 0 and female 1 and cut-off points for obesity are 35% in women 25% in men.

- Palafolls formula³¹.
Men = (BMI/waist]*10) + BMI. Women = (BMI/waist]*10) + BMI + 10.
- Deuremberg formula³².
1,2 x (BMI) + 0,23 x (age) - 10,8 x (gender) - 5,4
Male = 0 Female = 1

Body Roundness Index³³ (BRI)

$$\text{BRI} = 364,2 - 365,5 \times \sqrt{1 - \left(\frac{\text{WC}/(2\pi)}{(0,5 \text{ height})^2} \right)^2}$$

Non-alcoholic fatty liver scales:

- Fatty liver index (FLI)³⁴
$$\text{FLI} = \left(e^{0,953 \cdot \log_e(\text{triglycerides})} + 0,139 \cdot \text{BMI} + 0,718 \cdot \log_e(\text{ggt}) + 0,053 \cdot \text{waist circumference} - 15,745 \right) / \left(1 + e^{0,953 \cdot \log_e(\text{triglycerides})} + 0,139 \cdot \text{BMI} + 0,718 \cdot \log_e(\text{ggt}) + 0,053 \cdot \text{waist circumference} - 15,745 \right) \times 100$$

Cutoff for high risk 60.

- Hepatic steatosis index (HSI)³⁵
HSI = 8 x ALT/AST + BMI (+ 2 if type 2 diabetes yes, + 2 if female)
- Zhejiang University index (ZJU)³⁶
BMI + FPG mmol L + TG mmol L + 3 ALT/AST + 2 if female
- Fatty liver disease index (FLD)³⁷
BMI + TG + 3 x (ALT/AST) + 2 x Hyperglycaemia (presence= 1; absence = 0)
Values <28.0 or >37.0 excluded the possibility of NAFLD
BMI ≥ 28 = 1 point, AST/ALT ≥ 0.8 = 2 points, type 2 diabetes mellitus = 1 point.
Cut off for high risk 2 points
- Lipid accumulation product³⁸
In men: (waist circumference (cm) - 65) x (triglyceride concentration (mMol)).
In women: (waist circumference (cm) - 58) x (triglyceride concentration (mMol))

A smoker was considered to be any person who had regularly consumed at least 1 cigarette/day (or the equivalent in other types of consumption) in the last month, or had quit smoking less than one year ago.

Statistical analysis

Frequency was calculated for categorical variables and mean and standard deviation for quantitative variables. Bivariate analysis was performed using the chi-square test (with a correction with Fisher's exact test, when conditions required it) and a Student's t test for independent samples. Multivariate analysis was performed by binary logistic regression with the Wald method, with calculation of the Odds ratio, and the Hosmer-Lemeshow goodness-of-fit test was performed. The SPSS 27.0 program was used for the statistical analysis, and it was considered statistically significant when p<0.05.

Considerations and ethical aspects

The Clinical Research Ethics Committee of the Illes Balears Health Area approved the study n° IB 4383/20. The procedures were performed following the ethical standards of the institutional research committee and with the 2013 Declaration of Helsinki. All patients signed written informed consent documents before participating in the study.

Results

The mean values by sex of the different anthropometric, clinical and analytical variables of the sample are shown in **table I**. The high percentage of smokers in both sexes stands out, especially in men. In all the variables the results were worse in male farmers, the differences being statistically significant in all cases.

Most of the data analyzed show more negative results in male farmers, this is true for overweight and obesity indices (waist/height, BMI, BRI, ABSI, BSI, VAI and conicity index) but not for NWA, cardiovascular risk scales (SCORE, REGICOR and vascular age), metabolic syndrome, atherogenic indices, Triglyceride-glucose index and waist triglyceride index.

Fatty liver index and Framingham steatosis index are higher in men while hepatic steatosis index and Zhejiang University index are higher in women. The formulas for estimating body fat have higher values in women, since the female sex has a higher fat content under normal conditions. The complete results can be found in **table II**.

When analyzing the prevalence of altered values of the different scales studied, we observed a trend similar to that found in the mean values, that is, most prevalences are higher in men. There are only higher prevalences in women in BMI, CUN BAE, ECORE-BF, Deuremberg formula, hepatic steatosis index and Zhejiang University index. All the data can be consulted in **table III**.

Table I: Characteristics of Spanish farmers.

	Men n=3.695 Mean (SD)	Women n=1.675 Mean (SD)	p-value
Age (years)	40.9 (11.2)	41.5 (10.5)	0.068
Height (cm)	173.7 (7.0)	161.6 (6.6)	<0.0001
Weight (cm)	79.8 (14.9)	69.1 (15.0)	<0.0001
Waist (cm)	84.1 (11.6)	74.5 (11.6)	<0.0001
Systolic Blood Pressure (mmHg)	126.5 (16.1)	117.1 (15.9)	<0.0001
Dyastolic Blood Pressure (mmHg)	76.5 (10.9)	71.3 (10.3)	<0.0001
Cholesterol (mg/dl)	195.1 (40.8)	191.3 (35.4)	0.001
HDL-c (mg/dl)	51.0 (7.8)	56.3 (6.9)	<0.0001
LDL-c (mg/dl)	119.2 (38.7)	115.6 (34.3)	0.001
Triglycerides (mg/dl)	126.3 (90.3)	97.5 (44.7)	<0.0001
Glycaemia (mg/dl)	92.5 (25.6)	86.3 (19.6)	<0.0001
ALT (U/l)	28.8 (16.6)	19.0 (11.8)	<0.0001
AST (U/l)	26.0 (12.1)	19.2 (9.2)	<0.0001
GGT (U/l)	34.5 (34.0)	20.3 (22.9)	<0.0001
	Percentage	Percentage	p-value
18-29 years	18.4	15.7	<0.0001
30-39 years	27.5	26.0	
40-49 years	29.1	34.3	
50-69 years	25.0	24.0	
Non-Smokers	63.6	65.4	<0.0001
Smokers	36.4	34.6	

Multivariate analysis using binary logistic regression showed that males (except in the metabolic syndrome with the IDF criteria) and age over 50 years (except in the waist to weight ratio, hypertriglyceridemic waist and fatty liver index) are the two factors that most influence the appearance of altered values of scales related to cardiovascular risk. Smoking affects few scales and does so on the one hand by decreasing the prevalence (ECORE-BF, CUN BAE, Palafolls formula, Deuremberg formula and Framingham liver disease index) and on the other by increasing it (total and LDL cholesterol, Atherogenic dyslipidemia, lipid triad, LDL/HDL, REGICOR and SCORE scales). To see all the results, please refer to **table IV**

Table II: Mean values of the different cardiovascular risk and fatty liver scales according to gender in Spanish farmers.

	Men n=3.695 Mean (SD)	Women n=1.675 Mean (SD)	p-value
Waist to weight ratio	0.48 (0.06)	0.46 (0.07)	<0.0001
Body mass index (BMI)	26.4 (4.6)	26.4 (5.4)	0.999
CUN BAE	25.2 (6.7)	37.0 (7.3)	<0.0001
ECORE-BF	25.2 (6.4)	36.9 (7.5)	<0.0001
Relative fat mass	22.0 (5.3)	31.7 (6.0)	<0.0001
Palafolls formula	29.6 (4.8)	40.0 (5.7)	<0.0001
Deuremberg formula	24.9 (6.5)	35.9 (7.3)	<0.0001
Body surface index	57.1 (8.0)	52.2 (8.6)	<0.0001
Normalized weight adjusted index	0.6 (1.4)	0.8 (1.4)	0.001
Body roundness index	3.1 (1.2)	2.7 (1.3)	<0.0001
Body shape index	0.072 (0.006)	0.067 (0.006)	<0.0001
Visceral adiposity index	7.2 (6.6)	2.9 (1.6)	<0.0001
Conicity index	1.1 (0.1)	1.0 (0.1)	<0.0001
Fatty liver index	35.1 (27.6)	21.8 (23.5)	<0.0001
Hepatic steatosis index	35.7 (6.9)	37.0 (7.0)	<0.0001
Zhejiang University index	36.5 (6.1)	37.5 (6.2)	<0.0001
Fatty Liver Disease index	31.4 (5.7)	30.8 (6.0)	0.010
Lipid accumulation product	29.6 (36.6)	19.3 (19.3)	<0.0001
Triglyceride glucose index	8.5 (0.6)	8.2 (0.4)	<0.0001
Triglyceride glucose index-BMI	225.6 (47.0)	218.8 (49.9)	<0.0001
Triglyceride glucose index-waist	716.0 (122.5)	615.5 (109.1)	<0.0001
Triglyceride glucose index-WtWR	4.1 (0.7)	3.8 (0.7)	<0.0001
Waist triglyceride index	122.4 (98.3)	83.1 (44.5)	<0.0001
ALLY vascular age SCORE*	7.9 (7.2)	4.1 (5.0)	<0.0001
SCORE scale*	1.9 (2.4)	0.5 (0.9)	<0.0001
ALLY vascular age Framingham**	6.6 (10.7)	2.0 (12.2)	<0.0001
REGICOR scale***	3.5 (2.4)	2.4 (2.0)	<0.0001
N° factors of metabolic syndrome NCEP ATPIII	1.2 (1.2)	0.9 (1.1)	<0.0001
N° factors of metabolic syndrome JIS	1.6 (1.3)	1.0 (1.1)	<0.0001
Cardiometabolic index	1.3 (1.2)	0.8 (0.5)	<0.0001
Atherogenic index total cholesterol/HDL-c	3.9 (1.2)	3.5 (0.9)	<0.0001
Atherogenic index triglycerides/HDL-c	2.6 (2.1)	1.8 (0.9)	<0.0001
Atherogenic index LDL-c/HDL-c	2.4 (1.0)	2.1 (0.8)	<0.0001

(*) Women n=974 Men n= 1987 (**) Women n= 1412 Men n=3016 (***) Women n=1246 Men n=2584

Table III: Prevalence of altered values of the different cardiovascular risk and fatty liver scales by gender in Spanish farmers.

	Men n=3.695	Women n=1.675	
Waist to weight ratio > 0.50	35.3	23.1	<0.0001
Body mass index obesity	19.3	23.3	<0.0001
CUN BAE obesity	51.2	61.0	<0.0001
ECORE-BF obesity	51.2	60.2	<0.0001
Relative fat mass obesity	44.2	34.7	<0.0001
Palafolls formula obesity	83.9	80.1	<0.0001
Deuremberg formula obesity	48.6	77.0	<0.0001
Hypertension	24.8	11.8	<0.0001
Total cholesterol ≥ 200 mg/dl	42.1	38.1	0.005
LDL-c ≥ 130 mg/dl	36.8	32.0	0.001
Triglycerides ≥ 150 mg/dl	24.8	9.1	<0.0001
Glycaemia 100-125 mg/dl	16.2	8.7	<0.0001
Glycaemia ≥ 126 mg/dl	4.3	1.9	<0.0001
Metabolic syndrome NCEP ATPIII	14.5	9.6	<0.0001
Metabolic syndrome IDF	9.6	8.1	0.035
Metabolic syndrome JIS	23.2	10.8	<0.0001
Atherogenic dyslipidemia	5.7	3.6	0.001
Lipid triad	2.1	1.2	0.020
Hipertrigliceridemic waist	7.2	1.3	<0.0001
Atherogenic index total cholesterol/HDL-c moderate-high	16.8	11.1	<0.0001
Atherogenic index triglycerides/HDL-c high	26.1	7.1	<0.0001
Atherogenic index LDL-c/HDL-c high	25.0	12.0	<0.0001
SCORE scale moderate-high*	27.6	3.9	<0.0001
REGICOR scale moderate-high**	23.5	12.5	<0.0001
Fatty liver index high risk	21.3	10.0	<0.0001
Hepatic steatosis index high risk	42.6	51.3	<0.0001
ZJU index high	34.2	43.2	<0.0001
Framingham liver disease index high	55.2	49.9	<0.0001

(*) Women n=974 Men n= 1987 (**) Women n=1246 Men n=2584

Discussion

The first thing that is striking about the results obtained in this study is that the prevalence of altered values of parameters related to cardiovascular risk is high despite the fact that the mean age of the workers is low, 41 years, and the work also involves a high physical workload. In our sample we found, despite the relative youth of the sample, more than 20% obesity, arterial hypertension and hypertriglyceridemia, almost 40% hypercholesterolemia, high prevalence of metabolic syndrome and high values of cardiovascular risk scales such as SCORE or REGICOR, and also a high percentage of people at high risk of suffering from fatty liver disease according to the different scales.

These data are much higher than those found in a study carried out in Ireland³⁹ in 310 farmers in which the prevalence of smoking was much lower (9.3%) but much lower than those presented in 502 farmers in Crete⁴⁰ (52.7%).

As we have said, almost 20% of our workers present obesity values using BMI, these figures are lower than

Table IV: Logistic regression analysis.

	≥ 50 years OR (95% CI)	Men OR (95% CI)	Smokers OR (95% CI)
Waist to weight ratio > 0.50	ns	1.82 (1.59-2.07)	ns
Body mass index obesity	1.33 (1.15-1.55)	0.78 (0.68-0.90)	ns
CUN BAE obesity	3.45 (3.00-3.97)	0.65 (0.58-0.73)	0.86 (0.76-0.96)
ECORE-BF obesity	3.26 (2.84-3.74)	0.67 (0.60-0.76)	0.85 (0.76-0.96)
Relative fat mass obesity	1.19 (1.05-1.35)	1.49 (1.32-1.68)	ns
Palafolls formula obesity	1.91 (1.58-2.30)	1.30 (1.12-1.51)	0.80 (0.69-0.93)
Deuremberg formula obesity	6.57 (5.56-7.75)	0.25 (0.21-0.28)	0.83 (0.73-0.94)
Hypertension	3.46 (3.00-3.99)	2.55(2.15-3.02)	ns
Total cholesterol ≥ 200 mg/dl	2.51 (2.21-2.84)	1.18 (1.04-1.33)	1.18 (1.05-1.33)
LDL-c ≥ 130 mg/dl	2.60 (2.29-2.96)	1.23 (1.09-1.40)	1.19 (1.06-1.34)
Triglycerides ≥ 150 mg/dl	1.45 (1.24-1.68)	3.31 (2.75-3.97)	ns
Glycaemia ≥ 126 mg/dl	4.14 (3.08-5.56)	2.36 (1.60-3.50)	ns
Metabolic syndrome NCEP ATPIII	3.56 (3.02-4.19)	1.62 (1.34-1.96)	ns
Metabolic syndrome IDF	1.59 (1.30-1.94)	ns	ns
Metabolic syndrome JIS	3.23 (2.79-3.73)	2.57 (2.15-3.06)	ns
Atherogenic dyslipidemia	2.20 (1.71-2.83)	1.62 (1.21-2.17)	1.38 (1.08-1.78)
Lipid triad	1.91 (1.26-2.89)	1.76 (1.07-2.89)	1.99 (1.33-2.97)
Hipertrigliceridemic waist	ns	6,11 (3,90-9,56)	ns
Atherogenic index total cholesterol/HDL-c moderate-high	2.85 (2.43-3.33)	1.62 (1.36-1.94)	ns
Atherogenic index triglycerides/HDL-c high	1.64 (1.41-1.90)	4.65 (3.80-5.68)	ns
Atherogenic index LDL-c/HDL-c high	2.79 (2.41-3.21)	2.46 (2.08-2.91)	1.25 (1.08-1.43)
SCORE scale moderate-high	56.26 (38.64-81.91)	19.37 (13.06-28.73)	6.85 (5.15-9.10)
REGICOR scale moderate-high	12.46 (10.17-15.26)	2.46 (1.98-3.06)	4.17 (3.43-5.07)
Fatty liver index high risk	ns	2.42 (1.99-2.95)	ns
Hepatic steatosis index high risk	1.44 (1.20-1.71)	0.70 (0.59-0.81)	ns
ZJU index high	1.59 (1.33-1.90)	0.68 (0.58-0.80)	ns
Framingham liver disease index high	1.53 (1.28-1.83)	1.23 (1.05-1.44)	0.83 (0.70-0.98)

those found by other authors, thus the Irish study³⁹ presented a prevalence of 35% and a study carried out in 27 farmers in Minnesota⁴¹ found that 40.7% were obese. Other studies found figures similar to ours, 21.8% of the 1792 Australian farmers included in a study⁴² presented figures compatible with obesity. Approximately 35% of our farmers had abdominal obesity, a figure lower than that found in the Australian study⁴² which was 38.4%, much lower than that found in the Irish study (80.5%)³⁹.

The prevalence of hypertension in 20% of our workers is much lower than that found among Irish (46%)³⁹ and Australian (54%)⁴² farmers.

Hypercholesterolemia was found in 40% of our farmers, lower than among the Irish³⁹ (46%), in Crete (73.6%)⁴⁰ and in Minnesota⁴¹ (76.9%). Elevated triglyceride levels

in our study represent 20%, a much lower prevalence than that found in Irish farmers (49.4%)³⁹.

We have not found studies in farmers that have assessed the other parameters that we have included in our study (atherogenic indices, cardiovascular risk scales, fatty liver scales, etc.) and therefore we cannot compare them.

As strong points of our study, we can highlight the large sample size, more than 5000, and the large number of variables analyzed.

The main limitation of our study is that it was carried out in a specific country, which prevents us from extrapolating our results to other countries.

Bibliografía

1. Organización Mundial de la Salud. Carta de Ottawa para el Fomento de la Salud. Primera Conferencia Internacional sobre Fomento de la Salud, Ottawa, Canadá, 17-21 de noviembre de 1986. Ginebra: OMS; 1986. Available at: http://www.who.int/hpr/NPH/docs/ottawa_charter_hp.pdf.
2. Organización Mundial de la Salud. Enfermedades cardiovasculares. Available at: http://www.who.int/cardiovascular_diseases/about_cvd/es.
3. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*, 2006, 3(11): e442.
4. Instituto Nacional de Estadística. Defunciones según la causa de muerte. Resultados Nacionales. Año 2015. Madrid: Instituto Nacional de Estadística; 2017. Available at: http://scielo.isciii.es/scielo.php?script=sci_nlinks&pid=S1132-6255201700040025700007&lng=en
5. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;33(Suppl 1):S62-9.
6. López González ÁA, Rivero Ledo YI, Vicente Herrero MT, Gil Llinás M, Tomás Salvá M, Riutord Fe B. Índices aterogénicos en trabajadores de diferentes sectores laborales del área mediterránea española. *Clin Investig Arterioscler*. 2015;27(3):118-28
7. Zimmet P, M M Alberti KG, Serrano Ríos M.A new international diabetes federation worldwide definition of the metabolic syndrome: the rationale and the results. *Rev Esp Cardiol*. 2005;58(12):1371-6.
8. Cabrera-Roe E, Stusser B, Cáliz W, Orlandi N, Rodríguez J, Cubas-Dueñas I, et al. Concordancia diagnóstica entre siete definiciones de síndrome metabólico en adultos con sobrepeso y obesidad. *Rev Peru Med Exp Salud Publica*. 2017;34(1):19-27.
9. Sam S, Haffner S, Davidson MH, D'Agostino RB, Feinstein S, Kondos G, et al. Hypertriglyceridemic Waist Phenotype Predicts Increased Visceral Fat in Subjects With Type 2 Diabetes. *Diabetes Care*. 2009 Oct; 32(10): 1916-20
10. Marrugat J, Subirana I, Comín E, Cabezas C, Vila J, Elosua R, et al Investigators. Validity of an adaptation of the Framingham cardiovascular risk function: the VERIFICA Study. *J Epidemiol Community Health*. 2007; 61: 40-7.
11. Marrugat J, D'Agostino R, Sullivan L, Elosua R, Wilson P, Ordovas J, et al. An adaptation of the Framingham coronary risk function to southern Europe Mediterranean areas. *J Epidemiol Comm Health* 2003; 57(8): 634-8.
12. Sans S, Fitzgerald AP, Royo D, Conroy R, Graham I. Calibrating the SCORE cardiovascular risk chart for use in Spain. *Rev Esp Cardiol*. 2007;60(5):476-85.
13. Buitrago F, Cañón Barroso L, Díaz Herrera N, Cruces E. Analysis of predictive value of Framingham-REGICOR and SCORE functions in primary health care. *Med Clin (Barc)*. 2007;129(20):797.
14. Ramírez M. La edad vascular como herramienta de comunicación del riesgo cardiovascular. Centro Integral para la Prevención de Enfermedades Crónicas. 2010. Disponible en: <http://pp.centramerica.com/pp/bancofotos/267-2570.pdf>
15. Cuende JL. La edad vascular frente al riesgo cardiovascular: aclarando conceptos. *Rev Esp Cardiol*. 2016;69(3):243-6
16. Cuende JI. Edad vascular, RR, ALLY, RALLY y velocidad de envejecimiento, basados en el SCORE: relaciones entre nuevos conceptos de prevención cardiovascular. *Rev Esp Cardiol*. 2018;71:399-400
17. Amato MC, Giordano C. Visceral adiposity index: an indicator of adipose tissue dysfunction. *Int J Endocrinol*. 2014;2014:730827.
18. Yang RF, Liu XY, Lin Z, Zhang G. Correlation study on waist circumference-triglyceride (WT) index and coronary artery scores in patients with coronary heart disease. *Eur Rev Med Pharmacol Sci*. 2015;19(1):113-8
19. Bertoli S, Leone A, Krakauer NY, Bedogni G, Vanzulli A, Redaelli V, et al. Association of Body Shape Index (ABSI) with cardio-metabolic risk factors: A cross-sectional study of 6081 Caucasian adults. *PLoS One*. 2017 25;12(9):e0185013.
20. Doménech-Asensi G, Gómez-Gallego C, Ros-Berrueto G, García-Alonso FJ, Canteras-Jordana M. Critical overview of current anthropometric methods in comparison with a new index to make early detection of overweight in Spanish university students: the normalized weight-adjusted index. *Nutr Hosp*. 2018;35(2):359-67.
21. Andrade MD, Freitas MC, Sakumoto AM, Pappiani C, Andrade SC, Vieira VL, et al. Association of the conicity index with diabetes and hypertension in Brazilian women. *Arch Endocrinol Metab*. 2016;60(5):436-42.
22. Wakabayashi I, Daimon T. The "cardiometabolic index" as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus. *ClinChim Acta*. 2015;438:274-8.
23. Unger G, Benozzi SF, Peruzza F, Pennacchiotti GL. Triglycerides and glucose index: A useful indicator of insulin resistance. *Endocrinol Nutr*. 2014;61(10):533-40
24. Zheng S, Shi S, Ren X, Han T, Li Y, Chen Y, et al. Triglyceride glucose-waist circumference, a novel and effective predictor of diabetes in first-degree relatives of type 2 diabetes patients: cross-sectional and prospective cohort study. *Journal of translational medicine*. 2016; 14(1):260.

25. Bestehorn K, Smolka W, Pittrow D, Schulte H, Assmann G. Atherogenic dyslipidemia as evidenced by the lipid triad: prevalence and associated risk in statin-treated patients in ambulatory care, *Current Medical Research and Opinion* 2010; 26(12):2833-9
26. Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev*. 2010;23(2):247-69.
27. Shirazu I , Sackey1 TH A, Tiburu EK , Mensah YB , Forson A. The use of Body Surface Index as a Better Clinical Health indicators compare to Body Mass Index and Body Surface Area for Clinical Application. *Int. J. S. Res. Sci. Engg. Technol.* 2018; 4(11): 131-6
28. Woolcott OO, Bergman RN. Relative fat mass (RFM) as anew estimator of whole-body fat percentage-A cross-sectional study in American adults individuals. *Sci Rep*. 2018;8(1):10980.
29. Gómez-Ambrosi J, Silva C, Catalán V, Rodríguez A, Galofré JC, Escalada J, et al. Clinical usefulness of a new equation for estimating body fat. *Diabetes Care*. 2012;35(2):383-8.
30. Molina-Luque R, Romero-Saldaña M, Álvarez-Fernández C, Bannasar-Veny M, Álvarez-López Á, Molina-Recio G. Equation Córdoba: A Simplified Method for Estimation of Body Fat (ECORE-BF). *Int J Environ Res Public Health*. 2019;16(22):4529.
31. Mill-Ferreyra E, Cameno-Carrillo V, Saúl-Gordo H, Camí-Lavado MC. Estimation of the percentage of body fat based on the body mass index and the abdominal circumference: Palafolls Formula. *Semergen*. 2019;45(2):101-8.
32. Deurenberg P, Wetstrate JA, Seidell JC. Body mass index as a measure of body fatness: age- and sex- specific prediction formulas. *Br J Nutr* 1991; 65: 105-14.
33. Chang Y, Guo X, Chen Y, Guo L, Li Z, Yu S, et al. A body shape index and body roundness index: two new body indices to identify diabetes mellitus among rural populations in northeast China. *BMC Public Health*. 2015 19;15:794.
34. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, Tiribelli C. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol*. 2006; 6:33.
35. Lee JH, Kim D, Kim HJ, Lee CH, Yang JI, Kim W, et al. Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. *Dig Liver Dis*. 2010 ;42(7):503-8.
36. Wang J, Xu C, Xun Y, Lu Z, Shi J, Yu Ch, et al. ZJU index: a novel model for predicting nonalcoholic fatty liver disease in a Chinese population. *Sci Rep* 2015;5:16494.
37. Fuyan S, Jing L, Wenjun C, Zhijun T, Weijing M, Suzhen W, et al. Fatty liver disease index: a simple screening tool to facilitate diagnosis of nonalcoholic fatty liver disease in the Chinese population. *Dig Dis Sci*. 2013;58(11):3326-34.
38. Chiang JK, Koo M. Lipid accumulation product: a simple and accurate index for predicting metabolic syndrome in Taiwanese people aged 50 and over. *BMC Cardiovasc Disord*. 2012; 12:78
39. Van Doorn D, Richardson N, Osborne A. Farmers have hearts: The prevalence of risk factors for cardiovascular disease among a subgroup of Irish Livestock farmers. *Journal of Agromedicine* 2017;22(3):264-74
40. Vardavas CI, Linardakis MK, Hatzis CM, Saris WHM, Kafatos AG. Cardiovascular disease risk factors and dietary habits of farmers from Crete 45 years after the first description of the Mediterranean diet. *European Journal of Cardiovascular Prevention and Rehabilitation* 2010;17:440-46
41. Prokosch AJ, Dalleck LC, Pettitt RW, Cardiac risk factors between farmers and non-farmers. *JEPonline* 2011;14(3):91-100
42. Brumby S, Chandrasekara A, MCCoombe S, Kremer P, Lewandowski P. Cardiovascular risk factors and psychological distress in Australian farming communities. *Aust. J. Rural Health* 2012;20:131-7

Reduction of the average length of stay in internal medicine: difficult, but not impossible

Disminución de la estancia media en medicina interna: difícil, pero no imposible

**Daniel Nan¹ , Marta Fernández-Ayala¹ , Gonzalo Martínez de las Cuevas¹ ,
Eloísa Canga², José Manuel Olmos¹ , José Luis Hernández¹ **

1. Internal Medicine Department. Marqués de Valdecilla University Hospital- IDIVAL. University of Cantabria. Santander

2. Admission and Clinical Documentation Service. Marqués de Valdecilla University Hospital. Santander

Corresponding author

Daniel Narcis Nan Nan
Internal Medicine Department
Marqués de Valdecilla-IDIVAL University Hospital
Cantabria University - 39008 Santander
E-mail: danielnarcis.nan@scsalud.es

Received: 15 - II - 2021

Accepted: 29 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.34

Abstract

Objective: To analyze the variables that influence the average length of stay (LOS), mortality and readmissions in an Internal Medicine Department (IMD) of a tertiary University Hospital.

Method: Retrospective observational study of all patients admitted to an IMD from 2017 to 2019. The LOS, number of occupied beds, total number of admissions, urgent admissions, destination of the patient at discharge, hospital mortality, and early readmissions were analyzed. The age of the physicians, hours on call, work in the University and involvement in the plan of the multi-pathological patients (MPP) and the average delay of the diagnostic imaging procedures were collected. A descriptive analysis of the data was carried out.

Results: 18,129 patients (mean age: 81 years) were studied. There was a progressive decrease in the LOS (8.6 days in 2017 and 6.4 in 2019; 26% reduction) and in overall mortality (12.9% in 2017 and 11.3% in 2019). The rate of early readmissions was maintained (around 15%). In the clinical wards, differences were observed in the LOS, related to the profile of the internists with respect to both the mean age, as well as the monthly number of hours on call, and participation in the MPP.

Conclusion: We here present our experience in reducing LOS in an IMD. LOS is a key indicator to optimize hospital beds in periods of peak occupancy.

Keywords: Internal Medicine, hospitalization, hospital mortality.

Resumen

Objetivo: Analizar las variables que influyen en la estancia media (EM), mortalidad y reingresos en un Servicio de Medicina Interna (SMI) de un Hospital Universitario de tercer nivel.

Método: Estudio observacional retrospectivo de todos los pacientes ingresados en un SMI durante 2017 a 2019. Se analizó la EM, número de camas ocupadas, número total de ingresos, ingresos urgentes, destino del paciente al alta, mortalidad hospitalaria y reingresos precoces. Se recogió la edad de los facultativos, horas de guardia, vinculación con la universidad e implicación en el plan del paciente pluripatológico (MPP) y la demora media de las pruebas complementarias. Se realizó un análisis descriptivo de los datos.

Resultados: Se estudiaron 18.129 pacientes (media de edad: 81 años). Se observó una disminución progresiva de la EM (8,6 días en 2017 y 6,4 en 2019; reducción del 26%) y de la mortalidad global, (12,9% en 2017 y 11,3% en 2019). La tasa de reingresos precoces se mantuvo (alrededor del 15%). En las diferentes plantas, se observaron diferencias en la EM relacionadas con el perfil de los internistas respecto tanto a la media de la edad, como al número mensual de horas de guardia, y a la participación en el MPP.

Conclusión: Presentamos nuestra experiencia en la reducción de la EM en un SMI. La EM es un indicador clave para optimizar el uso de las camas hospitalarias, principalmente en periodos de máxima ocupación.

Palabras clave: Medicina Interna, hospitalización, mortalidad hospitalaria.

Introduction

The average length of stay (LOS) is an indicator that reflects the time that elapses from the time a patient is admitted to hospital until he or she recovers sufficient health to be able to receive care in his or her usual environment^{1,2}. It therefore represents the speed with which the diagnosis and treatment of diseases and conditions in hospitalized patients is carried out, i.e., it is linked to effective and appropriate use of available resources^{3,4}.

The aim of the present study was to analyze the variables that influence the decrease in the LOS, mortality and readmissions in the different hospitalization wards belonging to the same Internal Medicine Department of a tertiary care University Hospital.

Methods

Retrospective observational study of all patients admitted to the Internal Medicine Department (IMD) of the Marqués de Valdecilla University Hospital of Santander (HUMV). This is a hospital with a capacity of 700 beds and covers a population of about 350,000 inhabitants in the Autonomous Community of Cantabria. The study period runs from June 1, 2017 to December 31, 2019. The IMD is distributed over three hospitalization floors (floor A, floor B and floor C), each with 42 functional beds, staffed by 5 internists on staff and a similar number of resident physicians on each floor. The structure of the nursing teams is the same on all three floors and consists of a nursing supervisor, 4 nurses and 5 auxiliary nurses per floor on the morning shift.

Patients are admitted to the IMD, mostly from the Emergency Department and, to a lesser extent, from outpatient consultations or are transferred from other medical or surgical services. There is no prior selection of patients admitted from the Emergency Department, since it is the physician from that department who indicates the admission, and the Admitting Service staff assigns the

hospitalization bed, indistinctly, to any of the three floors of the IMD.

The working day of IMD physicians is from Monday to Friday, from 8:00 am to 3:00 pm. All the physicians on floor A are linked to the IMD's Pluripathological Patient Plan (MPP) and, in addition to the on-call duties of the IM, they perform a specific duty where, in addition to the patients of the service, patients included in the MPP are attended from 3 to 10 p.m. from Monday to Friday and from 9 a.m. to 3 p.m. on Saturdays.

Data collection was carried out by means of a structured questionnaire in a computerized database. The variables analyzed in the present study were average stay, number of occupied beds, total number of admissions, number of emergency admissions and those of average stay less than 48 hours, patient destination at discharge, mortality during admission, and early readmissions (in the first 30 days after discharge) to the different hospitalization wards. These data were provided by the hospital's Admissions and Clinical Documentation Service. In addition, the mean age of the staff physicians, their monthly number of on-call hours, their link to the university and their direct involvement in the MPP were collected. Finally, data were collected on the mean delay of the main complementary tests performed in hospital wards (endoscopy, computed tomography -CT- and echocardiography).

Given the type of study, informed consent was not required. A descriptive analysis of the data was performed. Quantitative variables were expressed as mean \pm standard deviation and qualitative variables as numbers and percentages.

Results

The results of the care variables are shown in **table I**. The number of patients hospitalized in IMD increased progressively during the study period and most of them (approximately 90%) came from the Emergency

Table I: Mean annual stay and other indicators in the different hospitalization wards of the Internal Medicine Department.

INDICATOR	Plant A			Plant B			Plant C			Total		
	2017	2018	2019	2017	2018	2019	2017	2018	2019	2017	2018	2019
Occupied beds	33	32	31	32	34	33	33	35	34	133	118	110
Total Admissions	1081	2263	2378	736	1598	1722	728	1363	1420	2545	6153	6277
Urgent Admissions	952	2112	2224	684	1478	1627	675	1276	1340	2311	5559	5799
Admissions < 48h	206	587	800	88	263	319	65	124	149	359	1165	1460
Average stay (days)	6	5,1	4,7	9,5	7,8	6,9	9,8	9,5	8,7	8,6	7	6,4
Total discharges	1034	2265	2382	728	1598	1724	716	1365	1423	2478	6172	6296
Discharges at home	812	1788	1890	545	1222	1365	579	1095	1029	1445	4828	4970
Discharges due to service transfer	73	155	172	37	104	87	38	67	61	148	431	417
Discharges due to hospital transfer	24	61	84	20	44	29	14	34	25	58	164	179
Exitus	125	255	234	125	226	240	85	166	165	335	737	708
Mortality / 100 admissions (%)	11,6	11,3	9,8	17,1	14,1	13,9	11,4	12,2	12,9	12,9	12,0	11,3
Early readmissions < 30 days (%)	15,8	14,3	16,5	14,8	15,3	16,0	17,0	17,4	14,7	15,8	15,3	15,8

Data are expressed as numbers or percentages.

Department. During the year prior to the start of the study the IMD beds were 131, with a total of 4844 patients discharged from hospital. The respective figures in the years 2017, 2018 and 2019 were 133, 118 and 110 occupied beds in the IMD and 5661, 6172 and 6296 discharged patients (a 10% increase during the study period).

The mean patient age was 80.8 ± 3.2 years and remained stable throughout the study (mean age 81.1 years in 2017, 80.5 in 2018 and 81 in 2019). A significant percentage of these patients were older than 90 years, specifically 22.5% in 2017, 21.5% in 2018 and 24% in 2019.

There was a progressive decrease in average stay (8.6 days in 2017, 7 days in 2018 and 6.4 days in 2019; an overall reduction of 26%) and overall mortality, which decreased from 12.9% in 2017 to 11.3% in 2019. However, the rate of early readmissions has remained stable (around 15%).

Analyzed separately the three hospitalization wards of the IMD, ward A had a shorter average stay and lower mortality than wards B and C, with an average annual stay of 4.7 days in 2019. The number of discharges due to hospital transfer (mainly to a chronic hospital) or service transfer, from this floor was slightly higher than in the other floors. There were no differences in age and percentage of nonagenarians among the three wards.

Table II shows the characteristics of the medical staff on the three floors of the IMD. It can be seen that there are differences in the profile of internists with respect to mean age, monthly number of on-call hours, participation in the MPP and affiliation with the University of Cantabria.

The average delay for non-urgent digestive endoscopies, went from an average of about 9 days in 2016 (the year before the start of the study) to less than 72 hours in 2019. The respective numbers for CT and echocardiogram went from 6.5 and 7.5 days in 2016 to 4 and 3 days in 2019.

Discussion

The decrease in the LOS of the HUMV IMD has been constant and progressive over the last three years in the different hospitalization wards, going from 8.6 days

in 2017 to 6.4 days in 2019. And this, despite the fact that the average age of patients seen in our IMD, during the period 2017-2019, was about 81 years, 5 years older than that published in the RECALMIN 2019 study, in Internal Medicine units of similar hospital⁵. One reason is that, in these last three years, the percentage of nonagenarian patients admitted to our units has increased. In fact, it is well known that a prolonged stay of very elderly patients does not necessarily result in an improvement in their health⁶.

Coinciding with the improvement in the LOS in our IMD, a slight decrease in overall mortality was also observed, which is lower than that reported in the RECALMIN study 2019⁵. However, the percentage of early readmissions to the service has remained at similar level, although also somewhat lower than that described in the RECALMIN study, in hospitals of the same level of complexity⁶.

There are several reasons that could explain the constant and progressive decrease in the LOS over the last three years. In this sense, several factors common to the entire IMD could have had an influence, such as the clear decrease in the delay in the main diagnostic tests requested during admission, the decrease in the number of beds per physician, due to a reduction in the number of occupied beds in the IMD, but which led to a progressive increase in the number of discharges (a 10% increase during the 3 years of the study) and access to the patient's electronic history from the home of the responsible physician, through a VPN connection.

However, there are a number of differences between the IMD wards that may have influenced the reduction in average stay and are worth commenting on. Thus, the average stay on floor A is lower than on the other two floors, and we were able to note that this shorter length of stay was not associated with an increase in mortality or early readmissions, compared to the data for the other floors. Floor A was opened in June 2017, after the completion of the reconstruction works of our hospital. The physicians who make up this team had been part of an IMD unit that had had to move to a hospital that primarily cared for elderly and multi-pathological patients. The stay in this center allowed them to gain experience in the specific care of these patients, both for the physicians and the nursing teams. In addition, the mean age of the

Table II: Differences in faculty staffing on the three hospitalization floors of the Internal Medicine Department.

	Plant A	Plant B	Plant C
Mean age of the physicians (years), mean \pm SD	45.6 \pm 4.8*	55.6 \pm 8.2	58.4 \pm 4.7
Physicians on duty, n (%)	5 (100)	3 (60)	2 (40)
On-call hours per physician per month, mean \pm SD	51.2 \pm 2.9**	22.5 \pm 19.5	12.3 \pm 16.9
Total on-call hours per floor per month, mean \pm SD	256	112	62
Professors linked to the University, n (%)	2 (40)	3 (60)	2 (40)
Physicians linked to the MPP, n (%)	5 (100)	1 (20)	0 (0)

MPP: Care Plan for the Pluripathologic Patient. *p=0.046 vs. plant B y p=0.003 vs. plant C. ** p=0.03 vs. plant B y p=0.007 vs. plant C.

IMD physicians was 53 years, higher than that described in the RECALMIN study (47 years)⁵.

In plant A, however, the average age of the physicians is more than 10 years younger than in the other two plants. In this regard, studies analyzing the association between age and employee productivity have yielded contradictory results. In general, workers' skills tend to increase up to a certain age and then begin to decrease, although older workers tend to develop a greater ability to plan, supervise and react to day-to-day problems^{7,8}.

Motivation is an internal state that activates, directs and maintains behavior⁹. Motivation and job satisfaction are aspects that complement each other within the business structure, and even more so in the healthcare setting¹⁰. It is a fundamental characteristic for the achievement of objectives and difficult to quantify in work teams¹¹. The team on floor A had undergone various organizational changes that finally led to a high degree of motivation, especially focused on achieving high healthcare performance. Some changes, but of lesser intensity, arose on floor B linked to the renewal of the staff, which implied a rejuvenation and increase in the degree of motivation of the physicians on this floor. However, on floor C, where there was no organizational change, the older age of the team physicians may have influenced the degree of their motivation. However, the opening of floor A and the improvement of its care indicators has had a motivational "knock-on" effect on the other floors of the IMD, also reactivated, in part, by a change in the Head of Service during the first year of the study period. Finally, the fact that the different hospitalization units have been able to be located in the same building, following the completion of the reconstruction work on our hospital, may also have played a role.

The organizational structure of public hospitals generally allows for few logistic adjustments in hospitalization wards, where work is usually carried out from Monday to Friday, from 8 am to 3 pm, with the rest of the day covered by on-call teams. This means that there is little care activity during weekends and holidays, which has been one of the reasons behind the creation of short-stay or high-resolution units^{12,13}. In this regard, a key factor in the reduction of average stay has been the implementation of a MPP on-call schedule, from 15:00 to 22:00 hours from Monday to Friday and from 9:00 to 15:00 hours on Saturdays. Although this on-call service was initially aimed at the care of MPP patients, the physician also performed care activities on his floor, which may have had an impact on the reduction of average stay. On floor A, all the physicians were on call and the average number of hours on call per attending was higher compared to the internists assigned to the other hospitalization floors (**see table II**). The link to the MPP is vital in improving the length of stays, since it allows better interpretation of the needs of these types of patients and more effective coordination

of care with Primary Care Services¹⁶. In this regard, it was observed that on floor A there was a greater number of discharges due to transfer to another hospital (mainly for chronic patients) or transfer to other services, doubling the number of discharges for this reason on the other floors. However, the number of discharges for this reason does not reach 10% and does not have a significant weight in the improvement of average stay.

On the other hand, it has been suggested that, in university hospitals, the link between the medical staff and the university may lead to a longer average stay, both because of the complexity of the patients attended in this type of center and because of the more teaching-oriented approach^{14,15}. However, in all the wards of our IMD the medical staff was linked to the university and there were no differences in the teaching given, so this factor does not seem to play a relevant role in our study.

Regarding the role of the nursing teams, the IMD wards had a similar structure, in terms of patient/nurse ratio (10/1), to the average for hospitals in Spain, according to data from the RECALMIN study⁵. However, the nursing team on Floor A had acquired greater experience in the care of the very elderly patient during their stay in the satellite hospital of the central hospital and that applied in daily care may possibly have played a role in the lower average stay on this floor.

Therefore, we believe that the main factors that have influenced a shorter stay on floor A have been: the younger age of the physicians, a higher degree of motivation, the application of geriatric care measures in very elderly patients, a greater presence on the hospitalization floor (due to the implementation of the afternoon and Saturday shift), which allowed for better discharge planning and participation in the MPP plan.

On the other hand, it has been shown that the decrease in the LOS of a ward had a beneficial effect on the overall average stay of the IMD, which has been decreasing over the last few years to around 6 days at present. This has been beneficial both for the patients, with fewer days of hospitalization, and for the hospital, avoiding the collapse of services such as the Emergency Department, especially in winter periods, and increasing the number of beds available for surgery programs.

With respect to the limitations of the study, we found several. An analysis by degree of severity of the patients admitted to the different wards was not carried out, since this information was not available. However, admission to the different wards was decided by the Admission Service, maintaining homogeneous distribution criteria. Likewise, the patients integrated in the MPP were also admitted indistinctly to the 3 floors, with a similar distribution. Another limitation is the lack of a tool to quantify the degree of motivation among the different physicians.

Conclusion

It should be noted that this improvement in the average stay of the IMD has been achieved with minimal changes in the organization and without these entailing a significant increase in costs. In addition to the improvement in MS, there has also been an improvement in in-hospital mortality, with the percentage of early readmissions remaining stable during this period. The hours of on-call duty, when not excessive in number, can be an economic incentive and at the same time an activity enhancer that has repercussions on better health care results. The maintenance over time of this efficiency of care has meant that, during 2020, in the midst of the SARS-CoV-2 pandemic, our hospital has not been overwhelmed with the care of patients affected by COVID-19, who have been attended mainly by internists.

Authorship contributions

D. Nan: conception, study design, data collection and drafting of the original version of the manuscript. M. Fernández Ayala, G. Martínez de las Cuevas and E. Canga: study conception, data collection and analysis, and critical

revision of the paper. J.M. Olmos: conception of the study, data analysis and critical revision of the manuscript. J.L. Hernández: conception and design of the study, analysis of the data, critical revision of the manuscript and writing of the final version of the manuscript. All authors approved the final version of the manuscript.

Funding

This work has not received any funding.

Acknowledgments

To all the staff of the Internal Medicine Service of the HUMV for their excellent daily work and their enormous dedication and involvement in the care of our patients.

Conflict of interest

None.

References

- Peiró S, Menéu R, Roselló ML, Martínez E, Portella E. ¿Qué mide la estancia media de los grupos relacionados de diagnóstico? *Med Clin (Barcelona)*. 1994; 103:413-7.
- Ministerio de Sanidad, Servicios Sociales e Igualdad: Subdirección General de Información Sanitaria e Innovación – Evolución de la Estancia Media en los Hospitales Generales del Sistema Nacional de Salud: Años 2001-2012. Serie Informes Breves CMBD. Madrid 2014. (Consultado el 18/8/20). Disponible en: <http://www.msssi.gob.es/estadEstudios/estadisticas/cmbdhome.htm>
- Cruz Caparrós G, Zambrana García JL, Delgado Fernández M, Díez García F. Reingresos hospitalarios en Medicina Interna y estancia media. *Rev Clin Esp*. 2001; 201:164
- Peiró MS, Portella E. Identificación del uso inapropiado de la hospitalización: la búsqueda de la eficiencia. *Med Clin (Barc)*. 1994; 103:65-71.
- Sociedad Española Medicina Interna y Fundación IMAS. RECALMIN 2019. Recursos y Calidad en Medicina Interna. La atención al paciente en las unidades de Medicina Interna del Sistema Nacional de Salud. Recursos, actividad y calidad asistencial; 2019. 66 p.
- Martínez-Sellés M, Vidán MT, López-Palop R, Rexach L, Sanchez E, Datino T et al. El anciano con cardiopatía terminal. *Rev Esp Cardiol*. 2009; 62:409-21.
- Desjardins R, Wamke A. Ageing and SkillLOS: A Review and Analysis of Skill Gain and Skill Loss Over the Lifespan and Over Time. OECD Education Working Papers No. 72. Paris: OECD Publishing; 2012. 84p.
- Börsch-Supan A, M Weiss. Productivity and age: evidence from work teams at the assembly line. *J Economics Ageing*. 2016; 7:30-42.
- Leboeuf M, Muro F. *El Gran Secreto de la Motivación*. Barcelona: Editorial Empresa Activa; 2009. p160.
- Macho Stadler I. Incentivos en los servicios sanitarios. En: *Incentivos y contratos en los servicios de salud*. Pere Ibern, editor. Barcelona: Editorial Springer Science & Business Media; 1999. p19-47.
- Real de Asúa E. Educar en liderazgo: requisito y reto del internista actual. *Rev Clin Esp*. 2011; 211: 423-6.
- Cots F, Castellós X, García A, Sanz M. Relación de los costes directos de la hospitalización con la duración de la estancia. *Gac Sanit*. 1997; 11:287-95.
- Marcos M, Hernández-García I, Ceballos-Alonso C, Martínez-Iglesias R, Mirón-Canela JA, Laso FJ. Influencia de las unidades de corta estancia en la calidad de la atención hospitalaria en España. Revisión sistemática. *Rev Calid Asist*. 2013; 28:197-8.
- Kämäräinen VJ, Peltokorpi A, Torkki P, Tallbacka K. Measuring healthcare productivity-from unit to system level. *Int J Health Care Qual Assur*. 2016; 29:288-99.
- Grosskopf S, Margaritis D, Valdmanis V. The effects of teaching on hospital productivity. *Socio-Econ Plann Sci*. 2001; 35:189-204.
- Minué-Lorenzo S, Fernández-Aguilar C. Visión crítica y argumentación sobre los programas de atención de la cronicidad en Atención Primaria y Comunitaria. *Aten Primaria*. 2018; 50:114-29.

ORIGINAL

Evaluation of the prevalence of hearing loss and associated patterns in hemodialysis patients: A cross-sectional study in Iran

Evaluación de la prevalencia de hipoacusia y patrones asociados en pacientes en hemodiálisis: un estudio transversal en Irán

Gholam-Ali Dashti Khavidaki , Reza Gharibi 

Department of ENT Disorder, AL-Zahra Hospital, Zahedan University of Medical Sciences, Zahedan, Iran

Corresponding author

Reza Gharibi

Department of ENT Disorder, AL-Zahra Hospital,
Zahedan University of Medical Sciences, Zahedan, Iran
E-mail: Hessam.gharibi@gmail.com

Received: 1 - II - 2021

Accepted: 20 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.39

Abstract

Objective: There are many similarities between renal nephrons and the cochlear duct in the ear. On the other hand, the prevalence, extent, and patterns of hearing loss associated with chronic kidney disease (CKD) reported by different studies are significantly different. Therefore, this study aimed to determine the prevalence of hearing loss and associated patterns in patients undergoing dialysis.

Methods: In this cross-sectional study, patients undergoing hemodialysis referred to Khatam al-Nabia Hospital in Zahedan, Iran in 2020, were studied. The samples that met the inclusion and exclusion criteria were entered into the study by census method, and finally, 60 people were examined. After recording demographic information, patients underwent an audiometric evaluation, and the information was assessed and recorded by a specialist.

Results: Out of 60 patients, in terms of hearing loss, 24 patients (40%) were healthy, and 36 patients (60%) were unhealthy; also, the most common type of hearing loss in patients was sensorineural hearing loss in the right ear (32 patients, 88.9%) and left ear (32 patients, 91.4%), respectively. Besides, in patients with right and left ear involvement, the mean duration of renal failure in mild and moderate hearing loss was 65.76 ± 49.17 , 42.10 ± 37.78 , 63.10 ± 45.92 , and 43.90 ± 43.61 months, respectively, which demonstrated a statistically significant difference. ($P < 0.05$).

Conclusion: Hearing loss is common in patients with chronic kidney disease, and an increase in the duration of kidney disease can directly affect hearing loss in patients undergoing hemodialysis.

Keywords: Hearing loss, renal insufficiency, chronic, audiometry, Iran.

Resumen

Objetivo: Existen muchas similitudes entre las nefronas renales y el conducto coclear del oído. Por otro lado, la prevalencia, el alcance y los patrones de la pérdida de audición asociada a la enfermedad renal crónica (ERC) comunicados por distintos estudios son significativamente diferentes. Por lo tanto, este estudio tenía como objetivo determinar la prevalencia de la pérdida de audición y los patrones asociados en pacientes sometidos a diálisis.

Métodos: En este estudio transversal se estudiaron los pacientes sometidos a hemodiálisis remitidos al Hospital Khatam al-Nabia de Zahedan (Irán) en 2020. Las muestras que cumplían los criterios de inclusión y exclusión se introdujeron en el estudio mediante el método de censo, y finalmente se examinaron 60 personas. Tras registrar la información demográfica, los pacientes se sometieron a una evaluación audiométrica, y la información fue evaluada y registrada por un especialista.

Resultados: De los 60 pacientes, en cuanto a la pérdida de audición, 24 pacientes (40%) estaban sanos, y 36 pacientes (60%) no estaban sanos; además, el tipo de pérdida de audición más común en los pacientes era la pérdida de audición neurosensorial en el oído derecho (32 pacientes, 88,9%) y en el izquierdo (32 pacientes, 91,4%), respectivamente. Además, en los pacientes con afectación del oído derecho e izquierdo, la duración media de la insuficiencia renal en la pérdida de audición leve y moderada fue de $65,76 \pm 49,17$, $42,10 \pm 37,78$, $63,10 \pm 45,92$ y $43,90 \pm 43,61$ meses, respectivamente, lo que demostró una diferencia estadísticamente significativa. ($P < 0.05$).

Conclusiones: La pérdida de audición es frecuente en los pacientes con enfermedad renal crónica, y un aumento de la duración de la enfermedad renal puede afectar directamente a la pérdida de audición en los pacientes sometidos a hemodiálisis.

Palabras clave: Pérdida auditiva, insuficiencia renal crónica, audiometría.

Introduction

The incidence of chronic kidney disease (CKD) has increased significantly in the last few years due to the significant increase in the number of diabetes and hypertension patients, which are the main risk factors for CKD¹. Patients with advanced CKD require kidney transplantation or dialysis to survive². Dialysis has been shown to affect the function of almost all parts of the body system. Sensorineural hearing loss (SNHL), which has a more significant effect on high frequencies than low frequencies, has been diagnosed in patients with CKD^{3,4}.

There are many anatomical, physiological, pharmacological, and pathological similarities between renal tubular cells and cochlear stria of the ear at the ultrastructural level. Both structures have epithelium near the arteries and basement membrane. This is most evident in the capillary endothelium in the Bowman capsule in the kidney's proximal tube and the cochlear stria vascularis. Thus, in addition to antigenic similarity, the cochlea and the kidney have similar physiological mechanisms, i.e., the active transfer of fluids and electrolytes is achieved by the stria vascularis in the cochlea and the glomeruli in the kidney^{3,5-7}. It has previously been reported that the cochlea is affected by systemic-metabolic, hydro electrolytic, and hormonal changes associated with CKD. Several factors may be related to the etiopathogenetic mechanisms of hearing loss in CKD, including factors related to the disease's severity and duration, electrolyte disorders, drug toxicity, age, and comorbid conditions such as diabetes mellitus, hypertension, and hemodialysis^{8,9}. Hearing loss is widespread in patients with CKD compared to the general population¹⁰. The possible mechanism is a common antigenic reaction between the kidneys and labyrinths of the ear due to osmotic changes induced by dialysis and the ototoxic effects of diuretics¹¹. Besides, hearing loss and uremia is associated with each other and can negatively affect a patient's quality of life by restricting communication and creating a risk of social isolation and emotional problems⁴.

Different results have been reported on the effect of hemodialysis on hearing in patients with chronic renal failure; some studies demonstrated that hemodialysis does not affect the hearing of patients^{12,13} and others suggested that this treatment method is effective in inducing hearing disorders. Studies in adults, especially on the effect of hemodialysis, are highly contradictory, indicating the need for further studies in this field. Therefore, considering the cases mentioned above, in this study, we decided to investigate the frequency and types of hearing loss in hemodialysis patients. Early diagnosis of hearing loss, followed by informing the patient and utilizing appropriate treatment, can prevent this complication^{14,15}.

Materials and methods

Selection of patients

In this cross-sectional study, hemodialysis patients referred to Khatam al-Nabia Hospital in Zahedan, Iran, in 2020 were studied. The present study was carried out after the ethics committee's approval and the research committee of Zahedan University of Medical Sciences. Inclusion criteria were 25 to 65 years of age, at least 6 months of hemodialysis treatment, definitive diagnosis of chronic kidney disease by a specialist, lack of previous hearing problems (such as trauma or congenital heart problem) personal consent of the patient. Exclusion criteria were peritoneal dialysis, non-chronic kidney disease (acute kidney disease, etc.), and history of age-related or congenital hearing problems and previous trauma. Accordingly, 60 patients were included in the study. In addition to examining the demographic factors of age and sex, other variables such as hearing loss, involved ear, degree of hearing loss, type of underlying disease, duration of renal failure, duration of dialysis, and several dialysis sessions were assessed a week.

Method of study

Following the researcher's evaluation of demographic information at the hemodialysis site, patients who met the inclusion criteria were transferred to the audiometry ward of Khatam al-Nabia Hospital. The available audiometers were Madsen audiometer model MIDIMATE622 and Madsen tympanometer model ZODIAC 90. An ENT specialist then evaluated the information, and the type of hearing loss (SNHL OR CHL) and the degree of hearing loss (mild, moderate, severe, very severe) were assessed, and the related information was recorded.

Data analysis

Descriptive statistics, including statistical tables and graphs and frequencies in percentages, were used to describe the data, and the Kruskal-Wallis test was used to compare frequencies in groups. The significance level was considered less than 0.05.

Results

In the present study, 60 hemodialysis patients were evaluated. Amongst the studied patients, 33 (55%) were male, and 27 (45%) were female, and the mean age of patients was 48.53 ± 13.08 years. Also, 24 patients (40%) were healthy, and 36 patients (60%) had hearing loss. In terms of hearing loss (HL), 19 patients (31.7%) had moderate HL in the right ear, and 20 patients (33.3%) had mild HL in the left ear (**table I**); Also, the study of hearing loss pattern showed that sensorineural hearing loss (SNHL) in the right ear (32 patients, 88.9%) and left ear (32 patients, 91.4%) was the most common type of hearing loss in patients (**table I**).

Table I: Degree and pattern of hearing loss in patients undergoing hemodialysis.

Variables		Ear	
		Right (N/%)	Left (N/%)
Degree of hearing loss	Healthy (<20)	24/40%	26/43.3%
	Mild (21-40)	17/28.3	20/33.3%
	Moderate (41-70)	19/31.7%	13/21.7%
	Severe (71-90)	-	1/1.7%
	Total	60/100%	60/100%
The pattern of hearing loss	Conductive (CHL)	3/8.3%	2/5.7%
	Sensorineural (SNHL)	32/88.9%	32/91.4%
	Conductive and Sensorineural (Mix)	1/2.8%	1/2.9%
	Total	36/100%	35/100%

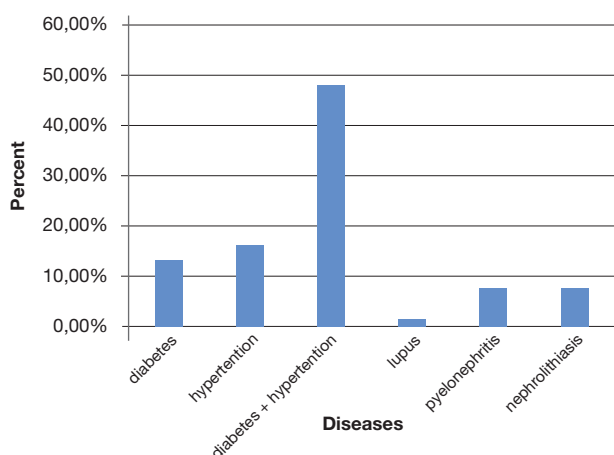
Table II: Results of audiometry test in both ears, mean duration of kidney disease, the mean duration of each dialysis session, and the number of dialysis sessions per week.

Variables		SD± Mean	Min	Max
Audiometry test	Right ear	31.75 ± 20.36	6	70
	Left ear	28.83 ± 17.99	5	80
Duration of kidney disease (months)		44.16 ± 37.62	6	180
Duration of each dialysis session (hours)		3.48 ± 0.62	2	4
Number of dialysis sessions per week		2.80 ± 0.40	2	3

Table III: Association between kidney disease duration and number of dialysis sessions per week, and hearing loss in hemodialysis patients.

Variables			SD± Mean	P-value*
Duration of kidney disease	Right ear	Healthy	30.50 ± 16.99	0.01
		Mild	65.76 ± 49.17	
		Moderate	42.10 ± 37.78	
	Left ear	Healthy	31.11 ± 17.53	0.02
		Mild	63.10 ± 45.92	
		Moderate	43.61 ± 43.90	
Number of dialysis sessions per week	Right ear	Healthy	2.70 ± 0.46	0.34
		Mild	2.88 ± 0.33	
		Moderate	2.84 ± 0.37	
	Left ear	Healthy	2.73 ± 0.45	0.50
		Mild	2.90 ± 0.30	
		Moderate	2.76 ± 0.43	

Figure 1: Frequency distribution of underlying diseases in hemodialysis patients.



According to **table II**, the mean results of the audiometry test of the right and left ears were 31.75 ± 20.36 dB and 28.83 ± 17.99 dB, respectively. Also, the mean duration of kidney disease, duration of each dialysis session, and the number of dialysis sessions per week was determined.

The study of the underlying diseases also showed that most people (29 patients, 48.3%) had both diabetes and hypertension, and 10 patients (16.7%) had high blood pressure (**Figure 1**).

The frequency distribution of involved ears in dialysis patients with HL showed that 2 patients (5.6%) had right ear involvement, 4 patients (11.1%) had left ear involvement, and 30 patients (83.3%) had involvement of both ears. According to **table III**, in patients with right and left ear involvement, renal failure's mean duration was significantly different in mild and moderate hearing loss. (P <0.05). The average number of dialysis sessions per week in mild and moderate hearing loss also showed no statistically significant difference in patients with right and left ear involvement (P >0.05).

Discussion

Kidney nephrons and cochlear ducts have been shown to have a similar epithelium, which includes a sodium-potassium pump that uses ATPase. Carbonic anhydrase is also present in both nephrons and cochlear stria¹⁶. Various pharmacological factors affect both the kidney and the inner ear, including aminoglycoside antibiotics, both ototoxic and nephrotoxic¹⁷. It has also been shown that there is an immunological link between the kidney and the ear, as antibodies produced against nephrons settle in the stria vascularis. The prevalence of cochlear hearing loss in patients with renal failure is more than in ordinary people that their hearing is affected by their age and gender^{18,19}.

This study aimed to evaluate the prevalence of hearing loss and associated patterns in patients with chronic kidney disease and undergoing dialysis. Our results demonstrated mild to moderate hearing loss in the right, and left ear was observed in 60% and 55% of

patients, respectively. About 90% of these patients had sensorineural hearing loss (SNHL) in the right and left ears. Also, the duration of renal failure had significant effects on patients' hearing loss. However, there was no statistically significant relationship between the number of dialysis sessions per week and hearing loss.

Similar to the results of the present study, HK Saeed et al., to evaluate sensory hearing loss in patients with chronic renal failure undergoing hemodialysis, showed that 66.1% of patients had sensory hearing loss, and during 12 months of follow-up, 6 other patients were also diagnosed with HL (67.3% in total). Also, the mean hearing threshold at the beginning of the study was 29.2 ± 21.2 dB and at the end of the study was 36.9 ± 17.3 dB, which was a significant difference⁹. Kohansal et al. also observed SNHL in 73.4% of all patients¹³. Additionally, our results were almost consistent with the studies by Sharma et al. (HL in 73.7% of patients)²⁰ and Singh et al. (HL in 70.9% of patients)²¹. However, low frequencies of SNHL have been reported in previous studies on hemodialysis patients in Iran (46%)²² and other countries^{15,23}. This difference may be due to changes in sample size, differences in age, kidney disease duration and hemodialysis, or a hearing assessment procedure.

In another study by Reddy et al., conducted on 200 patients with CKD, 52% of patients had high-frequency hearing loss, 9% had moderate-frequency hearing loss, and 2.5% had low-frequency hearing loss; 2.5% of patients had hearing loss at all frequencies. 61% of patients had bilateral ear involvement, and 5.5% had unilateral involvement²⁴. The findings of this study were similar to the present study, but the frequency of hearing loss in our study, in contrast to this study, was mainly at moderate frequencies in the right ear and low frequencies in the left ear.

Regarding the effect of chronic kidney disease on hearing loss, Risvi et al. reported that hearing deterioration in patients with CKD increases with disease progression and the need for dialysis. Anatomical changes such as endolymphatic system collapse, swelling, and atrophy have been shown to occur in the ear's labyrinth, and these changes have been attributed to osmotic imbalance due to hemodialysis²⁵. A study by Kusakari et al. it was reported that inner ear dysfunction was not associated with hematocrit, levels of blood urea nitrogen, creatinine, and duration of hemodialysis²⁶. According to studies, histopathological changes in the inner ear of patients with CKD undergoing hemodialysis may result in mild loss of cochlear outer hair cells and spiral ganglion cells or complete absence of the organ of Corti. However, these histopathological changes' patterns and importance need to be widely investigated to identify the effect of dialysis on the auditory pathways^{3,27}. In a study, Fidan et al. reported that sensorineural hearing loss was more common in CKD patients requiring dialysis than normal controls and that hemodialysis patients were more affected than peritoneal dialysis patients³. Jamaldeen et al.

also reported that hearing loss was present in 41.7% of patients with CKD, which was significantly higher than the control group. However, contrary to our study results, they stated that hearing loss might be inversely related to the number of hemodialysis sessions, but it is not associated with the disease's duration²⁸. This difference in results may be due to the number of samples in their study, 120 people. Also, Wu et al. showed in their study that CKD patients were at a significantly higher risk for SNHL compared to the non-CKD group. According to their results in the CKD group, the degree of SNHL in patients undergoing hemodialysis was higher than those without hemodialysis. Having CKD for a more extended period was also associated with a significant increase in the frequency of SNHL. The disease's duration was also confirmed as a risk factor in animal models of CKD, in which exacerbation of cochlear impairment overtime was confirmed²⁹. Additionally, some studies have suggested that the causes of hearing loss may be vascular changes and loss of cells in the organ of Corti during hemodialysis, and osmotic, electrolytic, and biochemical changes during dialysis, especially long-term dialysis³⁰. Osmotic oscillations and osmotic pressure during dialysis are greatly important factors that exacerbate hearing loss in these patients³¹. Other important factors that cause the exacerbation of HL in dialysis patients include changes in volume and blood pressure, which impair blood flow to the cochlea and its function³².

In general, apart from the initial findings, this study demonstrated our current understanding of hearing loss in CKD. Although there is no doubt that hearing loss is common among patients with CKD, studies with larger sample sizes are needed to elucidate the association between hearing loss in CKD and hemodialysis. Another question that arises in this regard is whether the audiometric screening of all CKD patients helps identify mild hearing loss and prevent HL severity progression, significantly if the definitive role of hemodialysis can be determined in prospective longitudinal studies. Moreover, the association between hearing loss in CKD and ototoxic medications needs to be assessed by further research as it can have significant clinical implications.

Conclusion

The results showed that hearing loss is common in CKD patients, and most studied patients were diagnosed with sensorineural hearing loss in the right and left ears. There was also a significant relationship between hearing loss and the duration of kidney disease and hemodialysis.

Acknowledgments

The authors appreciated the Department of ENT Disorder, AL-Zahra Hospital, Zahedan University of Medical Sciences, Zahedan, Iran.

References

- Jakić M, Mihaljević D, Zibar L, Jakić M, Kotromanović Ž, Roguljić H. Sensorineural hearing loss in hemodialysis patients. *Collegium antropologicum*. 2010;34(1):165-71.
- Rose C, Gill J, Gill JS. Association of kidney transplantation with survival in patients with long dialysis exposure. *Clinical Journal of the American Society of Nephrology*. 2017;12(12):2024-31.
- Fidan V, Binici DN, Borazan A. The prevalence of hearing loss in dialysis patients. *Acta Acustica united with Acustica*. 2012;98(5):800-3.
- Kang S-M, Lim HW, Yu H. Idiopathic sudden sensorineural hearing loss in dialysis patients. *Renal failure*. 2018;40(1):170-4.
- dos Reis A, Dalmolin SP, Dallegrave E. Animal models for hearing evaluations: a literature review. *Revista CEFAC*. 2017;19(3):417-28.
- El-Anwar MW, Elsayed H, Khater A, Nada E. Audiological findings in children with chronic renal failure on regular hemodialysis. *The Egyptian Journal of Otolaryngology*. 2013;29(3):182.
- Shi X. Physiopathology of the cochlear microcirculation. *Hearing research*. 2011;282(1-2):10-24.
- Pirodda A, Cicero AFG, Borghi C. Kidney disease and inner ear impairment: a simpler and closer pathogenic analogy? *Internal and emergency medicine*. 2012;7(2):93-5.
- Saeed HK, Al-Abbasi AM, Al-Maliki SK, Al-Asadi JN. Sensorineural hearing loss in patients with chronic renal failure on hemodialysis in Basrah, Iraq. *Tzu-Chi Medical Journal*. 2018;30(4):216.
- Seo YJ, Ko SB, Ha TH, Gong TH, Bong JP, Park D-J, Park SY. Association of hearing impairment with chronic kidney disease: a cross-sectional study of the Korean general population. *BMC nephrology*. 2015;16(1):154.
- Otukesh H, Moosavi A, Hosseini R, Goodarzi R, Roozbahani M. The Evaluation of Hearing Loss and Audiometric Disorders in Patients with Chronic Renal Failure, Chronic Hemodialysis and Transplantation Referred to Ali Asghar Pediatric Hospital from 2002 to 2003. *Razi Journal of Medical Sciences*. 2005;11(44):901-6.
- Gierek T, Markowski J, Kokot F, Paluch J, Wiecek A, Klimek D. Electrophysiological examinations (ABR and DPOAE) of hearing organ in hemodialysed patients suffering from chronic renal failure. *Otolaryngologia polska = The Polish otolaryngology*. 2002;56(2):189-94.
- Kohansal B, Saeedi N, Beigi MH, Moslemi A, Valizadeh A. Comparison of sensorineural hearing loss characteristics in different hemodialysis vascular accesses. *Auditory and Vestibular Research*. 2020.
- Renda R, Renda L, Selçuk ÖT, Eyigör H, Yılmaz MD, Oşma Ü. Cochlear sensitivity in children with chronic kidney disease and end-stage renal disease undergoing hemodialysis. *International journal of pediatric otorhinolaryngology*. 2015;79(12):2378-83.
- Bawa A, Singh G, Uzair G, Garg S, Kaur J. Pattern of hearing loss among chronic kidney disease patients on haemodialysis. *Int J Med Res Prof*. 2017;3:193-6.
- Torban E, Goodyer P. The kidney and ear: emerging parallel functions. *Annual review of medicine*. 2009;60:339-53.
- Nozu K, Nakanishi K, Abe Y, Udagawa T, Okada S, Okamoto T, Kaito H, Kanemoto K, Kobayashi A, Tanaka E. A review of clinical characteristics and genetic backgrounds in Alport syndrome. *Clin Exp Nephrol*. 2019;23(2):158-68.
- Okano T. Immune system of the inner ear as a novel therapeutic target for sensorineural hearing loss. *Frontiers in pharmacology*. 2014;5:205.
- Sam S, Subramaniam V, Pai S, Kallikkadan HH. Hearing impairment in patients with chronic renal failure. *J Med Sci Clin Res*. 2014;2:406-16.
- Sharma R, Gaur S, Gautam P, Tiwari R, Narain A, Lalchandani T. A study on hearing evaluation in patients of chronic renal failure. *Indian Journal of Otolaryngology*. 2011;17(3):109.
- Singh KK, Trivedi A, Jain N, Irteza M. To study auditory functions in chronic kidney disease. *Indian Journal of Otolaryngology*. 2018;24(4):261.
- Peywandi A, Roozbahany NA. Hearing loss in chronic renal failure patient undergoing hemodialysis. *Indian Journal of Otolaryngology and Head & Neck Surgery*. 2013;65(3):537-40.
- Acharya S, Pati N, Nayak AA. Pattern of hearing loss in patients of chronic kidney disease-a prospective comparative study. *Journal of Evolution of Medical and Dental Sciences-JEMDS*. 2017;6(47):3656-9.
- Reddy E, Prakash DS, Krishna MGR. Proportion of hearing loss in chronic renal failure: Our experience. *Indian Journal of Otolaryngology*. 2016;22(1):4.
- Rizvi SS, Holmes RA. Hearing loss from hemodialysis. *Archives of Otolaryngology*. 1980;106(12):751-6.
- Kusakari J, Kobayashi T, Rokugo M, Arakawa E, Ohyama K, Kawamoto K, Sekino H. The inner ear dysfunction in hemodialysis patients. *The Tohoku journal of experimental medicine*. 1981;135(4):359-69.
- Tamae A, Ishizu K, Yoshida T, Kubo K, Matsumoto N, Yasui T, Masutani K, Tsuruya K, Nakagawa T. Evaluation of the Effects of Chronic Kidney Disease and Hemodialysis on the Inner Ear Using Multifrequency Tympanometry. *The Journal of International Advanced Otolaryngology*. 2018;14(3):447.
- Jamaldeen J, Basheer A, Sarma AC, Kandasamy R. Prevalence and patterns of hearing loss among chronic kidney disease patients undergoing haemodialysis. *The Australasian medical journal*. 2015;8(2):41.
- Wu K-L, Shih C-P, Chan J-S, Chung C-H, Lin H-C, Tsao C-H, Lin F-H, Chien W-C, Hsiao P-J. Investigation of the relationship between sensorineural hearing loss and associated comorbidities in patients with chronic kidney disease: A nationwide, population-based cohort study. *PLoS one*. 2020;15(9):e0238913.
- Gatland D, Tucker B, Chalstrey S, Keene M, Baker L. Hearing loss in chronic renal failure-hearing threshold changes following haemodialysis. *Journal of the Royal Society of Medicine*. 1991;84(10):587.
- Singh AT, Mc Causland FR, editors. Osmolality and blood pressure stability during hemodialysis. *Seminars in dialysis*; 2017: Wiley Online Library.
- Babiker S, Elsayed ME, Dhaygude A, Madgula I. A complex case of hemodialysis induced increased intraocular pressure. *European Journal of Ophthalmology*. 2019;29(1_suppl):15-17.

Influence of tobacco consumption, age and sex on cardiovascular risk levels

Influencia del consumo de tabaco, la edad y el sexo en los niveles de riesgo cardiovascular

**Kristýna Mudrychová¹ , Jitka Mudrychová² , Martina Houšková Beránková¹ ,
Bárbara Altisench Jané² , María Albaladejo Blanco² , José Ignacio Ramírez Manent³ **

1. Czech University of Life Sciences, Prague 2. Family Doctor Practice, Calvià Primary Care Center, Health Service of Balears
3. Director of Calvià Primary Care Center, Health Service of Balears

Corresponding author

Jitka Mudrychová
Calvià Primary Care Center, Health Service of Balears
E-mail: jtkamudrych@gmail.com

Received: 1 - II - 2021
Accepted: 28 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.44

Abstract

Introduction: For the World Health Organization, cardiovascular disease is responsible for the highest number of deaths in the world.

Material and methods: Descriptive and transversal study in 418343 workers from different Spanish regions in which the influence of sociodemographic variables such as age and sex and tobacco use is valued on the values of different parameters related to cardiovascular risk. Parameters related to overweight and obesity, atherogenic indices, risk scales such as SCORE, REGICOR or vascular age, fatty liver risk scales and metabolic syndrome are determined.

Results: In smokers the prevalence of altered values is lower on scales related to overweight and obesity, atherogenic indices, high blood pressure, lipid profile, metabolic syndrome and fatty liver scales. Cardiovascular risk scales such as SCORE, REGICOR and vascular age have worse values in smokers.

Conclusions: Age and sex influence the appearance of all the parameters studied. There is variability in the results of cardiovascular risk, obesity and fatty liver when related to tobacco consumption.

Keywords: Cardiovascular risk, tobacco, sociodemographic variables.

Resumen

Introducción: La Organización Mundial de la Salud describe las enfermedades cardiovasculares con las responsables del mayor número de muertes en el mundo.

Material y métodos: Estudio descriptivo y transversal en 418.343 trabajadores de diferentes regiones españolas en el que se valora la influencia de variables sociodemográficas como edad y sexo y consumo de tabaco en los valores de diferentes parámetros relacionados con riesgo cardiovascular. Se determinan parámetros relacionados con sobrepeso y obesidad, índices aterogénicos, escalas de riesgo como SCORE, REGICOR o edad vascular, escalas de riesgo de hígado graso y síndrome metabólico

Resultados: En los fumadores la prevalencia de valores alterados es inferior en las escalas relacionadas con sobrepeso y obesidad, índices aterogénicos, hipertensión arterial, perfil lipídico, síndrome metabólico y escalas de hígado graso. Las escalas de riesgo cardiovascular como SCORE, REGICOR y edad vascular presentan peores valores en los fumadores.

Conclusiones: La edad y el sexo influyen en la aparición de todos los parámetros estudiados. Existe variabilidad en los resultados de riesgo cardiovascular, obesidad e hígado graso cuando se relacionan con el consumo de tabaco.

Palabras clave: Riesgo cardiovascular, tabaco, variables sociodemográficas.

Introduction

According to the World Health Organisation's Global Status Report on Health, cardiovascular diseases are responsible for the greatest number of deaths in the world¹. In developed countries, especially the United States and Europe, one person dies every 39 seconds², and in Spain there are 51,870 deaths per year due to this cause.

Although its frequency is higher in people over 60 years of age, one in four deaths under this age is related to them. This suggests that the increase in the prevalence of cardiovascular disease may be secondary to an increase in the different risk factors, also influenced by multiple extra-health factors: political, economic, socio-cultural and environmental³⁻⁵.

Among the risk factors, tobacco use, high cholesterol, high blood pressure, insufficient physical activity, obesity and diabetes are the major contributors to the development of CVD⁶.

The world's population is growing at the same time as the population is ageing, leading to an increase in the different cardiovascular risk factors (CVRFs) that have an impact on the health status of the general population. Cardiovascular disease (CVD) is currently one of the main public health concerns in all countries and involves different sectors of society, as health promotion should extend throughout an individual's life, from the earliest ages, when healthy lifestyle habits begin to be acquired, to adulthood and old age⁷.

As the working stage is a considerable period in people's lives and their behavioural habits will have an impact on both their current and future health. The aim of this study is to estimate cardiovascular risk in the Spanish working population and its relationship with sociodemographic variables and tobacco consumption.

Material and methods

Retrospective, cross-sectional study in a sample of 418,343 workers from different Spanish regions and different productive sectors during the period from January 2019 to June 2020. Participants were selected among those who attended periodic occupational health check-ups.

Inclusion criteria

- Age between 18 and 80 years.
- Be in active employment.
- Agree to participate in the study.
- Consent to the use of the data for epidemiological purposes

Socio-demographic variables were collected: age (years) and sex (male/female). Lifestyle habits: tobacco consumption, a smoker was considered to be a person who had regularly consumed at least 1 cigarette/day (or the equivalent in other types of consumption) in the last month, or who had given up consumption less than one year ago.

Parameters related to cardiovascular risk: overweight and obesity, atherogenic indices, CV risk scales: SCORE, REGICOR or vascular age, fatty liver risk scales and metabolic syndrome.

All measurements were taken by the healthcare staff of the different occupational health units participating in the study, after standardising the measurement techniques. Weight and height: a scale-measuring device is used: SECA model 700; Abdominal waist circumference is measured in cm with a tape measure: SECA model 20; BMI is calculated by dividing weight by height in metres squared. Obesity is considered to be 30 or more.

To estimate the percentage of body fat we use the CUN BAE⁸ equation (Clínica Universitaria de Navarra Body Adiposity Estimator) whose formula is:

$$44,988 + (0,503 \times \text{edad}) + (10,689 \times \text{sexo}) + (3,172 \times \text{IMC}) - (0,026 \times \text{IMC}^2) + (0,181 \times \text{IMC} \times \text{sexo}) - (0,02 \times \text{IMC} \times \text{edad}) - (0,005 \times \text{IMC}^2 \times \text{sexo}) + (0,00021 \times \text{IMC}^2 \times \text{edad})$$

A value of 0 is applied to the male and 1 to the female. The CUN BAE cut-off points for obesity are from 25% in men and 35% in women.

Blood pressure was examined in the supine position with a calibrated OMRON M3 automatic sphygmomanometer after 10 minutes of rest. Three determinations were made at one-minute intervals and the mean value of the three determinations was obtained. Blood samples were obtained by peripheral venipuncture after fasting for 12 hours and were sent to the reference laboratories where they were processed within 48-72 hours. Blood glucose, total cholesterol and triglycerides were determined by automated enzymatic methods, expressing the values in mg/dl. HDL was calculated by precipitation with dextran-sulphate Cl2Mg, and values were expressed in mg/dl. LDL is estimated by the Friedewald formula (provided triglycerides are below 400 mg/dl) and expressed in mg/dl.

Fórmula de Friedewald:

$$\text{LDL} = \text{colesterol total} - \text{HDL} - \text{triglicéridos}/5$$

Blood glucose values are classified according to the recommendations of the American Diabetes Association⁹, with hyperglycaemia being considered to be 125 mg/dl or higher or if the person is taking hypoglycaemic treatment.

Three atherogenic indices are calculated: Cholesterol/HDL (high values from 5 in men and 4.5 in women), LDL/HDL and Triglycerides/HDL (high values from 3)¹⁰.

Metabolic syndrome is determined using three models:

1st NCEP ATP III (National Cholesterol Educational Program Adult Treatment Panel III) is considered to exist if three or more of these factors are present: waist circumference greater than 88 cm in women and 102 in men, triglycerides from 150 mg/dl or specific treatment, blood pressure from 130/85 mm Hg or antihypertensive treatment, HDL less than 40 mg/dl in women or less than 50 in men or specific treatment and fasting blood glucose from 100 mg/dl or with specific treatment.

2nd International Diabetes Federation (IDF)¹¹ the presence of central obesity (waist circumference over 80 cm in women and 94 cm in men) is essential, in addition to two of the other factors indicated above for ATP III (triglycerides, HDL, blood pressure and glycaemia).

3rd IJS Model¹² criteria similar to NCEP ATP III but with waist circumference cut-off points from 80 cm in women and 94 cm in men.

The REGICOR scale is an adaptation of the Framingham scale to the Spanish population¹³ and assesses the risk of suffering a cerebrovascular event over a 10-year period. It allows calculation between 35 and 74 years of age. The risk is considered moderate at 5% and high at 10% and above¹⁴.

SCORE scale for low-risk countries is the one used in Spain¹⁵⁻¹⁶ and determines the risk of suffering a fatal cerebrovascular event in a 10-year period. It allows calculation between 40 and 65 years of age. Moderate risk is defined as 4% and high risk as from 5%. For vascular age, calibrated tables¹⁷ are used to assess the degree of ageing of the arteries and can be calculated from the age of 30.

Visceral adiposity index (VAI)¹⁸

Male:

$$VAI = \left(\frac{WC}{39,68 + (1,88 \times BMI)} \right) \times \left(\frac{TG}{1,03} \right) \times \left(\frac{1,31}{HDL} \right)$$

Female:

$$VAI = \left(\frac{WC}{39,58 + (1,89 \times BMI)} \right) \times \left(\frac{TG}{0,81} \right) \times \left(\frac{1,52}{HDL} \right)$$

The Body Roundness index¹⁹ (BRI) is calculated using the following formula where WC represents waist circumference, BMI represents BMI and height represents height.

$$BRI = 364,2 - 365,5 \times \sqrt{1 - \left(\frac{WC/(2 \times BMI)}{(0,5 \times height)^2} \right)}$$

Lipid accumulation product (LAP)²⁰

- Men: (waist circumference (cm) – 65) x (triglycerides (mMol)).
- Women: (waist circumference (cm) – 58) x (triglycerides (mMol))

Fatty liver index (FLI)²¹ Determination of the risk of non-alcoholic fatty liver disease is determined by the formula:

$$FLI = \left(e^{0,953 \times \log_e(\text{triglycerides}) + 0,139 \times BMI + 0,718 \times \log_e(\text{ggT}) + 0,053 \times \text{waist circumference} - 15,745} \right) / \left(1 + e^{0,953 \times \log_e(\text{triglycerides}) + 0,139 \times IMC + 0,718 \times \log_e(\text{ggT}) + 0,053 \times \text{waist circumference} - 15,745} \right) \times 100$$

High risk is considered to be 60

Atherogenic dyslipidaemia²² is characterised by high triglyceride concentrations (>150 mg/dl), low HDL (<40 mg/dl in men and <50 mg/dl in women) and normal or slightly elevated LDL. If LDL values are high (>160 mg/dl) we speak of lipid triad.

Statistical analysis

A descriptive analysis of the categorical variables is carried out, calculating the frequency and distribution of responses for each of them. For quantitative variables, the mean and standard deviation are calculated, and for qualitative variables, the percentage is calculated. The bivariate analysis of association was carried out using the 2 test (with correction of Fisher's exact statistic when conditions required it) and Student's t-test for independent samples. For the multivariate analysis, binary logistic regression was used with the Wald method, with the calculation of Odds ratios and the Hosmer-Lemeshow goodness-of-fit test. The statistical analysis was carried out with the SPSS 27.0 programme, the accepted level of statistical significance being 0.05.

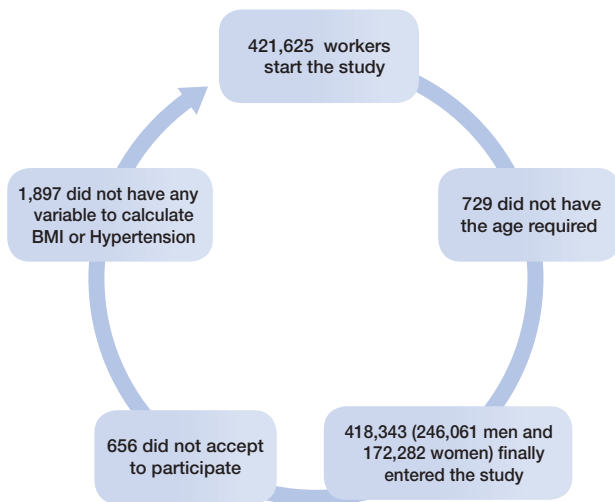
Ethical considerations and aspects

The study was approved by the Clinical Research Ethics Committee of the Illes Balears health area no. 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 patients signed written informed consent documents before participating in the study.

Results

Of the 421,625 workers who were invited to participate in the study, 1,897 were excluded as they did not have all the variables needed to calculate cardiovascular risk indicators, 656 did not agree to participate and 729 were under 18 or over 80 years of age and were therefore discarded. The final number of workers included in the study was 418,343 (246,061 men and 172,282 women) (Figure 1).

Figure 1: Participant flow chart.



The characteristics of the sample and the values of the sociodemographic, anthropometric, clinical and analytical parameters of our population are presented in table I.

The parameters related to overweight and obesity (BMI, CUN BAE, and BRI) show somewhat lower values in the group of smokers of both sexes; however, the CVR scales (vascular age, REGICOR and SCORE) show much higher values among smokers, both in women and men. The results for fatty liver (FLI and LAP) in female smokers are lower than in non-smokers, while in men the FLI shows very little difference between smokers and non-smokers. Atherogenic indices, in general, are somewhat lower in smokers of both sexes. Table II.

The prevalence of overweight and obesity is lower in both men and women among smokers, as is the case for metabolic syndrome. Similar results were found for arterial hypertension and lipid profile (with the exception of triglycerides in men) which give better results in smokers. Elevated cholesterol/HDL and LDL/HDL atherogenic indices are more frequent in non-smokers of both sexes, while high triglycerides/HDL is more frequent in smokers. Elevated CVR scores on the REGICOR and SCORE scales are much more frequent among men and women who smoke. In contrast, high-risk FLI is less frequent among smokers, with a very high difference between the two female sex groups (Table III).

In the multivariate analysis by means of binary logistic regression, male sex, age from 50 years onwards and tobacco consumption were established as covariates. Age and sex show influence on the occurrence of all parameters analysed, in the case of age the Odds ratios range from 1.51 (95% CI 1.49-1.53) for waist/height >0.50 to 73.44 (95% CI 69.96-77.08) for moderate-high SCORE, while in sex they range from 1.10 (95% CI 1.09-1.12) for high cholesterol to 16.02 (95% CI 15.36-16.70) for moderate-high SCORE. Tobacco appears as a mild protective factor for overweight and obesity parameters and high HBP and high LDL and moderate inducer for high triglycerides, atherogenic dyslipidaemia, lipid triad, atherogenic triglycerides/HDL and high REGICOR. In the SCORE scale, smoking greatly increases the risk (Odds ratio 7.62 CI 95% 7.35-7.90). The other parameters analysed were not influenced by smoking (Table IV).

Discussion

The results of our work show that the prevalence of high levels of overweight and obesity is lower in both women and men among smokers. These results are in line with other studies in which this discrepancy is observed between the prevalence of these health outcomes in relation to lifestyle and tobacco use, where caution is recommended when using data obtained from these databases when relating aspects such as the prevalence of tobacco use and overweight/obesity²³.

However, CVR scales (vascular age, REGICOR and SCORE) show much higher values among smokers in both women and men. Tobacco use has been considered by some authors as the forgotten factor in the calculation of cardiovascular risk despite the fact that

Table I: Characteristics of the sample.

	Women n=172282 Mean (dt)	Man n=246061 Mean (dt)	Total n=418343 Mean (dt)	p
Age	39,58 (10,78)	40,57 (11,06)	40,16 (10,96)	<0.0001
Height	161,83 (6,49)	174,62 (6,97)	169,35 (9,25)	<0.0001
Weight	66,23 (13,98)	81,36 (14,71)	75,13 (16,23)	<0.0001
Waist	74,77 (10,55)	86,16 (11,09)	81,47 (12,23)	<0.0001
SBP	117,43 (15,66)	128,17 (15,53)	123,74 (16,45)	<0.0001
DBP	72,59 (10,40)	77,75 (10,96)	75,62 (11,03)	<0.0001
Cholesterol	190,62 (35,82)	192,55 (38,87)	191,75 (37,65)	<0.0001
HDL	56,75 (8,65)	50,30 (8,49)	52,96 (9,13)	<0.0001
LDL	116,10 (34,80)	118,03 (36,69)	117,23 (35,93)	<0.0001
Triglycerides	89,11 (46,18)	123,71 (86,39)	109,46 (74,56)	<0.0001
Glucose	87,80 (15,14)	93,28 (21,26)	91,02 (19,17)	<0.0001
ALT	20,21 (13,56)	31,00 (20,20)	26,64 (18,58)	<0.0001
AST	18,15 (7,91)	24,42 (13,30)	21,71 (11,73)	<0.0001
GGT	20,41 (19,69)	35,77 (39,25)	29,56 (33,64)	<0.0001
	%	%	%	p
16-29 years	20,67	18,78	19,56	<0.0001
30-39 years	29,67	27,55	28,42	
40-49 years	29,61	30,05	29,87	
50-59 years	16,81	19,72	18,52	
60-80 years	3,24	3,90	3,63	
Non-smokers	67,17	66,62	66,85	<0.0001
Smokers	32,83	33,38	33,15	

Table II: Mean values of CVR-related parameters according to tobacco use by gender.

	Women			Men		
	Non smoker n=115727 Mean (dt)	Smoker n=56555 Mean (dt)	p	Non smoker n=163920 Mean (dt)	Smoker n=82141 Mean (dt)	p
Age	39,71 (10,79)	39,32 (10,76)	<0.0001	40,75 (11,05)	40,22 (11,07)	<0.0001
BMI	25,34 (5,16)	25,20 (5,14)	<0.0001	26,71 (4,47)	26,57 (4,46)	<0.0001
Waist to height ratio	0,46 (0,06)	0,46 (0,06)	<0.0001	0,49 (0,06)	0,49 (0,06)	<0.0001
CUN BAE scale	35,25 (7,13)	35,02 (7,14)	<0.0001	25,57 (6,61)	25,29 (6,64)	<0.0001
Body roundness index	2,76 (1,20)	2,74 (1,19)	<0.0001	3,31 (1,17)	3,30 (1,17)	<0.0001
Visceral adiposity index	2,70 (1,65)	2,72 (1,66)	<0.0001	7,36 (6,40)	7,46 (6,63)	<0.0001
Years lost of vascular age SCORE	2,67 (4,31)	7,39 (5,40)	<0.0001	5,27 (5,48)	12,65 (6,95)	<0.0001
SCORE	0,36 (0,71)	0,71 (1,33)	<0.0001	1,32 (1,64)	2,69 (3,01)	<0.0001
Years lost vascular age Framingham	-1,93 (10,81)	6,69 (12,06)	<0.0001	2,93 (8,59)	14,33 (9,88)	<0.0001
REGICOR scale	2,85 (2,20)	2,97 (2,23)	<0.0001	3,15 (2,15)	3,65 (2,50)	<0.0001
Fatty liver index	18,22 (21,77)	18,16 (21,77)	<0.0001	37,86 (27,48)	37,64 (27,52)	<0.0001
Lipid accumulation product	18,10 (18,23)	18,03 (18,43)	<0.0001	31,69 (32,90)	31,98 (33,71)	<0.0001
Atherogenic index cholesterol/HDL	3,45 (0,88)	3,44 (0,87)	<0.0001	3,96 (1,13)	3,96 (1,16)	<0.0001
Atherogenic index triglycerides/HDL	1,63 (0,98)	1,63 (0,98)	<0.0001	2,60 (2,09)	2,64 (2,15)	<0.0001
Atherogenic index LDL/HDL	2,12 (0,79)	2,11 (0,78)	<0.0001	2,45 (0,96)	2,44 (0,97)	<0.0001

Table III: Prevalence of altered values of CVR-related parameters according to tobacco consumption by gender.

	Women			Men		
	Non smoker n=115727 %	Smoker n=56555 %	p	Non smoker n=163920 %	Smoker n=82141 %	p
Waist to height ratio >0,50	21,72	21,18	<0.0001	41,65	41,20	<0.0001
Overweight BMI	27,49	26,92	<0.0001	41,79	41,00	<0.0001
Obesity BMI	16,51	16,04	<0.0001	19,84	19,14	<0.0001
Overweight CUN BAE	27,17	26,72	<0.0001	28,33	28,49	<0.0001
Obesity CUN BAE	48,18	47,17	<0.0001	52,40	50,76	<0.0001
Hypertension	13,74	13,12	<0.0001	29,01	28,35	<0.0001
Cholesterol ≥ 200	37,11	36,56	<0.0001	40,24	39,90	<0.0001
LDL ≥ 130	32,21	31,48	<0.0001	36,31	35,74	<0.0001
Triglycerides ≥ 150	7,99	7,94	<0.0001	23,75	24,13	<0.0001
Diabetes	1,33	1,33	<0.0001	3,57	3,53	<0.0001
Metabolically unhealthy	50,67	50,02	<0.0001	68,99	68,47	<0.0001
Metabolic syndrome ATPIII	9,66	9,44	<0.0001	16,94	16,67	<0.0001
Metabolic syndrome IDF	9,41	9,23	<0.0001	13,21	13,22	<0.0001
Metabolic syndrome JIS	11,21	10,98	<0.0001	27,75	27,31	<0.0001
Atherogenic dyslipidemia	4,00	3,93	<0.0001	7,54	8,11	<0.0001
Lipid triad	0,99	1,01	<0.0001	2,04	2,50	<0.0001
Cholesterol/HDL moderate-high	11,83	11,17	<0.0001	16,74	16,42	<0.0001
Triglycerides/HDL high	7,06	7,10	<0.0001	26,60	26,83	<0.0001
LDL/HDL high	13,13	12,63	<0.0001	25,93	25,83	<0.0001
SCORE moderate-high	2,09	10,39	<0.0001	19,61	41,87	<0.0001
REGICOR moderate-high -very high	17,69	18,42	<0.0001	19,79	26,85	<0.0001
FLI high risk	7,73	1,28	<0.0001	24,25	24,08	<0.0001

Table IV: Multivariate analysis using binary logistic regression.

	≥ 50 years			Male			Smokers		
	OR	IC 95%	p	OR	IC 95%	p	OR	IC 95%	p
Waist to height ratio >0,50	1,51	1,49-1,53	<0.0001	2,56	2,53-2,60	<0.0001	0,98	0,97-0,99	0,012
Obesity BMI	1,75	1,72-1,78	<0.0001	1,22	1,20-1,24	<0.0001	0,97	0,95-0,98	<0.0001
Obesity CUN BAE	4,57	4,49-4,64	<0.0001	1,13	1,11-1,14	<0.0001	0,96	0,95-0,97	<0.0001
Hypertension	3,78	3,72-3,84	<0.0001	2,60	2,56-2,64	<0.0001	0,98	0,96-0,99	0,008
Cholesterol ≥ 200	2,87	2,83-2,91	<0.0001	1,10	1,09-1,12	<0.0001			ns
LDL ≥ 130	2,92	2,88-2,96	<0.0001	1,16	1,15-1,18	<0.0001	0,98	0,97-0,99	0,024
Triglycerides ≥ 150	1,91	1,88-1,95	<0.0001	3,58	3,51-3,65	<0.0001	1,02	1,01-1,04	0,010
Diabetes	6,57	6,40-6,75	<0.0001	1,97	1,91-2,03	<0.0001			ns
Metabolically unhealthy	3,91	3,83-3,98	<0.0001	1,86	1,83-1,90	<0.0001			ns
Metabolic syndrome ATPIII	2,31	2,26-2,36	<0.0001	1,43	1,40-1,46	<0.0001			ns
Metabolic syndrome IDF	3,78	3,71-3,84	<0.0001	3,08	3,03-3,14	<0.0001			ns
Metabolic syndrome JIS	2,56	2,49-2,62	<0.0001	1,96	1,90-2,02	<0.0001	1,07	1,04-1,10	<0.0001
Atherogenic dyslipidemia	2,79	2,66-2,92	<0.0001	2,13	2,02-2,25	<0.0001	1,20	1,14-1,26	<0.0001
Lipid triad	3,29	3,23-3,35	<0.0001	1,49	1,47-1,52	<0.0001			ns
Cholesterol/HDL moderate-high	2,25	2,21-2,29	<0.0001	4,76	4,66-4,85	<0.0001	1,02	1,00-1,04	0,014
Triglycerides/HDL high	3,19	3,14-3,25	<0.0001	2,33	2,29-2,37	<0.0001			ns
LDL/HDL high	73,44	69,96-77,08	<0.0001	16,02	15,36-16,70	<0.0001	7,62	7,35-7,90	<0.0001
SCORE moderate-high	2,09	2,06-2,13	<0.0001	1,27	1,24-1,29	<0.0001	1,33	1,30-1,35	<0.0001
REGICOR moderate-high -very high	1,78	1,75-1,82	<0.0001	3,76	3,68-3,85	<0.0001			ns

its crucial role is acknowledged, and that its approach and treatment should be a priority in both primary and secondary prevention of cardiovascular disease (CVD). Despite this, hypertension, diabetes or dyslipidaemia are usually addressed preferentially, accompanied by the advice "you should stop smoking"²⁴. The results obtained in our study demonstrate the impact of smoking on cardiovascular risk, which are supported by previous studies showing that smoking reduction is not associated with a reduction in the risk of cardiovascular and pulmonary mortality and morbidity. Reducing smoking by 50% or less has little or no effect on morbidity and mortality. The review conducted by Undemer et al. between 1980 and 2018 shows that smoking cessation is the only effective strategy to reduce the harm caused by smoking²⁵.

In relation to fatty liver disease (FLI), our results find a lower frequency of FLI among smokers, with much more pronounced differences between groups of women. These results do not agree with those obtained in the literature review in which a systematic review and meta-analysis significantly associate smoking with non-alcoholic fatty liver disease, although it leaves open the option of prospective studies exploring the underlying mechanisms of this association. This review states that passive smoking increases the risk of non-alcoholic fatty liver disease by about 1.38-fold, and that the effects of cigarette smoking in active smokers (current, former and total smokers) are smaller than those in passive smokers. The different criteria and disparity of results suggest that further studies should be conducted to assess the

effects of passive and active smoking on non-alcoholic fatty liver disease²⁶.

In our results, male sex and age over 50 years increase CVR in smokers. Prospective studies relating CV risk associated with tobacco consumption confirm a higher risk of all cardiovascular disease subtypes in active smokers and a greater severity for women than for men when they suffer a major coronary event²⁷.

Scientific studies show that the prevalence of the main cardiovascular risk factors and non-communicable diseases is higher among older people and men, but more preventive actions and programmes are recommended in all cases, such as health education for workers²⁸.

Smoking increases the risk of all types of CVD, doubling the probability of suffering from them, and is the leading cause of avoidable illness, death and disability in Spain²⁹. Among the different cardiac pathologies, paroxysmal tachycardia is a recently identified smoking-related risk. Where comparisons can be made, the relative risks of fatal and non-fatal outcomes associated with smoking are similar. And smoking cessation significantly reduces the risk.

In today's society, smoking remains a widespread and established habit, and government action is insufficient to contain this pandemic. Tobacco use represents an essential trigger for a high proportion of premature CVD events and action against it should be a public health priority³⁰.

References

1. World Health Organization. Global status report on non communicable diseases 2014. Disponible en: <http://www.who.int/nmh/publications/nccd-status-report-2014/en/>
2. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. Heart disease and stroke statistics-2011 update: a report from the American Heart Association. *Circulation*. 2011;123:e18-209.
3. Butler D. UN targets top killers. International summit considers how to stem the rise in non-communicable diseases. *Nature*. 2011;477: 260-1.
4. Abegunde DO, Mathers CD, Adam T, Ortegón M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet*. 2007;370:1929-38.
5. Brownson RC, Haire-Joshu D, Luke DA. Shaping the context of health: a review of environmental and policy approaches in the prevention of chronic diseases. *Annu Rev Public Health*. 2006;27:341-70.
6. Editorial. Las enfermedades cardiovasculares: un problema de salud pública y un reto global. *Biomédica*. 2011;31(4):469-73
7. Castellano JM, Narula J, Castillo J, Fuster V. Promoción de la salud cardiovascular global: estrategias, retos y oportunidades. *Rev Esp Cardiol*. 2014; 67(9):724-30
8. CUN BAE Gómez-Ambrosi J, Silva C, Catalán V, Rodríguez A, Galofré JC, Escalada J, et al. Clinical usefulness of a new equation for estimating body fat. *Diabetes Care*. 2012;35(2):383-8.
9. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;33(Suppl 1):S62-9.
10. López González AA, Rivero Ledo YI, Vicente Herrero MT, Gil Llinás M, Tomás Salvá M, Riutord Fe B. Índices aterogénicos en trabajadores de diferentes sectores laborales del área mediterránea española. *Clin Investig Arterioscler*. 2015;27(3):118-28

11. Zimmet P, M M Alberti KG, Serrano Ríos M. A new international diabetes federation worldwide definition of the metabolic syndrome: the rationale and the results. *Rev Esp Cardiol.* 2005;58(12):1371-6.
12. Cabrera-Roe E, Stusser B, Cáliz W, Orlandi N, Rodríguez J, Cubas-Dueñas I, et al. Concordancia diagnóstica entre siete definiciones de síndrome metabólico en adultos con sobrepeso y obesidad. *Rev Peru Med Exp Salud Publica.* 2017;34(1):19-27.
13. Marrugat J, Subirana I, Comín E, Cabezas C, Vila J, Elosua R, et al. Investigators. Validity of an adaptation of the Framingham cardiovascular risk function: the VERIFICA Study. *J Epidemiol Community Health.* 2007; 61: 40-7.
14. Marrugat J, D'Agostino R, Sullivan L, Elosua R, Wilson P, Ordovas J, et al. An adaptation of the Framingham coronary risk function to southern Europe Mediterranean areas. *J Epidemiol Comm Health* 2003; 57(8): 634-8.
15. Sans S, Fitzgerald AP, Royo D, Conroy R, Graham I. Calibrating the SCORE cardiovascular risk chart for use in Spain. *Rev Esp Cardiol.* 2007;60(5):476-85.
16. Buitrago F, Cañón Barroso L, Díaz Herrera N, Cruces E. Analysis of predictive value of Framingham-REGICOR and SCORE functions in primary health care. *Med Clin (Barc).* 2007;129(20):797.
17. Ramírez M. La edad vascular como herramienta de comunicación del riesgo cardiovascular. Centro Integral para la Prevención de Enfermedades Crónicas. 2010. Disponible en: <http://pp.centramerica.com/pp/bancofotos/267-2570.pdf>
18. Amato MC, Giordano C. Visceral adiposity index: an indicator of adipose tissue dysfunction. *Int J Endocrinol.* 2014;2014:730827.
19. Chang Y, Guo X, Chen Y, Guo L, Li Z, Yu S, et al. A body shape index and body roundness index: two new body indices to identify diabetes mellitus among rural populations in northeast China. *BMC Public Health.* 2015 19;15:794.
20. Chiang JK, Koo M. Lipid accumulation product: a simple and accurate index for predicting metabolic syndrome in Taiwanese people aged 50 and over. *BMC Cardiovasc Disord.* 2012; 12:78
21. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, Tiribelli C. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol.* 2006; 6:33.
22. Bestehorn K, Smolka W, Pittrow D, Schulte H, Assmann G. Atherogenic dyslipidemia as evidenced by the lipid triad: prevalence and associated risk in statin-treated patients in ambulatory care. *Curr Med Res Opin* 2010; 26:2833-9
23. Julia G Solomon, Kristina A Monteiro, Mark R Zonfrillo. Prevalence of Tobacco Use and Overweight/Obesity in Rhode Island: Comparisons of Survey and Claims Data. *R I Med J* (2013). 2019 Mar 1;102(2):19-23.
24. César Minué-Lorenzo, Eduardo Olano-Espinosa. Tobacco consumption, the forgotten factor in the calculation and approach of cardiovascular risk. *Medicina Clínica (English Edition)*, Volume 152, Issue 4, 15 February 2019, Pages 154-8
25. M Underner, G Peiffer, J Perriot, G Harika-Germaneau, N Jaafari. Is reduction of tobacco consumption associated with reduced risk of cardiovascular and pulmonary mortality and morbidity? *Rev Pneumol Clin.* 2018 Jun;74(3):188-95.
26. Arash Akhavan Rezaayat, Malihe Dadgar Moghadam, Mohammad Ghasemi Nour, Matin Shirazinia, Hamidreza Ghodsi, Mohammad Reza Rouhbakhsh Zahmatkesh, Mitra Tavakolizadeh Noghabi, Benyamin Hoseini, Kambiz Akhavan Rezaayat. Association between smoking and non-alcoholic fatty liver disease: A systematic review and meta-analysis. *SAGE Open Med.* 2018 Jan 24;6:2050312117745223.
27. Q Shen, N B Zhu, C Q Yu, Y Guo, Z Bian, Y L Tan, P Pei, J S Chen, Z M Chen, J Lyu, L M Li, China Kadoorie Biobank (CKB) Collaborative Group. Sex-specific associations between tobacco smoking and risk of cardiovascular diseases in Chinese adults. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2018 Jan 10;39(1):8-15.
28. Nahid Khademi, Mehran Babanejad, Atefeh Asadmobini, Hossein Karim. The Association of Age and Gender with Risk Factors of Noncommunicable Diseases among Employees in West of Iran. *Int J Prev Med.* 2017 Feb 20;8:9.
29. Rodrigo Córdoba García, Francisco Camarells Guillem, Elena Muñoz Seco, Juana M. Gómez Puente, Joaquín San José Arango, Jose Ignacio Ramírez Manent, Carlos Martín Cantera, María del Campo Giménez, Juan Revenga Frauca y Grupo de Educación Sanitaria y Promoción de la Salud del PAPPS. Grupo de expertos del PAPPS. Recomendaciones sobre el estilo de vida. *Atencion Primaria* 2020;52(S2):32-43
30. Emily Banks, Grace Joshy, Rosemary J Korda, Bill Stavreski, Kay Soga, Sam Egger, Cathy Day, Naomi E Clarke, Sarah Lewington, Alan D Lopez. Tobacco smoking and risk of 36 cardiovascular disease subtypes: fatal and non-fatal outcomes in a large prospective Australian study. *BMC Med.* 2019 Jul 3;17(1):128.

Nigella sativa extract attenuates benzene induced oxidative DNA damage and abnormality in hematological parameters in rats

El extracto de Nigella sativa atenúa el daño oxidativo del ADN inducido por el benceno y la anomalía en los parámetros hematológicos en ratas

Mohamed M. El-Khawanky¹ , Basel A. Abdel-Wahab² ,
Metwalli E Abdalla³ , Abdulmohsen M. Alruwetei⁴ 

1. Department of Clinical Hematopathology, College of Medicine, Najran University 2. Department of Pharmacology, College of Medicine, Najran University 3. Department of Forensic Medicine and Toxicology, College of Medicine, Suez Canal University, Ismailia, Egypt 4. Medical Laboratories Department, College of Applied Medical Sciences, Qassim University

Corresponding author

Abdulmohsen M. Alruwetei
Medical Laboratories Department, College of Applied Medical
Sciences, Qassim University
Qassim, Saudi Arabia
E-mail: Roietai@qu.edu.sa

Received: 5 - II - 2021

Accepted: 14 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.51

Abstract

Background: Benzene exposure harms the genetic material and hematopoietic system. This effect appears in the form of excess 8-hydroxy-2-deoxyguanosine (8-OHdG) plasma levels and abnormalities in peripheral blood cells' count. Nigella sativa showed antioxidant properties that may overcome benzene exposure side effects. This study aimed to evaluate the potential protective effect of N. sativa against benzene-induced DNA damage and hepatotoxicity in rats.

Methods: The study was conducted on 26 Wistar rats. They were divided into three groups; group (A) eight rats (30,8%) were administered 100 mg benzene/ kg body wt, 5d/week, group (B) nine rats (34.6%) were administered (100 mg/kg BW/day) benzene plus (100 mg/kg BW/day) Nigella sativa extract via gastric gavage for 4 weeks, and nine normal rats (34.6%) without any chemical agents designated as a control group. Plasma 8-OHdG levels and peripheral blood count were used to evaluate Nigella sativa protective effect in the face of benzene exposure.

Results: A significant increase of 8-OHdG plasma levels among benzene-exposed rats compared to the control group ($p = .000$). Nigella sativa and benzene administered group showed a significant decreased 8-OHdG plasma levels as compared to benzene exposed animals. There was a significant improvement of RBC count, hemoglobin concentration, WBC count, and platelet count ($P = .003, .000, .000; .000$ respectively) in N. sativa and benzene administered group when compared to benzene exposed rats..

Conclusions: The current study provided evidence that the DNA damage and the hematotoxic effect of benzene can be counteracted by Nigella sativa.

Keywords: Benzene, Nigella Sativa, 8-OHdG, blood cells, antioxidant, hematotoxicity, genotoxicity.

Resumen

Antecedentes: La exposición al benceno tiene un efecto perjudicial sobre el material genético y el sistema hematopoyético. Este efecto se manifiesta en forma de un exceso de niveles plasmáticos de 8-hidroxi-2-deoxiguanosina (8-OHdG) y de anomalías en el recuento de células sanguíneas periféricas. La Nigella sativa demostró tener propiedades antioxidantes que pueden superar los efectos secundarios de la exposición al benceno. El objetivo de este estudio es evaluar el potencial efecto protector de la N. sativa contra el daño al ADN y la hematotoxicidad inducidos por el benceno en ratas.

Métodos: El estudio se realizó en 26 ratas Wistar. Se dividieron en tres grupos: el grupo (A), en el que se administró a ocho ratas (30,8%) 100 mg de benceno/kg de peso corporal, 5 días/semana; el grupo (B), en el que se administró a nueve ratas (34,6%) (100 mg/kg de peso corporal/día) benceno más (100 mg/kg de peso corporal/día) extracto de Nigella sativa por vía gástrica durante 4 semanas, y nueve ratas normales (34,6%) sin ningún agente químico, designadas como grupo de control. Se utilizaron los niveles de 8-OHdG en plasma y el recuento de sangre periférica para evaluar el efecto protector de Nigella sativa frente a la exposición al benceno.

Resultados: Hubo un aumento significativo de los niveles plasmáticos de 8-OHdG entre las ratas expuestas al benceno en comparación con el grupo de control ($p = .000$). El grupo administrado con Nigella sativa y benceno mostró una disminución significativa de los niveles plasmáticos de 8-OHdG en comparación con los animales expuestos al benceno. Hubo una mejora significativa del recuento de glóbulos rojos, la concentración de hemoglobina, el recuento de glóbulos blancos y el recuento de plaquetas ($p = 0,003, 0,000, 0,000; 0,000$ respectivamente) en el grupo administrado con N. sativa y benceno en comparación con las ratas expuestas al benceno.

Conclusiones: El presente estudio aporta pruebas de que el daño al ADN y el efecto hematotóxico del benceno pueden ser contrarrestados por Nigella sativa.

Palabras clave: Benceno, Nigella Sativa, 8-OHdG, células sanguíneas, antioxidante, hematotoxicidad, genotoxicidad.

Introduction

Benzene, a hydrocarbon chemical compound derived from crude oil and gasoline, is broadly used as a solvent or intermediate for the synthesis of industrial chemicals such as plastics, polymers and detergents and is also a component of petroleum products^{1,2}. It is considered an environmental pollutant and known for its hazardous effect against human health, especially when administered at substantial levels^{3,4}. It is widely used in our daily life activities. It can be administered through cigarette smoking, combusting and evaporation of gasoline, and automobile emissions, which make its exposure unavoidable and poses a serious risk to both industry workers' health as general population^{5,6}. Certainly, there is much evidence indicating the direct link between chronic exposure to high concentration of benzene and suppression of bone marrow, development of aplastic anemia, and various hematological malignancies^{3,7,8}. Other studies have also reported the cyto-reduction of blood cells in workers exposed to benzene's low concentration, indicating that benzene can exert hepatotoxic effects even at the lower permissible exposure limit^{9,10}.

The harmful effect of benzene on blood cells is recognized over 30 years, yet the mechanisms by which benzene induce toxicity are not clear¹¹. The metabolism of benzene is most likely responsible for its cytotoxic effect by introducing an oxidative stress. Human body can eliminate 50% of the absorbed quantity of benzene through inhalation, while a low quantity of benzene accumulates in lipid tissues due to its solubility in lipid, and the rest is metabolized mainly in the liver through the cytochrome P4502E1 (CYP2E1) systems^{12,13}. The resultant metabolites, including benzene oxide, catechol, and hydroquinone 2, can form redox cycling and lead to the generation of reactive oxygen species (ROS)¹³. These ROS can induce direct oxidative damage to the cellular components such as nucleic acid, proteins, and lipids and may also act through signaling molecules¹⁴. In normal conditions, the accumulation of ROS in the human body is regulated by antioxidant defense systems through certain metabolizing and scavengers to counteract the ROS oxidative damage¹⁵. However, both the increase in ROS production and insufficient protection by antioxidant factors result in inadequate protection from oxidative stress, which allows for an increase in DNA damage and subsequent genomic instability if the damage overwhelmed DNA repair capacity mechanisms¹⁵. Various studies have utilized different biomarkers, such as 8-hydroxy-2-deoxy Guanosine (8-OHdG), for evaluating the oxidative DNA damage¹⁶.

Recently, there is an interest in utilizing plant-derived natural products as a natural antioxidant source with a beneficial effect on general health and different diseases, including cancer¹⁷. *Nigella sativa* L. (*N. sativa*), also called black seed, is historically used as a remedy with

versatile medicinal applications¹⁸. *N. sativa* contains various compounds, such as thymoquinone (TQ), volatile oil, fixed oil, proteins, carbohydrates, minerals, vitamins, saponins, and alkaloids, which are essential for different biological properties of the seed¹⁹. Several studies have shown wide biological and pharmacological properties of *N. sativa* including, antioxidant, anti-inflammatory, antidiabetic, anti-hypertensive, anti-tumor and anti-microbial effects²⁰⁻²⁴. The antioxidant activity of *N. sativa* has been well documented in the literature and shown through studies that demonstrated the ability of *N. sativa* extracts to protect blood or organ tissues from oxidative damage induced by various chemicals such as alpha-lipoic acid, Streptozotocin, in animal models²⁵⁻²⁷. Given the recognized benzene-induced oxidative hematotoxicity and DNA damage linked with hematological malignancies, a search for protective agents against such toxic effects is required. *N. sativa* is an attractive strategy in this context. The current study aimed to assess the potential protective effect of *N. sativa* against benzene-induced DNA damage and hepatotoxicity in rats.

Materials and methods

Chemicals

N. Sativa extract and benzene were purchased from Sigma Aldrich, St. Louis, USA, and an 8-hydroxy-2-deoxy Guanosine (8-OHdG) assay kit were purchased from Cayman's Chemical Co. (USA). All the reagents used in this study were of analytical grade.

Animal and experimental protocol

Male Wistar rats with 200-250g body weight from the animal house of Najran University, Najran, Saudi Arabia were used in this study. All experimental works were conducted according to the National Institutes of Health guidelines for the use, handling of laboratory animals (NIH Publications No. 8023, revised 1978). All protocols and experiments related to animal work were approved by the Institutional Animal Use and Care Committee in Najran University.

A total of 26 rats were employed in the study. The animals were divided into three groups; group (A) of eight rats (30.8%) were administered 100 mg benzene (Sigma Aldrich, > 99.8% purity)/ kg body wt, 5d/week for 4 weeks. Benzene was administered in 1 ml of corn oil via gastric gavage. Group A designated as Benzene exposed. Group B of nine rats (34.6%) were administered (100 mg/kg BW/day) benzene plus (100 mg/kg BW/day) *Nigella sativa* extract via gastric gavage for 4 weeks. Group B is denoted as NIGL+Benzene. Group (C) of nine normal rats (34.6%) without any chemical additive served as a control group. Group C designated as control. Blood samples were collected via cardiac puncture post-anesthesia with light ether. About two ml of blood was collected in two EDTA-containing

sterile tubes; Blood samples were processed for plasma detection of 8-OHdG and complete blood count.

Blood picture

Hematological parameters were studied using an automated Blood Cell Counter (COULTER® LH 500 Hematology Analyzer - Beckman Coulter, USA).

Determination of 8-ohdg levels

8-OHdG plasma levels were measured using Cayman's 8-hydroxy-2-deoxy guanosine assay kit purchased from Cayman's Chemical Co. (USA). This assay detects both free 8-OHdG and DNA-incorporated 8-OHdG. This assay principle is based on the competition between 8-OHdG and 8-OHdG acetylcholinesterase (AChE) conjugate (8- OHdG Tracer) for a limited amount of 8-OHdG monoclonal antibody.

Statistical analysis

The 8-OHdG plasma levels and hematological parameters were analyzed statistically using the SPSS software (IBM SPSS Inc., version 20, Chicago, Illinois, USA), and results were expressed as mean values. The statistical measurements for the differences in plasma mean 8-OHdG levels and mean values of hematological parameters between studied groups were based on student *t*-test. Significant difference is denoted by *P*-value < 0.05 and highly significant if the *P*-value < 0.001.

Results

Evaluation of the oxidative stress response

Plasma 8-OHdG was measured between animal groups to detect the oxidative DNA damage induced by benzene and the potential protective effect of *N. sativa* against benzene-induced DNA damage. The first analysis focused on comparing the difference in plasma concentration of 8-OHdG between group A (Benzene exposed) and Group C (Control). The analysis revealed a significant increase of mean plasma concentration of 8-OHdG in benzene exposed rats in comparison to the control rat group (*p* value = .000), indicating that benzene resulted in oxidative stress, which recognized by an increase in the concentration level of 8-OHdG in animals exposed to benzene (Figure 1, Table I). Interestingly, Group B (NIGL+Benzene) showed a significantly decreased mean concentration level of 8-OHdG as compared to group A (benzene exposed animals) (*p*-value = .001). In contrast, the mean level of 8-OHdG in Group B (NIGL+Benzene) is significantly higher than that in group C (Control Group), indicating that co-administration of *N. sativa* extract along with benzene may result in scavenging the oxidative stress generated by benzene (Figure 1, Table I).

Evaluation of hematological parameters

The hematological parameters were also measured in all groups and results were compared with control groups.

Figure 1: Evaluation of the difference in plasma concentration of 8-OHdG in studied groups. The plasma concentration of 8-OHdG in the benzene-exposed rats was significantly higher when compared with the control group (*p* < 0.05). NIGL+ benzene group showed a significantly decreased plasma concentration of 8-OHdG than the benzene exposed group only (*p* < 0.05). NIGL denotes *N. Sativa*.

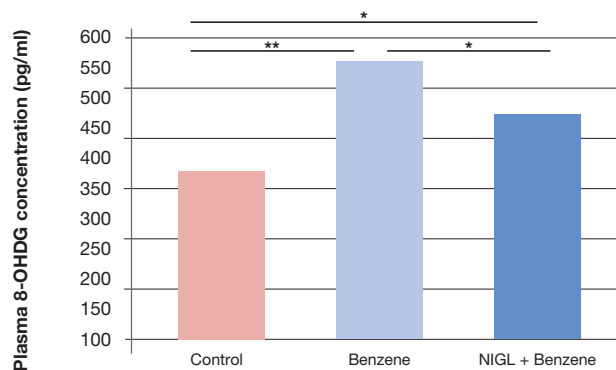


Table I: Significance of changes in plasma concentration of 8-OHdG.

Groups	Mean value + Standard Deviation	t- test	p value
1) Control VS. Benzene			
Control	383.78 + 57.779	8.286	0**
Benzene	564.75 + 22.676		
2) Control VS. NIGL+Benzene			
Control	383.78 + 57.779	3.436	0.004**
NIGL+Benz	480.00 + 44.721		
2) Benzene VS. NIGL+Benzene			
Benzene	564.75 + 22.676	4.661	0.001**
NIGL+Benzene	480.00 + 44.721		

***p*-value is significant at the 0.01 level.

**p*-value is significant at the 0.05 level. NIGL denote *N. Sativa*

The exposure to benzene showed a noticeable effect on blood cell as depicted by the changes in RBC count, Hb concentration, RBC indices, WBC count and platelet count between Group A (Benzene exposed) and group C (Control) (Figure 2, Table II). Certainly, there was a significant decrease in WBC count (*p*-value = .000) and platelet count ((*p*-value = .000) in Group A (Benzene exposed) as compared to group C (Control). Intriguingly, Group B (NIGL+Benzene) showed no statistical difference in RBC count, Hb and RBC indices compared to Group C (control rats). However, there was significant decrease in WBC count and significant increase in platelet counts between Group B (NIGL+Benzene) and Group C (control rats) (*P*-value = .000, *P*-value = .000, respectively) (Figure 2, Table II). Furthermore, a comparison of hematological parameters between Group A (Benzene exposed) and Group B (NIGL+Benzene) revealed a pronounced difference in all hematological parameters except MCV, MCH values. There was significant decrease in RBC count, hemoglobin concentration and WBC count (*P* value= .003, *P* value= .000, *P*-value = .000; respectively) and significant increase in platelet count (*P* value= .000) between Group A (Benzene exposed) and Group B (NIGL+Benzene). These results indicate the influence of *N. sativa* extract in reducing the hematotoxicity induced by benzene in rats.

Figure 2: Comparison of hematological parameters between studied groups. A) RBC Count, B) Hb Concentration, C) Mean Corpuscular Volume (MCV), D) Mean Hemoglobin Concentration (MCH), E) Platelet Count and F) WBC count. N.S indicates non-significant ($p \geq 0.05$), * indicates $p < 0.05$ and ** indicates $p < 0.01$. NIGL denote *N. Sativa*.

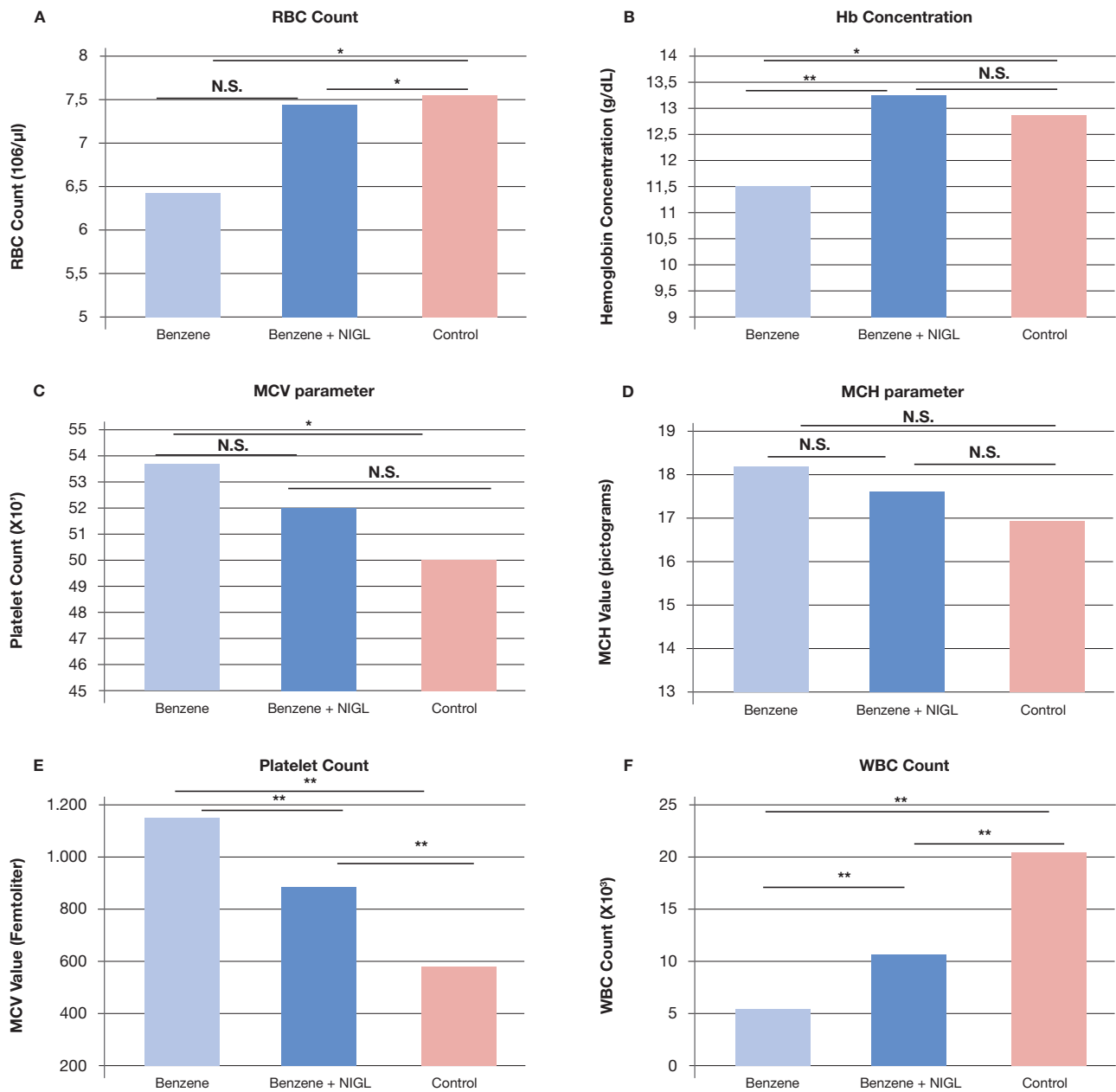


Table II: Significance of changes in Hematological Parameters.

Parameters	Mean value + Standard Deviation			Benzene VS. Control		NIGL+ Benzene VS. Control		NIGL+Benzene VS. Benzene	
	Control	Benzene	Benzene + NIGL	t- test	p value	t- test	p value	t- test	p value
RBCs	7.58 + 0.82	6.40 + 0.58	7.45 + 0.43	3.364	0.004**	0.36	0.72	3.69	0.003*
Hb	12.77 + 1.48	11.50 + 0.27	13.13 + 0.50	2.386	0.031*	0.559	0.58	7.823	0.000**
MCV	49.96 + 3.08	53.62 + 2.83	52.01 + 0.83	2.535	0.023*	1.571	0.14	1.337	0.20
MCH	16.88 + 1.15	18.17 + 1.43	17.65 + 0.39	2.046	0.059	1.534	0.14	0.866	0.40
WBCs	20.06 + 3.33	5.50 + 1.10	10.51 + 0.97	11.76	0.000**	6.748	0.000**	8.84	0.000**
PLT	575.89 + 162.89	1148.88 + 26.50	888 + 19.21	9.8	0.000**	4.614	0.000**	20.34	0.000**

*p-value is significant at the 0.05 level and **p-value is significant at the 0.01 level. NIGL denote *N. Sativa*

Discussion

Benzene and benzene-derived agents, widely used industrial chemicals and components of valuable products in modern life, have been reported to induce oxidative DNA damage linked with hematopoietic system disorders malignancies^{5,20,28,29}. *N. Sativa* is an antioxidant rich plant and several studies prove its protective effects against oxidative damage mediated by free radicals from chemical agents in animal models^{30,31}. However, there is uncertainty about the impact of *N. Sativa* against benzene-induced oxidative DNA damage and toxicity to hematological parameters. The present study is concerned with assessing the potential protective effect of *N. sativa* against benzene-induced DNA damage and hepatotoxicity in rats.

The in vivo models for benzene induced oxidative DNA damage has been established previously by several studies and the increase in the concentration of 8-OhdG is frequently reported as a reliable biomarker for assessing oxidative damage to DNA as well as the risk of cancer development and, therefore, quantifying plasma 8-OhdG is useful for detecting the oxidative stress response induced by benzene in an *in vivo* model^{29,32-36}. The results from the analysis of the difference in plasma 8-OhdG levels between study groups revealed consistent finding to what have been previously reported, as demonstrated by the significant increase in plasma 8-OhdG levels in rats exposed to benzene compared to control group, indicating for induction of oxidative stress by benzene in rats³²⁻³⁷. Interestingly although the plasma 8-OhdG level was increased in rats co-administered *N. Sativa* along with benzene. However, its level was significantly lower than observed in benzene-exposed rats, demonstrating that *N. Sativa* exerted an antioxidant effect against the

oxidative stress response induced by benzene in rats. Many studies supported the beneficial antioxidant effects of *N. Sativa* or its derived compounds in animal models^{30,31,38}. These observations suggest the potential benefit of using *N. Sativa* as an antioxidant strategy to manage unfavorable effects caused by exposure to benzene and its derivatives.

To investigate the potential protection role of *N. Sativa* against the toxic effect of benzene toward hematopoietic system, this study evaluated the difference in hematological parameters among rats groups. The analysis indicated abnormal hematological parameters upon administration of benzene as depicted by the significant decrease in RBC count, hemoglobin concentration and increase in platelet count compared to that observed in the control group. The finding agrees with results from several studies that reported benzene-induced hematotoxicity in animal models^{32,39,40}. The co-administration of *N. Sativa* extract and benzene had resulted in attenuation of the toxic effect of benzene against hematological cells. In particular, RBC count, Hb concentration, WBC count in rats that co-administered *N. Sativa* along with benzene were significantly higher than that observed in rats treated with benzene only, suggesting that *N. Sativa* could work as an antidote for benzene induced hematotoxicity.

Conclusions

The current study provided evidence that the DNA damage and the hematotoxic effect of benzene can be counteracted by *N. Sativa*. Further experiments are required to study the mechanisms by which *N. Sativa* provides antioxidant stress against benzene-induced oxidative stress.

Reference

1. Belingheri M, Fustinoni S, De Vito G, Porro A, Riva MA. Benzene and leukemia: from scientific evidence to regulations. A historical example. *La Med del lavoro*. 2019;110(3):234.
2. Rappaport SM, Kim S, Lan Q, Vermeulen R, Waidyanatha S, Zhang L, Li G, Yin S, Hayes RB, Rothman N, Smith MT. Evidence that humans metabolize benzene via two pathways. *Environ Health Perspect*. 2009;117(6):946-52.
3. Galbraith D, Gross SA, Paustenbach D. Benzene and human health: a historical review and appraisal of associations with various diseases. *Crit Rev Toxicol*. 2010;40(sup2):1-46.
4. Duarte-Davidson R, Courage C, Rushton L, Levy L. Benzene in the environment: an assessment of the potential risks to the health of the population. *Occup Environ Med*. 2001;58(1):2-13.
5. Kamal A, Malik RN. Hematological evidence of occupational exposure to chemicals and other factors among auto-repair workers in Rawalpindi, Pakistan. *Osong Publ Health Res Perpect*. 2012;3(4):229-38.
6. Maksoud HA, Elharrif MG, Mahfouz MK, Omnia MA, Abdullah MH, Eltabey ME. Biochemical study on occupational inhalation of benzene vapours in petrol station. *Resp Med Case Reports*. 2019;27:100836.
7. Snyder R. Leukemia and benzene. *Int J Environ Res Publ Health*. 2012;9(8):2875-93.
8. Hayes RB, Songnian Y, Dosemeci M, Linet M. Benzene and lymphohematopoietic malignancies in humans. *Am J Indust Med*. 2001;40(2):117-26.
9. Lan Q, Zhang L, Li G, Vermeulen R, Weinberg RS, Dosemeci M, Rappaport SM, Shen M, Alter BP, Wu Y, Kopp W. Hematotoxicity in workers exposed to low levels of benzene. *Science*. 2004;306(5702):1774-6.
10. Swaen GM, van Amelsvoort L, Twisk JJ, Verstraeten E, Slootweg R, Collins JJ, Burns CJ. Low level occupational benzene exposure and hematological parameters. *Chemico-Biol Interact*. 2010;184(1-2):94-100.

11. Ross D. The role of metabolism and specific metabolites in benzene-induced toxicity: evidence and issues. *J Toxicol Environ Health Part A*. 2000;61(5-6):357-72.
12. Raj HG, Malik S, Parmar VS, Kohli E, Tyagi YK, Rohil V, Dwarakanath BS, Adhikari JS, Bose M, Jain SC, Olsen CE. Chemoprevention of benzene-induced bone marrow and pulmonary genotoxicity. *Teratog Carcinog Mutagen*. 2001;21(2):181-7.
13. Rappaport SM, Kim S, Lan Q, Li G, Vermeulen R, Waidyanatha S, Zhang L, Yin S, Smith MT, Rothman N. Human benzene metabolism following occupational and environmental exposures. *Chemico-Biol Interact*. 2010;184(1-2):189-95.
14. Gut I, Nedelcheva V, Soucek P, Stopka P, Tichavska B. Cytochromes P450 in benzene metabolism and involvement of their metabolites and reactive oxygen species in toxicity. *Environ Health Perspect*. 1996;104(suppl 6):1211-8.
15. Poljsak B, Šuput D, Milisav I. Achieving the balance between ROS and antioxidants: when to use the synthetic antioxidants. *Oxidative Med Cell Longevity*. 2013;2013.
16. Valavanidis A, Vlachogianni T, Fiotakis C. 8-hydroxy-2'-deoxyguanosine (8-OHdG): a critical biomarker of oxidative stress and carcinogenesis. *J Environ Sci Health Part C*. 2009;27(2):120-39.
17. Lourenço SC, Moldão-Martins M, Alves VD. Antioxidants of natural plant origins: From sources to food industry applications. *Molecules*. 2019;24(22):4132.
18. Gali-Muhtasib H, El-Najjar N, Schneider-Stock R. The medicinal potential of black seed (*Nigella sativa*) and its components. *Adv Phytomed*. 2006;2:133-53.
19. Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, Damanhoury ZA, Anwar F. A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pacific J Trop Biomed*. 2013;3(5):337-52.
20. Gholamnezhad Z, Havakhah S, Boskabady MH. Preclinical and clinical effects of *Nigella sativa* and its constituent, thymoquinone: A review. *J Ethnopharmacol*. 2016;190:372-86.
21. Randhawa MA, Alghamdi MS. Anticancer activity of *Nigella sativa* (black seed)-a review. *Am J Chinese Med*. 2011;39(06):1075-91.
22. Ikhsan M, Hiedayat N, Maeyama K, Nurwidya F. *Nigella sativa* as an anti-inflammatory agent in asthma. *BMC Res Notes*. 2018;11(1):1-5.
23. Hamdan A, Haji Idrus R, Mokhtar MH. Effects of *nigella sativa* on type-2 diabetes mellitus: a systematic review. *Int J Environ Res Publ Health*. 2019;16(24):4911.
24. Jaarin K, Foong WD, Yeoh MH, Kamarul ZY, Qodriyah HM, Azman A, Zuhair JS, Juliana AH, Kamisah Y. Mechanisms of the antihypertensive effects of *Nigella sativa* oil in L-NAME-induced hypertensive rats. *Clinics*. 2015;70(11):751-7.
25. Abbasnezhad A, Hayatdavoudi P, Niazmand S, Mahmoudabady M. The effects of hydroalcoholic extract of *Nigella sativa* seed on oxidative stress in hippocampus of STZ-induced diabetic rats. *Avicenna J Phytomed*. 2015;5(4):333.
26. Burits M, Bucar F. Antioxidant activity of *Nigella sativa* essential oil. *Phytotherap Res*. 2000;14(5):323-8.
27. Mansour MA, Nagi MN, El-Khatib AS, Al-Bekairi AM. Effects of thymoquinone on antioxidant enzyme activities, lipid peroxidation and DT-diaphorase in different tissues of mice: a possible mechanism of action. *Cell Biochem Function*. 2002;20(2):143-51.
28. Dewi R, Hamid ZA, Rajab NF, Shuib S, Razak SA. Genetic, epigenetic, and lineage-directed mechanisms in benzene-induced malignancies and hematotoxicity targeting hematopoietic stem cells niche. *Human Exp Toxicol*. 2020;39(5):577-95.
29. Sun R, Cao M, Zhang J, Yang W, Wei H, Meng X, Yin L, Pu Y. Benzene exposure alters expression of enzymes involved in fatty acid β -oxidation in male C3H/He mice. *Int J Environ Res Publ Health*. 2016;13(11):1068.
30. Hosseini SM, Taghiabadi E, Abnous K, Hariri AT, Pourbakhsh H, Hosseinzadeh H. Protective effect of thymoquinone, the active constituent of *Nigella sativa* fixed oil, against ethanol toxicity in rats. *Iran J Basic Med Sci*. 2017;20(8):927.
31. Erisgin Z, Atasever M, Cetinkaya K, Dizakar SÖ, Omeroglu S, Sahin H. Protective effects of *Nigella sativa* oil against carboplatin-induced liver damage in rats. *Biomed Pharmacother*. 2019;110:742-7.
32. El Batsh MM, Zakaria SS, Gaballah HH. Protective effects of alpha-lipoic acid against benzene induced toxicity in experimental rats. *Eur Rev Med Pharmacol Sci*. 2015;19(14):2717-24.
33. Fenga C, Gangemi S, Teodoro M, Rapisarda V, Golokhvast K, Docea AO, Tsatsakis AM, Costa C. 8-Hydroxydeoxyguanosine as a biomarker of oxidative DNA damage in workers exposed to low-dose benzene. *Toxicol Reports*. 2017;4:291-5.
34. Ibrahim KS, Saleh ZA, Farrag AR, Shaban EE. Protective effects of zinc and selenium against benzene toxicity in rats. *Toxicol Indust Health*. 2011;27(6):537-45.
35. Yu K, Yang KY, Ren XZ, Chen Y, Liu XH. Amifostine protects bone marrow from benzene-induced hematotoxicity in mice. *Int J Toxicol*. 2007 Jul;26(4):315-23.
36. Zhao J, Sui P, Wu B, Chen A, Lu Y, Hou F, Cheng X, Cui S, Song J, Huang G, Xing C. Benzene induces rapid leukemic transformation after prolonged hematotoxicity in a murine model. *Leukemia*. 2021;35(2):595-600.
37. Tuo J, Deng X, Loft S, Poulsen HE. Dexamethasone ameliorates oxidative DNA damage induced by benzene and LPS in mouse bone marrow. *Free Radical Res*. 1999;30(1):29-36.
38. Beheshti F, Norouzi F, Abareshi A, Khazaei M, Alikhani V, Moussavi S, Biglari G, Soukhtanloo M, Hosseini M. *Nigella sativa* prevented liver and renal tissue damage in lipopolysaccharide-treated rats. *Saudi J Kidney Dis Transp*. 2018;29(3):554-66.
39. Farris GM, Robinson SN, Gaido KW, Wong BA, Wong VA, Hahn WP, Shah RS. Benzene-induced hematotoxicity and bone marrow compensation in B6C3F1 mice. *Fund Appl Toxicol*. 1997;36(2):119-29.
40. Takahashi M, Tsujimura N, Yoshino T, Hosokawa M, Otsuka K, Matsunaga T, Nakasono S. Assessment of Benzene-Induced Hematotoxicity Using a Human-Like Hematopoietic Lineage in NOD/Shi-scid/IL-2R γ null Mice. *Plos One*. 2012;7(12):e50448.

Identifying the Factors Affecting Integrated Care of the Elderly in Iran

Identificación de los factores que afectan la atención integral de las personas mayores en Irán

Mansoor Khojamli¹ , Fatemeh Dabbaghi² , Ghahraman Mahmoodi² 

1. Ph.D Candidate of health services Administration, Sari Branch, Islamic Azad University, Sari, Iran
2. Associated Professor, Hospital Administration Research Center, Sari Branch, Islamic Azad University, Sari, Iran

Corresponding author

Fatemeh Dabbaghi
Hospital Administration Research Center Sari Branch
Islamic Azad University, Sari, Iran
E-mail: f_dabbaghi@yahoo.com

Received: 27 - I - 2021

Accepted: 26 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.57

Abstract

Objective: The aging of the population has created profound challenges in the economic, social, and health fields, which require to be addressed by elderly care, which varies from country to country both in terms of concentration and method of implementation. This study aimed to identify the factors affecting integrated care for the elderly in Iran.

Methods: This study was an applied study that was performed in combination (qualitative and quantitative). The qualitative part was to compare the condition of old-age care in selected countries of the six regions of the World Health Organization by comparative studies with interviews with 31 health experts, and the quantitative part was to evaluate the old age care program in Iran by a questionnaire between 200 experts and health specialists. Data were analyzed by SPSS21 and LISREL software..

Results: Quantitative analysis of the items showed that the executive management dimension had the highest average with an average of 4.12 and the service provision dimension had the lowest average with an average of 2.26. By exploratory factor analysis, data adequacy (KMO) was equal to 0.983. The amount of common variance between one variable and other variables used in factor analysis was examined whose square of multiple correlations of all items with q1 was equal to 0.532.

Conclusion: The results of the confirmatory factor analysis showed that all dimensional variables were confirmed; therefore, managers and policymakers can make the best decisions by creating an integrated model of aging.

Keywords: Health care delivery, Integrated; Aged, Comparative study.

Resumen

Antecedentes: El envejecimiento de la población ha creado profundos desafíos en los ámbitos económico, social y sanitario, que requieren ser abordados por la atención a las personas mayores, que varía de un país a otro tanto en términos de concentración como de método de aplicación. Este estudio tenía como objetivo identificar los factores que afectan a la atención integrada a las personas mayores en Irán.

Métodos: Este estudio fue un estudio aplicado que se realizó de forma combinada (cualitativa y cuantitativa). La parte cualitativa consistió en comparar el estado de la atención a la tercera edad en países seleccionados de las seis regiones de la Organización Mundial de la Salud mediante estudios comparativos con entrevistas a 31 expertos sanitarios, y la parte cuantitativa consistió en evaluar el programa de atención a la tercera edad en Irán mediante un cuestionario entre 200 expertos y especialistas sanitarios. Los datos se analizaron con los programas SPSS 21.0 y LISREL.

Resultados: El análisis cuantitativo de los ítems mostró que la dimensión de gestión ejecutiva tenía la media más alta, con una media de 4,12, y la dimensión de prestación de servicios tenía la media más baja, con una media de 2,26. Mediante el análisis factorial exploratorio, la adecuación de los datos (KMO) fue igual a 0,983. Se examinó la cantidad de varianza común entre una variable y otras variables utilizadas en el análisis factorial, cuyo cuadrado de las correlaciones múltiples de todos los ítems con q1 fue igual a 0,532.

Conclusiones: Los resultados del análisis factorial confirmatorio mostraron que todas las variables dimensionales se confirmaron; por lo tanto, los gestores y los responsables políticos pueden tomar las mejores decisiones creando un modelo integrado de envejecimiento.

Palabras clave: Prestación de asistencia sanitaria, integrado, envejecimiento, estudio comparativo,

Introduction

The increase in the world's elderly population, especially in developing countries such as Iran, is undeniable¹. Population aging is a process known as population transfer in which mortality and fertility rates decrease and life expectancy increases². Advances in medical knowledge have enhanced the average life expectancy of humans. In developing countries, population aging is occurring more rapidly, and it is predicted that by 2050, 80% of the world's elderly will be concentrated in developing countries³. According to the Eastern Mediterranean Office, in 2025, the elderly population will increase to 8.7% and by 2050 to 15% of the region's total population. The elderly population in Iran will reach more than 10% by 2025 and about 21.7% by 2050⁴.

Despite the increase in the elderly population and the country's changing demographic pyramid, it is still not focused on the needs of this vulnerable group of society, and in-depth studies are felt on their needs⁵. Therefore, planning in this field should be one of the priorities of health policymakers. It must also be acknowledged that population aging poses profound economic, social, and health challenges that require a change in existing structures⁶.

The current situation of the population of Iran is such that the population has changed from the explosive situation of the child population to the increase of the elderly population. Psychological problems caused by aging cause anxiety and depression as well as feelings of inefficiency and uselessness in the elderly⁷⁻⁹ along with physical problems¹⁰; in this period, the person is isolated, and his social relations are reduced, and in general, it causes many changes in the lifestyle of this group¹¹. Meanwhile, in most societies, the elderly are at the most significant risk of diminishing physical, mental, and cognitive abilities and are more likely to rely on formal or informal support to maintain health, performance, and self-sufficiency^{12, 13}. Old age is associated with chronic and costly diseases. Studies show that the average number of visits to the elderly by doctors is three times, and the number of hospitalizations is five times higher than the number of non-elderly people¹⁴.

Public insurance and the provision of integrated hospital services have improved the satisfaction and quality of life of the elderly with several chronic diseases¹⁵. A study examining health policy trends for the elderly in three European countries, France, the United Kingdom, and Sweden, found that integrated government insurance systems, such as those in Sweden, could design a coherent health model for quality care and improvement. The lives of the elderly are practical¹⁶.

The purpose of the elderly health program is to ensure, maintain, and promote the health of the elderly¹⁷.

Additionally, this program seeks to increase the level of awareness and skills of elderly service providers and increase awareness and coverage of elderly health services. In this regard, strategies such as providing comprehensive health-oriented services (prevention, early diagnosis), control of interfering risk factors at the individual level, and training and counseling are utilized to improve behavior and lifestyle^{18,19}. The World Health Organization (WHO) considers supporting research and education in aging and community care as a basic principle for the new strategy¹⁶.

It is necessary for those involved in the health system to pay serious attention to the aging population and take the necessary measures to face this inevitable fact²⁰. Studies on the health needs and quality of life of the elderly have been conducted in the form of integrated models of the elderly in different countries globally, all of which indicated that meeting health needs increases the quality of life in the elderly population²¹⁻²⁷.

In Iran, although some research studies have been conducted in the field of health care for the elderly, the provision of appropriate models that improve the health indicators of the elderly has been neglected. Therefore, this study aimed to improve the health of senior citizens (elderly) and organize the country's existing health services to study the integrated care of the elderly in selected countries of the six regions of the WHO and provide a model for Iran.

Materials and methods

This study is an applied study conducted in two parts, qualitative and quantitative, in 2019. The qualitative part was employed to compare the status of geriatric care in selected countries of the six regions of the WHO by comparative studies, and the quantitative part was used to evaluate the elderly care program in Iran using a questionnaire.

The qualitative part was performed in three stages. In the first stage, to identify and collect the elderly care program's patterns, the components and factors affecting elderly care in Iran were purposefully studied. Internal and external databases such as Irandoc, Science direct, Iranmedex, Medline, PubMed, Scope, Elsevier, etc., search engines such as Scholar Google, official reports, as well as searching for reputable organizations in this field (NHS, WHO, AHRO, ICAHO) and other documents were reviewed. After ensuring the findings' saturation, using the content analysis method, the findings were coded, classified, and concluded. Finally, the results were collected in a matched manner in the matching matrix, and the variables affecting the geriatric care program were identified. By classifying these variables, the conceptual model of this research

includes seven components (organizational structure, how to provide human resources, financing, equipment procurement, executive management, how to provide services in selected countries, and service package in selected countries) to perform the next steps on which the research was set up.

In the second stage, comparative studies were conducted, and the countries were selected from the six regions of the WHO which had a successful geriatric care program in the health system. To this end, first, by referring to the latest statistics and information published by the WHO to examine the indicators and health data of countries, including high life expectancy, high elderly population, aging mortality rate, having integrated aging care models, leading in the provision of geriatric services, and availability of information as well as six countries from six regions were selected as selected countries. Finally, an adaptive matrix was formed to identify the variables.

In the third stage, the Delphi technique was surveyed and performed by experts on the model obtained from comparative studies, and then the theoretical model was modified and revised according to experts' views. In this regard, 35 experts were purposefully selected from 31 provinces of the country.

A small part of this study was conducted to investigate the factors affecting Iran's integrated geriatric care program. For this purpose, the questionnaire of the

integrated geriatric care program components was first designed and validated using the identified quality factors. The prepared questionnaire was then distributed among experts and health specialists in geriatrics, and the dimensions of the integrated geriatric care model were determined using exploratory factor analysis. At this stage, 200 experts and health specialists in geriatrics were randomly selected from 31 provinces.

Finally, the completed questionnaires were entered into SPSS21 software to perform exploratory factor analysis. After confirming/eliminating the practical factors, the obtained data were entered into LISREL software to perform confirmatory factor analysis, extract the mathematical model, and test for better fitting and modeling.

Results

First, by comparing the comparative studies of each dimension of integrated care for the elderly in seven selected countries, including the United States, Japan, Thailand, Egypt, the United Kingdom, South Africa, and Iran. Then, the content analysis by Scott's method was utilized to investigate the practical and essential factors in the integrated care for older people (ICOPE) with a survey of experts (**Table I**). The William Scott formula calculated the reliability of the questions in **table I**, and the agreement coefficient was 85%.

Table I: Practical and essential factors in integrated care of the elderly with a survey of experts.

Factors affecting integrated care for the elderly	Indicator	Confirmation	Practical	Result-oriented	Interactive	Comparative	Predictor	Practical	Total
Does executive management help integrated geriatric care?	Frequency/Percentage	22.63	11.20	7.63	23.27	13.41	22.96	14.95	91.33
Does funding help integrated care for the elderly?	Frequency/Percentage	43.71	29.19	52.22	34.17	52.26	18.15	24.30	93.62
Does the organizational structure contribute to integrated care?	Frequency/Percentage	38.83	19.75	26.57	29.19	37.20	19.59	36.37	91.43
Does the provision of equipment contribute to the integrated care of the elderly?	Frequency/Percentage	48.17	29.22	35.90	29.15	41.32	32.70	29.40	90.21
Does human resource provision contribute to integrated geriatric care?	Frequency/Percentage	28.77	27.16	29.08	36.19	39.85	29.12	28.29	96.30
Does providing services help integrated care for the elderly?	Frequency/Percentage	15.63	19.14	16.33	13.17	18.29	17.75	14.30	90.61
Does the service package help with integrated geriatric care?	Frequency/Percentage	11.69	12.32	11.29	13.10	8.44	16.63	12.03	89.50

By analyzing the quantitative findings of the data obtained from the experts' questionnaire, the results indicate that the executive management dimension had the highest average with an average of 4.12. The service provision dimension had the lowest average with an average of 2.26 (Table II).

Table II: Mean of indicators (dimensions) after exploratory factor analysis.

Dimensions	Experts	
	Mean	SD
Organizational Structure	2.2635	0.9632
Human Resources	3.8242	0.0362
Executive Management	4.1258	0.0236
Providing Services	2.2653	0.2051
Financial Resources	3.8061	0.1212
Service Package	3.1120	0.5241

To initiate the stage of exploratory factor analysis, the adequacy of the data was first measured. The KMO value was equal to 0.983, whose high rate indicates the data for classification. Bartlett test and its corresponding level of significance show that the data matrix is not a single matrix of correlation between variables. The data are capable of factor analysis (Table III).

Table III: Bartlett and KMO test.

Kaiser Meyer criterion for sample volume adequacy		0.983
Bartlett test	Chi-squared	95230.232
	Degrees of freedom	12675
	P-Value	0.000

The share of each item was calculated by combining all items linearly. The amount of common variance

between one variable and other variables used in factor analysis has been examined. This analysis indicates that the square of the multiple correlations of all items with q1 is equal to 0.532.

After factor analysis and rotation by the Varimax method, six factors were finally identified. The first factor's eigenvalue is equal to 14.225, and the sixth factor is equal to 6.854. The share of factors in explaining variance is descending, i.e., the first factor with 14.902 has the largest share in explaining variance. Meanwhile, the sixth factor with 365.7%, had the lowest share in explaining the variance, so that the six extracted factors can explain a total of 67.321% of the variance of the variables.

After determining the optimal number of factors from the set of factors, using the factor load values after rotation, items were categorized in the extracted factors. For this purpose, only variables whose factor load is higher than 0.3 were considered. Then, the content validity of the variables that make up each of the factors (dimensions) was extracted, and the factor, mean, and standard deviation of the respondents' opinions for the items of each dimension were obtained. Table IV below shows the fit indices of each dimension.

Based on the findings in table IV, the set of fit indicators shows that the collected data generally supports the service package's service structure dimension. Table V shows the confirmatory factor analysis statistics in all dimensions affecting the implementation of integrated care for the elderly in Iran.

Table IV: Mean of indicators (dimensions) after exploratory factor analysis.

Variable	Chi-Squared Relative	P-Value	CFI	NFI	PCFI	RMSEA
Organizational Structure Dimension (First Factor)	19.03	0.122	0.951	0.937	0.817	0.074
Human Resources Dimension (Second Factor)	36.59	0.260	0.959	0.949	0.776	0.041
Financial Resources Dimension (Third Factor)	12.40	0.490	0.987	0.982	0.599	0.000
Executive Management Dimension (Fourth Factor)	11.44	0.530	0.977	0.969	0.711	0.061
Providing Services Dimension (Fifth Factor)	3.870	0.690	0.976	0.970	0.692	0.000
Service Package Dimension (Sixth Factor)	10.61	0.220	0.990	0.985	0.613	0.062

Table V: Confirmatory factor analysis statistics in all dimensions affecting the implementation of integrated care for the elderly in Iran.

Variable	Abbreviation	Parameter Estimation	Impact Factor	P-Value	T-Value	Skewness
Providing Services	V	0.703	0.684	0.000	20.15	0.48
Financial Resources	P	1.000	0.742	0.000	27.53	0.22
Executive Management	D	0.812	0.832	0.000	25.79	0.33
Organizational Structure	R	1.017	0.715	0.000	21.60	0.47
Service Package	M	0.723	0.707	0.000	19.92	-0.17
Human Resources	K	0.771	0.800	0.000	18.07	0.22

Table VI: Fitness indices of the model confirming the pattern of integrated care for the elderly in Iran.

Fit Indicators	Criterion	Values Obtained	Model Fit
Chi-Squared	A lower value of this indicator indicates that the model is more suitable	12563.115	----
P-Value	More than 0.05	0.000	Not Suitable
Chi-Squared Relative	Between 2-5	4.163	Suitable
RMSEA	Less than 0.08 and preferably less than 0.05	0.028	Suitable
CFI	More than 0.9	0.927	Suitable
NFI	More than 0.9	0.945	Suitable
PCFI	More than 0.6	0.661	Suitable

The findings in **table V** show that all model paths based on scale items in the domains are significant, and these values range (T-Value) from 18.07 to 27.53. Also, the executive management factor with a coefficient of 0.832 has the most impact, and the service delivery factor with a coefficient of 0.684 has the lowest weight in the implementation of integrated care for the elderly in Iran.

According to **table VI**, the set of mentioned indicators shows that the model fit was appropriate. Therefore, according to the fit indices of the whole model, it can be mentioned that the above factors can be named as practical factors on the integrated care model of the elderly in Iran. Finally, a confirmatory factor analysis of the integrated care model for the elderly in Iran was performed (**Figure 1**).

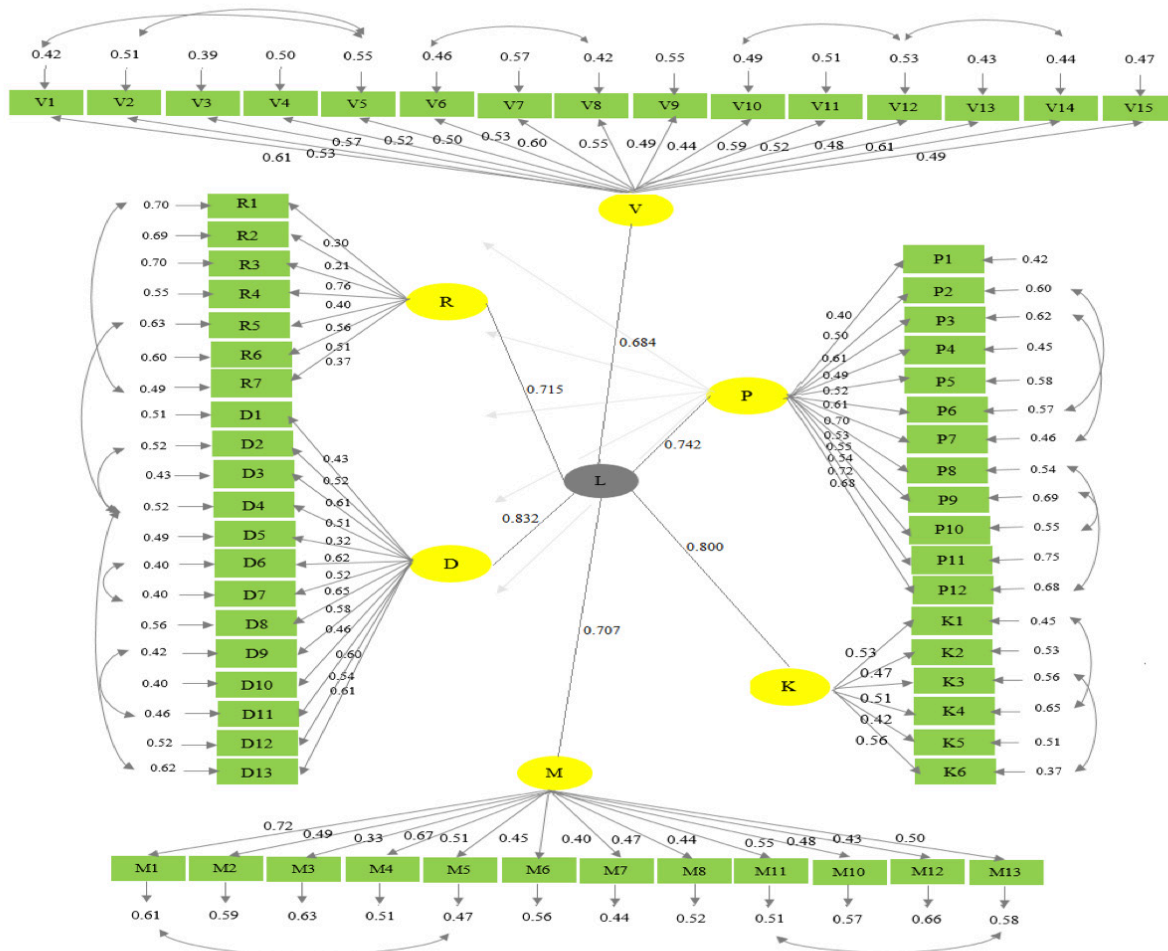
Discussion

Based on the results, the proposed model of this research was extracted and finalized in six stages. In the sixth stage, to validate and extract the final model, the exploratory factors obtained from the fifth stage, using

LISREL software, confirmatory factor analysis method, validation, and final study pattern, were confirmed. Finally, 65 selected variables were loaded on six main dimensions, which formed the final model of integrated care for the elderly in Iran. These dimensions include executive management dimension (0.832), human resources dimension (0.800), financial resources dimension (0.742), organizational structure dimension (0.715), service package dimension (0.707), and service delivery dimension (0.684), respectively.

Pourhadi stated the importance of organizational structure and highlighted how people deal with old age and disability, and dependence in this period has an essential role in caring for them²³. Safdari et al. also stated that in Iran, the executive bodies and institutions responsible for the elderly, within the scope of their current duties and allocated funds, take measures to protect the elderly. However, these measures do not seem to be sufficient²². Rahimi identified five main categories of experience-based services for the elderly. These five categories, including market management, inadequate structure

Figure 1: Factor analysis model and integrated care items for the elderly in Iran based on standardized coefficients..



Chi-Square=12563.115, df=12674, P-Value=0.00000, RMSEA=0.028

for care, insufficient resources of care and conflicting environment, maintenance instead of care, peaceful coexistence, and low expectations of the elderly, have been achieved²⁸. In line with this study, these studies have highlighted and discussed the organizational structure dimension. After exploratory factor analysis, confirmatory factor analysis was performed on the loaded variables in the organizational structure dimension. The results of the confirmatory factor analysis also showed that the variables of this dimension were all confirmed. Today, one of society's key issues is developing a suitable organizational structure for the elderly. There are several approaches to an organizational structure whose advantages and disadvantages should be considered.

The human resources component has also been extracted and considered in this study. Samaram Amin Aghayi, in this regard, also states that in Iran, industrial development is still moving alongside traditional culture. Thus we need economic and cultural contexts to use resources, especially human resources, in inclusive support programs²⁹. Analysis of the present study's findings indicates that the use of human resources in integrated geriatric care should train family members or elderly caregivers, and periodic training should be provided to general practitioners, nurses, and geriatricians. Also, organizational resource planning is a crucial indicator of integrated care for older people (ICOP).

Financial resources are essential because the resources available in geriatric health care are scarce, but their demand is continuously increasing. The non-payment of insurance claims has faced many problems in the health sector³⁰. Shoaei and Nejati consider the existence of a strong and diverse social security system in the United States to be the most prominent finding in comparing the two aging systems in Iran and the United States³¹. The financial resources of the variables of this dimension were all approved, and since the main problem in providing health care services lies in its economic problem, and the centers providing health care services are one of the most essential and costly units in any country, the need for health insurance is required with a wide range of insurance policies.

Studies have shown alignment with the results of this study in terms of executive management. Samaram and Amin Aghayi, in a study, stated that that the most essential reason to present administrative policies in Iran is the limitations of facilities in supporting the elderly²⁹. Eamer et al. also mentioned that improving executive management will reduce the length of recovery and hospitalization and reduce treatment costs²⁴. The results of the confirmatory factor analysis show that the variables of this dimension were all confirmed. According to the results of similar studies and in line with the present research, it can be stated that empowerment and self-efficacy of the elderly, social support programs, collection of demographic data on the elderly, adaptation of the elderly home environment,

telemedicine, city and pharmacy in the elderly and coordination between elderly health-related organizations are among the activities that should be considered in executive management and well-considered in strategic and operational planning for the elderly.

In terms of providing services based on need assessment, the need for the elderly has had the most significant impact. The results of the confirmatory factor analysis also showed that the variables of this dimension were all confirmed. Asefzadeh and Ghodoosian stated that the greatest need of the elderly in the care of cardiovascular diseases, surgeries, infectious and internal and eye diseases that need to be considered before organizing services³². Spoorenberg et al. also stated that to measure the effectiveness of service delivery, it is important to measure the how of using health services, costs, and quality of care²⁷. According to what was stated, first, the needs of the elderly should be identified, and then based on the needs, various resources, including human, economic, and physical, should be provided. Furthermore, appropriate software, including the structure and executive management, should be considered and designed based on experts' views.

In the service package component, screening tests and examinations for communicable diseases of the elderly had the highest factor, but the variables of this dimension were all approved. In all studies, there has been a strong emphasis on identifying types of services. Veras et al. stated that geriatric services include prevention, treatment, rehabilitation, long-term care, and palliative care, which were identified after comprehensive assessments of the elderly²⁶. Spoorenberg et al. also identified four key elements: self-management support, service delivery system design, decision support, and clinical information systems for integrated geriatric care²⁷.

Conclusion

According to the findings of the study, all dimensions were confirmed. Therefore, among the practical solutions, according to the designed model, it is possible to formulate an appropriate organizational structure according to the needs assessments; utilization of human resources in integrated geriatric care with the benefit of family members or home caregivers, periodic training of general practitioners, nurses and geriatricians, organizational resource planning as critical indicators of integrated geriatric care, empowerment and self-efficacy of the elderly, creation Social support programs, collection of demographic data on the elderly, adaptation of the elderly home environment, telemedicine, city and pharmacy friendly to the elderly, coordination between organizations related to elderly health, needs assessment including human, economic and physical resources and development of appropriate software including the structure and executive management.

Acknowledgments

The authors would like to thank the Hospital Administration Research Center, Sari Branch, Islamic Azad University, Sari, Iran for the significant supports.

References

1. Organization WH. Interesting facts about ageing [Internet]. Geneva: WHO; 2012 [cited 2013 Aug 29]. 2014.
2. Sadoughi F, Shahi M, Ahmadi M, Davaridolatabadi N. The Comparison of the Minimum Data Set for Elderly Health in Selected Countries. *Acta Inform Med*. 2015;23(6):393-7.
3. Afsharkohan J, Koolivand S. Structured study of the quality of life in the elderly in Iran (2004-13). *Iran J Ageing*. 2015;10(3):192-201. [Persian]
4. Tanjani PT, Motlagh ME, Nazar MM, Najafi F. The health status of the elderly population of Iran in 2012. *Arch Gerontol Geriatr*. 2015;60(2):281-7.
5. Sheiham A. Oral health, general health and quality of life. *Bull World Health Org*. 2005;83(9):644.
6. Jin K, Simpkins JW, Ji X, Leis M, Stambler I. The Critical Need to Promote Research of Aging and Aging-related Diseases to Improve Health and Longevity of the Elderly Population. *Aging Dis*. 2015;6(1):1-5.
7. Gardiner C, Geldenhuys G, Gott M. Interventions to reduce social isolation and loneliness among older people: an integrative review. *Health Soc Care Community*. 2018;26(2):147-57.
8. Shankar A, McMunn A, Demakakos P, Hamer M, Steptoe A. Social isolation and loneliness: Prospective associations with functional status in older adults. *Health Psychol*. 2017;36(2):179-87.
9. Cacioppo JT, Cacioppo S. Social Relationships and Health: The Toxic Effects of Perceived Social Isolation. *Soc Personal Psychol Compass*. 2014;8(2):58-72.
10. Chen H, Wang H, Crimmins EM, Chen G, Huang C, Zheng X. The contributions of diseases to disability burden among the elderly population in China. *J Aging Health*. 2014;26(2):261-82.
11. Allen J, Balfour R, Bell R, Marmot M. Social determinants of mental health. *Int Rev Psychiatry*. 2014;26(4):392-407.
12. Tanjani PT, Azadbakht M, Gamaroudi G, Sahaf R, Fekrizadeh Z. Validity and Reliability of Health Promoting Lifestyle Profile II in the Iranian Elderly. *Int J Prev Med*. 2016;7:74.
13. Kagan SH. The advanced practice nurse in an aging society. *Nurse Pract*. 2003;16:12-4.
14. Alizadeh M, Fakhzadeh H, Sharifi F, Zanjari N, Ghassemi S. Comparative study of physical and mental health status of old people in aged groups of 60-64 and 65-69 years old in Tehran metropolitan area. *Iran J Diabetes Metab*. 2013;13(1):50-61.
15. Bayliss EA, Ellis JL, Shoup JA, Zeng C, McQuillan DB, Steiner JF. Effect of continuity of care on hospital utilization for seniors with multiple medical conditions in an integrated health care system. *Ann Fam Med*. 2015;13(2):123-9.
16. Dall TM, Gallo PD, Chakrabarti R, West T, Semilla AP, Storm MV. An aging population and growing disease burden will require a large and specialized health care workforce by 2025. *Health Affairs*. 2013;32(11):2013-20.
17. Fulmer T, editor Health care reform and the changing training needs for those who care for the elderly. 141st APHA Annual Meeting 2013; USA.
18. Den Ambtman A, Beirão G, Kandampully J, Dias J, De Pouroq K, De Regge M, editors. Enhancing the healthcare experience: the role of technology in elderly care. *Frontiers in Service Conference 2017*; 2017; New York.
19. Rebok GW, Ball K, Guey LT, Jones RN, Kim HY, King JW, et al. Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. *J Am Geriatr Soc*. 2014;62(1):16-24.
20. Mirzaie M, Darabi S. Population aging in Iran and rising health care costs. *Iran J Ageing*. 2017;12(2):156-69. [Persian]
21. Borji M, Motaghi M. The effect of collaborative care model on social support and general self-efficacy of the elderly. *Iran J Psychiatric Nursing*. 2017;5(1):22-9. [Persian]
22. Safdari R, Sadeghi F, Mohammadiazar M. Aged care and services programs in Iran: Looking at the performance of relevant organizations. *Payavard-Salamat*. 2016;10(2):155-66. [Persian]
23. Pourhadi S. Designing a model for the care of the Iranian elderly. [Master's Thesis]. Tehran: University of Social Welfare and Rehabilitation Sciences; 2016. [Persian]
24. Eamer G, Taheri A, Chen SS, Daviduck Q, Chambers T, Shi X, et al. Comprehensive geriatric assessment for improving outcomes in elderly patients admitted to a surgical service. *Cochrane Database Syst Rev*. 2017;2017(1):CD012485.
25. Gungur S, Ghimire S. Role of family in elderly care. Finland: Lapland University of Applied Sciences; 2014.
26. Veras RP, Caldas CP, Motta LBd, Lima KCd, Siqueira RC, Rodrigues RTdSV, et al. Integração e continuidade do cuidado em modelos de rede de atenção à saúde para idosos frágeis. *Rev Saúde Públ*. 2014;48:357-65.
27. Spoorenberg SL, Uittenbroek RJ, Middel B, Kremer BP, Reijneveld SA, Wynia K. Embrace, a model for integrated elderly care: study protocol of a randomized controlled trial on the effectiveness regarding patient outcomes, service use, costs, and quality of care. *BMC Geriatrics*. 2013;13(1):62.
28. Rahimi M. Study of the process of caring for the elderly living in a nursing home. [Ph.D. Dissertation]. Tehran: University of Social Welfare and Rehabilitation Sciences; 2015. [Persian]
29. Samaram E, Amin Aghayi M. Social policy in Japan and Sweden: A proper pattern for Iranian elderlies. *Iran J Ageing*. 2007;1(2):88-100. [Persian]
30. Ghaffari S, Mohamadzadeh A, Akbari S, Salem Safi P, Yousefi M. Costing in hospital services: economists and accountants' approaches. *Hospital*. 2013;11(4):75-84. [Persian]
31. Shoaief F, Nejati V. Elderly-caring service pattern in USA comparing With Iran. *Iran J Ageing*. 2008;3(1):68-77. [Persian]
32. Asefzadeh S, Ghodoosian A. Recognition of the health related factors of aged population of minoodar in order to design research interventions (2009). *Iran J Ageing*. 2010;5(1):53-60. [Persian]

Relationship between alcohol consumption and obesity determined with different scales

Relación entre el consumo de alcohol y la obesidad determinada con diferentes escalas

**Yarianne Inalvis Rivero Ledo¹ , Dorey Arderi Guerra² , Yamileris Patchana³ ,
María Ladisa⁴ , Onel Valdes Garcia¹ , Hilda González San Miguel⁵ ,
María del Mar Rigo Vives⁵**

1. Larkin Community Hospital. Florida. USA 2. Lifestar Patient Management Services. Florida. USA. 3. Department of Public Health, Epidemiology and Disease Control Clinic. Womack Hospital, Fort Bragg. North Carolina, USA. 4. Occupational Health Service. Virgen Macarena University Hospital. Seville, Spain. 5. ADEMA University School. Palma. Balearic Islands. Spain.

Corresponding author

Yarianne Inalvis Rivero Ledo
Larkin Community Hospital
1475 W 49th Pl, Hialeah. FL 330
E-mail: yrivero80@gmail.com

Received: 22 - I - 2021
Accepted: 14 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.64

Abstract

Introduction: Alcohol consumption is linked to the development of various diseases, including obesity.

Methods: A descriptive, cross-sectional study was carried out on 60798 workers in which the relationship between high alcohol consumption and the appearance of overweight and obesity determined with different scales (BMI, waist to height ratio, body roundness index, body shape index, visceral adiposity index, conicity index and scales predicting body fat) was assessed.

Results: The mean values and the prevalence of obesity as determined by the different scales are higher among people who consume high amounts of alcohol. The multivariate analysis shows that alcohol consumption is one of the factors that most increase the risk of obesity.

Conclusion: Excessive alcohol consumption increases all the parameters related to overweight and obesity in Spanish workers.

Keywords: Alcohol consumption, obesity, overweight, visceral adiposity index, body fat.

Resumen

Introducción: El consumo de alcohol guarda relación con la aparición de diferentes enfermedades, entre ellas la obesidad.

Material y métodos: Se realiza un estudio descriptivo y transversal en 60798 trabajadores en los que se valora la relación entre el elevado consumo de alcohol y la aparición de sobrepeso y obesidad determinada con diferentes escalas (IMC, cintura/altura, body roundness index, body shape index visceral adiposity index, conicity index y escalas predictoras de grasa corporal).

Resultados: Los valores medios y la prevalencia de obesidad determinada con las diferentes escalas es más elevada entre las personas que consumen altas cantidades de alcohol. En el análisis multivariante se observa que el consumo de alcohol es uno de los factores que más aumentan el riesgo de padecer obesidad.

Conclusiones: El consumo excesivo de alcohol aumenta todos los parámetros relacionados con sobrepeso y obesidad en trabajadores españoles.

Palabras clave: Consumo de alcohol, obesidad, sobrepeso, índice de adiposidad visceral, grasa corporal.

Introduction

Alcohol use has been associated with significant health problems, both physical and mental, as well as social and personal problems. Many clinical decisions, both in terms of treatment of the associated pathology and management of alcohol use itself, will depend on the type of assessment made of alcohol consumption. For all these reasons, it is essential to make an adequate assessment of alcohol consumption and drinking patterns¹.

Overweight and obesity have been defined as the abnormal or excessive accumulation of fat that can be detrimental to health. The traditional way of measuring them is through the body mass index, although there are other indicators such as excess body fat.

Overweight and obesity are considered as a systemic, chronic, multi-causal disease, not exclusive to economically developed, involving all age groups, ethnicities and social classes².

According to WHO², the main cause of overweight and obesity is an imbalance between calories consumed and calories expended. However, obesity is known to have a multifactorial origin, involving genetic susceptibility, lifestyles (including alcohol consumption) and the environment (globalization, culture, economy, education and the political and social environment).

There are different mechanisms linking alcohol consumption to the development of overweight and obesity. It seems clear that light and moderate alcohol consumption is a protective factor and heavy drinking a risk factor for overweight and obesity. This may be due not only to the energy provided by alcohol but also to the fact that alcohol may stimulate the intake of other foods simultaneously³⁻⁵. Alcohol consumption has been shown to influence some hormones linked to satiety, especially by inhibiting the effects of leptin (the hormone responsible for satiety), or glucagon-like peptide-1 (GLP-1)⁶⁻⁷. Alcohol may also influence appetite through several central mechanisms. The effects of alcohol on opioid, serotonergic, and GABAergic pathways throughout the brain suggest the potential to increase appetite and energy intake⁸⁻⁹. Alcohol also acts on energy storage by inhibiting fat oxidation, i.e., it prevents fat from being used as energy, which means that long-term frequent alcohol consumption could lead to the formation of more fat rather than using existing fat for energy, which resulting in an increased likelihood of becoming overweight or obese⁸.

For the above reasons, in this study we are interested in finding out the relationship between alcohol consumption and the prevalence of obesity determined with different scales in a group of workers.

Methods

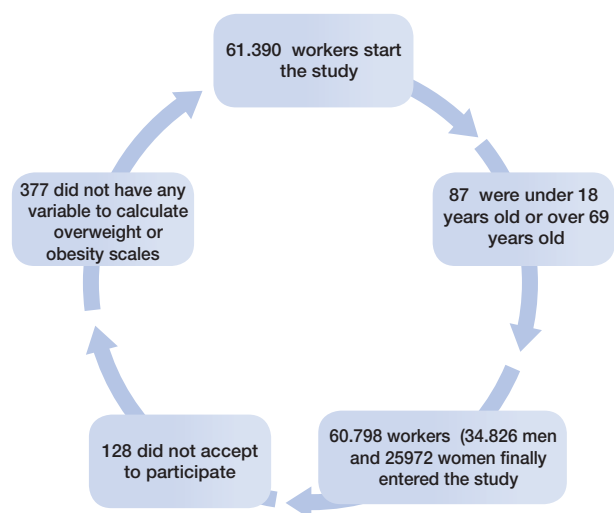
A retrospective, cross-sectional study is conducted on 60,798 Spanish workers during the period from May 2018 to January 2020. Workers were selected among those who attended occupational health follow up appointments periodically.

Inclusion criteria

- Age between 18 and 69 years.
- Agree to participate in the study.

The flow chart of the people involved in the study is shown in **Figure 1**.

Figure 1: Mean of indicators (dimensions) after exploratory factor analysis.



Anthropometric (height, weight, waist circumference), clinical and analytical measurements were performed by the occupational health professionals of the companies after having homogenized the measurement techniques.

Weight and height were determined with a scale-measuring device: model SECA 700. Abdominal waist circumference was measured with a tape measure: SECA 200. Blood pressure was assessed with a calibrated OMRON M3 automatic sphygmomanometer and after 10 minutes of rest. Three determinations were made at one-minute intervals and the mean value of the three was obtained. Blood tests were obtained after fasting for at least 12 hours. The samples were sent to reference laboratories where they were processed.

BMI was calculated by dividing weight by height in squared meters. Obesity was considered over 30. The waist-to-height ratio was considered risky over 0.50¹⁰.

Five formulas were used to estimate body fat percentage:

- CUN BAE¹¹ (Clínica Universitaria de Navarra Body Adiposity Estimator):
 $-44.988 + (0.503 \times \text{age}) + (10.689 \times \text{gender}) + (3.172 \times \text{BMI}) - (0.026 \times \text{BMI}^2) + (0.181 \times \text{BMI} \times \text{gender}) - (0.02 \times \text{BMI} \times \text{age}) - (0.005 \times \text{BMI}^2 \times \text{gender}) + (0.00021 \times \text{BMI}^2 \times \text{age})$
- ECORE BF¹² (Cordoba Equation for body fat estimation):
 $-97.102 + 0.123 (\text{age}) + 11.9 (\text{sex}) + 35.959 (\text{LnIMC})$

Where male equals 0 and female equals 1. The CUN BAE and ECORE-BF cut-off points for obesity were from 25% in men and 35% in women.

- Formula Palafolls¹³.
 Men = $([\text{BMI}/\text{PA}] \times 10) + \text{BMI}$. Women = $([\text{BMI}/\text{PA}] \times 10) + \text{BMI} + 10$. The authors propose the same cut-off points as CUN BAE.
- Deuremberg formula¹⁴.
- Fat mass % = $1.2 \times (\text{BMI}) + 0.23 \times (\text{Age in years}) - 10.8 \times (\text{gender}) - 5.4$

Where female equals 0 and male equals 1.

Obesity was considered to be 25% or more in men and 32% or more in women.

Relative fat mass¹⁵

Women: $76 - (20 \times (\text{height}/\text{waist}))$
 Men: $64 - (20 \times (\text{height}/\text{w waist}))$

Height and waist circumference are expressed in meters. The cut-off points for obesity are from 32% in women and 25% in men.

Other indicators of overweight and obesity calculated are:

- Visceral adiposity index¹⁶ (VAI).

Male:

$$VAI = \left(\frac{WC}{39,68 + (1,88 \times \text{BMI})} \right) \times \left(\frac{TG}{1,03} \right) \times \left(\frac{1,31}{HDL} \right)$$

Female:

$$VAI = \left(\frac{WC}{36,58 + (1,89 \times \text{BMI})} \right) \times \left(\frac{TG}{0,81} \right) \times \left(\frac{1,52}{HDL} \right)$$

- Conicity index¹⁷

$$\frac{\text{waist circumference (in metres)}}{0,109} \times 1/\sqrt{\frac{\text{weight (in kilogram)}}{\text{height (in metres)}}}$$

- Body Roundness Index¹⁸ (BRI) is calculated using the following formula, where WC represents the waist circumference.

$$BRI = 364,2 - 365,5 \times \sqrt{1 - \left(\frac{WC/(2r)}{(0,5 \text{ height})^2} \right)}$$

- Body shape index (ABSI)¹⁹.

$$ABSI = \frac{WC}{\text{BMI}^{2/3} \times \text{height}^{1/2}}$$

Smoking, diet, and physical activity were assessed by a clinical interview. Tobacco was considered a dichotomous variable (yes/no), and an individual was considered a smoker if they had regularly consumed at least 1 cigarette/day (or the equivalent in other types of consumption) in the last month or had stopped smoking less than a year ago. Healthy eating was considered as a diet that includes daily consumption of vegetables and fruits, and adequate physical activity was defined as performing at least 30 minutes a day or 150 minutes a week of moderate intensity aerobic physical activity or 75 minutes a week of vigorous activity. Quantification of consumption in standard drinking units is currently the reference method at all levels of care. The assessment of consumption in standard drinking units allows a rapid quantification of consumption and its easy conversion into grams of pure alcohol¹. The value of standard drinking units in Spain is set at 10 g of alcohol and is equivalent to one consumption of wine (100 ml), champagne (100 ml) or beer (200 ml) and half a consumption of spirits or mixed drinks (25 ml). If a man goes over 35 standard drinking units in a week and a woman over 20 in a week, there is a significant risk to their long-term health²⁰.

Social class is determined on the basis of the 2011 National Classification of Occupations (CNO-11) and based on the proposal made by the social determinants group of the Spanish Society of Epidemiology²¹. We opted for classification into 3 categories: Class I. Directors/managers, university professionals, sportsmen, women and artists. Class II. Intermediate occupations and self-employed workers without employees. Class III. Unskilled workers.

Statistical analysis

A descriptive analysis of the categorical variables was carried out, calculating the frequency and distribution of responses for each of them. For quantitative variables, the mean and standard deviation were calculated, and for qualitative variables, the percentage was calculated. The bivariate analysis of association was performed using the 2's test (with correction for Fisher's exact statistic when conditions required it) and Student's t-test for independent samples. For the multivariate analysis, binary

logistic regression was used with the Wald method, with the calculation of Odds ratios and the Hosmer-Lemeshow goodness-of-fit test was performed. Statistical analysis was performed with the SPSS 27.0 programme, the accepted level of statistical significance being 0.05.

Ethical considerations and issues

The study received approval from the Clinical Research Ethics Committee. All procedures were performed in accordance with the ethical standards of the institutional research committee and the 2013 Declaration of Helsinki. All patients signed written informed consent documents before participating in the study.

Results

The average age of our workers is not too old (40 years), almost 35% of them smoke and almost 15% consume alcohol to a high degree. Most of them belong to social class III. The clinical and analytical parameters are more unfavorable in men with statistically significant differences. All data are presented in **table I**.

The mean values of all scales related to overweight, and obesity are higher in the group of people who consume high amounts of alcohol, and this was observed in both sexes. The full data can be found in **table II**.

The prevalence of obesity as determined by the different scales is higher in the group of people who consume alcohol compared to those who do not, both in women and men. The full data can be found in **table III**.

Table I: Anthropometric, clinical, analytical, sociodemographic and healthy habits characteristics of the sample.

	Women n=25972	Men n=34826	Total n=60798	p-value
Age	39.5 ± 10.2	40.4 ± 10.5	40.0 ± 10.4	<0.0001
Height	161.3 ± 6.5	173.9 ± 7.1	168.5 ± 9.2	<0.0001
Weight	65.1 ± 13.1	81.3 ± 13.9	74.4 ± 15.8	<0.0001
Systolic Blood Pressure	114.6 ± 15.1	125.4 ± 15.7	120.8 ± 16.3	<0.0001
Dyastolic Blood Pressure	70.4 ± 10.4	76.0 ± 10.8	73.6 ± 11.0	<0.0001
Cholesterol	193.1 ± 36.4	197.6 ± 38.5	195.7 ± 37.7	<0.0001
HDL-c	55.0 ± 9.2	50.5 ± 7.6	52.4 ± 8.6	<0.0001
LDL-c	120.5 ± 36.9	121.8 ± 37.3	121.2 ± 37.1	<0.0001
Triglycerides	87.9 ± 45.9	126.2 ± 88.5	109.9 ± 75.8	<0.0001
Glucose	85.2 ± 15.1	90.6 ± 21.2	88.3 ± 19.0	<0.0001
	%	%	%	p-value
Alcohol consumption	8.5	19.6	14.8	<0.0001
Tobacco consumption	32.5	36.6	34.8	<0.0001
Healthy food consumption	50.6	40.1	44.6	<0.0001
Physical activity	52.2	44.1	47.5	<0.0001
Social class I	14.1	7.4	10.3	<0.0001
Social class II	32.7	23.5	27.4	
Social class III	53.2	69.1	62.3	
Elementary	47.1	68.8	59.1	<0.0001
Secondary	40.5	25.5	31.9	
University student	12.4	6.5	9.0	

Table II: Mean values of different obesity scales according to alcohol consumption by gender.

	Women			Men		
	n=23768 No alcohol mean ± SD	n=2204 Yes alcohol mean ± SD	p	n=28011 No alcohol mean ± SD	n=6815 Yes alcohol mean ± SD	p
Body mass index	24.4 ± 4.4	31.5 ± 5.6	<0.0001	25.9 ± 3.6	30.9 ± 4.2	<0.0001
Waist to height ratio	0.46 ± 0.1	0.54 ± 0.1	<0.0001	0.50 ± 0.0	0.57 ± 0.1	<0.0001
Relative fat mass	32.0 ± 5.0	38.5 ± 5.0	<0.0001	23.3 ± 3.7	28.5 ± 3.4	<0.0001
Palafolls formula	37.7 ± 4.7	45.2 ± 6.	<0.0001	28.9 ± 3.9	34.0 ± 4.5	<0.0001
Deuremberg formula	32.8 ± 6.1	43.5 ± 7.1	<0.0001	23.8 ± 5.3	31.6 ± 5.4	<0.0001
ECORE-BF	33.9 ± 6.4	44.2 ± 6.4	<0.0001	24.4 ± 5.3	31.7 ± 4.9	<0.0001
CUN BAE	34.0 ± 6.4	43.8 ± 5.9	<0.0001	24.3 ± 5.6	31.9 ± 5.0	<0.0001
Conicity index	1.09 ± 0.1	1.13 ± 0.1	<0.0001	1.18 ± 0.1	1.24 ± 0.1	<0.0001
Body roundness index	2.7 ± 1.0	4.3 ± 1.7	<0.0001	3.3 ± 0.9	4.8 ± 1.2	<0.0001
Visceral adiposity index	2.7 ± 1.6	4.4 ± 3.5	<0.0001	6.7 ± 6.0	12.4 ± 11.0	<0.0001
Body shape index	0.070 ± 0.01	0.070 ± 0.01	<0.0001	0.075 ± 0.01	0.077 ± 0.01	<0.0001

Table III: Prevalence of obesity determined with different scales according to alcohol consumption by gender.

	Women			Men		
	n=23768 No alcohol %	n=2204 Yes alcohol %	p	n=28011 No alcohol %	n=6815 Yes alcohol %	p
BMI obesity	10.2	60.4		11.1	56.7	
WtHR >0.5	19.5	69.7	<0.0001	44.5	91.8	<0.0001
RFM obesity	35.1	83.7	<0.0001	56.7	94.4	<0.0001
Palafolls obesity	53.0	94.1		56.4	93.7	
Deuremberg obesity	64.3	97.9	<0.0001	39.5	90.7	<0.0001
ECORE-BF obesity	39.8	92.3		44.5	93.0	
CUN BAE obesity	40.8	92.6		44.6	93.1	
Conicity index obesity	7.4	19.6	<0.0001	18.9	47.0	<0.0001

Table IV: Binary logistic regression.

	Male	≥ 50 years	Social class III	Smokers	Non-Physical exercise	Non healthy food	Alcohol
Obesity	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Body mass index	0.88 (0.83-0.93)	0.74 (0.70-0.78)	ns	ns	6.41 (6.11-6.72)	1.71 (1.61-1.81)	5.17 (4.88-5.48)
Relative fat mass	2.67 (2.57-2.77)	1.20 (1.14-1.26)	1.25 (1.07-1.46)	0.86 (0.82-0.89)	3.27 (3.06-3.48)	1.67 (1.56-1.78)	4.97 (4.58-5.39)
Deuremberg formula	0.17 (0.16-0.18)	13.10 (12.21-14.16)	1.48 (1.24-1.76)	0.78 (0.75-0.82)	6.79 (6.30-7.32)	1.98 (1.84-2.13)	4.51 (4.12-4.94)
ECORE-BF	1.18 (1.13-1.23)	3.32 (3.13-3.52)	1.34 (1.12-1.60)	0.71 (0.68-0.74)	8.09 (7.55-8.68)	1.87 (1.75-2.01)	4.67 (4.27-5.11)
CUN BAE	1.11 (1.06-1.16)	3.79 (3.57-4.02)	1.35 (1.12-1.61)	0.71 (0.67-0.75)	8.18 (7.63-8.77)	1.83 (1.70-1.96)	4.66 (4.25-5.10)
Conicity index	2.97 (2.82-3.13)	ns	0.77 (0.61-0.96)	1.36 (1.30-1.43)	1.25 (1.14-1.37)	1.24 (1.13-1.36)	3.26 (3.08-3.46)
Waist to height ratio	3.83 (3.68-4.00)	1.11 (1.06-1.17)	1.38 (1.15-1.65)	0.91 (0.88-0.95)	3.38 (3.15-3.63)	1.80 (1.68-1.93)	5.50 (5.14-5.90)

In the multivariate analysis using binary logistic regression, male, age 50 years and older, social class III, tobacco use, non-heart-healthy eating and not performing regular physical activity were established as covariates.

It was observed that sex, alcohol, physical exercise and healthy food were the variables that affected all the parameters related to cardiovascular risk, whereby the effect of social class and tobacco was less powerful in general. The complete data set is presented in **table IV**.

Discussion

The most important finding of this study is the effect of alcohol consumption on the values of the different scales of overweight and obesity. The multivariate study shows that alcohol is one of the variables studied that most increases the risk of obesity.

This relationship between alcohol consumption and the development of obesity is observed in most of the studies reviewed. A European study of nearly 100,000 men and 159,000 women found a positive association between long-term alcohol consumption and abdominal and general adiposity in men, while in women the association was only found with abdominal adiposity²². Other studies assess the influence of different levels of

alcohol consumption and obesity, for example a study in 250,000 Chinese adults²³ showed that light drinking decreased the proportion of obese people while heavy drinking increased the number of obese people. An American study²⁴ indicated that men who consumed two or more drinks per day increased the risk of being overweight, whereas if they consumed four or more drinks per day, the risk of obesity increased. In the same study, women who consumed alcohol had a lower prevalence of obesity. An Australian study²⁵ of 534 men also showed an increase in obesity in heavy drinkers (5 or more drinks per day).

Other studies showed similar results, one in 7855 French men²⁶, another in 141 Korean workers²⁷, a Spanish study in almost 3000 people²⁸, another in Canadians²⁹, in Koreans³⁰ and in English³¹ showed similar results. A study of Ugandan adults³² found no association between alcohol consumption and obesity. The strengths of this study are the large sample size, almost 61,000 workers, and the large number of scales assessing overweight and obesity, namely eleven, including five scales predicting body fat.

The main limitation is that alcohol consumption was self-reported and could not be objectified. Moreover, it is only taken into account if the person consumes alcohol in a significant way, there is no graduation of consumption.

References

1. Silla Stael M, Rosón Hernández B. Evaluación del consumo de alcohol y diagnóstico de patrón de consumo. *Trastornos Adictivos*. 2009;11(3):191-9
2. Organización Mundial de la Salud. 2016. Obesidad y sobrepeso. Available at: <http://www.who.int/mediacentre/factsheets/fs311/es/>
3. Yeomans MR. Alcohol, appetite and energy balance: is alcohol intake a risk factor for obesity? *Physiology & behavior* 2010; 100(1):82-9.
4. Schrieks IC, Staffleu A, Griffioen-Roose S, de Graaf C, Witkamp RF, Boerigter-Rijneveld R, et al. Moderate alcohol consumption stimulates food intake and food reward of savoury foods. *Appetite* 2015; 89:77-83.
5. Kase CA, Piers AD, Schaumburg K, Forman EM, Butryn ML. La relación del consumo de alcohol para la pérdida de peso en el contexto del tratamiento de la pérdida de peso de comportamiento. *Apetito* 2016; 99:105-11.
6. Röjdmarm S, Calissendorff J, Brismar K. Alcohol ingestion decreases both diurnal and nocturnal secretion of leptin in healthy individuals. *Clinical endocrinology* 2001; 55(5):639-47.
7. Raben A, Agerholm-Larsen L, Flint A, Holst JJ, Astrup A. Meals with similar energy densities but rich in protein, fat, carbohydrate, or alcohol have different effects on energy expenditure and substrate metabolism but not on appetite and energy intake. *The American Journal of Clinical Nutrition* 2003; 77(1):91-100.
8. Yeomans MR, Caton S, Hetherington MM. Alcohol and food intake. *Current Opinion in Clinical Nutrition & Metabolic Care* 2003; 6(6):639-44.

9. Widdowson PS, Holman RB. Ethanol-Induced Increase in Endogenous Dopamine Release May Involve Endogenous Opiates. *Journal of neurochemistry* 1992;59(1):157-63.
10. Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev.* 2010;23(2):247-69.
11. Gómez-Ambrosi J, Silva C, Catalán V, Rodríguez A, Galofré JC, Escalada J, et al. Clinical usefulness of a new equation for estimating body fat. *Diabetes Care.* 2012;35(2):383-8.
12. Molina-Luque R, Romero-Saldaña M, Álvarez-Fernández C, Bennasar-Veny M, Álvarez-López Á, Molina-Recio G. Equation Córdoba: A Simplified Method for Estimation of Body Fat (ECORE-BF). *Int J Environ Res Public Health.* 2019;16(22):4529.
13. Mill-Ferreyra E, Cameno-Carrillo V, Saúl-Gordo H, Camí-Lavado MC. Estimation of the percentage of body fat based on the body mass index and the abdominal circumference: Palafolls Formula. *Semergen.* 2019;45(2):101-8.
14. Deurenberg P, Wetstrate JA, Seidell JC. Body mass index as a measure of body fatness: age- and sex- specific prediction formulas. *Br J Nutr* 1991; 65: 105-14.
15. RFM Woolcott OO, Bergman RN. Relative fat mass (RFM) as a new estimator of whole-body fat percentage-A cross-sectional study in American adults individuals. *Sci Rep.* 2018;8(1):10980.
16. Amato MC, Giordano C. Visceral adiposity index: an indicator of adipose tissue dysfunction. *Int J Endocrinol.* 2014; 2014:730827.
17. Andrade MD, Freitas MC, Sakumoto AM, Pappiani C, Andrade SC, Vieira VL, et al. Association of the conicity index with diabetes and hypertension in Brazilian women. *Arch Endocrinol Metab.* 2016;60(5):436-42.
18. Chang Y, Guo X, Chen Y, Guo L, Li Z, Yu S, et al. A body shape index and body roundness index: two new body indices to identify diabetes mellitus among rural populations in northeast China. *BMC Public Health.* 2015 19; 15:794.
19. Bertoli S, Leone A, Krakauer NY, Bedogni G, Vanzulli A, Redaelli VI, et al. Association of Body Shape Index (ABSI) with cardio-metabolic risk factors: A cross-sectional study of 6081 Caucasian adults. *PLoS One.* 2017 25;12(9): e0185013.
20. Rodríguez-Martos A, Gual A, Llopis Llacer JJ. La unidad de bebida estándar: un registro simplificado del consumo de bebidas alcohólicas. *Med Clin (Barc)* 1999; 112: 446-50
21. Domingo-Salvany A, Bacigalupe A, Carrasco JM, Espelt A, Ferrando J, Borrell C. Propuesta de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011. *Gac Sanit* 2013;27(3):263-72
22. Bergmann MM, Schütze M, Steffen A, Boeing H, Halkjaer J, Tjønneland A, et al. The association of lifetime alcohol use with measures of abdominal and general adiposity in a large-scale European cohort. *Eur J Clin Nutr.* 2011 Oct;65(10):1079-87.
23. Xu X, Zhou M, Gao RQ, Guo Y, Tian XC, Bian Z, et al. [Study on correlation between alcohol consumption and obesity in adults in China]. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2019 10;40(7):759-64.
24. Tayie FA, Beck GL. Alcoholic beverage consumption contributes to caloric and moisture intakes and body weight status. *Nutrition.* 2016 Jul-Aug;32(7-8):799-805.
25. Coulson CE, Williams LJ, Brennan SL, Berk M, Kotowicz MA, Lubman DI, Pasco JA. Alcohol consumption and body composition in a population-based sample of elderly Australian men. *Aging Clin Exp Res.* 2013 May;25(2):183-92.
26. Dumesnil C, Dauchet L, Ruidavets JB, Bingham A, Arveiler D, Ferrières J, et al. Alcohol consumption patterns and body weight. *Ann Nutr Metab.* 2013;62(2):91-7
27. Dumesnil C, Dauchet L, Ruidavets JB, Bingham A, Arveiler D, Ferrières J, et al. Alcohol consumption patterns and body weight. *Ann Nutr Metab.* 2013;62(2):91-7
28. Schröder H, Morales-Molina JA, Bermejo S, Barral D, Soler-Mandoli E, Grau M, et al. Relationship of abdominal obesity with alcohol consumption at population scale. *Eur J Nutr* 2007; 46:369-76
29. Traversy G, Chaput JP. Alcohol Consumption and Obesity: An Update. *Curr Obes Rep* (2015) 4:122-30
30. Park KY, Park HK, Hwang HS. Relationship between abdominal obesity and alcohol drinking pattern in normal-weight, middle-aged adults: the Korea National Health and Nutrition Examination Survey 2008–2013. *Public Health Nutrition:* 20(12), 2192-200
31. Adults. Shelton NJ, Knott CS. Association Between Alcohol Calorie Intake and Overweight and Obesity in English. *American Journal of Public Health* 2014;104(4):629-31
32. Tumwesigyea NM, Mutungi G, Bahendeka S, Wesonga R, Katureebe A, Biribawa C, et al. Alcohol consumption, hypertension and obesity: Relationship patterns along different age groups in Uganda. *Preventive Medicine Reports* 2020; 19:101141

The effectiveness of nutrition care training program to nurses of Intensive Care Unit on patient's nutritional consequences

La efectividad del programa de capacitación en atención nutricional para enfermeras de la unidad de cuidados intensivos sobre las consecuencias nutricionales del paciente

Fakhrudin Faizi¹ , Ali Bahramifar² , Masoud Sirati Nir³ ,
Hamid Soleymanzadeh⁴ , Abolfazl Rahimi⁵ 

1. Assistant Professor in Pain Research & Management, Nursing Faculty and Atherosclerosis Research Center, Baqiatallah University of Medical Sciences, Tehran, Iran. 2. Assistant Professor of Anesthesiology, Trauma Research Center, University of Medical Sciences, Iran. 3. Associated professor in Nursing Education, Nursing Faculty and Behavioral Science Research Center, Baqiatallah University of Medical Sciences, Tehran, Iran. 4. Nursing student of Nursing Faculty, Student Research Committee of Baqiatallah University of Medical Sciences, Tehran, Iran. 5. Associated professor in Nursing Education, Nursing Faculty and Behavioral Science Research Center, Baqiatallah University of Medical Sciences, Tehran, Iran.

Corresponding author

Abolfazl Rahimi

Faculty of Nursing, Baqiyatallah University of Medical Sciences,
Tehran, Iran.

E-mail: fazel123@yahoo.com

Received: 18 - I - 2021

Accepted: 21 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.70

Abstract

Objective: Malnutrition is a common problem among hospitalized patients. The problem is worse in patients under intensive care units. This study evaluated the effectiveness of nutritional care training in intensive care units and its effects on patients.

Methods: In the interventional study with parallel design 60 patients (30 in each group) of ICU were selected by available sampling amongst 104 hospitalized patients according to input/output criteria. The intervention was designed according to the Nutritional Care Guidelines of the American Society for Parenteral and Enteral Nutrition (ASPEN) and the American Association of Critical-care Nurses (AACN) then the nurses of the mentioned wards were trained for one month (4 one-hour sessions). The pre and post-intervention nutritional status of the patients were assessed using a checklist previously has ordered by the Ministry of Health (IR, Iran) to be applied in the patients. Both groups were homogeneous, and the collected data were analyzed applying the Kolmogorov-Smirnov, Mann-Whitney-U, and Friedman test using SPSS software ver19.

Results: There were no significant differences between the groups in terms of age, sex, body weight, APACHE score, admission/hospitalization, alcohol consumption, smoking, history of hospitalization, marital status, type of insurance, and surgery ($p < 0.05$). Results showed a significant reduction of nausea ($p = 0.001$), vomiting ($p = 0.0001$), constipation ($p = 0.002$), diarrhea ($p = 0.004$) but no significant in body weight gain and aspiration rate ($p < 0.05$).

Conclusion: Regarding the importance of nutrition and its effect on improving patients' condition, it is more highlighted that cohering to standard nutrition principles then continuous training of the nurses can lead to better patient outcomes.

Keywords: Malnutrition, Intensive Care Unit (ICU), APACHE, Nutritional Support.

Resumen

Introducción: La desnutrición es un problema común entre los pacientes hospitalizados. El problema se agrava en los pacientes sometidos a unidades de cuidados intensivos. Este estudio evaluó la eficacia de la formación en cuidados nutricionales en las unidades de cuidados intensivos y sus efectos en los pacientes.

Material y métodos: En el estudio de intervención con diseño paralelo se seleccionaron 60 pacientes (30 en cada grupo) de la UCI por muestreo disponible entre 104 pacientes hospitalizados según criterios de entrada/salida. La intervención se diseñó de acuerdo con las Guías de Cuidados Nutricionales de la Sociedad Americana de Nutrición Parenteral y Enteral (ASPEN) y de la Asociación Americana de Enfermeras de Cuidados Críticos (AACN) y luego se entrenó a las enfermeras de las salas mencionadas durante un mes (4 sesiones de una hora). Se evaluó el estado nutricional de los pacientes antes y después de la intervención utilizando una lista de comprobación que el Ministerio de Sanidad (IR, Irán) había ordenado previamente que se aplicara a los pacientes. Ambos grupos eran homogéneos, y los datos recogidos se analizaron aplicando las pruebas de Kolmogorov-Smirnov, Mann-Whitney-U y Friedman utilizando el software SPSS 19.0.

Resultados: No hubo diferencias significativas entre los grupos en cuanto a edad, sexo, peso corporal, puntuación APACHE, ingreso/hospitalización, consumo de alcohol, tabaquismo, antecedentes de hospitalización, estado civil, tipo de seguro y cirugía ($p < 0,05$). Los resultados mostraron una reducción significativa de las náuseas ($p = 0,001$), los vómitos ($p = 0,0001$), el estreñimiento ($p = 0,002$) y la diarrea ($p = 0,004$), pero no fueron significativos en el aumento de peso corporal ni en la tasa de aspiración ($p < 0,05$).

Conclusiones: En cuanto a la importancia de la nutrición y su efecto en la mejora del estado de los pacientes, se destaca que la coherencia con los principios de nutrición estándar y la formación continua de las enfermeras pueden conducir a mejores resultados en los pacientes.

Palabras clave: Malnutrición, Unidad de Cuidados Intensivos, APACHE, soporte nutricional

Introduction

Nutrition is one of the primary and physiological needs of human beings and is essential for the maintenance of life, growth, development, tissue repair, and the function of limbs and organs then cells changed when a person is hospitalized^{1,2}. Patients with high stress or severe injury are exposed to breakage of body proteins and energy storage loss, leading to the compromised treatment, infection increase, recovery delay, lasting hospitalization time, increased hospital costs, and mortality rate³⁻⁵. Malnutrition is more prevalent in ICU patients than in conventional care units^{6,7}. The term "malnutrition" implies inappropriate feeding. Though recently published data from developed countries report overfeeding and overestimating patients' nutritional needs, evermore received food volume has bettered patients' outcomes⁸⁻¹⁰, but we encounter some Iran controversies. While a few studies reporting the nutritional status is "better than other countries,"¹¹ and 62% of critical nurses have good performance in nutrition care¹², others say malnutrition (less than body requirements) doubled in discharge day in comparison to admission¹³, sometimes prepared nutritional solutions have less energy index but higher in bacterial colony count according to allowed amounts. At least 40% of patients in intensive care units do not have adequate nutritional support^{14,15} and finally, the patients' energy intake was lower than his/her requirements¹⁶ even if the various type of feeding was applied in terms of continuous, intermittent and or parenteral nutritional feeding methods¹⁷.

According to ASPEN and AACN, nurses are considered as the primary member of the nutrition team in intensive care units¹⁸, but the latest (2020) article in the field from a well-known Namazi Hospital of Shiraz indicating that more than 75% of ICU nurses have not adequate knowledge in enteral feeding¹⁹ warning all medicals to stir in the field.

The study evaluates a nutritional support program's effectiveness based on ASPEN and AACN to ICU nurses on patients' nutritional consequences.

Materials and methods

The work derived from an MSc thesis carried out in the Nursing Faculty of Baqiyatallah University of Medical Sciences with ethical code of IR.BMSU.Rec.1397.020.

This clinical trial study was done with two parallel-group designs at the intensive care unit of Baqiyatallah Hospital in Tehran, Iran. In the study, the medical intensive care unit (ICU3) and all nurses working in this unit were selected based on research according to input criteria through available sampling. Inclusion

criteria: working in the unit (for nurses), GCS 15 and ability to verbal communication, age over 18 years, and hospitalization stay probably would last at least for one week (for patients). Exclusion criteria: patient's death/transfer or underwent mechanical ventilation within one week of sampling, hospitalization for more than one month, patient's discharge before the end of the first week.

Considering the difference between the mean and standard deviation of the previous studies' variables, the total required sample size was estimated 56 samples using Altman plot with $\alpha = 0.05$ and $\beta = 0.10$ and power =90 %. Based on the calculation, 30 patients were randomly assigned to each group with 10% attrition²⁰. The collected data were entered into SPSS statistical software version 19 and analyzed using descriptive and analytic statistics. The Kolmogorov-Smirnov test was used to determine the normality of the data then Mann-Whitney-U and Friedman tests were applied to comparison using SPSS software ver19.

At first, a training program for nurses was designed, and educational material was provided using ASPEN and AACN guidelines, including the following topics:

- Enteral nutrition and problems (nausea and vomiting, diarrhea, constipation, pulmonary aspiration and prohibition of enteral nutrition and precautions
- Parenteral nutrition
- Enteral nutrition in specific diseases
- Short and long term enteral feeding methods
- Determining nutritional needs
- And positioning of the patients.

They were receiving an agreement letter of action from the deputy for IR's research and ethical code.BMSU. Rec.1397.020, the first phase of sampling run for 76 days to obtain 30 patients. Basic relevant data and nutritional consequences of patients, including APACHE score, body weight, nausea, vomiting, constipation, diarrhea, and pulmonary aspiration, were assessed using a checklist (extracted from the specialized evaluation questionnaire of nutrition status of the Ministry of Health, Iran) and patients who did not have the input and output conditions of the study were excluded from the study.

In the second phase, all nurses responsible for caring for patients in the unit participated in a 4 weeks training period containing 4 one-hour sessions. The educational materials taken from ASPEN and AACN, educational pamphlets, and related PowerPoint files have been given to the nurses alongside the sessions.

In the third (post-training) phase, 30 patients were selected again during 74 days according to input criteria and full accordant to the first phase.

Results

Dropouts

We primarily included 104 patients in the study based on the inclusion criteria. Twenty-first out of 51 patients in the comparison and 23 out of 53 in the intervention group were excluded due to transfer to other wards or dying.

Demographics

Comparing the two groups' demographics, there was no significant difference in terms of sex, admission/hospitalization, marital status, type of insurance support, literacy level, employment status, APACHE score, and the patients' bodyweight ($p < 0.05$). The majority of the sample (65%) were in the elementary level of literacy, and 56% were female. Comparison between the two groups is summarized in **tables I and II**.

APACHE score

Since the groups were homogeneous in terms of demographic information, the APACHE score was used to homogenize the patients accurately, which evaluates the level of the patient's physiological status that there was no statistically significant difference (**Table II**) ($P > 0.05$).

Bodyweight

The study's main target was increased day-to-day in the intervention group in comparison and weight loss was reduced, but it was not significant ($P > 0.05$) as shown in **table III**.

Nausea, Vomiting, Diarrhea, Constipation and pulmonary aspiration:

The intervention group reported more nausea rate reduction than the comparison group considering 1st, 4th and 7th day of hospitalization in ICU ($P = 0.001$). The group's total nausea was significantly reduced in contrast to the comparison group ($P = 0.0001$). The reduction of vomiting rate comparing the two groups during the 3-time measurement was not significant ($p > 0.05$), but total vomiting rate reduction was significant considering the comparison group on day 7th of hospitalization ($p < 0.0001$). The same occurred for diarrhea status in the intervention group ($p > 0.05$), but the group has reported

less diarrhea rate than the comparison group on day 7 of hospitalization ($p < 0.002$). The intervention group on 7th day was less constipated than the comparison group ($p > 0.004$), but the rate in the groups did not significantly differ comparing the 3-time measuring ($p > 0.05$). Pulmonary aspiration rate differences were not significant in 3-time measuring and compared to the comparison group on the 7th day of hospitalization ($p > 0.5$). Details are summarized in **table IV**.

Discussion

After training ICU nurses on nutrition in the present study, the intervention group reported lower nausea, vomiting, diarrhea, and constipation but no more pulmonary aspiration rate than the comparison group. Day-by-day improvement in the intervention group was occurred comparing the comparison group, but no significant differences were observed in terms of diarrhea, constipation, and pulmonary aspiration.

Accordingly, Ros et al. (2009) conducted a review and concluded that a multidisciplinary approach should be established to improve patients' nutrition in ICUs then critical care nurses are well placed on the core of such a line²⁰. Additionally, Elpern et al. (2004) reported a significant reduction in nausea, vomiting, and aspiration rate during the 3 months of enteral feeding on patients hospitalized in medical ICU. They used the "precautionary interruptions" technique to decreased aspiration rate²¹ as we applied in our study.

We summarized ASPEN and AACN guidelines in the forms of pamphlets and PowerPoint files in the ward's bookshelves accessible to the nurses' to promote their knowledge. In an observational study, Mistry (2019) assessed satisfactory level of knowledge, unsatisfactory level of practice, and positive attitude of nasogastric tube feeding of ICU nurses in Egypt, recommending that the nursing procedure book be available ICUs²².

Incomplete adherence to the standards repeatedly is frequently reported in indoor studies. Al-Jalali et al.

Table I: The distribution of demographics and comparison between the groups.

Variable	Frequency	Comparison group Number (%)	Intervention group Number (%)	Total Number (%)	The significance Level (P Value)
Literacy level	Elementary	20 (66.7)	19 (63.3)	39 (65)	(P > 0.05)
	Middle	0 (0)	3 (10)	3 (5)	
	Under the diploma	1 (3.3)	1 (3.3)	2 (3.3)	
	Diploma	7 (23.3)	3 (10)	10 (16.65)	
	Academic	2 (6.6)	4 (13.3)	6 (10)	
Gender	Male	12 (40)	14 (46.7)	26 (43.3)	(P > 0.05)
	Female	18 (60)	16 (53.3)	34 (56.7)	
Type of admission	Hospital wards	13 (43.3)	16 (53.3)	29 (48.3)	(P > 0.05)
	Emergency	17 (56.7)	14 (46.7)	31 (51.7)	

Table II: The mean and standard deviation of the APACHE score.

Groups and frequency ↓ Variable →	Comparison group	Intervention group	Significance Level (P-Value)
Number of patients	30	30	P< 0.05
The mean APACHE score	18.73	17.36	
Standard deviation	6.8	7.1	

Table III: Comparison of weight between the comparison and intervention groups.

Bod Weight → ↓ Time of measuring	Mean (SD) (kg)		Significance Level
	Comparison group	Intervention group	
First day in ICU	67.2 (12.8)	68.3(11)	P< 0.05
Fourth day in ICU	66.7 (12.6)	68.1(10.4)	P< 0.05
Seventh day in ICU	66.2 (13.2)	67.9(10.3)	P< 0.05
Difference between the 1st and 7th day	0.9	0.3	P< 0.05
Significance Level	P< 0.05	P< 0.05	

Table IV: Comparing the frequency of nausea, vomiting, constipation, diarrhea, and aspiration in two comparison and intervention groups.

Variable	First day in ICU		4th day in ICU		7th day in ICU		Significance Level (P-Value)	
	Comparison group % (time)	Intervention group	Comparison group	Intervention group	Comparison group	Intervention group		
Nausea (times)	No	15 (50)	17 (56.7)	12 (40)	26 (86.7)	14 (46.7)	27 (90)	Friedman test† P = 0.001 Mann-Whitney‡ P = 0.0001
	Once	1 (3.3)	1 (3.3)	7 (23.3)	1 (3.3)	10 (33.3)	1 (3.3)	
	Twice	7 (23.3)	8 (26.7)	10 (33.3)	10 (33.3)	5 (16.7)	2 (6.7)	
	Three	5 (16.7)	4 (13.3)	1 (3.3)	0	1 (3.3)	0	
	Four	2 (6.7)	0	0	0	0	0	
Vomiting (times)	No	16 (53.3)	24 (80)	17 (56.7)	28 (93.3)	20 (66.7)	30 (100)	Friedman test P<0.05 Mann-Whitney P = 0.0001
	Once	26.7(8)	3 (10)	10 (33.3)	1 (3.3)	7 (23.3)	0	
	Twice	4 (13.3)	3 (10)	3 (10)	1 (3.3)	3 (10)	0	
	Three	1 (3.3)	0	0	0	0	0	
	Four	1 (3.3)	0	0	0	0	0	
Diarrhea	No	20 (66.7)	25 (83.3)	22 (73.3)	26 (86.7)	20 (66.7)	29 (96.7)	Friedman test P >0.05 Mann-Whitney P = 0.002
	Once	5 (16.7)	4 (13.3)	6 (20)	4 (13.3)	6 (20)	1 (3.3)	
	Twice	4 (13.3)	1 (3.3)	2 (6.7)	0	4 (13.3)	0	
	Three	1 (3.3)	0	0	0	0	0	
	Four	0	0	0	0	0	0	
Constipation	Yes	4 (13.3)	4 (13.3)	3 (10)	4 (13.3)	5 (16.7)	2 (6.7)	Friedman test P>0.05 Mann-Whitney P = 0.004
	No	26 (86.7)	26 (86.7)	27 (90)	26 (86.7)	25 (83.3)	28 (93.3)	
Aspiration	Yes	9 (30)	2 (6.7)	11 (36.7)	2 (6.7)	8 (26.7)	2 (6.7)	Friedman test P > 0.05 Mann-Whitney P > 0.05
	No	21 (70)	28 (93.3)	19 (63.3)	28 (93.3)	22 (73.3)	28 (93.3)	

† Friedman test to compare 3 times of measurement in the two groups; ‡Mann-Whitney-U to compare between the two group

(2019) from North Khorasan province reported merely 86% conformity to standard feeding was observed “during tube feeding” but the conformity rate reduced to 3.8% and 2.3% in pre and post feeding phases respectively highlighting a crucial need to adherence to standards of feeding²³ as previously reported by Ashuri et al. (2012) mentioning the mean score of the measures (during, pre and post phases) in gastrostomy feeding was significantly lower than standards and concluded a comprehensive training program is needed both to train the nurses and the patients²⁴.

Although Rubin et al.. (2019) reported a one-day held workshop for community nurses could significantly improve their knowledge about enteral feeding²⁵. However, to obtain more effectiveness, our training program was designed to be run for a month (one session per week) to let the nurses review and practice the educational reminder pamphlets. The positioning of the patients was the last topic our training program

based on ASPEN and AACN to attain adequate patient’s intake^{1,2}, Rezaee et al. (2018) accordantly reported positioning the patients on the right side after enteral feeding resulted in lower Gastric Residual Volume (GRV) improving patient’s condition ²⁶.

According to AACN and ASPEN, we raised the patient’s enteral intake to 500 mL of gavage each time if there was no nausea and vomiting, and there was no significant difference considering the comparison group. More studies have rejected any relation between pulmonary aspiration rate and increased GRV^{27,28}, but more nurses give enteral feeding if GRV measured is less than 250cc in fear of aspiration pneumonia²⁹.

According to the study, it was found that patients’ weight loss has been reduced by increasing the level of nurses’ awareness AACN and ASPEN guidelines accordant to Nematy et al. (2012) from Ghaem Educational Hospital reporting a slight improvement in patient’s weight and

BMI during a hospital stay³⁰, but the finding is discordant to more reported studies in the country as Kimiaei et al. (2017) echoed a significant reduction in BMI and body weight in a couple of weeks of ICU stay³¹ or Hoseini et al. (2006) that reported a significant reduction in BMI of patients in comparison to admission data at Shariati Educational Hospital of Tehran³².

Conclusion

Educating nutrition support to ICU nurses and adherence to standard principles such as ASPEN and AACN

improved patients' outcomes, decreasing nausea, vomiting, diarrhea, constipation, weight loss, and no a significant increase in aspiration rates. It is recommended that nutritional support education should be a primary concern of stakeholders in the country.

Acknowledgments

Authors like to thank Baqiyatallah University of Medical Sciences, Tehran, Iran

References

1. Chulay M, Burns S. AACN essentials of critical care nursing pocket handbook: McGraw-Hill Professional; 2010.
2. McClave SA, Martindale RG, Vanek VW, McCarthy M, Roberts P, Taylor B, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). *Journal of Parenteral and Enteral Nutrition*. 2009;33(3):277-316.
3. Alberda C, Graf A, McCargar L. Malnutrition: Etiology, consequences, and assessment of a patient at risk. *Best Practice & Research Clinical Gastroenterology*. 2006;20(3):419-39.
4. Wyszynski DF, Perman M, Crivelli A. Prevalence of hospital malnutrition in Argentina: preliminary results of a population-based study. *Nutrition*. 2003;19(2):115-9.
5. Wischmeyer PE. Malnutrition in the acutely ill patient: is it more than just protein and energy? *South African Journal of Clinical Nutrition*. 2011;24(3):S1-S7.
6. O'meara D, Mireles-Cabodevila E, Frame F, Hummell AC, Hammel J, Dweik RA, et al. Evaluation of delivery of enteral nutrition in critically ill patients receiving mechanical ventilation. *American Journal of Critical Care*. 2008;17(1):53-61.
7. Doig GS, Simpson F, Finfer S, Delaney A, Davies AR, Mitchell I, et al. Effect of evidence-based feeding guidelines on mortality of critically ill adults: a cluster randomized controlled trial. *JAMA*. 2008;300(23):2731-41.
8. Walker R, Probstfeld L, Tucker A. Hang Height of Enteral Nutrition Influences the Delivery of Enteral Nutrition. *Nutrition in clinical practice: official publication of the American Society for Parenteral and Enteral Nutrition*. 2018;33(1):151-7.
9. Amato L, Fusco D, Acampora A, Bontempi K, Rosa AC, Colais P, et al. Volume and health outcomes: evidence from systematic reviews and from evaluation of Italian hospital data. *Epidemiologia e prevenzione*. 2017;41(5-6 (Suppl 2)):1-128.
10. ApSimon M, Johnston C, Winder B, Cohen SS, Hopkins B. Narrowing the Protein Deficit Gap in Critically Ill Patients Using a Very High-Protein Enteral Formula. *Nutrition in Clinical Practice*. 2020;Feb.
11. Javid Mishamandani Z, Norouzy A, Hashemian SM, Khoundabi B, Rezaeisadrabadi M, Safarian M, et al. Nutritional status of patients hospitalized in the intensive care unit: A comprehensive report from Iranian hospitals, 2018. *Journal of Critical Care*. 2019;54:151-8.
12. Taherkhani A, Shahrokhi A, Barikani A, Rashvand F. Compare the Quality of Nursing Care Related to Enteral Nutrition with Standards in Patients at Intensive Care Unit (ICU) in Hospitals of Qazvin University of Medical Sciences. *Alborz University Medical Journal*. 2019;8(4):377-86.
13. Hejazi N, Mazloom Z, Zand F, Rezaianzadeh A, Amini A. Nutritional Assessment in Critically Ill Patients. *Iran J Med Sci*. 2016;41(3):171-9.
14. Moghadam AD, Chabok SY, Ramezani F, Leili EK, Rahimi V. Evaluation of nutritional quality and microbial contamination of enteral feeding solutions in hospitalized patients referred to neurosurgical ICU of Poursina Hospital in Rasht. *Pejouhandeh*. 2010;15(5):213-9.
15. Khalili H, Mojtahedzadeh M, Oveysi M, Tavakoli F. Do critically ill patients receive adequate nutritional support? *Research Bulletin of Medical Sciences (PEJOUHANDEH)*. 2004;9(1(37)):45-50.
16. Davari M, Moludi J, Jafarabadi MA, Ahmadi-Nejad M, Sanaie S, Aref-Hosseini S-R. Impact of clinical factors on calorie and protein intakes during lcu stay in adults trauma patients: results from a prospective observational study. *International journal of burns and trauma*. 2019;9(3):59-65.
17. Mazaherpur S, Khatony A, Abdi A, Pasdar Y, Najafi F. The Effect of continuous enteral nutrition on nutrition indices, compared to the intermittent and combination enteral nutrition in traumatic brain injury patients. *Journal of clinical and diagnostic research: JCDR*. 2016;10(10):1-5.
18. Singer P, Berger MM, Van den Berghe G, Biolo G, Calder P, Forbes A, et al. ESPEN guidelines on parenteral nutrition: intensive care. *Clinical nutrition*. 2009;28(4):387-400.

19. Jamshidi S, Hejazi N, Mazloom Z. ICU Nurses' Knowledge about Enteral Feeding in Critically Ill Patients in Nemazee Hospital in Shiraz, Iran. *Int J Nutr Sci March*. 2020;5(1):2-6.
20. Ros C, McNeill L, Bennett P. Review: nurses can improve patient nutrition in intensive care. *Journal of Clinical Nursing*. 2009;18(17):2406-15.
21. Elpern EH, Stutz L, Peterson S, Gurka DP, Skipper A. Outcomes associated with enteral tube feedings in a medical intensive care unit. *American Journal of Critical Care*. 2004;13(3):221-7.
22. Mistry MV. Knowledge regarding Total Parenteral Nutrition (TPN) among the ICU Nurses in Selected Hospital of Pune City. *Indian Journal of Public Health Research & Development*. 2019;10(7).
23. Al-Jalil T, Gray G, Rasouli M, Hoseini Azizi T, Hejazi S-S. Auditing of enteral nutrition nursing care in critical care patients. *Journal of Nursing Practice Today*. 2019;6(1):25-18.
24. Ashouri E, Fatehi N. A comparison of performing tube feeding with the standard procedures at selected educational and treatment centers of Isfahan University of Medical Sciences, Iran. *Iranian journal of nursing and midwifery research*. 2012;17(2 Suppl1):S80.
25. Rudin NMN, editor Community Nurses' Knowledge and Nursing Care Skill on Enteral Nutrition in caring for Critically Ill Patient in Kuantan and Pekan, Pahang: An Interventional Study. The 4th International Conference for Global Health (ICGH); 2019.
26. Rezaee J, Kadivarian H, Abdi A, Rezaei M, Karimpour H, Rezaei S. The Effect of Body Position on Gavage Residual Volume of Gastric in Intensive Care Units Patients. *IRAN JOURNAL OF NURSING (IJN)*. 2018;30(110):58-67.
27. Metheny NA, Schallom L, Oliver DA, Clouse RE. Gastric Residual Volume and Aspiration in Critically Ill Patients Receiving Gastric Feedings. *American Journal of Critical Care*. 2008;17(6):512-19.
28. Mizock BA. Risk of aspiration in patients on enteral nutrition: Frequency, relevance, relation to pneumonia, risk factors, and strategies for risk reduction. *Current Gastroenterology Reports*. 2007;9(4):338.
29. Faramarzi E, Mahmoodpoor A, Hamishehkar H, Shadvar K, Iranpour A, Sabzevari T, et al. Effect of gastric residual volume monitoring on incidence of ventilator-associated pneumonia in mechanically ventilated patients admitted to intensive care unit. *Pakistan Journal of Medical Sciences*. 2020;36(2).
30. Nematy M, Mohajeri SAR, Moghadam SA, Safarian M, Norouzy A, Parizadeh SMR, et al. Nutritional status in intensive care unit patients: a prospective clinical cohort pilot study. *Mediterranean Journal of Nutrition and Metabolism*. 2012;5(2):163-8.
31. Kimiaei-Asadi H, Tavakolitalab A. The assessment of the malnutrition in traumatic ICU patients in Iran. *Electron Physician*. 2017;9(6):4689-93.
32. Hosseini S, Amirkalali B, Nayebe N, Heshmat R, Larjani B. Nutrition Status of Patients During Hospitalization, Tehran, Iran. *Nutrition in Clinical Practice*. 2006;21(5):518-21.

The anti-tumor molecular mechanisms of mentioned fruits in the holy Quran; a systematic review

Los mecanismos moleculares antitumorales de las frutas mencionadas en el sagrado Corán; una revisión sistemática

Atefeh Ashtari^{1,4} , Firoozeh Niazvand³ , Narges Chamkouri²

1. Cellular & Molecular Research Center, Medical basic sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

2. Assistant Professor, Department of Anatomical Sciences, Faculty of Medicine, Abadan University of Medical Sciences, Abadan, Iran.

3. Assistant Professor, Department of Biochemistry, Faculty of Medicine, Abadan University of Medical Sciences, Abadan, Iran.

4. Department of Anatomical Sciences, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Corresponding author

Firoozeh Niazvand

Faculty of Medicine, Abadan University of Medical Sciences,
Abadan, Iran.

E-mail: niazvandf@gmail.com

Received: 1 - II - 2021

Accepted: 30 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.76

Abstract

Background: Various fruits are discussed in many verses of the Qur'an. Fruits such as pomegranates, grapes, olives, figs, and dates are considered gifts from God because of their myriad benefits. On the other hand, these fruits play an essential role in treating diseases such as cancer. Cancer is the second leading cause of death in developed countries, resulting in the uncontrolled division of cells. Due to high amounts of useful antioxidant compounds, these fruits kill cancer cells by stimulating cell death mechanisms such as apoptosis and necroptosis. This review study investigates the anti-cancer properties of the fruits mentioned in the Quran from a cellular and molecular perspective.

Methods: In this review study, conducted and available researches in databases such as ISI, PubMed, Scopus, Google Scholar, ISC, and SID have been used according to keywords.

Results: We examined the association of these fruits with the mechanism of cell death in cancer cells. As a result of analyzing these fruits' anti-cancer properties, it has been found that they can play an essential role in cancer prevention and treatment via different molecular mechanisms.

Conclusion: We found that the interpretations of the Holy Quran, which is the reference book in Islam, are entirely consistent with the new findings of medical sciences. So, there are many facts in the Quran that need further study and research.

Keywords: Holy Quran fruits, Cancer, Cell death, Molecular Signalling pathway.

Resumen

Antecedentes: En muchos versículos del Corán se habla de varias frutas. Frutas como las granadas, las uvas, las aceitunas, los higos y los dátiles se consideran regalos de Dios por sus innumerables beneficios. Por otra parte, estas frutas desempeñan un papel esencial en el tratamiento de enfermedades como el cáncer. El cáncer es la segunda causa de muerte en los países desarrollados y se debe a la división incontrolada de las células. Debido a las elevadas cantidades de compuestos antioxidantes útiles, estas frutas eliminan las células cancerosas estimulando mecanismos de muerte celular como la apoptosis y la necroptosis. Este estudio de revisión investiga las propiedades anticancerígenas de las frutas mencionadas en el Corán desde una perspectiva celular y molecular.

Métodos: En este estudio de revisión se han utilizado investigaciones realizadas y disponibles en bases de datos como ISI, PubMed, Scopus, Google Scholar, ISC y SID según palabras clave.

Resultados: Examinamos la asociación de estas frutas con el mecanismo de muerte celular en las células cancerosas. Como resultado del análisis de las propiedades anticancerígenas de estas frutas, se ha descubierto que pueden desempeñar un papel esencial en la prevención y el tratamiento del cáncer a través de diferentes mecanismos moleculares.

Conclusión: Hemos comprobado que las interpretaciones del Sagrado Corán, que es el libro de referencia en el Islam, son totalmente coherentes con los nuevos descubrimientos de las ciencias médicas. Por lo tanto, hay muchos hechos en el Corán que necesitan más estudio e investigación.

Palabras clave: Frutos del Sagrado Corán, Cáncer, Muerte celular, Vía de señalización molecular.

Introduction

In the holy Quran, special attention is paid to nutrition. The Holy Quran is available as a religious book for Muslims in different languages. It has 114 suras, some of which were revealed in Mecca and some in Medina. Each surah is divided into verses. The Quran is one of the best reference books that the importance of fruits can be read in its various chapters, such as Al-Muminun, Al-Rahman, Al-Baqarah, etc. Considering that the Holy Quran has recommended the use of different fruits, but some fruits have been given special attention as a blessing from God and a heavenly gift, which is probably due to their higher nutritional value than other fruits, including; Grapes, pomegranates, dates, figs, and olives¹. Cancer is the uncontrolled growth of abnormal cells anywhere in the body. Cells become cancerous due to the accumulation of defects or mutations in their DNA. Congenital infections, environmental factors, and poor lifestyle choices such as smoking and heavy alcohol use can also damage DNA and lead to cancer. If a cell is severely damaged and cannot repair itself, it undergoes programmed cell death or apoptosis. Cancer disease occurs when damaged cells grow, divide, and spread abnormally instead of self-destructing as they should². Millions of people worldwide are diagnosed with cancer and, it is estimated that by 2025 this number will reach about 20 million people³. Therefore, it is essential to know the drug to prevent and treat cancer.

Methodology

In this review study, conducted and available researches in databases such as ISI, PubMed, Scopus, Google Scholar, ISC, and SID have been used according to keywords: Holy Quran fruits, Cancer, Cell death, Molecular Signalling pathway. The present study is an overview of some properties of the fruits mentioned in the Holy Quran and their application to treat various cancers. The direct relationship between nutrition and cancer has been studied and proven in many studies. Diet can affect the tumor's symptoms, the response to patients' treatment, and the prognosis of the disease⁴.

In the mentioned fruits in the Quran, there are polyphenolic compounds that have significant anti-cancer activity. Several studies have demonstrated that these fruits and their constituents have different amounts of polyphenolic compounds in the last few decades, including; ellagitannins, ellagic acid, and other flavonoids quercetin kaempferol, myricetin, and luteolin. In recent years, the consumption of these fruits has been considered in cancer patients⁵. Additionally, several in vitro and in vivo studies have shown that the combination of natural polyphenols with chemotherapeutics can increase the anti-cancer efficacy, reduce the side effects

of chemotherapy and overcome the chemo- or radio-resistant cancer cells.

Results

Apoptosis

Cell death and cell cycle control are two critical factors in cancer cell growth progression or inhibition. Apoptosis is a type of regulated cell death program that can happen via various pathways in response to different stimuli and characterize by Deoxyribonucleic acid (DNA) fragmentation, nuclear condensation, and membrane blebbing, and cell shrinkage. A group of proteases called caspases are responsible for this action by activating these pro-enzymes via proteolytic cleavage hence disintegrate cells into apoptotic bodies. Two distinct apoptosis pathways are available, typically the extrinsic and intrinsic pathways. The intrinsic pathway (mitochondrial pathway) is usually activated in response to DNA fragmentation, chromatin degradation, protein cross-linking, and formation of apoptotic bodies wherewith extrinsic pathway is induced by death receptor-ligand binding (fas ligand (FasL) and tumor necrosis factor-alpha (TNF- α))⁶. After DNA damage, the p53 gene is activated and promotes the high expression of pro-apoptotic regulator, Bcl-2-associated X protein (Bax), and low anti-apoptotic gene expression B-cell lymphoma 2 (Bcl-2). Finally, the Bcl-2 family proteins' modulation initiates caspases cascade reaction and activates caspase-3 resulting in nuclear apoptosis⁷.

Necroptosis

Recent studies suggest that programmed cell death is not limited to caspase-dependent apoptosis but includes necroptosis, a form of necrotic death governed by receptor-interacting protein kinase 1 (RIPK1), receptor-interacting protein kinase 3 (RIPK3), and mixed lineage kinase domain-like (MLKL). Necroptosis is a vital cell killing mechanism that responds to cellular oxidative stress or blocked apoptosis and can be induced by inflammatory cytokines or chemotherapeutic drugs. At the signaling pathway, necroptosis is caspase-independent and signals by RIPK1, RIPK3, and MLKL, although apoptosis requires caspase activation and is mediated by interplays of the Bcl-2 family proteins or activation of death receptors⁸.

Fruits properties

Pomegranate

Pomegranate (*Punica granatum*) is the fruit of a tree belonging to the family Lythraceae. It is also cultivated in parts of Asia and the United States. The different parts of this fruit, including its seeds, root, bark, and leaves, have healing properties. Hydrolyzable tannins (punicalagin, pedunculagin, punicalin, gallagic acid, ellagic acid,

and esters of glucose) and anthocyanins (delphinidin-3-glucoside, cyanidin-3-glucoside, delphinidin-3, 5-diglucoside, cyanidin-3, 5-diglucoside, pelargonidin-3, 5-diglucoside, and pelargonidin-3-glucoside) among the most important identified contents are pomegranate seeds⁹. Some antioxidants have been found in pomegranates, such as butylated hydroxyanisole and Trolox; it is significantly higher than green tea¹⁰. Medicinal products and supplements of pomegranate fruit have been considered to treat various cancers¹¹.

Grape

Grape (*Vitis vinifera*) is one of the world's most commonly consumed fruits. The beneficial effects of grape and relevant grape-derived food products are believed to be related to various bioactive components in grapes¹². One major group of these components is phenolic antioxidants, including anthocyanins, catechins, resveratrol, phenolic acids, and procyanidins. Flavonoids constitute the majority of phenolic compounds (65–76%) in grapes. In red grapes, anthocyanins are the primary group of flavonoids¹¹. Most grape phenolic antioxidants are distributed in grape skins or seeds. For instance, resveratrol, anthocyanins, and catechins are concentrated in the skin, while procyanidins are concentrated in grape seeds¹³. Grape antioxidants could act as free radical scavengers, and chelating agents reduce physiological reactive oxygen species (ROS). ROS is an essential mediator of apoptosis since apoptosis initiation and regulation are associated with modifications in the oxidative environment¹⁴. Grapes contain potent flavonoids such as myricetin and quercetin that help protect the cells against free radicals' harmful effects¹⁵. Previous studies have shown that myricetin has anti-cancer effects on different cancer cells through various cell death mechanisms¹⁵.

Olive

The olive, known by *Olea europaea*, is a species of small tree in the family Oleaceae. In the Quran, the olive tree has a long history of medicinal and nutritional values¹⁶. Olive oil chemicals can be classified into two groups of saponifiers and non-saponifiers, from 90-99% and 0.4-5% of the oil. The most essential Saponifiers compounds are free fatty acids and their derivatives such as mono- and diacylglycerols, phosphatides, waxes, and esters. Olive oil polyphenols, especially hydroxytyrosol, tyrosol and their derivatives oleuropein, oleoresin and oleocanthal, express anti-cancer activity on different cancer cells. These polyphenolic compounds can act on gene expression that controls proliferation, apoptosis, and differentiation of cancer cells. The concentrations are easily reachable after the usual intake of olive oil¹⁶.

Fig

The fig (common fig), known by the scientific name *Ficus carica*, is belongs to the family Moraceae. Fig has long been used as a cancer treatment in different cultures

and is one of the Quran's fruits. Many scientific studies have used in vitro and in vivo methods to point out this natural medicine's anti-cancer properties. It is divided into three groups based on their geographical distribution, mainly Central and South America, Asia, Australasia, and Africa. Each part of the fig tree is used to treat various diseases such as cuts and wounds, diarrhea, cholera, mumps, jaundice, and cancer⁶. *Ficus carica* leaves and fruits contain active polyphenolic compounds and their derivatives. Therefore, they are considered an anti-cancer agent. Quercetin and luteolin are the main phenolic compounds found in fig leaves. Quercetin can stimulate the apoptosis of colon cancer cells (Caco-2 and HT-29) and leukemia cancer cells (HL-60) by stimulating the release of cytochrome c from mitochondria¹⁷.

Date

The date or date palm, scientifically known by the name *Phoenix dactylifera*, is the oldest and most authentic tree in southwest Asia and North Africa. The most important quality features to grade dates are color, flavor (sugar level), moisture (26-30%), and absence of defects such as insect, damage, cracks, and surface damage. The date fruit is a good source of valuable nutrients. It is rich in carbohydrates, dietary fibers, proteins, minerals, and vitamin B complexes, such as thiamine (B1), riboflavin (B2), niacin (B3), pantothenic (B5), pyridoxine (B6), and folate (B9).

Essential Minerals in date fruits are calcium, iron, magnesium, selenium, copper, phosphorus, potassium, zinc, sulfur, cobalt, fluorine, manganese, and boron¹⁸. The aglycone metabolites of Ajwa dates such as luteolin, myricetin, apigenin, quercetin, and petunidin have been reported to induce apoptosis in cancers¹⁹. The dates mentioned in the Holy Quran are known as a popular food among the people. "A fresh date tree falls to the ground, shaking its trunk"¹.

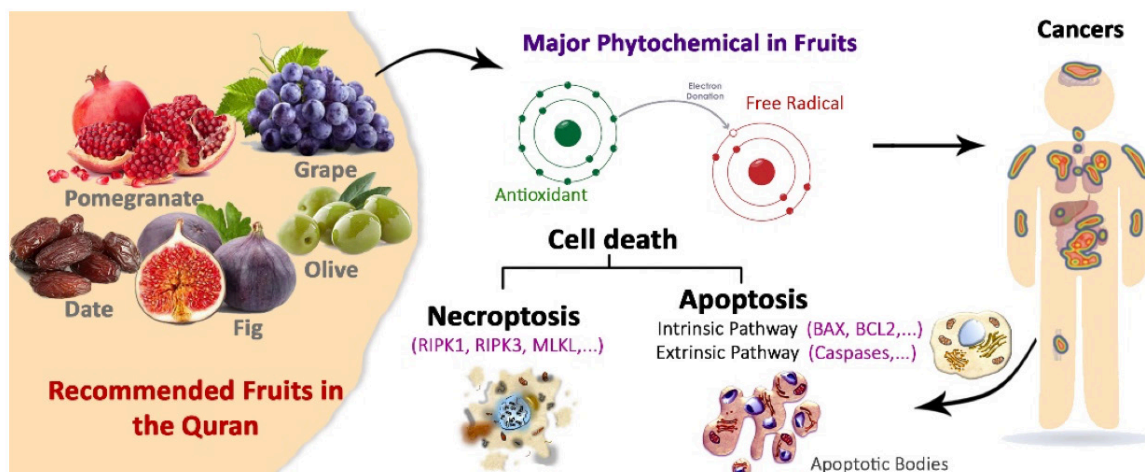
The effect of the mentioned fruits in the Holy Quran on different cancer cells' molecular mechanisms is described here (**Figure 1**).

Fruits anti-cancer activities

Breast cancer

The second most common cancer in women worldwide is breast cancer. Studies show the beneficial effects of pomegranate products on the process of breast cancer. In vivo research of breast cancer cells of the estrogen-dependent type has been²⁰ demonstrated that methanolic pomegranate extract has a modulating effect on estrogen deficiency in the absence of estrogen inhibits the growth of these cells²¹. Another study shows that the compounds in pomegranate extract can affect the expression of pro-apoptotic and anti-apoptotic genes (Bax/Bcl-2 ratio) and cascading waterfall (cytochrome c, Caspase-3, caspase-7, caspase-9) and eventually, by regulating the expression of these genes, it increases

Figure 1: The effect of the mentioned fruits in the Holy Quran on the molecular mechanisms of different cancer cells.



apoptosis²². Since high expression of aromatase (an enzyme that converts androgen to estrogen) is an essential factor in the development of breast cancer, and inhibition of aromatase/estrogen biosynthesis is considered as a therapeutic potential for this cancer, on the other hand, grape juice was the most effective in inhibiting the activity of human aromatase (methanol extract of grape juice and red wine suppresses aromatase in a dose-dependent)²³. Quercetin induced breast cancer cell apoptosis by modulating signaling pathways (protein kinase B (AKT), nuclear factor-kappa B (NF- κ B)) or regulatory molecules associated with apoptosis (p53, Bcl-2 family, FasL)²⁴. Luteolin inhibited metastatic breast cancer cell lines by reducing vascular endothelial growth factor (VEGF)²⁵. Quercetin has also been found to modulate the phosphoinositide 3-kinases (PI3K)/AKT/ mammalian target of rapamycin (mTOR) signaling pathway. The flavonoid has structural homology to the PI3K inhibitor, LY294002 (LY), and as expected, the phytochemical was found to inhibit the PI3K/AKT pathway to the inhibition elicited by LY in the breast cancer cell line²⁶. Pinosresinol showed cytotoxic, anti-proliferative, and pro-oxidant activity in human breast tumor cells, independent of their estrogen receptor status. Also, pinosresinol exerted antioxidant activity and prevented DNA damage associated with oxidative stress in human mammary epithelial cells²⁷. The active components in fig leaves, including bergapten and psoralen benzaldehyde, amylose, and selenium, have known anti-cancer effects and increase the expression of genes associated with apoptosis, including (Bax, and p53)¹⁹. Through up-regulation of pro-apoptotic molecules such as; p53, Bax, Fas, and FasL and down-regulation of Bcl-2 and suppression of AKT/mTOR signaling pathway²⁸.

Prostate cancer

About 9.7% of cancers in men are due to prostate cancer; it is the second most common cause of death after lung cancer. The effects of pomegranate extract

on prostate cancer have been proven by cell culture studies, clinical trials, and animal studies. Pomegranate compounds such as ellagic acid, caffeic acid, luteolin, and punicalic have been shown to reduce invasiveness and metastasis in prostate cancer cells (PC3 cells). Pomegranate fruit extract (PFE) regulated the expression of cyclin-dependent kinases (CDK) and the expression of cell cycle regulatory cyclins D1, D2, E, as well as decreased Bcl-2 expression and increased Bax expression, increasing the incidence of apoptotic cell death in these cells [29]. Grape seed compounds such as proanthocyanidin induced apoptosis in the PC3 cells through an activation caspase-dependent pathway.

Furthermore, Bax/Bcl-2 ratio in these cells increased after treatment with grape seed extract³⁰. Olive leaf hexane extract has cytotoxic effects on the human prostate cancer cell line³¹. In these cancer cells treated with ethyl acetate fractions of Ajwa dates, all the evidence for apoptosis, including (cell shrinkage, loss of cytoskeletal structure, DNA fragmentation), has been seen³².

Lung cancer

Lung cancer is one of the most common and severe types of cancer. There are studies on the inhibition of pomegranate extract on lung cancer cells (A549 and H1299), which suggest that this effect has been achieved by inhibiting the signaling pathways of mitogen-activated protein kinase (MAPK), PI3K/AKT, and NF- κ B³³. Previous studies about non-small cell lung cancer (NSCLC) proliferation have shown that grape seed extract (GSE) releases cytochrome c to the cytosol and activates caspases 3 and 9. Moreover, it phosphorylates extracellular signal-regulated kinase 1/2 (ERK1/2) and c-Jun N-terminal kinase 1/2 (JNK1/2), and these results indicate an increase in apoptosis in these cells³⁴. A high amount of oleic acid in olive oil can inhibit lung cancer progression through inhibition of prostaglandin E (PGE2) production and inactivation of the ERK pathway³⁵. An

investigation has shown that Fig (*F. auriculata*) activates apoptosis in the human lung cancer adenocarcinoma cancer cells (A549) through a pathway independent of caspases⁶. Studies have shown that extracts of both types, both Barhi date palm kernels (BDPK) extracts, and purified phytochemicals, cause apoptosis on A549 and HT-29 cells. BDPK extracts exhibited a dependent mitochondrial signaling pathway, reported with caspase-9 and induced receptor-mediated (extrinsic) apoptotic pathway as seen with caspase-8²⁸.

Colorectal cancer

Colorectal cancer is also known as bowel cancer, colon cancer, or rectal cancer. It is the second leading cause of cancer death in women and the third for men. The risk of developing this cancer is somewhat reduced by eating fresh fruits and vegetables that contain polyphenols. Consumption of pomegranate extract has shown to increase the expression of peroxisome proliferator-activated receptor (PPAR) gamma protein in non-tumor colonies, indicating the ability to inhibit the tumor³⁵. The GSE inhibits cell growth and induces cell cycle (G1 phase) arrest and apoptosis in human colorectal cancer cells, and modulates cell cycle regulators with a substantial effect for Cip1/p21 up-regulation³⁶.

Activating transcription factor (ATF3) is one of the critical transcription factors involved in mechanisms such as apoptosis, cell proliferation, and invasion, and its reduction has been seen in various cancers. Studies have shown that resveratrol in grapes can induce apoptosis by increasing ATF3 expression in colorectal cancer cells³⁷. Olive oil contains different polyphenolic compounds, which can induce apoptosis in various cancer cells. The Mediterranean diet is rich in extra virgin olive oil and associated with a lower incidence of colorectal cancer¹⁶. One of the critical polyphenolic compounds in virgin olive oil is hydroxytyrosol, which can induce apoptosis cell death in human colon adenocarcinoma cells (DLD1) via ROS generation¹⁹. Research has shown that Leaves and latex extracts of *F. carica* have strong anti-proliferative properties on colon cancer cells (HT-29 and HCT-11)³⁸.

Skin cancer (Squamous cell carcinoma)

Skin cancer is one of the most common cancers in the world. Non-melanoma skin diseases refer to a group of diseases that slowly develop in the skin's upper layer. Studies in nude mice have shown that pomegranate extract can play a role in repairing pathways on DNA damage and inflammation caused by ultraviolet B (UVB) in skin cells. Ingredients in pomegranate peel can stop the cell cycle in the G0 / G1 phase, increase caspase activity, and increase the NF- κ B factor in human skin fibroblast cells³⁹. Examining skin cancer cells in mice showed that proanthocyanidins in grape seeds had protective effects on these skin cells. The grape seed results have been reported to activate two mitogen-activating kinases and the NF- κ B signaling pathway⁴⁰. Olive oil contains large

quantities of squalene, which, found in large amounts in the Mediterranean diet, reduces skin cancer incidence. Although alpha-tocopherol (vitamin E) and carotenoid contents in the number of olive oil consumed daily are low, continuous consumption of olive oil will have considerable antioxidant effects in humans⁴¹. Fig latex inhibited cell growth and induced apoptosis through caspase and the Bcl-2 family signaling pathway and by extrinsic death receptor and intrinsic mitochondrial-dependent apoptotic signaling pathway in human hypopharynx squamous carcinoma cells (FaDu). These findings point to the potential of the latex of *Ficus carica* to provide a novel chemotherapeutic drug due to its growth inhibition effects and the induction of apoptosis in human oral cancer cells⁴². Date fruit extracts specifically inhibited oral squamous carcinoma cell line viability but did not have a toxic effect on human gingival epithelial cells at a concentration between 5-100 mg/mL for 24 hours (The crude extracts from the Khalal stage demonstrated the best inhibitory effect on reducing of oral squamous carcinoma cell growth)⁴³.

Liver cancer

Liver cancer is one of the deadliest gastrointestinal diseases. Research into pomegranate extract in mice has shown that its ingredients can reduce the expression of cytochrome p450 and affect the liver's cancer cells by acting on antioxidant and apoptotic mechanisms. Examination of rat cancer hepatic cells showed an increase in pro-apoptotic protein expression (Bax) and anti-apoptotic protein inhibition (Bcl-2) during pomegranate extract consumption. Signaling pathways involved in liver diseases such as NF- κ B and Wnt / β -catenin were affected by pomegranate extract⁴⁴. Quercetin reduced the phosphorylation of ERK1/2 and AKT phosphorylation and inhibited the NF- κ B pathway in HepG2 liver cancer cells. In HepG2 cells, kaempferol induced apoptosis via endoplasmic reticulum (ER) stress and the CHOP pathway²⁵.

A study has recently reported that oleuropein promotes apoptosis in liver cancer cells by activating caspases (3, 8, and 9) and regulating mitochondrial proteins, in addition to via reduction PI3K/AKT signaling pathway⁴⁵.

F. Carica leaf and fruit extracts' ability to cause liver cancer cells (Huh7it cell) apoptosis is through its ability to induce cell cycle arrest and increase the activity of apoptotic regulating genes (p53 and p21). The potential anti-cancer activity of original fresh fig fruit latex (FFL) against hepatocellular carcinoma cells *in vitro* has investigated the results demonstrated that FFL has an anti-proliferation effect by inducing apoptotic cells, inhibiting DNA synthesis of cancer cells and causing G0/G1 phase arrest of cancer cells¹⁷. The past studies have revealed the potent growth-inhibitory impact of ethanolic extract of Ajwa date pulp (ADP) against human liver carcinoma (HepG2) cells with little to no effect on

healthy Vero cells. The result was associated with ROS generation and mitochondrial membrane potential (MMP) depletion in cancer cells. ADP extract induced DNA damage in HepG2 cells, leading to cell cycle arrest at S and G2/M phases, followed by apoptosis through a p53-independent pathway⁴⁶.

Brain tumors

The most common brain tumor is resistant to treatment and therefore has a poor prognosis in glioma. In the human glioma cell line (U87MG), an increase in cyclin E proteins and a decrease in cyclin A had observed. The compounds in pomegranate peel increase the activity of caspases 3 and 9 and thus increase cell death. It was

also reported that cell death of autophagy type in cells treated with pomegranate extract increases, which results from the study of LC3-II protein. Obtained as a proprietary autophagy marker⁴⁷. Studies show that GSE affects p53 and interleukin 6 proteins' expression, thereby acting as an anti-inflammatory to the nervous system⁴⁸. The potential anti-cancer activity of original fresh FFL against human glioma cells in vitro investigated. The results demonstrated that FFL has an anti-proliferation effect by inducing apoptotic cells, inhibiting cancer cells' DNA synthesis, and causing G0/G1 phase arrest of cancer cells⁴⁹.

The molecular mechanisms of fruits mentioned in the Holy Quran are summarized in **table I**.

Table I: Cell death molecular mechanisms of fruits in different cancers.

Cancers	Fruits	The molecular mechanism(s)	References
Breast cancer	Pomegranate	Regulating the expression of these genes: cytochrome c, Caspase-3, caspase-7, caspase-9)	22
	Grape	Inhibition of aromatase/estrogen biosynthesis modulating AKT, NF- κ B, p53, Bcl-2 family, FasL Reducing expression of VEGF Modulated the PI3K/AKT/mTOR Inhibited the PI3K-AKT pathway	23-26
	Olive	Prevented DNA damage associated with oxidative stress in human mammary epithelial cells	27
	Fig	Increased the expression of Bax, p53, and p21	19
	Date	Up-regulation of p53, Bax, Fas, and FasL along with down-regulation of Bcl-2 suppression of AKT/mTOR signaling pathway	28
Prostate cancer	Pomegranate	Regulated the expression of CDK and the expression of cyclins D1, D2, E decreased Bcl-2	29
	Grape	Increased the Bax/Bcl-2 ratio	30
	Olive	Cytotoxic effects on the human prostate cancer cell line	31
	Date	Induced apoptosis and arrest the cell cycle in S phase	32
Lung cancer	Pomegranate	Inhibiting the signaling pathways of MAPK, PI3K/AKT, and NF- κ B Released cytochrome c caspases 3 and 9 Regulated the expression of CDK and the Expression of cell cycle regulatory cyclins D1, D2, E, as well as decreased Bcl-2 expression and increased Bax expression	29, 33
	Grape	Released cytochrome c to the cytosol and activates caspases 3 and 9. Phosphorylated ERK1/2 and NK1/2	34
	Olive	Inhibition of PGE2 production Inactivation of the ERK pathway	35
	Fig	Activated the pathway independent of caspases	6
	Date	Induced receptor-mediated (extrinsic) apoptotic pathway as seen with caspase-8	28
Colorectal cancer	Pomegranate	I increased the expression of (PPAR) gamma protein.	35
	Grape	Inhibited cell growth and induces cell cycle (G1 phase) increasing ATF3 expression	36, 37
	Olive	Regulated apoptosis/necrosis by activation of caspase cascade and inhibition of TNF- α -induced NF- κ B pathway	16
	Fig	Strong anti-proliferative properties	38
Skin cancer	Pomegranate	Stopped the cell cycle in the G0 / G1 phase, increased caspase activity, and increased the NF- κ B factor in human skin fibroblast cells	39
	Grape	Activated two mitogen-activating kinases and the NF- κ B signaling pathway	40
	Fig	Inhibited cell growth and induced apoptosis through caspase and the Bcl-2 family signaling pathway	42
	Date	The inhibitory effect on reducing oral squamous carcinoma cell growth	43
Liver cancer	Pomegranate	Increased in the expression of Bax and inhibition of Bcl-2	44
	Grape	Reduced the phosphorylation of ERK1/2 and AKT phosphorylation and inhibited the NF- κ B pathway Induced apoptosis via ER stress and CHOP pathway in HepG2 cells	25
	Fig	Induced cell cycle arrest and increase the activity of apoptotic regulating genes (p53 and p21) FFL inhibited DNA synthesis of cancer cells and caused G0/G1 phase arrest	17
	Olive	Promoted apoptosis in liver cancer cells by activating caspases (3, 8, and 9) and regulating mitochondrial proteins, in addition to via reduction PI3K/AKT signaling pathway	45
	Date	ROS generation and MMP depletion ADP extract induced cell cycle arrest at S and G2/M phases and followed by apoptosis through a p53-independent pathway	46
Brain tumors	Pomegranate	Increased the activity of caspases 3 and 9	47
	Grape	GSE affected the expression of p53 and interleukin 6 proteins	48
	Fig	FFL induced apoptotic cells, inhibit DNA synthesis of cancer cells and cause G0/G1 phase arrest of cancer cells	49

Conclusion

This study showed that in the Quran, the Muslims' Holy Book, all aspects of human life had been considered. According to the reviewed studies in the Quran, God has paid particular attention to foodstuffs' therapeutic and beneficial properties, mostly fruits such as pomegranate, grape, olive, date, and fig. In recent years, clinical research has shown that all these fruits' components have important therapeutic activities, such as anti-cancer and antioxidant effects. By studying the types of cell death molecular mechanisms and signaling pathways of mentioned fruits in the Quran, their role in cell death,

including apoptosis, is prominent. So, the results can be used in deciphering the treatment of cancers. On the other hand, by referring researchers to the Holy Quran and the cases mentioned in it, there is hope for treating diseases such as cancer.

Acknowledgments

This work was supported by a research fund (No: IR.ABADANUMS.REC.1398.097) from the Research Council of Abadan Faculty of Medical Sciences

References

1. The Holy Quran.
2. Pogribny IP, Rusyn I. Environmental toxicants, epigenetics, and cancer. *Adv Exp Med Biol* 2013; 754: 215-32.
3. World Health Organization. (2020). WHO report on cancer: setting priorities, investing wisely and providing care for all. World Health Organization. Available at: <https://apps.who.int/iris/handle/10665/330745>. License: CC BY-NC-SA 3.0 IGO (electronic version).
4. Paula R. Nutrition in cancer patients. *J Clin Med* 2019; 8(8): 1211-23.
5. Cas MD, Ghidoni R. Cancer prevention and therapy with polyphenols: sphingolipid-mediated mechanisms. *Nutrients* 2018; 10(7): 940-66.
6. Jamil EF, Abdul Ghani R. *Ficus auriculata* (fig) extracts induced cell cycle profile changes and apoptosis through caspase-independent pathway in human lung adenocarcinoma cell line, A549. *J Med Plants* 2017; 16(63): 57-67.
7. Dutoir MR, Averill-Bates DA. Activation of apoptosis signalling pathway by reactive oxygen species. *Biochim Biophys Acta* 2016; 1863(12): 2977-92.
8. Chen D, Yu J, Zhang L. Necroptosis: an alternative cell death program defending against cancer. *Biochim Biophys Acta* 2016; 1865(2): 228-36.
9. Elfalleh W, Hannachi H, Tlili N, Yahia Y, Nasri N, Ferchichi A. Total phenolic contents and antioxidant activities of pomegranate peel, seed, leaf and flower. *J Med Plants Res* 2012; 6: 4724-30.
10. Orak HH, Yagar H, Isbilir SS. Comparison of antioxidant activities of juice, peel, and seed of pomegranate (*Punica granatum L.*) and inter-relationships with total phenolic, Tannin, anthocyanin, and flavonoid contents. *Food Sci Biotechnol* 2012; 21: 373-87.
11. Faria A, Calhau C. The bioactivity of pomegranate: Impact on health and disease. *Crit Rev Food Sci Nutr* 2011; 51: 626-34.
12. Zhou K, Raffoul JJ. Potential anti-cancer properties of grape antioxidants. *J Oncol* 2012; e803294.
13. Farhangi H, Ajilian M, Saeidi M, Khodaei GH. Medicinal fruits in Holy Quran. *International Journal of Pediatrics* 2014; 2(3,2): 89-102.
14. Nayak BS, Ramdath DD, Marshall JR, Isitor G, Xue S, Shi J. Wound healing properties of the oils of *Vitis vinifera* and *Vaccinium macrocarpon*. *Phytother Res* 2011; 25(8): 1201-08.
15. Khorsandi L, Mansouri E, Rashno M, Karami MA, Ashtari A. Myricetin loaded solid lipid nanoparticles upregulate MLKL and RIPK3 in human lung adenocarcinoma. *Int J Pept Res Ther* 2020; 26: 899-910.
16. Torić J, Marković AK, Brala CJ, Brala CJ, Barbarić M. Anticancer effects of olive oil polyphenols and their combinations with anti-cancer drugs. *Acta Pharm* 2019; 69(4): 461-82.
17. Purnamasari R, Winami D, Permanasari AA, Agustina E, Hayaza S, Darmanto W. Anticancer activity of methanol extract of *Ficus carica* leaves and fruits against proliferation, apoptosis, and necrosis in Huh7it cells. *Cancer Inform* 2019; 18: 1-7.
18. Al-Alawi RA, Al-Mashiqri JH, Al-Nadabi JSM, Al-Shihi BI, Baqi Y. Date palm tree (*Phoenix dactylifera L.*): Natural products and therapeutic options. *Front Plant Sci* 2017; 8: 845-56.
19. Khan F, Ahmed F, Pushparaj PN, Abuzenadah A, Kumosani T, Barbour E, et al. Ajwa Date (*Phoenix dactylifera L.*) Extract inhibits human breast adenocarcinoma (MCF7) cells in vitro by inducing apoptosis and cell cycle arrest. *PLoS One*. 2016; 11(7): e0158963.
20. Sreeja S, Santhosh Kumar TR, Lakshmi BS. Pomegranate extract demonstrate a selective estrogen receptor modulator profile in human tumor cell lines and *in vivo* models of estrogen deprivation. *J Nutr Biochem* 2012; 23: 725-32.
21. Anupam B, Mandal A, Bhattacharyya P, Bhatia D. Pomegranate exerts chemoprevention of experimentally induced mammary tumorigenesis by suppression of cell proliferation and induction of apoptosis. *Nutr Cancer* 2016; 68(1): 120-30.
22. Battino M, Forbes-Hernández TY, Gasparini M, Afrin S, Cianciosi D, Zhang J, et al. Relevance of functional foods in the Mediterranean diet: The role of olive oil, berries and honey in the prevention of cancer and cardiovascular diseases. *Crit Rev Food Sci Nutr* 2019; 59(6): 893-920.

23. Huang TT, Shang XJ, Yao GH, Ge JP, Teng WH, Sun Y, et al. Grape seed extract inhibits the growth of prostate cancer PC-3 cells. *J Androl* 2012; 14(4): 331-3.
24. Priyadarsini RV, Murugan RS, Maitreyi S, Ramalingam K, Karunakaran D, Nagini S. The flavonoid quercetin induces cell cycle arrest and mitochondria-mediated apoptosis in human cervical cancer (HeLa) cells through p53 induction and NF- κ B inhibition. *Eur J Pharmacol* 2010; 649: 84-91
25. Abotaleb M, Samuel SM, Varghese E, Varghese S, Kubatka P, Liskova A, et al. Flavonoids in Cancer and Apoptosis. *Cancers* 2019; 11(1): 28-66.
26. Niazvand F, Orazizadeh M, Khorsandi L, Abbaspour M, Mansouri E, Khodadai A. Effects of quercetin-loaded nanoparticles on MCF-7 human breast cancer cells. *Medicina* 2019; 55(4): 114-29.
27. López-Biedma A, Sánchez-Quesada C, Beltrán G, Delgado-Rodríguez M, Gaforio JJ. Phytoestrogen (+)-pinoresinol exerts antitumor activity in breast cancer cells with different oestrogen receptor statuses. *BMC Complement Altern Med* 2016; 16(1): 350-63.
28. Zhang Y, Wan Y, Huo B, Li B, Jin Y, Hu X. Extracts and components of *Ficus carica* leaves suppress survival, cell cycle, and migration of triple-negative breast cancer MDA-MB-231 cells. *Onco Targets Ther* 2018; 11: 4377-86.
29. Malik A, Afaq F, Sarfaraz S, Adhami VM, Syed DN, Mukhtar H. Pomegranate fruit juice for chemoprevention and chemotherapy of prostate cancer. *Proc Natl Acad Sci USA* 2015; 102: 14813-8.
30. Mingshun Ch, Shu-Juan Y. Lipophilic grape seed proanthocyanidin exert anti-proliferative and pro-apoptotic effects on PC3 human prostate cancer cells and suppresses PC3 xenograft tumor growth *in vivo*. *J Agric Food Chem* 2019; 67(1): 229-35.
31. Boss A, Bishop KS, Marlow G, Barnett MPG, Ferguson LR. Evidence to support the anti-cancer effect of olive leaf extract and future directions. *Nutrients* 2016; 8(8): 513-34.
32. Mirza MB, Elkady AI, Al-Attar AM, Syed FQ, Mohammad FA, Hakeem KR. Induction of apoptosis and cell cycle arrest by ethyl acetate fraction of *Phoenix dactylifera L.* (Ajwa dates) in prostate cancer cells. *J Ethnopharmacol* 2018; 218: 35-44.
33. Şen HS, Şen V, Bozkurt M, Türkcü G, Güzel A, Sezgi C, et al. Carvacrol and pomegranate extract in treating methotrexate-induced lung oxidative injury in rats. *Med Sci Monit* 2014; 20: 1983-90.
34. Alpna T, Komal R, Subhash G, Kaur M, Agarwal R, Agarwal C. Differential effect of grape seed extract against human non-small-cell lung cancer cells: the role of reactive oxygen species and apoptosis induction. *Nutr Cancer* 2013; 65(01): 1-16.
35. Check JH, Sansoucie L, Chern J, Dix E. Mifepristone treatment improves length and quality of survival of mice with spontaneous lung cancer. *Anticancer Res* 2010; 30(1): 119-22.
36. Kohno H, Suzuki R, Yasui Y, Hosokawa M, Miyashita K, Tanaka T. Pomegranate seed oil rich in conjugated linolenic acid suppresses chemically induced colon carcinogenesis in rats. *Cancer Sci* 2014; 95: 481-6.
37. Whitlock NC, Bahn JH, Lee SH, Eling TE, Baek SJ. Resveratrol-induced apoptosis is mediated by early growth response-1, krüppel-like factor 4, and activating transcription factor 3. *Cancer Prev Res* 2011; 4(1): 116-27.
38. Soltana H, Pinon A, Limami Y, Zaid Y, Khalki L, Zaid N, et al. Antitumoral activity of *Ficus carica L.* on colorectal cancer cell lines. *Cell Mol Biol* 2019; 65(6): 6-11.
39. Pacheco-Palencia LA, Noratto G, Hingorani L, Talcott ST, Mertens-Talcott SU. Protective effects of standardized pomegranate (*Punica granatum L.*) polyphenolic extract in ultraviolet-irradiated human skin fibroblasts. *J Agric Food Chem* 2018; 56: 8434-41.
40. Afaq F, Katiyar SK. Polyphenols: skin photoprotection and inhibition of photocarcinogenesis. *Mini Rev Med Chem* 2011; 11(14): 1200-15
41. Sanchez-Rodriguez E, Lima-Cabello E, Biel-Glesson S, Fernandez-Navarro JR, Calleja MA, Roca M, et al. Effects of virgin olive oils differing in their bioactive compound contents on metabolic syndrome and endothelial functional risk biomarkers in healthy adults: a randomized double-blind controlled trial. *Nutrients* 2018; 10(5): 626-42.
42. Shin, BS, Lee SA, Moon SM, Han SH, Hwang EJ, Kim SG, et al. Latex of *Ficus carica L.* induces apoptosis through caspase and Bcl-2 family in FaDu human hypopharynx squamous carcinoma cells. *Int J Oral Biol* 2017; 42(4): 183-90.
43. Chaiyarit P, Weerayuttil P, Wongraweewiwat R, Kotchoom A, Rattanathongkum A. Inhibitory effects of date fruit (*Phoenix dactylifera L.*) extracts on oral cancer cell lines. *Khon Kaen Dent J* 2019; 22(1): 53-9
44. Bhatia D, Thoppil RS, Mandal A, Samtani KA, Darvesh AS, Bishayee A. Pomegranate bioactive constituents suppress cell proliferation and induce apoptosis in an experimental model of hepatocellular carcinoma: role of Wnt/ β -catenin signalling pathway. *Evid Based Complement Alternat Med* 2013; 2013: 1-15.
45. Yan CM, Chai EQ, Cai HY, Miao GY, Ma W. Oleuropein induces apoptosis via activation of caspases and suppression of phosphatidylinositol 3-kinase/protein kinase B pathway in HepG2 human hepatoma cell line. *Mol Med Rep* 2015; 11(6): 4617-24.
46. Siddiqui S, Ahmad R, Ali Khan M, Upadhyay S, Husain I, Srivastava AN. Cytostatic and Anti-tumor Potential of Ajwa Date Pulp against Human Hepatocellular Carcinoma HepG2 Cells. *Sci Rep* 2019; 9(1): 245-56.
47. Wang SG, Huang MH, Li JH, Lai FI, Lee HM, Hsu YN. Punicalagin induces apoptotic and autophagic cell death in human U87MG glioma cells. *Acta Pharmacol Sin* 2013; 34(11): 1411-9.
48. Roleira FMF, Tavares-da-Silva EJ, Varela CL, Costa SC, Silva T, Garrido, et al. Plant derived and dietary phenolic antioxidants: anti-cancer properties. *Food Chem* 2015; 183: 235-58.
49. Imran M, Nadeem M, Gilani S, Khan S, Sajid MW, Amir RM. Anti-tumor perspectives of oleuropein and its metabolite hydroxytyrosol: recent updates. *J Food Sci* 2018; 83(7): 1781-91.

Investigating the relationship between job stress and coronary mental health (Covid Virus 19) in Iranian companies and families

Investigación de la relación entre el estrés laboral y la salud mental coronaria (virus Covid 19) en empresas y familias iraníes

Hanieh Sadat Safavi Homami 

Faculty of Psychology and Education, Tehran, Iran

Corresponding author

Hanieh Sadat Safavi Homami
Faculty of Psychology and Education, Tehran, Iran
E-mail: haniehsafavi94@gmail.com

Received: 8 - II - 2021

Accepted: 1 - V - 2021

doi: 10.3306/AJHS.2021.36.02.84

Abstract

The **main** purpose of this study was to investigate the relationship between job stress and coronary artery health (Covid virus 19) in Iranian companies and families.

Methods: 241 employees (214 males and 27 females) were selected from the employees of Iranian companies using Cochran's formula by stratified random sampling method and using the Helrigel job stress questionnaire. And Slocum, the Stress Response Styles Questionnaire (CISS) and the Goldberg - Hiller General Health Questionnaire (GHQ-28) were evaluated. The obtained data were statistically evaluated using path analysis method.

Results: The findings showed that job stress and its dimensions are able to predict changes related to mental health as well as problem-oriented and emotion-oriented coping strategies of the subjects. The findings also confirmed the mediating role of coping with problem-oriented and coronary-induced stress in the relationship between job stress and mental health.

Conclusions: According to the findings, mental health can be improved by increasing problem-oriented strategy by teaching the use of these types of strategies as well as reducing emotion-oriented strategies.

Keywords: Covid-19, Job stress, mental health, coping strategies, employees.

Resumen

El **objetivo** principal de este estudio era investigar la relación entre el estrés laboral y la salud arterial coronaria (virus Covid 19) en empresas y familias iraníes

Metodología: Se seleccionaron 241 empleados (214 hombres y 27 mujeres) de entre los empleados de las empresas iraníes mediante la fórmula de Cochran por el método de muestreo aleatorio estratificado y utilizando el cuestionario de estrés laboral de Helrigel Además, se evaluaron el Cuestionario de Estilos de Respuesta al Estrés (CISS) y el Cuestionario de Salud General de Goldberg y Hiller (GHQ-28). Los datos obtenidos se evaluaron estadísticamente mediante el método de análisis de trayectorias.

Resultados: Se observó que el estrés laboral y sus dimensiones son capaces de predecir los cambios relacionados con la salud mental, así como las estrategias de afrontamiento orientadas a los problemas y a las emociones de los sujetos. Los resultados también confirmaron el papel mediador del afrontamiento del estrés orientado a los problemas y del estrés inducido por las emociones en la relación entre el estrés laboral y la salud mental.

Conclusiones: Según los resultados, la salud mental puede mejorarse aumentando la estrategia orientada a los problemas mediante la enseñanza del uso de este tipo de estrategias, así como reduciendo las estrategias orientadas a las emociones.

Palabras clave: Covid-19, estrés laboral, salud mental, estrategias de afrontamiento, empleados.

Introduction

Epidemic and new virus control

The corona virus family is becoming a global health crisis. The various aspects of the virus are still unknown to the public. This study aims to introduce the general aspects of this virus. This study is a narrative review that uses the keywords COVID-19 and New Coronavirus 2019 to review available texts. Published articles from 1/20/2020 to 3/3/2020 were reviewed. PubMed and Google Scholar are mainly used in the search. Free search in Google search engine is used to collect background information¹⁻³.

Aspects of prevalence, control and prevention of the disease were studied and presented. This study showed that the routes of transmission of Covid-19 virus are through respiratory droplets and direct contact with secretions containing the virus. One of the causes of the uncontrollable and surprising prevalence of this disease is the long incubation period of its cause and how it is transmitted in these asymptomatic, mild or pre-emergence periods of the disease. Undoubtedly, in today's society, it is not possible to live without a job, and every person needs to have a job in order to join the social organization and find a place and status in society. However, work is not only a way to meet the essential needs of life, but also a vital element in the social status of individuals⁴⁻⁶.

However, people's jobs are one of the main causes of stress in their lives. For each person, job is considered as a component of social identity, a source of living needs and a component of social identity, and is an important source of stress. There is more tension in jobs in which human communication is important⁷⁻⁹. Job stress has become a common and costly problem in the workplace today¹⁰⁻¹². Almost all thinkers acknowledge that stress is the result of an interaction between a person and a situation in which the individual considers his or her ability to respond to demands and insufficient pressure, so that the National Institute for Occupational Safety and Health (1999) treats job stress. Defines a person as harmful physical and emotional responses when working conditions do not match the abilities, facilities available, or needs of the workforce.

Job stress is one of the stresses that, if excessive, can endanger a person's health by causing physical, psychological and behavioral complications. Also, the existence of these pressures, by threatening organizational goals, can reduce the quality of individual performance¹³⁻¹⁵.

Organizational consequences of stress are decreased performance, increased absenteeism, resignations, decreased organizational commitment and job insecurity of employees, etc. (Francois, 2008). Extensive research

shows that there is a lot of job stress and physical and mental analysis in employees, which leads to dismissal from work, clashes between employees and severe displacement, health disorders and inability to perform tasks, vulnerability in professional communication, decreased quality of care provided and ultimately dissatisfaction and leaving the job¹⁶⁻¹⁹. In several studies on the effect of job stress on mental health job stress has been introduced as one of the most important causes of mental injuries and reduced mental health in most of these studies, stress is considered as a response that is experienced directly under the influence of stress sources.

But it is important to emphasize that stress does not always come directly from stressful sources, but how a person perceives stress in their experience, because studies have shown that stressful events. Similarly, they produce different effects in different people. Hence, the belief that there are variables that modulate the relationship between stress and mental health has been reinforced. Efficient manpower is the richest and most valuable wealth and property of any country. Many societies, despite having abundant natural resources, are not able to use these divine gifts due to the lack of qualified human resources. Efficient human resources are those who, while having knowledge and skills, have the necessary abilities to perform adequate and effective job tasks with mental health²⁰⁻²².

Mental health has been defined as a balanced and coordinated behavior with society, recognizing and accepting social realities, the ability to adapt to them and satisfy one's balanced needs²⁵.

In this regard, the World Health Organization (WHO) (2005) considers mental health to be a balance between different aspects of life, global, social, spiritual, spiritual and emotional, and the way we manage our environment and to the life we decide is of particular importance.

Mental health is a state of functioning and successful mental activity that results in fruitful activities, satisfying relationships with others, the ability to adapt to change, and coping with adversity. Promoting mental health in the community improves the quality of life. According to the World Health Organization, 1 in 4 people (25%) suffer from one or more mental disorders at any stage of life. According to the US Centers for Disease Control (CDC), 7.8 percent of men and 12.3 percent of women between the ages of 18 and 24 suffer from mental health problems, especially stress. Characteristics of people with mental health include self-awareness, self-motivation, aspirations, and environment. In Iran, this statistic is not less than other countries; So that in the National Plan for the Study of Health and Disease in Iran, the average of disorders in people over 15 years of age in Iran was reported to be 21%. The World Health Organization also estimates that mental illness, including stress related to

mental disorders, will be the second leading cause of disability by 2020. However, several studies conducted in different occupational groups have shown a significant relationship between mental health and job satisfaction; In a way, people with less job satisfaction had less mental health²⁶⁻²⁹. One of the factors that can affect people's mental health is job stress. People who suffer from a lot of stress pay less attention to their work and therefore may harm themselves and others in the organization.

Holmes (2002) considers one of the factors affecting the performance of individuals in organizations is job stress, which puts the mental health of many people at risk. Therefore, in the last decade, the issue of stress and its effects in the organization has become one of the main issues of organizational behavior³⁰. Job stress occurs when expectations of a person are greater than his or her powers and abilities. When a person is deprived of the opportunity to show creativity, decision-making, and tact in the workplace, he or she experiences stress, which ultimately leads to reduced efficiency; This is one of the major problems and threats to human health in modern societies³¹⁻³³.

Most studies that have examined job stress have shown that the labor force exposed to job stress in developed countries is about 30%, which is much higher in developing countries¹⁶. There is evidence that stress can also affect individual health and important organizational outcomes such as productivity³⁶⁻⁴⁰. Job dissatisfaction is a consequence of job stress and will have economic and social costs for the individual⁴¹. Job stress also increases productivity, reduces absenteeism, reduces productivity, relocates, labor conflicts, medical expenses, disability, and hires new staffing costs. There is an exaggeration of organizations and companies⁴².

The International Labor Organization (ILO) estimates that the cost to countries due to job stress is 1 to 3.5 percent of GDP and announces that this amount is increasing⁴³. Therefore, by identifying and modifying the stressors of the workplace, it is possible to prevent the development of mental illness in this group of people and prevent the costs imposed by it.

On the other hand, Linden (2005) believes that stress management increases people's ability to reduce stress and adapt properly to stressful situations. One way to mitigate the destructive effects of job stress is to look at the ways in which job stress affects mental health. One of these ways is coping strategies with stressful events through which job stress seems to target the mental health of the employed person. Stress coping techniques are the process by which people take control of issues caused by stress and negative emotion⁴⁴⁻⁴⁶.

Coping strategies are a set of cognitive and behavioral efforts that are used to interpret and correct a stressful

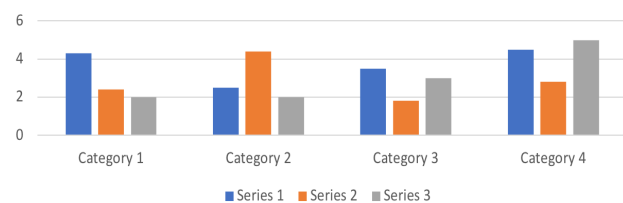
situation and reduce the suffering caused by it⁴⁷. The three main coping strategies are: Emotional coping strategies, which include efforts to regulate the emotional consequences of a stressful event and maintain emotional balance by controlling the emotions resulting from the stressful situation; Problem-oriented coping strategy involves constructive actions of the individual in relation to stressful situations and tries to eliminate or change the source of stress; And avoidant coping strategies include actions in which the individual tries to avoid the stress factor⁴⁸⁻⁵⁰.

In the field of the relationship between mental health and coping strategies, it can be said that mental health in a two-way interaction on the one hand is the result of selecting and using coping strategies effective and commensurate with change and stress, and on the other hand It is the foundation of a healthy psychological atmosphere in the light of which it is possible to correctly recognize and evaluate the stressful situation in order to choose an effective coping strategy. Health psychology attaches great importance to the role of coping strategies in how physical and mental health is⁵¹.

Table 1: Frequency distribution and mean age of the subjects by gender.

Standard deviation of age scores	Age average	Abundant	Gender
5/77	41/65	214	Men
4/95	40/85	27	Female
5/68	41/56	241	Total

Figure 1: Frequency distribution and mean age of the subjects by gender.



Data Collection Tools

Measurement and data collection tools in this study are: Hellerigel - Slocum (2000) Occupational Stress Questionnaire, CISS (1990) and Goldberg - Hiller General Health Questionnaire information on each of which is provided separately below⁵²⁻⁵⁵.

Hellergel and Slocum Job Stress Questionnaire

The Job Stress Assessment Questionnaire was developed by Helrigan and Slocum (2000) and measures

a person's level of job stress. This questionnaire has 3 factors of physical environment, job conflict and role ambiguity, each factor has 3, 4 and 3 questions, respectively. This questionnaire has five options including "always", "usually", "sometimes", "rarely" and "never". The scoring method of this questionnaire is as follows: To sum up the scores, the option "Always" is given a score of 10, "Usually" a score of 8, "Sometimes" 6, "Rarely" a score of 4 and "Never" a score of zero. To take. The scoring of the questionnaire for the agents is obtained by adding the scores of the questions of each agent and for the whole questionnaire the sum of the scores of the agents. The score range in this questionnaire is 0 to 100⁵⁶⁻⁶⁰.

Achieving a high score in this questionnaire indicates excessive stress in the job and low job satisfaction. The interpretation of the scores obtained from this questionnaire is such that for each factor, a score of 8-10 indicates that a lot of attention should be paid to the improvement of the factor, and for the whole questionnaire, a total score of 74 or more indicates that the stress level is higher. It is optimal, job satisfaction is low, the tendency to underemployment and absenteeism is also high⁶¹⁻⁶³.

The questionnaire is designed based on strong theories and based on the opinions of two famous management thinkers, has a high formal validity and content⁶⁴. In a study by Hassanzadeh (2008), its reliability was calculated to be 0.84. In the research of Hassanzadeh, Shirbeigi and Olizadeh (2012), the reliability of the questionnaire is 0.82 Bust Amo, which is a desirable and satisfactory coefficient. In the present study, internal consistency coefficients were obtained by Cronbach's alpha method for 0.78 questionnaire⁶⁵.

Stress Management Incident Questionnaire (CISS)

This questionnaire was developed by Parker and Andler (1990) to assess the coping patterns of individuals (adolescents and adults) in stressful and critical situations. They first administered a questionnaire consisting of 70 items to 599 male and female students. Respondents were asked to consider a personal crisis or stressful event they had recently experienced and to complete the questionnaire items according to how they dealt with it. Then, using factor analysis, they interpreted the data and extracted three major coping methods. Problem-oriented confrontation, emotion-oriented confrontation and avoidance-oriented confrontation⁶⁶.

Packer and Andler (1990) revised the questionnaire and reduced it to 66 items. The questionnaire was then administered to 394 students and 284 adults, and finally, after factor analysis of the data, it was reduced again to

48 items. The CISS questionnaire with 48 items is one of the reliable tools for measuring crisis management methods. Are considered stressful events. Each coping method has a separate scale with 16 items⁶⁷.

The Avoidance Coping Scale has two subscales: community-oriented, activity-oriented, and problem-oriented coping. Which a person uses to control, eliminate, or reduce unpleasant external or internal stimuli. These methods focus on the problem itself or the unpleasant stimulus. Emotion-oriented coping method: This method is the escape and (physical) distance of the person from the stress factor. Parker and Andler (1990) reported the internal consistency of the questionnaire from 41% to 66%. Agham Mohammadian et al. (1999) in their study on 100 students (50 girls and 50 boys) of Ferdowsi University of Mashhad. Credit and validity were reported by 73%.

Also, Hosseini Tabatabai (1998) obtained Cronbach's alpha coefficient for problem-oriented coping strategies 0.81 and 0.78, respectively. In the present study, Cronbach's alpha internal consistency coefficients for scales of coping strategies of problem-oriented, emotion-oriented and avoidance-oriented and subscales of turning to activities and turning to community, respectively / 75 0, 0.87, 0.73, 0.82 and 0.59 were obtained⁶⁸.

Research Method

To conduct this research, first by referring to and obtaining the necessary permits and agreements to conduct the research, the samples are randomly classified from among the employees working in the field of human resources, improving crop production, improving production. Animal and Deputy Minister of Planning and Economic Affairs were elected. After that, by providing the necessary explanation about the purpose of the research and obtaining the consent of the research units, the researcher was present at one of the low office hours at the employees' workplace and provided them with questionnaires. All research units completed the questionnaires with the knowledge that participation in research is optional and will not have any effect on their work process, including promotion or demotion. In the next step, the scoring questionnaires were statistically analyzed.

Method of statistical analysis of data

In analyzing the data of this research, two software's, SPSS-19 and AMOS-20, have been used. SPSS-19 software is used to describe and analyze raw data and regression analysis simultaneously and to determine the fit of the studied model from the structural equation model in AMOS-20 software to analyze the path of observation variables. Exploitation was performed using correlation

matrix. The results of this analysis will come in the next chapter. The maximum likelihood method was used to determine the fit of the model. It should be noted that there are several indicators to estimate the good fit of the overall model. These include chi-square indices, good fit index (GFI), adjusted good fit index (AGFI), mean square root remainder (RMR), and barbell index (CN). The chi-square index is strongly affected by the sample size, so in models with a sample size greater than 200, the null hypothesis is rejected. Therefore, model fit will usually not be verified. In such studies, it is used to compare the fit of the model with a random model⁶⁸.

In this study, the chi-square index will be reported, but the criterion for fitting the model will be other indicators in question. It should be noted that all calculations in this study were performed by statistical software with a statistical inference limit of $P < 0.05$. Descriptive findings related to research variables **table II** shows the mean, standard deviation and range of scores observed by the research subjects in the variables (coping styles, job stress and mental health)⁶⁹.

Correlation matrix of research variables **table III** shows the zero-order correlation matrix of the variables of the studied model. Significance levels and the relationship between exogenous, mediating and endogenous variables can

show a linear relationship between the variables under study. The existence of these relationships allows path analysis in the model studied in this study.

Path analysis findings

In the continuation of this section, the findings of the path analysis of sub-models and the final research model will be examined. In the study of model paths, β coefficients are the path coefficient index that is shown on the path arrows. Obviously, the paths leading to the endogenous variable will form an equation, in which the variance of the error of each equation or the residual values are also given to the variables. Below each equation, the indices R and R2, or in other words, the amount of variance explained by the predictor variables, are presented. It should be noted that at each stage, the research hypotheses as well as the proposed model that was presented in the second chapter will be examined. At the end of each section, there will be other findings that may result from data analysis in addition to the assumptions made⁷⁰.

Predicting mental health based on job stress

In order to investigate the predictive role of job stress on the mental health of the subjects, linear regression analysis was used in a simultaneous manner. The results of the analyzes are shown in **tables IV** and **V**.

As can be seen in **table VI**, based on the obtained results, the observed F value is significant ($P = 0.0005$) and can be 6.4% ($R2_{adj} = 0.064$) variance of the subject's mental health variable. Explained through job stress. Therefore, it is concluded that job stress can predict changes in subjects' mental health. According to the results obtained

Table II: Mean, standard deviation and range of scores of the studied variables.

Scope range		The standard	Average	Variable
Max	Min	deviation		
55	7	8/56	33/84	Problem-oriented coping methods
66	9	10/43	37/68	Emotional coping style
60	29	6/65	42/29	Avoidance-oriented coping methods
18	1	14/14	9/60	Physical environment stress
24	4	4/56	11/39	Job Conflict Stress
21	4	3/03	9/51	Stress ambiguity role
48	13	8/10	30/49	Job stress (total score)
61	7	10/62	26/13	Mental health

Table III: Zero-order correlation matrix between research variables.

Variables	1	2	3	4	5	6	7	8
1. Dealing with problem-oriented	1							
2. Exciting coping	**222/0-	1						
3. Avoiding confrontation	**264/0	**185/0	1					
4. Physical environment stress	**241/0-	**358/0	011/0	1				
5. Stress of job conflict	**208/0-	**223/0	009/0-	**360/0	1			
6. Role ambiguity stress	**355/0-	*165/0	116/0-	084/0	103/0	1		
7. Job stress	**373/0-	**370/0	042/0-	**745/0	**785/0	**474/0	1	
8. Mental health	**306/0-	**279/0	009/0-	*125/0	**200/0	**226/0	**261/0	1

Table IV: Results of analysis of variance (ANOVA) for predicting mental health based on job stress.

Source of Dispersion	Total Squares	df	Average Square	R	R2adj	F	P
Regression	97/1839	1	97/1839	261/0	064/0	423/17	0005/0
Left over	78/25239	239	61/105				
Total	75/27079	240	-				

Table V: Regression analysis coefficients for predicting subjects' mental health based on job stress.

Criterion variable	Predictive Variables	B	β	t	P
Mental Health	Job Stress	342/0	261/0	174/4	0005/0

Table VI: Results of analysis of variance (ANOVA) for predicting mental health based on job stress dimensions.

Source of dispersion	Total Squares	df	Average Square	R	R ² _{adj}	F	P
Regression	59/2291	3	86/763	291/0	073/0	303/7	0005/0
Left Over	16/24788	237	59/104				
Total	75/27079	240	-				

Table VII: Regression analysis coefficients for predicting job satisfaction of subjects based on job stress dimensions.

Criterion variable	Predictive Variables	B	β	t	P
Mental health	Physical environment stress	127/0	050/0	744/0	457/0
	Job Conflict Stress	375/0	161/0	413/2	017/0
	Stress ambiguity role	718/0	205/0	274/3	001/0

Table VIII: Results of analysis of variance (ANOVA) for predicting coping strategies based on job stress.

Variable property	Source of dispersion	Total squares	df	Average square	R	R ² _{adj}	F	P
Problem-oriented strategy	regression	86/2447	1	86/2447	373/0	136/0	647/38	0005/0
	left over	15/15138	239	34/63				
	Total	01/17586	240	-				
Excitement strategy	regression	73/3579	1	73/3579	370/0	134/0	982/37	0005/0
	left over	03/22525	239	25/94				
	Total	75/26104	240	-				
Circuit avoidance strategy	regression	15/19	1	15/19	042/0	002/0-	432/0	512/0
	left over	52/10596	239	34/44				
	Total	67/10615	240	-				

Table IX: Regression analysis coefficients to predict subjects' coping strategies on job stress.

Criterion variable	Predictive variables	B	β	t	P
Problem-oriented strategy	Job stress	394/0-	373/0-	217/6-	0005/0
Excitement strategy	Job stress	477/0	370/0	163/6	0005/0
Circuit avoidance strategy	Job stress	035/0-	042/0-	657/0-	512/0

in **table VI**, job stress with a beta coefficient ($\beta = 0.261$) and a significant level ($P = 0.0005$) is able to predict mental health (confirmation of the first hypothesis). As can be seen, job stress has a negative effect on mental health (it should be noted that the higher the score in the mental health questionnaire, the lower the mental health). In order to investigate which of the dimensions of job stress can predict mental health, multiple regression analysis was used in a simultaneous manner. The results of the analyzes are shown in **tables VI** and **VII**.

As shown in **tables VII**, based on the results, the amount of F observed is significant ($P = 0.0005$) and can be 7.3% ($R^2_{adj} = 0.073$) of the variance of the variable mental health of the subjects through Explained the dimensions of job stress. Therefore, it is concluded that the dimensions of job stress are able to predict changes related to the mental health of the subjects. According to the results in **table IV-VI**, physical environment stress with a beta coefficient of equal ($\beta = 0.050$) and a significant level ($P = 0.457$) is not able to predict mental health. Job stress conflict with beta coefficient ($\beta = 0.161$) and significance level ($P = 0.017$) can predict the mental health of subjects. Also, the role of role ambiguity stress with a beta coefficient ($\beta = 0.205$) and a significant level ($P = 0.001$) is able to predict the mental health of subjects. As can be seen, the dimensions of job stress have a

negative effect on mental health (it should be noted that the higher the score in the mental health questionnaire, the lower the mental health)³⁶.

Predicting coping strategies based on job stress

In order to investigate the predictive role of job stress on the level of coping strategies of the subjects, multiple regression analysis was used in a simultaneous manner. The results of the analyzes are shown in **tables VIII** and **IX**.

As can be seen in **table VIII**, based on the results, the observed F value is significant for the criterion variables of problem-oriented strategies ($P = 0.0005$) and emotion-oriented ($P = 0.0005$). But the observed F value is not significant for the avoidance strategies variable ($P = 0.512$). According to the findings, 13.6% ($R^2_{adj} = 0.136$) of variable variance of problem-oriented strategies can be explained through job stress; It is also possible to explain 13.4% ($R^2_{adj} = 0.134$) of the variance of variable emotion-driven strategies through job stress; Therefore, it can be concluded that job stress is able to predict changes related to problem-oriented and emotion-oriented strategies, but does not have the power to predict avoidance-oriented strategies.

According to the results in **table IX**, job stress with a beta coefficient of equivalent ($\beta = -0.373$) and a significant level ($P = 0.0005$) is a negative predictor of problem-oriented strategies with a coefficient. Equivalent beta ($\beta = 0.370$) and significance level ($P = 0.0005$) are positive predictors of emotion-driven strategies.

As can be seen, job stress has a negative effect on problem-oriented strategy and a positive effect on emotion-oriented strategy. In order to investigate which of the dimensions of job stress can predict coping strategies, multiple regression analysis was used in a simultaneous manner. The results of the analyzes in **tables X** and **XI**.

As can be seen in **table X**, based on the results, the observed F value is significant for the criterion variables of problem-oriented strategies ($P = 0.0005$) and emotion-oriented strategies ($P = 0.0005$). But the observed F value is not significant for the avoidance strategies variable ($P = 0.347$). According to the findings, 17.2% ($R^2_{adj} = 0.172$) of variable variance of problem-oriented strategies can be explained through the dimensions of job stress; Also, 14.4% ($R^2_{adj} = 0.144$) of the variance of emotion-driven strategies can be explained through the dimensions of job stress.

According to the results in **table XI**, physical environment stress with equivalent beta coefficient ($\beta = -0.174$) and significance level ($P = 0.006$) can predict the problem-oriented coping strategy. Job stress conflict with beta coefficient ($\beta = -0.111$) and significance level ($P = 0.079$) is not able to predict the problem-oriented coping strategy. Also, the role of role ambiguity stress with equal beta coefficient ($\beta = -0.232$) and significance

level ($P = 0.0005$) is able to predict the problem-oriented coping strategy. Physical environment stress with a beta coefficient ($\beta = 0.312$) and a significant level ($P = 0.0005$) is able to predict the strategy of emotional coping. Stress of job conflict with equivalent beta coefficient ($\beta = 0.098$) and significance level ($P = 0.129$) is not able to predict emotion coping strategy. Also, the role of role ambiguity stress with equal beta coefficient ($\beta = 0.129$) and significance level ($P = 0.034$) is able to predict the strategy of emotional coping. Also, physical environment stress with equivalent beta coefficient ($\beta = 0.023$) and significance level ($P = 0.739$); Stress of job conflict with equivalent beta coefficient ($\beta = -0.0000$) and significance level ($P = 0.939$) and role ambiguity stress with equivalent beta coefficient ($\beta = -0.117$) and significance level ($P = 0.073$) Are unable to predict avoidance-oriented coping strategies. As can be seen, the dimensions of job stress have a negative effect on coping strategies and a positive effect on emotional strategies³⁷.

Predicting mental health based on coping strategies with job stress management

In order to investigate the predictive role of coping strategies on the mental health of subjects with job stress control, multiple regression analysis in a simultaneous manner was used.

As shown in **tables XII** based on the obtained results, the amount of F is significant ($P = 0.0005$) and can be 13.5% ($R^2_{adj} = 135.135$) variance of variable mental health of subjects through Explained problem-solving, emotion-oriented, avoidance-oriented, and job-stress

Table X: Results of Analysis of variance (ANOVA) for predicting coping strategies based on job stress dimensions.

Variable property	Source of dispersion	Total squares	df	Average square	R	R ² _{adj}	F	P
Problem-oriented strategy	regression	76/3202	3	59/1067	427/0	172/0	591/17	0005/0
	left over	25/14383	237	69/60				
	Total	01/17586	240	-				
Excitement strategy	regression	87/4041	3	29/1347	393/0	144/0	473/14	0005/0
	left over	88/22062	237	09/93				
	Total	75/26104	240	-				
Circuit avoidance strategy	regression	73/146	3	91/48	118/0	001/0	107/1	347/0
	left over	93/10468	237	17/44				
	Total	67/10615	240	-				

Table XI: Regression analysis coefficients for predicting subjects' coping strategies on the dimensions of job stress.

Variable property	Predictive variables	B	β	t	P
Problem-oriented strategy	Physical environment stress	359/0-	174/0-	755/2-	006/0
	Job Conflict Stress	209/0-	111/0-	763/1-	079/0
	Stress ambiguity role	931/0-	329/0-	570/5-	0005/0
Excitement strategy	Physical environment stress	786/0	312/0	873/4	0005/0
	Job Conflict Stress	224/0	098/0	523/1	129/0
	Stress ambiguity role	443/0	129/0	138/2	034/0
Circuit avoidance strategy	Physical environment stress	037/0	023/0	334/0	739/0
	Job Conflict Stress	008/0-	005/0-	077/0-	939/0
	Stress ambiguity role	257/0-	117/0-	801/1-	073/0

coping strategies. Therefore, it is concluded that problem-oriented, emotion-oriented and avoidance-coping strategies with job stress control are able to predict changes in subjects' mental health. According to the results obtained in **table XIII**, the problem-solving strategy with an equivalent beta coefficient ($\beta = -0.231$) and a significant level ($P = 0.001$) can predict the mental health of the subject.

Emotional coping strategy with equivalent beta coefficient ($\beta = 0.184$) and significance level ($P = 0.007$) is able to predict the subjects' mental health. Also, avoidance coping strategy with equivalent beta coefficient ($\beta = 0.022$) and significance level ($P = 0.728$) is not able to predict the mental health of subjects.

Also, in this model, job stress with a beta coefficient of equal ($\beta = 0.108$) and a significant level ($P = 0.116$) is not able to predict the mental health of the subjects. Job stress is not significant on mental health. In order to investigate the predictive role of coping strategies on the mental health of subjects by controlling the dimensions of job stress, multiple regression analysis in a simultaneous manner was used, the results of the analysis in **tables XIV**.

As in **tables XIV**, based on the obtained results, the observed amount of F is significant ($P = 0.0005$) and can be 14.2% ($R^2_{adj} = 0.142$) variance of variable mental health of the subjects through Explained problem-

oriented, emotion-oriented, avoidance-oriented coping strategies, and dimensions of physical environment stress, job conflict, and role ambiguity stress.

Therefore, it is concluded that problem-oriented, emotion-oriented and avoidance-coping coping strategies by controlling the dimensions of job stress can predict changes in subjects' mental health. According to the results obtained in **table XV**, the problem-oriented coping strategy with equivalent beta coefficient ($\beta = -0.217$) and significance level ($P = 0.002$) and the emotion-coping coping strategy with Equivalent beta coefficient ($\beta = 0.200$) and significance level ($P = 0.003$) are able to predict the mental health of subjects. Also, avoidance coping strategy with equivalent beta coefficient ($\beta = 0.026$) and significance level ($P = 0.728$), physical environment stress with equivalent beta coefficient ($\beta = -0.051$) and significance level (454). $P = 0.0$, job conflict stress with equivalent beta coefficient ($\beta = 0.118$) and significance level ($P = 0.071$) and also in this model, role ambiguity stress with equivalent beta coefficient ($\beta = 0.111$) Significance level ($P = 0.087$) is not able to predict the mental health of subjects. In these cases, coping strategies have a relative mediation role as a mediator between the relationship between job stress dimensions and mental health. Findings related to mediation of coping strategies in relation to the dimensions of job stress and mental health are presented in detail in the following sections.

Table XII: Results of ANOVA for predicting mental health based on coping strategies with stress and job stress.

Source of dispersion	Total Squares	df	Average Square	R	R^2_{adj}	F	P
Regression	88/4048	4	96/16072	387/0	135/0	372/10	0005/0
Left over	87/23030	236	30/208				
Total	75/27079	240	-				

Table XIII: Regression analysis coefficients for predicting mental health based on coping strategies with stress and job stress.

Criterion variable	Predictive variables	B	β	t	P
Mental health	Problem-oriented strategy	286/0-	231/0-	387/3-	001/0
	Excitement strategy	187/0	184/0	736/2	007/0
	Circuit avoidance strategy	036/0	022/0	348/0	728/0
	Job stress	141/0	108/0	576/1	116/0

Table XIV: Results of ANOVA for predicting mental health based on coping strategies and dimensions of job stress.

Source of dispersion	Total Squares	df	Average Square	R	R^2_{adj}	F	P
Regression	62/4435	6	27/739	405/0	142/0	639/7	0005/0
Left over	13/22644	234	77/96				
Total	75/27079	240	-				

Table XV: Regression analysis coefficients for predicting mental health based on coping strategies and dimensions of job stress.

Criterion variable	Predictive variables	B	β	t	P
Mental health	Problem-oriented strategy	269/0-	217/0-	128/3-	002/0
	Excitement strategy	203/0	200/0	960/2	003/0
	Circuit avoidance strategy	041/0	026/0	398/0	691/0
	Physical environment stress	131/0-	051/0-	750/0-	454/0
	Job Conflict Stress	274/0	118/0	812/1	071/0
	Stress ambiguity role	389/0	111/0	721/1	087/0

The final research models

One of the important research questions is that job stress, along with which coping strategies, better predicts the mental health of employees? The results show a linear combination of job stress, problem-oriented stress coping strategy and emotion-oriented stress coping strategy predicts employees' mental health, which in Among these, job stress had both direct ($P < 0.01$, $\beta = 0.107$) and indirect effects ($P < 0.01$, $\beta = 0.154$) on mental health.

The results show a linear combination of dimensions of job conflict stress and role ambiguity, problem-oriented stress coping strategy and emotion-oriented stress coping strategy, predicting employees' mental health. They show that job stress has had a direct effect on mental health ($P < 0.01$, $\beta = 0.104$) and an indirect effect ($P < 0.01$, $\beta = 0.075$). The role of ambiguity stress also had a direct effect on mental health ($P < 0.01$, $\beta = 0.112$) and an indirect effect ($P < 0.01$, $\beta = 0.096$).

Finally, the main hypothesis of the research is the fourth hypothesis, which states that "coping strategies with stress play a mediating role in the relationship between job stress and mental health." Approved. Because by comparing the job stress path coefficients by reducing the direct path stress coefficients to mental health, the strategy variable Coping with stress (problem-oriented and emotion-oriented) is considered to mediate the relationship between job stress and mental health.

Also, by comparing the path coefficients of the dimensions of job stress (job conflict and role ambiguity), and by reducing the direct path coefficients of stress, job conflict to mental health and by reducing the direct path coefficients of stress, the ambiguity of the role to mental health, the variable of strategies to deal with stress (problem Orbital and emotion-oriented) are considered as mediators in the relationship between the dimensions of job stress (job conflict and role ambiguity) and mental health. Therefore, the main hypothesis of the research is confirmed and it is concluded that coping strategies have a mediating role in the relationship between job stress and mental health of employees.

Table XVI: Direct, indirect and significant total effects for the final modified model.

Variable	Direct effects	Interface variable (criterion)	Indirect effects	Total effects
Job stress	107/0	mental health	154/0	107/0
Job stress	373/0-	Problem-solving strategy	-	373/0-
Job stress	370/0	Exciting strategy	-	370/0
Problem-solving strategy	224/0-	mental health	-	224/0-
Exciting strategy	190/0	mental health	-	190/0

Table XVII: Direct, indirect and significant total effects for the final modified model.

Variable	Direct effects	Interface variable (criterion)	Indirect effects	Total effects
Job Conflict Stress	104/0	mental health	075/0	180/0
Job Conflict Stress	173/0-	Problem-solving strategy	-	173/0-
Job Conflict Stress	209/0	Exciting strategy	-	209/0
Stress ambiguity role	112/0	mental health	096/0	208/0
Stress ambiguity role	338/0-	Problem-solving strategy	-	338/0-
Stress ambiguity role	143/0	Exciting strategy	-	143/0
Problem-solving strategy	203/0-	mental health	-	203/0-
Exciting strategy	193/0	mental health	-	193/0

Table XVIII: Fitting of the final model, (N = 241).

Fit indicators	Admission scope	Calculated value
Chi-square of two models (df / CMIN)	$3 \geq$	274/2
Fit Goodness Index (GFI)	$9/0 \leq$	995/0
Adjusted Fit Goodness Index (AGFI)	$9/0 \leq$	953/0
Second Root Mean Mean Squared Error Squares (RMSEA)	$09/0 \geq$	073/0
Normalized Fit Index (NFI)	$9/0 \leq$	980/0
Comparative Brush Index (CFI)	$9/0 \leq$	988/0
Indicator HOELTRE	05/0	406
	01/0	701

Table XIX: Fitting of the final model (N = 241).

Fit indicators	Admission scope	Calculated value
Chi-square of two models (df / CMIN)	$3 \geq$	032/5
Fit Goodness Index (GFI)	$9/0 \leq$	992/0
Adjusted Fit Goodness Index (AGFI)	$9/0 \leq$	877/0
Second Root Mean Mean Squared Error Squares (RMSEA)	$09/0 \geq$	130/0
Normalized Fit Index (NFI)	$9/0 \leq$	953/0
Comparative Brush Index (CFI)	$9/0 \leq$	959/0
Indicator HOELTRE	05/0	184
	01/0	317

Fitting the final model

The ratio of chi-square to its degree of freedom (CMIN / Df) is one of the absolute equivalence indicators of the structural equation model. In this study, this ratio was calculated to be 2.274. Also, the major adaptive fit indices for a model are the good fit index (GFI), the adjusted fit good index (AGFI), the second root mean square error approximation index (RMSEA), the normalized fit index (NFI) and the brush index. All values related to the comparative index of the model also indicate the appropriate fit of the model in this study. Also, the CN barbell index at the alpha level of 0.05 in this study was 406 and at the alpha level of 0.01 in this study was calculated to be 701, which indicates the adequacy of the sample to refer to the relevant analyzes. According to the goodness of fit indicators, it can be said that the final model of this research has a good goodness of fit.

Discuss To explain this result, it can be said that job stress reduces the power of adaptation, the feeling of physical fatigue and the analysis of emotional resources in employed people, and this issue on the one hand negative, faulty or very personal reactions to the relationship. Follows other people in daily interactions and in the workplace (Story and Rapti, 2006) and on the other hand, if these conditions continue and negative and destructive feelings and emotions continue in the person, these emotions will target the mental health of the person. Will lead to reduced mental health.

In general, in explaining these results, it can be said that the stressors of the work environment such as lack of support resources, high workload, conflict with colleagues and facing the problems of clients, with increasing levels of anxiety, changes in Cardiovascular system, endocrine glands and immune system and decreased adaptive strength of individuals causing physical and mental fatigue, behavioral symptoms such as absenteeism, leaving work and increasing Accidents at work and the occurrence of psychological and physical symptoms such as depression, anxiety disorders, sleep disorders, gastrointestinal ulcers Hypertension, Heart Diseases Gastrointestinal Disorders, Headache, Respiratory Disorders and Skin Diseases Endangers the physical and mental health of employees. On the other hand, having mental health is one of the factors inhibiting the negative effects of job stress and one of the characteristics of people resistant to stressful events is having mental health.

In fact, it can be said that the lower the level of mental health of people, the more difficult it is to deal with job stress and its effects will be far more destructive. In another explanation of the results of the present study, according to Bandura (1996), when people are exposed to stress, those who find themselves empowered and efficient in the face of problems, make more efforts to deal with and cope with They do their problems, but people

who find themselves helpless in the face of problems give in easily and feel depressed, anxious and frustrated.

In explaining the findings, problem-oriented strategy is a shield against stress for mental health due to finding the root cause of stress and dealing with it rationally, but emotion-oriented coping strategy temporarily reduces stress and or it just eliminates the symptoms of stress while the stressor is still present and its effects are likely to occur in other ways and elsewhere. In other words, problem-oriented coping strategies are cognitive methods for coping with problems. This finding shows that the use of rational approach to the stressors can estimate the level of mental health and therefore Using a problem-oriented coping strategy conveys a sense of control and mastery over the situation, which in turn affects the improvement of mental health. Also, using an emotion-oriented strategy modulates emotion and may eliminate the symptoms but does not eliminate the stressor, so it can inadvertently lead to health problems, so less use of this strategy can predict increased mental health.

Also, in another explanation of the findings of this study, it can be stated that effective coping methods lead to the modulation of stress and consequently increase the better performance of individuals. Since coping is problem-oriented, it is a logical way to find and deal with stress it can have a more lasting and effective effect on job performance, and this effect Positive can bring mental health to the employed person.

The results of this study show that mental health has a significant relationship with the strategies that people use to cope with their stress, it can be realized the importance of coping strategies in increasing and decreasing people's mental health. Findings showed that coping with the problem can be more effective and sustainable strategy due to a rational approach to the stressor or factors, but coping with the problem due to instability and temporary reduction of stress does not have such an effect.

Explaining this hypothesis, it has been found that choosing appropriate ways to deal with stress can reduce the impact of stress on mental health and lead to mental adjustment. On the other hand, in the theory of defense mechanisms, the method of coping has been treated as a personality trait which justifies the result obtained from this study. It can also be mentioned that according to the model of Folkman and Lazarus in the coping process, cognitive skills are used to solve the problem. The individual uses cognitive skills to solve problems by applying an effective problem-oriented coping style. Based on this, the ways to deal with the problem are directly examined and psychological satisfaction is usually obtained by finding appropriate solutions to the problem.

On the other hand, this situation causes mental order and cohesion and reduces emotional turmoil. The source

of stress is better identified and can be assessed as controllable due to the obtained mental cohesion and emotional calm. Knowing the source of control on the one hand and evaluating it controllably on the other hand helps to increase mental health. Recognizing the source of stress also increases confidence and anxiety by increasing self-confidence and improving mental health, resulting in increased job satisfaction. Conversely, the use of emotion-oriented strategy prevents the person from directly and effectively dealing with the problem and reduces his ability to solve the problem.

This condition disrupts mental cohesion and emotional turmoil and reduces mental health. Mental and emotional turmoil also undermines the ability to properly identify the source of stress and negatively affects mental health.

Therefore, it can be said that in the context of the relationship between coping strategies and mental health, it can be said that job stress in a two-way interaction is one of the results of selecting and using coping strategies effective and commensurate with change and stress. On the other hand, it creates a healthy psychological atmosphere in the light of which it is possible to correctly recognize and evaluate the stressful situation in order to choose an effective coping strategy, which makes the job satisfaction of the person not undergo negative changes.

As a result, the mental health of the person is not challenged. The results of the analysis showed that job stress can affect the mental health of employees in two ways: first, directly and secondly, through problem-oriented and emotion-oriented coping methods. The direct effect of job stress on mental health has been discussed in the previous explanations. However, in order to explain the mediating role of problem-oriented and emotion-oriented coping methods, the following materials are presented.

Explaining the mediating role of problem-oriented coping strategies in the relationship between job stress and mental health, it can be said that in people who use problem-oriented coping style, the level of stress is low and the level of stress is low. Emotions enable a person to better use cognitive and dynamic skills to deal with the problem in the shadow of peace of mind, and as a result, achieve greater satisfaction and achieve higher mental health. Also, in explaining this finding, it can be said that people who use problem-oriented coping style have low levels of stress, and low levels of emotional stress make a person better able to use cognitive skills in the shadow of peace of mind.

Use dynamism to deal with the problem and thus achieve greater satisfaction and higher mental health. Thus, the mediating role of problem-oriented coping style in the relationship between job stress and mental health is justified.

Also, in explaining the mediating role of emotion-coping strategies in the relationship between job stress and mental health, it can be said that emotion-coping is the best option to manage the response to stressors that people cannot. To control them, their use is inevitable in some situations, and it can be said that their use can be a way to escape the effects of stress; Because emotional coping seeks to reduce the negative emotions associated with stress to control their reactions, but these people do not try. Solve infrastructure problems or use a logical strategy. Therefore, the person has resorted to these strategies to reduce negative emotions and escape from stress, and on the other hand, the use of this strategy cannot be effective because the logic and cognition of the person has not yet been able to accept the stress of work and this causes health.

The person's psyche is challenged. On the other hand, denial and passivity are two characteristics of those who use the emotional coping style, denial of the stressful situation to avoidance behavior and passivity in the face of the stressful situation and inability to use potential abilities and The initiative of the person leads and by reducing the person's self-confidence increases the problems and dissatisfaction and thus reduces the mental health of the person, so the negative relationship between these two variables can be justified. Finally, considering the issues raised, predicting mental health with regard to the level of job stress and the use of problem-oriented and emotion-oriented coping strategies seems logical, but this fact is supported by the findings. Statistically, this study was confirmed.

Conclusion

The corona virus is becoming a global health crisis. The various aspects of the virus are still unknown to the public. This study aims to introduce the general aspects of this virus. This study is a narrative review that uses the keywords COVID-19 and New Coronavirus 2019 to review available texts. Published articles from 1/1/2020 to 3/3/2020 were reviewed. The search mainly used PubMed and Google Scholar. Free search in Google search engine is used to collect background information. Aspects of disease prevalence, control and prevention were studied and presented. This study showed that the routes of transmission of Covid-19 virus are through respiratory droplets and direct contact with secretions containing the virus. One of the causes of the uncontrolled and surprising prevalence of this disease is the long incubation period of the cause and how it is transmitted in the same asymptomatic, mild or pre-emergence periods. According to the study, the symptoms of the virus in people with chronic diseases such as cardiovascular disease, diabetes, cancer, high

blood pressure and chronic respiratory diseases are more severe and the risk of the virus increases with age and is still a definitive treatment.

Not discovered for it. The results showed that the epidemic of this new virus will continue for 3 months and according to prevention methods and management of effective factors in its transmission, it can be prevented. It should be noted that the proposed ways to treat this disease are also being researched and tested. Currently the only way to control coronavirus 19 is to maintain good personal hygiene, increase immunity and avoid crowding in crowded places. Regarding the effect of job stress on mental health, job stress has been introduced as one of the most important causes of mental disorders.

In most of these studies, stress is considered as a response that is directly experienced by stressful sources. The role of job stress in employees' mental health agrees with the results of previous research in this field and shows that stress caused by working conditions has a significant effect on employees' mental health. Stress factors in the workplace reduce behavioral and physical symptoms and endanger his mental health.

According to what has been said, today job stress is known as one of the most important pests of organizations that on the one hand affects the physical and mental health of individuals and on the other hand can lead to other negative consequences and Most importantly, the stress on employees leads to a decline in the quality and quantity of services in the organization, which will have adverse effects on public health. Therefore, given that job stress is always present in different forms, using a permanent and effective method to deal with stress as

well as feeling understood and supported by others can affect their response to stress and as a result, controlling such situations will have an impact that will improve both job performance and employees' mental health.

Having mental health problems leads to dysfunction, decreased motivation, anxiety, fear and worry and causes a person to spend a significant part of their mental energy on such problems. As a result, it is certain that he will not have enough power and interest to work in the organization. Since human resources are one of the largest resources and assets of any organization, their health plays a decisive role in increasing productivity. Therefore, any planning and even investment in this sector that leads to maintaining and improving the health of employees, can ultimately lead to increased efficiency and be accompanied by a return on investment, so it is necessary to intervene that can improve Employees' mental health should be effective, planned and implemented periodically for employees to prevent mental health decline. Finally, as the findings of the present study showed, job stress is a cause of damage to health, and effective coping strategies such as problem-solving that leads to the modulation of job stress can be effective in maintaining and improving health. This finding shows that a person's mental health can be improved by increasing problem-oriented strategies through training in the use of these types of strategies as well as reducing their emotion-oriented strategies.

Conflict of interest

No conflict of interest

References




1. WHO Novel Coronavirus (2019-nCoV): Situation Report--13: WHO website; 2020 [cited 2020 February 3]. Available from: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200202-sitrep-13-ncov-v3.pdf>.
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* 2020;382(8):727-33. DOI: 10.1056/NEJMoa2001017 PMID: 31978945
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497-506. DOI: 10.1016/S0140-6736(20)30183-5 PMID: 31986264
4. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet.* 2020;395(10223):507-13. DOI: 10.1016/s0140-6736(20)30211-7
5. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020; 395(10223):514-23. DOI: 10.1016/S0140-6736(20)30154-9 PMID: 31986261
6. CDC. 2019 Novel Coronavirus: Interim Guidance for Healthcare Professionals: CDC website; [updated February 2, 2020; cited 2020 February 3]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html>.
7. WHO. Clinical Management of Severe Acute Respiratory Infection When Novel Coronavirus (nCoV) Infection Is Suspected: Interim Guidance: WHO website; [updated January 28, 2020; cited 2020 February 3,]. Available from: [https://www.who.int/publications-detail/clinical-management-of-severe-acuterespiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acuterespiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected).
8. CDC. 2019 Novel Coronavirus: How 2019-nCoV Spreads: CDC website; [updated January 31, 2020; cited 2020 February 3]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html>.
9. WHO. Novel Coronavirus (2019-nCoV): Situation Report--7: WHO website; [cited 2020 February 3]. Available from: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200127-sitrep-7-2019-ncov.pdf>.

10. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. *N Engl J Med*. 2020;382(10):970-1. DOI: 10.1056/NEJMc2001468 PMID: 32003551
11. WHO. Disease Outbreak News: Pneumonia of Unknown Cause--China: WHO website; [cited 2020 February 3]. Available from: <https://www.who.int/csr/don/05-january-2020-pneumonia-of-unknown-cause-china/en/>.
12. Li Q. An Outbreak of NCIP (2019-nCoV) Infection in China — Wuhan, Hubei Province, 2019–2020. *China CDC Weekly*. 2020;2(5):79-80. DOI: 10.46234/ccdcw.2020.022
13. CDC. 2019 Novel Coronavirus: Confirmed 2019-nCoV Cases Globally: Global Map: CDC website; [updated January 31, 2020; cited 2020 February 3]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/locations-confirmed-cases.html>.
14. CDC. 2019 Novel Coronavirus: Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens From Patients Under Investigation (PUIs) for 2019 Novel Coronavirus (2019-nCoV): CDC website; [cited 2020 February 3]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html>.
15. CDC. 2019 Novel Coronavirus: Interim Guidance for Implementing Home Care of People Not Requiring Hospitalization for 2019 Novel Coronavirus (2019-nCoV): CDC website; [updated January 31, 2020; cited 2020 February 3]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-home-care.html>.
16. CDC. 2019 Novel Coronavirus: Interim Infection Prevention and Control Recommendations for Patients With Confirmed 2019 Novel Coronavirus (2019-nCoV) or Patients Under Investigation for 2019-nCoV in Healthcare Settings: CDC website; [updated February 3, 2020; cited 2020 February 3]. Available from: <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html>.
17. Chu CM, Cheng VC, Hung IF, Wong MM, Chan KH, Chan KS, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax*. 2004;59(3):252-6. DOI: 10.1136/thorax.2003.012658 PMID: 14985565
18. Arabi YM, Allothman A, Balkhy HH, Al-Dawood A, AlJohani S, Al Harbi S, et al. Treatment of Middle East Respiratory Syndrome with a combination of lopinavir-ritonavir and interferon-beta1b (MIRACLE trial): study protocol for a randomized controlled trial. *Trials*. 2018; 19(1):81. DOI: 10.1186/s13063-017-2427-0 PMID: 29382391
19. News B. China Names HIV Drugs in Treatment Plan for New Virus: Bloomberg News website; 2020 [cited 2020 February 3]. Available from: <https://www.bloomberg.com/news/articles/2020-01-26/china-names-abbvie-s-hiv-drugs-in-treatment-plan-for-new-virus>.
20. Agostini ML, Andres EL, Sims AC, Graham RL, Sheahan TP, Lu X, et al. Coronavirus Susceptibility to the Antiviral Remdesivir (GS-5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease. *mBio*. 2018;9(2). DOI: 10.1128/mBio.00221-18 PMID: 29511076
21. Sheahan TP, Sims AC, Leist SR, Schafer A, Won J, Brown AJ, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat Commun*. 2020;11(1):222. DOI: 10.1038/s41467-019-13940-6 PMID: 31924756
22. Organization WH. Coronavirus disease (COVID-19) outbreak [cited 2020 January 30]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
23. Prevention CfDCa. Coronavirus disease 2019 (COVID-19) [cited 2020 January 30]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/index.html>.
24. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, et al. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med*. 2003;348(20):1953-66. DOI: 10.1056/NEJMoa030781 PMID: 12690092
25. Drosten C, Gunther S, Preiser W, van der Werf S, Brodt HR, Becker S, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med*. 2003;348(20):1967-76. DOI: 10.1056/NEJMoa030747 PMID: 12690091
26. de Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, et al. Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the Coronavirus Study Group. *J Virol*. 2013;87(14):7790-2. DOI: 10.1128/JVI.01244-13 PMID: 23678167
27. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med*. 2012;367(19):1814-20. DOI: 10.1056/NEJMoa1211721 PMID: 23075143
28. Radonovich LJ, Jr., Simberkoff MS, Bessesen MT, Brown AC, Cummings DAT, Gaydos CA, et al. N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel: A Randomized Clinical Trial. *JAMA*. 2019;322(9):824-33. DOI: 10.1001/jama.2019.11645 PMID: 31479137
29. Zhao S, Ling K, Yan H, Zhong L, Peng X, Yao S, et al. Anesthetic management of patients with suspected or confirmed 2019 novel coronavirus infection during emergency procedures. *J Cardiothorac Vasc Anesth*. 2020 1:28.
30. Wang LS, Wang YR, Ye DW, Liu QQ. A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. *Int J Antimicrob Agents*. 2020; 105948. [DOI:10.1016/j.ijantimicag.2020.105948]
31. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Sci China Life Sci*. 2020; 63(3):457-60. [DOI:10.1007/s11427-020-1637-5]
32. Chan JF, To KK, Tse H, Jin DY, Yuen KY. Interspecies transmission and emergence of novel viruses: Lessons from bats and birds. *Trends Microbiol*. 2013; 21(10):544-55. [DOI:10.1016/j.tim.2013.05.005]
33. He J, Tao H, Yan Y, Huang SY, Xiao Y. Molecular mechanism of evolution and human infection with the novel coronavirus (2019-nCoV). *BioRxiv*. 2020.
34. Ding N, Zhao K, Lan Y, Li Z, Lv X, Su J, et al. Induction of atypical autophagy by porcine hemagglutinating encephalomyelitis virus contributes to viral replication. *Front Cell Infect Microbiol*. 2017; 7:56.
35. Segars J, Katler Q, McQueen DB, Kotlyar A, Glenn T, Knight Z, et al. Prior and Novel Coronaviruses, COVID-19, and human reproduction: What is known? *Fertil Steril*. 2020 April.
36. Kearney J. Chloroquine as a potential treatment and prevention measure for the 2019 Novel Coronavirus: A review. *Preprints*. 2020; 2020030275.
37. Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. *Science*. 2020; 367(6485):1444-8.

38. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. *J Pharm Anal*. 2020 March.
39. Read R. Flawed methods in "COVID-19: Attacks the 1-Beta chain of hemoglobin and captures the porphyrin to inhibit human heme metabolism". *ChemRxiv*. 2020 April.
40. Gundlapally J, Kumar A, Kashyap A, Saxena AK, Sanyal A. In search of Novel Coronavirus 19 therapeutic targets. *Helix*. 2020; 10(2):01-08. [DOI:10.29042/2020-10-2-01-08]
41. Boccia S, Ricciardi W, Ioannidis JPA. What other countries can learn from Italy during the COVID-19 pandemic. *JAMA Intern Med*. 2020.
42. Lai CC, Liu YH, Wang CY, Wang YH, Hsueh SC, Yen MY, et al. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths. *J Microbiol Immunol Infect*. 2020; 53(3):404-12.
43. Sun J, He WT, Wang L, Lai A, Ji X, Zhai X, et al. COVID-19: Epidemiology, evolution, and cross-disciplinary perspectives. *Trends Mol Med*. 2020; 26(5):483-95.
44. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020; 579(7798):270-3.
45. World Health Organization, United Nations Children's Fund (UNICEF). Water, sanitation, hygiene, and waste management for the COVID-19 virus: Interim guidance [Internet]. 2020 [Updated 2020 April 23]. Available from: <https://apps.who.int/iris/handle/10665/331846>
46. Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA*. 2020; 323(14):1406-7.
47. Yang Y, Lu Q, Liu M, Wang Y, Zhang A, Jalali N, et al. Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China. *medRxiv*. 2020.
48. Filatov A, Sharma P, Hindi F, Espinosa PS. Neurological complications of coronavirus disease (COVID-19): Encephalopathy. *Cureus*. 2020; 12(3):e7352.
49. Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19. *Brain Behav Immun*. 2020; S0889-1591(20)30465-7.
50. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and thrombotic or thromboembolic disease: Implications for prevention, antithrombotic therapy, and follow-up. *J Am Coll Cardiol*. 2020.
51. Nickbakhsh S, Ho A, Marques DFP, McMenamin J, Gunson RN, Murcia PR. Epidemiology of seasonal coronaviruses: Establishing the context for the emergence of coronavirus disease 2019. *J Infect Dis*. 2020; jiaa185.
52. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020; 395(10223):497-506.
53. Wan S, Yi Q, Fan S, Lv J, Zhang X, Guo L, et al. Characteristics of lymphocyte subsets and cytokines in peripheral blood of 123 hospitalized patients with 2019 Novel Coronavirus Pneumonia (NCP). *medRxiv*. 2020
54. Ganji A, Farahani I, Khansarinejad B, Ghazavi A, Mosayebi G. Increased expression of CD8 marker on T-cells in COVID-19 patients. *Blood Cells Mol Dis*. 2020; 83:102437.
55. Ghazavi A, Ganji A, Khaki M, Mosayebi Gh. [Existential philosophy of the immune system: Defense or homeostasis? (Persian)]. *J Arak Univ Med Sci*. 2018; 21(5):110-20.
56. Khaki M, Ghazavi A, Ghasami K, Rafiei M, Payani MA, Ghaznavi-Rad E, et al. Evaluation of viral antibodies in Iranian multiple sclerosis patients. *Neurosciences*. 2011; 16(3):224-8.
57. Wan Y, Shang J, Sun S, Tai W, Chen J, Geng Q, et al. Molecular mechanism for antibody-dependent enhancement of coronavirus entry. *J Virol*. 2020; 94(5):e02015-19.
58. Tang YW, Schmitz JE, Persing DH, Stratton CW. The laboratory diagnosis of COVID-19 infection: Current issues and challenges. *J Clin Microbiol*. 2020; JCM.00512-20.
59. Lu H. Drug treatment options for the 2019-new coronavirus (2019-nCoV). *Biosci Trends*. 2020; 14(1):69-71.
60. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends*. 2020; 14(1):72-3
61. Aimo A, Baritussio A, Emdin M, Tascini C. Amiodarone as a possible therapy for coronavirus infection. *Eur J Prev Cardiol*. 2020; 2047487320919233.
62. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, Cleary P, Khaw FM, Lim WS, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: A systematic review and exploratory meta-analysis. *J Infect Dis*. 2015; 211(1):80-90.
63. Anti-2019-nCoV Volunteers, Li Z, Wu M, Yao J, Guo J, Liao X, et al. Caution on kidney dysfunctions of COVID-19 patients. *medRxiv*. 2020.
64. Tsukamoto Y, Tamura T, Maeda Y, Miyake K, Ato M. N6-methylated adenine on the target sites of mamA from *Mycobacterium bovis* BCG enhances macrophage activation by CpG DNA in mice. *Tuberculosis*. 2020; 121:101890
65. Weir RE, Gorak-Stolinska P, Floyd S, Lalor MK, Stenson S, Branson K, et al. Persistence of the immune response induced by BCG vaccination. *BMC Infect Dis*. 2008; 8:9.
66. Broxmeyer DL. MD. "Promising antimicrobial hope for "coronavirus", but is it working against a virus?" *Pulm Res Respir Care*. 2020; 4:19-28.
67. Miller A, Reandelar MJ, Fasciglione K, Roumenova V, Li Y, Otazu GH. Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: An epidemiological study. *medRxiv*. 2020
68. Tozzi A, D'Amato G, Guarino A. Towards cross-reaction between SARS-CoV-2 and a childhood vaccine? *ResearchGate*. 2020
69. Mostaan S, Yazdanpanah B, Moukha R, Hozouri HR, Rostami M, Khorashadizadeh M, et al. Adverse effects of BCG vaccine 1173 P2 in Iran: A meta-analysis. *Adv Biomed Res*. 2016; 5:99.
70. Moliva JL, Turner J, Torrelles JB. Immune responses to bacillus Calmette-Guérin vaccination: Why do they fail to protect against *Mycobacterium tuberculosis*? *Front Immunol*. 2017; 8:407.
71. Tanner R, Villarreal-Ramos B, Vordermeier M, McShane H. The humoral immune response to BCG vaccination. *Front Immunol*. 2019; 10:1317.
72. Hemilä H. Vitamin C intake and susceptibility to pneumonia. *Pediatr Infect Dis J*. 1997; 16(9):836-7.
73. Nonnecke BJ, McGill JL, Ridpath JF, Sacco RE, Lippolis JD, Reinhardt TA. Acute phase response elicited by experimental Bovine Diarrhea Virus (BVDV) infection is associated with decreased vitamin D and E status of vitamin-replete preruminant calves. *J Dairy Sci*. 2014; 97(9):5566-79.

The cryonic medical application from the perspective of Islamic jurisprudence and ethics; a review of theories

La aplicación médica criónica desde la perspectiva de la jurisprudencia y la ética islámicas; una revisión de teorías

Laila Fakher¹ , Rajab Akbarzadeh² , Mohammad Reza Zamiri² ,
Ahmad Hossain Fallahi² , Sayed Morteza Mosavi³ ,
Sayed Mohamad Saeid Mohamadi⁴ 

1. Ph.D Student of Islamic Education, Payame Noor University, Qom, Iran 2. Assistant Professor, Department of Islamic Education, Payame Noor University, Qom, Iran 3. Ph.D of Islamic Education, Payame Noor University, Qom, Iran
4. Master of Quranic Sciences, Mofid University, Qom, Iran

Corresponding author

Rajab Akbarzadeh
Assistant Professor, Department of Islamic Education,
Payame Noor University, Qom, Iran
E-mail: rajab.akbarzadeh@yahoo.com

Received: 30 - I - 2021

Accepted: 28 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.98

Abstract

Objective: In studying new phenomena, it is necessary to consider their moral and religious aspects. Because everyone has accepted ideas and principles in their thoughts and minds, all of them are based on external principles that are common. As a golden rule in all divine and even non-divine religions and sects, it is acceptable and defensible that whatever you do not like for yourself, do not like for others. However, whether can we confirm or reject the cryonic discussion in terms of moral aspects? The objective investigation of this subject is from the perspective of Islamic ethics.

Methods: In this research, it has been attempted with expert studies in published articles to examine whether, according to the teachings of Islam, can be found a confirm or reject for the cryonic discussion.

Results: Since Islam has a moral school of realism and assesses everything on a predetermined basis, this matter will be possible, and perhaps in non-Islamic thoughts and even some Islamic sects due to the unrealistic nature of ethics, cannot be obtained the verdict of this issue. At first, this argument is to be raised that the meaning of death is the limits of human authority over the corpse after death; finally, the reasonable possibilities in this field and its attention are discussed.

Conclusion: In the end, according to what is stated in the fundamentals of Islamic ethics, it has been ruled that this subject, if it complies with the conditions and regulations, has no conflict with Islamic ethics.

Keywords: Cryonics, cryopreservation, medical, ethics, Islam, death.

Resumen

Objetivo: Al estudiar los nuevos fenómenos, es necesario considerar sus aspectos morales y religiosos. Como todo el mundo tiene ideas y principios aceptados en sus pensamientos y mentes, todos ellos se basan en principios externos que son comunes. Como regla de oro en todas las religiones y sectas divinas e incluso no divinas, es aceptable y defendible que lo que no te guste para ti, no te guste para los demás. Sin embargo, ¿podemos confirmar o rechazar la discusión sobre la criogenia en términos de aspectos morales? La investigación objetiva de este tema se realiza desde la perspectiva de la ética islámica.

Métodos: En esta investigación, se ha intentado con estudios de expertos en artículos publicados examinar si, de acuerdo con las enseñanzas del Islam, se puede encontrar una confirmación o rechazo para la discusión criónica.

Resultados: Dado que el Islam tiene una escuela moral de realismo y evalúa todo sobre una base predeterminada, esta cuestión será posible, y tal vez en los pensamientos no islámicos e incluso algunas sectas islámicas debido a la naturaleza irreal de la ética, no se puede obtener el veredicto de esta cuestión. En primer lugar, se va a plantear el argumento de que el significado de la muerte son los límites de la autoridad humana sobre el cadáver después de la muerte; finalmente, se discuten las posibilidades razonables en este campo y su atención.

Conclusiones: Al final, de acuerdo con lo establecido en los fundamentos de la ética islámica, se ha dictaminado que este tema, si cumple con las condiciones y regulaciones, no tiene ningún conflicto con la ética islámica.

Palabras clave: Criónica, criopreservación, medicina, ética, Islam, muerte

Introduction

Not much research activity has been done regarding cryonics, and since it is an emerging issue, but cannot be obtained any information from ancient scientific texts. Therefore, to obtain new and religious information, it has been paid to study the opinions in this regard. There is no research history in medical ethics in cryonics, and this research is considered the first step in this category. The following research subjects have investigated this issue from the perspective of Shiite jurisprudence and jurisprudential religions^{1,2}.

Although we have a better Latin resource situation, none of them have dealt with its moral aspect from the Islamic point of view. For example, the article "Seeking Life After Death" by David Shaw, University of Glasgow 2009; in this article it has been paid to the cryonic process, and the arguments put forward by proponents are included the potential for community benefit, the ability to cheat death for at least a few years, and the prospect of immortality if resuscitation is successful.

The article "Immortality Technology" 2012; Brain on Ice, Cambridge King's College, which has studied the scientific and medical ways which through of them can treat various diseases.

The article "Cryopreservation technique" Merkel, Coyote Hilljah; Which it has paid to explain cryonics from a scientific aspects and expresses that icy air is a method of stabilizing the situation everyone who is incurable; So that they can be treated with medical facilities and care that will probably be available in the future.

For the lexicography of this research, it is necessary to say that "ethics" in the word is the plural of the word "Temper" and has the same root as the word "Creation", with this the difference that the word "Creation" is used about the face and appearance form and the word "Temper" refers to the mysterious character³.

Moreover, the meaning of "Islamic ethics" refers to the rules of the practical intellect, which expresses the requirements of intellect in the position of action and determines the correct way of doing things that are guided the human from the aspect of the moral agent so that act them requires the human perfection and happiness⁴.

Regarding the principles of Islamic jurisprudence and ethics and the similarity of these two sciences, it should be said that both of these sciences provide direct and infallible knowledge of religion to the representatives of God on earth, namely the Infallibles (peace be upon them). Both of these sciences consider the sense, intellect, and revelation as the means of acquiring knowledge;⁴ both of them recognizes material, immaterial, and rational matters

that there is also the accessible possibility to it, and both of them also consider possible the acquisition of useful knowledge only in this way, that each tool of knowledge is used correctly and about its source. In other respects, these two sciences have many similarities, including considering the legislation of the rulings in accordance with the right and truth and human interests. They consider the tasks according to reality and perform them as comfortable and in harmony with nature⁵.

However, concerning the subject of cryonics, we should also mention in this report that a girl was asked the High Court in London to allow her to freeze her body after her death so that her hopes for a long life in the future would not be destroyed. This girl, who did not want to reveal her name for legal reasons, was acquainted with cryonics through the Internet in the last months of her life. The judge of the High Court and accepting her request was ruled that the trial trend should not be issued until the girl's death. The judge agreed with this action for the first time was performed after passing a legal process⁶. This young girl died on November 17, 2016, and the court had banned news coverage of this event⁷. The lawyer of this British teenager says: "She could convince the court and me that she had reached the necessary maturity and capacity to make such a decision"⁷. This teenage girl wrote to the judge: "I think that my body freezing based on cryonics method will give me a chance to recover and come back to life in the future, maybe hundreds of years from now." "I think my disease treatment will be discovered in the future, and the futurists can revive me, so I want to have this opportunity. This is my wish"⁸. The judge had acknowledged that to prevent undue pressure on the sick girl, the news of this case and the course of the trial proceedings remain confidential until her death.

The father of this girl, who also has cancer, was opposed her. In order to prevent this request, execution was referred to court, because he believes that even if her daughter is to be cured and wakes up again in 200 years, she will have no relatives and will remember anything and be placed in an unpleasant situation, especially that she is a 14-year-old girl without a family, and after revive may not be able to adapt herself with the conditions of the United States⁷.

The father says: "I believe that they are using false promises to abuse those who fear the death and are vulnerable from the people." None of them do think that cryonics ever be successful. I am a rationalist, and I have confidence in my medical perspective. When I asked that if there was this probability even one in a million that my daughter come back to life again, they could not give the positive answer"⁸.

The corpse of this girl after her death was sent to Michigan in America in a container filled with dry ice so that it is to be placed in a tank with computer-controlled

temperature and is frozen by liquid nitrogen at the cost of about 37000 thousand Pound which this girl's grandparents paid. The body will eventually be placed in a cryopreservation tank at minus 196 ° C temperature⁹ for long-term maintenance⁶.

By reading this report, the human is first affected by the emotional and human nature of the daughter and father; A girl who has cancer and with a brief acquaintance with bio-freezing and under the influence of the possibility of resuscitation in the future persuades the lawyer and the judge to freeze her body after death and a father who, like many people¹⁰ believes that her daughter deceived the false promises of cryonic companies and they have abused her child. She, who also has cancer, does not believe in resuscitation, especially since the Cryonics Company managers have not guaranteed her daughter's resuscitation.

Several points can talk about this subject. Should we accept the promise of this girl's father? This issue can be examined from two points. One point is that we still have no trust regarding the outcome of this event. This is only a probability. Moreover, with such costs that some have counted, this probability is not amplified¹¹, and the second point is that if after 200 years it is found a cure for her daughter's illness, she will be in a world without relatives and will be alone. Besides, the girl's father accuses cryonic companies of abusing his daughter in the immortality debate.

Should we accept mother and daughter's promise that they have sought what is known as immortality and, based on the same low probability, have chosen cryonics? To investigate this issue from the Islamic ethics perspective, it is necessary to see this issue's jurisprudential principles from different aspects. And for this reason, we must first know to what in the definition of death Islamic jurisprudence

Definition of death in Islam

Is what refers to it in the original jurisprudential books "Legal death"¹² or get out of the soul from the body, so that there is no return for it^{15, 38}. It is said that whether it is included the topic of cryonics or not. Moreover, if not, what extent control do we have over our bodies before we die? If it is ok, we need to see that after death, how can we control our bodies. (Which, of course, we will address in a separate section).

Some of the jurisprudence books say: "The signs of the difference between life and death or between living beings and inanimate objects, it is one of the things that is innately understood the living being breathes, eats, grows, reproduces and moves"¹³.

Moreover, after stating this issue, although some people are considered death as an unknown from some aspects, ultimately life is the opposite of death³⁶, and even dictionaries have introduced it as the opposite of death³⁷, while some of them consider the five cases to conclude the death debate." Human life has five categories; *First*: Conscious human life, *Second*: Unconscious human life, or in other words, physical life, which is not based on consciousness and sense and movements, such as sleep state or drunkenness or the use of sleeping pills, of course, considering the health of the central part of the brain, which becomes like plant life that its feeding and growing and breathing is without sense. *Third*: The life of the organs outside the body after death, which is done under intensive-care conditions. *Fourth*: The life of the body's stem cells; *Fifth*: The single-cell life that takes place in the lining of the uterus and grows into multiple cells to make the body organs"¹³.

Moreover, after stating these subjects, it says: "Human life is the same, conscious and unconscious life (The first and second part of life) until the soul is not separated from the body. However, the life of some organs of the body and the like after death is not called human life"¹³.

By this definition, it is possible to declare the cases that have become involved the brain death, or similar cases, in fact, a dead person, because their human life does not exist¹⁴. That according to jurisprudence opinion, a dead person is said to a person that according to custom, the soul has been separated from her/his body^{39, 40} and brain death is known as someone whose brain has been dismembered or whose head has been separated⁴¹ and from the point of view of medicine science., brain death is equal to the death of a patient⁴².

This topic is more straightforward; because official death has been announced, but definitive death is not. Moreover, our discussion in this article is about the whole body, not the cases that cryo-preservation only one part of the limbs.

Some other Islamic thinkers in the expression time of dying and others' duties say about the deceased: "What is known among the religious man is that the death is the time of separation of the soul from the body. People say about this field that the king of death pulls the soul out of the human head, so the first part of the body that becomes soulless is the legs, and then the rest of the parts until it reaches the head, and the last part which dies is the head. In the parts of the head, the first part which the soul separates from it, the mouth and the tongue, then it reaches to the eyes and after that, the ears are died and then it goes up to the brain. Furthermore, after that, the soul generally separates from the body. Furthermore, this graduation [Which is common in the words of the people] can be found in the noble tradition of the Prophet and some of the sermons of Nahj al-Balaghah."¹⁵.

Of course, this does not mean that the soul, which there is the soul in the legs, is transferred to the rest of the body, and the soul of the body is transferred to the head. Because the soul of each organ of the body is unique; And even if it is transferred, it will not be useful in the survival of that organ¹⁵.

Then he introduces death as the separation of the soul from the body and distinguishes it from life and the state of life that if the soul is in the body, it will affect the body, stimulate it, and reciprocally is affected from the body. After death, this relationship between soul and body will be disconnected¹⁵.

With this definition, it is possible to imagine a situation in which the cryonics argument, official death is far from definitive death, and at the same time, it is possible to carry out an activity in cryo-preservation of a person.

Of course, according to this quotation, the only problem is that until the last part of the body is not empty of soul, there is no death or die and cannot be considered a person as a dead person. Regarding brain death, religious thinkers also say that the survival or death of a person depends on the view of custom, and whatever the community recognizes about a person is associated with the criterion of action¹⁶, as mentioned.

In addition to the questions and answers that have been emulated from the religious authorities in this regard, it has also been said whether it is possible to have the organs of a person who has suffered brain death (and medically, there is no hope for his survival, but some organs like the heart work for a while) transplanted to a patient who is needed? (Considering that if they are waiting, they may no longer be linked)

His answer to such a question is that because at the same time that the heart is working and the brain is dead, a drug may be invented or discovered that activates the brain (Although this issue may be certainty in many populations, this issue may be uncertainty in some people and individuals; because the finding of some drugs that are invented or discovered for some diseases is instantaneous) therefore, with this possibility, it is not permissible¹⁷.

The limits of a human's authority over his/her corpse after the death

In the case of the cryonic debate, which is usually related to the after death, this point is also remarkable whether a person in Islamic law has the authority after the death over his body or not. If it is ok, what is the extent?

Cryonics involves cooling the body of a person who has just been announced his/her official death, and this is

done to the point of freezing and glass transition with liquid nitrogen. The purpose of cryonics is to keep the body in a particular freezing state for several years to find a solution and treatment for his/her disease in the future and the advancement of various sciences. In cryonics, the tissues of the human body remain healthy¹⁸.

But in this case, what has been confirmed is related to the death of the person who turned him into a corpse. According to the Alcor website, the cryopreservation process begins precisely at the time of the complete cardiac arrest. It means that after attempts to resuscitate the patient, he/she could not reach a conclusion, and his death was officially announced. What is essential is that the intracellular chemical balance has not been disturbed yet. Therefore, at this stage, the corpse is connected to the artificial heart and lung system so that the blood circulates in the body, and doctors can inject a specific type of chemical drug into the body¹⁹.

According to the Cryonic Life Extension Foundation website, Alcor¹⁹ states that during the cryonic process, the body is frozen so that its vital tissues are not damaged. In the future, whenever it was needed, they can be using the "Cardiopulmonary resuscitation device" re-circulate blood flow and return life to the sick person.

Injectable drugs cause the brain oxygen level to remain at an acceptable level and do not interfere; rapid freezing of the brain at this time also causes the brain to fail without state changing or its cells becoming crystalline. The ideal purpose for doing such an action is to allow the brain to resume its function without problems after freezing years. In any case, since such a person is considered a person dead in the Islamic jurisprudence perspective, it is necessary to examine whether a person has authority over his corpse after his death. In the case of a positive answer, to what extent is this authority?

Because bequest and its importance have been emphasized in Islamic narrations and even a chapter of narration books has been dedicated to it²², we must say that requesting that after official death, how people act depends on conditions, including *First*. It is a testament to the knowledge of how to act so that, according to what has been said, the patients who become crypto, with the knowledge and knowledge of their destiny, accept this matter. Moreover, he should not have been deceived or forced to make this will. Because a person who has been forced to do something has no rule in Islamic jurisprudence and ethics such as retribution or compensation^{23, 44}. *Second*. The amount paid for this work should not be more than one-third of the person's property at the time of death. That is, if these large expenses, which are required for cryonics, are more than one-third of the deceased's property, it must be with the permission of the heirs, and if they do not allow it, this is excluded and does not have to be enforced^{24, 25}.

Third. However, since he is considered dead from the jurisprudential point of view, his property can be divided and given to the heirs. However, if, after years, that person is revived and they can heal him, all his possessions must be returned to him to decide. So perhaps it can be said that the property will be in the hands of the trust's heirs²⁵.

On the other hand, we see that a person can bequeath that he in what conditions and where is buried²⁰, so he has authority. Nevertheless, on the other hand, in testimony about his/her properties, we cannot order more than one-third²¹, so the limits of a person's authority over his successor, although it is existing, it is limited. Although the property is different from the corpse, however, the corpse's powers are also the same manner. That is, as, in the case of property, he has the right to occupy one-third of the property, and his authority is not absolute⁴³. In the case of the corpse, his authority is not absolute.

Considering this fact that is requesting and its importance have been emphasized in Islamic narrations and even a chapter of narration books has been dedicated to itself²², so we must say that requesting after official death, how act for the people depends on following conditions, including:

First, this testament should be aware in terms of how to act so that, according to what has been said, the patients who become crypto, with the knowledge and information of their destiny, accept this matter; And he should not have been deceived or forced to make this testament; Because a person who has been forced to do something, he/she does not have a ruling in Islamic jurisprudence and ethics such as retribution or compensation^{23, 44}.

Second. The costs paid for this work should not be more than one-third of the person's property at the time of death. It means that if these large expenses, which are required for cryonics, to be more than one-third of the deceased's property, it must be with the permission of the heirs, and if they do not allow it, this matter is excluded and is not enforceable^{24, 45}.

Third. From the jurisprudential perspective, he/she is considered a dead person so his/her property can be divided and given to the heirs. Nevertheless, if, after the years, those person is revived and they could treat him/his, all his/her possessions must be returned to him/his in order to decide again about it. So perhaps it can be said that the property will be in the heirs' hands²⁵.

Attention to the probabilities at the reasonable level

There is disagreement among all people about whether cryonics reach conclude outcome or not. According to the story we were mentioned in the introduction section, almost in all cases, the general agreement and

disagreement of people, scientists, and thinkers with cryonics can be seen¹⁹.

Among the experts who have expressed concern about the resuscitation of the girl's corpse and the ethical issues surrounding it, Calligo Cohen, is a professor and neurologist at King's College London. He said:" This issue morally is very complicated. He got rid of the disease and could receive comfort, but others may be affected by this decision at present. The court's decision to allow this teenager body freeze could have an unintended impact on the other people for this false hopes."

British philosopher, Mario Warwick, says:" People need to be more aware of this freezing, even though it is not prohibited or protected by law. People are brutally abused and exploit those who are vulnerable to disease. This is a real moral dilemma"⁸.

Professor Martin Reese, a cosmologist, and astrophysicist, has said:" The promises made by the proponents of cryonics are ridiculous and unserious. In our opinion, this is unlikely this action to be possible, and even if it is possible, it should be ignored. From a moral point of view, if people want to be frozen and revived, even if they can survive, they will make a significant commitment to future generations, and any revived person will be a nuisance or incompatibility for the future."⁸

Anders Sandberg, a researcher at the Institute for the Future of Humanity at Oxford University, said:" Cryopreservation is a controversial discussion that is better known in science fiction than in real life. The individual who wants to keep frozen are like refugees who are fleeing from the present time to the future; "Because they cannot live here."¹⁹

Professor Niels Hope, a professor of ethics and teacher in the life sciences, has said:"

"Until the cryonics is not successful, we do not have to talk about its rules. Nevertheless, if it advances in the next 10 years, there may be ethical, legal, and social questions to answer in this case. The legal effects of successful freezing and resuscitation can be complex and out of reach. If death is reversible, the other body is something higher than the property that must be buried and destroyed."⁸

This possibility of resuscitation was caused by the incidence of legal and moral dilemmas, including that only wealthy people would have access to this expensive technology and whether people would decide to freeze when they became ill. Moreover, as well as inheritance laws to be endangered.

Hope also said: "We should be avoided the Restrictive rules or regulations. Strict rules can lead to the innovations which we need in this area. If it is successful, it would be

extraordinary, but it can be extremely problematic in addition to attraction. It is very dangerous to say that something is impossible in science and technology in the 21st century. People who use the word "Impossible" are courageous!"⁸.

In the dialog of this thinker, it may be not reached conclusion cryonics has been documented, but it should also be noted this point that any work has necessary preliminary; If we want to know whether cryonics reach the outcome or not, it should be done on several people to determine being or not being the outcome.

Tim Gibson from the England nonprofit Cryonics Group, which was prepared the body of a 14-year-old girl for transportation to a freezing facility in Michigan, said that all of their staff are crypto volunteers and will abide well by the laws and rules.

He said:" The danger for us is that cryonics will become more to an advertising idea, and more profit-seeking companies, by abusing customers will harm us and this idea."¹⁹

Dr. Raymond Risko, a chiropractor and physiologist who teaches at the university, says that "If the controversial science of the body freezing of a person living with 14-year-old cancer is used, scientists and doctors are at risk of harming their jobs, and they are removed of the scientific community, so they should avoid discussing it". Nevertheless, Risko argued that fiction science signs could not be dismissed merely as fiction science and said that it is likely that within five to 10 years, experts would be able to resuscitate a small mammal, such as a mouse, after preserving it in liquid nitrogen.

Risko also has said that "But those who were interested in freezing, they were hoped that scientific advances would be able to resuscitate the humans who were frozen. He added that "Unconventional concepts" such as in vitro fertilization, space travel, and organ transplants all have experienced" Initial distrust."

He said:" We do not need to start a big debate. We are still trying to endure all the hardships in keeping and maintaining the organs, and eventually we will find a solution for the whole body."²⁶

Christoph Koch, a neuroscientist at the California Institute of Technology, has said, "If this chemical change in the brain does not destroy the memory synapses, the cryopreservation process will be amazing."²⁷

According to **Ray Kurzweil**, an American scientist, and futurist, "When the world changes thousands of centuries later, the human will reach immortality."²⁸

The proponents of this topic that any subject that was once a fictional story have been later realized; Therefore, the cryopreservation process will be possible one day.

Nevertheless, there are also opposing ideas about the cryopreservation subject. Some scientists consider that death is another side of the coin of life and believes that preventing death will never be realized; it contradicts the nature of life and the nature of living beings.

According to these quotations, many cases can be mentioned that were accompanied by denial or even ridicule of others, but in later years, it has been proven, and no one could deny them. As an example, remembering the following points about the fantasy of space travel is not without merit:

Dr. Forrest Remalton, an astronomer at the University of Chicago, was said in 1932 that: "There is no hope for the imaginary idea of reaching the moon because of insurmountable obstacles to escaping the earth's gravity. Also, SIR Richard vali, an England Royal astronomer, was told in 1956 that:" All these writing about space travel is quite difficult".

While **Neil Armstrong** and **Baz Aldrin** were the first astronauts to set foot on the moon in 1969.

In this case, whether the possibility of cryonic impact is a reasonable and acceptable thing or not, it should be said that about the numerous cases of significant advances in the medical and technical fields, it must be accepted that patients return to life. Their treatment is not a matter which cannot be quickly ruled out, so such a possibility is rational and acceptable.

Cryonics is often performed on people who have an incurable disease and are waiting for definitive death according to current medical, scientific definitions. Furthermore, in the definition of death, modern medical sciences should be used, which this definition is different from the past²⁹.

Besides, in the verses of the Qur'an, giving life to one person is as valuable as reviving all human beings³⁰.

In Islamic jurisprudence and ethics, preserving the lives of oneself and others has been considered as the obligatory topics. Moreover, even in case of conflict with other rulings, it precedes them³¹. So, saving a patient's life depends on stopping freezing itself; it will be enforceable. Of course, if we are sure to save his/her life or there is a strong possibility in this regard.

Conclusion

After the brain's oxygen supply is complete, the brain cells gradually stop working and begin to degenerate, but many of its cells are still alive. Therefore, a person's personality information can be encrypted in a short period and up to a few hours after his biological death. The loss

of this information will be the final death of information and even irreversible³².

Modern science cannot define the exact moment of information death. However, the theoretical death of information depends not only on current knowledge of the mechanisms of the human brain but also on the ability of future medical technologies to recover and restore information in the damaged brain in order to move towards of patients rehabilitation and improve their personality²⁸.

Stopping the electrical activity of the brain during freezing storage does not mean losing personal identity and memory. Although short-term memory is likely to be lost, there are many reasons why we believe that identity and long-term memory are preserved at the synapse and in the connection between neurons. If today we can bring life back to people who have been drowned for "A few minutes" and even a few hours, it should be able to save their life after a while, which is one of the benefits of future technologies.

It can be said that "Absolute death" occurs only when the essential information of the brain is destroyed, and the preservation of the brain and its memory is exactly what the cryonic goal is to achieve.

Of course, no one can guarantee success because no one can guarantee the future. No one can predict scientific progress with certainty. The Cryonics Institute believes that this is an influential theory with a high probability of success, but it does not mean that we do not consider crises and social problems. Nuclear wars, economic collapse, political conflicts, and terrorism are all possible and can destroy the body of cryonics patients as much as they can take the life of any human being.

Therefore and considering the reasonable possibility that exists in this field and the limits of the authority that exists for human beings about their death, it can be said that the issue ruling in Islamic ethics is that this is permissible by observing some of its preconditions and there is nothing wrong with it.

Acknowledgments

The authors would like to thank the Department of Islamic Education, Payame Noor University, Qom, Iran, for their reference preparation support.

References

1. Tabatabaee SF, Husseinzadeh ARM, Molavifar S. The cryonic order of the patient is in vain from the shiite jurisprudence. *Feghh J*. 2017; 9(30-31):21-32.
2. Tawaf M. The legitimacy of freezing the terminally ill patient in terms of jurisprudential religions. Master thesis. University of Religions and Denomination, Qom, Iran, 2014.
3. Haeri Esfahani MH. *Al-Fosol Al-Gharviat Fel Osol-Alfeghhiat*, Dar Al Hayat Islamic Sciences Publisher, 1st edition, Qom, 1984, pp. 337-8.
4. Motahhari M. *Human Social Evolution*, Sadra Press. 1st ed, Qom, Iran, 2011.
5. Ahmadpour M. *Islamic jurisprudence and ethics: a comparative science*. 2nd edition, Islamic Sciences and Culture Academy press. Qom, 2016, p. 208.
6. TIME magazine. Current & Breaking News, National & World Updates. Available from: <https://www.time.com>.
7. CNN website, Breaking News, Latest News and Videos2016 . Available from: <https://edition.cnn.com/2016/11/18/health/uk-teenager-cryonics-body-preservation/index.html>.
8. The guardian. Available from: <https://www.theguardian.com>.
9. Bolte RG, Black PG, Bowers RS, Thorne JK, Corneli HM. The use of extracorporeal rewarming in a child submerged for 66 minutes. *J Am Med Assoc*. 1988;260(3):377-9.
10. Jones G, Whitaker M, King M. Speculative ethics: Valid enterprise or tragic cul-de-sac? *Bioethics in the 21st Century: IntechOpen*;2011..
11. Cron R. *Is Cryonics an Ethical Means of Life Extension?* Dissertation, University of Exeter, 2014.
12. Sabzevari SAA. *Mahzib al-Hikam*, Vol 30. Al-Manar Institute - Ayatollahs Office Fourth; Qom: 1413.
13. Qandehari MAM. *Al-Fiqh and Medical Problems*, Vol 2. Publication of Islamic Propagation Office of Qom Seminary, Qom, Iran. 2003, P. 152.
14. Khomeini SRM. *Towdhiih Al-Masa'el*. Vol 2, Ministry of Islamic Guidance Publications, Tehran, Iran, 2003.
15. Al Sadr MS. *Ma Wara Al-fiqh*. Vol 10, Dar Al-Azvae press, Beirut: Lebanon; 1st edition, 1999.
16. Lankarani MFM. *Medical and Patient Orders (Fazel)*, Vol 1. Jurisprudence Center of infallible Imams, 2008.
17. Behjat MT. *Estafatat*. Vol 4, Office of the Grand Ayatollah Behjat, Qom, 2007.
18. Apleyard B. *How to live forever or die trying: on the new immortality*. Simon & Schuster, 2007, p. 307.
19. Alcor Life Extension Foundation: Cryonics, 2012. Available from: <https://alcor.org/Library/videos/sandberg2012.html>.

20. Naraq MAMM. Documentary of the Shi'a Fel-ahkam al-Shari'ah, Vol 19. 1st edition, Al-Bait Institute, Qom, Iran, 1994.
21. Majlesi MBMT. Bahar al-Anwar. Vol 1. Institute of Al-Tab and Al-Nasha, Beirut, Lebanon. 1990.
22. Al-Hurr al-Aamili. Wasail of Shia (Wasail al-Shia). 2nd Volume. 4th Edition. al-rabbani A, editor. Beirut: Dar Ahya al-Torath al-Arabi; 1960. p. 13. [Arabic]
23. Kulayni AMY. Usul al-Kafi. Vol 15. Al-Hadith Publisher, Qom, Iran, 1987.
24. Sadough Qomi MAB. Man La Yahzar al-Fiqh. Vol 4. Seminary of Islamic Publications Office, Qom, Iran, 2nd edition, 1993.
25. Jeebe Ameli (Shahid Sani) Z. [Masalek Al-Atham Ela Tanqih Al-Sharayeh AlEslam]. Vol. 7. 1st Edition. Qom, Iran, Maaref Islami Institute, 1993 [in Arabic].
26. The Science Surrounding Cryonics - MIT Technology Review. Available from: <https://www.technologyreview.com/s/542601/the-science-surrounding-cryonics>.
27. Humans immortal - Believe or Not - medical cases. Available from: <https://medicalcases.info/featured/humans-immortal-belive-not/>.
28. KrioRus where you can be FROZEN to come back from the dead. Available from: www.kriorus.ru/english.html.
29. Goudarzi F, Kiani M. Forensic Medicine. Samt Organization, Tehran, Iran, 2013.
30. Ali MM. Holy Quran. Ahmadiyya Anjuman Ishaat Islam Lahore, USA, 2011.
31. Mercer C. Resurrection of the Body and Cryonics. Religions. 2017;8(5):96.
32. Buetow HA. Medical-Legal Aspects of Cryonics: Prospects for Immortality Ethical-Legal and Social Challenges to a Brave New World Genetics-Ethics and the Law. J Contemporary Health Law & Policy (1985-2015). 1986;2(1):173-88.
33. Safari N, Bouzari S. Comparative Study of Legal Aspects of Cryonics in Iran and US Law. Iranian J Med Law. 2020;13(51):155-76.
34. Beauchamp TL, Childress JF. Principles of biomedical ethics. Oxford University Press, USA, 2001.
35. Tierney TF. The preservation and ownership of the body. Perspectives on embodiment: The intersections of nature and culture. 1999:233-61.
36. Majlesi MB. Maladh al-akhyar fi fahm Tahdhib al-akhbar. Ayatollah Marashi Najafi Library Press, Qom, Iran. 1986, P. 50.
37. Manzur I. Lisan al-'arab. Dar Ihya Turath Arabiy; Vol 15, 1997, pp 15-409.
38. Huxtable R. Cryonics in the Courtroom: Which Interests? Whose Interests?. Medical law review. 2018;26(3):476-99.
39. Montazeri Najafabadi HA. Risalah Istifta'at. 1st edition. Vol 2, Qom, Iran, 2009, P. 381.
40. Movahedi Lankarani MF. Judgments of Physicians and Patients (Fazel). Qom, Iran, P. 149.
41. Makarem Shirazi N. Medical Rules. Imam Ali ibn Abi Talib, Qom, Iran, 2008; P. 113.
42. Kubar OI, Mikirtichian G, Nikitina A. Ethical Review of Biomedical Research in the CIS Countries: social and cultural aspects. Saint-Petersburg: Fenix. 2007.
43. Seifi Mazandarani AA. Dalil Tahrir Alwasilat - Alwasia. 1st ed. Tehran-Iran: Arranging and Publishing the Works of Imam Khomeini Institute. P. 129.
44. Kulayni M. Al-Kafi(Printed - Islamic). 4th edition. Dar Alkutub Al'islamia, Tehran, Iran, 1987. P. 129.
45. Mousavi Khomeini SR. Tawdih Almasayil (Imam Khomeini). 8th edition. Office of Islamic Publications affiliated with the Society of Teachers of the Seminary of Qom; Qom, Iran, 2003, Vol 2, P. 674.

Extra-articular manifestations in rheumatoid arthritis and its relationship with serology markers in Saudi patients

Identificación de los factores que afectan la atención integral de las personas mayores en Irán

Fehaid Ghali Alanazi 

Department of Medicine, College of Medicine, Majmaah University, 11952 Saudi Arabia

Corresponding author

Fehaid Ghali Alanazi

Department of Medicine, College of Medicine

Majmaah University, Al-Majmaah 11952 Saudi Arabia

E-mail: f.alanazi@mu.edu.sa

Received: 2 - II - 2021

Accepted: 24 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.106

Abstract

Introduction: Extra-articular manifestations of Rheumatoid arthritis (ExRA) are defined as all the diseases and symptoms which are not directly linked to the musculoskeletal system and can occur at any age after onset. The study aimed to investigate the frequency of ExRA patients and to assess its relationship to serology markers.

Methods: This observational cross-sectional study was carried out on 60 Saudi patients with newly or previously diagnosed RA according to 2010 American College of Rheumatology-European League against Rheumatism criteria. They were followed in the Rheumatology Clinic at King Khalid Majmaah Hospital (KKMH) from January 2017 to December 2020. Data collected was analyzed by SPSS 26 and appropriate statistical tests were applied.

Results: A total of sixty patients (52 women; 8 men) who visited KKMH were included in this study. The mean age of the patients was 47.87 ± 11.55 years, and the female-to-male ratio was 6.5:1. Out of the total, 14 patients (23.3%) had a family history of RA. 18 patients developed ExRA features; anemia occurred in 30%, Sjögren's syndrome in 8.3%, thrombocytosis in 6.7%, and leukopenia in 3.3%. Further, 40 patients (66.7%) were positive for RF, 47 (78.3%) for anti-CCP antibodies, and both markers were positive in 36 (60%) of the patients. Among 18 patients with ExRA, the percentage of positive RF and anti-CCP were 25% and 32%, respectively, while 42 patients with no ExRA, both markers were positive in 75 % and 68 %, respectively.

Conclusion: Anemia is the most common extra-articular manifestation of TA, however, no significant relationship was observed between serology markers and extra-articular manifestations of RA.

Keywords: Rheumatoid arthritis, extra-articular manifestations, serology markers, Saudi patients.

Resumen

Introducción: Las manifestaciones extra articulares de la artritis reumatoide (ExRA) se definen como todas las enfermedades y síntomas que pueden relacionarse directamente con el sistema musculoesquelético y que pueden aparecer a cualquier edad tras su inicio. El estudio tuvo como objetivo investigar la frecuencia de los pacientes con ExRA y evaluar su relación con los marcadores serológicos.

Métodos: Este estudio observacional transversal se llevó a cabo en 60 pacientes saudíes con AR recién diagnosticada o previamente diagnosticada según los criterios del American College of Rheumatology-Liga Europea contra el Reumatismo de 2010. Fueron seguidos en la Clínica de Reumatología del Hospital King Khalid Majmaah (KKMH) desde enero de 2017 hasta diciembre de 2020. Los datos recogidos se analizaron con SPSS 25 y se aplicaron las pruebas estadísticas adecuadas.

Resultados: Un total de sesenta pacientes (52 mujeres; 8 hombres) que visitaron el KKMH fueron incluidos en este estudio. La edad media de los pacientes era de $47,87 \pm 11,55$ años, y la proporción entre mujeres y hombres era de 6,5:1. Del total, 14 pacientes tenían antecedentes familiares de AR. 18 pacientes desarrollaron rasgos ExRA; la anemia se presentó en el 30%, el síndrome de Sjögren en el 8,3%, la trombocitosis en el 6,7% y la leucopenia en el 3,3%. Además, 40 pacientes fueron positivos para el FR, 47 para los anticuerpos anti-CCP, y ambos marcadores fueron positivos en 36 de los pacientes. Entre los 18 pacientes con ExRA, el porcentaje de RF y anti-CCP positivos fue del 25% y el 32%, respectivamente, mientras que en 42 pacientes sin ExRA, ambos marcadores fueron positivos en el 75% y el 68%, respectivamente.

Conclusiones: La anemia es la manifestación extra articular más frecuente de la AT, sin embargo, no se observó una relación significativa entre los marcadores serológicos y las manifestaciones extra articulares de la AR.

Palabras clave: Artritis reumatoide, manifestaciones extra articulares, marcadores serológicos.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune condition characterized by inflammatory polyarthritis that is recurring and progressive, leads to tenosynovitis, erosion, destruction of the joint surface, and deformity¹. RA affects 1-2% of the world's population and occurs two to three times more frequently in women than in men². Extra-articular manifestations of RA (ExRA), defined as all the diseases and symptoms which are not directly linked to the musculoskeletal system³. ExRA can occur at any age after onset, and it is more common in men than women⁴. Several studies have reported an ExRA with a frequency ranging from 18% to 41%, reasons for the wide range due to study design and differences in the enrolled population⁵. Although there are no reliable predictors for the development of ExRA, some scientific reviews have reported that risk factors could be associated with it, such as male gender, smoking, and positive serology markers (RF, CCP and ANA) and HLA-region gene⁶. Many of these ExRA are related to the more active and severe RA, so it is considered a severe condition and emphasized the role of ExRA as predictors of premature mortality in patients with RA⁷. ExRA patients should be monitored and treated aggressively⁸.

In this study, we reviewed the incidence and frequency of ExRA among RA patients from the Majmaah province population attended at the rheumatology clinic in King Khalid Majmaah Hospital (KKMH), Saudi Arabia (SA), and identified the relationship between serology markers and ExRA.

Materials and methods

This is a cross-sectional retrospective study involving 60 RA patients from Saudi Arabia. They were newly or previously diagnosed with RA according to the 2010 American College of Rheumatology/European League Against Rheumatism Diagnostic Criteria⁹. The patients were selected from the rheumatology clinic in KKMH from January 2017 to December 2020. The research was approved by the central institutional review board of the Ministry of Health, SA.

The demographic profiles of the patients, as well as the length of the disease at the time of the initial presentation (classified as Less than 5 years, Between 5 to 10 years, and more than 10 years), and presence of extra-articular manifestations of RA (ExRA) were evaluated based on their medical records. Family history was considered positive if at least one first-degree relative had been diagnosed with RA. Laboratory blood tests, including rheumatoid factor (RF) and anti-cyclic citrullinated peptide (Anti-CCP) levels, were performed routinely at admission to the clinic.

Extra-articular manifestations of RA included Sjogren syndrome, which was defined by xerophthalmia and xerostomia. Hematological changes included leucopenia (WBC count $<4 \times 10^9/\text{ul}$), thrombocytosis (platelet count $>400 \text{ K}/\text{ul}$) and anemia (normochromic or hypochromic). During the study, the relationship between serology markers and extra-articular manifestations was assessed. All characteristic features of patients with RA seen at KKMH were statistically analyzed using IBM SPSS version 26 (IBM Corp., Armonk, NY, USA). Age was defined as mean and SD, whereas categorical data was expressed as frequencies and percentages. Pearson's chi-square and Fisher's exact tests were used to test for associations between study variables. A p-value of 0.05 was considered important.

Results

Clinical characteristics of the RA patients

This research included a total of sixty patients (52 women, 86.7 percent; 8 men, 13.3 percent) who visited KKMH. The patients' average age was 47.87 \pm 11.55 years, with a female-to-male ratio of 6.5:1. The duration of the disease at the time of the study for most of the patients was Less than 5 years, 36 subjects (60%), followed by Between 5 to 10 years, 13 subjects (21.7%), and more than 10 years, 11 subjects (18.3%). Out of the total, 14 patients (23.3%) had a family history of RA. In our study, extra-articular manifestations were found in 18 patients (30%). Further, 40 (66.7%) patients were positive for RF, 47 (78.3%) for anti-CCP antibodies, and both markers were positive in 36 (60%) of the patients. **Table I** illustrates the clinical characteristics of the RA patients.

Table I: Characteristics features of rheumatoid arthritis population (n=60).

Parameter	n (%)
Mean age (years)	47.87 \pm 11.55
Gender	
Female	52 (86.7)
Male	8 (13.3)
Female: Male ratio	
Duration of the disease (years)	
Less than 5	36 (60.0)
Between 5 - 10	13 (21.7)
More than 10	11 (18.3)
Family history of RA	
No	46 (76.7)
Yes	14 (23.3)
Extra-articular manifestation	
No	42 (70)
Yes	18 (30)
Rheumatoid factor (RF)	
Positive	40 (66.7)
Negative	20 (33.3)
Anti-cyclic citrullinated peptide (Anti-CCP)	
Positive	47 (78.3)
Negative	13 (21.7)
Rheumatoid factor (RF) and Anti-cyclic citrullinated peptide (Anti-CCP)	
Positive	36 (60.0)
Negative	24 (40.0)

Main extra-articular features

The main extra-articular features are shown in **table II**. Anemia was found in 18 patients (30%). Normochromic normocytic and hypochromic microcytic were the commonest, affecting 7 (11.7%) anemic patients, while hypochromic normocytic anemia affects only four (6.7%) patients. Sjogren syndrome and thrombocytosis were present in 5 (8.3%) and 4 (6.7%) patients. Leukopenia was the least frequent feature found in RA patients, occurring in 2 patients only (3.3%).

Relationship between RF, Anti-CCP, and extra-articular manifestation in RA patients

The relationship between RF, Anti-CCP, and extra-articular manifestation in RA patients is shown in **table III**. The percentage of positive RF and anti-CCP in 18 patients with ExRA, were (25%) and (32%), respectively, while in

Table II: Main extra-articular manifestations of rheumatoid arthritis population (n=60).

Extra-articular manifestations	n (%)
Sjogren syndrome	5 (8.3)
Anemia	18 (30.0)
Normochromic normocytic	7 (11.7)
Hypochromic normocytic	4 (6.7)
Hypochromic microcytic	7 (11.7)
Leukopenia	2 (3.3)
Thrombocytosis	4 (6.7)

42 patients with no ExRA, both markers were positive in (75 %) and (68 %), respectively. We did not report any statistically significant between the status of serology markers in the two RA groups (with and without ExRA).

Discussion

This study aimed to investigate the extra-articular manifestations in rheumatoid arthritis and its relationship with serology markers among about 60 Saudi patients attending the rheumatology clinic at KKMh. Based on our search of the literature, no previous study has evaluated the ExRA in the Majmaah province, SA. The mean age of patients in the RA group was 47.87 ± 11.55 years, and the majority, 52 (86.7%), were female (female-to-male ratio, 6.5:1). These findings are consistent with previously published reports^{10,11}. The duration of the disease at the time of the first presentation for the majority of the patients was Less than 5 years (60%) and higher than that observed in the Al-Ghamdi study¹².

Family history considers as one of the strongest risk factors for developing RA and may predict the disease course. It is an integral part of the workup and diagnosis of RA. In the present review, fourteen patients reported at least one first-degree relative affected by RA, higher than the proportion reported by Al-Herz¹³.

Table III: Determine the association between the RF, Anti-CCP and extra-articular manifestation in RA patients.

Associations		RF -20 (33.3)	RF +40 (66.7)	p-value	Anti-CCP - 13(21.7)	Anti-CCP + 47(78.3)	p-value
Items	Overall n=60 (%)						
Extra-articular manifestation							
No	42(70)	12(60)	30 (75)	0.231	10 (77)	32 (68)	0.538
Yes	(30)18	8 (40)	10 (25)		3 (23)	15 (32)	
Sjogren syndrome							
No	55 (91.7)	19 (95)	36 (90)	0.508	13 (100)	42(89.4)	0.219
Yes	5 (8.3)	1 (5)	4 (10)		0 (0)	5 (10.6)	
Anemia							
No	42 (70.0)	15 (75)	17(67.5)	0.185	11(84.6)	31(66)	0.943
Yes	18 (30.0)	5 (25)	13(32.5)		2 (15.4)	16 (34)	
Normochromic Normocytic							
No	53 (88.3)	17(85)	36 (90)	0.569	12(92.3)	41(87.3)	0.614
Yes	7 (11.7)	3 (15)	4 (10)		1(7.7)	6 (12.7)	
Normocytic Hypochromic							
No	56 (93.3)	19 (95)	37(92.5)	0.714	13 (100)	43 (91.5)	0.276
Yes	4 (6.7)	1 (5)	3 (7.5)		0 (0)	4 (8.5)	
Microcytic Hypochromic							
No	53 (88.3)	19 (95)	34 (85)	0.255	12(92.3)	41(87.3)	0.614
Yes	7 (11.7)	1 (5)	6(15)		1(7.7)	6 (12.7)	
Leukopenia							
No	58(96.7)	19 (95)	39(97.5)	0.611	13 (100)	45(95.7)	0.449
Yes	2 (3.3)	1 (5)	1 (2.5)		0 (0)	2 (4.3)	
Thrombocytosis							
No	56 (93.3)	19 (95)	37(92.5)	0.714	12(92.3)	44 (93.6)	0.866
Yes	4 (6.7)	1 (5)	3 (7.5)		1(7.7)	3 (6.4)	

At present, biomarkers such as RF and Anti-CCP have important diagnostic value for RA. Several studies prove that Anti-CCP is a more specific marker than RF due to their high specificity to RA. Our cross-study showed patients positive for RF, anti-CCP and both of them were (66.7%), (78.3%) and (60%), respectively. These results are comparable to the proportion reported by other studies¹⁴⁻¹⁵.

Extra-articular can involve many systems and organs such as the skin, cardiopulmonary, hematology, nervous, eyes, gastrointestinal and renal, and it is significantly present more frequent in seropositive patients¹⁶. However, there is no agreed classification for these manifestations due to the variation in definitions and criteria observed in different study designs. In our study, the frequency of ExRA was 30% among our patients. However, these results disagreed with previous investigations¹².

In scientific reviews, the main ExRA has been evaluated. The hematological abnormalities of ExRA are broad and include anemia, leukopenia, thrombocytopenia, thrombocytosis, and malignancies, and could present either at the time of diagnosis or during the course of the disease¹⁷. Anemia is one of the most common ExRA symptoms, and it can be caused by a number of factors including disease activity, medication side effects, dietary deficiencies, and gastrointestinal bleeding¹⁸. Anemia was the most common ExRA in our population, occurring in 18 (30.0%) of patients, with normochromic normocytic and hypochromic microcytic were much higher among our patients (11.7%), followed by hypochromic normocytic found in 4 (6.7%) of patients. These findings are consistent with those of Cojocar et al.⁴. The percentage of thrombocytosis was (6.7%) among our patients, while leukopenia occurred in (3.3%), and these findings were less than the reported data by Al-Ghamdi¹².

Keratoconjunctivitis sicca is, by far, the most common ocular manifestation in individuals with RA¹⁹, and it is described as an aqueous tear deficiency. The incidence of keratoconjunctivitis sicca is between 11.6% to 50%²⁰, and it is frequently observed together with xerostomia in a secondary Sjögren's syndrome¹⁹. This disorder needs artificial tears for a lifetime 21. In our study, Sjögren's syndrome was found in 8.3% of patients, and it is comparable to that reported in the Al-Ghamdi study 6%¹².

Table II presents the details of the main ExRA found in this study.

Table III presents the details of the association between the RF, Anti-CCP, and ExRA patients found in this study. Many studies have examined the relationship between them, such as Turesson et al., suggested that both serology markers (Anti-CCP and RF) were associated with severe ExRA²². Also, Kim study found that Anti-CCP levels are significantly high in patients with ExRA²³. Moreover, the results of the Egypt study showed that

ExRA patients have significantly high titer and positivity of RF and Anti-CCP, and they found (67.2%) ExRA patients have positive Anti-CCP²⁴. However, another study postulated that Anti-CCP levels tended to be higher in patients with ExRA, but this was not statistically significant²².

In our study, among 18 patients with ExRA, the percentage of positive RF and anti-CCP were (25%) and (32%), respectively, while 42 patients with no ExRA, the percentage of positive RF and anti-CCP were (75%) and (68%), respectively. We compared the status of RF and anti-CCP in the two RA groups (with and without the main ExRA), and we did not observe any statistical significance. These results are inconsistent with previously published reports²²⁻²⁴.

Overall, ExRA can involve multiple organs that cause comorbidities and may also have psychological and social consequences. ExRA has an association with RA disease activity; therefore, it has had a role as a predictor of early mortality among RA patients. Based on our findings, the incidence and frequency of ExRA among studied groups are comparable to the proportion reported by others. On the other hand, the serology markers were not prevalent in the presence or absence of ExRA among RA. However, in future studies, the number of investigated patients must be increased to confirm our findings and to accurately represent the entire population.

Conclusion

Anemia is the most common extra-articular manifestations of RA and present in up to one-third of the studied group. However, our data did not observe any relationship between serology markers and extra-articular manifestations of RA. More extensive sample size studies are needed in the future to confirm our findings.

Acknowledgments

The author would like to thank the Deanship of Scientific Research at Majmaah University, Saudi Arabia for supporting this research under Project Number: R-2021-88.

References

- Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet*. 2016; 388: 2023-38.
- Turesson C, Matterson EL. Management of extra-articular disease manifestations in rheumatoid arthritis. *Curr Opin Rheumatol*. 2004;16(3):206-11.
- Mielants H, Van den Bosch F. Extra-articular manifestations. *Clin Exp Rheumatology* 2009; 27(Suppl. 55):S56-S61.
- Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD, Tanasescu R. Extra-articular Manifestations in Rheumatoid Arthritis. *Maedica (Bucur)*. 2010;5(4):286-91.
- Kishore S, Maher L, Vikas M. Rheumatoid vasculitis: a diminishing yet devastating menace. *Curr Rheumatol Rep*. 2017;19: 39.
- Al-Ghamdi A, Attar SM. Extra-articular manifestations of rheumatoid arthritis: a hospital-based study. *Ann Saudi Med*. 2009; 29(3):189-93.
- Bongartz T, Cantaert T, Atkins SR, Harle P, Myers JL, Turesson C, Ryu JH, Baeten D, Matteson EL. Citrullination in extra-articular manifestations of rheumatoid arthritis. *Rheumatol (Oxford)* 2007;46(1):70-5.
- Young A, Koduri G. Extra-articular manifestations and complications of rheumatoid arthritis. *Best Pract Res Clin Rheumatol*. 2007; 21(5): 907-27.
- Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham III CO, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, Combe B. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis & Rheumatism*. 2010;62(9):2569-81.
- Dougados M. Comorbidities in rheumatoid arthritis. *Curr Opin Rheumatol*. 2016;28(3):282-8.
- Al-Swailem R, Al-Rayes H, Sobki S, Arfin M, Tariq M. HLA-DRB1 association in Saudi rheumatoid arthritis patients. *Rheumatol Int*. 2006;26(11):1019.
- Al-Ghamdi A, Attar SM. Extra-articular manifestations of rheumatoid arthritis: a hospital-based study. *Ann Saudi Med* 2009; 29:189-93.
- Al-Herz A, Al-Awadhi A, Saleh K, Al-Kandari W, Hasan E, Ghanem A, Abutiban F, Alenzi A, Hussain M, Ali Y, Khadrawy A. A comparison of rheumatoid arthritis patients in Kuwait with other populations: results from the KRRD registry. *J Adv Med Med Res*. 2016:1-1.
- Mewar D, Wilson AG. Autoantibodies in rheumatoid arthritis: a review. *Biomed Pharmacother*. 2006;60(10):648-55.
- Zemri K, Sellam F, Harir N, Beniassa Z, Hebri ST, Bensaber O, Elmehadji D, Nadji Z, Karoubi K. Is there an association between Anti-Citrullinated Peptide Antibodies and the Severity of Rheumatoid Arthritis Parameters in Algerian Patients?. *J Drug Delivery Therap*. 2020;10(4):17-24.
- Sahatçiu-Meka V, Rexhepi S, Manxhuka-Kërliu S, Rexhepi M. Extraarticular manifestation of seronegative and seropositive reumatoid arthritis Bosn. *J Basic Med Sci*. 2010; 10(1): 27-31.
- Bowman SJ. Haematological manifestations of rheumatoid arthritis. *Scand J Rheumatol*. 2002; 31: 251-9.
- Agrawal S, Misra R, Aggarwal A. Anemia in rheumatoid arthritis high prevalence of iron-deficiency anemia in Indian patients. *Rheumatol Int*. 2006; 26(12): 1091-5.
- Crostein BN. Interleukin-6 – a key mediator of systemic and local symptoms in rheumatoid arthritis. *Bull NYU Hosp J Dis*. 2007; 65(suppl 1):S11-S15.
- Goto E, Matsumoto Y, Kamoi M, Endo K, Ishida R, Dogru M. Tear evaporation rates in Sjögren syndrome and non- Sjögren dry eye patients. *Am J Ophthalmol* 2007; 144(1):81-5.
- Zlatanović G, Veselinović D, Cekić S, Zivković M, Dorđević-Jocić J, Zlatanović M. Ocular manifestation of rheumatoid arthritis-different forms and frequency. *Bosn J Basic Med Sci*. 2010;10(4):323-327.
- Turesson C, Jacobsson LT, Sturfelt G, Matteson EL, Mathsson L, Rönnelid J. Rheumatoid factor and antibodies to cyclic citrullinated peptides are associated with severe extra-articular manifestations in rheumatoid arthritis. *Ann Rheum Dis*. 2007;66(1):59-64.
- Kim SK, Park SH, Shin IH, Choe JY. Anti-cyclic citrullinated peptide Antibody, smoking, alcohol consumption, and disease duration as risk factors for extra-articular manifestations in Korean patients with rheumatoid arthritis. *J Rheumatol*. 2008; 35(6):995-1001.
- El Sawi HA, Abd EL-Ghaffar N, Mansour MA. Relationship between anti-cyclic citrullinated peptide antibodies and disease activity and extra-articular manifestations of rheumatoid arthritis in Egyptian patients. *Al-Azhar Assiut Med J*. 2011;9(1):21-35.

ARTICLE ESPECIAL

La colisión de dos pandemias: retos y oportunidades

The collision of two pandemics: challenges and opportunities

Luis Masmiquel Comas 

Servicio de Endocrinología y Nutrición. Hospital Universitario Son Llàtzer. IdISBa

Correspondencia

Luis Masmiquel Comas

Servicio de Endocrinología y Nutrición.

Hospital Universitario Son Llàtzer. IdISBa

E-mail: lmasmiquel@hsl.es

Received: 21 - I - 2021

Accepted: 31 - III - 2021

doi: 10.3306/AJHS.2021.36.02.111

Resumen

Se revisan los datos epidemiológicos, fisiopatológicos y clínicos que permiten afirmar que la COVID-19 ha entrado en colisión con la gran pandemia de obesidad. La obesidad implica un aumento del riesgo de infección y multiplica las posibilidades de mala evolución y muerte por COVID-19. También, al igual que la COVID-19, supone una carga económica y sociosanitaria de primera magnitud.

Reconocer el impacto de la obesidad sobre la COVID-19 implica retos y oportunidades en ámbitos que abarcan desde la investigación y la prevención hasta el tratamiento ambulatorio y hospitalario de ambas entidades.

Por otra parte, debemos admitir que la interrelación obesidad-COVID-19 es compleja y subyace sobre determinantes sociales de salud.

Así pues, para entender y abordar COVID-19 deberemos abordar la obesidad y sus derivadas; es decir, otras enfermedades no comunicables como la diabetes, las enfermedades cardiovasculares, las enfermedades respiratorias crónicas y el cáncer. También, deberemos articular políticas y programas que reviertan las desigualdades. Realizar esfuerzos en esta línea sin duda mejorará nuestra salud e incrementará nuestra resiliencia frente a amenazas futuras.

Palabras clave: COVID-19, obesidad, hipertensión, diabetes mellitus, inflamación sistémica.

Abstract

The epidemiological, pathophysiological and clinical data that allow us to affirm that COVID-19 has collided with the great pandemic of obesity are reviewed.

Obesity confers an increased risk of infection and multiplies the chances of poor evolution and death from COVID-19. Also, like COVID-19, it supposes an economic, health and social burden of the first magnitude. Recognizing the impact of obesity on COVID-19 implies challenges and opportunities in areas ranging from research and prevention to outpatient and hospital treatment of both entities.

On the other hand, we must admit that the obesity-COVID-19 interrelation underlies social determinants of health that substantially increase its toll. Thus, to understand and address COVID-19 we must address obesity and its derivatives; that is, other non-communicable diseases such as diabetes, cardiovascular diseases, chronic respiratory diseases and cancer. Also, we must articulate policies and programs that reverse inequalities. Making efforts in this line will undoubtedly improve our health and increase our resilience against future threats.

Key words: COVID-19, obesity, hypertension, diabetes mellitus, systemic inflammation.

Introducción

La enfermedad por coronavirus de 2019 (COVID-19), producida por el nuevo coronavirus de tipo 2 causante del síndrome respiratorio agudo grave (SARS-CoV2), fue declarada pandemia por la Organización Mundial de la Salud (OMS) el día 11 de marzo de 2020¹. Aunque sus tasas de mala evolución pueden variar de un país a otro, se estima que alrededor de 1 de cada 5-10 adultos sintomáticos ingresan en el hospital. De éstos, las tasas de ingreso en UCI, dependiendo del país, oscilan entre el 5 y el 32%²⁻⁵. A finales de diciembre, el SARS CoV2 había infectado a alrededor de 82 millones de personas y provocado 1.800.000 muertes⁶.

Hace ya 3 años, como endocrinólogo, les hablaba de la obesidad como otra gran pandemia que es causa de grandes sufrimientos. La obesidad y el sobrepeso afectan conjuntamente a cerca del 50% de la población en los países industrializados y son el camino que nos lleva a muchas otras enfermedades no comunicables. La obesidad per se, supone un incremento del riesgo de hospitalización, de sufrir una enfermedad grave y de morir de forma prematura⁷.

Desafortunadamente, estas dos pandemias han entrado en colisión con repercusiones muy importantes para los individuos, las familias, los sistemas de salud, y la sociedad en general.

La infección por SARS-CoV2 tiene algunas similitudes con la gripe, por lo que podríamos decir que, en cierta manera, estábamos avisados. Desde la mal llamada gripe española de 1918, se sabe que la malnutrición, tanto por exceso como por defecto, comporta un peor pronóstico. En la misma línea, los datos recogidos durante las epidemias de gripe asiática de 1960 y de Hong Kong de 1968, indicaban que la obesidad se asociaba a una enfermedad más prolongada y a una mayor mortalidad. Finalmente, en 2009, la pandemia de gripe A (H1N1) permitió confirmar que la obesidad incrementaba la gravedad, el riesgo de hospitalización y el riesgo de muerte por gripe⁸.

En las próximas líneas revisaremos los datos epidemiológicos de la relación COVID-19-Obesidad, sus mecanismos potenciales y, finalmente, los retos terapéuticos y las oportunidades futuras derivadas de la colisión obesidad-COVID-19.

Evidencias clinicoepidemiológicas

Influencia de la obesidad sobre la COVID-19

Cai y colaboradores⁹, comunicaron por primera vez, en una serie de casi 400 pacientes de Shenzhen, que la obesidad incrementaba el riesgo de neumonía

en pacientes con COVID-19. La razón de riesgos de neumonía grave fue de 1,96 y 5,7 para los pacientes con sobrepeso y obesidad, respectivamente, en comparación con los individuos con normopeso. Poco después, en Francia, Simonnet y colaboradores¹⁰ mostraron, en una serie de 124 pacientes consecutivos ingresados en UCI, que aquellos con un índice de masa corporal (IMC) mayor de 35 tenían 7 veces más riesgo de precisar ventilación mecánica. La prevalencia de obesidad en estos pacientes fue casi del 50%. En la serie americana de Petrelli¹¹ de 4103 pacientes, 445 precisaron ventilación mecánica. De éstos fallecieron el 36,4%. En esta serie, el factor de riesgo más importante de hospitalización fue la obesidad con IMC >40 kg/m², unas 6 veces más en comparación con el normopeso.

Algunas series que han estratificado la muestra por edad observan un riesgo de 2 a 4 veces mayor de ingreso en UCI en pacientes de menos de 60 años con IMC >30 kg/m². Parece pues que el efecto de la obesidad es especialmente dramático entre la población más joven¹². Por otra parte, es bien conocido que existe una relación muy potente entre la edad avanzada y el riesgo de mala evolución de la COVID-19. Probablemente por ello, la influencia de la obesidad se pierde en la población anciana, especialmente a partir de los 70 años¹³.

Como bien saben ustedes, los datos basados en centros únicos son menos generalizables al estar sometidos a mayores sesgos. Sin embargo, estas observaciones vienen refrendadas por estudios multicéntricos y metaanálisis recientes.

A modo de ejemplo, la serie de Hendren y colaboradores¹³ aporta datos muy consistentes para las primeras economías al estudiar el *American Heart Association's COVID19 Cardiovascular Disease Registry* que recoge datos de 88 hospitales y más de 7000 pacientes. En él se observa que el riesgo combinado de muerte o ventilación mecánica fue un 28%, un 54% y un 80% más elevado para los IMC >30 kg/m², >35 kg/m² y >40 kg/m², respectivamente. El incremento aislado del riesgo de intubación fue de un 28%, un 88% y un 208% para las mismas categorías. Esta asociación fue particularmente intensa en menores de 50 años. Por último, en los pacientes con obesidad, también se objetivó, un riesgo aumentado de hemodiálisis y tromboembolismo. Parece claro pues que la obesidad incrementa el riesgo de mala evolución de la COVID-19 especialmente en los sujetos más jóvenes.

Finalmente, destacar los resultados del metanálisis de Popkin y colaboradores¹⁴ que recoge datos de 75 estudios sobre obesidad y COVID-19. En éste se concluye que la obesidad aumenta en un 100% el riesgo de hospitalización. Se objetiva que el riesgo de ingreso en UCI y de ventilación mecánica, en particular cuando el IMC es mayor de 35 Kg/m², se incrementa un 74% y un 69%, respectivamente; y también, se confirma un exceso de mortalidad del 48%.

Otro aspecto crucial es saber si los pacientes con obesidad son más susceptibles de ser infectados por SARS-CoV2. Existen pocos datos al respecto, pero el análisis de 2494 muestras del *UK Biobank* parece indicar que la respuesta es sí. El riesgo de tener una muestra positiva para SARS-CoV2 fue un 31%, un 55% y un 57% más elevado para pacientes con sobrepeso, obesidad con IMC >30 kg/m² y obesidad con IMC>35 kg/m², respectivamente¹⁵. En este mismo registro, un estudio de aleatorización mendeliana que compara 1211 pacientes europeos positivos con 387.079 individuos negativos indica que los pacientes en las categorías genéticas de alto riesgo para obesidad y dislipemia tienen mayor predisposición a la infección por SARS-CoV2¹⁶.

Influencia de la COVID-19 sobre la obesidad

La COVID-19 ha provocado la pérdida de puestos de trabajo y la falta de ingresos en una gran parte de la población. Esto se ha relacionado con un incremento de un bajo peso y malnutrición en los países pobres de Asia y África subsahariana¹⁷. Sin embargo, en los países con ingresos medios o elevados, algunos estudios objetivan un cambio hacia una mayor ingesta de alimentos procesados, con mayor densidad calórica, y de peor calidad nutricional. De la misma manera, se aprecia una mayor tendencia al sedentarismo^{18,19}. Todo ello, a pesar de no disponer de datos fidedignos en el momento actual, hace esperar un aumento de la prevalencia de obesidad y otras enfermedades no comunicables²⁰.

Mecanismos potenciales de la relación entre la COVID-19 y la obesidad

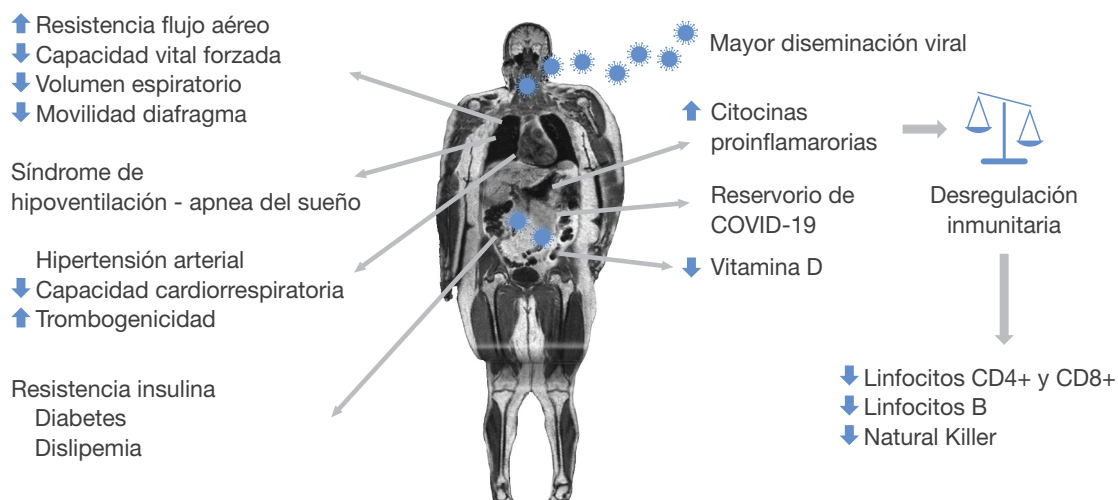
Diferentes mecanismos pueden explicar la relación COVID19-Obesidad (**Figura 1**).

La disfunción inmunológica

La obesidad es un estado inflamatorio sistémico de bajo grado que implica una activación crónica del sistema inmunológico. Esto afecta negativamente a los mecanismos de defensa y se asocia a una alta tasa de complicaciones infecciosas y fracasos de vacunación²¹.

El tejido adiposo es un órgano que juega un papel central en múltiples procesos fisiológicos entre los que se incluyen la inmunidad y la inflamación²². Secreta multitud de factores pro y antiinflamatorios que mantienen la homeostasis tisular. Cuando existe hipertrofia adiposa, se evidencia una infiltración por macrófagos que producen múltiples sustancias y se comunican con otras células del sistema inmune²³. En este estado, se observa un aumento de citocinas proinflamatorias (ej, la IL-6 y TNF- α) y una disminución de moléculas antiinflamatorias (ej. adiponectina). Todo ello, favorece la inflamación.

Como consecuencia de la inflamación, la inmunidad innata - primera línea de defensa- en la que participan interferones y células *natural killer*, y la inmunidad adaptativa, en la que participan linfocitos T-citotóxicos y B generadores de anticuerpos contra antígenos virales, están alteradas en los sujetos con obesidad²³. Por ello, responden peor frente a las infecciones víricas, observándose mayor carga viral, un ciclo vital más prolongado del virus y una peor capacidad de recuperación. En esta línea, se ha descrito una menor efectividad de antivirales y vacunas en los pacientes con obesidad. A modo ilustrativo, en las personas con obesidad, se describe una peor respuesta de células T CD8+ y de títulos de anticuerpos frente a la gripe tras la vacunación²⁴.



Por último, en los pacientes infectados por SARS-CoV2, si bien la respuesta inmune es vital para eliminar el virus, en algunas ocasiones, es persistente y exagerada causando una producción masiva de citocinas proinflamatorias. Como resultado, se produce una gran lesión tisular. Este fenómeno es lo que se conoce como "tormenta de citocinas". La tormenta de citocinas es una de las principales causas de progresión y muerte en los estadios finales de la enfermedad²⁵⁻²⁷. Curiosamente, estos pacientes con mala evolución, en sus estadios iniciales, presentan menor contaje de linfocitos CD4+, CD8+ y NK, así como mayores niveles de IL-6 y TNF. Por tanto, muestran un cierto paralelismo con lo que se observa en los pacientes con obesidad, aunque lógicamente, a una mayor escala²⁸.

El sistema Renina-Angiotensina

El sistema renina angiotensina (RAS) comprende péptidos implicados en procesos fisiológicos clave. Entre sus principales funciones está la regulación de la presión arterial y del equilibrio hidroelectrolítico. Uno de sus componentes principales es el enzima conversor de la angiotensina de tipo 1 (ACE1), que convierte la angiotensina I en angiotensina II. Esta última es el principal efector del sistema. Sin embargo, también promueve señales inflamatorias, protrombóticas y profibróticas que contribuyen a cambios patológicos en diferentes enfermedades como la insuficiencia renal y cardíaca. Múltiples evidencias implican al RAS en la patofisiología de la diabetes y de la enfermedad cardiovascular, ambas, comorbilidades bien reconocidas de la obesidad^{29,30}.

Por otro lado, el ACE de tipo 2 (ACE2) mitiga las acciones deletéreas de la angiotensina II al convertirla en angiotensina [1-7] (inactiva). Esta enzima, ha sido identificada como el receptor del SARS-CoV2³¹. La unión ACE2-SARS-CoV2, además de reducir la actividad de la enzima, se considera pues un factor de infectividad. Asimismo, los macrófagos alveolares que expresan ACE2 se han postulado como objetivos primarios del virus y actores importantes de la tormenta de citocinas. Por ello, la cantidad tisular de ACE2 se relaciona con la gravedad de las complicaciones y el pronóstico de los pacientes³².

Puesto que la obesidad se caracteriza por una hiperactividad del RAS, tanto a nivel adiposo como sistémico, es tentador especular que el eje RAS-SARS-CoV2 contribuye a las complicaciones y a la mala evolución de los pacientes con obesidad. También, puesto que el tejido adiposo expresa ACE2, se ha argumentado que la grasa visceral puede servir como lugar de reserva del virus. Este hecho podría contribuir a la mayor carga viral y al mayor tiempo de diseminación observado en los pacientes con obesidad³³.

La comorbilidad metabólica, renal y cardíaca de la obesidad

La obesidad es una de las principales causas de diabetes y de enfermedad cardiovascular. Estas comorbilidades están aceptadas como factores de riesgo de mala evolución de la COVID-19³⁴⁻³⁶. El mal control de la glucemia se ha relacionado con un aumento de mortalidad. También, se asocia a complicaciones crónicas implicadas en la mala evolución de la COVID-19 como microangiopatía, la enfermedad renal diabética y la enfermedad cardiovascular³⁷. La obesidad per se también provoca glomeruloesclerosis y favorece la aparición de insuficiencia renal. La enfermedad renal crónica está entre las 10 comorbilidades principales asociadas a la mala evolución de la COVID 19^{38,39}.

Es destacable también que la obesidad es una de las principales causas de fibrilación auricular e insuficiencia cardíaca. Una publicación del Instituto Nacional de Salud Italiano indica que la fibrilación auricular estaba presente en el 25% de los fallecidos por COVID-19 y era la cuarta comorbilidad por orden de frecuencia. El Departamento de Salud del Estado de Nueva York también ha situado a la fibrilación auricular entre las 10 comorbilidades más prevalentes^{38,40}.

Por último, la obesidad se asocia a enfermedad del hígado graso no alcohólico. Una revisión sistemática reciente indica que esta comorbilidad se relaciona de forma independiente con una mala evolución de la COVID-19⁴¹.

La hipercoagulabilidad y la trombosis

Los pacientes con COVID tienen un alto riesgo de tromboembolismo venoso y de coagulación intravascular diseminada, incluso a pesar de ser sometidos a anticoagulación sistémica. Este estatus de hipercoagulabilidad y trombosis se conoce como "coagulopatía asociada a COVID-19" y es proporcional a su gravedad⁴².

Es importante destacar que los pacientes con obesidad, con y sin síndrome metabólico, presentan hipercoagulabilidad y mayor riesgo de trombosis venosa de manera proporcional al IMC. La lista de mecanismos implicados es muy larga, desde la disfunción endotelial y la hipoactividad del inhibidor del activador del plasminógeno hasta la hiperactividad del fibrinógeno, FVII, FVIII y Factor Von Willebrand, pasando por el desequilibrio de citocinas y del RAS⁴³. Por tanto, es posible especular que el estatus procoagulante de la propia obesidad contribuye a la coagulopatía asociada a COVID.

La malnutrición y la obesidad sarcopénica

Los pacientes con obesidad suelen presentar anomalías metabólicas complejas, cambios en el estilo de vida y un historial de terapias de pérdida de peso. En conjunto, estos elementos pueden contribuir a un estatus nutricional y físico inadecuado que dificulta el mantenimiento de la masa muscular. Así pues, paradójicamente, la malnutrición y la sarcopenia son frecuentes en la obesidad. En los últimos años, múltiples estudios demuestran una relación directa entre sarcopenia y morbimortalidad en los pacientes con obesidad. Así, la *European Association for the Study of Obesity (EASO)* ha reconocido a la obesidad con baja masa muscular como un problema clínico y científico prioritario⁴⁴. En esta línea, investigadores de nuestro grupo junto con otros, hemos relacionado el estatus nutricional con la mala evolución y el pronóstico de la infección por SARS-CoV2^{45,46}.

De la misma manera, y quizás en relación con la nutrición y la sarcopenia, se describen niveles de vitamina D bajos en las personas con obesidad. Los niveles de vitamina D se correlacionan de forma inversa con los niveles de citocinas inflamatorias y podrían estar relacionados con la tormenta de citocinas de la COVID-19. Asimismo, la vitamina D se relaciona con la secreción de catelicidinas y defensinas que interfieren en la replicación viral. También modula la expresión de ACE 2 y se ha objetivado que tiene un efecto protector sobre la lesión pulmonar inducida por lipopolisacárido⁴⁷⁻⁴⁹. Sin embargo, hoy en día, no se sabe con seguridad si los niveles de vitamina D y su normalización podrían influir en la evolución de la COVID-19.

La disfunción respiratoria de la obesidad

Diferentes alteraciones respiratorias que coexisten con la obesidad podrían deteriorar el curso de la infección por SARS-CoV2. En primer lugar, se describe un deterioro del intercambio de gases en comparación con las personas delgadas⁵⁰. El exceso de grasa abdominal disminuye la

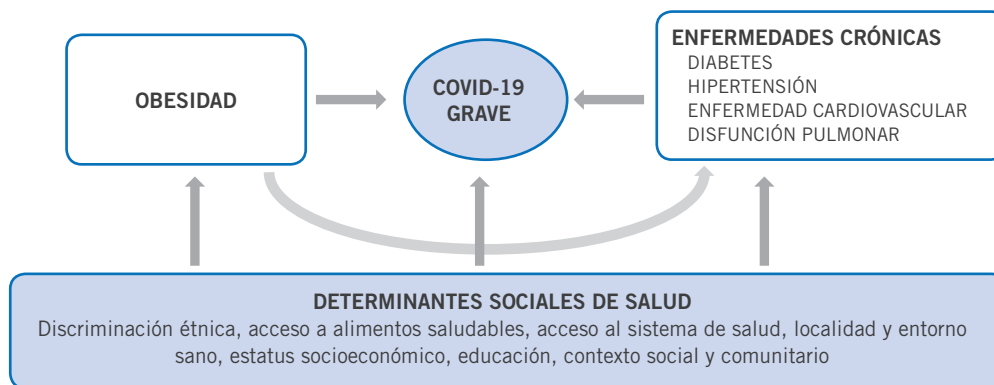
excursión del diafragma y reduce la ventilación de las bases pulmonares con la consiguiente menor saturación de oxígeno. Además, tanto el volumen pulmonar como la fuerza muscular son menores. Se ha demostrado que el aumento del IMC reduce de forma exponencial la capacidad funcional residual y el volumen de reserva espiratorio. En los pacientes con obesidades extremas, la capacidad vital y la capacidad pulmonar total también se ven afectadas⁵¹. En segundo lugar, la obesidad se asocia a asma, EPOC, síndrome de hipoventilación asociado a la obesidad, hipertensión pulmonar y apnea obstructiva del sueño. Todo ello puede favorecer el deterioro de la EPOC, el síndrome de hipoventilación en UCI y la evolución al fracaso respiratorio cuando existe un *distress* respiratorio^{52,53}.

En el asma, el SAOS y la mala evolución del *distress* respiratorio asociados a la obesidad, al igual que en la COVID-19 grave, se han implicado el incremento de la leptina, de las citocinas proinflamatorias y la deficiencia de interferón⁵⁴.

Los determinantes sociales de salud

Por último, he de destacar que la COVID-19 está afectando de forma desproporcionada a las comunidades más desfavorecidas. Entre las condiciones no médicas implicadas y que claramente influyen en la salud podemos enumerar a la estabilidad económica, el entorno físico, el racismo, la discriminación, el acceso a una nutrición de calidad, el acceso a los sistemas de salud y el acceso a una buena educación, todas ellas dependientes del contexto socio-comunitario. Con todas, la obesidad se relaciona de forma bidireccional y podríamos considerarla un denominador común⁵⁵. No debemos olvidar que tanto la pandemia de COVID-19 como la pandemia de obesidad se enmarcan dentro del concepto de sindemia, acuñado por Merrill Singer en 1990⁵⁶. Según Singer, el concepto sindémico revela interacciones biológicas y sociales que son importantes para el pronóstico y el tratamiento de las enfermedades (**Figura 2**).

Figura 2: Interacción entre obesidad, enfermedades no comunicables y determinantes sociales de salud relacionados con la COVID-19.



Retos y oportunidades

El binomio COVID-19 obesidad nos enfrenta a una serie de retos y también, por qué no, si los solventamos, nos abre una ventana de oportunidad para mejorar las perspectivas actuales y futuras.

Puesto que el impacto de la infección por SARS-CoV2 y la respuesta a las diferentes estrategias terapéuticas es diferente en el paciente con obesidad, es absolutamente crucial que se recoja el fenotipo metabólico en todos los casos. Esto es el IMC, las circunferencias de la cintura y la cadera y los niveles de glucosa. Estos datos nos ayudarán en la toma de decisiones y permitirán estratificar los resultados de estudios observacionales y ensayos clínicos.

En el ámbito hospitalario

A nivel individual, el paciente con obesidad que precisa hospitalización presenta una mayor complejidad terapéutica. Su intubación es más difícil, se necesitan camas, camillas y sillas bariátricas que fuera de los hospitales con unidades especializadas pueden no estar disponibles. La obtención de pruebas de imagen, por la limitación física de algunos equipos, puede ser complicada y retrasar algunos diagnósticos. El transporte y colocación de los pacientes es más complejo y, al igual que las gestantes, la posición prona puede ser, en ocasiones, imposible. De la misma manera, la decisión del momento de extubación de los pacientes con grandes obesidades es más difícil. La puesta en evidencia de estas limitaciones quizás favorecerá la mejora de la atención a los pacientes con obesidad grave en el futuro.

Desde el punto de vista farmacológico, el comportamiento de algunos fármacos es peor conocido en pacientes con grandes obesidades y sería deseable disponer de más datos. En este sentido se ha objetivado un mayor aclaramiento para algunos antivirales como por ejemplo el oseltamivir⁵⁷. De la misma manera, es posible que su capacidad de control de la replicación viral sea diferente en pacientes con obesidad grave. También, algunos autores sugieren que los individuos con enfermedad por hígado graso podrían presentar mayor hepatotoxicidad⁵⁸. Asimismo, se ha descrito que el efecto de la dexametasona sobre la atenuación de la producción de IL6 está alterado en los pacientes obesos, por lo que es posible que esta estrategia deba modificarse en función del IMC⁵⁹.

En referencia al uso de ARA2 o IECAs, con frecuencia utilizados por los pacientes con obesidad, las sociedades científicas remarcan que no hay evidencias que justifiquen su retirada y que ésta, podría descompensar a los pacientes de alto riesgo, o a aquellos con antecedentes de insuficiencia cardíaca o infarto de miocardio⁶⁰. Por otra

parte, la obtención de datos clínicos y experimentales sobre el efecto de los IECAs o ARA2 sobre la COVID-19 es importante ya que podría tratarse de un arma de doble filo dependiendo de la fase de la enfermedad. En los primeros momentos, un aumento de expresión de ACE2 precipitado por el uso de estos fármacos podría incrementar la infectividad. Por el contrario, en fases más avanzadas, su sobreexpresión podría tener efectos protectores sobre la lesión tisular⁶¹.

En el ámbito ambulatorio

En el ámbito ambulatorio, parece importante aumentar la vigilancia y priorizar la detección de la COVID-19. También, mantener una actitud terapéutica proactiva sobre la obesidad. Esto es más crítico para aquellas personas con IMCs en los rangos superiores. Enfatizando la proactividad, algunos estudios indican que el antecedente de cirugía bariátrica reduce el riesgo de muerte y de ventilación mecánica por COVID^{62,63}.

Por otro lado, es destacable que, en la actualidad, no existen guías específicas sobre la prevención, diagnóstico y tratamiento de la COVID-19 en personas con obesidad, pero parece lógico acoger las siguientes recomendaciones:

En referencia a la dieta y al estilo de vida, es aconsejable perder peso y mantener un buen control de la tensión arterial y de la glucemia. La dieta deberá introducir un déficit calórico moderado y ser equilibrada garantizando la ingesta adecuada de proteínas, vitaminas, minerales y ácidos grasos poliinsaturados W3 esenciales para una adecuada función inmunológica^{64,65}. Es remarcable que estas recomendaciones se emiten en base a datos experimentales y observacionales que indican que influirán de forma beneficiosa en los parámetros inflamatorios. Sin embargo, aún no se han desarrollado ensayos clínicos aleatorizados orientados a resolver estas cuestiones. Por último, puesto que la deficiencia de vitamina D se ha relacionado con el riesgo de desarrollar infecciones, parece recomendable mantener unos niveles adecuados. En el momento actual, se están realizando estudios para valorar la relación entre los niveles de vitamina D3 y el pronóstico de la COVID-19. También se están desarrollando ensayos sobre los beneficios de su suplementación⁶⁶.

En referencia a los aspectos psicológicos, es importante tener en cuenta que los pacientes con obesidad son más vulnerables al estrés y al impacto psicológico del aislamiento social. Estos aspectos pueden influir de forma negativa en el manejo adecuado de la obesidad. Por ello, al igual que en condiciones normales, el apoyo psicológico debe ser uno de los elementos del manejo del binomio obesidad-COVID-19. Sin embargo, de manera similar a la dieta, sería deseable investigar en

ensayos clínicos cómo el apoyo psicológico ayudará a esta población más vulnerable al estrés y al aislamiento⁶⁷.

En referencia al ejercicio físico, es destacable un estudio reciente con la cohorte del *UK Biobank* en el que, datos objetivos obtenidos mediante acelerómetro, indican que tiene un efecto protector sobre la evolución de la COVID⁶⁸. El ejercicio tiene una influencia positiva sobre la inflamación, la salud cardiometabólica y la función pulmonar; además, reduce el riesgo de infecciones respiratorias y puede en parte contrarrestar la unión SARS-CoV2 al receptor ACE2. Por tanto, parece recomendable prescribir ejercicio de intensidad moderada, particularmente en los pacientes en los que una ganancia adicional de peso puede tener consecuencias serias, incluidas una rápida pérdida de capacidad residual funcional y de volumen de reserva espiratoria^{69,70}. En esta línea, sería interesante investigar si las apps u otras iniciativas virtuales como videos o webinars pueden reducir el sedentarismo y el tiempo de inactividad durante la pandemia.

De cara a la vacunación, artículos clave demuestran que existen células T de memoria, de supervivencia larga, que reconocen al SARS-CoV2 y, también, que la generación de la respuesta inmune mediada por éstas es crítica para el desarrollo de la vacuna. Desafortunadamente, la respuesta de las células T está alterada en los sujetos con obesidad. Por tanto, es posible que las vacunas sean menos eficaces en poblaciones con una alta prevalencia de obesidad⁷¹. Así pues, incluir el IMC como variable de confusión en los estudios sobre eficacia y seguridad de las diferentes vacunas parece de importancia capital. En este sentido es remarcable que el IMC medio en uno de los estudios recientes en los que se publican los resultados de la fase 2 del desarrollo de la vacuna de nanopartículas de la proteína Spike recombinante (NVX-CoV2373) es de 25.19 +/- 3,6 Kg/m².⁷² En cuanto a la fase 3 del desarrollo clínico, en diciembre se habían publicado, con buenos resultados de eficacia y seguridad, los datos de la vacuna BNT162b2 mRNA (*Pfizer*) y de la vacuna mRNA-1273 SARS-CoV2 (*Moderna*) con 43.548 y 30.420 participantes, respectivamente. Aunque ambos ensayos no tenían potencia estadística suficiente para el análisis por subgrupos de IMC, cabe pensar que la obesidad (IMC >30 Kg/m²) estaba bien representada. En el primer estudio, los pacientes con IMC >30 kg/m² suponían el 35% de la muestra. Por otro lado, *Moderna* comunicaba un IMC medio de 29,3 kg/m² y una prevalencia de obesidad grave del 6,7%^{73,74}.

En el ámbito de la política sanitaria

Debido a la elevada prevalencia global de obesidad, los gobiernos deben tener como objetivos prioritarios reconocer a la obesidad como una enfermedad y

actuar en consecuencia priorizando la investigación, la prevención y el tratamiento. Si logramos reducir la carga de la obesidad probablemente reduciríamos el número futuro de casos de COVID-19 y mejoraremos su evolución. También, disminuiríamos la incidencia de enfermedades no comunicables que afectan negativamente a las estadísticas de la pandemia.

Entre las estrategias preventivas y terapéuticas posibles a nivel poblacional caben todas aquellas que favorezcan la monitorización y regulación del consumo de alimentos ultraprocesados y de baja calidad. También las que favorezcan el consumo de alimentos saludables y el ejercicio físico. Algunos datos demuestran que la subvención parcial de frutas y vegetales favorece su consumo^{75,76}. Asimismo, a pesar de que las experiencias son escasas, modelos como el israelí, que combinan políticas fiscales con leyes de etiquetado de alimentos y promoción de hábitos saludables han demostrado cierto impacto positivo⁷⁷. Por otra parte, es vital combinar educación con regulación por lo que parecen imprescindibles las políticas basadas en las escuelas⁷⁸.

Por último, el enfoque sindémico del tándem COVID-obesidad invita a un tratamiento amplio del problema que abarca todos los factores relacionados. Aquí debo reiterar que tanto la COVID-19 como la obesidad subyacen sobre determinantes sociales y económicos de salud. No importa cuán efectiva sea una vacuna o un tratamiento. Si perseguimos puramente una solución biomédica, probablemente fracasaremos⁵⁵. De hecho, según un editorial de la prestigiosa revista *Lancet*, limitar el daño causado por la COVID-19 exigirá mucha más atención a las enfermedades no transmisibles y a la desigualdad socioeconómica que lo admitido hasta el momento⁵⁶. Por tanto, habilitar políticas en esta dirección debería considerarse una obligación por parte de los gobiernos.

Conclusión o reflexión final

Durante el último año, la pandemia de COVID-19 ha tenido un impacto global sin precedentes en los sistemas sanitarios. También, un coste social y económico que perdurará años e incluso décadas.

Tenemos suficientes datos epidemiológicos, fisiopatológicos y clínicos para afirmar que la COVID-19 ha entrado en colisión con otra gran pandemia: la obesidad. La obesidad implica un aumento del riesgo de infección y multiplica las posibilidades de mala evolución y muerte por COVID-19. También, al igual que la COVID-19, supone una carga económica y sociosanitaria de primera magnitud.

Reconocer el impacto de la obesidad sobre la COVID-19 implica retos y oportunidades en ámbitos que abarcan

desde la investigación y la prevención hasta el tratamiento ambulatorio y hospitalario de ambas entidades.

Por otra parte, debemos admitir que la interrelación obesidad-COVID-19 es compleja y subyace sobre determinantes sociales de salud que incrementan de forma sustancial su peaje.

Así pues, para entender y abordar COVID-19 deberemos abordar la obesidad y sus derivadas; es decir, otras

enfermedades no comunicables como la diabetes, las enfermedades cardiovasculares, las enfermedades respiratorias crónicas y el cáncer. También, deberemos articular políticas y programas que reviertan las desigualdades, con una agenda que no deberá ser exclusiva de los países ricos, ya que son causa desatendida de enfermedad, especialmente cuando existen pocos recursos. Realizar esfuerzos en esta línea sin duda mejorará nuestra salud e incrementará nuestra resiliencia frente a amenazas futuras.

Bibliografía

1. <https://www.who.int/es/news/item/27-04-2020-who-timeline---covid-19>.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020 Feb 15;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5. Epub 2020 Jan 24. Erratum in: *Lancet*. 2020 Jan 30;; PMID: 31986264; PMCID: PMC7159299.
3. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW; the Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gittlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA*. 2020 May 26;323(20):2052-2059. doi: 10.1001/jama.2020.6775. Erratum in: *JAMA*. 2020 May 26;323(20):2098. PMID: 32320003; PMCID: PMC7177629.
4. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, Cereda D, Coluccello A, Foti G, Fumagalli R, Iotti G, Latronico N, Lorini L, Merler S, Natalini G, Piatti A, Ranieri MV, Scandroglio AM, Storti E, Cecconi M, Pesenti A; COVID-19 Lombardy ICU Network. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020 Apr 28;323(16):1574-1581. doi: 10.1001/jama.2020.5394. PMID: 32250385; PMCID: PMC7136855.
5. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, Holden KA, Read JM, Dondelinger F, Carson G, Merson L, Lee J, Plotkin D, Sigfrid L, Halpin S, Jackson C, Gamble C, Horby PW, Nguyen-Van-Tam JS, Ho A, Russell CD, Dunning J, Openshaw PJ, Baillie JK, Semples MG; ISARIC4C investigators. Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ*. 2020 May 22;369:m1985. doi: 10.1136/bmj.m1985. PMID: 32444460; PMCID: PMC7243036.
6. <https://coronavirus.jhu.edu/map.html>. Acceso 30 de diciembre de 2020
7. Masmiquel L. Obesidad: visión actual de una enfermedad crónica (Obesity as a chronic disease: current approach). *Medicina Balear* 2018; 33(1):48-58. DOI 10.3306/MEDICINABALEAR 33.01.48
8. Luzi L, Radaelli MG. Influenza and obesity: its odd relationship and the lessons for COVID-19 pandemic. *Acta Diabetol*. 2020 Jun;57(6):759-764. doi: 10.1007/s00592-020-01522-8. Epub 2020 Apr 5. PMID: 32249357; PMCID: PMC7130453.
9. Cai Q, Chen F, Wang T, et al. Obesity and COVID-19 severity in a designated hospital in Shenzhen, China. *Diabetes Care* 2020;43:1392-1398. PMID: 32958624 PMCID: PMC7510038 DOI: 10.2337/dc20-1195.
10. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, Labreuche J, Mathieu D, Pattou F, Jourdain M; LICORN and the Lille COVID-19 and Obesity study group. High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation. *Obesity (Silver Spring)*. 2020 Jul;28(7):1195-1199. doi: 10.1002/oby.22831. Epub 2020 Jun 10. Erratum in: *Obesity (Silver Spring)*. 2020 Oct;28(10):1994. PMID: 32271993; PMCID: PMC7262326.
11. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, Tobin KA, Cerfolio RJ, Franco F, Horwitz LI. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ*. 2020 May 22;369:m1966. doi: 10.1136/bmj.m1966. PMID: 32444366; PMCID: PMC7243801.
12. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, Stachel A. Obesity in Patients Younger Than 60 Years Is a Risk Factor for COVID-19 Hospital Admission. *Clin Infect Dis*. 2020 Jul 28;71(15):896-897. doi: 10.1093/cid/ciaa415. PMID: 32271368; PMCID: PMC7184372.
13. Hendren NS, de Lemos JA, Ayers C, Das SR, Rao A, Carter S, Rosenblatt A, Walchok JG, Omar W, Khara R, Hegde AA, Drazner MH, Neeland IJ, Grodin JL. Association of Body Mass Index and Age With Morbidity and Mortality in Patients Hospitalized With COVID-19: Results From the American Heart Association COVID-19 Cardiovascular Disease Registry. *Circulation*. 2020 Nov 17. doi: 10.1161/CIRCULATIONAHA.120.051936. Epub ahead of print. PMID: 33200947.
14. Popkin BM, Du S, Green WD, Beck MA, Algaith T, Herbst CH, Alsukait RF, Alluhidan M, Alazemi N, Shekar M. Individuals with obesity and COVID-19: A global perspective on the epidemiology and biological relationships. *Obes Rev*. 2020 Nov;21(11):e13128. doi: 10.1111/obr.13128. Epub 2020 Aug 26. PMID: 32845580; PMCID: PMC7461480.
15. Yates T, Razieh C, Zaccardi F, Davies MJ, Khunti K. Obesity and risk of COVID-19: analysis of UK biobank. *Prim Care Diabetes*. 2020 Oct;14(5):566-567. doi: 10.1016/j.pcd.2020.05.011. Epub 2020 May 28. PMID: 32493608; PMCID: PMC7254007.
16. Aung N, Khanji MY, Munroe PB, Petersen SE. Causal Inference for Genetic Obesity, Cardiometabolic Profile and COVID-19 Susceptibility: A Mendelian Randomization Study. *Front Genet*. 2020 Nov 11;11:586308. doi: 10.3389/fgene.2020.586308. PMID: 33262790; PMCID: PMC7686798.

17. Independent Expert Group of the Global Nutrition Report. 2020 Global nutrition report: action on equity to end malnutrition. Development Initiatives: Bristol, UK 2020; 172.
18. Kantar. Covid-19: wave 2, 27-30 March among connected South African consumers. Kantar World Panel: Johannesburg 2020.
19. Euromonitor Passport . The impact of coronavirus on packaged and fresh food. Euromonitor International London 2020.
20. Pries AM, Ferguson EL, Sharma N, Upadhyay A, Fliteau S. Exploratory Analysis of Nutritional Quality and Metrics of Snack Consumption among Nepali Children during the Complementary Feeding Period. *Nutrients*. 2019 Dec 4;11(12):2962. doi: 10.3390/nu11122962. PMID: 31817203; PMCID: PMC6950298.
21. Talbot HK, Coleman LA, Crimin K, Zhu Y, Rock MT, Meece J, Shay DK, Belongia EA, Griffin MR. Association between obesity and vulnerability and serologic response to influenza vaccination in older adults. *Vaccine*. 2012 Jun 6;30(26):3937-3943. doi: 10.1016/j.vaccine.2012.03.071. Epub 2012 Apr 3. PMID: 22484350; PMCID: PMC3770527.
22. Rosen ED, Spiegelman BM. What we talk about when we talk about fat. *Cell*. 2014 Jan 16;156(1-2):20-44. doi: 10.1016/j.cell.2013.12.012. PMID: 24439368; PMCID: PMC3934003.
23. Khan S, Chan YT, Revelo XS, Winer DA. The Immune Landscape of Visceral Adipose Tissue During Obesity and Aging. *Front Endocrinol (Lausanne)*. 2020 May 15;11:267. doi: 10.3389/fendo.2020.00267. PMID: 32499756; PMCID: PMC7243349.
24. Sheridan PA, Paich HA, Handy J, Karlsson EA, Hudgens MG, Sammon AB, Holland LA, Weir S, Noah TL, Beck MA. Obesity is associated with impaired immune response to influenza vaccination in humans. *Int J Obes (Lond)*. 2012 Aug;36(8):1072-7. doi: 10.1038/ijo.2011.208. Epub 2011 Oct 25. PMID: 22024641; PMCID: PMC3270113.
25. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y, Bai C, Gao T, Song J, Xia P, Dong J, Zhao J, Wang FS. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020 Apr;8(4):420-422. doi: 10.1016/S2213-2600(20)30076-X. Epub 2020 Feb 18. Erratum in: *Lancet Respir Med*. 2020 Feb 25; PMID: 32085846; PMCID: PMC7164771.
26. Mahallawi WH, Khabour OF, Zhang Q, Makhdoum HM, Suliman BA. MERS-CoV infection in humans is associated with a pro-inflammatory Th1 and Th17 cytokine profile. *Cytokine*. 2018 Apr;104:8-13. doi: 10.1016/j.cyt.2018.01.025. Epub 2018 Feb 2. PMID: 29414327; PMCID: PMC7129230.
27. Wong CK, Lam CW, Wu AK, Ip WK, Lee NL, Chan IH, Lit LC, Hui DS, Chan MH, Chung SS, Sung JJ. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. *Clin Exp Immunol*. 2004 Apr;136(1):95-103. doi: 10.1111/j.1365-2249.2004.02415.x. PMID: 15030519; PMCID: PMC1808997.
28. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020 Mar 28;395(10229):1033-1034. doi: 10.1016/S0140-6736(20)30628-0. Epub 2020 Mar 16. PMID: 32192578; PMCID: PMC7270045.
29. Goossens GH. The renin-angiotensin system in the pathophysiology of type 2 diabetes. *Obes Facts*. 2012;5(4):611-24. doi: 10.1159/000342776. Epub 2012 Sep 5. PMID: 22986649.
30. Ferrario CM, Strawn WB. Role of the renin-angiotensin-aldosterone system and proinflammatory mediators in cardiovascular disease. *Am J Cardiol*. 2006 Jul 1;98(1):121-8. doi: 10.1016/j.amjcard.2006.01.059. Epub 2006 May 9. PMID: 16784934.
31. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*. 2020 Apr 16;181(2):271-280.e8. doi: 10.1016/j.cell.2020.02.052. Epub 2020 Mar 5. PMID: 32142651; PMCID: PMC7102627.
32. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, Wang Z, Li J, Li J, Feng C, Zhang Z, Wang L, Peng L, Chen L, Qin Y, Zhao D, Tan S, Yin L, Xu J, Zhou C, Jiang C, Liu L. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci*. 2020 Mar;63(3):364-374. doi: 10.1007/s11427-020-1643-8. Epub 2020 Feb 9. PMID: 32048163; PMCID: PMC7088566.
33. Ryan PM, Caplice NM. Is Adipose Tissue a Reservoir for Viral Spread, Immune Activation, and Cytokine Amplification in Coronavirus Disease 2019? *Obesity (Silver Spring)*. 2020 Jul;28(7):1191-1194. doi: 10.1002/oby.22843. Epub 2020 May 31. PMID: 32314868; PMCID: PMC7264526.
34. Deng SQ, Peng HJ. Characteristics of and Public Health Responses to the Coronavirus Disease 2019 Outbreak in China. *J Clin Med*. 2020 Feb 20;9(2):575. doi: 10.3390/jcm9020575. PMID: 32093211; PMCID: PMC7074453.
35. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, Bi Z, Zhao Y. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020 May;109(5):531-538. doi: 10.1007/s00392-020-01626-9. Epub 2020 Mar 11. PMID: 32161990; PMCID: PMC7087935.
36. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. *Aging (Albany NY)*. 2020 Apr 8;12(7):6049-6057. doi: 10.18632/aging.103000. Epub 2020 Apr 8. PMID: 32267833; PMCID: PMC7185114.
37. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, Lei F, Wang H, Xie J, Wang W, Li H, Zhang P, Song X, Chen X, Xiang M, Zhang C, Bai L, Xiang D, Chen MM, Liu Y, Yan Y, Liu M, Mao W, Zou J, Liu L, Chen G, Luo P, Xiao B, Zhang C, Zhang Z, Lu Z, Wang J, Lu H, Xia X, Wang D, Liao X, Peng G, Ye P, Yang J, Yuan Y, Huang X, Guo J, Zhang BH, Li H. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. *Cell Metab*. 2020 Jun 2;31(6):1068-1077.e3. doi: 10.1016/j.cmet.2020.04.021. Epub 2020 May 1. PMID: 32369736; PMCID: PMC7252168.
38. New York State Department of Health. Fatalities. <https://covid19tracker.health.ny.gov/views/NYS-COVID19-Tracker/NYSDOHCOVID-19Tracker-Fatalities?%3Aembed%2Fyes&%3Atoolbar%2Fno>.
39. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol*. 2020 Jun;52(6):1193-1194. doi: 10.1007/s11255-020-02451-9. Epub 2020 Mar 28. PMID: 32222883; PMCID: PMC7103107.
40. COVID-19 Surveillance Group. Characteristics of COVID-19 patients dying in Italy Report based on available data on April 6th, 2020. https://www.epicentro.iss.it/en/coronavirus/bollettino/Report-COVID-2019_6_april_2020.pdf.
41. Sachdeva S, Khandait H, Kopel J, Aloysius MM, Desai R, Goyal H. NAFLD and COVID-19: a Pooled Analysis. *SN Compr Clin Med*. 2020 Nov 6:1-4. doi: 10.1007/s42399-020-00631-3. Epub ahead of print. PMID: 33173850; PMCID: PMC7646222.

42. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, Heinrich F, Mushumba H, Kniep I, Schröder AS, Burdelski C, de Heer G, Nierhaus A, Frings D, Pfeufferle S, Becker H, Brederke-Wiedling H, de Weerth A, Paschen HR, Sheikhzadeh-Eggers S, Stang A, Schmiedel S, Bokemeyer C, Addo MM, Aepfelbacher M, Püschel K, Kluge S. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. *Ann Intern Med.* 2020 Aug 18;173(4):268-277. doi: 10.7326/M20-2003. Epub 2020 May 6. PMID: 32374815; PMCID: PMC7240772.
43. Samad F, Ruf W. Inflammation, obesity, and thrombosis. *Blood.* 2013 Nov 14;122(20):3415-22. doi: 10.1182/blood-2013-05-427708. Epub 2013 Oct 3. PMID: 24092932; PMCID: PMC3829115.
44. Barazzoni R, Bischoff S, Boirie Y, Busetto L, Cederholm T, Dicker D, Toplak H, Van Gossum A, Yumuk V, Vettor R. Sarcopenic Obesity: Time to Meet the Challenge. *Obes Facts.* 2018;11(4):294-305. doi: 10.1159/000490361. Epub 2018 Jul 18. PMID: 30016792; PMCID: PMC6189532.
45. de la Rica R, Borges M, Aranda M, Del Castillo A, Socias A, Payeras A, Rialp G, Socias L, Masmiquel L, Gonzalez-Freire M. Low Albumin Levels Are Associated with Poorer Outcomes in a Case Series of COVID-19 Patients in Spain: A Retrospective Cohort Study. *Microorganisms.* 2020 Jul 24;8(8):1106. doi: 10.3390/microorganisms8081106. PMID: 32722020; PMCID: PMC7463882.
46. Nicolau J, Ayala L, Sanchís P, Olivares J, Dotres K, Soler AG, Rodríguez I, Gómez LA, Masmiquel L. Influence of Nutritional Status on Clinical Outcomes Among Hospitalized patients with COVID-19. *Clinical Nutrition (en Revisión)*
47. Palaniswamy S, Gill D, De Silva NM, Lowry E, Jokelainen J, Karhu T, Mutt SJ, Dehghan A, Sliz E, Chasman DI, Timonen M, Viinamäki H, Keinänen-Kiukkaanniemi S, Hyppönen E, Herzig KH, Sebert S, Järvelin MR. Could vitamin D reduce obesity-associated inflammation? Observational and Mendelian randomization study. *Am J Clin Nutr.* 2020 May 1;111(5):1036-1047. doi: 10.1093/ajcn/nqaa056. PMID: 32232398; PMCID: PMC7198294.
48. Grant WB, Lahore H, Rockwell MS. The Benefits of Vitamin D Supplementation for Athletes: Better Performance and Reduced Risk of COVID-19. *Nutrients.* 2020 Dec 4;12(12):3741. doi: 10.3390/nu12123741. PMID: 33291720; PMCID: PMC7761895.
49. Carter SJ, Baranaukas MN, Fly AD. Considerations for Obesity, Vitamin D, and Physical Activity Amid the COVID-19 Pandemic. *Obesity (Silver Spring).* 2020 Jul;28(7):1176-1177. doi: 10.1002/oby.22838. Epub 2020 May 21. PMID: 32299148; PMCID: PMC7311254.
50. Huang JF, Wang XB, Zheng KI, Liu WY, Chen JJ, George J, Zheng MH. Letter to the Editor: Obesity hypoventilation syndrome and severe COVID-19. *Metabolism.* 2020 Jul;108:154249. doi: 10.1016/j.metabol.2020.154249. Epub 2020 Apr 22. PMID: 32333938; PMCID: PMC7195293.
51. Jones RL, Nzekwu MM. The effects of body mass index on lung volumes. *Chest.* 2006 Sep;130(3):827-33. doi: 10.1378/chest.130.3.827. PMID: 16963682.
52. McCallister JW, Adkins EJ, O'Brien JM Jr. Obesity and acute lung injury. *Clin Chest Med.* 2009 Sep;30(3):495-508, viii. doi: 10.1016/j.ccm.2009.05.008. PMID: 19700048; PMCID: PMC2731710.
53. Spelta F, Fratta Pasini AM, Cazzoletti L, Ferrari M. Body weight and mortality in COPD: focus on the obesity paradox. *Eat Weight Disord.* 2018 Feb;23(1):15-22. doi: 10.1007/s40519-017-0456-z. Epub 2017 Nov 6. PMID: 29110280.
54. Almond MH, Edwards MR, Barclay WS, Johnston SL. Obesity and susceptibility to severe outcomes following respiratory viral infection. *Thorax.* 2013 Jul;68(7):684-6. doi: 10.1136/thoraxjnl-2012-203009. Epub 2013 Feb 22. PMID: 23436045.
55. Belanger MJ, Hill MA, Angelidi AM, Dalamaga M, Sowers JR, Mantzoros CS. Covid-19 and Disparities in Nutrition and Obesity. *N Engl J Med.* 2020 Sep 10;383(11):e69. doi: 10.1056/NEJMp2021264. Epub 2020 Jul 15. PMID: 32668105.
56. Horton R. Offline: COVID-19 is not a pandemic. *Lancet.* 2020 Sep 26;396(10255):874. doi: 10.1016/S0140-6736(20)32000-6. PMID: 32979964; PMCID: PMC7515561.
57. Chairat K, Jittamala P, Hanpithakpong W, Day NP, White NJ, Pukrittayakamee S, Tarning J. Population pharmacokinetics of oseltamivir and oseltamivir carboxylate in obese and non-obese volunteers. *Br J Clin Pharmacol.* 2016 Jun;81(6):1103-12. doi: 10.1111/bcp.12892. Epub 2016 Mar 4. PMID: 26810861; PMCID: PMC4876175.
58. Ferron PJ, Gicquel T, Mégarbane B, Clément B, Fromenty B. Treatments in Covid-19 patients with pre-existing metabolic dysfunction-associated fatty liver disease: A potential threat for drug-induced liver injury? *Biochimie.* 2020 Dec;179:266-274. doi: 10.1016/j.biochi.2020.08.018. Epub 2020 Sep 3. PMID: 32891697; PMCID: PMC7468536.
59. Huang CJ, Acevedo EO, Mari DC, Randazzo C, Shibata Y. Glucocorticoid inhibition of leptin- and lipopolysaccharide-induced interleukin-6 production in obesity. *Brain Behav Immun.* 2014 Jan;35:163-8. doi: 10.1016/j.bbi.2013.10.004. Epub 2013 Oct 11. PMID: 24126150.
60. Center for Disease Control and Prevention. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19). [Internet]. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>. 2020 [cited 2020 Apr 3]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>
61. Gurwitz D. Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics. *Drug Dev Res.* 2020 Aug;81(5):537-540. doi: 10.1002/ddr.21656. Epub 2020 Mar 4. PMID: 32129518; PMCID: PMC7228359.
62. Lannelli A, Bouam S, Schneck AS, Frey S, Zarca K, Gugenheim J, Alifano M. The Impact of Previous History of Bariatric Surgery on Outcome of COVID-19. A Nationwide Medico-Administrative French Study. *Obes Surg.* 2020 Nov 18:1-9. doi: 10.1007/s11695-020-05120-z. Epub ahead of print. PMID: 33210274; PMCID: PMC7673863.
63. Aminian A, Fathalizadeh A, Tu C, Butsch WS, Pantalone KM, Griebeler ML, Kashyap SR, Rosenthal RJ, Burguera B, Nissen SE. Association of prior metabolic and bariatric surgery with severity of coronavirus disease 2019 (COVID-19) in patients with obesity. *Surg Obes Relat Dis.* 2021 Jan;17(1):208-214. doi: 10.1016/j.soard.2020.10.026. Epub 2020 Nov 23. PMID: 33243670; PMCID: PMC7682430.
64. Naja F, Hamadeh R. Nutrition amid the COVID-19 pandemic: a multi-level framework for action. *Eur J Clin Nutr.* 2020 Aug;74(8):1117-1121. doi: 10.1038/s41430-020-0634-3. Epub 2020 Apr 20. PMID: 32313188; PMCID: PMC7167535.
65. Calder PC, Carr AC, Gombart AF, Eggorsdorfer M. Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections. *Nutrients.* 2020 Apr 23;12(4):1181. doi: 10.3390/nu12041181. PMID: 32340216; PMCID: PMC7230749.

66. Mitchell F. Vitamin-D and COVID-19: do deficient risk a poorer outcome? *Lancet Diabetes Endocrinol.* 2020 Jul;8(7):570. doi: 10.1016/S2213-8587(20)30183-2. Epub 2020 May 20. PMID: 32445630; PMCID: PMC7239633.
67. Sockalingam S, Leung SE, Cassin SE. The Impact of Coronavirus Disease 2019 on Bariatric Surgery: Redefining Psychosocial Care. *Obesity (Silver Spring).* 2020 Jun;28(6):1010-1012. doi: 10.1002/oby.22836. PMID: 32294297; PMCID: PMC7262315.
68. Zhang X, Li X, Sun Z, He Y, Xu W, Campbell H, Dunlop MG, Timofeeva M, Theodoratou E. Physical activity and COVID-19: an observational and Mendelian randomisation study. *J Glob Health.* 2020 Dec;10(2):020514. doi: 10.7189/jogh-10-020514. PMID: 33312507; PMCID: PMC7719276.
69. Zbinden-Foncea H, Francaux M, Deldicque L, Hawley JA. Does High Cardiorespiratory Fitness Confer Some Protection Against Proinflammatory Responses After Infection by SARS-CoV-2? *Obesity (Silver Spring).* 2020 Aug;28(8):1378-1381. doi: 10.1002/oby.22849. Epub 2020 Jul 9. PMID: 32324968; PMCID: PMC7264673.
70. Rahmati-Ahmadabad S, Hosseini F. Exercise against SARS-CoV-2 (COVID-19): Does workout intensity matter? (A mini review of some indirect evidence related to obesity). *Obes Med.* 2020 Sep;19:100245. doi: 10.1016/j.obmed.2020.100245. Epub 2020 Apr 27. PMID: 32342019; PMCID: PMC7184978.
71. Altmann DM, Boyton RJ. SARS-CoV-2 T cell immunity: Specificity, function, durability, and role in protection. *Sci Immunol.* 2020 Jul 17;5(49):eabd6160. doi: 10.1126/sciimmunol.abd6160. PMID: 32680954.
72. Keech C, Albert G, Cho I, Robertson A, Reed P, Neal S, Plested JS, Zhu M, Cloney-Clark S, Zhou H, Smith G, Patel N, Frieman MB, Haupt RE, Logue J, McGrath M, Weston S, Piedra PA, Desai C, Callahan K, Lewis M, Price-Abbott P, Formica N, Shinde V, Fries L, Lickliter JD, Griffin P, Wilkinson B, Glenn GM. Phase 1-2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. *N Engl J Med.* 2020 Dec 10;383(24):2320-2332. doi: 10.1056/NEJMoa2026920. Epub 2020 Sep 2. PMID: 32877576; PMCID: PMC7494251.
73. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW Jr, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med.* 2020 Dec 10;NEJMoa2034577. doi: 10.1056/NEJMoa2034577. Epub ahead of print. PMID: 33301246; PMCID: PMC7745181.
74. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Kehtan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham BS, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Ivarsson M, Miller J, Zaks T; COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med.* 2020 Dec 30. doi: 10.1056/NEJMoa2035389. Epub ahead of print. PMID: 33378609.
75. Mozaffarian D, Rogoff KS, Ludwig DS. The real cost of food: can taxes and subsidies improve public health? *JAMA.* 2014 Sep 3;312(9):889-90. doi: 10.1001/jama.2014.8232. PMID: 25182094; PMCID: PMC6129188.
76. Kanter R, Boza S. Strengthening Local Food Systems in Times of Concomitant Global Crises: Reflections From Chile. *Am J Public Health.* 2020 Jul;110(7):971-973. doi: 10.2105/AJPH.2020.305711. Epub 2020 May 14. PMID: 32407131; PMCID: PMC7287531.
77. Gillon-Keren M, Kaufman-Shrqui V, Goldsmith R, Safra C, Shai I, Fayman G, Berry E, Tirosh A, Dicker D, Froy O, Gordon E, Chavia Ben-Yosef AC, Nitsan L, Altman H, Blaychfeld-Magnazi M, Endevelt R. Development of Criteria for a Positive Front-of-Package Food Labeling: The Israeli Case. *Nutrients.* 2020 Jun 23;12(6):1875. doi: 10.3390/nu12061875. PMID: 32585990; PMCID: PMC7353345.
78. Garden EM, Pallan M, Clarke J, Griffin T, Hurley K, Lancashire E, Sitch AJ, Passmore S, Adab P. Relationship between primary school healthy eating and physical activity promoting environments and children's dietary intake, physical activity and weight status: a longitudinal study in the West Midlands, UK. *BMJ Open.* 2020 Dec 22;10(12):e040833. doi: 10.1136/bmjopen-2020-040833. PMID: 33371029.

TSUNAMI COVID-19. Reflexions d'entitats de l'entorn de les Cures Pal·liatives

COVID-19 TSUNAMI. Palliative Care environment entity reflections

Joana Maria Juliá Mora¹ , **Mercé Llagostera Pagés^{1,2}** , **Carmen Moreno Hoyos^{1,2}** ,
Javier Cortés Bordoy³ , **Catalina Rosselló Forteza¹** , **Susana Jordá Martí⁴** ,
Jorge Calvín Gil-Mascarell⁴ , **Bárbara Massó Pomés⁵** 

1. Societat Balear de cures pal·liatives, Illespal. 2. Centre Coordinador del Programa de Cures Pal·liatives de les Illes Balears. IBSALUT. 3. Junta de Balears Associació Espanyola Contra el Càncer, AECC. 4. Associació Àngeles sin alas. 5. DIME, Associació de voluntaris de cures pal·liatives de les Illes Balears.

Correspondencia

Merce Llagostera
Societat Balear de cures pal·liatives, Illespal
E-mail: merce.llagostera@ssib.es

Rebut: 29 - I - 2021

Acceptat: 30 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.122

Resum

La pandèmia per la COVID19 va aturar a la societat de manera sobtada, interferint a tota l'activitat, a tots els programes de Cures Pal·liatives provocant canvis importants en l'atenció. A les Illes Balears diverses entitats que treballen en pro de les Cures Pal·liatives (AECC, Àngeles Sin Alas, Centre Coordinador del Programa de Cures Pal·liatives, DIME i Illespal) no han quedat al marge d'aquestes importants limitacions, provocant així, grans canvis en les seves dinàmiques, havent-se de reinventar noves maneres per arribar a la població i oferir l'ajuda necessària. Aquest article recull les experiències viscudes de les entitats que treballen en benefici de les CP i convidar a la reflexió sobre la capacitat d'adaptació que han tingut davant els canvis i modificacions que ha provocat la crisi sanitària en el nostre dia a dia. Cal destacar, l'esperança de totes elles a poder iniciar novament les activitats i que els socis se'n sentin beneficiats, la seva actitud resilient, la seva capacitat d'adaptació i de compromís davant les noves circumstàncies. Davant els nous reptes les respostes han estat variables, donant l'oportunitat de introduir conceptes, formació i atenció al final de la vida a diferents serveis com urgències, UCI i residències geriàtriques on les CP no eren l'objectiu prioritari d'entrada.

Paraules clau: Cures pal·liatives, pediatria, final de vida, COVID19, sistemes de salut, voluntaris.

Abstract

The Covid -19 Pandemic has brought society abruptly to a halt, interfering with many activities and social interactions. Palliative Programs haven't been spared, necessitating major changes. In the Balearic Islands several entities working for Palliative Care (AECC, Angeles Sin Alas, the Coordinating Center for Palliative Care Programs, DIME and Illespal) have not been sidelined by these changes. These companies had to re-invent ways to reach the population in order to provide the necessary help, causing major changes in their dynamics. This article calls for a moment of reflection on the experiences of the above-mentioned companies and their adjustability to changes which brought about health crises on a daily basis. Their resilience and commitment to face and deal with new circumstances are truly awe-inspiring. Faced with new challenges, responses have been variable, giving opportunities for the introduction of new concepts, training and attention to different end of life services such as Emergency Department, ICU and nursing homes which have never viewed Palliative Care as a priority before.

Key words: Palliative care, hospice care, pediatrics, end-of-life, COVID19, health systems, volunteers.

Introducció

Portem ja més d'un any des de l'aparició a Wuhan dels primers casos de pacients amb COVID-19, malaltia provocada pel nou virus SARS-COV-2. Un virus amb gran capacitat pel contagi que en poc temps va ocasionar la pandèmia que encara ara, a inicis de 2021, resta amb nosaltres amb importants restriccions en tots els àmbits, tant sanitaris, socials, culturals, econòmics i de formació, entre altres. La nostra vida ha canviat molts

aspectes de les relacions personals i de l'assistència sanitària, generant conflictes ètics amb important impacte emocional en el dia a dia dels professionals de la salut així com en la població en general¹.

La pandèmia per la COVID19 va aturar a la societat de manera sobtada, interferint en tota l'activitat de tots els programes de Cures Pal·liatives (CP) i dels seus equips.

Aquest fet va provocar canvis importants en l'atenció pal·liativa: canvis en les necessitats dels pacients, dificultats d'accés presencial tant als centres sanitaris com als domicilis i com a conseqüència aparegueren noves maneres d'intervenció com la telemedicina amb les seves avantatges i limitacions².

Kotalik³, al 2005, fent referència a les pandèmies anunciava que, tots els sectors de la societat i tots els individus es veuran afectats per una pandèmia, i es requerirà la col·laboració de tots. Per tant, és essencial que es desenvolupin plans i s'implementin programes de comunicació, que no només informin, sinó que també creïn una atmosfera de confiança mútua i solidaritat, qualitats que en el moment d'una pandèmia seran molt necessàries. En el nostre cas es pot dir que la previsió que pogués arribar una pandèmia era bastant imprevisible ja que per les manifestacions i els discursos de la població general, així com el de les societats científiques va ser una situació que els va agafar completament desprevinguts, simplement no estàvem preparats per això.

A les Illes Balears diverses entitats que treballen en pro de les Cures Pal·liatives (AECC, Ángeles Sin Alas, Centre Coordinador del Programa de Cures Pal·liatives, DIME i Illespal) no han quedat al marge d'aquestes importants limitacions, provocant així, grans canvis en les seves dinàmiques, havent-se de reinventar noves maneres per arribar a la població i oferir l'ajuda necessària.

Aquest article recull les experiències viscudes d'aquestes entitats que treballen en benefici de les Cures Pal·liatives i convida a la reflexió sobre la capacitat d'adaptació que han tingut davant els canvis i modificacions que ha provocat i provoca el virus SARS-COV-2 en el nostre dia a dia. És per això, que a continuació exposarem quines han estat les estratègies de cada una de les entitats per tal de fer front a la situació i no quedar-se al marge de les adversitats i amenaces que ha suposat el virus per a la població més fràgil i vulnerable.

AECC. Junta de Balears de l'Associació Espanyola Contra el Càncer

En col·laboració amb totes les societats científiques concernides, l'Associació Espanyola contra el Càncer (AECC) ha realitzat a nivell nacional un estudi per a avaluar l'impacte que ha ocasionat la pandèmia pel virus SARS-CoV-2 als pacients amb malaltia oncològica a nivell nacional, amb avaluacions per comunitats autònomes. En general i amb dades molt similars a les Illes Balears, s'ha detectat una disminució de l'activitat diagnòstica de càncer un 30% menys en citologies i un 23,5% menys en biòpsies. També s'han vist afectats els pacients atesos als hospitals de dia amb una disminució del 14%, els tractaments amb

quimioteràpia ha baixat un 9,5% i amb radioteràpia un 5%. A més a les Illes Balears, s'ha produït un retràs en l'actualització i aplicació dels tres programes de cribratge que estaven en marxa, amb matisos diferents: és necessari la consolidació del cribratge de mama femenina, la redifinició global del cribratge de càncer de cèrvix - amb una estructura obsoleta en l'aplicació - i implementació potent del cribratge de colon, que presenta una cobertura molt baixa, de les pitjors d'Espanya.

Una àrea prioritària d'acció oncològica preventiva és la lluita contra el tabaquisme el 30% dels càncers incidents estan relacionats causalment amb el consum de tabac, aquesta àrea també s'ha vist afectada degut a l'anul·lació de les activitats presencials complint amb la normativa existent de prevenció de contagis de la COVID19.

Ha augmentat l'atenció telefònica, multiplicant-se quasi per tres les consultes respecte al 2019 invertint el mateix temps com si fos presencial. L'AECC Illes Balears ha destinat un 20% més del pressupost al suport econòmic i psicològic dels malalts de càncer, així com, en assessorament nutricional.

Les línies d'acció del 2021 per a l'AECC Illes Balears, decidides pel consell provincial són les següents:

- Promoció de la salut mitjançant accions encaminades a actualitzar l'acció dels programes de cribratge, amb atenció prioritària al càncer de colon i a reforçar la lluita contra el tabaquisme amb educació per evitar l'inici del consum i ajuda a la desintoxicació dels fumadors.
- Ajuda prioritària per a cobrir qualsevol de les necessitats dels pacients i a les seves famílies.
- Mantenir el suport a la investigació oncològica, tant amb l'aportació a la "Fundación Científica Nacional", com amb el programa de beques a grups d'investigadors de la nostra comunitat.
- Seguir col·laborant per a que millori el coneixement del que són i representen les cures pal·liatives, tant a la població general com en el sector sanitari, així com incentivant l'accés de manera equitativa.

Totes aquestes accions es continuaran realitzant com en els últims anys en col·laboració ferma amb les institucions polítiques, acadèmiques i professionals de la comunitat autònoma, així com les altres organitzacions no governamentals que treballen en l'àrea oncològica.

Associació ÀNGELES SIN ALAS

A *Ángeles Sin Alas* hem hagut de batallar moltes vegades per a poder seguir endavant complint la nostra missió. Però el que mai haguéssim imaginat és que un enemic com la COVID19 ens posaria en una situació tan crítica.

La suspensió dels esdeveniments programats degut a les tan necessàries mesures de seguretat per fer front a la pandèmia, ha estat la causa per la qual no hem pogut obtenir una de les fonts d'ingressos més importants. Com a conseqüència hem hagut de reduir alguns dels nostres serveis, com l'atenció presencial i telefònica, o les xerrades divulgatives. Per ara, hem pogut fer front a la cessió i compra de material ortoprotèsic que, des de la Unitat de Cures Pal·liatives Pediàtriques, ens han sol·licitat per als nins i nines, extremant les precaucions higièniques segons la normativa.

Gràcies a les noves tecnologies, hem pogut mantenir algunes sessions de musicoteràpia que ja oferíem des de fa temps. Les càmeres, micròfons i altaveus han substituït la presència de la música en directe i el poder interactuar amb els instruments, així com amb els nins i les seves famílies. Però hem reaprès, una vegada més, a adaptar-nos a situacions adverses. I és que és innat en els que componem *Ángeles Sin Alas*: per estar a l'alçada dels nostres nins hem de ser resilients, afrontar nous reptes i anar de la mà de situacions canviants.

Necessitem socis que aportin una petita quantitat mensual per ajudar-nos a seguir endavant. És la manera que tenim per a sobreviure sense actes programats.

Gràcies, infinites gràcies a les persones que ens han ajudat i ens estan ajudant en aquests moments. Tots junts aconseguirem continuar acompanyant als nostres nins i a les seves famílies per a millorar les seves vides.

Centre coordinador del programa de CP de les Illes Balears

Com ens ha afectat

D'entrada va ser una gran frenada, una aturada de pràcticament totes les coses que teníem en marxa, i amb uns dies d'"Standby", d'anar al ralenti, a l'espera de si aquesta situació era curta o llarga, i mentre això passava posàvem en marxa els mecanismes de readaptació en tots els àmbits, no només al laboral.

Vam aturar totes les accions formatives previstes al nostre centre, totes les sessions divulgatives previstes a diferents pobles i barris de Palma incloses en el projecte col·laboratiu "Cures Pal·liatives, un dret, una necessitat", es van haver de cancel·lar múltiples reunions que impulsaven projectes que teníem en marxa.

A hores d'ara continuem estant en més d'un 70% centrades en temes COVID enlloc dels habituals d'impulsar CP.

Que hem fet

D'entrada vam empapar-nos llegint documents i ens

vàrem coordinar per elaborar un document de consens que pogués ajudar a professionals que estessin tractant pacients amb necessitats d'atenció pal·liativa infectats pel virus SARS-CoV-2. Aquesta tasca va ser possible gràcies a la participació de professionals de diferents equips específics de CP. El document "Recomendaciones de actuación en casos de infección por SARS-Cov-2 en pacientes con necesidades de atención paliativa"⁴.

Vàrem entrar també al grup redactor dels diferents protocols i recomanacions sobre "Recomendaciones de prevención y protección en Centros Sociosanitarios y residencias de personas mayores y discapacidad en la CCAA de las Islas Baleares"⁵ i de les múltiples actualitzacions que se n'han fet.

La pandèmia ens ha fet normalitzar les trobades, reunions, webinars i congressos virtuals.

A la primera onada de la pandèmia quan es van intervenir dues residències pels importants brots que hi havia, vam anar-hi a fer feina de manera presencial per ajudar a redirigir la part sanitària. Un cop allà, una de les coses que hi vam introduir a part de les estrictament sanitàries, va ser el suport del voluntariat de DIME que feia acompanyament telefònic.

A la segona onada, s'ha treballat i editat des de la subdirecció d'atenció a la cronicitat, conjuntament amb la Gerència d'atenció primària i del SAMU-061, un "Protocolo de detección, seguimiento y traslado de pacientes con COVID-19 en centros residenciales y de vulnerabilidad social" en el que hi hem participat activament i en el que s'ha proposat un nou model d'intervenció per ajudar, millorar i protocol·litzar les actuacions que cal fer en cas d'un brot a un d'aquests centres, amb la posada en marxa de nous "dispositius" d'intervenció i suport com l'Equip de Suport d'Infermeres a Residències (ESIRs), el vehicle d'intervenció ràpida del 061 per residències (MIR) i l'ESAD en cas de precisar-ho per tenir situacions de final de vida.

També hem participat activament amb la coordinació i estructuració de circuits amb la central COVID de vulnerables i amb les valoracions in situ i de suport i seguiment a les múltiples residències on apareixen nous brots de la infecció.

S'ha fet, des de l'equip tècnic d'atenció a la cronicitat i cures pal·liatives múltiples formacions a ESIRs, a professionals de centres residencials de gent gran i discapacitat de totes les illes, de centres de dia i de monitors del clubs socials. També des del mateix equip es coordina tot el seguiment i l'assistència de les residències en brot per part de les ESIRs i des del mes de juliol es controla la monitorització diària de totes les residències de gent gran i discapacitat de les illes Balears per poder tenir-la actualitzada a diari i facilitar les dades a la Conselleria i a Fiscalia.

Projectes de futur

Ens plantegem reorganitzar i seguir donant formació al voltant de les cures pal·liatives virtualment.

Hem incorporat l'atenció pal·liativa a l'àmbit residencial com un punt important a tenir en compte. Estem treballant, juntament amb l'equip d'atenció a la cronicitat, per generar maneres d'atendre a la gent gran de l'àmbit residencial d'una manera més integrada entre la pròpia residència, l'àmbit social i el sanitari.

Estam reiniciant les reunions i gestions necessàries per posar en marxa els projectes que teníem prevists abans del COVID i que estan inclosos dins el Programa de Cures Pal·liatives de la nostra comunitat 2019-2023.

DIME, Associació de voluntaris de cures pal·liatives de les Illes Balears

Des del primer moment de confinament degut a la COVID19, la nostra associació va haver de deixar la seva activitat d'acompanyament a les unitats de cures pal·liatives (UCP). Encara que l'esperança era que fos circumstancial, el temps ens va dur a una aturada de més de 9 mesos.

Atenent a les peticions d'hospitals i residències vàrem proporcionar material tecnològic (tauletes) per a que els pacients es poguessin comunicar amb els seus familiars. També vàrem iniciar un acompanyament telefònic amb les persones majors de les residències per oferir un espai per a la comunicació.

No obstant la incertesa, la prudència i el fet que tots ens trobéssim en una nova situació, no va afavorir que es pogués crear una xarxa de recolzament així com ens hagués agradat per la situació que vivíem.

Sentíem una sensació d'impotència davant tanta necessitat d'atenció pal·liativa a la que no podíem accedir. Ara és temps de reinventar-se, reconnectar i el més important, revaloritzar l'atenció pal·liativa tan necessària i que aquesta pandèmia ha deixat al descobert la seva cara més amarga, un final de vida en aïllament i solitud.

Des de DIME seguim treballant conjuntament amb institucions i associacions en la divulgació d'una atenció pal·liativa de qualitat. Dels grans reptes sorgeixen noves oportunitats i amb la col·laboració dels nostres voluntaris, la seva il·lusió, les seves idees i la seva energia segur que iniciarem nous projectes que ens permetran continuar amb la tasca de l'acompanyament i poder aportar el nostre petit gra de sorra a l'atenció pal·liativa.

ILLESPAL Societat balear de cures pal·liatives

La pandèmia ens va sorprendre a tots descol·locats i, com a la resta del món, el seu primer efecte va ser paraitzar-nos. Ens va obligar a cancel·lar les activitats que teníem previstes pel 2020: una activitat formativa en espiritualitat amb la professora Sara Pons dirigida a professionals, i una divulgativa, seguir amb les xerrades sobre Cures Pal·liatives amb la projecció del documental "el viatge definitiu"⁶ dirigit a la ciutadania.

Segons anava evolucionant la pandèmia, amb la intensitat del símptomes que provocava i l'alta mortalitat, ens adonàvem com a societat científica, que l'àrea de coneixement de les cures pal·liatives tenia molt a aportar a aquesta situació de crisi, i conjuntament amb el centre coordinador de CP de les Illes Balears vàrem realitzar un document de recomanacions pràctiques dirigides al maneig clínic dels pacients infectats per SARS-Cov-2 amb necessitats pal·liatives, expressant també la nostra disponibilitat.

A més, juntament amb altres societats científiques es varen escriure dues cartes a la premsa local, una fou amb la intenció d'aclarir conceptes sobre bones pràctiques que estaven generant dubtes als professionals sanitaris a l'hora de la presa de decisions ètiques, l'altra per a visibilitzar la professionalitat i la qualitat de l'atenció cap a les persones majors.

Pel que fa a l'activitat dirigida als socis, s'ha aturat completament.

- Amb motiu de la celebració del Dia Mundial de CP, es va fer una gran campanya divulgativa amb la intenció de visibilitzar les CP:
 - Ens vàrem unir a la campanya de la SECPAL i AECPAL amb el lema "Mi Cuidado, Mi Bienestar"
 - A més es va realitzar una enquesta dirigida a la ciutadania amb el mateix lema i amb preguntes obertes per promocionar la participació i reflexió.
 - Visibilitzar de les CP també en temps de pandèmia: Participació en diferents mitjans de comunicació: premsa escrita, televisió i radio local⁷⁻¹⁰.
- Es dóna suport a Palma Compassiva
- Hem participat al Festival "Dando vida a la Muerte"

Cap a on anar

Illespal vol seguir amb la missió de fer difusió i formació en cures pal·liatives. Denunciar la manca d'equitat a l'accés a les CP com un dret universal. Visibilitzar que la bona mort no només es decidir quan i com un vol morir, sinó que, són molts els ciutadans que demanen viure el final de vida de manera digna amb bon suport per a pal·liar el sofriment¹¹. L'accés a les cures pal·liatives són un dret que tenim les persones, però no una realitat en el nostre país, ja que no les reben tots els ciutadans que les necessiten.

Discussió i conclusions

L'anàlisi de les experiències viscudes per les diferents societats i associacions ens porten a identificar quines han estat les mancances, les fortaleses i les àrees de millora en situació de crisi sanitària. Com a punt en comú cal destacar l'aturada en sec de tota la programació i cancel·lació de totes les activitats programades, el canvi en la manera de fer les coses, l'adaptació a la nova situació i la capacitat de resiliència. En general l'adaptació dels professionals sanitaris fou ràpida, intensa i altament efectiva, principalment gràcies al sobreesforç personal¹². D'aquesta reflexió s'ha de tenir en consideració la necessitat de l'elaboració de polítiques de resposta davant crisis sanitàries provocades per pandèmies o altres situacions de crisi humanitàries².

No es pot oblidar que s'ha deixat de banda molta atenció i activitats encaminades a persones amb necessitats

pal·liatives, amb malalties avançades i fragilitat, centrant l'atenció a les persones amb COVID19. La manca de recursos de tot tipus, tant humans com materials, que venim patint des de fa molts anys, ha quedat al descobert en aquesta situació de pandèmia, el virus ha tret a la llum les mancances que sofreix el sistema sanitari espanyol reclamades en tantes ocasions per a moltes societats científiques i col·legis professionals¹³.

Així mateix, cal destacar l'esperança de les diferents societats científiques, associacions i equips de salut per a poder tornar a iniciar les activitats i que els socis se'n sentin beneficiats, l'actitud resilient, d'adaptació i de compromís amb les noves circumstàncies. Davant els nous reptes les respostes han estat variables, donant l'oportunitat de introduir conceptes, formació i atenció al final de la vida a diferents tipus de serveis com urgències, UCI i residències geriàtriques on les CP no eren l'objectiu prioritari d'entrada.

Bibliografia

- Bertran J, Sánchez I, Ibañez JJ. Conflictos éticos relacionados con la enfermedad por Coronavirus Covid-19. *Bioética & Debat*. 2020;26(87):22-5.
- Gómez-Batiste X, Leiva JP, Tuca A, Beas E, Montoliu RM, Gálvez R, et al. Organización paliativa durante la pandemia de la COVID-19 y propuestas para la adaptación de los servicios y programas de cuidados paliativos y de atención psicosocial ante la posibilidad de reactivación de la pandemia y época pos-COVID-19. *Med Paliativa*. 2020;27(3):242-54.
- Kotalik J. Preparing for an influenza pandemic: ethical issues. *Bioethics*. 2005;19(4):422-31.
- Centre Coordinador del programa de cures pal·liatives de les Illes Balears, Illespal. Recomendaciones de actuación en casos de infección por SARS-CoV-2 en pacientes con necesidades de atención paliativa [Internet]. 2020. Disponible en: <http://www.caib.es/sites/urespaliatives/f/313934>
- Dirección General de salud pública y participación. Recomendaciones de prevención y protección en Centros Sociosanitarios y Residencias de personas mayores y discapacidad en la Comunidad Autónoma de las Islas Baleares ante la epidemia de COVID-19 [Internet]. Palma; 2020. Disponible en: <http://www.caib.es/sites/urespaliatives/f/317784>
- Centre Coordinador del programa de cures pal·liatives de les Illes Balears. El viatge definitiu [Internet]. Palma: Youtube; 2016. Disponible en: <https://www.youtube.com/watch?v=hHeBgNSKvcY>
- Sansó Martínez N. Día internacional de los cuidados paliativos. *Diario Última Hora*. 2020;
- Rosselló Forteza E. Día mundial de los cuidados paliativos. *Diario de Mallorca* [Internet]. 2020; Disponible en: <https://www.diariodemallorca.es/opinion/2020/10/10/dia-mundial-cuidados-paliativos-17650416.html>
- Benito Oliver E. Cuidados «peliagudos». *Diario de Mallorca* [Internet]. 2020; Disponible en: <https://www.diariodemallorca.es/opinion/2020/10/10/cuidados-peliagudos-17650466.html>
- Rosselló Forteza C. Dia internacional de les cures pal·liatives [Internet]. IB3 radio; 2020. Disponible en: <https://ib3.org/aldiaradio?pl=1&cont=0eb656c5-62c1-45c9-b0fc-a7d0e3d87507>
- Sociedad Española de Cuidados Paliativos, Asociación Enfermería de Cuidados Paliativos. Comunicado sobre la proposición de Ley Orgánica de Regulación de la Eutanasia [Internet]. 2020. Disponible en: <http://infocuidadospaliativos.com/comunicado-de-secpal-y-aecpal-sobre-la-proposicion-de-ley-organica-de-regulacion-de-la-eutanasia/>
- Esquerda M, Rubio O, Amblàs J, Pifarré J. La medicina cambia rápidamente. En un instante, la medicina tal como la conoces acaba. *Bioética & Debat*. 2020;26(87).
- Arias-Casais N, Garralda E, Rhee JY, Lima L De, Pons JJ, Clark D, et al. *EAPC Atlas of Palliative Care* EAPC Atlas of Palliative Care. EAPC Press, editor. Vilvoorde; 2019.

ESTUDI DE CASOS

Anemia ferropénica refractaria en la infancia ¿Y si la causa no es tan frecuente?

Iron deficiency anemia in children. What if the etiology is not that common?

**Unai Díaz-Moreno¹, Margarita Cañellas-Fuster¹, Georgina Sanchís-Blanco²,
Susana Fuertes-Blas¹, Carmen Vidal-Palacios¹, Claudia Marhuenda²**

1. Departamento de Pediatría. Hospital Universitario Son Llàtzer.

2. Departamento de Cirugía Pediátrica. Hospital Universitario Son Espases.

Correspondencia

Unai Díaz-Moreno

Department of Pediatrics. Hospital Universitario Son Llàtzer
Carretera Manacor km 4, 07198 - Palma de Mallorca, Spain

E-mail:

Recibido: 3 - II - 2021

Aceptado: 29 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.127

Resumen

La anemia ferropénica afecta a un 50% de los niños a lo largo de su infancia. En nuestro país, suele ser secundaria a deficiencias dietéticas, sangrado y malabsorción gastrointestinal. Sin embargo, ¿Por dónde comenzamos a buscar una vez se han descartado estas etiologías? La hernia hiatal se ha descrito como causa de anemia ferropénica en adultos. En niños, se han reportado muy pocos casos, y todos ellos tenían un test de sangre oculta en heces (SOH) positivo, que dio pistas para llegar al diagnóstico. Presentamos el caso de un niño de 4 años con test de SOH negativo hasta en tres ocasiones, cuya hernia hiatal fue la causante de una anemia ferropénica severa, crónica y recurrente. Después de la corrección quirúrgica, el paciente se recuperó completamente.

Palabras clave: Anemia, hernia hiatal, fallo de medro.

Summary

Iron-deficiency anemia (IDA) affects around 50% of all children at any point. In our country, lack on dietary iron intake, gastrointestinal tract bleeding and malabsorption syndromes are the most common etiologies. However, where would you look into once these have been ruled out? Hiatal hernia (HH) has been described as a cause of IDA in adults. In children, a few cases have been reported. To our knowledge, all of them had a positive fecal occult blood test, which lead to the diagnosis. We report a case of a 4-year-old boy with three-times negative fecal occult blood test in whom a hiatal hernia was recognized as the cause of severe, recurrent and chronic IDA. After surgical intervention, he was completely recovered.

Key words: Anemia, hiatal hernia, failure to thrive.

Descripción del caso

Varón 4 años con palidez cutánea y decaimiento de 7 meses evolución. Asociaba abdominalgia 1 año evolución, diaria, postprandial, periumbilical, de escasa duración, asociado a saciedad precoz. Su madre refería que desde siempre había sido "mal comedor". No asociaba otros síntomas. El paciente se encontraba taquicárdico, y en la exploración física destacaba la afectación estado general, intensa palidez mucocutánea, sin adenomegalias. Se realizó la antropometría, que resultó ser compatible con desnutrición moderada. Como antecedentes, es el primer hijo pareja joven, origen magrebí, consanguíneos (Primos hermanos). Había ingresado 6 meses antes en otro centro hospitalario por anemia grave (Hb 3,2g/dl), atribuida a Parvovirus B19, que resolvió parcialmente tras transfusión concentrado hematíes (TCH) (Hb 7g/dl). Analítica de control al mes de la transfusión con Hb 12 g/dl. Presentaba una curva ponderarla aplanada desde los 6 meses. Resto sin interés.

Evolución y exploraciones complementarias:

Se realizó analítica inicial, en la que destacaba: Hb 2.88g/dl, Hto 10,10%, VCM 56,40fL, RDW 20.70%, Ferritina 3,44 ng/ml. No signos de hemólisis. Morfología sangre periférica: Aninopoiquilocitosis moderada, microcitosis e hipocromía marcadas. No esquistocitos. Serie blanca y plaquetas sin alteraciones morfológicas. Dada la anemia grave, sintomática, precisó transfusión de concentrado de hematíes urgente y terapia con hierro (Fe) oral 6mg/kg/día.

Se completó el estudio:

- Electroforesis: Normal.
- Serología celiacía: negativo
- H pylori test aliento: positivo, tratado y erradicado.
- Sangre oculta heces: (repetidamente, hasta en tres ocasiones) negativo.

- Gastroscopia: hernia hiatal (HH) moderada, sin lesiones esofágicas ni gástricas
- Biopsias: normales
- Gammagrafía Tc99: no mucosa gástrica ectópica.
- Tránsito esofagogastroduodenal presencia de HH mixta (por deslizamiento y paraesofágica).

Tras 5 meses de Fe oral Hb max.10.20 g/dl, ante AFR se pauta Fe endovenoso consiguiendo Hb. 12.90 g/dl y recaída tras interrupción (Hb.10.20 g/ dl). Comentado con cirugía pediátrica, y tras revisión bibliografía, se orienta como AFR secundaria a HH congénita. Se reparó quirúrgicamente con reducción de la hernia, cierre del gran defecto de pilares diafragmáticos y funduplicatura Nissen. La evolución posterior ha sido satisfactoria con desaparición de la clínica abdominal, aumento de 1 kg de peso en un mes, sin nuevos episodios de anemia.

Discusión

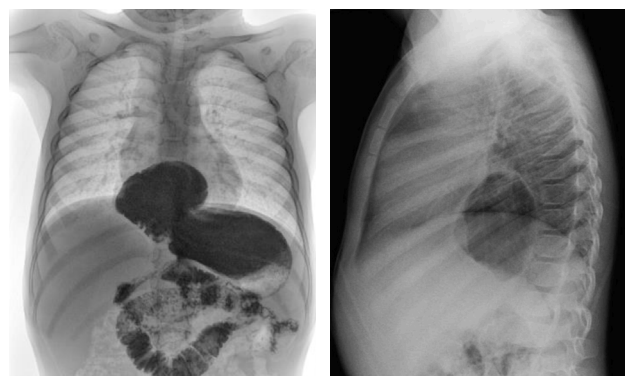
En adultos, la hernia hiatal (HH) suele ser debida a un aumento de la presión intraabdominal debido a obesidad o hiperlaxitud de la membrana esofagodiafragmática. En niños, la mayoría de los casos reportados son congénitos, y responden peor al tratamiento conservador con inhibidores de la bomba de protones, por lo que hay que plantearse la cirugía de entrada. El mecanismo exacto por el cual la hernia hiatal provoca la anemia es desconocido. Se han propuesto varias teorías: 1ª. La HH provoca reflujo de contenido ácido del estómago, y esto a su vez provoca erosión de la pared esofágica, con el consiguiente sangrado. 2ª. el sangrado provendría de las úlceras de Cameron, pequeñas erosiones lineales localizadas en el cuerpo de la hernia. Pero, ¿Qué pasa cuando en la gastroscopia no se evidencia ningún punto de sangrado, como en nuestro caso?. Aquí viene el

tercer mecanismo, propuesto por Shih et al en 2016 tras reportar un caso de HH con test de SOH débilmente positivo. Defienden que la anemia ferropénica no se produce por un sangrado directo, sino por una malabsorción de hierro causada por la hernia hiatal.

Juicio clínico final

Los casos AFR y HH descritos en la literatura son frecuentes en adultos. En la edad pediátrica son muy pocos, pero similares al nuestro. Si bien, nuestro paciente es el primer caso reportado de anemia grave refractaria debida a HH con test repetidos de sangre oculta en heces negativos. Una vez descartadas las causas más habituales de AF en la infancia, el diagnóstico de HH debe ser considerado como posible causa de AFR. El tratamiento de la HH, aunque asintomática, debe ser siempre quirúrgico ante la presencia de AFR y HH.

Imagen 1: tránsito esofagogastro-duodenal, en el que se objetiva hernia hiatal tipo III. **Imagen 2:** radiografía lateral de tórax.



Bibliografía

1. Shih TC, Shih HH, Chang YT, Dai ZK, Chen IC. Hiatal Hernia: A rare cause of iron-deficiency anemia in children. *Pediatrics and neonatology* 2017; 58, 460-1.
2. Ajj M, Shambhavi, Gupta S. Hiatus hernia presenting as resistant iron deficiency anaemia in a child. *Trop Doct.* 2017;47(1):58-60.
3. Sinaki B, Jayabose S, Sandoval C. Iron-deficiency anemia associated with hiatal hernia: Case reports and literature review. *Clinical Pediatrics* 49 (10) 984-5.
4. Karpelowsky JS, Wieselthaler N, Rode H. Primary paraesophageal hernia in children. *J Pediatr Surg* 2006; 41(9): 1588-93.
5. Patoulías D, Kalogirou M, Feidantsis T, Kallergis I, Patoulías I. Paraesophageal hernia as a cause of chronic asymptomatic anemia in a 6 years old boy: Case report and review of the literature. *Acta Medica (Hradec Králové)* 2017; 60(2): 76-81

ESTUDI DE CASOS

Manifestaciones cutáneas con implicación pronóstica

Cutaneous manifestations with prognostic implication

Amador Solá Truyols 

Hospital Universitario Son Llàtzer

Correspondencia

Amador Solá Truyols
Hospital Universitario Son Llàtzer
Carretera Manacor. 07198. Palma de Mallorca
E-mail: stamador@gmail.com

Recibido: 1 - II - 2021

Aceptado: 28 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.129

Resumen

El desarrollo de lesiones de sarcoidosis sobre cicatrices, aparece descrito en numerosos estudios. Se presenta el caso de un varón de 39 años con extensas quemaduras de segundo y tercer grado, en más del 15% de la superficie corporal, que un año después del accidente desarrolla unas lesiones de aspecto distinto sobre las regiones sometidas a quemaduras. Estaban entremezcladas con otras lesiones de aspecto eccematoso, descamativas, que habían sido tratadas ocasionalmente con corticoides tópicos.

En estas áreas cicatriciales, aparecían múltiples placas anaranjadas, con telangiectasias en la superficie sugestivas de un proceso granulomatoso, por lo que se realizó una anamnesis dirigida.

El paciente refería disnea a esfuerzos moderados, por lo que la sospecha de sarcoidosis era elevada. Se realizó una biopsia cutánea, en la que se apreciaban granulomas no caseificantes, y se llevó a término una prueba de imagen con lesiones compatibles con nuestra sospecha principal. Conociendo este conjunto de hallazgos clínico patológicos, finalmente se llegó al diagnóstico de sarcoidosis sistémica con afectación cutánea y pulmonar. Viendo las implicaciones pronósticas que posee esta entidad, la exploración física de un órgano tan accesible como es la piel, resulta fundamental.

Palabras clave: Sarcoidosis, cicatriz, granulomas, dermatoscopia.

Abstract

The development of sarcoidosis lesions on scars has been described in numerous studies. We present the case of a 39-year-old man with extensive second and third degree burns, in more than 15% of the body surface, who one year after the accident developed different-looking lesions on the regions subjected to burns. They were mixed with other eczematous, scaly-looking lesions that had been occasionally treated with topical corticosteroids.

In these scar areas multiple orange plaques appeared with telangiectasias on the surface, suggestive of a granulomatous process, for which reason a directed anamnesis was performed.

The patient reported a recent moderate limitation of physical activity, so that the suspicion of sarcoidosis was high. A skin biopsy was performed, showing non-caseifying granulomas, and an imaging test with compatible lesions was completed.

Knowing this set of findings, the diagnosis of systemic sarcoidosis with skin and lung involvement was finally reached. Due to the prognostic implications of this entity, the physical examination of an organ as accessible as the skin is essential.

Key words: Sarcoidosis, scar, granulomas, dermoscopy.

Caso clínico

Varón de 39 años, alérgico a la penicilina y fumador de 20 cigarrillos diarios. Como antecedentes patológicos relevantes destacamos hipertensión arterial, dislipemia y portador de virus Hepatitis C. Un año antes, fue accidentalmente rociado con un producto inflamable, y sufrió extensas quemaduras de segundo y tercer grado, en más del 15% de la superficie corporal. Las áreas afectas incluían ambas manos y antebrazos, alcanzando toda la extremidad superior derecha y gran parte de la zona posterior cefálica. Requirió múltiples injertos y cirugías para revertir la extensa retracción cicatricial.

Acudió a nuestro servicio de urgencias refiriendo la aparición de múltiples lesiones asintomáticas sobre las áreas que habían sufrido quemaduras. El cuadro se inició 2 meses antes de la visita actual, con la extensión progresiva de las lesiones y entremezcladas con otras lesiones de aspecto eccematoso, y descamación gruesa que habían sido tratadas puntualmente con corticoides tópicos, con escasa mejoría. Durante el examen físico del paciente, se detectaron múltiples placas cicatriciales hipertróficas y con severas retracciones, además de la pérdida de varias falanges en ambas manos, consecuencia de las severas quemaduras.

Figura 1:

- A.** Extensas áreas cicatriciales secundarias a quemaduras.
B. Detalle de las mismas a mayor aumento, donde se aprecia cierto tono anaranjado.



Al observar con detalle, sobre estas áreas cicatriciales, aparecían múltiples placas anaranjadas, con telangiectasias en la superficie. El aspecto anaranjado de las lesiones, y la reproducción de las mismas sobre regiones previamente sometidas a una agresión externa, suponía una alta sospecha de proceso granulomatoso. Al reinterrogar al paciente, se insistió en la posibilidad de padecer clínica respiratoria, confirmándose una disnea a esfuerzos moderados de 4 meses de evolución.

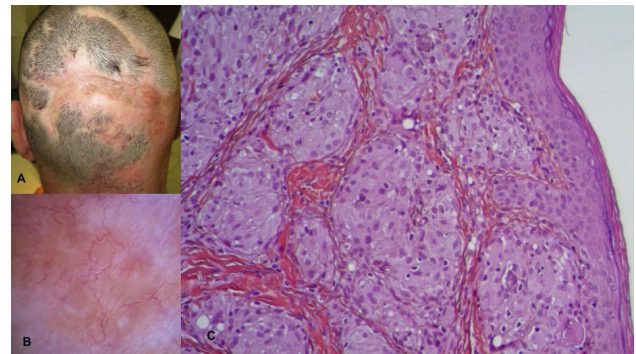
Dados los hallazgos en la exploración física y la clínica anteriormente descrita se orientó este caso como una posible sarcoidosis, por lo que se llevó a término una biopsia cutánea y se solicitó un TAC torácico de alta resolución. El estudio histológico mostraba granulomas de aspecto epitelioides en dermis con la presencia de células gigantes multinucleadas, sin la presencia de necrosis ni corona linfocitaria. En el estudio con luz polarizada no se detectaron cuerpos extraños.

El TAC identificaba adenopatías significativas supraclaviculares izquierdas, mediastínicas e hiliares bilaterales. También extensas condensaciones alveolares con broncograma aéreo, tanto centrales como periféricas, asociando múltiples micronódulos pulmonares de distribución perilinfática y centrolobulillar. Se llevaron a cabo pruebas de función respiratoria, cuyo resultado fue un patrón restrictivo, y en la broncoscopia el recuento CD4/CD8=10,25% y una ecografía-PAAF de mazacote subcarinal, revelaba linfadenitis granulomatosa no necrotizante.

Con estos hallazgos clínico-patológicos se llegó al diagnóstico final de sarcoidosis sistémica con afectación pulmonar estadio II (adenopatías hiliares y patrón reticulonodulillar bilateral) y afectación cutánea. El tratamiento del paciente en el momento de nuestra valoración consistió en una dosis diaria de 60 mg de prednisona, en pauta descendente, y la asociación de metotrexato a dosis de 17,5 mg semanales, con una buena evolución posterior.

Figura 2:

- A.** Placas de alopecia cicatricial secundarias a quemaduras. A simple vista se observan áreas anaranjadas y telangiectasias llamativas.
B. Imagen dermatoscópica de las lesiones previas.
C. Corte histológico en el que se visualizan formaciones redondeadas (granulomas de aspecto epitelioides) junto con células gigantes multinucleadas, sin corona linfocitaria ni necrosis. Compatibles con granulomas de tipo sarcoides.



Discusión

La sarcoidosis es una enfermedad granulomatosa de origen desconocido. Tiene una distribución a nivel mundial y afecta a personas de cualquier raza, edad y sexo. Se ve con mayor frecuencia en adultos jóvenes por debajo de los 40 años, con un ligero predominio por el sexo femenino. Aunque no se conoce con certeza, la prevalencia de esta enfermedad se ha estimado en 10-20 casos por 100.000 habitantes, y la incidencia anual parece variar entre regiones geográficas, agregación familiar y racial, siendo de tres a cuatro veces más común en negros.

En su etiopatogenia se ha involucrado una disregulación de la respuesta inmune frente a antígenos exógenos, capaces de producir la cascada inflamatoria responsable de la formación de los característicos granulomas epitelioides. Aunque son necesarios más estudios, para conocer en mayor detalle la patogénesis de la sarcoidosis.

La histopatología característica de esta enfermedad consiste en la presencia de granulomas no caseificantes, conformados por células gigantes, agregados de histiocitos epitelioides y macrófagos maduros. En general, sin la corona de linfocitos en la periferia (granulomas desnudos).

Se trata de una enfermedad multisistémica, que en más del 90% de los casos afecta a los pulmones y en un 30% de los pacientes se producen manifestaciones a nivel extra torácico. La afectación pulmonar clásica, es en forma de enfermedad pulmonar intersticial difusa, aunque también se incluyen otras presentaciones como el engrosamiento pleural, quilotórax, neumotórax e hipertensión pulmonar. La clínica respiratoria más habitual incluye la tos, la disnea y el dolor torácico. Es habitual la asociación de fiebre, pérdida de peso y malestar generalizado, con sensación de fatiga o debilidad muscular.

Durante la anamnesis será de suma importancia indagar la posible nueva aparición de lesiones cutáneas, sobre todo situadas en tatuajes o cicatrices, también posibles cambios a nivel visual, sequedad de mucosas, dolor o tumefacción articular, palpitaciones y síncope. Las manifestaciones clínicas a nivel dermatológico se observa en aproximadamente el 25 por ciento de los pacientes con sarcoidosis, según las distintas series publicadas, y con relativa frecuencia puede ser el primer signo de la enfermedad. La asociación entre lesiones cutáneas y enfermedad sistémica no se conoce con exactitud, dada la ausencia de estudios extensos bien diseñados.

Las lesiones cutáneas se clasifican en lesiones específicas de sarcoidosis y lesiones inespecíficas, éstas últimas son el resultado de la respuesta inmune que produce el paciente. Las lesiones específicas poseen granulomas sarcoideos a nivel histológico. Y la presentación específica más habitual es en forma de pápulas y placas de una tonalidad marrón, violácea o rojiza, que aparecen sobre todo en la cara, el tercio superior de la espalda y las extremidades. Menos habitual es la presentación de alopecia, y las formaciones nodulares, conocidas como sarcoidosis subcutánea, también las formas papulonodulares en mejillas, nariz y pabellones auriculares (lupus pernio). La presencia de granulomas sarcoideos en el tejido cicatricial es una manifestación característica y se puede ver con relativa frecuencia. Las lesiones habitualmente son asintomáticas, aunque los pacientes pueden quejarse de sensaciones como el prurito o la irritación. Hay que prestar atención al tejido cicatricial y explorar con detalle las lesiones, ya que pueden confundirse con cicatrices hipertróficas o queloides.

Las lesiones inespecíficas incluyen el eritema nodoso como la presentación más frecuente. Otras formas son el eritema multiforme, la calcinosis cutis, el prurigo y el síndrome de Sweet. El diagnóstico diferencial clínico, incluye numerosas entidades dependiendo de las distintas formas de presentación cutánea de sarcoidosis. Y a nivel histológico engloba las reacciones a cuerpo extraño e infecciones por micobacterias como la lepra tuberculoide y el lupus vulgar.

Bibliografía

1. Thomas KW1, Hunninghake GW. Sarcoidosis. JAMA. 2003 Jun 25;289(24):3300-3.
2. Ungprasert P1, Carmona EM2, Utz JP2, Ryu JH2, Crowson CS3, Matteson EL4. Epidemiology of Sarcoidosis 1946-2013: A Population-Based Study. Mayo Clin Proc. 2016 Feb;91(2):183-8.
3. Roberts SD1, Mirowski GW, Wilkes D, Kwo PY, Knox KS. Sarcoidosis. Part II: extrapulmonary and systemic manifestations. J Am Acad Dermatol. 2004 Oct;51(4):628-30.
4. Baughman RP1, Grutters JC2. New treatment strategies for pulmonary sarcoidosis: antimetabolites, biological drugs, and other treatment approaches. Lancet Respir Med. 2015 Oct;3(10):813-22.

El diagnóstico de sarcoidosis requiere un cuadro clínico-radiológico compatible, la demostración histológica de granulomas no caseificantes y la exclusión de otras enfermedades granulomatosas.

Estos pacientes requerirán una serie de pruebas complementarias que consistirán en radiografía de tórax, electrocardiograma, pruebas de función respiratoria (incluyendo la capacidad de difusión), pruebas de la tuberculina e interferón gamma, evaluación oftalmológica y análisis de sangre con hemograma, transaminasas y enzimas de colestasis, niveles de calcio, función renal, urianálisis y niveles de enzima convertidora de angiotensina.

En aquellos pacientes con estudios radiológicos compatibles y clínica sugestiva, la evaluación dermatológica puede ser fundamental, ya que la obtención de una biopsia de piel es una técnica sencilla.

El tratamiento de la sarcoidosis cutánea puede incluir una conducta expectante. Aunque, las lesiones sintomáticas, que resultan desfigurantes, o que presentan progresión o ulceración, se pueden manejar con terapias locales y sistémicas.

Las formas cutáneas localizadas se pueden tratar con infiltración de corticoides intralesionales o su aplicación tópica, incluso crioterapia o radioterapia entre otras. En las formas cutáneas diseminadas, los antipalúdicos, el metotrexato y las tetraciclinas son una opción a considerar.

En caso de afectación sistémica, el tratamiento de elección son los corticoides orales, aunque también se puede optar por otros agentes como el metotrexato, azatioprina, leflunomida y micofenolato.

Juicio clínico final

Sarcoidosis sistémica con afectación pulmonar estadio II (adenopatías hiliares y patrón reticulonodular bilateral) y afectación cutánea.

5. English JC 3rd1, Patel PJ, Greer KE. Sarcoidosis. J Am Acad Dermatol. 2001 May;44(5):725-43; quiz 744-6.
6. Sanchez M1, Haimovic A2, Prystowsky S2. Sarcoidosis. Dermatol Clin. 2015 Jul;33(3):389-416.
7. Yanardağ H1, Pamuk ON, Karayel T. Cutaneous involvement in sarcoidosis: analysis of the features in 170 patients. Respir Med. 2003 Aug;97(8):978-82.
8. García-Porrúa C1, González-Gay MA, Vázquez-Caruncho M, López-Lazaro L, Lueiro M, Fernández ML, et al. Erythema nodosum: etiologic and predictive factors in a defined population. Arthritis Rheum. 2000 Mar;43(3):584-92.

CASE REPORT

Traumatic retroclival epidural hematoma in a child

Hematoma epidural retroclival traumático en un niño

Aidin Shakeri¹ , **Rezvan Rahimifar²** , **Shima Zargar²** , **Alireza Kamali³** 

1. Department of Neurosurgery, Arak University of Medical Science, Arak, Iran.

2. Students Research Committee, Arak University of Medical Science, Arak, Iran.

3. Department of Anesthesiology and Critical Care, Arak University of Medical Sciences, Arak, Iran.

Corresponding Author

Rezvan Rahimifar
Students Research Committee,
Arak University of Medical Science, Arak, Iran
E-mail: rezvan.rahimi772212@gmail.com

Received: 27 - I - 2021

Accepted: 27 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.132

Abstract

Posterior fossa epidural hematomas are seldom encountered and vaguely understood. In this paper, we report on a 10-year-old child experiencing a traumatic retroclival epidural hematoma. A 10-year old boy was involved in a car-to-motorcycle accident. On admission, level of consciousness was assessed 11 on Glasgow Coma Scale. Brain computed tomography revealed a hyperdense lesion in favor of epidural retroclival hematoma mildly compressing the pons. The epidural retroclival hematoma was managed conservatively with close clinical observation. The level of consciousness improved after 8 hours. The patient then complained of headache; however, they had no sign or symptoms of neurologic deficits. Eventually, a repeat CT-Scan was obtained before discharge on day 6, which demonstrated partial resolution of the hemorrhage. Three and nine months later, follow-up physical examinations and CT-Scans demonstrated no new neurological deficits and revealed gradual resolution of the hematoma. Our observations that conservative treatment with close clinical monitoring and serial recording of CT-Scans are the mainstay of management are not new but agree with earlier studies.

Key words: Hematoma, epidural, cranial, intracranial hemorrhages, conservative treatment, consciousness, automobiles.

Resumen

Los hematomas epidurales de la fosa posterior son raros y poco conocidos. En este artículo, informamos sobre un niño de 10 años que sufrió un hematoma epidural retroclival traumático después de un accidente de tráfico. Al ingreso, el nivel de conciencia se evaluó en 11 en la escala de Glasgow. La Tomografía Computarizada (TC) cerebral reveló una lesión hiperdensa compatible con un hematoma retroclival epidural que comprimía ligeramente el puente de Varolio. El hematoma retroclival epidural se trató de forma conservadora con una estrecha observación clínica. El nivel de conciencia mejoró después de 8 horas. El paciente se quejó de dolor de cabeza; sin embargo, no tenía signos o síntomas de déficit neurológico. Finalmente, se repitió la tomografía computarizada antes del alta el día 6, que demostró la resolución parcial de la hemorragia. Tres y nueve meses más tarde, los exámenes físicos de seguimiento y las TC no demostraron nuevos déficits neurológicos y revelaron una resolución gradual del hematoma. El hecho de que el tratamiento conservador con un estrecho control clínico y el registro en serie de las TC son el pilar del tratamiento no es nuevo, pero coinciden con estudios anteriores.

Palabras clave: Hematoma, epidural, craneal, hemorragias intracraneales, tratamiento conservador, conciencia, automóviles

Introduction

Posterior fossa epidural hematomas are seldom encountered. Interestingly, retroclival hemorrhages are among the rarest, comprising an estimated 1.2% to 12.9% of all epidural hematomas^{1,2}. The pediatric population, aged between 3 to 16 years, is involved in high-speed vehicle accidents that are mostly affected^{1,3}.

Retroclival hematomas are a rare entity that is still vaguely understood. Traumatic events inducing neck hypermobility, i.e., hyperflexion and hyperextension, are predominantly responsible for retroclival hematomas. Both mechanisms may lead to soft tissue injuries or fractures and, therefore, venous bleeding⁴. Retroclival hemorrhage may be classified into epidural hematoma [RcEDH] or subdural hematoma [RcSDH] according to the tectorial membrane⁵.

The predominance of the condition among children aged between 3-16 years is mainly attributable to the craniocervical junction's unique anatomical features, which is mostly attributable to the craniocervical instability junction due to smaller occipital condyles and the more horizontal positioning of the atlantooccipital joint¹.

The craniocervical junction is a lax ligamentous apparatus providing mobility at the expense of stability^{5,7}. According to previous studies, atlantooccipital dislocation^{11,12}, atlantoaxial dislocation², rupture of the transverse ligament⁶, fractures of the occipital condyles¹³, spheno-occipital synchondrosis diastasis¹⁴, brain stem contusion, and intraventricular hemorrhage may be connected to the condition⁶.

Clinical manifestations

Retroclival hematomas may present with highly variable clinical symptoms, including nausea, headache, and cranial nerve palsies¹⁵. The sixth cranial nerve [i.e., Abducens] is the most commonly affected cranial nerve, which may be injured both unilaterally^{10,16} or bilaterally^{3,9,11,17-21}. Neurological impairment may be related to stretching, direct compression, or contusion of surrounding nerves and brain parenchyma. The optic, oculomotor, trigeminal, facial, glossopharyngeal, and hypoglossal nerves may also be injured. Patients may also manifest paresis or palsies of upper and lower extremities^{2,15}. Brain stem contusion with cardiorespiratory failure^{6,8,11,12,22} and progressive hydrocephalus¹¹ may infrequently occur in severe cases¹⁵.

Diagnosis and management

REDHs are frequently misdiagnosed; CT-Scans may initially appear normal or mislead the practitioner due

to the cranium's artifacts. Consequently, in high clinical suspicion MRI, it is crucial to demonstrate the disease entity's anatomical details and discover injury of the ligamentous apparatus⁸.

Common etiologies, including trauma and pituitary adenomas, can usually be established by comprehensive history taking. If no obvious mechanism is found, work-up for vascular or coagulation abnormalities must be undertaken²³.

Considering previous literature, most cases of REDH manifest a benign clinical course and resolve spontaneously within 2-11 weeks. Therefore, conservative treatment with close clinical observation and serial recording of CT-Scans are the mainstay of management⁴.

Illustrative case

A 10-year old boy was involved in a car-to-motorcycle accident. On admission, the patient suffered from nausea and vomiting. The patient was lethargic and confused on examination. Level of consciousness was assessed 11 [E₃V₃M₅] according to the Glasgow Coma Scale. The patient was hemodynamically stable with a BP=100/60 and PR=100. No focal neurologic findings, cranial nerve palsies, or clinical deterioration due to cerebral/brain stem contusion was observed. The pupils were bilaterally reactive to light and measured 3 mm.

As shown in **figure 1**, axial brain computed tomography revealed a 58 mm long hyperdense lesion with a maximum thickness of 4.3 mm extending from the superior posterior aspect of the clivus to the central posterior aspect of the odontoid in favor of epidural retroclival hematoma mildly compressing the pons. The spheno-occipital suture showed no evidence of fracture. As shown in **figure 1** (white arrow), the ossiculum terminal of the C2 odontoid process was seen that fused to the dens in follow-up imaging studies as part of a physiologic process typically seen at the age of 12. As shown in **figure 2**, subarachnoid blood was also noted in the basal cistern and left cerebellopontine angle, indicating subarachnoid hemorrhage. Brain CT-Angiography revealed no pathologic findings. It must be emphasized that cervical CT-Scan demonstrated no evidence of retropharyngeal hematoma, atlanto-occipital instability, or atlantoaxial dislocation.

The patient was transferred from the ED to the orthopedic ward due to a subtrochanteric fracture of the left femur managed subsequently by ORIF Surgery. No critical care was required. The epidural retroclival hematoma was managed conservatively. The level of consciousness improved after 8 hours, measuring 15 on Glasgow Coma Scale. Complaints of a headache and left hip and thigh pain were noted during the reassessment of the

patient. Physical examination revealed no cervical spine tenderness or cranial nerve deficits. The patient was hospitalized for 6 days. Eventually, a repeat CT-Scan was obtained before discharge on day 6, which demonstrated partial resolution of the hemorrhage.

Follow-up: Three months later, follow-up physical examination was unremarkable, and repeat CT-scan showed gradual resolution of the hematoma from the basion to the posterior aspect of the C2 body, declining to a maximum thickness of 4.0 mm and a length of 27mm

as can be seen from **figure 3**. A follow-up CT-Scan nine months later, as shown in **figure 4**, demonstrated no evidence of the hematoma in the retroviral region. In the retro-odontoid region, a hyperdensity with a maximum thickness of 3.4 mm was found.

Outcome: According to previous studies, partial recovery with minimal residual neurologic deficits was reported as the most common outcome^{2,8}; however, our case regained consciousness and demonstrated complete resolution of symptoms on the first day of admission.

Figure 1: Craniocervical CT Scan, sagittal view, in the first admission; illustrate ossiculum terminate and thickness of RCEDH.



Figure 2: Brain CT Scan ,Axial view. Shows subarachnoid hemorrhage in Basal and left CPA cisterns.

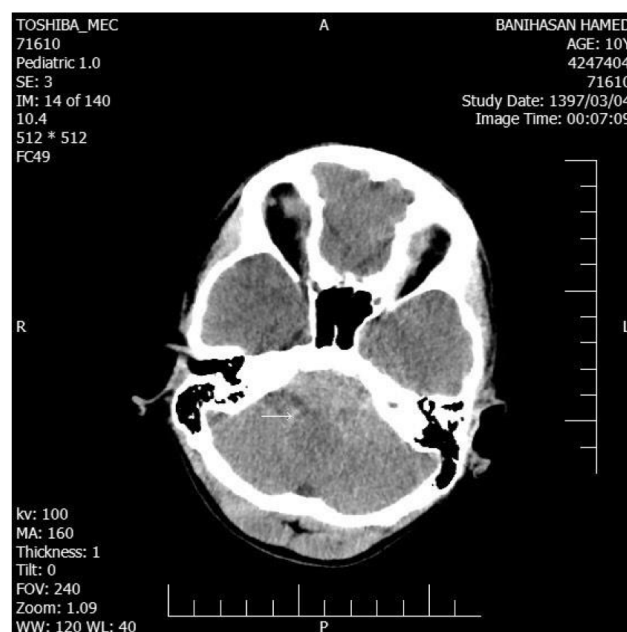


Figure 3: Craniocervical CT Scan, sagittal view, illustrate thickness of RCEDH that decreased after 3 month.



Figure 4: Craniocervical CT Scan, sagittal view, RCEDH resolved and only retro-odontoid hematoma remains after 9month.



The findings of a clinical series conducted by Tubbs et al. [39] are in good agreement with the case presented in our study; No correlation was revealed between hematoma sizes and clinical manifestations or initial GCS scores and clinical outcomes. [17, 22, 2]. The extra-axial hematoma may pressure the brainstem and cranial nerves, warranting surgical evacuation^{11,21,24,25}.

Conclusion

Retroclival hematomas are a rare entity still vaguely understood, usually manifesting with variable clinical

symptoms. Our observations that close clinical observation and serial recording of CT-Scans are the mainstays of management are not new but are in good agreement with earlier studies.

Acknowledgments

The authors want to thank the deputy of Research of Arak University of Medical Sciences, the Clinical Research Center of Valiasr Hospital, and all those who participated and helped us in this study.

References

1. Agrawal D, Cochrane DD. Traumatic retroclival epidural hematoma-a pediatric entity?. *Child's Nervous System*. 2006; 22(7):670-3.
2. Tubbs RS, Griessenauer CJ, Hankinson T, Rozzelle C, Wellons JC, Blount JP, et al. Retroclival epidural hematomas: a clinical series. *Neurosurgery*. 2010; 67(2):404-7.
3. Van Rijn RR, Flach HZ, Tanghe HL (2003) Spontaneous retroclival subdural hematoma. *JBR-BTR* 86:174-5.
4. Nguyen HS, Shabani S, Lew S. Isolated traumatic retroclival hematoma: case report and review of literature. *Child's Nervous System*. 2016; 32(9):1749-55.
5. Koshy J, Scheurkogel MM, Clough L, Huisman TA, Poretti A, Bosemani T. Neuroimaging findings of retroclival hemorrhage in children: a diagnostic conundrum. *Childs Nerv Syst* 2014; 30:835-9.
6. Orrison WW, Rogde S, Kinard RE, Williams JE, Torvik A, Sackett JF, et al. Clivus epidural hematoma: a case report. *Neurosurgery*. 1986; 18:194-6.
7. Tahir MZ, Quadri SA, Hanif S, Javed G. Traumatic retroclival epidural hematoma in pediatric patient-case report and review of literature. *Surg Neurol Int* 2011; 2:78.
8. Pérez-Bovet J, Garcia-Armengol R, Ferrer SM. Traumatic epidural retroclival hematoma with odontoid fracture and cardiorespiratory arrest. *Spinal cord*. 2013; 51(12): 926-8.
9. Khan N, Zumstein B. Transverse clivus fracture: case presentation and significance of clinico-anatomic correlations. *Surg Neurol* 2000; 54:171-7.
10. Paterakis KN, Karantanis AH, Hadjigeorgiou GM, Anagnostopoulos V, Karavelis A. Retroclival epidural hematoma secondary to a longitudinal clivus fracture. *Clin Neurol Neurosurg* 2005; 108:67-72.
11. Papadopoulos SM, Dickman CA, Sonntag VK, Rekatte HL, Spetzler RF. Traumatic atlantooccipital dislocation with survival. *Neurosurgery*. 1991; 28:574-9.
12. Vera M, Navarro R, Esteban E, Costa JM. Association of atlanto-occipital dislocation and retroclival haematoma in a child. *Childs Nerv Syst* 2007; 23:913-6.
13. Suliman HM, Merx HL, Wesseling P, van der Sluijs B, Vos PE, Thijssen HO. Retroclival extradural hematoma is a magnetic resonance imaging diagnosis. *J Neurotrauma* 2001; 18:1289-93.
14. Kurosu A, Amano K, Kubo O, Himuro H, Nagao T, Kobayashi N, et al. Clivus epidural hematoma. Case report. *J Neurosurg*. 1990; 72:660-2.
15. Dal Bo S, Cenni P, Marchetti F. Retroclival hematoma. *J Pediatr*. 2015;166:773.
16. McDougall CM, Sankar T, Mehta V, Pugh JA. Pediatric traumatic retroclival epidural hematoma. *Can J Neurol Sci*. 2011; 38:338-40.
17. Kwon TH, Joy H, Park YK, Chung HS. Traumatic retroclival epidural hematoma in a child: case report. *Neurol Med Chir (Tokyo)*. 2008; 48:347-50.
18. Ratilal B, Castanho P, Luiz CV, Antunes JO. Traumatic clivus epidural hematoma: case report and review of the literature. *Surgical neurology*. 2006 ;66(2):200-2.
19. Becco de Souza R, Brasileiro de Aguiar G, Sette Dos Santos ME, Acioly MA. Retroclival epidural hematoma in a child affected by whiplash cervical injury: a typical case of a rare condition. *Pediatr Neurosurg*. 2011; 47:288-91.
20. Mizushima H, Kobayashi N, Sawabe Y, Hanakawa K, Jinbo H, Iida M, et al. Epidural hematoma of the clivus. Case report. *J Neurosurg*. 1998; 88:590-3.
21. Sridhar K, Venkateswara PG, Ramakrishnaiah S, Iyer V. Posttraumatic retroclival acute subdural hematoma: report of two cases and review of literature. *Neurol India*. 2010; 58:945-8.
22. Yang BP . Traumatic retroclival epidural hematoma in a child. *Pediatr Neurosurg* 2003; 39:339-40.
23. Krishnan P, Kartikueyan R, Chowdhury SR, Das S. Retroclival subdural hematoma: an uncommon site of a common pathology. *Neurol India*. 2013; 61:550-2.
24. Datar S, Daniels D, Wijdicks EF. A major pitfall to avoid: retroclival hematoma due to odontoid fracture. *Neurocrit Care*. 2013; 19:206-9.
25. Marks SM, Paramaraswaren RN, Johnston RA. Transoral evacuation of a clivus extradural haematoma with good recovery: a case report. *Br J Neurosurg*. 1997; 11:245-7.

Fracture resistance of teeth with simulated cervical root resorptions restored by various materials

Resistencia a la fractura dental con reabsorciones radiculares cervicales simuladas y restauradas con diversos materiales

Fatemeh Mohammadian¹ , Seyyed Sina Hazinehei² , Sedighe Sadat Hashemi kamangar³ , Fatemeh Dibaji¹ , Mohammad Javad Kharrazifard⁴ 

1. Department of Endodontics, School of Dentistry, Tehran University of Medical Sciences, International Campus, Tehran, Iran.

2. School of Dentistry, Tehran University of Medical Sciences, International Campus, Tehran, Iran.

3. Department of Operative Dentistry, International Campus, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.

4. Statistical Advisor, Dental Research Center, Tehran University of Medical Sciences, Tehran, Iran

Corresponding Author

Fatemeh Dibaji

Department of Endodontics, School of Dentistry,

Tehran University of Medical Sciences, International Campus, Tehran, Iran

E-mail: f-dibaji@tums.ac.ir

Received: 21 - I - 2021

Accepted: 29 - IV - 2021

doi: 10.3306/AJHS.2021.36.02.136

Abstract

This study **aimed** to compare the fracture resistance of teeth with cervical root resorptions following restoration with resin composite, resin-modified glass ionomer (RMGI), Biodentine, and mineral trioxide aggregate (MTA).

Methods: 60 sound extracted single-rooted maxillary premolars were divided into 4 experimental (n=10) and 2 control (n=10) groups. Ten intact teeth served as the negative control group. In the remaining teeth, cavities were prepared with 2 mm depth, extending 1 mm above the cemento-enamel junction (CEJ), and 2 mm below it. The cavities remained unrestored in the 10 positive control teeth. The cervical cavities in the remaining teeth were restored with Z250 resin composite, Fuji II LC RMGI, ProRoot MTA, and Biodentine. The teeth' fracture resistance was measured using a universal testing machine and recorded in newton (N). Data were analyzed using one-way ANOVA followed by Tukey's test with a 95% confidence interval.

Results and conclusions: Significant differences were noted in the fracture resistance of composite resin and RMGI with the positive control group ($P < 0.05$). No significant difference was noted between the Biodentine and MTA groups with the positive control group in this respect ($P > 0.05$). Within this study's limitations, it seems that the resin composite and RMGI restorations can increase the fracture resistance of teeth with artificially-induced cervical resorption defects. However, Biodentine and MTA as bioactive cement have no strengthening effect on the tooth structure.

Keywords: Biodentine, cervical resorption, fracture resistance, mineral trioxide aggregate, resin composite.

Resumen

El **objetivo** de este estudio es comparar la resistencia a la fractura de dientes con reabsorciones radiculares cervicales tras la restauración con composite de resina, ionómero de vidrio modificado con resina (RMGI), Biodentina y agregado de trióxido mineral (MTA).

Metodología: Se dividieron 60 premolares maxilares de una sola raíz extraídos en 4 grupos experimentales (n=10) y 2 de control (n=10). Diez dientes intactos sirvieron de grupo de control negativo. En los dientes restantes, se prepararon cavidades de 2 mm de profundidad, que se extendían 1 mm por encima de la unión cemento-esmalte (CEJ) y 2 mm por debajo de ella. Las cavidades permanecieron sin restaurar en los 10 dientes de control positivo. Las cavidades cervicales de los dientes restantes se restauraron con composite de resina Z250, Fuji II LC RMGI, ProRoot MTA y Biodentine. La resistencia a la fractura de los dientes se midió con una máquina de ensayo universal y se registró en newton (N). Los datos se analizaron mediante un ANOVA unidireccional seguido de la prueba de Tukey con un intervalo de confianza del 95%.

Resultados y conclusiones: Se observaron diferencias significativas en la resistencia a la fractura de la resina compuesta y la RMGI con el grupo de control positivo ($P < 0,05$). No se observaron diferencias significativas entre los grupos de Biodentina y MTA con el grupo de control positivo a este respecto ($P > 0,05$). Dentro de las limitaciones de este estudio, parece que las restauraciones de resina compuesta y RMGI pueden aumentar la resistencia a la fractura de los dientes con defectos de reabsorción cervical inducidos artificialmente. Sin embargo, la biodentina y el MTA como cemento bioactivo no tienen ningún efecto reforzador sobre la estructura dental.

Palabras clave: Biodentina, reabsorción cervical, resistencia a la fractura, agregado de trióxido mineral, composite de resina.

Introduction

External invasive cervical resorption refers to a process through which progressive loss of dentin and cementum occurs because of odontoclasts' activity in the granulation tissues adjacent to the teeth' cervical region¹. The extent of resorption defects can be classified into four classes based on Hiethersay classification: class I, a small cervical lesion with shallow penetration into dentine; class II, a well-defined lesion close to the coronal pulp but with little or no extension into radicular dentine; class III, deeper invasion of the lesion into the coronal third of the root; class IV, a lesion extending beyond the coronal third of the root². More extensive and potentially more inaccessible lesions have a poorer prognosis³. The treatment should be promptly started after the definite diagnosis of cervical root resorption due to this condition's invasive nature⁴. If the resorption has not invaded the pulp chamber and has extended far below the gingival margin, a surgical flap should be reflected, the resorptive tissue should be completely removed, and the cavity should be restored with a suitable restorative material³. Based on the resorption defect position, various materials such as glass ionomer cement, resin-modified glass-ionomer cement, resin composite, amalgam, Biodentine, and mineral trioxide aggregate (MTA) have been suggested as appropriate restorative materials⁵.

Since tooth structure loss renders teeth susceptible to fractures, the long-term prognosis depends on the overall total volume loss of the resorption's affected root structure⁶. An appropriate restorative material should be applied to seal the area of tooth loss and optimally resist occlusal and masticatory forces⁷. However, there is no information about these dental materials' efficacy to reinforce teeth weakened by cervical lesions. Considering the significance of fracture resistance of the teeth and its effect on their long-term survival and function in the oral cavity, this study aimed to assess the fracture resistance of teeth with artificially-induced cervical resorption defects restored with different dental materials to find the more resistant material for this purpose.

Materials and methods

Sixty extracted single-rooted and single-canal maxillary human premolars were used in this study. The teeth were cleaned and stored in 0.5% thymol solution at 4°C until the testing. The selected teeth were sound and had no anomalies or caries. Also, the teeth were inspected under a stereomicroscope at x20 magnification to ensure the absence of cracks.

Since the artificially created cervical resorption defects had to have a 2 mm depth, and we had to ensure no exposure of root canal during cavity preparation, a minimum of 2.5 mm distance was required between

the external root surface and the internal root canal wall. Thus, the selected teeth had a minimum of 2.5 mm distance (dentin thickness) between the external root surface and the internal root canal wall in the mesiodistal and buccolingual directions on radiographs from 1 mm above the cemento-enamel junction (CEJ) to 2 mm apical to the CEJ in all directions.

To minimize the confounding effect of variations in size and shape of teeth, their buccolingual and mesiodistal dimensions were measured by a digital caliper (Mitutoyo, Hiroshima, Japan) with 0.01 mm accuracy. According to the tooth size obtained using the following formula, the teeth were divided into two control groups (n=10) and four experimental groups (n=10) using stratified complete block randomization.

$$\text{Tooth height} = \frac{\text{Height of palatal cusp from the CEJ} + \text{height of buccal cusp from the CEJ}}{2}$$

Tooth width = Mesiodistal width of the tooth at the height of contour

$$\text{Tooth size} = \frac{\text{Tooth height}}{\text{Tooth width}}$$

Next, the roots were dipped in melted wax to the level of their CEJ such that a layer of wax with 0.3 mm thickness covered the roots to stimulate the periodontal ligament (PDL). The teeth were mounted in self-cure acrylic resin blocks (Acropars, Tehran, Iran) with 25 mm diameter to the level of their CEJ such that the longitudinal axis of the root was perpendicular to the resin block. The wax-coated teeth were removed from the mounting block, and the wax layer was eliminated from the roots. Ten good teeth served as the negative control and did not undergo cavity preparation. In the remaining teeth, to simulate the class III of invasive root resorption classification of Hiethersay², extensive cavities with 2±0.1 mm in depth and 3±0.1 mm in width (from 1 mm above the CEJ to 2 mm apical to the CEJ) were prepared using a fissure bur (Dia. Tessin, Gordevio, Switzerland), such that they extended from the mesial half of the tooth to the distal half of the tooth involving the entire buccal surface (**Figure 1**).

Ten teeth served as the positive control, and the artificially created defects in them were not restored with any restorative material. In the rest of the teeth, Z250 resin composite (3M ESPE, St. Paul, MN, USA), Fuji II LC RMGI (GC America Inc., Alsip, IL, USA), Biodentine (Septodont, Saint Maur-des Fossés, France), and ProRoot MTA (Dentsply, Tulsa, OK, USA) were used for the restoration of artificially created cervical resorption defects.

To repair with Z250 resin composite, the teeth cavities were the first acid etched by 3M Scotch (3M ESPE,

Figure 1: Artificial cervical root resorption cavity.

Buccolingual view



Mesiodistal view

Minnesota, USA) for 15 seconds, and the cavities were rinsed thoroughly. Then Single Bond adhesive (3M ESPE, Minnesota, USA) was placed on the cavities, and to create a thin layer of bonding, the cavity was gently dried by air spray for 2-5 seconds. The bonding agent was light-cured for 15 seconds. Then Resin composite was placed incrementally (up to 2 mm-thick layers), and each resin composite layer was light-cured for 20 seconds.

At first, in the Fuji II LC group, the resin-modified glass ionomer's powder and liquid were mixed to achieve a suitable consistency. For this purpose, a spoonful of powder and two drops of its liquid were placed on a paper pad. With a spatula, the powder was divided into two equal parts, and the first part was mixed with the liquid for 10 seconds, and then the second part of the powder was added, and the ingredients were mixed for 10 seconds. Fuji II LC was placed in the cavities incrementally (up to 2 mm-thick layers), and each layer was light cured for 20 seconds.

According to the manufacturer's instructions, to repair the cervical cavity with Biodentine, after gently tapping the capsule containing dentine powder, 5 drops of its unique solution were poured into the capsule. Then, the capsule is placed in the amalgamator device (Kerr, Detroit, USA) to mix for 30 seconds, and the resulting cement was placed in the cavity incrementally and was gently compacted with Schilder pluggers (Hu, Friday, Chicago, IL, USA).

Finally, ProRoot MTA (Dentsply, Tulsa, OK, USA) was used to repair the last group. According to the manufacturer's instructions, after gradually incorporating its powder with liquid and mixing for one minute, MTA was placed in the cavity then the material was gently compacted by pluggers.

To allow the restorative materials' complete setting, they were incubated at 37°C and 100% humidity (Kavosh

Mega, Tehran, Iran) for 7 days⁸. The holes in acrylic blocks were filled with Impregum soft polyether impression material (3M ESPE, Minnesota, USA) to simulate the PDL then the teeth were mounted again in their respective holes in acrylic blocks.

After 1 hour, the teeth were transferred to a universal testing machine to measure fracture resistance (Zwick Roell, Zwick, Ulm, Germany). A flame-shaped bur (Dia. Tessin, Gordevio, Switzerland) was used to create small contact points on the buccal and lingual cusps to prevent lateral deviation upon load application. A compressive load was applied to the cusp slopes along the teeth' longitudinal axis by a round-end rod with 5 mm diameter at a crosshead speed of 0.5 mm/min. Maximum load causing tooth fracture was recorded in N. To determine the mode of failure, the teeth were removed from the resin blocks, and the mode of failure of each tooth was evaluated by two operators and considered as favorable (fractures stopped higher than 1 mm below the CEJ) and unfavorable (fractures stopped lower than 1 mm below the CEJ)⁹. Data were analyzed using SPSS version 25. One-way ANOVA was used to compare the fracture resistance of the groups. Pairwise comparisons were performed using Tukey's test. $P < 0.05$ was considered statistically significant.

Results

Table I shows the mean values of the fracture strength in the six groups. The results showed significant differences in fracture resistance of resin composite and RMGI groups with the unrestored positive control group ($P < 0.05$). However, the difference in fracture resistance of resin composite and RMGI groups was not significant ($P > 0.05$). The difference between Biodentine and MTA was not significant ($P > 0.05$), and the two groups had no significant difference with unrestored positive control teeth either ($P > 0.05$).

Table I: Fracture resistance of the study groups in Newton.

Group	Minimum	Maximum	Mean	Std. Deviation
Intact	1517.00	1831.00	1684.60	122.02
Resin composite	112.00	2243.00	1186.00	688.99
RMGI	180.00	1546.00	900.20	408.27
Biodentine	175.00	966.00	584.30	279.64
MTA	110.00	733.00	405.70	208.90
Unrestored	37.00	231.00	134.00	77.92

Table II: Frequency percentage of favorable and unfavorable modes of failure in the study groups.

Group	N	Favorable Fractures	Unfavorable Fractures
Resin composite	10	9 (90%)	1 (10%)
RMGI	10	8 (80%)	2 (20%)
Biodentine	10	7 (70%)	3 (30%)
MTA	10	4 (40%)	6 (60%)
Intact	10	8 (80%)	2 (20%)
Unrestored	10	2 (20%)	8 (80%)

Table II presents the modes of failure. Accordingly, the mode of failure in intact teeth, resin composite, RMGI, and Biodentine groups was mainly favorable while it was primarily unfavorable in MTA and unrestored positive control group.

Discussion

Different restorative materials should be necessarily used to reinforce the weakened tooth structure in order to confer resistance against masticatory loads or parafunctional forces¹⁰.

In the present study, maxillary single-canal, single-rooted premolar teeth were used for standardization because maxillary premolars, due to their particular anatomy, are highly fragile when subjected to occlusal forces, particularly when they have lost part of their structure⁷.

Cervical resorption is often invasive and results in losing an extensive tooth structure part in a short time⁶. After reaching the protective perianal resorption resistant sheet formed by the prevention and innermost layer of dentin, an extension of resorption towards the pulp often stops, and the defect further extends towards the lateral sides and in incisogingival direction⁶. Due to the lack of a similar study on creating artificial cervical invasive resorption, we considered class III classification of Hiethersay², and cavities were prepared as described above.

According to the current results, maximum fracture resistance was noted in teeth with cervical resorption defects restored with Z250 resin composite followed by Fuji II LC RMGI, Biodentine, and MTA. Subash et al.¹⁰ measured the fracture resistance of resin composite, RMGI, and Biodentine as core build-up materials. The resin composite showed maximum fracture resistance, while Biodentine showed minimum fracture resistance¹⁰. Also, Hiremath et al.¹¹ showed that the fracture resistance

of Biodentine was significantly lower than the reinforced resin composite and sound teeth. Yasa et al.¹² indicated that the fracture resistance of resin composite and glass ionomer when used as an intra-orifice barrier, was significantly higher than the control group; however, MTA Angelus and Micro Mega MTA did not increase the fracture resistance of the teeth compared with the control group; this result was likewise present study's results.

Gupta et al.⁸ measured the fracture resistance of RMGI and resin composite as an intra-orifice barrier and reported that their fracture resistance was significantly higher than the MTA. However, RMGI had significantly higher fracture resistance than resin composite⁸. The later result was different from our findings, which may be due to the difference in the two studies' methodology.

In the present study, maximum fracture resistance was noted in the group restored with resin composite. The reason may be the ability of resin composite to reinforce the remaining tooth structure¹³. Moreover, adhesive material provides adequate retention for the resin composite and serves as a bridge and splint between the cavity walls¹⁴.

Higher fracture resistance obtained by the use of RMGI compared with unrestored teeth with defects (positive control) is due to the inherent properties of RMGI, such as high flexural strength and a modulus of elasticity comparable to that of dentin (10 to 14 GPa)^{8,15}. Thus, it can resist high levels of stress. Moreover, its chemical bond to dentin surfaces can cause high resistance at the dentin-cementum interface and increase the integrity of the coronal structure and the fracture resistance of the tooth⁸.

In the present study, no significant difference was noted in fracture resistance of teeth with cervical defects restored with RMGI and Z250 resin composite. This finding was similar to that of Aboobakr et al.¹⁶, who found no significant difference in fracture resistance of Tetric N Flow resin composite and Fuji LC RMGI as intra-orifice barriers.

Considering that glass ionomer's clinical application in cervical areas is much easier and has lower technical sensitivity than resin composite¹⁷, this valuable clinical finding can help in the more efficient and more accessible restoration of cervical resorption defects.

Yasa et al.¹² showed that Biodentine significantly increased the fracture resistance of teeth compared with the control group. Some studies have shown that materials with calcium silicate base can chemically bond to root canal dentin^{18,19}. Biodentine, compared with MTA, releases higher amounts of calcium, leading to the formation of an intermediate layer and tag-like structures¹⁹. This property can increase the bonding ability of Biodentine 20. In addition to this, it has shown demonstrated that Biodentine caused higher absorption

of calcium and silicon ions by root dentin and resulted in the higher formation of tag-like structures compared with the MTA²¹. In the present study, although Biodentine, compared with the MTA and control groups, increase the fracture resistance of the teeth with cervical resorption defects, the differences were not significant.

Nagas et al.¹⁵ compared the efficacy of three intra-orifice barriers to reinforce root structure and concluded that MTA, compared with RMGI and fiber-reinforced composite, had no efficacy to reinforce the root structure; this result was in line with our findings. Low fracture resistance of the MTA group, compared with RMGI and resin composite, is due to its inability to bond to dentin, hardness under high pressure, and weakness under tension despite its optimal modulus of elasticity²².

In the clinical setting, the prognosis of teeth after restorative treatment failure depends on the mode of fracture and position of the fracture line. Dental restorations with fractures extending to below the CEJ are often very hard or impossible to repair²³. In the present study, the mode of failure in three resin composite, RMGI, and Biodentine were mainly favorable (90%, 80%, and 70%, respectively). However, the mode of failure was unfavorable in 60% of the cases in MTA group. This finding can be due to the MTA's inefficacy to obtain a suitable bond to tooth structure compared with the other three materials.

In general, it seems that although bioactive materials such as Biodentine and MTA enhance tissue healing when applied adjacent to biologic tissues^{24,25}, the current results revealed that Biodentine and MTA had no reinforcing effect on the tooth structure when applied for restoration of cervical resorption defects due to their physical

properties. New bioactive materials with more suitable physical properties are required to serve this purpose.

Some surveys have been conducted in different fields of medical sciences up to know²⁶⁻³¹. However, to the best of the authors' knowledge, no previous study is available on fracture resistance of the teeth with cervical resorption defects restored with different materials. Thus, it seems that the data obtained in this study can be used to design future studies to find more suitable restorative materials for this purpose. Finally, yet importantly, it should be noted that in the oral environment, the teeth are subjected to several factors such as continuous exposure to moisture, thermal and pH alterations due to the consumption of foods and drinks, different bacteria and enzymes, and masticatory forces. All these parameters have undeniable effects on fracture resistance of the teeth. The clinical setting cannot be completely simulated in vitro. Thus, the generalization of the results of in vitro studies to the clinical setting should be made cautiously.

Within the limitations of this in vitro study, it seems that resin composite and RMGI can increase the fracture resistance of teeth with artificially induced cervical resorption defects when used as a restorative material. However, Biodentine and MTA as bioactive agents have no significant efficacy to reinforce the tooth structure.

Acknowledgments

The authors would like to thank the Department of Endodontics, School of Dentistry, Tehran University of Medical Sciences, International Campus, Tehran, Iran, for the imperative supports.

References

1. Patel S, Mavridou AM, Lambrechts P, Saberi N. External cervical resorption-part 1: histopathology, distribution and presentation. *International endodontic journal*. 2018;51(11):1205-23.
2. Heithersay GS. Clinical, radiologic, and histopathologic features of invasive cervical resorption. *Quintessence international (Berlin, Germany : 1985)*. 1999;30(1):27-37.
3. Patel S, Foschi F, Condon R, Pimentel T, Bhuvu B. External cervical resorption: part 2 - management. *International endodontic journal*. 2018;51(11):1224-38.
4. Rotondi O, Waldon P, Kim SG. The Disease Process, Diagnosis and Treatment of Invasive Cervical Resorption: A Review. *Dentistry journal*. 2020;8(3).
5. Eftekhar L, Ashraf H, Jabbari S. Management of Invasive Cervical Root Resorption in a Mandibular Canine Using Biodentine as a Restorative Material: A Case Report. *Iranian endodontic journal*. 2017;12(3):386-9.
6. Matny LE, Ruparel NB, Levin M, Noujeim ME, Diogenes A. Response Regarding: A Volumetric Assessment of External Cervical Resorption Cases and Its Correlation to Classification, Treatment Planning, and Expected Prognosis. *Journal of endodontics*. 2020;46(12):1929-30.
7. Mondelli RF, Ishikiriama SK, de Oliveira Filho O, Mondelli J. Fracture resistance of weakened teeth restored with condensable resin with and without cusp coverage. *Journal of applied oral science : revista FOB*. 2009;17(3):161-5.
8. Gupta A, Arora V, Jha P, Nikhil V, Bansal P. An in vitro comparative evaluation of different intraorifice barriers on the fracture resistance of endodontically treated roots obturated with gutta-percha. *Journal of conservative dentistry: JCD*. 2016;19(2):111-5.
9. Firouzmandi M, Doozandeh M, Jowkar Z, Abbasi S. Effect of composite/amalgam thickness on fracture resistance of maxillary premolar teeth, restored with combined amalgam-composite restorations. *Journal of clinical and experimental dentistry*. 2016;8(3):e268-72.
10. Subash D, Shoba K, Aman S, Bharkavi SKI, Nimmi V, Abhilash R. Fracture Resistance of Endodontically Treated Teeth Restored

- with Biodentine, Resin Modified GIC and Hybrid Composite Resin as a Core Material. *Journal of clinical and diagnostic research : JCDR*. 2017;11(9):Zc68-zc70.
11. Hiremath H, Kulkarni S, Hiremath V, Kotipalli M. Evaluation of different fibers and biodentine as alternates to crown coverage for endodontically treated molars: An in vitro study. *Journal of conservative dentistry : JCD*. 2017;20(2):72-5.
 12. Yasa E, Arslan H, Yasa B, Akcay M, Alsancak M, Hatirli H. The force required to fracture endodontically roots restored with various materials as intra-orifice barriers. *Nigerian journal of clinical practice*. 2017;20(10):1237-41.
 13. Bholra S, Barker D. Composite Build-Ups: a Review of Current Techniques in Restorative Dentistry. *Dental Update*. 2020;47(3):186-98.
 14. Rezvani M, MOHAMMADI BM, Mollaverdi F, Moradi Z, Soboot A. Comparison of direct and indirect composite resin restorations effect on the fracture resistance of maxillary premolars (An in vitro study). 2012.
 15. Nagas E, Uyanik O, Altundasar E, Durmaz V, Cehreli ZC, Vallittu PK, Lassila LV. Effect of different intraorifice barriers on the fracture resistance of roots obturated with Resilon or gutta-percha. *Journal of endodontics*. 2010;36(6):1061-3.
 16. Aboobaker S, Nair BG, Gopal R, Jituri S, Veetil FR. Effect of intra-orifice barriers on the fracture resistance of endodontically treated teeth - an ex-vivo study. *Journal of clinical and diagnostic research : JCDR*. 2015;9(2):Zc17-20.
 17. Dias AGA, Magno MB, Delbem ACB, Cunha RF, Maia LC, Pessan JP. Clinical performance of glass ionomer cement and composite resin in Class II restorations in primary teeth: A systematic review and meta-analysis. *Journal of dentistry*. 2018;73:1-13.
 18. Lucas CP, Viapiana R, Bosso-Martelo R, Guerreiro-Tanomaru JM, Camilleri J, Tanomaru-Filho M. Physicochemical Properties and Dentin Bond Strength of a Tricalcium Silicate-Based Retrograde Material. *Brazilian dental journal*. 2017;28(1):51-6.
 19. Akcay H, Arslan H, Akcay M, Mese M, Sahin NN. Evaluation of the bond strength of root-end placed mineral trioxide aggregate and Biodentine in the absence/presence of blood contamination. *European journal of dentistry*. 2016;10(3):370-5.
 20. Guneser MB, Akbulut MB, Eldeniz AU. Effect of various endodontic irrigants on the push-out bond strength of biodentine and conventional root perforation repair materials. *Journal of endodontics*. 2013;39(3):380-4.
 21. Bansal K, Jain A, Aggarwal N, Jain A. Biodentine VS MTA: A comparative analysis. *International Journal of Oral Health Dentistry*. 2020;6(3):201-8.
 22. Kazemipoor M, Azizi N, Farahat F. Evaluation of Microhardness of Mineral Trioxide Aggregate After Immediate Placement of Different Coronal Restorations: An In Vitro Study. *Journal of dentistry (Tehran, Iran)*. 2018;15(2):116-22.
 23. Shafiei F, Memarpour M, Karimi F. Fracture resistance of cuspal coverage of endodontically treated maxillary premolars with combined composite-amalgam compared to other techniques. *Operative dentistry*. 2011;36(4):439-47.
 24. Maheaswari R, Jeeva R. Biodentine: Periodontal perspective. *Journ App Dent Sci*. 2017;3:12-6.
 25. Malkondu Ö, Karapinar Kazandağ M, Kazazoğlu E. A review on biodentine, a contemporary dentine replacement and repair material. *BioMed research international*. 2014;2014:160951.
 26. Ranjbar R, Farsani FY, Dehkordi FS. Phenotypic analysis of antibiotic resistance and genotypic study of the vacA, cagA, iceA, oipA and babA genotypes of the Helicobacter pylori strains isolated from raw milk. *Antimicrob Res Infect Control* 2018;7(1):1-4.
 27. Dehkordi FS. Prevalence study of Bovine viral diarrhea virus by evaluation of antigen capture ELISA and RT-PCR assay in Bovine, Ovine, Caprine, Buffalo and Camel aborted fetuses in Iran. *AMB Express* 2011;1(1):1-6.
 28. Abdolmaleki Z, Mashak Z, Dehkordi FS. Phenotypic and genotypic characterization of antibiotic resistance in the methicillin-resistant Staphylococcus aureus strains isolated from hospital cockroaches. *Antimicrob Res Infect Control* 2019;8(1):1-4.
 29. Dehkordi FS, Haghighi N, Momtaz H, Rafsanjani MS, Momeni M. Conventional vs real-time PCR for detection of bovine herpes virus type 1 in aborted bovine, buffalo and camel fetuses. *Bulgar J Vet Med* 2013;16(2):102-111.
 30. Dehkordi FS, Valizadeh Y, Birgani TA, Dehkordi KG. Prevalence study of Brucella melitensis and Brucella abortus in cow's milk using dot enzyme linked immuno sorbent assay and duplex polymerase chain reaction. *J Pure Appl Microbiol* 2014;8(2):1065-9.
 31. Halaji M, Farahani A, Ranjbar R, Heiat M, Dehkordi FS. Emerging coronaviruses: first SARS, second MERS and third SARS-CoV-2: epidemiological updates of COVID-19. *Infez Med* 2020;28(suppl 1):6-17.



www.ramib.org

Junta Directiva de la Reial Acadèmia de Medicina de les Illes Balears

President Macià Tomàs Salvà
Vicepresident Àngel Arturo López González
Secretari General Antonio Cañellas Trobat
Vicesecretari Sebastian Crespí Rotger
Tresorer Joan Besalduch Vidal
Bibliotecària Antonia Barceló Bennassar

Acadèmics d'honor

2003 - Excm. Sr. Santiago Grisolia García, Premi Príncep d'Astúries
2007 - Excm. Sr. Ciril Rozman, Premi Jaime I

Acadèmics numeraris

M. I. Sra. Juana M. Román Piñana
M. I. Sr. Josep Tomàs Monserrat
M. I. Sr. Bartomeu Anguera Sansó
M. I. Sr. Bartomeu Nadal Moncadas
M. I. Sr. Alfonso Ballesteros Fernández
M. I. Sr. Ferran Tolosa i Cabaní
Excm. Sr. Macià Tomàs Salvà
M. I. Sra. Joana M. Sureda Trujillo
M. I. Sr. Joan Buades Reinés
M. I. Sr. José L. Olea Vallejo
M. I. Sr. Pere Riutord Sbert
M. I. Sr. Joan Besalduch Vidal
M. I. Sr. Fèlix Grases Freixedas
M. I. Sr. Antoni Cañellas Trobat
M. I. Sr. Josep Francesc Forteza Albertí
M. I. Sr. Jordi Ibáñez Juvé
M. I. Sr. Joan March Noguera
M. I. Sr. Àngel Arturo López González
M. I. Sra. Pilar Roca Salom
M. I. Sr. Javier Cortés Bordoy
M. I. Sr. Lluís Masmiquel Comas
M. I. Sr. Sebastià Crespí Rotger
M. I. Sra. Antònia Barceló Bennassar
M. I. Sr. Javier Garau Alemany
M. I. Sr. Jordi Reina Prieto
M. I. Sr. Joan M. Benejam Gual
M. I. Sr. Claudio Rubén Mirasso Santos

Acadèmics supernumeraris

M.I. Sr. Àlvar Agustí García-Navarro
M.I. Sra. Marta Emma Couce Matovelle

Acadèmics emèrits

M.I. Sr. Arnau Casellas Bernat



www.ramib.org

Protectors de la Reial Acadèmia

Banca March
Conselleria de Presidència
ASISA
Conselleria de Salut
Col·legi Oficial de Metges de les Illes Balears
Fundació Patronat Científic del Col·legi de Metges de les Illes Balears

Benefactors de la Reial Acadèmia

Salut i Força

Patrocinadors de la Reial Acadèmia

Clínica Rotger
Metges Rosselló
Grup Hospitalari Quirónsalud
Col·legi Oficial d'Infermeria de les Illes Balears
Associació Espanyola contra el Càncer a les Illes Balears
Col·legi Oficial de Farmacèutics de Balears
Escola Universitària ADEMA

MEDICINA · BALEAR

PUBLICACIÓ DE LA REIAL ACADEMIA DE MEDICINA DE LES ILLES BALEARS

www.medicinabaleaer.org