

ACADEMIC JOURNAL OF HEALTH SCIENCES

MEDICINA BALEAR

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Assessment of cardiometabolic status in 5.994 german mechanics

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influence of age, sex, social class and tobacco consumption

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in students of the Higher Technological Institute Sucre

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Intramammary lymph nodes, clinical characteristics and prevalence

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Sociodemographic variables influencing the prevalence of insulin resistance in the italian population

Relationship between blood pressure levels and body mass index values in 41,093 ukrainians people

The epidemiological and preventive situation in Spain of causal human papilloma virus cancers

The role of environmental factors and molecular genetics diagnosis in treatment of breast cancer in Iran, Qom (2019-2020)

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Prevalence of overweight and obesity in spanish working population along the Covid-19 pandemic.
Adiposity indicators and related variables

Effect of a Coriolus versicolor-based vaginal gel on cervical epithelialization and vaginal microbiota
in HPV-positive women: EPICERVIX pilot study

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The study of gestational diabetes as a silent disease

The headquarters of the Royal Academy of Medicine of the Balearic Islands (1830-2022)

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Learning disability; the tip of the iceberg

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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).



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Índice
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EDITORIAL

Clinical ultrasound in Primary Care

José Ignacio Ramírez Manent

9-10

ORIGINALS ARTICLES

Relationship between different scales related to cardiovascular risk and Finrisk test values in workers 11-15

ZeinYarianne Inalvis Rivero Ledo, Fátima Zerquera, Milena Ayón, Yosmira Brito Domínguez, Flavio J. Leguen, Gloriana Madrigal Loria, Yesenia Aguilar Ortega

Assessment of cardiometabolic status in 5.994 german mechanics 16-21

María Teresa Bernal, Luis Alberto Ramos, Anke Jacobi, Waltraud Gutmann, Samantha Josephine Klein Reches, Pablo Díaz Cerezuola

Relationship between healthy habits and sociodemographic variables in the values of different atherogenic indices 22-27

Pere Riutord Sbert, Bartomeu Riutord, Neus Riutord Fe, Sebastiana Arroyo Bote, Ángel Arturo López González, José Ignacio Ramírez Manent

Classification of blood pressure with JNC-7 criteria in spanish working population: influence of age, sex, social class and tobacco consumption 28-32

Héctor Eugercios Escribano, Marta Pérez-Lerna, María José Recatalá Gimeno, Javier Lucas Tosoratto, Bárbara Carriedo, Ángel Arturo López González

Determination of different scales of cardiovascular risk in 1.979 spanish informatics workers 33-41

Caridad Sedeño Argilagos, Hilda María González San Miguel, Gregorio Martínez-Sánchez, Gema Pérez-Davison, María del Mar Rigo Vives

Variables that influence the degree of control in dyslipidemic patients under hypolipidemic treatment 42-48

Miguel C. Aguiló Juanola, Ivett Naviza Arroyo Buelvas, Jorge Elias Ayala Buelvas, Katrina Riera Routon

Risk factors associated with the use and consumption of drugs in students of the Higher Technological Institute Sucre 49-59

Darwin Raúl Noroña Salcedo, Vladimir Vega Falcón

Results of arthroscopic debridement in patients with osteoarthritis of the knee 60-64

Mohammad Reza Sobhan, Seyyed Mohammad Jalil Abrisham, Masoud Vaseghi, Zahra Sahraneshin Samani, Mohammad Shafiee

Evaluation of King's variceal prediction score as a marker of portal hypertension in children with chronic liver diseases 65-72

Maryam Niknam, Seyed Mohsen Dehghani, Maryam Ataollahi, Ahmadrza Sadeghi

Investigating the effect of ORS with probiotics, zinc and vitamin A on children's diarrhea: a randomized clinical trial 73-79

Abbas Taghavi Ardakani, Rahmat Yahyapour, Masoud Amiri, Mohammad Reza Sharif, Davood Khairkhan, Mohsen Taghizadeh, Hamid Reza Gilasi

Drug use evaluation of oral hypoglycemics in diabetic patients in a tertiary care hospital, India 80-83

Seyedsahand Gheybi, Peter Kandel

Designing a competency model for managers of health care networks in Iran 84-91

Afshin Poormenati, Somayeh Hesam, Shaghayegh Vahdat, Iravan Masoudi Asl

Intramammary lymph nodes, clinical characteristics and prevalence 92-95

Laleh Ebrahimipour, Masoumeh Gity

Preparation and implementation of standard therapeutic guidelines for poisoning cases in a tertiary care hospital, Mysuru, India 96-100

Yasaman Jafamiay Jahromi, Nisar Ahmed, Pouyan Haghpanah, Sadaf Hojjati

Anthropometric profile in 1.350 well being and beauty professionals 101-106

Cristina Núñez Fernández, Nildiana Cedeño Caballero, Martín Delgado, Clara Buitrago, Raquel Fernández de Castro

Sociodemographic variables influencing the prevalence of insulin resistance in the italian population 107-112

Sergio Rizzo

Relationship between blood pressure levels and body mass index values in 41,093 ukrainians people 113-117

Natalia Tretiak, Petro Tretiak Kravchuk, Oleksandr Sanyk, Valeri Loburets, Bárbara Altisench Jané, José Ignacio Ramírez Manent

The epidemiological and preventive situation in Spain of causal human papilloma virus cancers 118-121

Javier Cortés, Ana Forteza, Daniel Andía

The role of environmental factors and molecular genetics diagnosis in treatment of breast cancer in Iran, Qom (2019-2020) 122-126

Faegheh Miryousefiata, Sareh Sangy

Relationship between different scales related to cardiovascular risk and Finrisk test values in workers 127-131

Yarianne Inalvis Rivero Ledo, Fátima Zerquera, Milena Ayón, Yosmira Brito Domínguez, Flavio J. Leguen, Gloriana Madrigal Loria, Yesenia Aguilar Ortega

Prevalence of overweight and obesity in spanish working population along the Covid-19 pandemic. Adiposity indicators and related variable 132-138

M^l Teófila Vicente-Herrero, M^l Victoria Ramírez-Iñiguez de la Torre, Luisa Capdevila García, Angélica Partida-Hanon, Luis Reinoso-Barbero, Ángel Arturo López González

Effect of a *Corioli* *versicolor*-based vaginal gel on cervical epithelialization and vaginal microbiota in HPV-positive women: EPICERVIX pilot study 139-145

Silvia González, Luis Serrano, Javier Cortés, Teresa Vezza, José Garrido-Mesa, Francesca Algieri, Rocío Morón, María Elena Rodríguez Cabezas,

Julio Gálvez, Alba Rodríguez Nogales

Evaluation the effectiveness of the cognitive rehabilitation therapy model for improvement executive functions in high- functions autistic children, by using neuroimaging, neuropsychological and molecular genetics technique 146-152

Fazlollah Shahraki, Peyman Hassani-Abharian

The study of gestational diabetes as a silent disease 153-161

Fateme Momenzadeh, Fahimeh Khoshnejad

SPECIAL ARTICLES

The headquarters of the Royal Academy of Medicine of the Balearic Islands (1830-2022) 162-167

José Tomás Monserrat

Ozone therapy, scientific support and use as complementary therapy in COVID-19 168-172

Gregorio Martínez-Sánchez

CASE REPORT

Orbital lymphoma. Presentation of a small series 173-176

Tamara de las Mercedes Galbán Lueje, Lillian Gloria León Veitia, Agustín Arocha García, Neyda Alina González Pérez, Jesús Yasoda Endo Milan

Learning disability; the tip of the iceberg 177-179

Unai Díaz-Moreno Elorz, Monserrat Pons Rodríguez, Jorge Roldán Busto, Fernando Ferragut Agut, María Ángeles Ruiz Gómez



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EDITORIAL

Ecografía clínica en Atención Primaria

José Ignacio Ramírez Manent

9-10

ORIGINALS ARTICLES

Relación entre diferentes escalas relacionadas con el riesgo cardiovascular y valores del test de Finrisk en trabajadores

ZeinYarianne Inalvis Rivero Ledo, Fátima Zerquera, Milena Ayón, Yosmira Brito Domínguez, Flavio J. Leguen, Gloriana Madrigal Loria, Yesenia Aguiar Ortega

11-15

Evaluación del estado cardiometabólico en 5.994 mecánicos alemanes

María Teresa Bernal, Luis Alberto Ramos, Anke Jacobi, Waltraud Gutmann, Samantha Josephine Klein Reches, Pablo Díaz Cerezuela

16-21

Relación entre hábitos saludables y variables sociodemográficas en los valores de diferentes índices aterogénicos

Pere Riutord Sbert, Bartomeu Riutord, Neus Riutord Fe, Sebastiana Arroyo Bote, Ángel Arturo López González, José Ignacio Ramírez Manent

22-27

Clasificación de la presión arterial con criterios JNC-7 en la población laboral española: influencia de la edad, el sexo, la clase social y el consumo de tabaco

Héctor Eugercios Escribano, Marta Pérez-Lema, María José Recatalá Gimeno, Javier Lucas Tosoratto, Bárbara Carriedo, Ángel Arturo López González

28-32

Determinación de diferentes escalas de riesgo cardiovascular en 1.979 informáticos españoles

Caridad Sedeño Argilagos, Hilda María González San Miguel, Gregorio Martínez-Sánchez, Gema Pérez-Davison, María del Mar Rigo Vives

33-41

Variables que influyen en el grado de control de pacientes dislipémicos en tratamiento hipolipemiente

Miguel C. Aguiló Juanola, Ivett Naviza Arroyo Buelvas, Jorge Elias Ayala Buelvas, Katrina Riera Routon

42-48

Factores de riesgo asociados al uso y consumo de drogas en estudiantes del Instituto Superior Tecnológico Sucre

Darwin Raúl Noroña Salcedo, Vladimir Vega Falcón

49-59

Resultados del desbridamiento artroscópico en pacientes con osteoartritis de la rodilla

Mohammad Reza Sobhan, Seyyed Mohammad Jalil Abrisham, Masoud Vaseghi, Zahra Sahraneshin Samani, Mohammad Shafiee

60-64

Evaluación de la puntuación de predicción de varices de King como marcador de hipertensión portal en niños con enfermedades hepáticas crónicas

Maryam Niknam, Seyed Mohsen Dehghani, Maryam Ataollahi, Ahmadsreza Sadeghi

65-72

Investigación del efecto de las SRO con probióticos, zinc y vitamina A en la diarrea infantil: un ensayo clínico aleatorizado

Abbas Taghavi Ardakani, Rahmat Yahyapour, Masoud Amiri, Mohammad Reza Sharif, Davood Khairkhal, Mohsen Taghizadeh, Hamid Reza Gilasi

73-79

Evaluación del uso de fármacos de hipoglucemiantes orales en pacientes diabéticos en un hospital de atención terciaria, India

Seyedsahand Gheybi, Peter Kandel

80-83

Diseño de un modelo de competencias para gestores de redes sanitarias en Irán

Afshin Poormenati, Somayeh Hesam, Shaghayegh Vahdat, Iravan Masoudi Asl

84-91

Ganglios linfáticos intramamarios, características clínicas y prevalencia

Laleh Ebrahimpour, Masoumeh Gity

92-95

Preparación e implementación de pautas terapéuticas estándar para casos de intoxicación en un hospital de atención terciaria, Mysuru, India

Yasaman Jafamiy Jahromi, Nisar Ahmed, Pouyan Haghpahan, Sadaf Hojjati

96-100

Perfil antropométrico en 1.350 profesionales del bienestar y la belleza

Cristina Núñez Fernández, Nilciana Cedeño Caballero, Martín Delgado, Clara Buitrago, Raquel Fernández de Castro

101-106

Variables sociodemográficas que influyen en la prevalencia de resistencia a la insulina en población italiana

Sergio Rizzo

107-112

Relación entre los niveles de presión arterial y los valores del índice de masa corporal en ucranianos

Natalia Tretiak, Petro Tretiak Kravchuk, Oleksandr Sanyk, Valeri Loburets, Bárbara Altisench Jané, José Ignacio Ramírez Manent

113-117

Situación epidemiológica y preventiva en España de los cánceres causados por el virus del papiloma humano

Javier Cortés, Ana Forteza, Daniel Andía

118-121

El papel de los factores ambientales y el diagnóstico de genética molecular en el tratamiento del cáncer de mama en Irán, Qom (2019-2020)

Faegheh Miryousefiata, Sareh Sangy

122-126

Relación entre diferentes escalas relacionadas con el riesgo cardiovascular y valores del test de Finrisk en trabajadores

Yarianne Inalvis Rivero Ledo, Fátima Zerquera, Milena Ayón, Yosmira Brito Domínguez, Flavio J. Leguen, Gloriana Madrigal Loria, Yesenia Aguiar Ortega

127-131

Prevalencia de sobrepeso y obesidad en población laboral española durante la pandemia Covid-19. Indicadores de adiposidad y variables relacionadas

M^a Teófila Vicente-Herrero, M^a Victoria Ramírez-Iñiguez de la Torre, Luisa Capdevila García, Angélica Partida-Hanon, Luis Reinoso-Barbero, Ángel Arturo López González

132-138

Eficacia de un gel vaginal basado en Coriolus versicolor sobre la epitelización cervical y la microbiota vaginal en mujeres positivas al VPH: Estudio piloto EPICERVIX

Silvia González, Luis Serrano, Javier Cortés, Teresa Vezza, José Garrido-Mesa, Francesca Algieri, Rocío Morón, María Elena Rodríguez Cabezas, Julio Gálvez, Alba Rodríguez Nogales

139-145

Evaluación de la eficacia del modelo de terapia de rehabilitación cognitiva para la mejora de las funciones ejecutivas en niños autistas de altas funciones, mediante el uso de técnicas de neuroimagen, neuropsicológicas y de genética molecular

Fazlollah Shahrahi, Peyman Hassani-Abhari

146-152

El estudio de la diabetes gestacional como enfermedad silenciosa

Fateme Momenzadeh, Fahimeh Khoshnejad

153-161

SPECIAL ARTICLES

Las sedes de la Real Academia de Medicina de las Islas Baleares (1830-2022)

José Tomás Monserrat

162-167

Ozonoterapia, respaldo científico y uso como terapia complementaria en la COVID-19

Gregorio Martínez-Sánchez

168-172

CASE REPORT

Linfoma de orbita. Presentación de una pequeña serie

Tamara de las Mercedes Galbán Lueje, Lillian Gloria León Veitia, Agustín Arocha García, Neyda Alina González Pérez, Jesús Yasoda Endo Milan

173-176

Dificultad en el aprendizaje; la punta del iceberg

Unai Díaz-Moreno Elorz, Monserrat Pons Rodríguez, Jorge Roldán Busto, Fernando Ferragut Agut, María Ángeles Ruiz Gómez

177-179

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Ecografía clínica en Atención Primaria

Clinical ultrasound in Primary Care

Dr. José Ignacio Ramírez Manent

Médico especialista en Medicina Familiar y comunitaria. Centro de Salud de Calvià, Gerencia de Atención Primaria de Mallorca

En el año 2018 el Ibsalut y la Dirección General del Servicio de Salud de las Islas Baleares apostaron por la implantación de la ecografía clínica en todos los Centros de Atención Primaria de las Islas Baleares. Con este fin se adquirieron 59 ecógrafos con los que se dotó a los Centros de Salud de las Islas Baleares y se inició al mismo tiempo la formación en ecografía a sus médicos de familia. Esta adquisición respondía a la apuesta del Servicio de Salud por incrementar la resolución en los equipos de atención primaria, donde la ecografía clínica constituye una herramienta fundamental para alcanzar dicha meta.

Durante estos 4 años la ecografía clínica se ha desarrollado y acrecentado en todos los Centros de Salud de Baleares, con la formación paralela de más de 200 profesionales. En este período todos los MIR de la especialidad de medicina de familia han recibido un curso de ecografía abdominal básica, organizado por la "Unitat Docent Multiprofessional d'Atenció familiar i Comunitària de Mallorca", que se considera como una habilidad fundamental e indispensable del médico de familia.

Hasta hace pocos años, la ecografía ha sido principalmente una prueba de imagen confinada al servicio de radiología y realizada por especialistas en radiodiagnóstico. En los últimos años el ultrasonido se ha incorporado por el médico de familia y se ha trasladado a la cabecera de la cama del paciente («point of care ultrasound»). Durante décadas, el estetoscopio ha sido el símbolo de la profesión médica. Al principio los médicos solo disponían de unos pocos instrumentos para realizar su labor, entre ellos, el estetoscopio sigue siendo una herramienta importante en la exploración actual del paciente. Hoy en día, la ecografía y el estetoscopio tienen muchas similitudes al ser operador dependientes y necesitar de práctica y experiencia para realizar la técnica de forma adecuada. Cuando comparamos la auscultación con la ecografía, es evidente que esta última técnica proporciona mejores resultados en manos expertas. Varios estudios han demostrado que los médicos de familia formados en ecografía tienen la misma precisión y eficiencia que los exámenes realizados por radiólogos. Lo que hace que el ultrasonido se convierta en el estetoscopio del siglo XXI.

En estos momentos la ecografía es en muchos casos la primera prueba complementaria de diagnóstico por imagen que se realiza en medicina. Su carencia de

radiación nuclear, bajo coste y efectividad la convierten en una técnica de extremada utilidad en atención primaria. La ecografía realizada por médicos de familia formados mejora el estudio y evaluación de enfermedades frecuentes, y ajusta las derivaciones al segundo nivel asistencial además de aumentar la capacidad resolutive del médico de Atención Primaria.

La ecografía realizada por el clínico es distinta de la que se efectúa en los servicios de radiodiagnóstico. Se puede definir la ecografía clínica como la exploración ecográfica que realiza el médico que atiende en ese momento al paciente. Es decir, por el facultativo que evalúa, historia y explora al paciente y es responsable del diagnóstico y tratamiento del enfermo. Se busca que los resultados ecográficos tengan una relación con los signos y los síntomas que presenta el paciente explorado en ese instante, lo que posibilita al clínico disminuir la incertidumbre y ayudar a la toma de decisiones.

La ecografía aporta una serie de ventajas sobre otras técnicas de diagnóstico, como es su rápido aprendizaje y su posibilidad de realizarla donde se encuentre el paciente (pie de cama) sin pérdida de resolución de los equipos de ecografía. Hoy en día existen sondas de ecografía adaptables a dispositivos como tablets o móviles inteligentes.

Por otro lado, la ecografía en atención primaria constituye un nuevo elemento de motivación para el médico de familia, que se encuentra con una técnica novedosa que le asiste en su diagnóstico, favorece su desarrollo profesional y le hace sentirse más valorado por sus pacientes. Resulta muy útil también en medicina rural, donde el médico de familia aislado de las grandes ciudades puede presentar una duda diagnóstica y ayudado de la telemedicina puede enviar las imágenes obtenidas para ser valoradas por especialistas.

Sin embargo, aunque la ecografía clínica es una herramienta muy útil para completar el diagnóstico del médico de familia, no tiene sentido en el cribado de poblaciones asintomáticas ni en el cribado individual multiórganos como se realiza en los servicios de radiodiagnóstico. En esta coyuntura es necesario establecer las indicaciones de la ecografía clínica en atención primaria por su importancia clínica, eficiencia y en las que su utilización modifica la conducta del clínico adecuando en consecuencia sus decisiones.

Indicaciones de la ecografía clínica en atención primaria

Ecografía Hepática, Biliar, páncreas y bazo	Síndrome constitucional, diagnóstico de colelitiasis, colecistitis y dilatación de la vía biliar Seguimiento de lesiones benignas (quistes, hemangiomas...), hepatomegalia, sospecha de hepatopatía, ictericia, alteraciones de la bioquímica hepática, esplenomegalia. Sospecha de pancreatitis.
Ecografía de los grandes vasos abdominales	Masa abdominal pulsátil, Diagnóstico de Aneurisma de Aorta abdominal, Hipertensión portal, Síndrome constitucional con o sin masa epigástrica.
Ecografía urológica	Valoración de hidronefrosis, dolor cólico en fosa renal con o sin fiebre, Hematuria, sospecha de tumores de vejiga e infecciones de tracto urinario inferior en el varón adulto, valoración de la próstata y vesículas seminales, riñón transplantado, obstrucción del aparato urinario.
Ecografía del cuello	Estudio y valoración del tiroides, bocio, nódulos tiroideos, adenopatías, glándulas salivales.
Ecografía vascular	Sospecha de TVP en la extremidad inferior, estudio de carótidas, placas de ateroma y grado de estenosis. GIM carotídeo, velocidad de flujo.
Ecografía escrotal	Dolor testicular agudo o crónico, masa testicular, criptorquidia, aumento de tamaño de las bolsas escrotales, escroto agudo, evaluación de traumatismo escrotal, detección de varicocele.
Ecografía Musculoesquelética	Lesiones musculares, lesiones tendinosas, lesiones de los ligamentos, lesiones óseas, lesiones del tejido subcutáneo, lesiones articulares, lesiones de nervios periféricos.
Ecografía de piel y partes blandas	Caracterización de masa palpable superficial, Inflamación postraumática o postquirúrgica, masas o hernias de pared abdominal, estudio de adenopatías, abscesos, lipomas.
Ecografía en situaciones de urgencias	Valoración de traumatizado toracoabdominal. Detección de líquido libre abdominal. Valoración de la volemia. Pérdida de sensación de los movimientos fetales. Descartar rotura embarazo ectópico. Valorar hemorragia vaginal en gestante. Sangrado uterino disfuncional.
Ecocardiografía básica	Detección de derrame pericárdico y taponamiento cardíaco, cribado de valvulopatías, estudio del síncope, hipotensión, shock, valoración del paciente con insuficiencia cardíaca, valoración de la función sistólica y diastólica del VI, valoración de la hipertrofia de las cavidades cardíacas, evaluación del dolor pleuropericárdico, elevación de la presión venosa central.
Ecografía pulmonar	Derrame pleural, edema de pulmón, consolidación pulmonar, neumotórax, atelectasia.
Procedimientos ecoguiados	Canalización de vía venosa periférica, drenaje de articulaciones, paracentesis, infiltraciones articulares y peritendinosas, drenaje de hematomas, seromas o cavidades.

En conclusión podemos afirmar que la ecografía clínica realizada por el médico de familia, ayuda a reducir el diagnóstico diferencial que se instaura tras una correcta anamnesis y exploración del paciente, disminuye la incertidumbre y mejora el manejo del paciente proporcionándole un tratamiento más adecuado. Se trata de una técnica inocua, fácilmente repetible y que aumenta la satisfacción tanto del médico como del paciente.

Sin embargo, debemos reseñar que el uso indiscriminado de la ecografía sin una sospecha diagnóstica o una finalidad determinada (traumatismo toracoabdominal) puede incrementar la incertidumbre del médico de familia. Así pues, la exploración ecográfica debe utilizarse únicamente para responder a las preguntas clínicas que nos planteemos.

Bibliografía

- Andersen C.A, Holden S, Vela J, Rathleff M.S, Jensen M.B. Point-of-Care Ultrasound in General Practice: A Systematic Review. *Ann Fam Med*. 2019 Jan;17(1):61-69. doi: 10.1370/afm.2330.
- Touhami D, Merlo C, Hohmann J, Essig S. The use of ultrasound in primary care: longitudinal billing and cross-sectional survey study in Switzerland. *BMC Fam Pract*. 2020 Jul 1;21(1):127. doi: 10.1186/s12875-020-01209-7.4
- Conangla L, Domingo M, Lupón J, Wilke A, Juncà G, Tejedor X, Volpicelli G, Evangelista L, Pera G, Toran P, Mas A, Cediel G, Verdú JM, Bayes-Genis A. Lung Ultrasound for Heart Failure Diagnosis in Primary Care. *J Card Fail*. 2020 Oct;26(10):824-831. doi: 10.1016/j.cardfail.2020.04.019. Epub 2020 Jun 6.
- Pertierra-Galindo N, Salvo-Donangelo L, Salcedo-Joven MI, Román-Crespo B, Froilán Torres MC. Study of patient satisfaction when performing an ultrasound in Primary Care. *Semergen*. 2019 May-Jun;45(4):239-250. doi: 10.1016/j.semereg.2018.08.007. Epub 2018 Dec 19.
- Potter A, Pearce K, Hilmy N. The benefits of echocardiography in primary care. *Br J Gen Pract*. 2019 Jul;69(684):358-359. doi: 10.3399/bjgp19X704513.
- M M Malón Musgo. Ultrasound in clinical practice in Primary Care. *An Sist Sanit Navar*. 2018 Aug 29;41(2):157-160. doi: 10.23938/ASSN.0313.
- Esquerrà M, Roura Poch P, Masat Ticó T, Canal V, Maideu Mir J, Cruxent R. Abdominal ultrasound: a diagnostic tool within the reach of general practitioners. *Aten Primaria*. 2012 Oct;44(10):576-83. doi: 10.1016/j.aprim.2011.07.016.
- Kumar A, Kugler J, Jensen T. Evaluation of Trainee Competency with Point-of-Care Ultrasonography (POCUS): a Conceptual Framework and Review of Existing Assessments. *J Gen Intern Med*. 2019 Jun;34(6):1025-1031. doi: 10.1007/s11606-019-04945-4.
- Lindgaard K, Riisgaard L. Validation of ultrasound examinations performed by general practitioners. *Scand J Prim Health Care*. 2017 Sep;35(3):256-261. doi: 10.1080/02813432.2017.1358437.
- Andersen CA, Brodersen J, Rudbæk TR, Jensen MB. Patients' experiences of the use of point-of-care ultrasound in general practice - a cross-sectional study. *BMC Fam Pract*. 2021 Jun 18;22(1):116. doi: 10.1186/s12875-021-01459-z.

ORIGINAL

Relationship between different scales related to cardiovascular risk and Finrisk test values in workers

Relación entre diferentes escalas relacionadas con el riesgo cardiovascular y valores del test de Finrisk en trabajadores

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Abstract

Introduction: Cardiovascular diseases are the main cause of death in developed countries and one of the risk factors most closely related to them is diabetes. The aim is to study the relationship between the values of a test that determines the risk of suffering diabetes mellitus and the values of different scales related to cardiovascular risk.

Methods: Cross-sectional study in 59,042 workers in which the values of the Finrisk test were related to the values of some cardiovascular risk scales such as the body shape index, conicity index, visceral adiposity index, Cholindex and hypertriglyceridemic waist among others.

Results: All the scales included in this study increase their values in parallel to the increase in the values of the Finrisk test. This situation occurs in both women and men.

Conclusion: There is a relationship between the values of the Finrisk test and all the scales analyzed in this study.

Keywords: Finrisk test, diabetes mellitus, cardiovascular diseases.

Resumen

Introducción: Las enfermedades cardiovasculares son la principal causa de muerte en los países desarrollados y uno de los factores de riesgo que más se relaciona con ellas es la diabetes. El objetivo es estudiar la relación entre los valores de un test que determina el riesgo de sufrir diabetes mellitus y los valores de diferentes escalas relacionadas con el riesgo cardiovascular.

Material y métodos: Estudio transversal en 59,042 trabajadores en los que se relacionan los valores del test de Finrisk con los valores de algunas escalas de riesgo cardiovascular como el índice de forma del cuerpo, índice de conicidad, índice de adiposidad visceral, Cholindex y cintura hipertrigliceridémica entre otros.

Resultados: Todas las escalas incluidas en este estudio van incrementando su valor paralelamente al incremento de los valores del test de Finrisk. Esta situación se produce tanto en las mujeres como en los hombres.

Conclusión: Existe una relación entre los valores del test de Finrisk y todas las escalas analizadas en este trabajo.

Palabras clave: Test Finrisk, diabetes mellitus, enfermedades cardiovasculares.

Introduction

Cardiovascular diseases (CVD) cause great morbidity and mortality both in the developed and undeveloped countries. In recent years 80 percent of deaths from CVD have occurred in countries with medium or low income, and the number is growing¹. The cardiovascular risk (CVR) is defined as the likelihood of an event in a given period, usually 10 years, for its determination generally scales are based on cohort studies are used. Determining the CVR it is based on clinical guidelines that address cardiovascular prevention.

In the occurrence of CVD is influenced by different factors such as tobacco consumption, obesity, dyslipidemia and diabetes. The risk of diabetes can be determined with different scales among which we highlight the FINRISK (FINnish Diabetes Risk Score) questionnaire for being perhaps the most widely used. FINRISK has been successfully implemented as a practical screening instrument to assess diabetes risk and to detect undiagnosed type 2 diabetes in European populations²⁻⁴. However it has also become evident that it is not universally applicable among all ethnic groups and populations^{5,6}.

There are many indexes that help predict CVD from classic Body Mass Index (BMI), waist circumference and waist to height ratio to the most recent Body Adiposity Index (BAI)^{7,8}. There are other indices that could perhaps be useful in predicting these CVD among which are the Body Shape Index (ABSI) at some authors they have linked to an increased risk of cardiovascular mortality⁹, the Visceral Adiposity Index (VAI) which has been linked with visceral fat levels¹⁰, type 2 diabetes¹¹ and coronary artery disease¹², Cholinex which has been linked with coronary artery disease¹³, the Conicity Index (CI) which has been linked with high coronary risk¹⁴ and Hypertriglyceridemic waist (HTGW) has been associated with type 2 diabetes¹⁵, coronary artery disease¹⁶ and even acute myocardial infarction¹⁷.

An analysis of the scientific literature shows that previous indexes have not been used too much in cardiovascular prevention but perhaps can provide valuable information on the assessment of CVR.

For all these reasons, and trying to improve cardiovascular prevention, this study presents the main objective is to determine what relationship exists between FINRISK test values and the values of these indices.

Materials and methods

Subjects and Study Protocol

A cross-sectional study with adult workers (ages, 20-69 years) was performed. All subjects were belong to different productive sectors. Participants in the

study were systematic selected during their work health periodic examination between January 2018 and December 2019. Every day each worker was assigned a number and half of the examined workers were randomly selected using a random number table. Thus, from a total population of 130487 workers, 65200 of them were invited to participate in the study. 4402 (6.8%) refused to participate and 1756 (2.8%) they are excluded to be diabetic and not being able to perform the FINRISK test, being the final number of participants 59042 (90.4%), with 25510 women (43.2%) and 33532 men (56.8%). The mean of age of participants in the study was 39.70 years (SD±10.25). All participants were informed of the purpose of this study before they provided written informed consent to participate. Following the current legislation, members of the Health and Safety Committees were informed as well. The study protocol was in accordance with the Declaration of Helsinki and was approved by the relevant research ethics committee. After acceptance, a complete medical history, including family and personal history and FINRISK questionnaire, was recorded. The following inclusion criteria were considered: age between 18 and 70 (working age population), no diabetic, agreement to participate in the study and to be gainfully employed. Subjects who did not meet any of the inclusion criteria and those who refused to participate were excluded from the study.

Measurements and Calculations

All anthropometric measurements were made in the morning, after an overnight fast, at the same time (9 a.m.), and according to the recommendations of the International Standards for Anthropometric Assessment (ISAK)¹⁸. Furthermore, all measurements were performed by well trained technicians or researchers to minimize coefficients of variation. Each measurement was made three times and the average value was calculated. Weight and height were determined according to recommended techniques mentioned above. Body weight was measured to the nearest 0.1 kg using an electronic scale (Seca 700 scale, Secagmbh, Hamburg). Height was measured to the nearest 0.5 cm using a stadiometer (Seca 220 (CM) Telescopic Height Rod for Column Scales, Secagmbh, Hamburg). BMI was calculated as weight (kg) divided by height (m) squared (kg/m²). Criteria to define overweight were the ones of the World Health Organization (WHO)¹⁹ which considers obesity when BMI \geq 30 kg/m². Abdominal waist was measured using a flexible steel tape (Lufkin Executive Thinline W 606). The plane of the tape was perpendicular to the long axis of the body and parallel to the floor. Waist circumference was measured at the level of the umbilicus and superior iliac crest. The measurement was made at the end of a normal expiration while the subject stood upright, with feet together and arms hanging freely at the sides. Waist circumference (WC) was measured using a tapeline at the level midway between the lateral lower rib margin and iliac crest. Waist-to-height ratio (WtHR) was calculated by dividing WC by height in cm.

Venous blood samples were taken from the antecubital vein with suitable vacutainers without anticoagulant to obtain serum. Blood samples were taken following a 12 h overnight fast. Participants were seated at rest for at least 15 minutes before blood samples were taken. Serum was obtained after centrifugation (15 min, 1,000 g, 4°C) of blood samples. Serum was stored at -20°C and analysis were performed within 3 days. Concentrations of glucose, cholesterol and triglycerides were measured in serum by standard procedures used in clinical biochemistry laboratory using a clinical system Beckman Coulter SYNCHRON CX@9 PRO (Beckman Coulter, Brea, CA, USA).

Blood pressure was determined after a resting period of 10 minutes in the supine position using an automatic and calibrated sphygmomanometer OMRON M3 (OMRON Healthcare Europe, Spain). As indicated for the anthropometrical measures, blood pressure was measured three times with a one-minute gap between each measurement and an average value was calculated. FINRISK questionnaire value 8 items: age, BMI, waist circumference, physical activity, dietary consumption of fruits, vegetables, and berries, Use of antihypertensive medication, previously measured high blood glucose and family history of diabetes. The maximum achievable score is 26. Less than 7 points is considered low risk, 7-11 point slightly elevated risk, 11-14 points moderate risk, 15-20 points high risk and 21-26 points very high risk.

Real Body shape index (ABSI)⁹ was calculated using the equation:

$$- \text{Waist circumference (cm)} / \text{BMI}^{2/3} \text{ weight}^{1/2} \text{ (kg)}$$

Theoretical ABSI is set based on sex and age. The ratio between real and theoretical ABSI is called ABSI relative risk (ABSI RR). ABSI RR <1 is considered abnormal.

Conicity index(CI)¹⁴ was calculated using the equation:

$$- \text{Waist circumference (m)} / (0,109 \sqrt{\text{weight (kg)/height (m)}})$$

The cut-off to consider high CI were 1.18 for women and 1.25 for men.

Visceral Adiposity Index (VAI)²⁰ was calculated using the equations:

$$\text{Women (Waist circumference } / (39.68 + (1.89 \text{ BMI})) \times (\text{triglycerides} / 1.03) \times (1.31 / \text{HDL-C})$$

$$\text{Men (Waist circumference } / (36.58 + (1.89 \text{ BMI})) \times (\text{triglycerides} / 0.81) \times (1.52 / \text{HDL-C})$$

The cut-off to consider optimal VAI²¹ were < 30 years (≥ 2.52) 30-42 years (≥ 2.23) 43-51 years (≥ 1.92) 52-65 years (≥ 1.93) ≥ 66 years (≥ 2.00)

Cholindex¹³ was calculated using the equations:

$$- \text{LDLC-HDL-C (if triglycerides } < 400 \text{ mg/dl) or LDL-C-HDL-C+TG/5 (if triglycerides } \geq 400 \text{ mg/dl)}$$

The cut-off to consider high Cholindex was 80 mg/dl

We believe that there are Hypertriglyceridemic waist (HTGW)¹⁵ when:

- Waist circumference ≥ 88 cm in women and ≥ 102 cm in men and triglycerides ≥ 150 mg/dl.

Statistical Analyses

All the data were tested for their normal distribution (Kolmogorov-Smirnov test). Results are expressed as means and standard deviations (SD) and, when required, in percentages. Student t test for unpaired data was used to evaluate differences in anthropometric and biochemical characteristics between genders. Chi-square test was used for the difference of proportions. The existence of significant bivariate correlations between parameters such as ABSI, CI, VAI and Cholindex and FINRISK questionnaire was ascertained by determining Pearson or Spearman correlation coefficients. Statistical analysis was carried out using IBM SPSS Statistics 27.0 software (SPSS/IBM, Chicago, IL, USA). Significance was accepted at $p < 0.05$.

Results

Age and anthropometrical and clinical characteristics of the participants in the study as a whole and categorized by gender are shown in **table I**. Significant differences

Table I: Anthropometric, clinical and analytical characteristics of participants in the study.

Characteristics ¹	Women (n=25,510)	Men (n=33,532)	Total (n=59,042)	p-value
Age (years)	39.30 ± 10.10	40.01 ± 10.35	39.70 ± 10.25	<0.0001
Weight (kg)	161.32 ± 6.51	173.94 ± 7.04	168.49 ± 9.25	<0.0001
Height (cm)	64.87 ± 12.94	81.06 ± 13.75	74.06 ± 15.62	<0.0001
BMI (kg/m ²)	24.94 ± 4.84	26.78 ± 4.16	25.98 ± 4.56	<0.0001
Waist circumference (cm)	75.24 ± 9.66	88.37 ± 9.54	82.69 ± 11.59	<0.0001
WtHR	0.47 ± 0.06	0.51 ± 0.06	0.49 ± 0.06	<0.0001
Systolic BP (mmHg)	114.36 ± 14.94	124.91 ± 15.36	120.35 ± 16.06	<0.0001
Diastolic BP (mmHg)	70.29 ± 10.34	75.77 ± 10.74	73.40 ± 10.91	<0.0001
Total cholesterol (mg/dl)	192.78 ± 36.39	196.74 ± 38.63	195.03 ± 37.73	<0.0001
HDL-C (mg/dl)	55.03 ± 9.17	50.68 ± 7.53	52.56 ± 8.56	<0.0001
LDL-C (mg/dl)	120.39 ± 36.92	121.82 ± 37.18	121.20 ± 37.07	<0.0001
Triglycerides (mg/dl)	86.98 ± 43.77	123.24 ± 85.76	107.58 ± 72.99	<0.0001

BMI, Body mass index. WtHR, waist-to-height-ratio. Systolic BP, Systolic blood pressure. Diastolic BP, Diastolic blood pressure.

HDL-C, high-density lipoprotein cholesterol. LDL-C, low-density lipoprotein cholesterol.

1. data are expressed as means ± standard deviation. 2. Statistical significance was estimated by independent t-test

between men and women were found in all parameters analyzed with higher values of age, anthropometric characteristics (height, weight, body mass index, waist circumference, and waist to height ratio), systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides in men.

The mean values for the different indices according FINRISK questionnaire are shown in **table II**. The ABSI, VAI and Cholindex values in women are worsening in parallel with FINRISK test values, the same applies to men. The Conicity index values behave differently in men and women, in men also they are getting worse with increasing the value of the FINRISK test, however in women no clear relationship with the test was observed.

The prevalence of normal and altered values of the different indices according FINRISK questionnaire values are shown in **table III**. In women, the prevalence of high VAI, HTGW and high Cholindex is increasing in parallel with the increase in the value of the FINRISK test, in men we can observe the same with high VAI, HTGW, high CI and high Cholindex. ABSI altered shows no clear relationship with the FINRISK questionnaire values in women and men. In women this relationship was not seen with the high CI.

The Pearson correlations between parameters such as ABSI, CI, VAI and Cholindex and FINRISK questionnaire was -0.087 ABSI, 0.242 CI, 0.398 VAI and, 0.329 Cholindex, p-value <0.01.

Discussion

Tanto los valores medios como la prevalencia de valores elevados de todas las escalas analizadas en este estudio van aumentando a medida que lo hacen los valores del test de Finrisk, esta situación se puede apreciar tanto en las mujeres como en los hombres.

Sólo hemos encontrado un estudio que relacione los valores del test de Finrisk con escalas relacionadas con el riesgo cardiovascular como hemos hecho nosotros, aunque no empleando las mismas escalas. Este estudio realizado en población Española determinó los valores de diferentes parámetros antropométricos, clínicos (índice de masa corporal, perímetro de cintura, índice cintura altura, tensión arterial), analíticos (perfil lipídico y glucemia) y escalas relacionadas con riesgo cardiovascular (índices aterogénicos, síndrome metabólico, REGICOR, SCORE, edad del corazón y edad vascular) en más de 68000 personas y al igual que nosotros observó como todas las escalas aumentaban sus valores a medida que lo hacían los valores del test de Finrisk.

Entre las fortalezas de este estudio destacaremos el gran tamaño de la muestra que supera las 59000 personas y la variedad de escalas que se han tenido en cuenta.

Como limitación principal es que se ha realizado en población laboral por lo que se han excluido personas menores de 18 y mayores de 69 años lo que impide extrapolar los resultados a la población general.

Table II: Mean values of the different indices according FINRISK test.

		n ²	ABSI		CI		VAI		Cholindex	
			Mean (SD)	p value ¹	Mean (SD)	p value ¹	Mean (SD)	p value ¹	Mean (SD)	p value ¹
Women	Low	19,057	0.090 (0.080)	<0.0001	1.08 (0.08)	<0.0001	2.14 (1.09)	<0.0001	60.75 (40.78)	<0.0001
	Slightly raised	4,777	0.091 (0.012)		1.14 (0.14)		3.01 (1.94)		77.08 (41.26)	
	Moderate	1,017	0.088 (0.011)		1.12 (0.13)		3.33 (2.10)		84.26 (40.31)	
	High	643	0.088 (0.012)		1.15 (0.14)		4.15 (2.83)		88.81 (41.27)	
	Very high	16	0.084 (0.090)		1.11 (0.11)		6.06 (3.74)		99.66 (45.81)	
Men	Low	22,465	0.094 (0.070)	0.010	1.17 (0.07)	<0.0001	2.53 (1.63)	<0.0001	66.36 (39.56)	<0.0001
	Slightly raised	8,117	0.094 (0.090)		1.23 (0.11)		4.48 (3.96)		84.35 (43.70)	
	Moderate	1,856	0.093 (0.080)		1.24 (0.10)		5.17 (4.26)		89.74 (44.86)	
	High	960	0.093 (0.090)		1.25 (0.11)		6.28 (5.67)		90.37 (49.95)	
	Very high	134	0.092 (0.080)		1.25 (0.10)		7.14 (5.56)		99.63 (46.40)	

ABSI, Body shape index. CI, Conicity index.

1. Statistical significance was estimated by independent t-test 2. Number of participants in the study.

Table III: Cataloging the various indices according on the value of FINRISK test by sex.

	Low	Women Slightly raised	Moderate	High	Very high	Low	Men Slightly raised	Moderate	High	Very high	p value
High VAI	37.7	66.0	74.6	84.9	93.8	48.7	79.6	86.3	88.2	94.0	<0.0001
Normal VAI	62.3	34.0	25.4	15.1	6.3	51.3	20.4	13.7	11.8	6.0	
HTGW absence	99.9	90.1	85.1	71.2	43.8	98.3	76.6	67.6	57.2	44.0	<0.0001
HTGW presence	0.1	9.9	14.9	28.8	56.3	1.7	23.4	32.4	42.8	56.0	
ABSI Relative Risk altered	89.9	76.7	85.3	81.0	100.0	82.8	74.2	81.6	76.3	84.3	<0.0001
Normal ABSI Relative Risk	10.1	23.3	14.7	19.0	0.0	17.2	25.8	18.4	23.8	15.7	
High Conicity index	11.2	35.1	28.0	39.5	37.5	14.5	41.0	47.7	48.6	48.5	<0.0001
Normal Conicity index	88.8	64.9	72.0	60.5	62.5	85.5	59.0	52.3	51.4	51.5	
High Cholindex	31.0	46.8	51.4	60.2	75.0	34.9	51.9	57.5	54.4	68.7	<0.0001
Normal Cholindex	69.0	53.2	48.6	39.8	25.0	65.1	48.1	42.5	45.6	31.3	

VAI, Visceral Adiposity Index. HTGW, Hypertriglyceridemic waist. ABSI, Body Shape Index.

Conclusiones

Existe una relación directa entre los valores del test de Finrisk y los valores de todas las escalas relacionadas con el riesgo cardiovascular analizadas en este trabajo, de manera que a medida que se incrementan los valores del test lo hacen también los valores de todas las escalas.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Leeder S. A race against time: the challenge of cardiovascular disease in developing economies. Columbia University, New York. 2004.
2. Saaristo T, Peltonen M, Keinanen-Kiukkaanniemi S, Vanhala M, Saltevo J, Niskanen L, Oksa H, Korpi-Hyövälti E, Tuomilehto J. FIN-D2D Study Group. National type 2 diabetes prevention programme in Finland: FIN-D2D. *Int J Circumpolar Health*. 2007;66:101-12
3. Soriguer F, Valdes S, Tapia MJ, Esteve I, Ruiz de Adana MS, Almaraz MC, et al. Validation of the FINRISK (FINnish Diabetes Risk Score) for prediction of the risk of type 2 diabetes in a population of southern Spain. Pizarra Study. *Med Clin (Barc)* 2012;138:371-6.
4. Tankova T, Chakarova N, Atanassova I, Dakovska L. Evaluation of the Finnish Diabetes Risk Score as a screening tool for impaired fasting glucose, impaired glucose tolerance and undetected diabetes. *Diabetes Res Clin Pract*. 2011;92:46-52.
5. Makrilakis K, Liatis S, Grammatikou S, Perrea D, Stathi C, Tsiligris P, Katsilambros N. Validation of the Finnish diabetes risk score (FINRISK) questionnaire for screening for undiagnosed type 2 diabetes, dysglycaemia and the metabolic syndrome in Greece. *Diabetes Metab*. 2011;37:144-51
6. Hippisley-Cox J, Coupland C, Robson J, Sheikh A, Brindle P. Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. *BMJ*. 2009;338:b880.
7. Lopez AA, Cespedes ML, Vicente T, Tomas M, Bannasar-Veny M, Tauler P, et al. Body adiposity index utilization in a Spanish Mediterranean population: comparison with the body mass index. *PLoS One*. 2102;7(4):e35281
8. Bannasar-Veny M, Lopez-Gonzalez AA, Tauler P, Cespedes ML, Vicente-Herrero T, Yañez A, et al. Body adiposity index and cardiovascular health risk factors in Caucasians: a comparison with the body mass index. *PLoS One*. 2013;8(5):e63999.
9. Krakauer NY, Krakauer JC. A new Body Shape Index predicts mortality hazard independently of Body Mass Index. *Plos One*. 2012;7(7):e39504
10. Mohammadreza B, Farzad H, Davoud K, Fereidoun A. Prognostic significance of the Complex "Visceral Adiposity Index" vs simple anthropometric measures: Tehran lipid and glucose study. *CardiovascDiabetol*. 2012;11:20
11. Al-Daghri NM, Al-Attas OS, Wani K, Alnaamil AM, Sabico S, Al-Ajlan A, et al. Sensitivity of various indices in identifying cardiometabolic disease in Arab adults. *CardiovascDiabetol*. 2015;14:101
12. Patil VC, Parale GP, Kulkarni PM, Patil HV. Relation of anthropometric variables to coronary artery disease risk factors. *Indian Journal of Endocrinology and Metabolism*. 2011; 15(1):31-7.
13. Akpınar O, Bozkurt A, Acartürk E, Seydaoglu G. A new index (CHOLINDEX) in detecting coronary artery disease risk. *AnadoluKardiyolDerg*. 2013; 13:315-9.
14. Gondin-Pitanga FJ, Lessa I. Anthropometric indexes of obesity as an instrument of screening for high coronary risk in adults in the city of Salvador-Bahia. *Arquivos Brasileiros de Cardiologia*. 2005;85(1):26-31
15. Amini M, Esmailzadeh A, Sadeghi M, Mehvarifar N, Amini M, Zare M. The association of hypertriglyceridemic waist phenotype with type 2 diabetes mellitus among individuals with first relative history of diabetes. *JRMS*. 2011; 16(2):156-64.
16. Arsenault BJ, Lemieux I, Despres JP, Wareham NJ, Kastelein JJP, Khaw KT, et al. The hypertriglyceridemic-waist phenotype and the risk of coronary artery disease: results from the EPIC-Norfolk Prospective Population Study. *CMAJ*. 2010;182(13):1427-32
17. Egeland GM, Igland J, Nygard O, Sulo G, Tell GS. Hypertriglyceridemic-waist phenotype is a useful global assessment tool for predicting acute myocardial infarction. *J Cardiovasc Dis Diagn*. 2015; 3:4
18. Bioelectrical impedance analysis in body composition measurement: National Institutes of Health Technology Assessment Conference Statement. *Am J Clin Nutr*. 1996; 64:524S-532S.
19. Organization WH. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation. 2000. Ginebra:WHO
20. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral Adiposity Index. A reliable indicator of visceral function associated with cardiometabolic risk. *Diabetes Care*. 2010; 33(4):920-2
21. Amato MC, Giordano C, Pitrone M, Galluzzo A. Cut-off points of the visceral adiposity index (VAI) identifying a visceral adipose dysfunction associated with cardiometabolic risk in a Caucasian Sicilian population. *Lipids in Health and Disease*. 2011; 10:183-90.
22. López-González AA, García-Agudo S, Tomás-Salvá M, Vicente-Herrero MT, Queimadelos-Carmona M, Campos-González I. FINRISK Test: Relationship between cardiovascular risk parameters and scales in Spanish Mediterranean population. *Rev Med Inst Mex Seguro Soc*. 2017 May-Jun;55(3):309-16.

Assessment of cardiometabolic status in 5.994 german mechanics

Evaluación del estado cardiometabólico en 5.994 mecánicos alemanes

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Abstract

Introduction: Cardiometabolic disorders encompass a number of pathological processes that are highly prevalent especially in the developed world and are related to socioeconomic status.

Material and methods: Descriptive and cross-sectional study in 5994 German mechanics in which different indicators of obesity and overweight, insulin resistance scales, fatty liver and liver fibrosis scales and atherogenic indices were determined.

Results: Overall, 62.5% of German mechanics are obese or overweight, 27.3% have high blood pressure, 42% have high cholesterol, 22.7% have blood glucose above 100 mg/dl, a high percentage of metabolic syndrome (15.8% if NCEP-ATPIII criteria are applied, 25.2% if JIS criteria are applied), 11.3% have a high risk of insulin resistance and 23.3% a high risk of fatty liver disease.

Conclusions: The level of cardiometabolic risk among mechanics can be considered moderate-high and increases with age.

Keywords: Obesity, metabolic syndrome, dyslipidemia, insulin resistance, fatty liver.

Resumen

Introducción: Las alteraciones cardiometabólicas engloban una serie de procesos patológicos altamente prevalentes especialmente en el mundo desarrollado y que guardan relación con el nivel socioeconómico.

Material y métodos: Estudio descriptivo y transversal en 5994 mecánicos alemanes en los que se determinan diferentes indicadores de obesidad y sobrepeso, escalas de resistencia a la insulina, escalas de hígado graso y fibrosis hepática e índices aterogénicos.

Resultados: Globalmente el 62,5% de los mecánicos alemanes presentan obesidad o sobrepeso, el 27,3% hipertensión arterial, el 42% hipercolesterolemia, el 22,7% glucemia superior a 100 mg/dl, un alto porcentaje de síndrome metabólico (15,8% si aplicamos los criterios NCEP-ATPIII, y el 25,2% si los criterios aplicados son los JIS), el 11,3% presentan un alto riesgo de resistencia a la insulina y el 23,3% un alto riesgo de enfermedad de hígado graso.

Conclusiones: El nivel de riesgo cardiometabólico entre los mecánicos se puede considerar moderado-alto y se va incrementando con la edad.

Palabras clave: Obesidad, síndrome metabólico, dislipemia, resistencia a la insulina, hígado graso.

Introduction

Cardiometabolic risk refers to the probability that a person is likely to suffer cardiovascular alterations if he or she has at least one risk factor such as obesity, high LDL cholesterol, high triglyceride or low HDL levels, arterial hypertension, insulin resistance, smoking or a sedentary lifestyle¹. Each of these factors alone is already dangerous, but when a combination of them occurs, the risk of a cardiovascular event increases considerably. The World Health Organization (WHO) estimates that cardiometabolic diseases cause around 30% of deaths worldwide².

People who are overweight are at increased risk of cardiovascular disease because weight affects the way insulin acts in the body³. Insulin helps control blood glucose, cholesterol and triglyceride levels. Weight gain makes insulin more ineffective which causes our body to not respond properly. When the body is resistant or less susceptible to insulin, there is an accumulation of glucose in the blood, which is known as insulin resistance and can eventually lead to diabetes mellitus. It is also known that arterial hypertension is more frequent in people with insulin resistance.

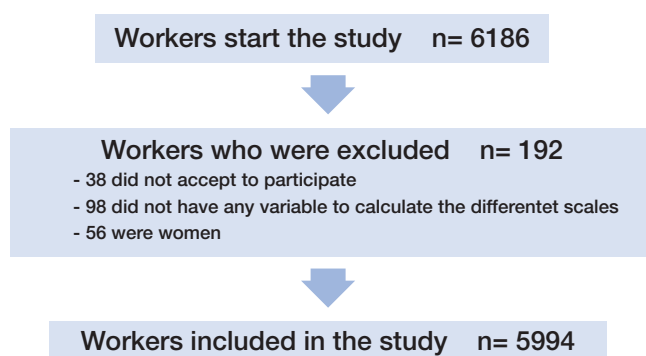
In Germany⁴ 37% of deaths are due to cardiovascular diseases and 3% to diabetes-related processes, so that the highest percentage of deaths in our country is related to cardiometabolic problems.

The aim of our study was to determine the prevalence of cardiometabolic disorders in a group of mechanics working in Germany.

Methods

A descriptive, cross-sectional study was performed in 6.186 german mechanics workers between January 2019 and December 2020. 192 of them were excluded (38 for not agreeing to participate, 98 for lacking any of the parameters necessary to calculate the different cardiovascular risk scales, and 56 were women), leaving 5.994 mechanics. See flow chart in **figure 1**.

Figure 1: Flow chart of the study participants.



Inclusion criteria

- Age between 18 and 69 years.
- Give consent to participate in the study and the use of the data for epidemiological purposes.
- Were man.

Anthropometric, clinical and analytical determinations were carried out by the healthcare professionals of the different occupational health units that participated in the study, after standardizing the measurement techniques.

The following parameters were included in the assessment:

Weight (in kg) and height (in cm) are determined with a SECA model 700 scale and a SECA 220 measuring rod. Abdominal waist circumference (in cm) is measured with a SECA model 200 tape measure. For the waist-to-height ratio (WtHR), the cut-off point is set at 0.50⁵. Blood pressure is measured in the decubitus supine position with a calibrated OMRON M3 automatic sphygmomanometer and after a 10-minute rest period. Three determinations are made at one minute intervals, obtaining the mean of the three hypertension is considered when the values are equal/higher than 140 mmHg systolic or 90 mmHg diastolic blood pressure or if the worker is receiving antihypertensive treatment⁶. Blood glucose, total cholesterol and triglycerides are determined by peripheral venipuncture after fasting for at least 12-hour. Glycemia, total cholesterol and triglycerides are determined by automated enzymatic methods. HDL is determined by precipitation with dextran sulfate Cl2Mg and LDL is calculated using the Friedewald formula (provided that triglycerides are less than 400 mg/dl). All the above values are expressed in mg/dl.

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

The following are considered altered values: 200 mg/dL for cholesterol, 130 mg/dL for LDL and 150 mg/dL for triglycerides or if they are under treatment for any of these analytical alterations⁷.

Blood glucose values are classified according to the criteria of the American Diabetes Association⁸ and are considered to be diabetes at 126 mg/dL or if they are receiving hypoglycaemic treatment.

BMI is calculated by dividing weight by height in meters squared. Obesity is considered to be 30 kg/m² or more.

We use to estimate the percentage of body fat: CUN BAE9 (Clínica Universitaria de Navarra Body Adiposity Estimator).

$-44,988 + (0.503 \times \text{age}) + (10.689 \times \text{gender}) + (3.172 \times \text{BMI}) - (0.026 \times \text{BMI}^2) + (0.181 \times \text{BMI} \times \text{gender}) - (0.02 \times \text{BMI} \times \text{age}) - (0.005 \times \text{BMI}^2 \times \text{gender}) + (0.00021 \times \text{BMI}^2 \times \text{age})$ where Male = 0 Female = 1

Other indicators related to overweight and obesity:

Visceral adiposity index (VAI)¹⁰

Females:

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

Males:

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

Body roundness index¹¹ (BRI) = $364.2 - 365.5 \times \sqrt{1 - ((\text{waist}/(2\pi))^2 / (0.5 \times \text{height})^2)}$

Body Surface Index (BSI)¹². BSA is calculated using the DuBois formula where w (weight) represents weight in kg and h (height) represents height in cm.

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

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

Conicity index (CI)¹³

$$\frac{\text{waist circumference (in metres)}}{0,109} \times 1 \sqrt{\frac{\text{Weight (in kilogram)}}{\text{Height (in metres)}}}$$

Body shape index (ABSI)¹⁴

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

Other indicators related to cardiovascular risk:

Triglyceride glucose index¹⁵

TyGindex = $\text{LN}(\text{TG} [\text{mg/dl}] \times \text{glycaemia} [\text{mg/dl}]/2)$.

METS-IR¹⁶. $\text{LN}(2 \times \text{blood glucose} + \text{Triglycerides}) \times \text{BMI} / \text{LN}(\text{HDL-c})$. Se considera riesgo alto de RI a partir de 50.

Cardiometabolic index (CMI)¹⁷

WtHR/(Triglycerides/HDL-c)

Metabolic syndrome was determined using three models:

a) NCEP ATP III (National Cholesterol Educational Program Adult Treatment Panel III), which considers metabolic syndrome when three or more of the following factors are present: waist circumference is greater than 88cm in women and 102 in men; triglycerides >150

mg/dl or specific treatment for this lipid disorder; blood pressure >130/85 mm Hg; HDL <40 mg/dl in women or <50 mg/dl in men or specific treatment is followed, and fasting blood glucose >100 mg/dl or specific glycaemic treatment.

b) The International Diabetes Federation (IDF) model¹⁸, which considers the presence of central obesity necessary, defined as a waist circumference of >80 cm in women and >94 cm in men, in addition to two of the other factors mentioned above for ATP III (triglycerides, HDL, blood pressure and glycemia).

c) The JIS model¹⁹, which follows the same criteria as NCEP ATP III but the waist circumference cut-off points start at 80 cm in women and 94 cm in men.

Atherogenic dyslipidemia (AD)²⁰ is characterized 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 (LT).

Fatty liver scales include:

Fatty liver index (FLI)²¹

$$FLI = \left(\frac{e^{0.953 \times \log_e(\text{triglycerides}) + 0.139 \times \text{BMI} + 0.718 \times \log_e(\text{GGT}) + 0.053 \times \text{waist circumference} - 15.745}}{(1 + e^{0.953 \times \log_e(\text{triglycerides}) + 0.139 \times \text{BMI} + 0.718 \times \log_e(\text{GGT}) + 0.053 \times \text{waist circumference} - 15.745})} \right) \times 100$$

BARD score²² BMI ≥ 28 1 point, AST/ALT ≥ 0,8 2 points, type 2 diabetes mellitus 1 point. Cutoff to high risk 2 points

Lipid accumulation product (LAP)²³

- Men: (waist (cm) - 65) x (triglycerides (mMol)).

- Women: (waist (cm) - 58) x (triglycerides (mMol))

The different atherogenic indices have different cutoff points²⁴: Total cholesterol/HDL-c index: low risk: < 5 in men and < 4.5 in women; moderate risk: between 5 and 9 in men and between 4.5 and 7 in women; and high risk: > 9 in men and > 7 in women. LDL-c/HDL-c ratio: low risk: < 3 and high risk ≥ 3. Triglycerides/HDL-c ratio is considered high risk from 3%. Cholesterol-HDL-c index: high risk as from 130.

A smoker is considered to be any person who has regularly consumed at least 1 cigarette/day (or the equivalent in other types of consumption) in the last month, or has quit smoking less than 12 months ago.

Statistical analysis

A descriptive analysis of the categorical variables was performed, 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 association analysis was performed using the chi2 test (with correction of Fisher's exact statistic when conditions required so). The statistical analysis was performed with the SPSS 27.0 program, with an accepted statistical significance level of 0.05.

Ethical aspects

The study was approved by the Clinical Research Ethics Committee. All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 2013 Declaration of Helsinki. All patients signed written informed consent documents prior to their participation in the study.

Results

Table I shows the anthropometric, sociodemographic, analytical and clinical characteristics of the 5994 mechanics. A total of 32.9% were smokers. All age groups were similarly represented.

Table II shows the mean values of the different cardiometabolic indicators analyzed in the study: overweight and obesity indicators (BMI, WtHR, BSI, BRI, ABSI, VAI, CI, CUN BAE), insulin resistance scales (TyG index, METS-IR), fatty liver and liver fibrosis scales (FLI, BARD score, LAP) and atherogenic indices.

Table III shows a bivariate analysis of the different scales related to cardiometabolic disorders in the different age groups. All the scales show a progressive worsening of the values obtained with increasing age.

Table I: Characteristics of the 5994 German mechanics.

Mechanics n=5994	Mean (SD)
Age (years)	39.4 (11.3)
Height (cm)	174.4 (6.7)
Weight (kg)	81.5 (14.7)
Waist (cm)	85.9 (10.7)
Systolic blood pressure (mmHg)	127.4 (15.2)
Diastolic blood pressure (mmHg)	77.2 (10.7)
Total cholesterol (mg/dl)	193.3 (38.8)
HDL-c (mg/dl)	50.6 (8.0)
LDL-c (mg/dl)	118.6 (36.9)
Triglycerides (mg/dl)	122.0 (76.1)
Glycaemia (mg/dl)	93.0 (19.9)
ALT (U/L)	32.0 (18.1)
AST (U/L)	24.5 (14.9)
GGT (U/L)	36.3 (45.8)
n (%)	
18-29 years	1357 (22.6)
30-39 years	1776 (29.6)
40-49 years	1553 (25.9)
50-69 years	1308 (21.8)
Non smokers	4023 (67.1)
Smokers	1971 (32.9)

Table II: Mean values of anthropometric and cardiometabolic parameters in German mechanics.

Mechanics n=5994	Mean (SD)
Body mass index	26.8 (4.5)
Waist to height ratio	0.49 (0.06)
Body surface index	57.9 (7.9)
Body roundness index	3.3 (1.1)
Body shape index	0.073 (0.01)
Visceral adiposity index	7.2 (6.0)
Conicity index	1.16 (0.09)
CUN BAE	25.5 (6.7)
TyG index	8.5 (0.6)
METS-IR	39.3 (8.4)
AI Total cholesterol/HDL-c	3.9 (1.1)
AI Triglycerides/HDL-c	2.6 (1.9)
AI LDL-c/HDL-c	2.4 (1.0)
AI Total cholesterol-HDL-c	142.7 (40.8)
Cardiometabolic index	1.3 (1.1)
Lipid accumulation product	31.4 (31.7)
Fatty liver index	37.2 (27.4)
BARD scoring	1.7 (1.1)

Table III: Prevalence of high values of anthropometric and cardiometabolic parameters in German mechanics by age.

	18-29 years n= 1357 % (95% CI)	30-39 years n= 1776 % (95% CI)	40-49 years n= 1553 % (95% CI)	50-69 years n= 1308 % (95% CI)	Total n= 5994 % (95% CI)	p-value
Waist to height ratio >0.50	31.3 (30.2-32.4)	38.9 (37.8-40.0)	45.5 (44.5-46.5)	47.0 (46.9-48.1)	40.7 (40.2-41.2)	<0.0001
Overweight BMI	31.7 (30.6-32.8)	39.2 (38.1-40.3)	47.8 (46.8-48.8)	49.5 (48.4-50.6)	42.0 (41.5-42.5)	<0.0001
Obesity BMI	11.6 (10.6-12.6)	19.1 (18.1-20.3)	24.7 (23.7-25.8)	26.8 (25.7-27.9)	20.5 (20.0-21.0)	<0.0001
Overweight CUN BAE	26.8 (25.7-27.9)	34.3 (33.3-35.3)	27.7 (26.7-28.7)	17.5 (16.4-18.6)	27.2 (26.5-27.5)	<0.0001
Obesity CUN BAE	25.9 (24.8-27.0)	42.5 (41.5-43.5)	65.2 (64.2-66.2)	79.4 (78.3-80.5)	52.7 (52.2-53.2)	<0.0001
Hypertension	13.9 (12.9-14.9)	17.5 (16.6-18.4)	31.3 (30.3-32.3)	49.8 (48.7-51.0)	27.3 (26.8-27.8)	<0.0001
Total cholesterol ≥ 200 mg/dl	15.0 (14.0-16.0)	36.8 (35.8-37.8)	57.6 (56.6-58.6)	58.5 (57.4-59.6)	42.0 (41.5-42.5)	<0.0001
LDL-c ≥ 130 mg/dl	13.9 (12.8-14.9)	30.8 (29.8-31.8)	51.3 (50.3-52.3)	55.0 (53.9-56.1)	37.6 (37.1-38.1)	<0.0001
Triglycerides ≥ 150 mg/dl	12.5 (11.5-13.5)	21.2 (20.2-22.3)	30.5 (29.5-31.6)	32.7 (31.6-33.8)	24.2 (23.7-24.7)	<0.0001
Glycaemia 100-125 mg/ml	10.5 (9.5-11.5)	14.7 (13.8-15.6)	23.1 (22.1-24.1)	31.7 (30.6-32.8)	19.6 (19.1-20.1)	<0.0001
Glycaemia > 125mg/dl	0.7 (0.5-0.9)	1.6 (1.3-2.0)	2.4 (2.0-2.8)	8.5 (7.6-9.4)	3.1 (2.7-3.5)	<0.0001
Metabolic syndrome NCEP-ATPIII criteria	4.4 (3.7-5.1)	9.2 (8.5-9.9)	19.4 (18.4-20.4)	32.3 (31.2-33.4)	15.8 (15.3-20.3)	<0.0001
Metabolic syndrome IDF criteria	5.2 (4.5-5.9)	9.7 (9.0-10.4)	16.0 (15.0-17.0)	16.1 (15.0-17.2)	11.7 (11.2-12.2)	<0.0001
Metabolic syndrome JIS criteria	9.9 (9.0-10.8)	16.9 (15.9-17.9)	30.0 (29.0-31.0)	46.7 (45.6-47.8)	25.2 (24.7-25.7)	<0.0001
Atherogenic dyslipidemia	2.5 (2.0-3.0)	4.4 (3.8-5.0)	10.0 (9.0-11.0)	13.6 (12.5-14.7)	7.4 (7.0-7.8)	<0.0001
Lipid triad	0.4 (0.3-0.6)	1.0 (0.7-1.3)	3.4 (3.3-3.5)	4.0 (3.2-4.8)	2.2 (1.9-2.5)	<0.0001
AI Total cholesterol/HDL-c moderate-high	3.0 (2.5-3.5)	9.7 (9.0-10.5)	21.3 (20.3-22.3)	30.3 (29.2-31.4)	15.7 (15.2-16.2)	<0.0001
AI Triglycerides/HDL-c high	12.3 (11.3-13.3)	21.2 (20.2-22.2)	32.1 (31.1-33.1)	39.1 (38.0-40.2)	25.9 (25.4-30.4)	<0.0001
AI LDL-c/HDL-c high	7.2 (6.3-8.1)	17.3 (16.3-18.3)	35.5 (34.5-36.5)	44.7 (43.6-45.8)	25.7 (25.2-26.2)	<0.0001
AI Total cholesterol-HDL-c	30.9 (29.8-32.0)	56.5 (55.5-57.5)	77.9 (76.7-78.7)	78.9 (78.8-80.0)	61.1 (60.6-61.6)	<0.0001
Lipid accumulation product high	22.1 (21.0-23.2)	32.7 (31.7-33.7)	43.1 (42.1-44.1)	44.8 (43.7-45.9)	35.6 (35.1-36.1)	<0.0001
METS-IR high	5.5 (4.8-6.3)	10.5 (9.7-11.2)	14.6 (13.6-15.6)	16.0 (15.0-17.1)	11.3 (10.8-11.8)	<0.0001
TyG index high	12.2 (11.2-13.2)	22.1 (21.1-23.1)	34.3 (33.3-35.3)	42.7 (41.6-42.8)	27.5 (27.0-28.0)	<0.0001
Fatty liver index high risk	12.8 (11.8-13.8)	20.9 (19.9-21.9)	29.6 (28.6-30.6)	29.9 (28.8-31.0)	23.3 (22.8-23.9)	<0.0001

The last column shows the overall prevalence of altered values for all the scales, with the most striking values being 20.5% obesity and 42% overweight, 27.3% arterial hypertension, 42% hypercholesterolemia, 22.7% of blood glucose above 100 mg/dl, a high percentage of metabolic syndrome (15.8% if we apply the NCEP-ATPIII criteria, and 25.2% if the criteria applied are JIS), 11.3% present a high risk of insulin resistance and 23.3% a high risk of fatty liver disease.

Discussion

In our study, we can consider that the cardiometabolic risk obtained in the group of mechanics by applying the different scales included in the study can be considered moderately high. A clear increase in this risk is observed with increasing age.

Our results are consistent with those obtained by the authors of the French RECORD²⁵ study which analysed data from 4.360 workers where BMI, waist circumference, blood pressure, lipid profile, and blood glucose were assessed. The conclusion of the study was that the most disadvantaged sectors of the workforce performed worse on all cardiometabolic scales. A Colombian study²⁶ conducted in a metal-mechanic company showed much higher prevalences of metabolic syndrome than ours, namely 41%. Other studies^{27,28}, also conducted in

mechanics, showed prevalences of metabolic syndrome similar to ours.

Translated with www.DeepL.com/Translator (free version) As strong points, we would highlight the large sample size, almost 6.000 mechanics, and the large number of scales used, which has allowed us to determine the cardiometabolic risk of this group with greater reliability.

As limitations, we found that the study was only carried out in men, as women were excluded due to their small number (specifically 56) and in a specific country, which may make it difficult to extrapolate the results to other geographical areas.

Conclusion

The cardiometabolic risk of German mechanics can be considered moderate-high, especially considering the very low average age of the population studied, mainly due to high prevalence of overweight-obesity, dyslipidemia, arterial hypertension, metabolic syndrome and high risk of insulin resistance and fatty liver.

Interests conflict

The researchers declare that they have no conflict of interest.

References

- Morales G, Balboa-Castillo T, Muñoz S, Belmar C, Soto A, Schifferli I, et al. Association between cardiometabolic risk factors, physical activity and sedentariness in Chilean university students. *Nutr Hosp* 2017;34(6):1345-52
- Maldonado Villalón JA, Carranza Cervantes CA, Ortiz González MJ, Gómez Alonso C, Cortés-Gallegos NL. Prevalencia de factores de riesgo cardiometabólico en estudiantes universitarios de la región centro-occidente, en la Universidad Michoacana de San Nicolás de Hidalgo, México. *Rev. Mex. Cardiol* . 2013; 24(2): 76-86.
- Ye J. Mechanisms of insulin resistance in obesity. *Front Med* 2013;7(1):14-24
- Organización Mundial de la Salud - ENT Perfiles de países, 2018. Available at: https://www.who.int/nmh/countries/deu_es.pdf
- Luengo-Pérez LM, Urbano-Gálvez JM, Pérez-Miranda M. Validación de índices antropométricos alternativos como marcadores del riesgo cardiovascular. *Endocrinol Nutr* 2009;56(9):439-46
- James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb CH, Handler J. Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014;311(5):507-20.
- Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L. ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J* 2020;41(1):111-88.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;33(Suppl 1):S62-9
- Gómez-Ambrosi J, Silva C, Catalán V, Rodríguez A, Galofré JC, Escalada J. Clinical usefulness of a new equation for estimating body fat. *Diabetes Care* 2012;35(2):383-8.
- Amato M, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M. Visceral Adiposity Index A reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care* 2010;33(4):920-2

11. Rico-Martín S, Calderón-García JF, Sánchez-Rey P, Franco-Antonio C, Martínez-Álvarez, M, & Sánchez-Muñoz-Torrero, JF. (2020). Effectiveness of body roundness index in predicting metabolic syndrome: A systematic review and meta-analysis. *Obes Rev.*;21(7): e13023
12. Shirazu I, Sackey THA, 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
13. Andrade MD, Freitas MC, Sakumoto AM, Pappiani C, Andrade SC, Vieira VL. Association of the conicity index with diabetes and hypertension in Brazilian women. 2016;60(5):436-42.
14. Bertoli S, Leone A, Krakauer NY, Bedogni G, Vanzulli A, Redaelli VI. 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.
15. 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
16. Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, Viveros-Ruiz T, Cruz-Bautista I, Romo-Romo A, et al METS-IR a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. *Eur J Endocrinol* 2018;178(5):533-44
17. 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.
18. Zimmet P, Alberti KG, Serrano-Rios 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.
19. Cabrera-Roe E, Stusser B, Cálix W, Orlandi N, Rodríguez J, Cubas-Dueñas I. 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.
20. Bestehom 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
21. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol* 2006; 6:33.
22. Ruffillo G, Fassio E, Alvarez E, Landeira G, Longo C, Dominguez N, et al. Comparison of NAFLD fibrosis score and BARD score in predicting fibrosis in nonalcoholic fatty liver disease. *J Hepatol* 2011;54(1):160-3
23. 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
24. 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.* 201;27(3):118-28
25. Lewin A, Thomas F, Pannier B, Chaix B. Work economic sectors and cardiovascular risk factors: cross-sectional analysis based on the RECORD Study. *BMC Public Health.* 2014 Jul 24;14:750.
26. Agredo-Zúñiga RA, García-Ordoñez ES, Osorio C, Escudero N, López-Albán CA, Ramírez-Vélez R. Obesidad abdominal y ausentismo por causa médica en una empresa de la industria metalmeccánica en Cali, Colombia. *Rev Peru Med Exp Salud Publica* 2013;30(2):251-5.
27. Martínez EG, Gutierrez AM. Metabolic Syndrome and Body Composition measurements in Blue-Collar Workers from a Metal-Mechanic Factory in Soledad. Preliminary Report. *Salud Uninorte. Barranquilla (Col)* 2017;33(1):1-6
28. 22. Suárez-Ortegón MF, Arbeláez A, Mosquera M, Ramírez-Vélez R, Aguilar-De Plata C. Evaluation of the relationship between self-reported physical activity and metabolic syndrome and its components in apparently healthy women. *Biomédica.* 2014;34:60-66.

Relationship between healthy habits and sociodemographic variables in the values of different atherogenic indices

Relación entre hábitos saludables y variables sociodemográficas en los valores de diferentes índices aterogénicos

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Abstract

Introduction: Atherosclerosis is the pathological lesion responsible for most cardiovascular diseases.

Methods: A descriptive, cross-sectional study was carried out in 1457 Spanish workers to assess the effect of healthy habits (physical exercise determined with the IPAQ questionnaire, Mediterranean diet, and tobacco consumption) and sociodemographic variables (age, sex, and social class) on the values of different atherogenic indices.

Results: The mean values and the prevalence of altered values in all the atherogenic indices analyzed were lower the higher the level of physical activity and also the greater the adherence to the Mediterranean diet. In men there was a greater risk of presenting elevated values in all atherogenic indices, whereas the highest social class only increased this risk in some indices.

Conclusion: Healthy habits such as physical exercise and the Mediterranean diet improve atherogenic indices and reduce the risk of presenting arteriosclerosis.

Keywords: Atherogenic index, Mediterranean diet, Physical activity, social class.

Resumen

Introducción: La aterosclerosis es la lesión patológica responsable de la mayoría de las enfermedades cardiovasculares.

Métodos: Se realizó un estudio descriptivo y transversal en 1457 trabajadores españoles para evaluar el efecto de los hábitos saludables (ejercicio físico determinado con el cuestionario IPAQ, dieta mediterránea y consumo de tabaco) y variables sociodemográficas (edad, sexo y clase social) sobre los valores de diferentes índices aterogénicos.

Resultados: Los valores medios y la prevalencia de valores alterados en todos los índices aterogénicos analizados fueron menores cuanto mayor era el nivel de actividad física y también cuanto mayor era la adherencia a la dieta mediterránea. En los hombres hubo un mayor riesgo de presentar valores elevados en todos los índices aterogénicos, mientras que la clase social más alta sólo aumentó este riesgo en algunos índices.

Conclusiones: Los hábitos saludables como el ejercicio físico y la dieta mediterránea mejoran los índices aterogénicos y reducen el riesgo de presentar arteriosclerosis.

Palabras clave: Índice aterogénico, dieta mediterránea, actividad física, clase social.

Introduction

Atherosclerosis is the anatomopathological process underlying most cardiovascular diseases, in which accumulations of lipids, monocytes, and T lymphocytes are observed in the intima, causing migration and proliferation of smooth muscle cells, and the elaboration of collagen. Atherosclerotic disease, which begins in the first decade of life, is relatively benign and slowly progressive, remaining asymptomatic until there is a significant reduction in the vascular lumen, an abrupt occlusion, or thrombotic complications. Like most diseases whose prevalence increases with age, it is a complex pathology that depends on the interaction of genetic and environmental factors^{1,2}. The combination of an unhealthy diet and low physical activity are the main risk factors for arteriosclerosis^{3,4}. The two parameters most associated with cardiovascular disease, both strongly correlated with each other, are the proportion of calories in the diet, – supplied by saturated fatty acids – and blood cholesterol levels⁵⁻⁷. For this reason, international organizations consider that 30 minutes of moderate physical activity a day and diets in which the percentage of lipids is less than 30% are essential to reduce the risk of developing cardiovascular disease⁸.

Although the multifactorial origin of arteriosclerosis is known, it is also recognized that almost half the risk of developing cardiovascular disease is related to the lipid metabolism⁹. In the search for a greater degree of prediction of cardiovascular disease, the need arose to develop different instruments to better assess it, and atherogenic indices are framed in this context. These indices provide important information on risk factors that are difficult to quantify by classical systematic analyses and are a better reflection of the clinical and metabolic interactions of lipid fractions. We believe that lipoprotein indices have been little used in cardiovascular prevention although they can provide valuable information on risk assessment. Their use as important predictors of cardiovascular risk is based on a large number of epidemiological studies that have shown that these indices have a higher correlation with cardiovascular disease and, as such, are better predictors of cardiovascular disease than simple lipid parameters¹⁰⁻¹². Therefore, in an attempt to improve the degree of knowledge of these tools, the main objective of the present study was to determine the influence of certain hygienic habits, such as tobacco consumption, diet, and physical exercise, on the values of different atherogenic indices in the Spanish Mediterranean population.

Material and methods

A retrospective, cross-sectional study was performed in 1584 Spanish workers from different productive sectors in the period between January 2017 and December 2017. One hundred and twenty-seven workers were

excluded (69 for not accepting to participate and 58 for being under 18 years old), leaving 1457 workers finally included in the study, 718 women (mean age 43.30 years) and 739 men (mean age 46.02 years). The workers were selected from among those who attended periodic occupational medical check-ups.

Inclusion criteria

- Aged between 18 and 67 years.
- Being an active worker.
- Belonging to one of the companies collaborating in the study.
- Accepting to participate in the study.

The different measurements (anthropometric, clinical, and analytical) were performed by health personnel from the participating occupational health units after homogenizing the measurement techniques.

Weight (in kilograms) and height (in cm) were obtained with a SECA 700 measuring scale with a capacity of 200 kg, which incorporated a SECA 220 telescopic measuring rod with millimetric division and a 60-200 cm interval.

Abdominal and hip girth were measured in both cases with a SECA model 200 tape measure with the person in a standing position with their feet together and trunk erect, abdomen relaxed, and upper limbs hanging on both sides of their body. For the former, the tape measure was placed parallel to the ground at the level of the last floating rib; and for the latter, horizontally at the level of the hip.

Blood pressure was obtained with an OMRON M3 automatic sphygmomanometer with the person in the supine position after 10 minutes of rest. Three measurements were taken at one-minute intervals and the mean of the three was obtained. Blood tests were obtained after 12 hours of fasting. Samples were sent to reference laboratories. Glycemia, total cholesterol and triglycerides use automated enzymatic methods, and the values are expressed in mg/dl. HDL was determined by precipitation with dextran sulfate Cl2Mg, and values are also expressed in mg/dl. LDL was calculated using the Friedewald formula (provided that triglycerides were less than 400 mg/dl). Values are expressed in mg/dl.

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

The different atherogenic indices have different cutoff points¹³:

Total cholesterol/HDL-c index: low risk: < 5 in men and < 4.5 in women; moderate risk: between 5 and 9 in men and between 4.5 and 7 in women; and high risk: > 9 in men and > 7 in women. LDL-c/HDL-c ratio: low risk: < 3 and high risk ≥ 3 . Triglycerides/HDL-c ratio is considered

high risk from 3%. Cholesterol-HDL-c index: high risk as from 130.

CHOLINDEX=LDL-C-HDL-C (Triglycerides<400 mg/dL), LDL-C-HDL-C + 1/5 of Triglycerides (Triglycerides \geq 400 mg/dL)¹⁴.

Cholindex is considered high at 80 and above.

A smoker was a person who regularly consumed at least 1 cigarette/day (or the equivalent in other types of consumption) in the previous month, or had stopped smoking in the preceding 12 months.

Social class was obtained from the 2011 National Classification of Occupations (CNO-11) based on the proposal made by the Spanish Society of Epidemiology¹⁵. We chose the classification in 3 categories: Class I. Directors/managers, university professionals, athletes and artists. Class II. Intermediate occupations and self-employed workers without employees. Class III. Unskilled workers.

Diet was assessed using the questionnaire on adherence to the Mediterranean diet¹⁶ which contains 14 questions with values of 0 or 1 point each. Values below 9 indicate low adherence and above 9 indicate good adherence.

Physical activity was assessed with the International Physical Activity Questionnaire (IPAQ)¹⁷, a self-administered questionnaire consisting of seven questions that assesses the physical activity performed in daily life in the previous seven days.

Results

Table I shows the values of the anthropometric, clinical, analytical, sociodemographic, and healthy habit variables of the population studied, where it can be observed that the values were more unfavorable, except for total cholesterol and tobacco consumption, among men.

All the atherogenic indices analyzed showed a decrease in the mean values as the level of physical activity increased, and this situation appeared in both women and men, as shown in **table II**.

Something similar to that observed with physical activity was seen with the Mediterranean diet, in that people, both men and women, who presented high scores in the questionnaire on adherence to the Mediterranean diet would present better values in all the atherogenic indices. The complete data are shown in **table III**.

The prevalence of altered values of all the atherogenic indices decreased as the level of physical exercise increased; this situation was seen in both men and women. (see **table IV**).

The prevalence of elevated values of the atherogenic indices also demonstrated better results in people with a high adherence to the Mediterranean diet, as shown in **table V**.

Sex, physical activity, and Mediterranean diet were the only variables to show an influence in all the scales

Table I: Characteristics of the population.

	Women (n=718) mean (SD)	Men (n=739) mean (SD)	Total (n=1457) mean (SD)	p-value
Age (years)	43.30 (8.44)	46.02 (8.50)	44.68 (8.57)	<0.0001
Height (kg)	66.29 (12.29)	82.24 (13.81)	74.38 (15.32)	<0.0001
Weight (m)	1.62 (0.06)	1.73 (0.07)	1.68 (0.09)	<0.0001
BMI (kg/m ²)	25.36 (4.61)	27.40 (4.13)	26.39 (4.49)	<0.0001
Waist (cm)	89.44 (16.36)	97.00 (10.65)	93.27 (14.27)	<0.0001
Hip (cm)	105.78 (13.22)	108.77 (10.27)	107.29 (11.91)	<0.0001
Systolic Blood Pressure (mm Hg)	121.31 (17.05)	133.76 (18.11)	127.62 (18.66)	<0.0001
Diastolic Blood Pressure (mm Hg)	75.03 (10.58)	80.63 (11.43)	77.87 (11.36)	<0.0001
Cholesterol (mg/dl)	186.02 (31.14)	183.37 (31.72)	184.67 (31.46)	0.108
HDL (mg/dl)	60.18 (13.55)	49.83 (12.16)	54.93 (13.86)	<0.0001
LDL (mg/dl)	107.88 (28.16)	108.94 (29.15)	108.42 (28.66)	0.483
Triglycerides (mg/dl)	86.57 (43.59)	119.55 (87.42)	103.30 (71.28)	<0.0001
Glycemia (mg/dl)	92.16 (16.31)	98.68 (19.54)	95.47 (18.30)	<0.0001
	Percentage	Percentage	Percentage	p-value
<35 years	16.71	10.42	13.52	<0.0001
35-49 years	57.80	51.01	54.36	
\geq 50 years	25.49	38.57	32.12	
Social class I	18.94	8.80	13.80	<0.0001
Social class II	63.65	82.67	73.30	
Social class III	17.41	8.53	12.90	
No tobacco	71.87	72.94	72.41	<0.0001
Yes tobacco	28.13	27.06	27.59	
MET low	23.68	19.08	21.35	<0.0001
MET moderate	48.05	36.4	42.14	
MET high	28.27	44.52	36.51	
Predimed low	36.49	48.17	42.42	<0.0001
Predimed high	63.51	51.83	57.58	

analyzed. Of these, the one showing the greatest influence was age, with odds ratios ranging from 1.64 (95% CI 1.32-2.06) for high non-HDL/HDL cholesterol to 6.04 (95% CI 4.26-8.58) for high triglycerides/HDL. Age only revealed an influence for high non-HDL/HDL cholesterol. All results are presented in **table VI**.

Discussion

In our study, all the atherogenic indices analyzed improved as the level of physical activity determined with the IPAQ questionnaire increased. Something similar was observed when adherence to the Mediterranean diet increased.

Table II: Mean values of the different atherogenic index scales according to physical activity by gender.

	Women				Men			
	MET low n=170 mean (SD)	MET moderate n=345 mean (SD)	MET high n=203 mean (SD)	p-value	MET low n=141 mean (SD)	MET moderate n=269 mean (SD)	MET high n=329 mean (SD)	p-value
Cholesterol/HDL-c	3.65 (0.91)	3.18 (0.76)	2.92 (0.65)	<0.0001	4.36 (1.14)	3.94 (1.05)	3.60 (0.90)	<0.0001
LDL-c/HDL-c	2.25 (0.75)	1.87 (0.65)	1.64 (0.58)	<0.0001	2.65 (0.89)	2.35 (0.86)	2.16 (0.74)	<0.0001
Triglycerides/HDL-c	1.97 (1.63)	1.50 (0.96)	1.36 (0.89)	<0.0001	3.50 (2.85)	2.79 (2.36)	2.23 (1.82)	<0.0001
HDL-c/LDL-c+VLDL-c	0.42 (0.16)	0.51 (0.18)	0.58 (0.20)	<0.0001	0.33 (0.12)	0.39 (0.17)	0.44 (0.18)	<0.0001
Cholesterol-HDL-c	140.64 (31.22)	124.63 (29.07)	115.50 (27.10)	<0.0001	144.45 (31.84)	136.12 (33.82)	126.76 (28.84)	<0.0001
Triglycerides/LDL-c	0.87 (0.51)	0.81 (0.39)	0.77 (0.56)	<0.0001	1.53 (2.83)	1.38 (2.82)	1.03 (0.72)	<0.0001
Cholesterol no HDL-c/HDL-c	0.71 (0.07)	0.67 (0.07)	0.64 (0.08)	<0.0001	0.76 (0.06)	0.73 (0.08)	0.70 (0.08)	<0.0001
Cholindex	64.52 (33.22)	46.94 (30.87)	35.83 (31.19)	<0.0001	70.70 (31.84)	62.03 (35.55)	55.12 (35.77)	<0.0001

Table III: Mean values of the different atherogenic index scales according to healthy food by gender.

	Women			Men		
	Predimed low n=262 mean (SD)	Predimed high n=456 mean (SD)	p-value	Predimed low n=356 mean (SD)	Predimed high n=383 mean (SD)	p-value
Cholesterol/HDL-c	3.29 (0.84)	3.18 (0.79)	<0.0001	4.02 (1.07)	3.73 (1.00)	<0.0001
LDL-c/HDL-c	1.95 (0.70)	1.87 (0.69)	<0.0001	2.42 (0.86)	2.23 (0.80)	<0.0001
Triglycerides/HDL-c	1.69 (1.25)	1.51 (1.10)	<0.0001	2.93 (2.55)	2.44 (2.00)	<0.0001
HDL-c/LDL-c+VLDL-c	0.50 (0.19)	0.52 (0.19)	<0.0001	0.38 (0.15)	0.42 (0.18)	<0.0001
Cholesterol-HDL-c	126.21 (30.61)	125.63 (30.32)	<0.0001	135.62 (33.01)	131.61 (30.91)	<0.0001
Triglycerides/LDL-c	0.87 (0.50)	0.82 (0.46)	<0.0001	1.41 (2.97)	1.11 (0.89)	<0.0001
Cholesterol no HDL-c/HDL-c	0.68 (0.08)	0.67 (0.08)	<0.0001	0.73 (0.07)	0.71 (0.08)	<0.0001
Cholindex	49.44 (32.48)	47.12 (33.52)	<0.0001	63.32 (34.44)	58.08 (36.15)	<0.0001

Table IV: Prevalence of altered values in the different atherogenic index scales according to physical activity by gender.

	Women				Men			
	MET low n=170 Percentage	MET moderate n=345 Percentage	MET high n=203 Percentage	p-value	MET low n=141 Percentage	MET moderate n=269 Percentage	MET high n=329 Percentage	p-value
Cholesterol/HDL-c moderate	14.71	6.96	2.46	<0.0001	27.66	13.01	7.60	<0.0001
Cholesterol/HDL-c high	0.59	0.00	0.00		0.00	0.00	0.00	
LDL-c/HDL-c high	15.88	6.96	2.46	<0.0001	34.04	24.10	13.67	<0.0001
Triglycerides/HDL-c high	10.59	6.38	3.45	<0.0001	41.13	31.97	20.06	<0.0001
Cholesterol no HDL-c/HDL-c high	62.35	42.32	28.57	<0.0001	67.38	57.25	43.77	<0.0001
Cholindex high	29.41	12.17	8.37	<0.0001	37.59	25.65	20.67	<0.0001

Table V: Prevalence of altered values in the different atherogenic index scales according to healthy food by gender.

	Women			Men		
	Predimed low n=262 Percentage	Predimed high n=456 Percentage	p-value	Predimed low n=356 Percentage	Predimed high n=383 Percentage	p-value
Cholesterol/HDL-c moderate	9.54	6.36	<0.0001	16.57	10.44	<0.0001
Cholesterol/HDL-c high	0.00	0.00		0.00	0.22	
LDL-c/HDL-c high	9.54	6.80	<0.0001	24.44	17.23	<0.0001
Triglycerides/HDL-c high	8.78	5.26	<0.0001	34.55	22.72	<0.0001
Cholesterol no HDL-c/HDL-c high	46.95	41.01	<0.0001	54.21	52.22	<0.0001
Cholindex high	16.41	14.47	<0.0001	28.65	22.98	<0.0001

Table VI: Logistic regression analysis.

	Men OR (CI 95%)	Age ≥50 years OR (CI 95%)	Smokers OR (CI 95%)	MET low-moderate OR (CI 95%)	Predimed low OR (CI 95%)	Social class II-III OR (CI 95%)
Cholesterol/HDL-c moderate-high	2.26 (1.56-3.26)	ns	1.73 (1.21-2.48)	2.69 (1.74-4.15)	1.53 (1.08-2.17)	ns
LDL-c/HDL-c high	3.81 (2.70-5.38)	ns	ns	2.40 (1.67-3.44)	1.48 (1.08-2.01)	0.60 (0.39-0.92)
Triglycerides/HDL-c high	6.04 (4.26-8.58)	ns	1.65 (1.21-2.25)	1.90 (1.37-2.63)	1.69 (1.26-2.26)	ns
Cholesterol no HDL-c/HDL-c high	1.64 (1.32-2.06)	1.97 (1.56-2.50)	ns	1.85 (1.47-2.34)	1.24 (1.01-1.54)	0.47 (0.34-0.65)
Cholindex high	2.16 (1.63-2.85)	ns	ns	1.65 (1.23-2.22)	1.32 (1.01-1.72)	0.50 (0.35-0.72)

In the multivariate analysis, the variable that most increased the risk of presenting high values of all the atherogenic indices was being over 50 years of age, followed by low or moderate physical activity and low adherence to the Mediterranean diet.

Practically, all the studies consulted reveal a beneficial effect of physical activity on the values of the atherogenic indices, as we have found.

A study carried out in the same geographical area as ours and also in the working population, specifically in more than 60.000 workers, assessed the influence of physical activity and a diet rich in vegetables and fruit on the prevalence of elevated values of different atherogenic indices, showing that both high cholesterol/HDL and LDL/HDL or triglycerides/HDL were more frequent in the groups that did not engage in frequent physical activity or in those who did not consume high amounts of fruit and vegetables¹⁸. These results are similar to ours. Another study in more than 200 Norwegian adults also found a beneficial effect of physical exercise, in this case on the atherogenic LDL/HDL index¹⁹. Data from two health surveys, one in the United States²⁰ and the other in Chile,²¹ assessed the effect of physical activity on the values of the log triglyceride/HDL atherogenic index, also finding, like us, a beneficial effect. Similar data were found in another study, in this case carried out in a younger population, specifically in almost a hundred Colombian recruits, in whom physical exercise improved the values of several atherogenic indices²².

The joint effect of physical activity and a low-calorie diet was evaluated in 327 overweight Romanian adults in whom an improvement in lipid profile and atherogenic indices was also observed²³. Something similar was found in the American National Health and Nutrition Examination Survey²⁴ conducted in more than 2700 adults in which an improvement in atherogenic indices was observed with physical exercise and healthy eating, although in this case an additive effect of both was not observed.

A sub study of the PREDIMED study carried out in 772 participants who were given a Mediterranean diet supplemented with olive oil and nuts showed that after 3 months there was an improvement in the lipid profile (increase in HDL and decrease in LDL) as well as a decrease in the markers of inflammation related to arteriosclerosis²⁵.

The effect of the different types of fat in the diet on the values of the log triglyceride/HDL atherogenic index were also studied²⁶ and the consumption of less healthy fats (saturated) was found to worsen their values.

Among the strengths of this study are the large sample size, the number of atherogenic indices analyzed (specifically eight), and the fact that the assessment of physical activity and adherence to the Mediterranean diet was conducted with validated questionnaires (IPAQ and Predimed).

The main limitation of the study is that it was carried out in a very specific geographical area, which may make it difficult to extrapolate the results to other countries.

Conclusions

High physical activity (high METs) and high adherence to the Mediterranean diet decrease the values of all the atherogenic indices analyzed in this study and thus the risk of suffering arteriosclerosis. People in social class I have a higher risk of presenting elevated values of LDL/HDL, non-HDL/HDL cholesterol, and Cholindex.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. EUROASPIRE. A European Society of Cardiology survey of secondary prevention of coronary heart disease: principal results. EUROASPIRE Study Group. European Action on Secondary Prevention through Intervention to Reduce Events. *Eur Heart J* 1997; 18(10):1569-82.
2. Fuster V, Topol E, Nabel E. *Atherothrombosis and coronary artery disease*. 2nd ed. Philadelphia: Lippincott Williams Wilkins; 2005.
3. Grande F. Dieta, lipoproteínas y aterosclerosis. En: Sáez de la Calzada C, Zarco P, editores. *Cardiopatía isquémica*. Barcelona: Doyma, 1985; 23-31.
4. Dayton S, Pearce ML, Hashimoto S. A controlled clinical trial of a diet high in unsaturated fat in preventing complications of atherosclerosis. *Circulation* 1969; 40 (Supl 2): 1-63.
5. Keys A. Coronary heart disease in seven countries. *Circulation* 1970; 41 (Supl 4): 1-211.
6. Pisa Z, Uemura K. Trends of mortality from ischemic heart disease in 27 countries, 1968-1977. *World Health Stat Q* 1982; 35: 11-47.
7. Uemura K, Pisa Z. Trends in cardiovascular disease mortality in industrialized countries since 1950. *World Health Stat Q* 1988;41(3-4):155-78
8. Human Energy Requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. Rome, 17-24 October 2001.
9. Yusuf S, Hawken S, Öunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:937-52.
10. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risks by levels and ratios. *Ann Intern Med* 1994;121:641-7.
11. Stampfer MJ, Krauss RM, Ma J, Blanche PJ, Holl LG, Sacks FM, et al. A prospective study of triglyceride level, low-density lipoprotein particle diameter, and risk of myocardial infarction. *JAMA* 1996;276:882-8.
12. Ridker PM, Stampfer MJ, Rifai N. Novel risk factors for systemic atherosclerosis: a comparison of C-reactive protein, fibrinogen, homocysteine, lipoprotein(a), and standard cholesterol screening as predictors of peripheral arterial disease. *JAMA* 2001;285:2481-5
13. 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
14. Akpınar O, Bozkurt A, Acartürk E, Şeydaoğlu G. A new index (CHOLINDEX) in detecting coronary artery disease risk. *Anadolu Kardiyol Derg* 2013; 13: 315-9
15. 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
16. Miró Ò, Martín-Sánchez FJ, Jacob J, Andueza JA, Herrero P, Llorens P. Valoración del grado de adherencia a la dieta mediterránea en pacientes con insuficiencia cardiaca: Estudio DIME-EAHFE. *Anales del Sistema Sanitario de Navarra* 2016;39(2): 261-8
17. Seron P, Muñoz S, Lanas F. Nivel de actividad física medida a través del cuestionario internacional de actividad física en población Chilena. *Rev. Med. Chile*. 2010;138(10):1232-9.
18. López-González AA, Rivero YI, Vicente-Herrero MT, Queimadelos M, Monroy N, Núñez C. Influencia del consumo de tabaco, actividad física, alimentación y edad en los valores de diferentes índices aterogénicos en población mediterránea española. *Medicina Balear* 2014;29(2):23-31
19. Holme I, Høstmark AT, Anderssen SA. ApoB but not LDL-cholesterol is reduced by exercise training in overweight healthy men. Results from the 1-year randomized Oslo Diet and Exercise Study. *J Intern Med*. 2007;262(2):235-43.
20. Edwards MK, Blaha MJ, Loprinzi PD. Influence of sedentary behavior, physical activity, and cardiorespiratory fitness on the atherogenic index of plasma. *J Clin Lipidol*. 2017;11(1):119-25.
21. Reyes-Ferrada W, Solís-Urra P, Plaza-Díaz J, Sadarangani KP, de Moraes Ferrari GL, et al. Cardiorespiratory Fitness, Physical Activity, Sedentary Time and Its Association with the Atherogenic Index of Plasma in Chilean Adults: Influence of the Waist Circumference to Height Ratio. *Nutrients*. 2020 ;12(5):1250.
22. García Muñoz AI, Melo Buitrago PJ, Rodríguez Arcila MA, Silva Zambrano DA. Índices aterogénicos y composición corporal en cadetes de una escuela de formación militar colombiana. *Sanid Mil* 2020; 76 (1): 13-18
23. Abdelhaq Abbes M, Bereksi-Repuig K. Impact of Low Caloric Diet and Exercise on Atherogenic Indices in Obese Hypertensive Adults. *Romanian Journal of Diabetes Nutrition and Metabolic Diseases* 2018; 25(4):369-75
24. Edwards MK, Loprinzi PD. Physical activity and diet on atherogenic index of plasma among adults in the United States: mediation considerations by central adiposity. *Eur J Clin Nutr*. 2018;72(6):826-31.
25. Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, RuizGutiérrez V, Covas MI, et al. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med* 2006; 145:1-11
26. Moussavi Javardi MS, Madani Z, Movahedi A, Karandish M, Abbasi B. The correlation between dietary fat quality indices and lipid profile with Atherogenic index of plasma in obese and non-obese volunteers: a cross-sectional descriptive-analytic case-control study. *Lipids Health Dis*. 2020;19(1):213.

Classification of blood pressure with JNC-7 criteria in spanish working population: influence of age, sex, social class and tobacco consumption

Clasificación de la presión arterial con criterios JNC-7 en la población laboral española: influencia de la edad, el sexo, la clase social y el consumo de tabaco

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Abstract

Introduction: The Hypertension is a major health problem and is considered the leading cause of death in the world. The aim of this study was to determine the influence of sociodemographic variables and tobacco consumption on the prevalence of arterial hypertension in a large group of Spanish workers.

Material and methods: Descriptive and cross-sectional study in 418,343 Spanish workers to determine the prevalence of blood pressure values using the JNC7 criteria by linking them to sociodemographic variables and tobacco consumption.

Results: The prevalence of Hypertension is 20.7% (27% in men and 11.9% in women). The variable that most influences the onset of Hypertension is age with an Odds ratio of 3.77 (95% CI 3.71-3.84), also sex and social class show influence, while tobacco consumption as a mild protective factor.

Conclusions: The prevalence of Hypertension in the working population increases with age and in the lowest social classes being the far higher values in men. It is therefore necessary to implement campaigns.

Keywords: Blood pressure, hypertension, sociodemographic variables, tobacco.

Resumen

Introducción: La hipertensión arterial es un importante problema de salud y se considera la primera causa de muerte en el mundo. El objetivo de este estudio fue determinar la influencia de las variables sociodemográficas y del consumo de tabaco en la prevalencia de hipertensión arterial en un amplio grupo de trabajadores españoles.

Material y métodos: Estudio descriptivo y transversal en 418.343 trabajadores españoles para determinar la prevalencia de los valores de presión arterial según los criterios del JNC7 relacionándolos con las variables sociodemográficas y el consumo de tabaco.

Resultados: La prevalencia de hipertensión es del 20,7% (27% en hombres y 11,9% en mujeres). La variable que más influye en la aparición de la hipertensión es la edad con una Odds ratio de 3,77 (IC 95% 3,71-3,84), también el sexo y la clase social muestran influencia, mientras que el consumo de tabaco como factor protector leve.

Conclusiones: La prevalencia de hipertensión en la población trabajadora aumenta con la edad y en las clases sociales más bajas siendo los valores muy superiores en los hombres. Por tanto, es necesario poner en marcha campañas de prevención, detección y tratamiento de la hipertensión arterial dirigidas a la población.

Palabras clave: Presión arterial, hipertensión, variables sociodemográficas, tabaco.

Introduction

The World Health Organization recognizes high blood pressure (HTA) as one of the major health problems and the leading cause of death in the world, with more than 9 million new diagnoses each year. It therefore considers it a global public health crisis with a prevalence of approximately 25% of adults, associated with a decline in life expectancy of 10-15 years¹.

The American Heart Association values Hypertension as the highest percentage risk factor for cardiovascular disease, constituting 40.6%, above smoking (13.7%), non-cardiac-healthy diet (13.2%), sedentary life (11.9%) and hyperglycemia (8.8%)².

It is the chronic disease most often treated by health professionals³. It is increasing in association with an aging population and an increase in obesity⁴. The greatest risk is its silent character, it is not perceived by the patient and only shows evident symptoms when it has already produced damage. From there the importance of realizing a periodic control in young people and, especially in adults as the age increases. The delay in diagnosis favors poor control and an increase in cardiovascular risk⁵.

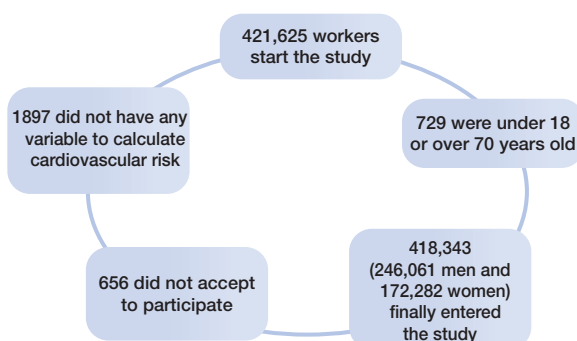
The aim of this study is to estimate the prevalence of blood pressure values, stratifying them by applying the criteria of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7)⁶ and relating them to clinical, social and demographic variables in the Spanish working population.

Materials and methods

Study design and setting.

A retrospective and transversal study is carried out on 418,343 workers from different Spanish geographical areas and belonging to different productive sectors during the period from January 2019 to June 2020. The workers were selected among those who attended the periodic occupational medical examinations. The flow chart is shown in **figure 1**.

Figure 1: Study participant flowchart.



1.1 Inclusión criteria

- Age between 18 and 70 years old.
- Be an active worker
- Agree to participate in the study.

Data collection and management

The anthropometric measurements of height and weight, clinical and analytical, have been made by the health personnel of the different occupational health units participating in the study, after homogenizing the measurement techniques.

To measure the weight (expressed in kilograms) and the height (expressed in cm), a scale/height meter was used: model SECA 700 with capacity for 200 kg and 50 gram divisions, which has an added telescopic height meter SECA 220 with millimetric division and 60-200 cm interval. The BMI is calculated by dividing the weight by the height in meters squared.

The abdominal waist perimeter was measured in cm with a measuring tape: SECA model 20, with 1-200 cm interval and millimetric division. For evaluation, the person is placed in a standing position, feet together and trunk upright, abdomen relaxed and upper extremities hanging on both sides of the body. The measuring tape is placed parallel to the floor at the level of the last floating rib.

The blood pressure was examined in supine position with a calibrated OMRON M3 automatic sphygmomanometer and after 10 minutes of rest. Three determinations were made at one-minute intervals, obtaining the mean value of the three. Blood pressure was classified according to criteria JNC-7.

The blood samples were obtained by peripheral venipuncture after 12 hours of fasting and were sent to the reference laboratories where they were processed within a maximum time of 48-72 hours. Glycaemia, total cholesterol and triglycerides were determined by automated enzymatic methods, expressing the values in mg/dl. HDL is calculated by precipitation with dextran-sulphate C12Mg, and values are expressed in mg/dl. The LDL is estimated by means of the Friedewald formula (provided that the triglycerides are lower than 400 mg/dl) and is expressed in mg/dl.

Friedewald formula: $LDL-c = \frac{\text{Total cholesterol} - \text{HDL-c} - \text{triglycerides}}{5}$

A smoker is a person who has regularly consumed at least 1 cigarette/day (or the equivalent in other types of consumption) in the last month, or has stopped smoking less than a year ago.

The social class is determined from the 2011 National Classification of Occupations (CNO-11), based on the proposal of the group of social determinants of the

Spanish Society of Epidemiology [7]. It is classified into 3 categories: Class I. Directors/managers, university professionals, athletes 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 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 association analysis is carried out by means of the test of chi 2 (with correction of the exact Fisher statistic when conditions require it) and the Student t for independent samples. For multivariate analysis, binary logistic regression with Wald's method has been used, with the calculation of Odds ratios and the Hosmer-Lemeshow goodness-of-fit test is performed. The statistical analysis is carried out with the program SPSS 27.0 with the accepted statistical significance level of 0.05.

Ethics statement

Approval for the study was obtained from Balearic Islands Health Area Clinical Research Ethics Committee (institutional review board approval number: IB 4383/20). The study was designed in accordance with the ethical guidelines of the Declaration of Helsinki. All participants sign written informed consent documents before participating in the study.

Study participant flowchart is shown in figure 1.

Results

Our sample corresponds to a male-dominated population, average age 39-40 years, overweight, average blood pressure within normal values and discreetly high total cholesterol figures.

All the studied parameters, anthropometric (height, weight, BMI and waist circumference), clinical (blood pressure) and analytical (lipid profile and glycaemia) present more unfavorable average values in males, with statistically significant differences. In both sexes, the most frequent age group is 30-49 years old and the predominant social class is III. One third of the participants in our study are smokers, being equally distributed in both genders.

Table I.

The prevalence of blood pressure values according to JNC7 classification in both sex is shown in figure 2.

Figure 2: Prevalence of blood pressure values according to JNC7 classification by sex (in percentage).

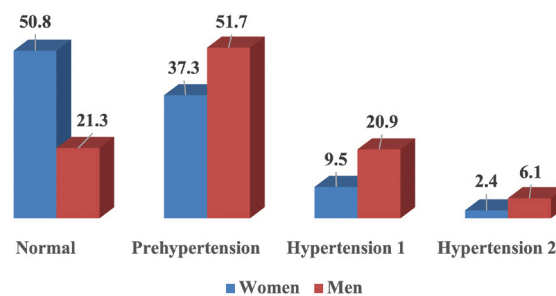


Table I: Sociodemographic, anthropometric, clinical and analytical characteristics of the sample.

	Women n=172.282 mean (SD)	Men n=246.061 mean (SD)	Total n=418.343 mean (SD)	p-value
Age	39.6 (10.8)	40.6 (11.1)	40.2 (11.0)	<0.0001
Height	161.8 (6.5)	174.6 (7.0)	169.4 (9.3)	<0.0001
Weight	66.2 (14.0)	81.4 (14.7)	75.1 (16.2)	<0.0001
BMI	25.3 (5.2)	26.7 (4.5)	26.1 (4.8)	<0.0001
Waist circumference	74.8 (10.6)	86.2 (11.1)	81.5 (12.2)	<0.0001
Systolic blood pressure	117.4 (15.7)	128.2 (15.5)	123.7 (16.5)	<0.0001
Dyastolic blood pressure	72.6 (10.4)	77.8 (11.0)	75.6 (11.0)	<0.0001
Total cholesterol	190.6 (35.8)	192.6 (38.9)	191.8 (37.7)	<0.0001
HDL-c	56.8 (8.7)	50.3 (8.5)	53.0 (9.1)	<0.0001
LDL-c	116.1 (34.8)	118.0 (36.7)	117.2 (35.9)	<0.0001
Triglycerides	89.1 (46.2)	123.7 (86.4)	109.5 (74.6)	<0.0001
Glycaemia	87.8 (15.1)	93.3 (21.3)	91.0 (19.2)	<0.0001
	Percentage	Percentage	Percentage	p-value
18-29 years	20.7	18.8	19.6	<0.0001
30-39 years	29.7	27.6	28.4	
40-49 years	29.6	30	29.9	
50-59 years	16.8	19.7	18.5	
60-70 years	3.2	3.9	3.6	
Social class I	6.9	4.9	5.7	<0.0001
Social class II	23.4	14.9	18.4	
Social class III	69.7	80.3	75.9	
No Smokers	67.2	66.6	66.9	<0.0001
Smokers	32.8	33.4	33.2	

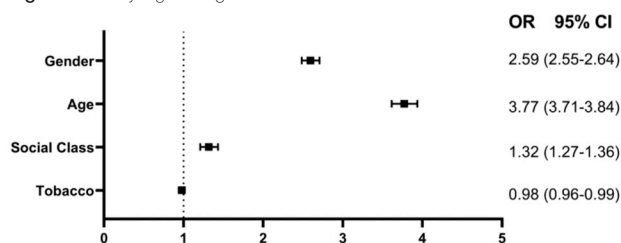
Table II: Prevalence of blood pressure values with JNC-7 classification according to age, social class and tobacco by sex.

	Women						Men					
	n	Normal %	Prehypertension %	Hypertension 1 %	Hypertension 2 %	p-value	n	Normal %	Prehypertension %	Hypertension 1 %	Hypertension 2 %	p-value
18-29 years	35617	63.8	32.5	3.3	0.4	<0.0001	46215	29.8	56.6	12.2	1.4	<0.0001
30-39 years	51115	61.6	32.6	4.9	0.9		67798	26.5	55.5	15.4	2.6	
40-49 years	51017	46.5	40.1	10.6	2.8		73935	18.8	51.8	22.8	6.6	
50-59 years	28951	29.4	45.0	19.6	6.0		48522	12.1	44.4	31.0	12.5	
60-70 years	5582	18.8	45.2	27.3	8.7		9591	8.7	39.6	36.0	15.7	
Social class I	11894	60.3	32.7	5.8	1.2	<0.0001	11950	22.0	53.9	19.2	4.9	<0.0001
Social class II	40266	53.6	36.5	8.0	1.9		36590	20.0	53.4	20.9	5.7	
Social class III	120122	48.9	38.0	10.3	2.8		197521	21.5	51.3	21.0	6.2	
No Smokers	115727	50.5	37.4	9.6	2.5	<0.0001	163920	21.1	51.8	21.0	6.1	<0.0001
Smokers	56555	51.3	37.1	9.2	2.4		82141	21.7	51.7	20.7	5.9	

The prevalence of arterial hypertension, both together and separately, increases as age increases in both genders. Similarly, its prevalence increases in parallel in men and women as they descend in social class. The prevalence of hypertension is slightly higher in the non-smoking group compared to that of smokers. In all cases the differences show statistical significance. (See **table II**).

The multivariate analysis by means of binary logistic regression establishes as covariates the male sex, the age from 50 years, the tobacco consumption and the social class II-III. The variable that shows greater influence in the appearance of hypertension is age with an Odds ratio of 3.77 (95% CI 3.71-3.84). Gender and social class also influence while tobacco consumption as a mild protective factor. (See **figure 3**).

Figure 3: Binary logistic regression



Discussion

Essential hypertension is still the most frequently diagnosed disease among patients who come to the Primary Care outpatient clinic today. Its importance lies in its high prevalence and its association with high cardiovascular and renal morbidity and mortality.

The absence of a clear threshold for the association of blood pressure and risk of cardiovascular events and the existence of lifestyle factors that predispose to hypertension and whose modification is very difficult in practice, despite having been shown to reduce CVD, means that primary prevention continues to be considered as a real possibility that is doubtful and has already been described as utopian in previous studies⁹.

In our study the overall prevalence of hypertension is 27% in men and 11.9% in women, data that differs from the study Di@bet.es⁹ conducted in the general population with 5,048 people over 18 years, where the overall prevalence of hypertension was 42.6%, however, coincide with our results by gender, with higher figures for men 49.9% than for women 37.1%.

The analysis of the relationship of blood pressure figures with age and gender in our results reveals that they increase with increasing age, with the most unfavorable values in all cases in men, although these differences decrease between genders at ages over 59. Our results coincide with other studies that find an increase in hypertension prevalence with age and male gender¹⁰. This association between high blood pressure values with age is also observed in various population studies and leads to strict control of patients throughout their lives, but especially with aging¹¹⁻¹³.

The young population is less aware of the idea of illness, so primary prevention activities are complex and not very effective. This task can be developed from the basic units of occupational health in companies that complement the function of primary health care. Previous studies obtain a better result at a higher educational level and social status with greater acceptance of the treatments in case of needing them. In this work, white collars were less likely to suffer from hypertension compared to blue collars¹⁴, which coincides with the results of our study of the worst results in terms of blood pressure in the population of both genders belonging to class III (which corresponds to blue collar workers) than in class I (white collar).

We found no relationship between the higher blood pressure figures and the consumption of tobacco referred to by other authors who defend that tobacco-induced mitochondrial oxidative stress contributes to endothelial dysfunction and the development of hypertension¹⁵.

Cardiovascular diseases are the leading cause of death in our country and also lead to a high degree of disability and health expenditure. Atherosclerosis is a disease with

a multifactorial cause, so its prevention requires a global approach that takes into account the different risk factors with which it is associated, among which hypertension occupies a prominent place¹⁶. Outpatient monitoring (MAPA) is by far the best clinical tool for estimating an individual's blood pressure. There is no scientific or clinical justification for ignoring these advantages, so MAPA should be part of the evaluation and follow-up of practically all hypertensive patients and to act in prevention with the advantages that its use implies for both the physician and the patient¹⁷.

Our results show that it is possible to carry out preventive activities in hypertension in the workplace with access to large population samples, as well as interventions from occupational health as has been referred to by other authors with results in controlling hypertension and modifying unhealthy lifestyle habits. These multilevel actions are recommended for large-scale use or inclusion in workplace hypertension control programs¹⁸.

The scope for improvement in the diagnosis and treatment of hypertension among employees in a company is very broad. Effective intervention programs based on epidemiological

studies of large samples such as the one presented here are urgently needed and constitute its greatest strength. Among the limitations of our study are the lack of a comparative group of non-working people, the limitation to age groups between 18 and 70 years, and the greater participation of men, which does not allow extrapolating the results to the general population. As this is a population that regularly attends its health check-ups in prevention services, better results could be obtained than in the general population. This could be a source of confusion.

Conclusion

The prevalence of high blood pressure in the working population increases with age and in lower social classes, in both genders. We propose to implement campaigns of prevention, detection and treatment of arterial hypertension directed to the general population, being of special interest the work in primary prevention from the units of labor health and by the doctor of the work.

Interests conflict

The researchers declare that they have no conflict of interest.

References

- Organización Mundial de la Salud. Información general sobre la Hipertensión en el mundo. Día mundial de la Salud 2013. Documento N(WHO/DCO/WHD/2013.2. Accedido el 24 julio 2014. Available at: http://apps.who.int/iris/bitstream/10665/87679/1/WHO_DCO_WHD_2013.2_spa.pdf?ua=1.
- Benjamin EM, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation* 2019; 139(10): e56-e528
- La hipertensión arterial, principal motivo de consulta en atención primaria. *Jano.es* 16 de mayo 2013. Available at: <https://jano.es/noticia-la-hipertension-arterial-principal-motivo-19743>
- El envejecimiento poblacional, la obesidad y el sedentarismo pueden elevar la prevalencia de hipertensión en España. Available at: <https://medicosypacientes.com/articulo/el-envejecimiento-poblacional-la-obesidad-y-el-sedentarismo-pueden-elevar-la-prevalencia-de-hipertension-arterial-en-Espana>
- De Burgos-Lunar C, Cura-González I, Salinero-Fort MA, et al. Retraso diagnóstico de la hipertensión arterial en pacientes diabéticos atendidos en atención primaria. *Rev Esp Cardiol* 2013;66(9):700-6
- Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7 Express). Available at: https://www.paho.org/hq/dmdocuments/2010/JNC7_interactivo.pdf
- Domingo-Salvany A, Bacigalupe A, Carrasco JM, et al. Propuesta de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011. *Gac Sanit* 2013;27(3):263-72
- Campo C, Roldán C, Segura J. Prevención primaria de la HTA: posibilidad real o utopía? Detección precoz de la HTA [Primary prevention of arterial HT: real possibility or utopia? Early detection of arterial HT]. *Nefrología*. 2005;25 Suppl 4:7-12.
- Menéndez E, Delgado E, Fernández-Vega F, et al. Prevalencia, diagnóstico, tratamiento y control de la hipertensión arterial en España. *Resultados del estudio Di@bet.es*. *Rev Esp Cardiol* 2016;69(6):572-8
- Bianchi MEV, Cusumano AM, Torres C, et al. Prevalencia de obesidad e hipertensión arterial y su asociación con edad y sexo en la ciudad de Resistencia (Argentina), años 2008-2014. *Hipertens Riesgo Vasc*. 2019 Jan-Mar;36(1):14-20.
- Wagner A, Sadoun A, Dallongeville J, et al. High blood pressure prevalence and control in a middle-aged French population and their associated factors: the MONA LISA study. *J Hypertens* 2011; 29:43-50
- Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. *JAMA* 201; 303:2043-50
- Guo F, He D, Zhang W, et al. Trends in prevalence, awareness, management, and control of hypertension among United States adults, 1999 to 2010. *J Am Coll Cardiol* 2012; 60:599-606.
- Shen Y, Wang X, Wang Z, et al. The Standardized Management of Hypertensive Employees Program. Prevalence, awareness, treatment, and control of hypertension among Chinese working population: results of a workplace-based study. *J Am Soc Hypertens*. 2018 Apr;12(4):311-322.e2.
- Dikalov S, Itani H, Richmond B, et al. Tobacco smoking induces cardiovascular mitochondrial oxidative stress, promotes endothelial dysfunction, and enhances hypertension. *Am J Physiol Heart Circ Physiol*. 2019 Mar 1;316(3):H639-H646.
- Mostaza JM, Pintó X, Armario P, et al. Standards for global cardiovascular risk management arteriosclerosis. *Clin Investig Arterioscler*. 2019 Jul;31 Suppl 1:1-43
- De la Sierra A. Ambulatory blood pressure monitoring is a useful tool for all patients. *Hipertens Riesgo Vasc*. 2017 Jan-Mar;34(1):45-49.
- Wang Z, Wang X, Shen Y, et al. Effect of a Workplace-Based Multicomponent Intervention on Hypertension Control: A Randomized Clinical Trial. *JAMA Cardiol*. 2020 May 1;5(5):567-575.

ORIGINAL

Determination of different scales of cardiovascular risk in 1.979 spanish informatics workers

Determinación de diferentes escalas de riesgo cardiovascular en 1.979 informaticos españoles

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Abstract

Introduction: Cardiovascular diseases are the leading cause of morbidity and mortality in almost all countries of the world. The aim of this study was to determine the level of cardiovascular risk in the group of computer workers.

Methods: A descriptive, cross-sectional study was carried out in 1979 computer scientists (1684 men and 2945 women) in which different scales related to cardiovascular risk were assessed: overweight and obesity, body fat estimation, cardiometabolic indicators, atherogenic indices, non-alcoholic fatty liver disease risk scales and cardiovascular risk scales.

Results: Among the computer scientists, a high prevalence of smoking was found (30.8% in men and 33.2% in women), a prevalence of obesity determined by BMI of 14.6% in women and 19.2% in men. The prevalence of hypertension was much higher in men (27.6%) than in women (6.8%). Metabolic syndrome with IDF criteria was present in 3.4% of women and 12.9% of men. Hypertension was observed in 27.6% of men and 6.8% of women. Finally, 10.3% of men had moderate or high risk levels according to the REGICOR model, while the percentage in women was 4.7%.

Conclusions: The level of cardiovascular risk found in IT workers can be considered high for a population with an average age of 37 years and especially in men.

Keywords: Cardiovascular risk, obesity, metabolic syndrome, body fat mass, atherogenic indices, workers.

Resumen

Introducción: Las enfermedades cardiovasculares son la principal causa de morbilidad y mortalidad en casi todos los países del mundo. El objetivo de este estudio fue determinar el nivel de riesgo cardiovascular en el grupo de trabajadores informáticos.

Métodos: Se realizó un estudio descriptivo y transversal en 1979 informáticos (1684 hombres y 2945 mujeres) en el que se valoraron diferentes escalas relacionadas con el riesgo cardiovascular: sobrepeso y obesidad, estimación de la grasa corporal, indicadores cardiometabólicos, índices aterogénicos, escalas de riesgo de enfermedad de hígado graso no alcohólico y escalas de riesgo cardiovascular.

Resultados: Entre los informáticos se encontró una alta prevalencia de tabaquismo (30,8% en hombres y 33,2% en mujeres), una prevalencia de obesidad determinada por el IMC de 14,6% en mujeres y 19,2% en hombres. La prevalencia de hipertensión fue mucho mayor en los hombres (27,6%) que en las mujeres (6,8%). El síndrome metabólico con criterios de la FID estaba presente en el 3,4% de las mujeres y el 12,9% de los hombres. La hipertensión se observó en el 27,6% de los hombres y en el 6,8% de las mujeres. Por último, el 10,3% de los hombres presentaban niveles de riesgo moderado o alto según el modelo REGICOR, mientras que el porcentaje en las mujeres era del 4,7%.

Conclusiones: El nivel de riesgo cardiovascular encontrado en los trabajadores de IT puede considerarse alto para una población con una edad media de 37 años y especialmente en los hombres.

Palabras clave: Riesgo cardiovascular, obesidad, síndrome metabólico, masa grasa corporal, índices aterogénicos, trabajadores.

Introduction

The World Health Organization launched in 2013 a global action plan for all countries to reduce premature mortality, this initiative focused on strengthening health, services and public policies with the aim of preventing and managing four major non-communicable diseases: cardiovascular diseases, cancer, diabetes mellitus and chronic respiratory diseases as these are the major contributors to global morbidity and mortality. Of all of them, cardiovascular diseases are the most susceptible to obtain rapid changes¹.

The main risk factors for cardiovascular diseases are well known and include mainly smoking, high blood pressure, dyslipidemia, diabetes mellitus, and obesity; thus, these are the most commonly used parameters to assess cardiovascular risk in the general population².

Low physical activity (considered as less than 30 minutes of moderate intensity at least 5 days per week, less than 20 minutes of vigorous intensity physical activity at least 3 days per week or less than 600 metabolic equivalents-min per week) is part of the cardiovascular risk factors although it does not rank first¹.

Computer science is considered as a science with a low volume of motor activity, sedentary, with prolonged postures in time and intense hours of mental work, elements that together with the ergonomic factors of the work can cause different discomforts and ailments that have been qualified as diseases of this profession³.

Control over excessive workloads and time pressures have been studied in these workers, factors that can increase work stress and foster or exacerbate a psychophysiological response, as well as the potential development of musculoskeletal symptoms and disorders⁴. The most prevalent health disorders in these professionals have been musculoskeletal, ocular, and mental disorders⁵. Studies of vision impairment have also been described, although it has been noted that the incidence of eye symptoms was somewhat lower than the incidence of symptoms in the neck, shoulders, arms, and hands⁶. Many studies have been aimed at determining musculoskeletal conditions among IT or computer workers⁷⁻¹⁰. Other conditions that can appear in computer scientists include cardiovascular and kidney problems, obsessive behaviors, eyestrain, migraines, weight gain¹¹. In summary, stress, headache, back pain, cervical pain, gastric problems, astigmatism, chest tightness, breathing difficulties, sadness, irritability, isolation, obesity, hypertension, depression, cardiovascular and renal problems are among the common conditions of these professionals¹².

Although the possible occurrence of cardiovascular diseases is mentioned in several of these investigations,

we have not found epidemiological studies that analyze the incidence of cardiovascular risk in this group of workers, which is why our work has set out to perform a detailed analysis of the factors and parameters related to cardiovascular risk among IT professionals.

Methods

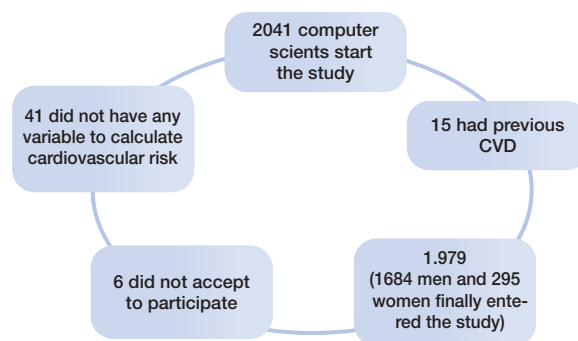
A retrospective and cross-sectional study was carried out in 1.979 informatics scientist between January 2019 and December 2020. The workers were selected based on their attendance to periodic occupational medical examinations.

Selection criteria:

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

Of the 2.041 informatics scientist initially included in the study, 41 were excluded due to not having data from all the necessary variables to calculate the cardiovascular risk indicators; 15 had suffered CVD previously; and 6 did not give permission to participate in the study. The final number of workers included in the study was 1.979. See flow chart in **figure 1**.

Figure 1: Participant flow chart.



Anthropometric, clinical and analytical measures were carried out by the healthcare professionals of the different 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 and height: weight (in kilograms) and height (in cm) were determined with a height bar scale (model: SECA 700 with a capacity of 200 kg and 50-gram divisions, to which was added a SECA 220 telescopic height bar with millimetric division and 60-200 cm intervals).
- Abdominal waist circumference (cm): was measured

with a SECA model 200 tape measure. The individual was placed in a standing position, with the feet together and the trunk erect, the abdomen relaxed and the upper extremities hanging on both sides of the body. The tape measure was then placed parallel to the ground at the height of the last floating rib.

- Blood pressure: blood pressure was measured in the supine position with a calibrated OMRON M3 automatic sphygmomanometer and after a 10-minute rest period. Three determinations were made at one-minute intervals, obtaining the mean of the three. Hypertension was considered when the values were equal to or higher than 140 mm Hg systolic or 90 mm Hg diastolic blood pressure.
- Blood glucose, total cholesterol and triglycerides: These were determined by peripheral venipuncture and after fasting for at least 12 hours. Automated enzymatic methods were used. HDL was determined by precipitation with dextran sulfate Cl2Mg. 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: $LDL = \text{total cholesterol} - HDL - \text{triglycerides} / 5$
- Blood glucose values were classified according to the recommendations of the American Diabetes Association¹³, considering hyperglycemia >125 mg/dL. High cholesterol >239 mg/dL, high LDL >159 mg/dL, and high triglycerides >200 mg/dL were considered high.

The cut-off points for the atherogenic indexes were¹⁴:

- Cholesterol/HDL (considered as high values >5 in men and >4.5 in women),
- LDL/HDL and Triglycerides/HDL (high values >3)

Metabolic syndrome was determined using three models:

a) The NCEP ATP III (National Cholesterol Educational Program Adult Treatment Panel III), which considers metabolic syndrome when three or more of the following factors are present: waist circumference >88 cm in women and 102 cm in men; triglycerides >150 mg/dL or specific treatment for this lipid disorder; blood pressure >130/85 mm Hg; HDL <40 mg/dL in women or <50 mg/dL in men or specific treatment is followed, and fasting blood glucose >100 mg/dL or specific glycemic treatment.

b) The International Diabetes Federation (IDF) model¹⁵ establishes as necessary the presence of central obesity, defined by a waist circumference >80 cm in women and >94 cm in men, and also at least two of the other factors mentioned above for ATP III.

c) The JIS¹⁶ model, which uses the same criteria as the NCEP ATPIII, but the waist cut-off points are those seen in the IDF model.

Hypertriglyceridemic waist¹⁷ required: waist circumference greater than 94 cm in men and greater than 80 cm in women and triglycerides greater than 150 mg/dl or treatment of hypertriglyceridemia.

The REGICOR scale is an adaptation of the Framingham scale to the Spanish population¹⁸ and estimates the risk of suffering a cerebrovascular event over a 10-year period. It can be applied between 35 and 74 years of age. It is considered moderate risk >5% and high risk >10%¹⁹. The SCORE scale is the version recommended for Spain²⁰⁻²¹ and estimates the risk of suffering a fatal cerebrovascular event over a 10-year period. It is used between 40 and 65 years of age and we speak of risk >4% and high >5%. To determine vascular age, calibrated tables²² are used to assess the degree of aging of the arteries and can be calculated from the age of 30 years.

Vascular age with the Framingham model²³ uses age, sex, HDL-c, total cholesterol, systolic blood pressure, antihypertensive treatment, smoking and diabetes. The scale can be calculated from the age of 30 years. Vascular age with the SCORE²⁴ model is calculated using age, sex, systolic blood pressure, smoking and total cholesterol. As with the SCORE scale from which it derives, it can be calculated in people between 40 and 65 years of age. An interesting concept applicable to both vascular ages is avoidable lost life years (ALLY)²⁵, which can be defined as the difference between biological age (BI) and vascular age (VE).

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

The different indicators are calculated using the following formulas:

Visceral adiposity index²⁶ (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:

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

Waist triglyceride index²⁷ Waist circumference (cm) x triglycerides (mmol).

Body shape index (ABSI)²⁸.

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

Normalized weight-adjusted index (NWA)²⁹

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

Conicity index³⁰

$$\frac{\text{waist circumference (in metres)}}{0,109} \times 1 \sqrt{\frac{\text{Weight (in kilogram)}}{\text{Height (in metres)}}$$

Lipid accumulation product³¹

- In men: (waist circumference (cm) - 65) x (triglyceride concentration (mMol)).
- In women: (waist circumference (cm) - 58) x (triglyceride concentration (mMol))

Cardiometabolic index³²

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

Triglyceride glucose index³³ = LN (triglycerides [mg/dl] x glycaemia [mg/dl]/2).

Triglyceride glucose index-BMI, Triglyceride glucose index-waist³⁴

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

Atherogenic dyslipidemia is characterized 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 LDL³⁵.

Body mass index (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 0.50³⁶.

Body Surface Index³⁷ (BSI). BSA is calculated using the DuBois formula where w represents weight in kg and h represents height in cm.

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

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

It is considered diabetes when the person has blood glucose levels above 126 mg/dl or is under treatment for diabetes and has a BMI of 30 kg/m² or more³⁸.

Formulas to estimate the percentage of body fat:

$$\text{- Relative fat mass}^{39} = 76 - (20 \times (\text{height/p waist}))$$

Where the height and waist circumference are expressed in meters. The cut-off points for obesity are 33.9% in women.

- CUN BAE⁴⁰ (University of Navarra Body Adiposity Estimator Clinic) using the following formula:

$$-44.988 + (0.503 \times \text{age}) + (10.689 \times \text{sex}) + (3.172 \times \text{BMI}) - (0.026 \times \text{BMI}^2) + (0.181 \times \text{BMI} \times \text{sex}) - (0.02 \times \text{BMI} \times \text{age}) - (0.005 \times \text{BMI}^2 \times \text{sex}) + (0.00021 \times \text{BMI}^2 \times \text{age})$$

- ECORE-BF (Equation COrdoba Estimator Body Fat)⁴¹

$$-97.102 + 0.123 (\text{age}) + 11.9 (\text{gender}) + 35.959 (\text{LnBMI})$$

Male = 0 Female = 1

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

- Palafolls formula⁴².

$$\text{Men} = (\text{BMI/waist}] \times 10) + \text{BMI}. \text{Women} = (\text{BMI/waist}] \times 10) + \text{BMI} + 10.$$

- Deuremberg formula⁴³.

$$1,2 \times (\text{BMI}) + 0,23 \times (\text{age}) - 10,8 \times (\text{gender}) - 5,4$$

Male = 0 Female = 1

Body Roundness Index⁴⁴ (BRI)

$$BRI = 365.2 - 365.5 \times \sqrt{1 - (((wc/2\pi)^2)/[(0.5 \times \text{height}]^2))}$$

Where WC represents the waist circumference.

Non-alcoholic fatty liver:

- Fatty liver index (FLI)⁴⁵

$$FLI = \left(\frac{e^{0.953 \times \log_e (\text{triglycerides}) + 0.139 \times \text{BMI} + 0.718 \times \log_e (\text{GGT}) + 0.053 \times \text{waist circumference} - 15.745}}{1 + e^{0.953 \times \log_e (\text{triglycerides}) + 0.139 \times \text{BMI} + 0.718 \times \log_e (\text{GGT}) + 0.053 \times \text{waist circumference} - 15.745}} \right) \times 100$$

FLI scores of 60 and above indicate high risk.

- Hepatic steatosis index (HSI)⁴⁶

$$HSI = 8 \times \text{ALT/AST} + \text{BMI} (+ 2 \text{ if type 2 diabetes yes, } + 2 \text{ if female})$$

- Zhejiang University index (ZJU)⁴⁷

$$\text{BMI} + \text{FPG mmol L} + \text{TG mmol L} + 3 \text{ ALT/AST} + 2 \text{ if female}$$

- Fatty liver disease index (FLD)⁴⁸
 $BMI + TG + 3 \times (ALT/AST) + 2 \times \text{Hyperglycaemia}$
 (presence= 1; absence = 0)

Values <28.0 or >37.0 excluded the possibility of NAFLD

BMI $\geq 28 = 1$ point, AST/ALT $\geq 0.8 = 2$ points, type 2 diabetes mellitus = 1 point.

Cut off for high risk 2 points

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

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. A bivariate association analysis was performed using the χ^2 test (with a correction with the Fisher's exact statistical test, when conditions required so) and a Student's t-test for independent samples. For the multivariate analysis, binary logistic regression was used with the Wald method, with the calculation of the Odds-ratio and the Hosmer-Lemeshow goodness-of-fit test was performed. Statistical analysis was performed with the SPSS 27.0 program, and a p value of <0.05 was considered as statistically significant.

Considerations and ethical aspects

The study was approved by the Clinical Research Ethics Committee of the Illes Balears Health Area in November 2020. 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 average age of the IT workers included in our study is not too high, around 37 years old. Women smoke more than men. The clinical and analytical variables are more unfavorable in men, the differences being statistically significant in most cases as can be seen in **table I**.

Most of the indicators related to cardiovascular risk analyzed in this study show higher mean values in men, as is the case for non-alcoholic fatty liver disease risk scales, cardiometabolic indicators, atherogenic indices and cardiovascular risk scales. When overweight and obesity scales are assessed we can see that those not related to body fat also show higher mean values in men, while when body fat predictive scales are analyzed the mean values are higher in women, as it is known that normal body fat values in women are higher than in men. The differences observed between the sexes for all scales show statistical significance. The complete data can be found in **table II**.

Something similar to that observed with the mean values occurs when analyzing the prevalence of altered values of the scales related to cardiovascular risk, in this case all the scales (overweight and obesity, non-alcoholic fatty liver disease risk, cardiometabolic risk, atherogenic indices and cardiovascular risk scales) show higher prevalence in men, with the differences observed always being statistically significant. All data can be found in **table III**.

Table I: Characteristics of the informatics scientist by gender.

	Women n=295 Mean (SD)	Men n=1684 Mean (SD)	p-value
Age (years)	36.2 (8.5)	37.3 (8.8)	0.051
Height (cm)	163.5 (6.5)	176.5 (7.1)	<0.0001
Weight (cm)	66.3 (15.0)	82.7 (15.2)	<0.0001
Waist (cm)	75.2 (11.5)	86.8 (11.8)	<0.0001
Systolic Blood Pressure (mmHg)	115.2 (12.8)	128.5 (14.1)	<0.0001
Diastolic Blood Pressure (mmHg)	71.8 (9.6)	78.3 (10.8)	<0.0001
Total cholesterol (mg/dl)	187.8 (32.6)	189.2 (32.3)	0.531
HDL-c (mg/dl)	59.5 (9.4)	51.8 (8.4)	<0.0001
LDL-c (mg/dl)	111.1 (29.9)	114.3 (34.1)	0.129
Triglycerides (mg/dl)	86.1 (42.5)	116.2 (65.4)	<0.0001
Glycaemia (mg/dl)	86.2 (10.5)	89.3 (14.9)	0.001
ALT (U/l)	18.1 (9.8)	30.1 (18.2)	<0.0001
AST (U/l)	14.6 (5.3)	22.0 (13.0)	<0.0001
GGT (U/l)	17.2 (11.7)	32.1 (29.7)	<0.0001
	Percentage	Percentage	p-value
18-29 years	24.4	21.0	0.015
30-39 years	40.3	38.4	
40-49 years	29.5	32.0	
50-69 years	5.8	8.6	
Non-Smokers	66.8	69.2	0.021
Smokers	33.2	30.8	

Table II: Mean values of the different CVR scales according to gender in informatics scientist.

	Women n=295 Mean (SD)	Men n=1684 Mean (SD)	p-value
Waist to height ratio	0.46 (0.07)	0.49 (0.06)	<0.0001
Body mass index (BMI)	24.8 (5.2)	26.5 (4.4)	<0.0001
CUN BAE	34.0 (7.2)	24.9 (6.3)	<0.0001
ECORE-BF	33.9 (7.1)	24.9 (5.9)	<0.0001
Relative fat mass	31.7 (5.6)	22.7 (4.9)	<0.0001
Palafolls formula	38.0 (5.5)	29.6 (4.5)	<0.0001
Deuremberg formula	32.6 (6.6)	24.2 (5.9)	<0.0001
Body surface index	50.3 (8.6)	58.4 (8.0)	<0.0001
Normalized weight adjusted index	0.3 (1.4)	0.6 (1.4)	<0.0001
Body roundness index	2.7 (1.3)	3.3 (1.2)	<0.0001
Body shape index	0.070 (0.006)	0.074 (0.006)	<0.0001
Visceral adiposity index	2.5 (1.5)	6.8 (5.0)	<0.0001
Conicity index	1.1 (0.1)	1.2 (0.1)	<0.0001
Fatty liver index	16.4 (21.1)	36.7 (27.5)	<0.0001
Hepatic steatosis index	34.9 (5.5)	37.5 (6.5)	0.001
Zhejiang University index	35.6 (5.4)	37.3 (5.3)	0.008
Fatty Liver Disease index	28.8 (5.2)	32.3 (5.1)	<0.0001
Lipid accumulation product	17.9 (18.7)	30.7 (28.1)	<0.0001
Triglyceride glucose index	8.1 (0.4)	8.4 (0.5)	<0.0001
Triglyceride glucose index-BMI	201.8 (46.6)	224.2 (44.4)	<0.0001
Triglyceride glucose index-waist	612.1 (106.6)	733.1 (121.3)	<0.0001
Triglyceride glucose index-WTHR	3.7 (0.6)	4.2 (0.6)	<0.0001
Waist triglyceride index	74.3 (43.4)	116.1 (72.3)	<0.0001
ALLY vascular age SCORE*	1.9 (4.7)	5.6 (6.0)	<0.0001
SCORE scale*	0.2 (0.9)	0.9 (1.5)	<0.0001
ALLY vascular age Framingham**	-2.8 (8.8)	4.5 (9.0)	<0.0001
REGICOR scale***	1.4 (1.2)	2.7 (1.6)	<0.0001
Nº factors of metabolic syndrome NCEP ATPIII	0.6 (0.9)	1.2 (1.1)	<0.0001
Nº factors of metabolic syndrome JIS	0.7 (0.9)	1.6 (1.3)	<0.0001
Cardiometabolic index	0.7 (0.5)	1.2 (0.9)	<0.0001
Atherogenic index total cholesterol/HDL-c	3.2 (0.6)	3.8 (1.0)	<0.0001
Atherogenic index triglycerides/HDL-c	1.5 (0.8)	2.4 (1.6)	<0.0001
Atherogenic index LDL-c/HDL-c	1.9 (0.6)	2.3 (0.9)	<0.0001

(*) Women n=104 Men n= 684 (**) Women n= 223 Men n=1331 (***) Women n=169 Men n=1030

Table III: Prevalence of altered values of the different CVR scales by gender in informatics scientist.

	Women n=295 Percentage	Men n=1684 Percentage	p-value
Waist to height ratio > 0.50	21.0	37.3	<0.0001
Body mass index obesity	14.6	19.2	<0.0001
CUN BAE obesity	38.6	45.2	<0.0001
ECORE-BF obesity	37.6	45.4	<0.0001
Relative fat mass obesity	26.8	47.0	<0.0001
Palafolls formula obesity	68.5	87.6	<0.0001
Deuremberg formula obesity	61.7	68.2	<0.0001
Hypertension	6.8	27.6	<0.0001
Total cholesterol ≥ 200 mg/dl	31.5	36.6	0.040
LDL-c ≥ 130 mg/dl	24.7	31.2	0.025
Triglycerides ≥ 150 mg/dl	5.1	21.4	<0.0001
Glycaemia 100-125 mg/dl	6.4	10.8	<0.0001
Glycaemia ≥ 126 mg/dl	0.3	1.8	<0.0001
Metabolic syndrome NCEP ATPIII	4.1	12.8	<0.0001
Metabolic syndrome IDF	3.4	12.9	<0.0001
Metabolic syndrome JIS	4.7	22.7	<0.0001
Atherogenic dyslipidemia	1.0	5.5	<0.0001
Lipid triad	0.0	1.2	<0.0001
Hypertriglyceridemic waist	2.0	7.9	<0.0001
Atherogenic index total cholesterol/HDL-c moderate-high	6.4	12.9	<0.0001
Atherogenic index triglycerides/HDL-c high	4.1	23.4	<0.0001
Atherogenic index LDL-c/HDL-c high	6.1	20.4	<0.0001
SCORE scale moderate-high	1.9	11.0	<0.0001
REGICOR scale moderate-high	4.7	10.3	<0.0001
Fatty liver index high risk	7.5	22.7	<0.0001
Hepatic steatosis index high risk	35.5	54.3	<0.0001
ZJU index high	25.8	37.6	<0.0001
Fatty liver disease index high	41.9	61.5	<0.0001

Table IV: Logistic regression analysis.

	≥ 50 years OR (95% CI)	Men OR (95% CI)	Smokers OR (95% CI)
Waist to height ratio > 0.50	ns	2.24 (1.66)	ns
Body mass index obesity	1.83 (1.27-2.63)	ns	1.30 (1.02-1.65)
CUN BAE obesity	4.11 (2.85-5.93)	ns	ns
ECORE-BF obesity	3.97 (2.76-5.71)	1.34 (1.04-1.73)	ns
Relative fat mass obesity	ns	2.41 (1.83-3.17)	ns
Palafolls formula obesity	2.27 (1.23-4.16)	3.20 (2.40-4.26)	ns
Deuremberg formula obesity	6.61 (4.46-9.80)	3.50 (2.87-4.65)	ns
Hypertension	3.27 (2.34-4.58)	5.16 (3.23-8.25)	ns
Total cholesterol ≥ 200 mg/dl	3.09 (2.22-4.30)	ns	ns
LDL-c ≥ 130 mg/dl	3.10 (2.24-4.30)	1.34 (1.00-1.78)	ns
Triglycerides ≥ 150 mg/dl	2.11 (1.48-3.01)	4.98 (2.92-8.50)	ns
Glycaemia 100-125 mg/dl	4.68 (3.26-6.72)	1.88 (1.16-3.05)	ns
Glycaemia ≥ 126 mg/dl	6.33 (2.97-13.49)	ns	ns
Metabolic syndrome NCEP ATPIII	4.62 (3.20-6.65)	3.37 (1.85-6.14)	ns
Metabolic syndrome IDF	2.44 (1.63-3.63)	4.17 (2.18-7.98)	ns
Metabolic syndrome JIS	3.51 (2.50-4.93)	5.84 (3.36-10.14)	ns
Atherogenic dyslipidemia	4.13 (2.51-6.79)	5.32 (1.67-16.96)	ns
Hypertriglyceridemic waist	1.81 (1.08-3.03)	4.03 (1.76-9.22)	ns
Atherogenic index total cholesterol/HDL-c moderate-high	2.74 (1.86-4.02)	2.10 (1.29-3.42)	ns
Atherogenic index triglycerides/HDL-c high	2.43 (1.72-3.44)	7.07 (3.92-12.76)	ns
Atherogenic index LDL-c/HDL-c high	2.71 (1.92-3.84)	3.85 (2.35-6.31)	ns
SCORE scale moderate-high	167.82 (60.21-467.75)	20.24 (3.79-108.18)	12.81 (5.58-29.46)
REGICOR scale moderate-high	31.68 (18.62-53.70)	3.02 (1.23-7.38)	7.65 (4.50-13.01)
Fatty liver index high risk	2.12 (1.48-3.05)	3.59 (2.24-5.76)	1.32 (1.03-1.68)
Hepatic steatosis index high risk	2.29 (1.10-4.79)	2.13 (1.32-3.42)	ns
ZJU index high	ns	1.72 (1.03-2.87)	ns
Fatty liver disease index high	ns	2.24 (1.40-3.56)	ns

In the multivariate analysis using binary logistic regression, age 50 years and older, tobacco use were established as covariates. Age over 50 years and male gender are the variables that most increase the risk of presenting high values of the scales related to cardiovascular risk, while smoking only increases the risk of obesity according to BMI, the risk with the REGICOR and SCORE scales and the risk of non-alcoholic fatty liver disease with the FLI. (See **table IV**)

Discussion

The most salient data obtained in our study are a high prevalence of smoking (30.8% in men and 33.2% in women), a prevalence of obesity determined by BMI of 14.6% in women and 19.2% in men. Hypertension was found in 27.6% of the men and 6.8% of the women, while only 3.4% of the women and 12.9% of the men had metabolic syndrome. Finally, 10.3% of the men had moderate or high risk levels according to the REGICOR model, the percentage in women being 4.7%.

We have not found any studies in the different databases consulted that analyze cardiovascular risk in the group of computer workers, so we decided to compare our results with those obtained in different studies that assessed cardiovascular risk in office workers, as both groups have a sedentary job and preferably use a computer for their work.

A study of 100 Pakistani office workers⁴⁹ (89% of them male) showed that the prevalence of smoking in this

group (19%) was much lower than that found in our work, while another study in the same country of 515 civil servants⁵⁰ (98% male) found a somewhat higher prevalence than ours (33.2%).

This same Pakistan study⁵⁰ also assessed the prevalence of excess weight, observing that 7.4% of the workers were obese (a much lower figure than ours), in contrast to the figures obtained in 235 Nigerian office workers⁵¹ (90% male) where the prevalence of obesity was 34.5%, although the average age was also higher than ours (43.3 years).

Two studies assessed the percentage of office workers with high blood pressure, and in both cases the prevalence found was lower than ours, in the first study 17.7% of 90 Iranian workers⁵² were hypertensive, while in the second study in Pakistan⁵⁰ the figure was somewhat higher (21.9%).

Metabolic syndrome using the IDF criteria in office workers was studied in 46 German male workers⁵³ with an average age of 45.8 years and found to have a very high prevalence of 33%, almost three times the figure found by us.

Three studies analyzed cardiovascular risk in office workers using the Framingham model, the first of which was conducted in 180 Iranian workers⁵⁴ of whom 70% were men, 9.5% had moderate or high risk levels. Slightly higher figures were obtained in Nigerian workers⁵¹ (16.5%

moderate and 5.5% high risk). The German study⁶³ mentioned above reported a prevalence of high risk of 10.7%. The values obtained in these three studies are higher than those obtained by us.

A study carried out on 249 women and 390 men working in offices in Vizcaya⁶⁵ found that 6% of the women and 23.9% of the men had high values of atherogenic indices, figures similar to ours in women but much higher in men.

Among the strong points of our study we can highlight that it is the first to analyze parameters and scales related to cardiovascular risk in computer workers, it is also

important to point out that the sample size is large, almost 2,000 workers, and the number of scales included is also very high. As limitations we would point out that the level of physical activity and diet, which are factors that can influence cardiovascular risk, have not been taken into account, as this information was not available.

We believe that it could be interesting to carry out studies similar to ours in other countries on a group such as IT workers, whose presence in companies is increasing.

Interests conflict

The researchers declare that they have no conflict of interest.

References

- Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, Mentz A, Yusuf S. Reducing the Global Burden of Cardiovascular Disease, Part 1: The Epidemiology and Risk Factors. *Circ Res*. 2017;121(6):677-94.
- Lacey B, Herrington WG, Preiss D, Lewington S, Armitage J. The Role of Emerging Risk Factors in Cardiovascular Outcomes. *Curr Atheroscler Rep* 2017;19:28.
- Merced Len, S. efDeportes.com. Revista Digital. Buenos Aires, Año 17, 173: Available at <https://www.efdeportes.com/efd173/prevenir-las-enfermedades-en-los-informaticos.htm> (accessed 10 october 2021)
- Griffiths KL, Mackey MG, Adamson BJ. *J Occup Rehabil* 2011;21:482-92.
- Blagojević L, Petrović B, Blagojević J. Risk Factors for Health Disorders in Computer Operators in Telecom Serbia. *International Journal of Occupational Safety and Ergonomics (JOSE)* 2012;18(3):321-27.
- Toomingas A, Hagberg M, Heiden M, Richter H, Westergren KE, Wigaeus TE. Incidence and risk factors for symptoms from the eyes among professional computer users. *Work* 2012;41:3560-2.
- Deepak S, Ajeesh P. Effect of Ergonomic and Workstyle Risk Factors on Work Related Musculoskeletal Disorders among IT Professionals in India. *Work* 2012;41:2872-5.
- Kaliniene G, Ustinaviciene R, Skemiene L, Vaiciulis V, Vasilavicius P. Associations between musculoskeletal pain and work-related factors among public service sector computer workers in Kaunas County, Lithuania. *BMC Musculoskeletal Disorders* 2016; 17:420.
- Malińska, M. Musculoskeletal disorders among computer operators. *Medycyna Pracy* 2019;70(4):511-21.
- Stanam A, Golla V, Vasa SJ, Taylor RD. Exposure to Computer Work and Prevalence of Musculoskeletal Symptoms Among University Employees: A Cross-Sectional Study. *Journal of Environmental Health* 2019; 81(7):14-20.
- Carter, K. P. (17 de julio de 2015). (A. D'Angelo, Editor, & A. D'Angelo, Productor) Recuperado el 9 de febrero de 2021, de Quora: <https://www.quora.com/What-chronic-illnesses-do-software-programmers-tend-to-suffer-from>
- Merino, D. (20 de julio de 2017). Programar produce ansiedad y depresión. Logroño, España: Calm Code. Recuperado el 4 de febrero de 2021, de <https://calmcode.es/blog/programar-causa-ansiedad-depresion/>
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;33(Suppl 1):S62-9.
- 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
- 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.
- 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.
- 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
- 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.
- 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.
- 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.
- 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.
- 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>
- 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>

24. Cuende JL. La edad vascular frente al riesgo cardiovascular: aclarando conceptos. *Rev Esp Cardiol.* 2016;69(3):243-6
25. Cuende JL. 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
26. Amato MC, Giordano C. Visceral adiposity index: an indicator of adipose tissue dysfunction. *Int J Endocrinol.* 2014;2014:730827.
27. 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
28. 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.
29. 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):359-367.
30. 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.
31. 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
32. 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.
33. 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
34. 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.
35. Bestehom 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
36. 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.
37. Shirazu I, Sackey 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
38. Kalra S. Diabesity. *J Pak Med Assoc.* 2013 Apr;63(4):532-4.
39. 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.
40. 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.
41. 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.
42. Mill-Ferreya 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.
43. 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.
44. 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.
45. 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.
46. 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.
47. 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.
48. 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.
49. Sultana A, Awais S, Hayat M. Risk Factors for Cardiovascular Diseases Among Office Workers. *Journal of Rawalpindi Medical College (JRMCC);* 2016;20(4): 328-30
50. Abbasi MSK, Aziz W, Habib N, Saleem H, Abbasi A. Prevalence and Awareness of Cardiovascular Disease Risk Factors in the Government Servants of Muzaffarabad, the Capital of Azad Kashmir. *IJAVMS* 2012;6(5):385-91
51. Oforia SN, Obosi J. Prevalence of hypertension among office workers in a multi-national company in the Niger-Delta with the 2017 American College of Cardiology/ American Heart Association Blood Pressure Guidelines. *Preventive Medicine Reports* 2019; 15:100899
52. Mirmohammadi SJ, Taheri M, Mehrparvar AM, Heydari M, Kanafi AS, Mostaghaci M. Occupational Stress and Cardiovascular Risk Factors in High-Ranking Government Officials and Office Workers. *Iran Red Crescent Med J* 2014; 16(8): e11747.
53. Strauss M, Foshag P, Leischik R. Prospective Evaluation of Cardiovascular, Cardiorespiratory, and Metabolic Risk of German Office Workers in Comparison to International Data. *Int. J. Environ. Res. Public Health* 2020, 17:1590
54. Nakhaie MR, Koor BE, Salehi SO, Karimpour F. Saudi. Prediction of Cardiovascular Disease Risk using Framingham Risk Score among Office Workers, Iran, 2017. *J Kidney Dis Transpl* 2018;29(3):608-14
55. Vallejo, G.; Prado, V.; Abasolo, E.; Extebarria, E.; Abecia, L.C. Factores de riesgo cardiovascular en trabajadores administrativos del País Vasco. *SEMST* 2005; 2:141-50

VARIABLES QUE INFLUYEN EN EL GRADO DE CONTROL DE PACIENTES DISLIPÉMICOS EN TRATAMIENTO HIPOLIPEMIANTE

Variables that influence the degree of control in dyslipidemic patients under hypolipidemic treatment

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Summary

Introduction: Dyslipidemia is an analytical alteration that, if not controlled, can cause important health problems. There are different treatments ranging from diet and physical activity to pharmacological treatment.

Material and methods: Retrospective and cross-sectional study in 23,627 Colombians (7,131 women and 16,496 men) with dyslipidemia under pharmacological treatment. The degree of control of the different lipid parameters (total cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides) was assessed according to the criteria of the American Heart Association. We also determined the influence of variables such as age, sex, social class, tobacco use and cardiovascular risk level on the degree of control.

Results: The overall degree of control of lipid parameters varied and ranged in men between 26.6% if we considered non-HDL cholesterol and 56% if we considered triglycerides, while in women these percentages were 25.9% and 75.1%, respectively. The variables that influence the degree of control are age, sex and level of cardiovascular risk. Smoking and social class had no influence.

Conclusions: The degree of control of lipid parameters in the Colombian population can be considered low, especially in men, in persons over 50 years of age, and in those with moderate to high cardiovascular risk.

Keywords: Dyslipidemia, estatín, Lipid lowering goals.

Resumen

Introducción: La dislipemia es una alteración analítica que en caso de no ser controlada puede ocasionar importantes problemas de salud. Existen diferentes tratamientos que van de la dieta y la actividad física hasta el tratamiento farmacológico.

Material y métodos: Estudio retrospectivo y transversal en 23,627 colombianos (7,131 mujeres y 16,496 hombres) con dislipemia en tratamiento farmacológico. Se valora el grado de control de los diferentes parámetros lipídicos (colesterol total, LDL colesterol, colesterol no HDL y triglicéridos) de acuerdo a los criterios de la Asociación Americana del Corazón. También se determina cómo influyen en el grado de control variables como edad, sexo, clase social, consumo de tabaco y nivel de riesgo cardiovascular.

Resultados: El grado de control global de los parámetros lipídicos varía y oscila en los hombres entre el 26,6% si consideramos el colesterol no HDL y el 56% si lo que consideramos son los triglicéridos mientras que en las mujeres estos porcentajes son del 25,9% y 75,1% respectivamente. Las variables que influyen en el grado de control son la edad, el sexo y el nivel de riesgo cardiovascular. El tabaco y la clase social no muestran influencia.

Conclusiones: El grado de control de los parámetros lipídicos en población colombiana puede considerarse bajo, especialmente en los hombres, en las personas a partir de 50 años y en aquellos con nivel de riesgo cardiovascular moderado-alto.

Palabras clave: Dislipemia, estatina, objetivos de reducción de lípidos.

Introduction

La dislipemia es una alteración de los niveles de lípidos y proteínas en la sangre. Incluye colesterol, triglicéridos o ambos, y es uno de los principales factores de riesgo de cardiopatía isquémica. También puede aparecer como consecuencia de una disminución del nivel de colesterol HDL. Es una enfermedad asintomática que generalmente se detecta en etapas avanzadas, normalmente cuando se manifiestan síntomas asociados a la afección, como: infarto cerebral, pancreatitis aguda o enfermedades coronarias¹. No obstante, puede prevenirse su desarrollo mediante un análisis de sangre.

La dislipemia puede ser heredada, lo que conocemos como dislipemia primaria, pero también puede aparecer como consecuencia de un estilo de vida poco saludable, lo que también se conoce como dislipemia secundaria². Las causas con una mayor incidencia en la dislipemia son el sedentarismo, la ingesta dietética excesiva de grasas saturadas y pobre en fibra y el tabaquismo.

El tratamiento de la dislipemia debe ser individualizado teniendo en cuenta las características del paciente y el estado en el que se encuentra la enfermedad. El tratamiento principal será aquel encaminado a controlar la dieta del paciente y promover el consumo de verduras, legumbres y hortalizas. En pacientes con alta concentración de colesterol será necesario administrar estatinas o asociar/sustituir por ezetimiba, mientras que en aquellos con niveles altos de triglicéridos se recurrirá a la niacina, fibratos y ácidos grasos omega-3. El tratamiento con estatina está indicado para reducir el riesgo de enfermedades cardiovasculares. No obstante, habrá casos en los que resultará necesario recurrir a la medicación para controlar la evolución de la enfermedad, sobre todo cuando los niveles de colesterol LDL se sitúen por encima de 190 mg/dL o cuando el paciente, de entre 40 y 75 años, padezca diabetes³.

Existen múltiples definiciones del término cumplimiento terapéutico. De forma simple se puede decir que representa la concordancia entre las instrucciones dadas y las conductas seguidas. La definición más comúnmente aceptada es la propuesta inicialmente por Haynes et al⁴ y avalada posteriormente por un grupo de expertos de la Organización Mundial de la Salud (OMS) que define al cumplimiento como “el grado hasta el cual la conducta del paciente, en términos de tomar medicamentos, seguir dietas o realizar cambios en el estilo de vida, coinciden con la prescripción clínica”. Existe cierto acuerdo al considerar como cumplidor a aquél que sigue dichas recomendaciones en al menos un 80%.

El objetivo de este trabajo fue determinar el nivel de control de pacientes dislipémicos en tratamiento farmacológico valorando también las variables asociadas a un buen o mal control terapéutico.

Material y métodos

Se lleva a cabo un estudio descriptivo y transversal en 23,898 dislipémicos en tratamiento farmacológico durante el periodo comprendido entre enero de 2019 y diciembre de 2020. Del total 271 se excluyen (81 al no aceptar participar y 190 por no tener los valores de los parámetros lipídicos, quedando finalmente 23.627 (7.131 mujeres y 16.496. hombres). Los datos se muestran en el diagrama de flujo (Figura 1).

Figura 1: Diagrama de flujo de los participantes en el estudio.



Criterios de inclusión

- Ser dislipémico
- Recibir tratamiento farmacológico
- Aceptar participar en el estudio

Para eliminar el sesgo inter observador, las mediciones tanto antropométricas, clínicas y analíticas, las realiza el personal sanitario que participa en el estudio, tras homogenizar las técnicas de medición.

La edad se clasifica en 4 grupos: 18-34 años, 35-44 años, 45-54 años y ≥ 55 años.

El peso (en kilogramos), y la altura (en cm) se determinan con una báscula con tallímetro modelo SECA 700 con capacidad para 200 kg que lleva anexo un tallímetro telescópico SECA 220 con división milimétrica e intervalo 60-200 cm.

El IMC se calcula dividiendo el peso en kg entre la altura en metros al cuadrado:

$$- \text{IMC} = \text{peso (kg)} / \text{altura}^2 \text{ (metros)}$$

El IMC se clasifica en normopeso ($< 25 \text{ kg/m}^2$), sobrepeso ($25-29,9 \text{ kg/m}^2$) y obesidad ($\geq 30 \text{ kg/m}^2$).

La presión arterial se determina en decúbito supino con un esfigmomanómetro automático OMRON M3 calibrado después de 10 minutos de descanso. Se obtienen tres mediciones con intervalos de un minuto obteniéndose la media de las tres. Los análisis de sangre se obtienen

tras 12 horas de ayuno. Las muestras se envían a los laboratorios de referencia. Glucemia, colesterol total y triglicéridos emplean métodos enzimáticos automatizados y los valores se expresan en mg/dl. El HDL se determina por precipitación con dextrano-sulfato Cl₂Mg, y los valores se expresan también en mg/dl. El LDL se calcula empleando la fórmula de Friedewald (siempre que los triglicéridos sean inferiores a 400 mg/dl). Los valores se expresan en mg/dl.

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

Consideramos fumador a aquella persona que regularmente ha consumido al menos 1 cigarrillo/día (o el equivalente en otros tipos de consumo) en el último mes, o ha dejado de fumar hace menos de un año.

La clase social se obtiene a partir de la Clasificación Nacional de Ocupaciones del año 2011 (CNO-11) partiendo de la propuesta realizada por el grupo de determinantes sociales de la Sociedad Española de Epidemiología⁵. Elegimos la clasificación en 3 categorías: Clase I. Directores/gerentes, profesionales universitarios, deportistas y artistas. Clase II. Ocupaciones intermedias y trabajadores por cuenta propia sin asalariados. Clase III. Trabajadores no cualificados. Se consideró white collar a las personas de las clases sociales I-II y blue collar a las de la clase social III.

REGICOR (Registro Gironí del Cor) es una adaptación de la escala de Framingham a las características de la población española mediante un probado proceso de calibración⁶. La escala ha sido validada en población española⁷. Estima el riesgo de sufrir un evento cardiovascular fatal o no fatal en un período de 10 años. Las tablas se aplican a personas entre 35 y 74 años de edad. Para el cálculo del riesgo se tienen en cuenta la edad, el sexo, el tabaquismo, la diabetes, la presión arterial sistólica y diastólica, el colesterol total y el HDL-c. Para clasificar el nivel de riesgo con las tablas REGICOR se utilizaron los puntos de corte recomendados⁸, considerando moderado a partir del 5%, alto a partir del 10% y muy alto para valores del 15% o más.

El tratamiento para la dislipemia se determinó mediante entrevista clínica. Para considerar a una persona en tratamiento hipolipemiante como controlada se emplean los criterios de la American Heart Association⁹.

Análisis estadístico

Se realiza un análisis descriptivo de las variables categóricas, calculando la frecuencia y distribución de respuestas de cada una de ellas. Para las variables cuantitativas, se calcula la media y la desviación estándar y para las variables cualitativas se calcula el porcentaje. El análisis de asociación bivariante se realiza mediante

el test de la χ^2 (con corrección del estadístico exacto de Fisher cuando las condiciones lo requirieran) y la *t* de Student para muestras independientes. Para el análisis multivariante se ha utilizado la regresión logística binaria con el método de Wald, con el cálculo de las Odds-ratio y se realiza la prueba de bondad de ajuste de Hosmer-Lemeshow. El análisis estadístico se realiza con el programa SPSS 27.0 siendo el nivel de significación estadística aceptado de 0,05.

Consideraciones y aspectos éticos

El estudio fue aprobado por el Comité de ética para la investigación en salud de la secretaría distrital de salud de Bogotá. Todos los procedimientos se realizaron de acuerdo con las normas éticas del comité de investigación institucional y con la Declaración de Helsinki de 2013. Todos los pacientes firmaron documentos de consentimiento informados por escrito antes de participar en el estudio.

Resultados

Todas las variables antropométricas, clínicas y analíticas de las personas incluidas en el estudio muestran valores más desfavorables en los varones. El grupo de edad más representado es el de 50 a 59 años con más del 50%. Más del 80% de las personas pertenecen a la clase social más desfavorecida. Un 32% son fumadores. Todos los datos se pueden consultar en la **tabla I**.

Los valores medios de todos los parámetros lipídicos de los varones en tratamiento van disminuyendo a medida que aumenta la edad. Estos valores medios en general son más altos en los hombres de la clase social I y en los fumadores. Las cifras de todos los parámetros lipídicos se van incrementando a medida que aumenta el valor de la escala REGICOR de riesgo cardiovascular. (Ver **tabla II**) En las mujeres la situación es similar salvo en lo referente a la edad, ya que no encontramos esa relación tan clara como la vista en los hombres, ni tampoco parece existir relación con el tabaco. (Ver **tabla III**)

En los varones el porcentaje de personas controladas con el tratamiento hipolipemiante va disminuyendo con la edad. También se observa un mayor grado de control en las personas de clases sociales más altas (salvo triglicéridos). En relación al nivel de riesgo cardiovascular el peor grado de control se aprecia entre las personas con valores de REGICOR más altas. El grado de control global oscila entre el 56% si valoramos los triglicéridos y el 26,6% si el parámetro elegido es el colesterol no HDL. (Ver **tabla IV**)

En las mujeres la edad no se comporta igual y no existe una relación lineal como la observada en los varones. El mayor grado de control se observa en las clases sociales intermedias. La relación con el nivel de riesgo cardiovascular es similar a la obtenida en los hombres.

Tabla I: Characteristics of the population.

	Men n=16.496 Mean (SD)	Women n=7.131 Mean (SD)	Total n=23.627 Mean (SD)	p-value
Age (years)	51.9 (7.5)	53.1 (7.5)	52.3 (7.5)	<0.0001
Height (cm)	172.1 (6.8)	158.9 (6.3)	168.1 (9.0)	<0.0001
Weight (kg)	85.6 (14.5)	70.3 (14.0)	81.0 (16.0)	<0.0001
BMI (kg/m ²)	28.9 (4.4)	27.8 (5.2)	28.5 (4.6)	<0.0001
Waist circumference (cm)	88.3 (10.7)	76.2 (10.8)	84.7 (12.1)	<0.0001
Waist to height ratio	0.51 (0.06)	0.48 (0.07)	0.50 (0.06)	<0.0001
Systolic blood pressure (mmHg)	135.3 (17.0)	128.5 (17.8)	133.3 (17.5)	<0.0001
Diastolic blood pressure (mmHg)	83.0 (10.6)	77.8 (10.6)	81.4 (10.9)	<0.0001
Total cholesterol (mg/dl)	203.8 (44.2)	212.7 (41.6)	206.5 (43.6)	<0.0001
HDL-c (mg/dl)	46.4 (8.2)	53.4 (7.8)	48.5 (8.7)	<0.0001
LDL-c (mg/dl)	125.2 (40.8)	134.6 (40.3)	128.1 (40.9)	<0.0001
Triglycerides (mg/dl)	168.5 (120.4)	126.0 (76.8)	155.7 (110.8)	<0.0001
Glycaemia (mg/dl)	107.2 (35.2)	98.5 (26.6)	104.6 (33.1)	<0.0001
	%	%	%	p-value
18-39 years	6.4	5.5	6.2	<0.0001
40-49 years	27.5	20.5	25.3	
50-59 years	51.1	54.2	52.1	
60-69 years	15.0	19.8	16.4	
Social class I	4.9	3.7	4.6	<0.0001
Social class II	14.5	16.3	15.0	
Social class III	80.6	80.0	80.4	
Blue collar	80.6	80.0	80.4	0.195
White collar	19.4	20.0	19.6	
Non-smokers	68.2	67.7	68.0	0.228
Smokers	31.8	32.3	32.0	

Tabla II: Mean values of lipid parameters according to different variables in men treated with lipid-lowering drugs.

Men	n	Total colesterol		LDL-c		Triglycerides		Cholesterol non HDL	
		Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
18-39 years	1062	214.8 (50.0)	<0.0001	131.9 (47.3)	<0.0001	179.8 (142.6)	<0.0001	165.3 (51.3)	<0.0001
40-49 years	4528	208.9 (45.4)		128.4 (42.6)		175.3 (119.9)		161.5 (46.0)	
50-59 years	8437	201.3 (43.5)		123.3 (39.5)		166.8 (124.8)		155.3 (44.1)	
60-69 years	2469	198.1 (40.2)		123.0 (38.3)		157.1 (90.9)		153.4 (41.3)	
Social class I	817	204.9 (39.41)	0.976	126.0 (38.3)	0.776	164.9 (104.1)	0.001	157.3 (40.0)	0.135
Social class II	2387	203.4 (40.3)		124.7 (37.4)		161.1 (99.0)		156.0 (40.8)	
Social class III	13292	203.8 (45.2)		125.2 (41.5)		170.1 (124.7)		157.7 (45.8)	
Blue collar	13292	203.8 (45.2)	0.981	125.2 (41.5)	0.774	170.1 (124.7)	0.001	157.7 (45.8)	0.133
White collar	3204	203.8 (40.1)		125.0 (37.6)		162.2 (100.4)		156.3 (40.6)	
Non-smokers	11249	203.2 (44.2)	0.021	124.6 (40.6)	0.008	168.7 (123.6)	0.724	156.8 (44.9)	0.013
Smokers	5247	204.9 (44.3)		126.5 (41.2)		168.0 (113.1)		158.7 (44.8)	
REGICOR low	11557	201.3 (43.8)	<0.0001	123.1 (40.5)	<0.0001	164.8 (116.1)	<0.0001	154.8 (44.5)	<0.0001
REGICOR moderate	4277	207.8 (44.3)		128.5 (40.2)		176.3 (127.1)		161.8 (44.6)	
REGICOR high	432	218.3 (44.1)		139.1 (43.2)		180.10 (120.8)		172.4 (44.8)	
REGICOR very high	93	231.4 (38.0)		153.6 (33.6)		198.6 (158.4)		188.0 (38.4)	

Tabla III: Mean values of lipid parameters according to different variables in women treated with lipid-lowering drugs.

Women	n	Total colesterol		LDL-c		Triglycerides		Cholesterol non HDL	
		Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
18-39 years	395	211.6 (47.9)	0.001	132.1 (45.6)	0.015	133.8 (160.0)	0.007	156.7 (48.9)	0.004
40-49 years	1461	212.9 (43.5)		133.7 (41.9)		128.3 (81.6)		158.6 (43.3)	
50-59 years	3864	214.0 (41.3)		135.9 (40.2)		126.3 (66.6)		160.8 (41.6)	
60-69 years	1411	209.0 (38.8)		132.4 (37.0)		120.8 (59.8)		156.5 (38.6)	
Social class I	264	215.9 (42.5)	0.312	136.2 (40.7)	0.624	130.4 (85.6)	0.589	161.3 (43.0)	0.656
Social class II	1159	213.4 (38.9)		133.7 (37.4)		126.3 (67.0)		158.7 (39.4)	
Social class III	5708	212.4 (42.0)		134.6 (40.8)		125.8 (78.2)		159.3 (42.3)	
Blue collar	5708	212.4 (42.0)	0.259	134.6 (40.8)	0.599	125.8 (78.2)	0.590	159.3 (42.3)	0.786
White collar	1423	213.8 (39.5)		134.0 (37.9)		127.0 (70.9)		159.0 (40.0)	
Non-smokers	4827	212.8 (41.0)	0.611	134.8 (40.0)	0.547	127.0 (77.3)	0.318	159.6 (41.4)	0.354
Smokers	2304	212.3 (42.8)		134.1 (40.8)		126.1 (75.6)		158.6 (42.8)	
REGICOR low	5218	212.1 (41.3)	0.025	133.7 (39.9)	0.002	125.2 (78.1)	0.547	158.3 (41.5)	<0.0001
REGICOR moderate	1683	213.6 (41.6)		136.4 (40.3)		128.3 (73.0)		161.5 (41.9)	
REGICOR high	123	233.6 (44.5)		146.4 (46.0)		131.5 (59.8)		172.1 (44.7)	
REGICOR very high	12	221.8 (50.3)		144.5 (43.6)		136.3 (48.0)		171.8 (50.4)	

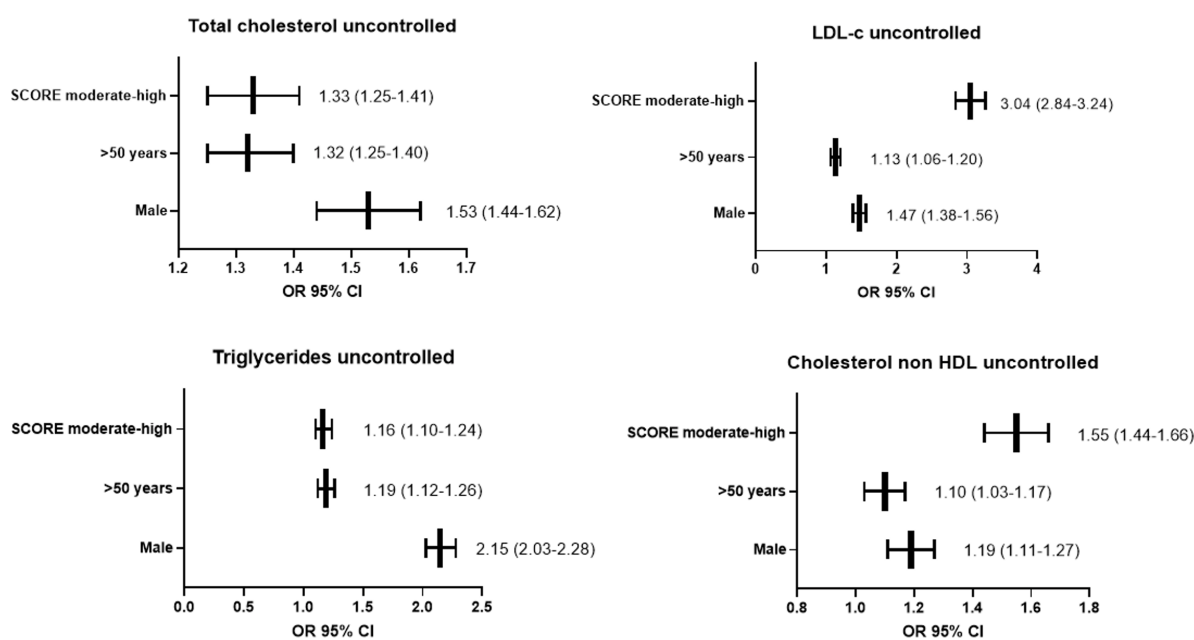
Tabla IV: Prevalence of elevated values of lipid parameters according to different variables in men treated with lipid-lowering drugs.

Men	n	Total colesterol		LDL-c		Triglycerides		Cholesterol non HDL	
		% (95% CI)	p-value	% (95% CI)	p-value	% (95% CI)	p-value	% (95% CI)	p-value
18-39 years	1062	58.6 (57.8-59.4)	<0.0001	66.3 (65.5-67.1)	0.008	44.6 (43.8-45.4)	<0.0001	74.6 (73.8-75.4)	0.002
40-49 years	4528	54.5 (54.1-54.9)		65.2 (64.8-65.6)		47.3 (46.9-47.7)		75.4 (75.0-75.8)	
50-59 years	8437	47.0 (46.8-47.2)		62.6 (62.4-62.8)		43.5 (43.3-43.7)		72.5 (72.3-72.7)	
60-69 years	2469	44.8 (44.3-45.3)		63.0 (62.5-63.5)		39.2 (38.7-39.7)		72.3 (71.8-72.8)	
Social class I	817	53.6 (52.2-55.0)	0.030	64.5 (63.1-66.0)	0.815	41.7 (40.3-43.2)	0.306	75.3 (74.0-76.6)	0.443
Social class II	2387	50.3 (49.6-51.0)		63.9 (63.2-64.6)		43.4 (42.7-44.1)		73.4 (72.7-74.1)	
Social class III	13292	49.1 (49.0-49.2)		63.5 (63.4-63.6)		44.2 (44.1-44.3)		73.2 (73.1-73.3)	
Blue collar	13292	47.2 (47.1-47.3)	0.019	63.5 (63.4-63.6)	0.294	44.2 (44.1-44.3)	0.117	73.2 (73.1-73.3)	0.235
White collar	3204	51.1 (50.6-51.6)		64.1 (63.6-65.6)		43.0 (42.5-43.5)		73.9 (73.4-74.4)	
Non-smokers	11249	48.8 (48.7-48.9)	0.007	62.9 (62.8-63.0)	0.002	44.0 (43.9-44.1)	0.432	72.9 (72.8-73.0)	0.033
Smokers	5247	50.9 (50.6-51.2)		65.2 (64.9-65.6)		43.9 (43.6-44.2)		74.3 (74.0-74.6)	
REGICOR low	11557	47.2 (47.1-47.3)	<0.0001	56.8 (56.7-56.9)	<0.0001	43.1 (43.0-43.2)	<0.0001	70.8 (70.7-70.9)	<0.0001
REGICOR moderate	4277	53.5 (53.2-53.8)		77.9 (77.6-78.2)		46.3 (46.0-46.6)		77.3 (77.0-77.6)	
REGICOR high	432	60.4 (59.0-61.8)		97.0 (95.7-98.4)		46.5 (45.1-48.0)		97.9 (96.2-99.6)	
REGICOR very high	93	80.6 (78.6-82.6)		100		51.6 (49.6-53.6)		100	
Total	16494	49.5 (49.4-49.6)		63.6 (63.5-63.7)		44.0 (43.9-44.1)		73.4 (73.3-73.5)	

Tabla V: Prevalence of elevated values of lipid parameters according to different variables in women treated with lipid-lowering drugs.

Women	n	Total colesterol		LDL-c		Triglycerides		Cholesterol non HDL	
		% (95% CI)	p-value	% (95% CI)	p-value	% (95% CI)	p-value	% (95% CI)	p-value
18-39 years	395	58.0 (56.5-59.5)	0.126	64.8 (63.3-66.3)	0.001	24.8 (24.3-25.3)	0.178	71.9 (71.4-74.4)	0.001
40-49 years	1461	59.2 (58.5-59.9)		67.8 (67.1-68.5)		25.7 (25.0-26.4)		73.6 (72.9-74.3)	
50-59 years	3864	59.9 (59.5-60.3)		72.2 (71.8-72.6)		25.4 (25.0-25.8)		77.8 (77.4-78.2)	
60-69 years	1411	56.3 (55.6-57.0)		71.3 (70.5-72.0)		22.6 (21.8-23.4)		75.0 (74.4-75.8)	
Social class I	264	60.2 (58.3-62.1)	0.667	70.5 (68.5-72.5)	0.351	23.1 (21.1-25.1)	0.261	77.3 (75.3-79.3)	0.099
Social class II	1159	60.0 (59.2-60.8)		72.5 (71.6-73.4)		26.7 (25.8-27.6)		78.4 (77.5-79.3)	
Social class III	5708	58.7 (58.4-59.0)		70.4 (69.8-71.0)		24.6 (24.0-25.2)		75.5 (74.9-76.1)	
Blue collar	5708	58.7 (58.4-59.0)	0.211	70.4 (69.8-71.0)	0.121	24.6 (24.0-25.2)	0.169	75.5 (74.9-76.1)	0.022
White collar	1423	59.9 (59.2-60.6)		72.0 (71.3-72.7)		25.9 (25.2-26.6)		78.1 (77.4-78.8)	
Non-smokers	4827	59.4 (59.1-59.7)	0.175	71.0 (70.6-71.5)	0.209	25.3 (24.9-25.7)	0.128	76.5 (76.1-77.0)	0.126
Smokers	2304	58.2 (57.5-58.9)		70.1 (69.4-70.8)		24.0 (23.3-24.7)		75.2 (74.5-75.9)	
REGICOR low	5218	58.0 (57.6-58.4)	0.029	65.9 (65.5-66.3)	<0.0001	24.3 (23.9-24.7)	0.043	74.8 (74.4-75.2)	<0.0001
REGICOR moderate	1683	61.1 (60.4-61.8)		83.8 (83.1-84.0)		26.0 (25.3-26.7)		78.7 (78-79.4)	
REGICOR high	123	69.1 (67.1-71.1)		96.7 (94.7-98.9)		34.1 (32.0-37.8)		97.6 (84.2-99.6)	
REGICOR very high	12	58.3 (54.3-65.7)		100		41.7 (21.3-69.3)		91.7 (57.3-99.8)	
Total	7131	59.0 (58.8-59.2)		70.7 (70.5-70.9)		24.9 (24.8-25.1)		76.1 (76.0-76.3)	

Figura 2: Regresión logística binaria.



El mayor grado de control global se observa cuando consideramos los triglicéridos (75,1%) y el menor cuando el parámetro elegido es el colesterol no HDL (23,9%) (Ver **tabla V**).

En el análisis multivariante se consideran como covariables aquellas que obtuvieron significación estadística en el análisis bivariante, es decir sexo masculino, edad a partir de 50 años, clase social III, consumo de tabaco y niveles de riesgo cardiovascular con la escala REGICOR moderados o altos. Los resultados muestran que el consumo de tabaco y la clase social no incrementan el riesgo de presentar un mal control terapéutico. Entre las variables que más influencia tienen en incrementar el riesgo de mal control del tratamiento encontramos que la que presenta unas Odds ratio más elevadas es REGICOR moderado-alto. (Ver **gráfica 2**).

Discusión

El grado de control de la dislipemia en tratamiento obtenido en nuestro trabajo oscila en los hombres entre el 56% cuando consideramos triglicéridos y el 26,6% si el parámetro es el colesterol no HDL. En las mujeres también son estos mismos parámetros los que marcan el rango de control siendo del 75,1% y 23,9% respectivamente. Las variables que han mostrado influencia en incrementar el riesgo de presentar un mal control tras el tratamiento son la edad a partir de 50 años, el sexo masculino y valores elevados de riesgo cardiovascular con la escala REGICOR.

Un estudio también colombiano¹⁰ realizado en 211 pacientes adultos de cuatro ciudades tratados con estatinas entre 2012 y 2013 encontró un grado de control similar al obtenido por nosotros, Otro estudio colombiano de los mismos autores obtuvo también tasas de control similares a la nuestras¹¹. Estudios españoles^{12,13} indican tasas de control también muy deficitarias similares a las obtenidas por nosotros.

En diferentes estudios^{10,14-16} tener alto riesgo

cardiovascular se asocia con aumento de la probabilidad de controlar la dislipidemia a diferencia de lo obtenido en nuestro estudio. Mientras que otros estudios¹⁷ coinciden con nosotros en cuanto al peor control en pacientes con alto riesgo cardiovascular. En este mismo sentido se expresaba el estudio CardioTeca¹⁸. Este mismo estudio CardioTeca mostraba un grado de control más deficiente en la mujeres a diferencia de lo que hemos encontrado nosotros en nuestra investigación.

Aunque nosotros no hemos encontrado asociación entre consumo de tabaco y peores niveles de control lipídico tras tratamiento, algunos autores si lo han hecho¹⁹. No hemos encontrado ningún estudio que valore la influencia de la clase social en el grado de control lipídico.

Como puntos fuertes del estudio podemos destacar el gran tamaño de la muestra (más de 23,000 personas), que se han considerado diferentes parámetros de perfil lipídico y que se han tenido en cuenta bastantes variables para ver su influencia en el grado de control tras el tratamiento.

Como limitaciones principales encontramos que el grado de cumplimiento ha sido autoreportado y por lo tanto no sabemos realmente si todas las personas incluidas en el estudio tomaban regularmente o no el tratamiento y que tampoco se ha comparado el efecto de los diferentes tratamientos. También el hecho de haber realizado el estudio sólo en población de Colombia impide extrapolar los resultados a otras áreas geográficas.

Conclusiones

El grado de control de las personas en tratamiento hipolipemiente en población colombiana se puede considerar bajo, especialmente en los varones, en las personas de 50 o más años de edad y en aquellos con alto riesgo cardiovascular.

Interests conflict

The researchers declare that they have no conflict of interest.

Bibliografía

1. Pallarés-Carratalá V, Pascual-Fuster V, Godoy-Rocatí D. Dyslipidaemia and vascular risk. A new evidence based review. *Semergen* 2015; 41(8):435-45
2. Dislipemia. Guías Fisterra. Available at: <https://www.fisterra.com/guías-clínicas/dislipemias/>

3. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019 Jun 18;139(25):e1082-e1143.

4. Haynes RB, Yao X, Degani A, Kripalani S, Grag A, McDonald HP. Intervenciones para mejorar el cumplimiento con la medicación (Revisión Cochrane traducida). En: La Biblioteca Cochrane Plus, 2006 Número 1. Oxford.
5. 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
6. Marrugat J, Solanas P, D'Agostino R, Sullivan L, Ordovas J, Cordón F, et al. Estimación del riesgo coronario en España mediante la ecuación de Framingham calibrada. *Rev Esp Cardiol* 2003; 56: 253-61.
7. 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.
8. 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.
9. Wilson PWF, Polonsky TS, Miedema MD, Khera A, Kosinski AS, Kuvin JT. Systematic Review for the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019 Jun 25;73(24):3210-27.
10. Machado-Alba JE, Machado-Duque ME, Yepes MC, Manrique S, Tobón LM. Lipid-lowering therapy and its effectiveness in patients from four Colombian cities. *Acta Médica Colombiana* 2016; 41(3):181-6
11. Machado-Alba JE, Murillo-Muñoz MM, Machado-Duque ME. Effectiveness of lipid-lowering therapy among a sample of patients in Colombia. *Rev Panam Salud Pública*. 2013; 33(6): 383-90
12. Banegas JR, López-García E, Dallongeville J, Guallar E, Halcox JP, Borghi C, et al. Achievement of treatment goals for primary prevention of cardiovascular disease in clinical practice across Europe: the EURIKA study. *Eur Heart J*. 2011 Sep;32(17):2143-52.
13. Galve E, Cordero A, Cequier A, Ruiz E, González-Juanatey JR. Grado de control lipídico en pacientes coronarios y medidas adoptadas por los médicos. Estudio REPAR. *Rev Esp Cardiol*. 2016;69:931-8.
14. Meyer JW, Schultz JS, O'Donnell JC, Patel PA, Sasane RM. Patterns and effectiveness of lipid-lowering therapies in a managed care environment. *Value Health*. 2005; 8(5): 601-12.
15. Alnouri F, Wood D, Kotseva K, Ibrahim ME. Which statin worked best to achieve lipid level targets in a European registry? A post-hoc analysis of the EUROASPIRE III for coronary heart disease patients. *J Saudi Heart Assoc*. 2014; 26(4): 183-91.
16. Ankam J, Feldman DI, Blaha MJ, Martin SS. Improving lipid control follow-ing myocardial infarction. *Curr Opin Cardiol*. 2014; 29(5): 454-66.
17. Gómez-Belda A, Rodilla E, González C, Costa JA, Serra B, Pascual JM. Objetivos del tratamiento hipolipemiante en pacientes con alto riesgo y muy alto riesgo cardiovascular: un reto posible? [Lipid lowering goals in high risk and very high cardiovascular risk patients: a reasonable challenge?]. *Rev Clin Esp*. 2006 Oct;206(9):417-21.
18. Félix-Redondo FJ, Lozano-Mera L, Mostaza JM, Saénz P, Fernández-Berges D, Buitrago F. Influence of Gender and Cardiovascular Risk on the Control of Low-density Lipoprotein in a Population From Extremadura. *Rev Esp Cardiol*. 2015 Dec;68(12):1184-6.
19. Laforest L, Souchet T, Moulin P, Ritleng C, Desamericq G, Le Jeune P, et al. Prevalence of low high-density lipoprotein cholesterol and hypertriglyceridaemia in patients treated with hypolipidaemic drugs. *Arch Cardiovasc Dis*. 2009 Jan;102(1):43-50.

Factores de riesgo asociados al uso y consumo de drogas en estudiantes del Instituto Superior Tecnológico Sucre

Risk factors associated with the use and consumption of drugs in students of the Higher Technological Institute Sucre

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Resumen

Objetivo: La presente investigación tuvo como objetivo determinar el grado en el que los factores socioeconómicos se encuentran asociados con el consumo de alcohol, cigarrillo, marihuana y cannabis en los estudiantes del Instituto Superior Tecnológico Sucre (ISTS), de Ecuador, durante el semestre 2020 ii.

Métodos: El estudio realizado tuvo un enfoque cuantitativo con diseño no experimental, transversal, descriptivo y correlacional. A una muestra de 1.755 estudiantes universitarios se les aplicó la *Encuesta Socioeconómica* ISTS y la *Encuesta EST-Diagnóstico de la situación del consumo de alcohol, tabaco y otras sustancias psicoactivas en la comunidad universitaria* de la Universidad Central del Ecuador, confirmándose la inferencia a través del estadístico Chi cuadrada y la razón de momios para el grado de asociación.

Resultados: Como resultados se obtuvo que las amistades, conflictos laborales y el tiempo libre destinado a fiestas y ocio están asociadas con el consumo de tabaco y alcohol. Por otro lado, factores como la relación con la familia y necesidad de aceptación social infirieron con el consumo de cocaína.

Conclusiones: Se concluye que los factores nominales de género, autoidentificación, ingreso mensual y responsabilidad de la familia obtuvieron asociación baja, y que la predicción de consumo obedece a la influencia de las amistades, conflictos laborales, y necesidades de aceptación.

Palabras clave: Factores de riesgo, consumo de drogas, estudiantes universitarios, encuesta Socioeconómica ISTS, Encuesta EST-Diagnóstico, razón de momios, Chi cuadrada, sustancias psicoactivas.

Summary

Objective: The objective of this research was to determine the degree to which socioeconomic factors are associated with the consumption of alcohol, cigarettes, marijuana and cannabis among students of the Sucre Higher Institute of Technology (ISTS), Ecuador, during semester 2020 ii.

Methods: The study had a quantitative approach with a non-experimental, cross-sectional, descriptive and correlational design. A sample of 1,755 university students were administered the ISTS Socioeconomic Survey and the EST-Diagnosis of the situation of alcohol, tobacco and other psychoactive substances consumption in the university community of the Central University of Ecuador, confirming the inference through the Chi-square statistic and the odds ratio for the degree of association.

Results: The results showed that friendships, labor conflicts and free time for parties and leisure are associated with the consumption of tobacco and alcohol. On the other hand, factors such as relationship with family and need for social acceptance inferred with cocaine use.

Conclusions: It is concluded that the nominal factors of gender, self-identification, monthly income, and family responsibility obtained low association, and that the prediction of consumption obeys the influence of friendships, work conflicts, and needs for acceptance.

Keywords: Risk factors, drug use, college students, Socioeconomic ISTS survey, EST-Diagnostic Survey, odds ratio, Chi-square, psychoactive substances.

Introducción

En la actualidad, el consumo de drogas y alcohol se manifiesta como una problemática que aumenta progresivamente en el ámbito mundial. El abuso de sustancias estupefacientes son factores de riesgo para el cometimiento de actos violentos, la ocurrencia de enfermedades crónico degenerativas y la siniestralidad vial. Por ello, Ecuador enfoca sus esfuerzos por mitigar su uso y consumo mediante la creación de políticas públicas basadas principalmente en la prevención y educación de la población.

La relación entre su uso y la ocurrencia de delitos que tienen como saldo negativo la inseguridad y los asesinatos en el país, coinciden con el dispendio de alcohol y drogas ilegales de los agresores en el 88% de los casos.¹ Paralelamente, la violencia en la vida en pareja responde a una influencia del alcohol hasta en el 40% de los altercados. El uso frecuente que ocasiona su dependencia compulsiva se manifiesta posteriormente en enfermedades cardíacas, cáncer, enfermedades pulmonares y patologías mentales.²

Respecto a los accidentes de tránsito, el 25% de personas fallece por conducir bajo los efectos del alcohol. La facilidad de distracción, disminución en la capacidad de reacción y sobrevaloración de las habilidades de los conductores embriagados, también causan incapacidades permanentes con costos altos en pensiones, subsidios e indemnizaciones para las familias y el Estado.³

Respecto a la legislación, la ley ecuatoriana sufre algunas reformas desde principios del siglo XX y en 1916 se expide la Ley de control del opio; en 1924 la Ley sobre la importación, venta y uso del opio, sus derivados y de los preparados de la morfina y de la cocaína; en 1958 la Ley sobre el tráfico de las materias primas, drogas y preparados estupefacientes; y en 1974 la Ley de control y fiscalización del tráfico de estupefacientes. En todas ellas se reprime con sanciones pecuniarias y privaciones de libertad el uso y consumo de las sustancias psicotrópicas bajo un evidente sistema de control punitivo y coercitivo.⁴

A principios del siglo XXI, la legislación ecuatoriana contiene las penas más drásticas para la tenencia de drogas en América Latina, y concede en 2008, reformas constitucionales, cuyo nuevo enfoque, impide la criminalización y la vulneración de derechos.^{5,6}

La dependencia gubernamental encargada de implementar esta gestión, es la Secretaría Técnica de Prevención Integral de Drogas (SETED), que el 23 de abril 2018 se suprime por decreto ejecutivo 376, y pasa las competencias al Ministerio de Salud Pública de Ecuador. No obstante, la SETED presenta un plan de trabajo integral 2017-2021 con base a un diagnóstico de varios estudios en colegios, universidades y empresas

con participación de profesionales de la salud. Si bien en este documento y sus estudios anexos no existen detalles explicativos de los factores asociados con el uso y consumo, si se arrojan datos descriptivos importantes desde el año 2012.⁷

El inicio aproximado de consumo de drogas empieza desde los 12 a 14 años de edad y continua hacia los 21 años. Los alumnos del Instituto Superior Tecnológico Sucre (ISTS), en Ecuador, lugar en donde se realiza el presente estudio, se encuentran dentro de este rango etario. El acceso fácil al mercado de la droga aumenta las posibilidades de consumo y de dependencia entre los estudiantes, además que su uso se asocia directamente con situaciones de violencia, deserción escolar y delincuencia. Los jóvenes de 17 a 24 años de edad, manifiestan consumir en algún momento alguna droga, lo cual incluye cocaína, marihuana u otra sustancia sujeta a control y fiscalización.

Respecto al consumo del alcohol, los informes de la Organización Panamericana de la Salud (OPS), señalan que un mayor porcentaje de hombres (7,6%) que mujeres (4%), mueren por causas relacionadas con el alcohol, aunque hay evidencia de que las mujeres pueden ser más vulnerables a los efectos nocivos del alcohol.⁸

Existe preocupación por el aumento constante en el consumo de alcohol entre las mujeres, el cual es un factor importante para el desarrollo de 200 enfermedades y trastornos físicos. Si se compara la ingesta de alcohol en América Latina, Ecuador está entre los tres países que más la consumen, por detrás de Chile y Colombia; la tasa oscila alrededor de los 9 litros de consumo anual.⁸

La marihuana es una sustancia sujeta a fiscalización cuyo consumo anual alcanza las 48 toneladas, de acuerdo con la Dirección Nacional de Antinarcóticos⁹, de alta demanda en población universitaria y su legalidad está en los 10 gramos para consumidores habituales. Su administración terapéutica demuestra clínicamente ser efectiva para el dolor crónico en pacientes terminales; para impedir el daño del nervio óptico en algunos casos de glaucoma; para disminuir convulsiones epilépticas; y sigue en debate su acción frenadora del cáncer.

Posiblemente, estos aspectos positivos de la marihuana medicinal nublen la conciencia de sus efectos nocivos sobre la salud, sobre todo en la población más joven.

El tetrahidrocannabinol (THC), compuesto psicoactivo del cannabis, altera el funcionamiento de la esfera socioafectiva, por lo que se relaciona con trastornos como depresión, ansiedad, nerviosismo, psicosis, suicidio y trastornos de personalidad. También están las enfermedades pulmonares, cardíacas y el cáncer de páncreas, entre los padecimientos de orden físico. El riesgo de problemas mentales graves se incrementa

con la menor edad de consumo y la inestabilidad familiar característica de la adolescencia y de adultos jóvenes.¹⁰

Respecto a la cocaína, opioides, y metanfetaminas, el porcentaje de consumidores es muy inferior al que registran el alcohol, el cigarrillo y la marihuana. Una explicación de este fenómeno se encontraría en el precio de adquisición del estupefaciente. Mientras un gramo de marihuana cuesta 2,00 usd., el mismo gramo de cocaína se consigue en hasta en 30,00 usd.¹¹ La adicción y los efectos de la cocaína en la salud suelen ser más agresivos que la marihuana. La esquizofrenia paranoide y la psicosis son las enfermedades más ligadas con su consumo, y en referencia a problemas físicos, se puede detallar destrucción de las vías aéreas superiores, neumonía, y problemas digestivos.¹²

Por ello, el Comité Interinstitucional de Prevención Integral del Fenómeno Socio Económico de las Drogas y de Regulación y Control del Uso de Sustancias Catalogadas Sujetas a Fiscalización (anteriormente SETED), dentro del ámbito de su competencia y en virtud de la Ley Orgánica de prevención; regula y gestiona en la educación superior ecuatoriana la implementación de programas y planes de prevención de consumo.

Estos esfuerzos no solucionan la problemática, puesto que los Institutos de Educación Superior no cuentan con diagnósticos que les permitan tener una línea base de indicadores que ilustren la realidad del uso y consumo de drogas de la comunidad educativa. Más aún, el desconocimiento de los factores asociados impide gestionar las probabilidades de resaltar ese consumo; y esta es la principal causa para que dichos programas de mitigación fracasen y no dejen de ser meros esfuerzos repetitivos que las unidades de bienestar institucional realizan con el único afán de cumplir, pero que no resuelven el problema.¹³

Por lo expuesto, la identificación de los factores de riesgo del uso y consumo de drogas en una Institución de Educación Superior supone no solamente establecer la línea base de consumo; el detalle descriptivo del tipo de droga; la frecuencia; las diferencias etarias, socioeconómicas o de género; sino la determinación de cómo las características de vida y educación se encuentran asociadas a conductas frecuentes de uso y abuso de estas sustancias.

Todo lo mencionado justifica la presente investigación, dado que el establecimiento de estos factores permitirá diseñar estrategias exclusivas encaminadas a la disminución de la probabilidad de consumo; y al mismo tiempo, fortalecer aquellos factores protectores eugenésicos que disminuyen ostensiblemente la probabilidad del uso de drogas en programas efectivos, susceptibles de ser medios y evaluados.

En tal virtud, este estudio tiene el objetivo de determinar el grado en el que los factores socioeconómicos se encuentran asociados con el consumo de alcohol, cigarrillo, marihuana y cannabis, en los estudiantes del Instituto Superior Tecnológico Sucre (ISTS), de Ecuador, durante el semestre 2020 ii.

Métodos

El diseño del estudio fue de tipo no experimental, transversal y prospectivo, correspondiendo al nivel correlacional.

La población diana estuvo conformada por 2.545 estudiantes matriculados en el semestre 2020 ii en el ISTS y se planificó contar con la totalidad del universo, sin embargo, al aplicar los criterios de selección se obtuvo una muestra final de 1.755 alumnos.

Como criterio de inclusión, se consideraron a los estudiantes de las diez carreras del ISTS y de todos los semestres para el período escolar señalado. Se excluyeron a los estudiantes que no estaban matriculados en el momento del levantamiento de información y que no tuviesen firmado el consentimiento informado; además, se a quienes no completaron los dos instrumentos de medición.

La encuesta Socio Económica ISTS fue un instrumento institucional de 80 preguntas, de sondeo autoadministrado en el momento de la matrícula, a través Google Forms, que exploró información categórica nominal dispuesta en cuatro ejes: indicadores de eficacia profesional; datos descriptivos; necesidades educativas especiales; y datos de vida familiar-trabajo.

La información recolectada permitió a la Coordinación de Bienestar Institucional identificar necesidades educativas especiales; condiciones de ingresos y gastos; números de contacto en caso de emergencia; y género y auto identificación étnica. Al ser un instrumento que midió condiciones y no categorías ordinales, sus resultados fueron expresados en porcentajes y frecuencias, sin necesidad de usar baremos.

La encuesta EST-Diagnóstico de la situación del consumo de alcohol, tabaco y otras sustancias psicoactivas en la comunidad universitaria, fue elaborada por la Universidad Central del Ecuador¹⁴ y evaluó el consumo en el último mes, el deseo de consumo y los problemas de consumo en alcohol, cigarrillo, marihuana y cocaína.

No se tomaron en cuenta los resultados de otras drogas como opiáceos, anfetaminas, inhalantes sedantes y alucinógenos.

La segunda dimensión del test evaluó los factores asociados al consumo, como problemas de estudios;

agrado de la carrera; cantidad de amistades; aceptación social; y conflictos laborales. La última dimensión fue el número de horas dedicadas al tiempo libre: a la televisión; deportes; programas; actividad física; fiestas; escuchar música; visitar amigos; redes sociales; paseos-excursiones y juegos de azar.

Respecto a la fiabilidad del predictor, el alfa de Cronbach fue alto, con valor de 0,82. Para el proceso de calificación del instrumento, se calcularon las frecuencias de los resultados del primer, segundo y tercer grupo de preguntas relacionadas con el consumo en el último mes, el deseo de consumo y los problemas de consumo. Las respuestas posibles en los tres grupos fueron: diariamente, semanalmente, una vez y nunca. Para la última dimensión, había cuatro posibles respuestas: no le dedica tiempo; entre 0 a 1 hora; entre 1 a 3 horas; y más de 3 horas.

Se realizaron tres análisis estadísticos. El primero descriptivo, permitió confirmar los porcentajes y frecuencias de los resultados de los factores socioeconómicos de la primera encuesta y de las tres dimensiones del segundo instrumento. En segundo orden, se aplicó la Chi cuadrada para determinar las relaciones estadísticamente significativas entre las variables nominales con la encuesta de drogas. La utilización de esta prueba permitió relacionar el tiempo libre y los factores asociados con la frecuencia/intensidad de consumo de drogas.

Para ambos casos, el nivel de significancia calculado fue de 0,05. Complementario a la Chi cuadrada, se utilizaron los estadísticos de V-Crammer y Gamma, para comprender la fuerza e intensidad de las asociaciones.

La investigación se basó en la hipótesis de que valoraciones altas en el agrado de la carrera; cantidad alta de amistades; alta aceptación familiar; y bajos conflictos laborales, estarían relacionados con baja frecuencia o intensidad de consumo de las sustancias estupefacientes.

Se calculó el Odd Ratio (razón de momios) para confirmar la probabilidad de ocurrencia de las inferencias estadísticas. En este punto, se generaron tablas de 2x2 conformándose grupos de expuestos y no expuestos. En las dimensiones de consumo en el último mes, deseo de consumo y problemas de consumo, las respuestas diariamente, semanalmente y una vez, fueron consideradas como presencia de consumo, presencia de deseo y presencia de problemas, respectivamente.

Las agrupaciones de las respuestas nunca, demostraron ausencia de consumo, ausencia de deseo y ausencia de problemas. Para la última dimensión del tiempo libre, no le dedica tiempo y entre 0 a 1 hora, correspondió al no uso de tiempo, y entre 1 a 3 horas y más de 3 horas indicaron tiempo de dedicación.

Respecto a las consideraciones éticas, se consideró para las encuestas, una pregunta adicional en la que los participantes aceptaban el consentimiento informado, así como el propósito y alcances de la investigación. Se resaltó en todo momento, la confidencialidad de los datos suministrados y que los resultados servirían para la implementación de planes de mejora de la comunidad educativa. Se respetaron los principios éticos de la Declaración de Helsinki para las investigaciones con seres humanos, difundidos por la Asociación Médica Mundial, así como sus posteriores actualizaciones.

Resultados

Variables sociodemográficas

Los resultados de la Encuesta Socioeconómica ISTS, evidenciaron, que predominó el género masculino con el 57,2% (N=1.003) sobre el femenino que representó el 42,8% (N=752).

Respecto a la edad, el grupo etario más representado fue el de 18-26 años con 85,4% (N=1.498); seguido del de 27-35 años con 11,4% (N=201); el de 36 a 44 años con un 2,4% (N=42); el de 45 a 53 años con un 0,5% (N=9); y finalmente el de hasta 17 años con un 0,3% (N=5).

La edad que más se repitió fue la de 20 años; el 50% de los estudiantes estaban por encima de los 22 años; y la media de la edad fue de 22,84 años del cual se desvían en promedio 4,6 años. La curva de distribución fue no paramétrica, con una segmentación de 0,000 en la prueba de Kolmogorov-Smirnov.

La etnia más representada fue la mestiza con el 94,3% (N=1.655); seguido por la indígena con el 3,0% (N=52); la afroecuatoriana con el 1,8% (N= 32); la blanca con el 0,5% (N=9); y finalmente la montubia con 0,4% (N=7).

El estado civil predominante fue el de soltero con 88,5% (N=1.553); seguido por casado con 6,9% (N=121); Unión Libre/Unión de Hecho con 3,5% (N=62); concluyendo con el de divorciado con un 1.1% (N=19).

El 99,1% (N=1.739) manifestó no presentar discapacidad y el 0,9% (N=16) si presentó algún tipo de discapacidad. Cinco personas registraron disminución auditiva, 4 intelectual, 1 psicosocial y 6 personas visual.

Además, el 79,7% (N=1.399) no trabajaba y el 20,3% (N=356) sí. De los estudiantes que se encontraban trabajando, el 81,3% lo hacían en el sector privado y el 18,7% en el público. El 73% tuvo relación de dependencia.

Eficacia profesional

Respecto a los resultados de la eficacia profesional, al analizarse cronológicamente los resultados en los ocho semestres analizados (2017 i; 2017 ii; 2018 i; 2018 ii; 2019

i; 2019 ii; 2020 i; y 2020 ii), resaltó que los estudiantes que no repitieron ninguna materia, se comportaron así: 1.635 (93,2%); 1.648 (93,9%); 1.575 (89,7%); 1.533 (87,4%); 1.498 (85,4%); 1.443 (82,2%); 1.469 (83,7%); y 1.555 (88,6%). Se aprecia que los estudiantes que no repitieron ninguna materia, disminuyeron 11,7% desde el período 2018 ii, hasta 2019 ii;

De igual forma, los que repitieron una materia, se comportaron de la forma siguiente: 61 (3,5%); 60 (3,4%); 96 (5,5%); 126 (7,2%); 140 (8,0%); 159 (9,1%); 173 (9,9%); y 104 (5,9%). Destaca que aquellos que arrastraron una materia, aumentaron en promedio 1,3% desde el 2017 ii.

Los que repitieron entre dos y cuatro materias tuvieron la siguiente evolución cronológica: 56 (3,2%); 44 (2,5%); 79 (4,5%); 88 (5,0%); 108 (6,2%); 137 (7,8%); 95 (5,4%); concluyendo con 80 (4,6%). En este caso se percibe un incremento desde el 2018 ii a un ritmo de 1,3% hasta 2020 i, punto en el que decrecen hasta 3,2%.

Por último, los que repitieron más de cuatro materias tuvieron el comportamiento siguiente: 3 (0,2%); 3 (0,2%); 5 (0,3%); 8 (0,5%); 9 (0,5%); 16 (0,9%); 18 (1,0%); finalizando con 16 (0,9%). En este caso se presenta una tendencia al alza con promedio del 0,1% hasta 2020 i, donde disminuyen en 0,11%.

Resultados del EST-Diagnóstico de la situación del consumo de alcohol, tabaco y otras sustancias psicoactivas en la comunidad universitaria

Los resultados del consumo, deseo y problemas asociados al uso de sustancias, evidenciaron los resultados siguientes:

Consumo en el último mes:

- Tabaco: diariamente o casi diariamente 13 (0,7%); semanalmente 56 (3,2%); una vez 322 (18,3%); nunca 1.364 (77,7%).
- Alcohol: diariamente o casi diariamente 7 (0,4%); semanalmente 72 (4,1%); una vez 832 (47,4%); nunca 844 (48,1%).
- Cannabis: diariamente o casi diariamente 3 (0,2%); semanalmente 7 (0,4%); una vez 52 (3,0%); nunca 1.693 (96,5%).
- Cocaína: diariamente o casi diariamente 2 (0,1%); semanalmente 2 (0,1%); una vez 4 (0,2%); nunca 1.747 (99,5%).

Deseo de consumir la sustancia:

- Tabaco: diariamente o casi diariamente 11 (0,6%); semanalmente 29 (1,7%); una vez 152 (8,7%); nunca 1.563 (89,1%).
- Alcohol: diariamente o casi diariamente 5 (0,3%); semanalmente 38 (2,2%); una vez 368 (21,0%);

nunca 1.344 (76,6%).

- Cannabis: diariamente o casi diariamente 2 (0,1%); semanalmente 4 (0,2%); una vez 22 (1,3%); nunca 1.727 (98,4%).
- Cocaína: diariamente o casi diariamente 1 (0,1%); semanalmente 1 (0,1%); una vez 1 (0,1%); nunca 1.752 (99,8%).

Problemas ocasionados por el consumo:

- Tabaco: diariamente o casi diariamente 1 (0,1%); semanalmente 8 (0,5%); una vez 86 (4,9%); nunca 1.660 (94,6%).
- Alcohol: diariamente o casi diariamente 0 (0%); semanalmente 11 (0,6%); una vez 179 (10,2%); nunca 1.565 (89,2%).
- Cannabis: diariamente o casi diariamente 0 (0%); semanalmente 2 (0,1%); una vez 8 (0,5%); nunca 1.745 (99,4%).
- Cocaína: diariamente o casi diariamente 0 (0%); semanalmente 1 (0,1%); una vez 2 (0,1%); nunca 1.752 (99,8%).

Otros factores relacionados al consumo de drogas

Respecto a los factores relacionados al consumo de droga, se evidenció que 160 estudiantes (9,1%) tuvo problemas de estudios y 1.595 (90,9%) no. Asimismo, 1.667 (95,0%) manifestaron que la carrera era de su agrado y 88 (5,0%) que no. En relación a los grupos amigos, 1.280 (72,9%) señaló que sí y 475 (27,1%) que no.

El factor aceptado por compañeros reflejó 1.645 (93,7%) contestando sí y 110 (6,3%) que no; mientras que el factor comparte problemas con compañeros reflejó 786 (44,8%) respuestas que sí y 969 (55,2%) que no.

Adicionalmente, 1.407 (80,2%) evidenciaron preocupación por problemas de sus amigos y 348 (19,8%) no; la pertenencia a organizaciones reflejó 125 (7,1%) con afirmaciones y 1.630 (92,9%) con negaciones.

Finalmente, 482 (27,5%) trabajan actualmente y 1.273 (72,5%) no lo hacen; mientras que manifestaron conflictos laborales 53 (3,0%) y 1.702 (97,0%) no.

En cuanto al agrado de los participantes hacia la carrera, el 5% de la población no le agrada la carrera, el 6,3% no se siente aceptado, el 19,8% no se interesa por los problemas de los demás, el 27,1% no tiene grupos de amigos en la institución, el 55,2% no comparte sus problemas con compañeros, el 9,1% tiene problemas de estudios y tan solo el 7,1% pertenece a organizaciones. El 30% tiene trabajo y de este grupo, un 3% experimenta conflictos laborales.

La **tabla I** refleja el número de horas dedicadas al tiempo libre.

Tabla I: Tiempo libre.

Tiempo libre	Lectura	TV	Deportes	Arte	Actividad Física
Más de 3 horas	80 (4,6%)	100 (5,7%)	182 (10,4%)	47 (2,7%)	167 (9,5%)
Entre 1 y 3 horas	492 (28,0%)	463 (26,4%)	509 (29,0%)	207 (11,8%)	529 (30,1%)
Entre 0 y 1 hora	973 (55,4%)	768 (43,8%)	753 (42,9%)	696 (39,7%)	871 (49,6%)
No le dedica tiempo	210 (12,0%)	424 (24,2%)	311 (17,7%)	805 (45,9%)	188 (10,7%)
Tiempo libre	Fiestas	Música	Amigos y familiares	Redes	Paseos
Más de 3 horas	930 (53,0%)	541 (30,8%)	175 (10,0%)	619 (35,0%)	157 (8,9%)
Entre 1 y 3 horas	498 (28,4%)	723 (41,2%)	484 (27,6%)	413 (24,0%)	352 (20,1%)
Entre 0 y 1 hora	258 (14,7%)	463 (26,4%)	725 (41,3%)	434 (25,0%)	539 (30,7%)
No le dedica tiempo	69 (3,9%)	28 (1,6%)	371 (21,1%)	289 (16,0%)	707 (40,3%)

Fuente: elaboración propia

Respecto a la relación entre las variables nominales de la encuesta socioeconómica, entre los resultados de frecuencia, deseo y problemas de consumo, destaca que las materias repetidas 2020 ii mostraron en su nexo con el deseo de consumo de tabaco un OR de 1,5, un p-valor de 0,039 y un V Cramer de 0,064. Al confrontarse dichas materias con el deseo de consumo de alcohol, se obtuvo un OR nulo, un p-valor de 0,000 y un V Cramer de 0,113.

Por su parte, respecto al nexo del género y el deseo de consumir tabaco, se evidenció un OR nulo, un p-valor de 0,000 y un V Cramer de 0,016; mientras que el vínculo entre género y el deseo de consumir alcohol, arrojó como resultados un OR nulo, un p-valor de 0,000 y un V Cramer de 0,09.

Finalmente, la relación entre autoidentificación y deseo de consumir tabaco mostró valores de un OR nulo, un p-valor de 0,000 y un V Cramer de 0,131; mientras que los valores que relacionaron a la autoidentificación y el deseo de consumo de alcohol fueron de un OR nulo, un p-valor de 0,000 y un V Cramer de 0,097.

En la **tabla II** se detallan las inferencias estadísticas entre los factores de la encuesta de drogas con la frecuencia de consumo-deseo de consumo y problemas por el consumo.

La **tabla III** refleja las inferencias entre factores de consumo y deseo de consumo.

Tabla II: Factores de consumo y frecuencia de consumo.

Frecuencia de consumo	Tabaco			Alcohol			Cannabis			Cocaína		
	p	Gamma	OR	p	Gamma	OR	p	Gamma	OR	p	Gamma	OR
Problemas de estudios	0,199	-	-	0,861	-	-	0,824	-	-	0,655	-	-
Carrera de agrado	0,164	-	-	0,012	0,052	-	0,038	0,262	-	0,032	0,463	-
Grupos amigos ists	0,018	-0,097	-	0,225	-	-	0,227	-	-	0,394	-	-
Aceptado por compañeros	0,589	-	-	0,19	-	-	0,804	-	-	0,029	-0,6	5
Comparte problemas con compañeros	0,376	-	-	0,105	-	-	0,183	-	-	0,373	-	-
Se preocupa por problemas de sus amigos	0,234	-	-	0,28	-	-	0,841	-	-	0,025	0,6	-
Pertenece a organizaciones	0,822	-	-	0,351	-	-	0,000	-0,5	-	0,004	-0,7	-
Trabaja actualmente	0,003	-0,2	-	0,141	-	-	0,903	-	-	0,07	-	-
Conflictos laborales	0,006	0,3	2	0,000	0,194	-	0,19	-	-	0,002	0,64	-

Fuente: elaboración propia

Tabla III: Factores de consumo y deseo de consumo.

Deseo de consumo	Tabaco			Alcohol			Cannabis			Cocaína		
	p	Gamma	OR	p	Gamma	OR	p	Gamma	OR	p	Gamma	OR
Problemas de estudios	0,54	-	-	0,53	-	-	0,032	0,09	-	0,017	0,66	-
Carrera de agrado	0,066	-	-	0	0,134	-	0,008	0,4	-	0	0,9	-
Grupos amigos ists	0,97	-	-	0,5	-	-	0,24	-	-	0,77	-	-
Aceptado por compañeros	0,301	-	-	0,152	-	-	0,451	-	-	0,002	0,7	-
Comparte problemas con compañeros	0,457	-	-	0,518	-	-	0,493	-	-	0,414	-	-
Se preocupa por problemas de sus amigos	0,38	-	-	0,64	-	-	0,311	-	-	0,209	-	-
Pertenece a organizaciones	0,024	-0,26	-	0	-0,122	-	0	-0,6	-	0,004	-0,7	-
Trabaja actualmente	0,215	-	-	0,448	-	-	0,686	-	-	0,334	-	-
Conflictos laborales	0,095	0,000	2	0,347	-	-	0,062	-	-	0	0,8	16

Fuente: elaboración propia

En la **tabla IV** se exponen las inferencias entre factores de consumo y problemas derivados del consumo.

En la **tabla V** se muestran los resultados del uso del tiempo libre relacionado con la frecuencia de consumo.

Finalmente, en la **tabla VI** se evidencia el uso del tiempo libre relacionado deseo de consumo.

Discusión

Respecto a los resultados de la eficacia profesional, resalta que en general se evidencia que, con diferentes magnitudes, el promedio de todos los registros es negativo, pero, en los dos últimos semestres hay menos materias reprobadas.

En relación a los resultados del EST-Diagnóstico de la situación del consumo de alcohol, tabaco y otras sustancias psicoactivas, se destaca que 391 personas (22,3%) consumen cigarrillos durante el último mes, de estos, 92 (23,5%) son mujeres y 299 (75,5%) hombres. Por cada mujer que consume cigarrillos hay 3 hombres que lo hacen.

En cuanto al alcohol, 911 (51,9%) indican que ingieren bebidas alcohólicas, de los cuales 374 (41,1%) son mujeres y 537 (58,9%) son hombres, con una razón de 1:1,4. Para cannabis, se registra consumo en 62 (3,5%) informantes, 14 mujeres (22,6%) y 48 hombres (77,4%), proporción 1:3,4.

Resalta que solo ocho estudiantes consumen cocaína (0,5%), de ellos, 2 son mujeres (25%) y 6 hombres (75%).

Tabla IV: Factores de consumo y problemas derivados del consumo.

Problemas por consumo	Tabaco			Alcohol			Cannabis			Cocaína		
	ρ	Gamma	OR	ρ	Gamma	OR	ρ	Gamma	OR	ρ	Gamma	OR
Problemas de estudios	0,87	-	-	0,032	0,28	-	0,018	0,623	-	0,126	-	-
Carrera de agrado	0,7	-	-	0,756	-	-	0,012	0,36	-	0	0,811	-
Grupos amigos ist	0,941	-	-	0,583	-	-	0,553	-	-	0,573	-	-
Aceptado por compañeros	0,003	0,1	-	0,015	0,14	-	0,029	0,58	-	0,001	0,76	-
Comparte problemas con compañeros	0,296	-	-	0,357	-	-	0,946	-	-	0,534	-	-
Se preocupa por problemas de sus amigos	0	0,36	-	0,002	0,29	-	0,355	-	-	0,498	-	-
Pertenece a organizaciones	0,78	-	-	0,944	-	-	0,009	-0,7	-	0,06	-	-
Trabaja actualmente	0,381	-	-	0,751	-	-	0,494	-	-	0,183	-	-
Conflictos laborales	0	0,58	3,8	0	0,33	-	0	0,56	-	0	0,88	-

Fuente: elaboración propia

Tabla V: Tiempo libre y frecuencia de consumo.

Uso tiempo libre	Tabaco			Alcohol			Cannabis			Cocaína		
	ρ	Gamma	OR	ρ	Gamma	OR	ρ	Gamma	OR	ρ	Gamma	OR
Horas de lectura	0,315	-	-	0,247	-	-	0,007	-0,36	-	0,567	-	-
Horas tv	0,052	-	-	0,204	-	-	0,031	-0,037	-	0,534	-	-
Deportes	0,02	-0,188	-	0,154	-	-	0,506	-	-	0,742	-	-
Arte	0,511	-	-	0,06	-	-	0,018	-0,321	-	0,493	-	-
Ejercicio	0,214	-	-	0,296	-	-	0,117	-	-	0,463	-	-
Fiestas	0	0,324	2	0	0,419	2,5	0,126	-	-	0,406	-	-
Música	0,098	-	-	0,102	-	-	0,007	-0,46	-	0,969	-	-
Visita fam	0,648	-	-	0	-0,158	-	0,622	-	-	0,248	-	-
Redes sociales	0,058	-	-	0,065	-	-	0,792	-	-	0,649	-	-
Paseos excursiones	0,000	-0,157	0	0,022	-0,111	-	0,14	-	-	7,14	-	-

Fuente: elaboración propia

Tabla VI: Tiempo libre y deseo de consumo.

Deseo de consumo	Tabaco			Alcohol			Cannabis			Cocaína		
	ρ	Gamma	OR	ρ	Gamma	OR	ρ	Gamma	OR	ρ	Gamma	OR
Horas de lectura	0,374	-	-	0,017	-0,133	-	0,187	-	-	0,249	-	-
Horas tv	0,26	-	-	0,122	-	-	0,028	-	-	0,313	-	-
Deportes	0,061	-	-	0	-0,189	-	0,578	-	-	0,343	-	-
Arte	0,483	-	-	0,264	-	-	0,382	-	-	0,375	-	-
Ejercicio	0,027	-0,153	-	0,075	-	-	0,175	-	-	0,653	-	-
Fiestas	0	0,338	2	0	0,409	2,3	0,255	0	-	0,538	-	-
Música	0,017	-0,196	-	0	-0,222	-	0,007	-0,674	-	0,373	-	-
Visita fam	0,343	-	-	0,118	-	-	0,496	-	-	0,683	-	-
Redes sociales	0,017	-0,174	-	0	-0,241	-	0,348	-	-	0,369	-	-
Paseos excursiones	0,315	0	-	0,281	0	-	0,574	0	-	0,642	-	-

Fuente: elaboración propia

Es notorio que 192 (10,9%) frecuentemente sienten un fuerte deseo de consumo de tabaco, de los cuales, 39 (20,3%) son mujeres y 153 (79,7%) son hombres.

Otros resultados que merecen atención es que 411 (23,4%) experimentan deseos de consumo de alcohol, de los que, 143 (34,8%) son de sexo femenino y 268 masculino (65,2%). Asimismo, 28 (1,6%) registran deseos de consumo para cannabis, de los cuales 7 (25%) son mujeres y 21 (75%) son hombres, mientras que 3 (0,2%) hombres se identifican en necesidad de consumo de cocaína. La razón entre hombres y mujeres es: 1:3,9 en tabaco, 1:1,8 en alcohol, 1:3 en cannabis, y en cocaína no hay frecuencia femenina.

Para responder con qué frecuencia el consumo de la droga causa problemas en los estudiantes, el tabaco evidencia que 95 (5,4%) de los sujetos presentan problemas de salud, sociales, legales o económicos. De estos individuos, 15 (15,8%) son mujeres y 80 (84,2%) son hombres. En el alcohol, aparecen 190 (10,8%) alumnos entre los cuales 58 (30,5%) son de género femenino y 132 (69,5%) son masculino.

Para el caso de cannabis, el número de participantes con problemas es de 10 (0,6%), de los cuales hay 2 (20%) mujeres y 8 (80%) hombres. La cocaína solo cuenta con 3 (0,2%) hombres. Al igual que en las dos dimensiones anteriores, los hombres evidencian la mayor frecuencia de problemas derivados del consumo, tal como lo indica las razones: 1:5,3 tabaco, 1:2,2 alcohol, 1:4 marihuana.

El número de hombres y mujeres con deseos de consumir tabaco, alcohol y marihuana es casi la mitad de la frecuencia de consumo en el último mes. El 50% de los estudiantes que consumen estas sustancias en los últimos 30 días, sienten un fuerte deseo o ansias de fumarlas o ingerirlas. Esto podría indicar que, 46 mujeres y 150 hombres tienen algún grado de adicción al cigarrillo, 187 mujeres y 269 hombres al alcohol, y 7 mujeres y 24 hombres a la marihuana.

El alcohol, con algo más del 50%, es la droga que se consume con mayor frecuencia en el último mes, seguida del tabaco con 22,3%, la marihuana con 3,5% y la cocaína con 0,5%. De la misma manera, el alcohol registra el porcentaje más alto en el deseo de consumo con el 23,4%, delante del tabaco con 10,9%, cannabis 1,6% y cocaína 0,2%. Los problemas que se originan por el consumo siguen el mismo patrón, 10,8% para alcohol, 5,4% tabaco, 0,6% cannabis y 0,2% cocaína.

En concordancia con la **tabla I**, de los participantes, 1.428 (81,4%) invierten su tiempo en fiestas y diversión. Este factor registra la mayor frecuencia. En segundo lugar, se posiciona el tiempo libre para la música, con un total de 1.264 (72,0%) estudiantes. Posteriormente se encuentran las horas en redes sociales, con 1.032

(58,8%); seguido de las horas de actividad física, con 696 (39,7%); y de las horas destinadas a deportes, con 691 (39,4%). El quinto lugar es para amigos y familiares, con 659 (37,5%), posteriormente, las horas de lectura, con 572 (32,6%); horas de televisión, con 563 (32,1%); paseos y excursiones con 509 (29,0%); y finalmente, actividades artísticas con 254 (14,5%).

A partir del nivel de significancia de 0,05, debe destacarse que, de todas las variables sociodemográficas, las materias repetidas 2020 ii, el ingreso mensual, el género y la autoidentificación étnica son estadísticamente significativas para deseo de consumo de alcohol y de tabaco. El estadístico que mide la fuerza de la relación para variables nominales es la V de Cramer que en todos los casos arroja valores de baja intensidad. No se evidencian probabilidades de ocurrencia significativas.

De acuerdo con la **tabla II**, existen 12 relaciones estadísticamente significativas entre factores asociados al consumo con la frecuencia de consumo. Los problemas de estudios, y el compartir problemas con compañeros, no registran ninguna asociación. La fuerza inferencial es baja para tabaco y alcohol, mientras que para cannabis y cocaína es media y alta. La direccionalidad de Gamma confirma la hipótesis de investigación en las 12 asociaciones. La dirección negativa de Gamma en cigarrillo, indica que los informantes sin trabajo y con menor cantidad de amigos en el ISTS, tienden a consumir más tabaco.

Con referencia a la probabilidad, los conflictos laborales aumentan 2 veces más el consumo de tabaco, y la falta de aceptación de los compañeros incrementa en 5 veces el consumo de cocaína.

La **tabla III** manifiesta que las amistades, los compañeros y el trabajo no registran relación significativa con el deseo de consumo en las cuatro sustancias. De las 11 inferencias, la participación en organizaciones se relaciona con el deseo de consumo de tabaco, alcohol, cannabis y cigarrillo. La fuerza de inferencia para tabaco y alcohol es baja, mientras que cannabis y cocaína es alta y media.

En todas las asociaciones se comprueba la hipótesis de investigación. La dirección negativa de las cuatro sustancias en el factor de pertenecer a organizaciones, indica que la necesidad de consumo se intensifica en virtud de la no afiliación del estudiante a una organización. Los conflictos labores aumentan el deseo del uso de cigarrillo hasta en 2 veces más, y hasta 16 veces más para el consumo de cocaína.

De acuerdo con la **tabla IV**, mientras que los grupos de amigos y el trabajo no se relacionan con problemas derivados del consumo de las sustancias, la aceptación por los compañeros y los conflictos laborales son los de mayor influencia. El alcohol y tabaco presenta fuerza

inferencial media y baja, mientras que cannabis y cocaína registran fuerza alta. Los conflictos laborales incrementan la probabilidad de problemas derivados del consumo de tabaco hasta en 3,8 veces más.

En concordancia con la **tabla V**, existen 10 inferencias con las sustancias con excepción de cocaína con una intensidad de baja y media. A mayores horas de música de lectura, tv y actividades artísticas, el consumo de cannabis disminuye. La práctica de deportes y excursiones influye en la disminución de consumo de tabaco, pero la mayor exposición de fiestas la intensifica. Las visitas a familiares y las excursiones, reducen el consumo de alcohol, mientras que las fiestas la aumentan. De hecho, los estudiantes expuestos a fiestas tienen 2 veces más probabilidad de consumo de tabaco y 2,5 veces más probabilidad de consumo de alcohol.

La **tabla VI** demuestra que no existen inferencias entre tiempo libre y problemas de consumo. La intensidad de las relaciones es baja para tabaco y alcohol, con excepción en el tiempo destinado a fiestas, en donde Gamma tiene una fuerza media. A mayor tiempo de dedicación a las actividades de ejercicio, a la música y a las redes sociales, disminuye el deseo de consumo de tabaco. A mayores horas de lectura, deportes, música y redes sociales, disminuye el deseo de consumo de alcohol. Existe una relación positiva entre exposición a fiestas y deseo de consumir tabaco y alcohol. Los participantes tienen una probabilidad de incrementar su deseo de consumo en hasta 2 veces más para tabaco, y hasta 2,3 veces más en alcohol. La actividad de escuchar música está inversamente relacionada con el consumo de cannabis.

Los resultados que se obtienen en el presente estudio evidencian que ninguna de las 10 inferencias se relaciona con cocaína.

Llegado este momento del análisis de resultados, es oportuno resaltar que las cifras que se advierten en¹⁵ sobre el consumo de tabaco indican la diferencia entre hombres y mujeres, y es que por cada mujer que fuma existen 4 hombres que lo hacen a nivel mundial. El razonamiento a este hecho está en la dinámica de los efectos de recompensa de la dopamina, que en los hombres se activa más.¹⁶

El consumo de alcohol también es superior en hombres que, en mujeres, sin que haya diferencias significativas por grupos etarios. En el estudio de¹⁷ se investiga la prevalencia de alcohol en 234 jóvenes universitarios de Jalisco, México, donde se analiza la frecuencia de consumo y el tipo de bebida alcohólica. En todos los análisis la mujer presenta menor exposición al licor y la afectación que causa el alcohol, perjudica más a la mujer porque en su composición corporal hay mayor concentración de grasa y menor porcentaje de agua,

además de una digestión más aletargada en comparación con el hombre.

Esta interpretación sumada a otros factores socioculturales como los estereotipos de género, explican las relaciones del consumo entre hombres y mujeres que se obtienen en estas investigaciones y las del presente estudio. El consumo de las drogas psicoactivas cannabis y cocaína, también tienen en el hombre a su mayor consumidor y de acuerdo con¹⁸, la razón recae en la mayor sensibilidad de la mujer por los efectos sobre el estrógeno y la progesterona.

Las personas con un deseo de consumo alto corresponden a la mitad de quienes presentan en el último mes alta frecuencia de consumo en tabaco, alcohol y cannabis. La frecuencia de consumo en el último mes no necesariamente explica el deseo, necesidad o pulsión, ni tampoco se pueden determinar características de dependencia.¹⁹

En este sentido, la mitad de los consumidores que coinciden con deseo alto de consumo deben ser analizados en ulteriores estudios para confirmar esta posible asociación.

El alcohol es la droga que más se consume en los estudiantes del ISTS, seguida del tabaco, marihuana y cocaína. Estas dos últimas no llegan a más del 4%. En un estudio sobre alcohol, cigarrillo y drogas ilícitas que se realiza por²⁰ en un preuniversitario de Perú, el licor resulta ser la droga de mayor frecuencia, seguido del cigarrillo con valores similares a los del presente estudio. En la muestra, en donde además participan 815 adolescentes, el consumo de la cocaína obtiene el tercer puesto con 7% y después la marihuana con 0,7%.

Sin embargo,²¹ descubre una prevalencia de consumo de cocaína de 5,3% y de marihuana de 44,1% en 1.577 estudiantes universitarios chilenos. Otro estudio al respecto, que se realiza en Colombia por²² sobre 1.264 estudiantes universitarios, indica el consumo de la marihuana (4,7%) por encima de la cocaína (2%). Estos registros sobrepasan la frecuencia de consumo de las sustancias sujetas a fiscalización y confirman el mayor consumo de marihuana sobre cocaína. El deseo de consumo de sustancias estupefacientes en los estudios de^{17,18,19,20} y ²² registran mayores valores para el alcohol, seguido del tabaco, marihuana y cocaína. Ninguno de los instrumentos de medición que se utilizan son específicos para conducta adictiva.

En referencia a la relación de variables sociodemográficas con la frecuencia y el consumo de estupefacientes,²³ encuentra que el género y el rendimiento académico se relacionan estadísticamente con el consumo de alcohol, en una población de 618 estudiantes universitarios.

Otros datos nominales como la raza, trabajo fijo, e ingreso económico, no son significativos. Al comparar estos

resultados con los del presente estudio, hay que recalcar que el sueldo, las materias reprobadas del semestre anterior, el género y la autoidentificación étnica tienen relación con el deseo de consumo de alcohol y tabaco, siempre con una fuerza baja y sin valor predictivo.

Para²⁴, el consumo de tabaco en adolescentes, a partir de los 16 años, está directamente relacionado con la existencia de familiares que fumen y no por el nivel académico, el aspecto laboral, la práctica de deportes, y la asistencia a fiestas. En este mismo aspecto²⁵, en un estudio de 146 adolescentes, concluye que el hábito de consumo de tabaco se incrementa por la exposición a la sustancia a través de los padres fumadores (OR:11,3); ausencia de actividades físicas (OR:3,3); disponibilidad de dinero; y número de asignaturas aprobadas.

Estos datos difieren a los encontrados en el presente estudio, ya que los factores que ejercen influencia son la presencia de los compañeros, la falta de un empleo (OR:2) y los conflictos laborales. Puede que las diferencias obedezcan a la mayor libertad que tienen los estudiantes al cumplir la mayoría de edad y la ocupación laboral.

En una investigación que realiza²⁶, se determina el grado de asociación del consumo de alcohol en 849 estudiantes universitarios y los factores relacionados son los amigos, la familia y el género, antes que el agrado de la carrera o conflictos laborales. El consumo de alcohol en el último mes se registra en 25,8%, que es la mitad del consumo medido en el ISTS.

En cuanto al consumo de marihuana,²⁷ halla la prevalencia de los factores asociados al consumo de cannabis en una universidad pública de Colombia, y demuestra que el consumo de cigarrillo (OR:23) y la edad de 20-21 años (OR: 3,05) tienen inferencias. Igualmente,²⁸ investiga sobre la prevalencia de factores en el consumo de cannabis en 814 adolescentes y descubre que el género; la edad (18-19 años); el estrato social; el nivel académico de los padres; y el consumo de cigarrillo, provoca un mayor consumo de marihuana.

En la presente investigación, las variables agrado de la carrera y pertenencia a organizaciones, resultan estadísticamente significativas con una intensidad media y baja, respectivamente. En ninguno de los anteriores resultados se confirman valores significativos de OR.

Los estudios de factores predisponentes al consumo de cocaína presentan poblaciones drogodependientes, como, por ejemplo, el que se realiza por²⁹ en una población mayor a 18 años en Colombia, donde se demuestra que la edad (18-25 años) OR:1,26 y el estrato social bajo (OR:1,43) aumentan la probabilidad de consumo.

Los datos arrojados en el estudio del ISTS muestran relaciones entre los problemas de estudio, el agrado

de la carrera, la aceptación de los compañeros, la no pertenencia a organizaciones y los conflictos laborales (OR: 16), como elementos relacionados. Estos resultados responden a tres estudiantes que tienen consumo habitual al estupefaciente.

Conclusiones

En el presente estudio se determinó el grado en el que los factores socioeconómicos se encuentran asociados con el consumo de alcohol, cigarrillo, marihuana y cannabis en los estudiantes del Instituto Superior Tecnológico Sucre (ISTS), de Ecuador, durante el semestre 2020 ii.

Se concluye que las variables socio demográficas género, la etnia, las materias repetidas en 2020 y el ingreso mensual influyeron en el consumo de tabaco y alcohol, con baja intensidad y sin presentar asociación predictiva OR.

Los factores que se relacionaron más con el consumo, deseo y problemas derivados del uso de las sustancias estupefacientes, fueron el desagrado a la carrera; la no pertenencia a organizaciones; los conflictos en el trabajo; los problemas de estudio; y la aceptación por los compañeros.

En cuanto a las asociaciones encontradas en el consumo de tabaco, las personas con conflictos laborales tuvieron el doble de probabilidad de deseo de consumo y más problemas derivados del uso de esta sustancia. La poca aceptación social que experimentaron en la institución, incrementó notablemente su consumo, así como los conflictos laborales su deseo de esta droga.

En cuanto a las actividades de ocio, el tiempo que los jóvenes dedicaron a la música, la televisión y el arte, disminuyeron el consumo de cannabis; y, por otro lado, los deportes, las visitas a familiares y las excursiones previnieron el consumo de tabaco y alcohol. Se evidenció que las reuniones sociales, las celebraciones y fiestas se relacionaron directamente con el consumo de alcohol y cigarrillo, lo cual intensificó la probabilidad de consumo de tabaco y de alcohol. Así mismo, los participantes expuestos a las fiestas duplicaron la intensidad del deseo de consumo de alcohol y cigarrillo.

La droga de mayor consumo en los estudiantes fue el alcohol, seguido del cigarrillo, la marihuana y la cocaína. En todos los resultados, fueron los hombres quienes presentaron mayor frecuencia y deseo de consumo. Los indicadores pedagógicos mostraron que desde 2017, disminuye el porcentaje de aprobación de materias, aunque desde el 2020, los indicadores presentan un leve mejoramiento. Esta situación es vinculante con un ligero aumento en el consumo de alcohol.

Las actividades que más practicaron fueron las fiestas; escuchar música; las redes sociales; la práctica de

ejercicio-deportes; las visitas a familiares; la lectura; la televisión; los paseos y las actividades artísticas. Se debe considerar a la música; la televisión; el arte; los deportes; y las excursiones en el diseño de actividades de mitigación de consumo droga, debido a que estos son factores protectores o eugenésicos que disminuyen

la probabilidad del deseo y consumo de marihuana, alcohol y cigarrillo.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses respecto a la presente investigación.

Referencias

1. EL Telégrafo. Más de \$ 144.000 millones sería el costo de droga incautada en 2020. 2020.
2. Laita AD,RAD,&CJP. Enfermedades por tóxicos: intoxicaciones agudas más frecuentes por medicamentos y drogas. *Medicine-Programa de Formación Médica Continuada Acreditado*. 2018; 12(69): p. 4043-54.
3. Muñoz J. Efectividad de un programa de educación emocional y habilidades interpersonales sobre la capacidad de resiliencia en adolescentes con trastorno mental. *Proyecto de investigación*.; 2018.
4. Álvarez Velasco C. Debut y despedida: la historia de la Secretaría Técnica de Prevención Integral de Drogas de Ecuador. Quito, Ecuador: Friedrich-Ebert-Stiftung (FES-ILDIS); 2019.
5. Zalamea Suárez JJ,&BSLA. La constitución ecuatoriana de 2008 y el precedente constitucional. *Revista Iuris*. 2018; 2(16): p. 203-23.
6. Constitución de la República del Ecuador. Constitución de la República del Ecuador. Registro oficial. Quito: Tribunal Constitucional del Ecuador, Asamblea Constituyente del Ecuador; 2008. Report No.: Nro, 449.
7. Secretaría Técnica de Drogas (SETED). Portal en línea SETED. [Online].; 2017 [cited 2018]. Available from: <http://www.prevenciondrogas.gob.ec>.
8. Organización Panamericana de la Salud. Informe de situación regional sobre el alcohol y la salud en las Américas. [Online].; 2015. Available from: http://iris.paho.org/xmlui/bitstream/handle/123456789/7708/9789275318553_esp.pdf.
9. Policía Nacional del Ecuador (PNE). Informe anual de incautación de drogas. [Online].; 2018. Available from: <https://www.policia.gob.ec/un-total-de-22-998-dosis-de-droga-incauta-la-policia-en-11-operativos-desarrollados-en-guayaquil/>.
10. Castañeda CP,ALM,IB,NR,MF,DC.&CNA. Uso de cannabis en jóvenes hospitalizados por un primer episodio de psicosis: un estudio caso-control. *Revista médica de Chile*. 2020; 148(11).
11. El Telégrafo. Seis Factores que explican la violencia.; 2021. Available from: <https://www.eltelegrafo.com.ec/noticias/judicial/12/implicados-homicidios-asesinatos-hombres-narcotrafico-corrupcion>.
12. Guerrón A. Discursos en torno al cuerpo de los jóvenes consumidores de pasta base de cocaína en Quito. Master's thesis. Universidad Andina Simón Bolívar, Sede Ecuador; 2016.
13. Kuri. D. Políticas sobre drogas en el Ecuador. Guayaquil: Universidad Espíritu Santo; 2021.
14. UCE. Diagnóstico de la situación del consumo de alcohol, tabaco y otras sustancias psicoactivas en la comunidad universitaria. Quito: Universidad Central de Ecuador; 2000.
15. OMS. Organización Mundial de la Salud. [Online].; 2017 [cited 2021]. Available from: ¡Error! Referencia de hipervínculo no válida..
16. National Institute on Drug Abuse. NACDA guidelines for administration of drugs to human subjects.. [Online].; 2020 [cited 2021]. Available from: <https://www.drugabuse.gov/research/clinical-research/nacda-guidelines-administr>.
17. Gómez. Z. Consumo de alcohol, tabaco y otras drogas en jóvenes universitarios. *RESPYN Revista Salud Pública y Nutrición*. 2018; 38: p. 547-51.
18. Callado L. Consumo de cannabis, juventud y género. *Trastornos adictivos*. 2011; 13(3): p. 89-90.
19. López M. Influencia del consumo de drogas en los estudiantes universitarios. *Rev Estomatol Herediana*. 2012 oct - dic; 22(4): p. 247-56.
20. Morales J. Consumo de alcohol y drogas ilícitas en adolescentes preuniversitarios. *Revista Cubana de Medicina General Integral*. 2019; 35(3): p. 878.
21. Sepúlveda M. Estudio cuantitativo del consumo de drogas y factores sociodemográficos asociados en estudiantes de una universidad tradicional chilena. *Revista Médica de Chile*. 2011; 139: p. 856-63.
22. Tirado J. Prevalencia y factores de riesgo para el consumo y dependencia de drogas en estudiantes de una universidad de Medellín, Colombia 2009. *Revista Facultad Nacional de Salud Pública*. 2012; 30(1): p. 38-44.
23. Camacho I. Consumo de alcohol en universitarios Relación funcional con los factores sociodemográficos, las expectativas y la ansiedad social. *Acta colombiana de psicología*. 2005; 8(1): p. 91-120.
24. Muñoz P. Práctica de actividad física, consumo de tabaco y alcohol y sus efectos en la salud respiratoria de los jóvenes universitarios. *Retos: nuevas tendencias en educación física, deporte y recreación*. 2019; 35: p. 130-5.
25. Villena A. Factores asociados al consumo de tabaco en adolescentes. *Revista Clínica de Medicina de Familia*. 2009; 2(7): p. 320-5.
26. Betancourth S. Consumo de alcohol en estudiantes universitarios colombianos. *Universidad y Salud*. 2017; 19(1): p. 37-50.
27. Martínez J. Prevalencia y factores asociados al consumo de marihuana en estudiantes de 18 a 25 años de una universidad pública, Colombia. *Universidad y Salud*. 2016; 18(3): p. 525-31.
28. Martínez-Torres J. Prevalencia de vida y factores asociados al consumo de marihuana en estudiantes escolarizados de Pamplona-Colombia, durante el primer período de 2015: estudio Emtamplona. *Revista médica de Chile*. 2018; 146(9): p. 1016-23.
29. D. B. Factores asociados al consumo de cocaína en usuarios de heroína inyectable en Colombia. *Salud mental*. 2016; 39(4): p. 205-11.

Results of arthroscopic debridement in patients with osteoarthritis of the knee

Resultados del desbridamiento artroscópico en pacientes con osteoartritis de la rodilla

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Abstract

Background: There are several treatments for osteoarthritis and Arthroscopic debridement is one of the them. We decided to consider Results of Arthroscopic Debridement in Patients with Osteoarthritis of the Knee in SHAHID SADOUGHI Hospital Since 2007 to 2015 review.

Methods: This study was analytic cross-sectional and retrospective. 36 patients with a previous diagnosis of osteoarthritis between 2007 and 2015 underwent arthroscopic debridement in SHAHID SADOUGHI Hospital were identified and their data completed by their files, phone call. For all patients WOMAC, SF-36 and Lysholm was calculated. Patient data analyzed by version 18 SPSS.

Results: Of the 36 patients entered into the study, 17 patients were females and 19 were males. The mean age was $54/3\pm 0.67$ years the Mean time of remission after surgery was 23.25 ± 14.23 of months. Arthroscopic debridement was performed for all patients and 34 patients underwent debridement of articular cartilage, and 3 patients underwent loose body removal. The mean preoperative and postoperative WOMAC was changed from 57 to 19, and SF-36 was changed from 25 to 73 either Lysholm was changed from 32 to 80.

Conclusion: It seems arthroscopy in cases that are properly selected, will improving symptoms and patient satisfaction.

Keywords: Debridement, arthroscopy, knee osteoarthritis.

Resumen

Antecedentes: Hay varios tratamientos para la osteoartritis y el desbridamiento artroscópico es uno de ellos. Decidimos considerar los resultados del desbridamiento artroscópico en pacientes con osteoartritis de la rodilla en el hospital SHAHID SADOUGHI desde 2007 hasta 2015.

Métodos: Este estudio fue analítico transversal y retrospectivo. Se identificaron 36 pacientes con diagnóstico previo de artrosis entre 2007 y 2015 sometidos a desbridamiento artroscópico en el Hospital SHAHID SADOUGHI y se completaron sus datos mediante sus expedientes y llamada telefónica. Para todos los pacientes se calculó el WOMAC, el SF-36 y el Lysholm. Los datos de los pacientes se analizaron con la versión 18 del SPSS.

Resultados: De los 36 pacientes que entraron en el estudio, 17 pacientes eran mujeres y 19 eran hombres. La edad media fue de $54/3\pm 0,67$ años y el tiempo medio de remisión tras la cirugía fue de $23,25\pm 14,23$ meses. Se realizó un desbridamiento artroscópico en todos los pacientes y en 34 de ellos se llevó a cabo un desbridamiento del cartílago articular, y en 3 pacientes se extrajo el cuerpo suelto. La media del WOMAC preoperatorio y postoperatorio pasó de 57 a 19, y el SF-36 pasó de 25 a 73, o el Lysholm pasó de 32 a 80.

Conclusión: Parece que la artroscopia, en los casos adecuadamente seleccionados, mejorará los síntomas y la satisfacción del paciente.

Palabras clave: Desbridamiento, artroscopia, artrosis de rodilla.

Introduction

Osteoarthritis is the result of biologic and biomechanical changes which breaks down the natural process of construction on the one hand and the destruction of the joint on the other hand and causing Changes in articular cartilage chondrocytes, extraocular material and subchondral bone¹. Osteoarthritis is seen in more than half of the people over 60 years of age. Osteoarthritis is expected to be the fourth cause of disability in the next decade. Knee osteoarthritis around the world involves 40% of people over the age of 70²⁻⁴. Symptoms include knee pain, morning stiffness, bone swelling, crepitation, and synovial effusion, and in general, the quality of life of a person is reduced. The usual diagnostic method is knee radiography that narrowing of the articular space, subchondral sclerosis and osteophytes formation are obvious in graphs⁵⁻⁷. The most common symptoms of osteoarthritis are progressive pain Which was mild initially, but could gradually become debilitating⁸. The pain of patients with osteoarthritis almost always gets better with a little rest and intensifying with movements and activities, especially movements that are associated with weighing⁹. Osteoarthritis can be divided into two primary and secondary types. The primary type is usually involving some joints, with unknown origin and different degrees in different joints and rarely shows up before reaching 35 years of age. The secondary type is usually single-joint and roughness of joint surface is the joint answers to this situation⁹. There are many ways to treat knee osteoarthritis which surgical treatments include osteotomy of the bone, replacement of a knee condyle and complete knee replacement¹⁰. Other non-surgical treatments include physiotherapy, training, weight loss, injectable corticosteroids, anti-inflammatory drugs, chondroitin sulfate and glucosamine and injectable hyaluronic acid¹¹. When the pain caused by osteoarthritis is not controlled by drug therapy, surgical procedures such as arthroscopic debridement are recommended¹². Debrided arthroscopy of degenerative knee is one of the methods of treatment for osteoarthritis which is used in certain cases. Generally, arthroscopy is a diagnostic method that can assess the exact stage of osteoarthritis. This method can be accompanied by the removal of free objects in the joint, limited synovectomy and also the knee joint lavage. Evidence suggests that arthroscopic debridement has improved the performance and pain of young patients with a history of knee injury. Arthroscopic debridement as a low-cost method with few complications and a quick return to everyday activities and Preventing complications and death followed by processes such as tibia osteotomy and arthroplasty¹³. The patient's choice for arthroscopic debridement should be based on the level of activity, the amount of joint mobility required, the age and overall health status of the patients. Some other factors, such as excessive surgical costs, rest periods, and distances from work, are also considered. The therapeutic goals in Osteoarthritis patients include reducing pain, improving physical disability, preventing

progression of cartilage damage and improving quality of life¹⁴. On the other hand, studies have shown the desirability of debridement results in improving the symptoms of the patient, especially patients with varus¹⁵. A study by Moseley and colleagues found no acceptable findings on the efficacy of arthroscopic debridement on knee function and its results did not differ from placebo and lavage¹⁶. Another retrospective study was conducted in 2003 has been shown that in patients with low degrees of osteoarthritis (Grade 1 and 2), after the operation, the symptoms of the disease are greater and their symptoms greatly decreased. Considering that similar studies have shown different results in the therapeutic effects of debridement of arthroscopy, Therefore, we decided to study the results of arthroscopic debridement in patients with knee osteoarthritis in SHAHID SADOUGHI Hospital in Yazd during a 7-years period (2007-2015).

Materials and methods

This research is a cross-sectional and retrospective study. Our study population included 36 patients with knee osteoarthritis who had undergone knee arthroscopy debridement at SHAHID SADOUGHI Hospital in Yazd from the beginning of 2007 to March 2015. Sampling method in this study was all patients who were under arthroscopic debridement due to knee osteoarthritis and did not have exit criteria. Patients with inflammatory diseases such as Rheumatoid Arthritis or Septic Arthritis, Patients with severe disturbances such as Valgus with over 8 degrees and Varus more than 3 degrees were excluded from the study. Our statistical population (36 patients) was identified and their information was collected from files or with calling them. The data collection method was with questionnaire which was designed to assess the pain and quality of life of patients with osteoarthritis. The parameters studied included age, sex, weight, height, body mass index (BMI), duration of symptoms of osteoarthritis, knee locking symptoms and articular fluid and WOMAC' SF-36' Lysholm scores. WOMAC is abbreviation of Western Ontario and McMaster universities which is graded in three areas: Pain intensity (0-8), joint stiffness (0-20), and patient's function in different situations (0-68). Finally, the total score in three areas is graded from 0 to 100 that the higher the number, the more advanced the osteoarthritis and the reduction of knee function. SF-36 is abbreviation of the short form 36 Health survey which includes 36 questions in 8 domains: Physical function, social function, physical role, emotional role, mental health, physical pain and general health. The questionnaire is scored from 0 to 100, the larger numbers represent better quality of life (improved knee performance). The reliability and stability of this questionnaire are calculated in the other study¹⁷. Other score is Lysholm that is dedicated to the knee and scored in 8 areas: Pain, support, impotence, swelling, lameness, locking, jumping and squatting. This scorecard is scored from 0 to 100, and larger numbers represent

improvements. Finally, the data is entered into the SPSS version 17 and Chi-square, ANOVA and Levene were used to analyze the data. The results were expressed as frequency distribution tables, percentages, mean and standard deviation. In all cases, P-value <0.05 was considered as a significant level.

Results

Thirty six patients had inclusion criteria. Patient information was fully recorded and then scored for all patients based on the WOMAC, SF-36, and Lysholm criteria. Of the 36 patients examined, 19 were female (54.1%) and 17 were male (45.9%). The mean age of patients who undergone arthroscopic debridement was 54.3 ± 0.67 years, the mean weight of patients was 74.18 ± 1.88 kg, The mean height of patients was 162.6 ± 1.89 cm and the average BMI was 27.5 ± 0.33 . Also, the length of recovery after surgery was 23.25 ± 13.23 months, the minimum recovery time after surgery was 4 months and most were 54 months. The results of the study showed that the total number of patients under arthroscopic debridement, joint dryness in 28 patients (75.7%), inflammation and swelling of the knee in 33 patients (91.7%), crepitation in 35 patients (97.2%) and Knee locking occurred was in 8 patients (22.2%). The results of the study indicate the duration of preoperative symptoms that 19 patients (52.8%) for 6 months, 14 persons (38.9%) for 12 months and 3 patients (8.3%) had symptoms for 18 months. Symptoms of osteoarthritis included pain, joint stiffness, swelling, locking or instability in the knee. According to **figure 1**, 34 patients (94.4%)

underwent arthroscopic arthroplasty with cartilage debridement, 13 (36.1%) patients underwent arthroscopic debridement of Minsk, 3 patients (8.3%) had removal of loose Body and 6 (16.7%) patients with synovectomy.

The results of the study revealed the distribution of pre-operative pain scored of 1 to 10 that 8 people (22.2%) have chosen 8 point. The frequency distribution of other pain scores is presented in **table I**.

The results of the study show the distribution of abnormal findings during arthroscopy that the rupture of meniscus was clearly seen in 14 patients (38.9%), loose body in 3 patients (8.3%) and articular cartilage damage in 35 (97.2%) patients. Findings in the MRI revealed that in 14 patients (38.9%) from 36 cases, Meniscus tears were reported, 8 patients (22.2%) had loose body and 35 patients (97.2%) had cartilage damage that had MRI report for cartilaginous damage. Based on **figure 2**, which represents WOMAC, SF-36, Lysholm before and after surgery, The WOMAC scoring system, before the operation, averaged 57.8 and after the operation was 19.7, scoring SF-36 before the operation is 25.3 and after it, is 73.4 and Lysholm scored, before surgery, 32.2 and then 80.1 were achieved.

The results of the study on the relationship between variables using ANOVA test showed that there is a significant relationship between articular cartilage damage in arthroscopy and MRI with BMI (P-value=0.006). In other words, weight gain can damage the articular cartilage. Also, there was a significant relationship between age and cartilage damage in MRI (P-value<0.05). Younger patients show better results. The results of the study using Levene test show that there is a significant statistical relationship between loose body formation in arthroscopy and age (**Table II**).

Figure 1: Distribution and frequency of arthroscopic operations in patients.

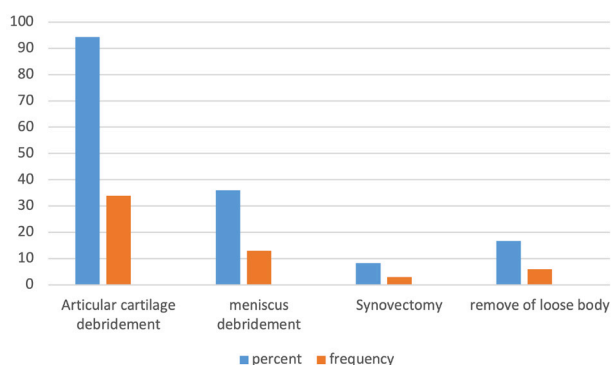


Table I: Distribution and prevalence of pain before and after surgery (10 points).

	Pain score	Prevalence	Percent
Before operation	9	19	52.8
	10	9	25
	8	8	22.2
After operation	2	14	38.9
	3	11	30.6
	4	6	16.7
	5	2	5.6
	6	2	5.6
	1	1	2.8

Figure 2: WOMAC, SF-36, Lysholm before and after surgery in patients.

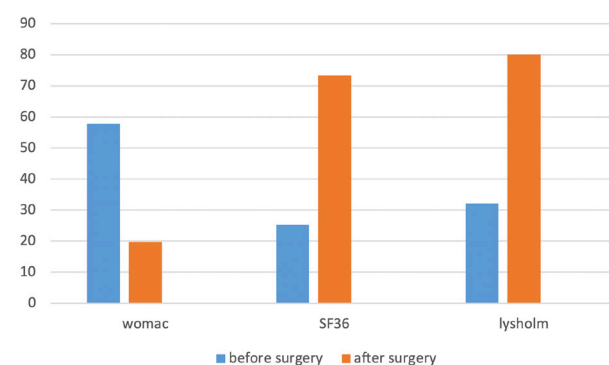


Table II: Relationship between Loose Body in Age Arthroscopy.

Loose age	Body	Mean	Standard deviation	P-value
yes		54.90	5.01	0.002
no		53.57	1.45	

As the age increases, the incidence of Loose Body increases in arthroscopy. The results of the study based on the ANOVA test showed no statistically significant relationship between sex and duration of Osteoarthritis symptoms with tearing of Meniscus and Loose body in MRI (P-value>0.05), But according to the Levene Test, there was a significant statistical relationship between sex with the numbers obtained in SF-36 (**Table III**). So that in higher man's numbers, shows better improvement after arthroscopy.

Table III: The relationship between sex with SF-36.

Sex	SF-36	Mean	Standard deviation	P-value
male		52.13	2.19	<0.05
female		44.42	13.43	

Discussion

Medical science faces many challenges and problems¹⁸⁻²³. For the first time, Mr. Bircher described the beneficial effect of arthroscopy on knee osteoarthritis in 1921 and later Masaaki and colleagues described the effects of lavage⁵. In all patients, the knee scores of osteoarthritis were calculated and Before and after surgery, they were recorded separately to study its difference between patients. Based on the results of these scores, all patients had a significant improvement in knee function, as a result, we had an average of 48 points on the WOMAC score's reduction. Nearly 85% of the patients were satisfied with the outcome of the surgery. In Harwine's study, 63% of patients were satisfied with surgical results 16 and in the Bonamo study, 83% of the patients were satisfied with surgical results¹⁶. Another score which examined by SF-36, before surgery was at least 14, and reached 36 after surgery. After surgery, the maximum was 32, which reached 82. This score was increased by an average of 50, indicating a significant improvement in patients. In McLaren's study, 65% of patients had a significant increase in knee score, which was close to the results of this study²⁴. The other score that was studied was Lysholm, the lowest amount before surgery was 20, which reached 75 after surgery and the highest was 47, which reached 94. These numbers

indicate improvement in the symptoms of the disease in patients and their satisfaction with the results of arthroscopic debridement. In Baumgartner et al., 60% of patients had excellent outcomes after surgery¹³.

Moseley did not find an acceptable result in the study of the efficacy of arthroscopic debridement on knee function and results did not differ from placebo and lavage²⁵. While this study showed a significant improvement in patients and a rise in SF-36 and Lysholm and a reduction in WOMAC. But Richard et al. said that arthroscopic debridement does not play a significant role in improving knee pain²⁶. The results showed that there is a significant relationship between articular cartilage damage in arthroscopy with BMI, this suggests that weight gain causes damage to the articular cartilage which is consistent with the Harwine and Kelly study results²⁷. There was a significant relationship between age and articular cartilage damage in MRI, Harwine study also mentions the age-related relationship with cartilage damage, and age mentioned as an important factor in evaluating arthroscopic results, so that patients with lower age showed better results²⁷. There is also a significant relationship between the creation of a loose body in arthroscopy with the patient age, As the age increased, the incidence of Loose Body increased in arthroscopy. Harwine et al. Also showed an increase in loose body in arthroscopy with increasing age²⁷.

Conclusion

Patients' pain was greatly reduced, so that the numbers WOMAC, SF-36, Lysholm all represent the improvement of the patient's condition and generally improving the quality of one's life. SF-36 numbers were also higher in males, indicating that the knee condition is better in male. So arthroscopy has caused a significant increase in scores measured as well as reducing the pain of the patients. Arthroscopy seems to improve patients' symptoms and satisfaction in cases that are properly selected.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Andreoli TE, Bennett JC, Carpenter CJ, Plum F. Cecil essentials of medicine. 4th ed. Saunders; 1997, p. 624-6.
2. Canale ST. Campbell's Operative Orthopedics. 10th ed. Mosby; 2002. p. 916-46.
3. Richards RN, Lonergan RP. Arthroscopic surgery for relief of pain in the osteoarthritic knee. *Orthopaedics*.1984;7:1705-7.
4. Jackson RW, Dieterichs C. The results of arthroscopic lavage and debridement of osteoarthritic knees based on the severity of degeneration. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*.2003;19(1):13-20.
5. Yegane Ali, Mottaghi Arash. Correlation of quantified MRI, physical exam and knee radiography in patients with knee osteoarthritis. *Tehran University Medical Journal*; Vol. 69, No. 3, June 2011: 185-190.
6. Spahn G, Hofmann GO, Klinger HM. The effects of arthroscopic joint debridement in the knee osteoarthritis: results of a meta analysis. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2012;78(13):1-9.
7. Rönn K, Reischl N, Gautier E, Jacobi M. Current surgical treatment of knee osteoarthritis. *Arthritis Journal*. 2011;43(11):89-95.
8. Rand JA. Role of arthroscopy in osteoarthritis of the knee. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*.1991;7(4):358-63.
9. Sihvonen R, Paavola M, Malmivaara A, Itälä A, Joukainen A, Nurmi H, et al. Arthroscopic partial meniscectomy versus sham surgery for a degenerative meniscal tear. *New England Journal of Medicine*.2013;369(26):2515-24.
10. Kelly MA. Role of arthroscopic debridement in the arthritic knee. *The Journal of arthroplasty*. 2006;21(4):9-13.
11. Fond J, Rodin D, Ahmad S, Nirschl RP. Arthroscopic debridement for the treatment of osteoarthritis of the knee: 2-and 5-year results. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*.2002;18(8):829-34.
12. van den Bekerom MP, Patt TW, Rutten S, Raven EE, van de Vis HM, Albers GR. Arthroscopic debridement for grade III and IV chondromalacia of the knee in patients older than 60 years. *Journal of Knee Surgery*. 2007;20(4):271.
13. Baumgartner MR, Cannon DC, Vitton JM, Schmidt ES, Mauer RC. Arthroscopic debridement of the arthritic knee. *Clin Orthop*.1990;253:197-202.
14. Dhawan A, Mather III RC, Karas V, Ellman MB, Young BB, Bach Jr BR, et al. An epidemiologic analysis of clinical practice guidelines for non-arthroplasty treatment of osteoarthritis of the knee. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*.2014;30(1):65-71.
15. Salisbury RB, Nottage WM, Gardner V. The effect of alignment on results in arthroscopic debridement of the degenerative knee. *Clin Orthop*. 1985;198(61):268-272.
16. Bonamo JJ, Kessler KJ, Noah J. Arthroscopic meniscectomy in patients over 40. *Am J Sports Med* 1992;20:422-428.
17. Montazeri A, Gashtasbi A, Vahdania MS. Determination of Reliability and validity of SF-36 Persian questionnaire. *Payesh Journal*.1384;5(1):49-56.[Persian]
18. Rahimi E, Yazdanpour S, Dehkordi FS. Detection of Toxoplasma gondii antibodies in various poultry meat samples using enzyme linked immuno sorbent assay and its confirmation by polymerase chain reaction. *J Pure Appl Microbiol*. 2014;8(1):421-7.
19. 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):6-17.
20. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of Brucella abortus and Brucella melitensis in Aborted Bovine, Ovine, Caprine, Buffaloes and Camelid Fetuses by application of conventional and real-time polymerase chain reaction. *The Thai Journal of Veterinary Medicine*. 2012;42(1):13.
21. Sheikhsahrokh A, Ranjbar R, Saeidi E, Dehkordi FS, Heiat M, Ghasemi-Dehkordi P, Goodarzi H. Frontier therapeutics and vaccine strategies for sars-cov-2 (COVID-19): A review. *Iranian Journal of Public Health*. 2020;49(Suppl 1):18.
22. Ranjbar R, Seif A, Dehkordi FS. Prevalence of antibiotic resistance and distribution of virulence factors in the shiga toxigenic Escherichia coli recovered from hospital food. *Jundishapur Journal of Microbiology*. 2019;12(5):8.
23. Nejat S, Momtaz H, Yadegari M, Nejat S, Safarpour Dehkordi F, Khamesipour F. Seasonal, geographical, age and breed distributions of equine viral arteritis in Iran. *Kafkas Univ Vet Fak Derg*. 2015;21(1):111-6.
24. McLaren AC, Blokker CP, Fowler PJ, Roth JN, Rock MG. Arthroscopic debridement of the knee for osteoarthritis. *Can J Surg* 1991;34:595-598.
25. Moseley JB, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *New England Journal of Medicine*.2002;347(2):81-8.
26. Richards RN, Lonergan RP. Arthroscopic surgery for relief of pain on the osteoarthritic knee. *Orthopedics* 1984;160(31):162-7.
27. Harwin SF. Arthroscopic debridement for osteoarthritis of the knee:predictors of patient satisfaction. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*. 1999;15(2):142-6.

ORIGINAL

Evaluation of King's variceal prediction score as a marker of portal hypertension in children with chronic liver diseases

Evaluación de la puntuación de predicción de varices de King como marcador de hipertensión portal en niños con enfermedades hepáticas crónicas

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Abstract

Background: Variceal bleeding is one of the serious complications of portal hypertension due to chronic liver disease in children which can be life threatening. There is limited useful tool to selection the children with chronic liver disease who will benefit from upper endoscopy for evaluation of clinically significant varices.

Materials and Methods: This study included all Patients of either sex, aged less than 18 years old with diagnosis of chronic liver disease (CLD) independently of etiology. All cases underwent esophagogastroduodenoscopy (EGD) for evaluation of esophageal varices presented in Pediatric Gastroenterology (GI) ward in Nemazee Hospital-a referral center in south of Iran- affiliated to Shiraz University of Medical Sciences. Patient demographics, etiologies and complications of chronic liver disease with clinical, biochemical and radiological data were collected. Kings variceal prediction score index and other prediction indices were calculated.

Results: Data on 104 patients were collected; 17.3% had Wilson disease and 16% had biliary atresia. Twenty seven (27%) children present with gastrointestinal bleeding and overall 62 (59.6%) had clinically significant (grade II- III) varices. Kings variceal prediction score (K-VaPS), Clinical prediction rule (CPR), Varices prediction rule (VPR), platelet count/spleen diameter ratio and platelet count/equivalent adult spleen diameter ratio had at optimal cut-off sensitivity and specificity of 51.61% and 69.05%, 43.55% and 73.81%, 51.61% and 73.81%, 53.33% and 71.43%, 51.61% and 69.05% respectively. Clinical prediction rule (CPR) had a favourable AUROC of 0.699 (0.59-0.80) compared to Kings variceal prediction score 0.646 (0.53-0.75). Kings variceal prediction score cut-off of 45.8 yielded a sensitivity and specificity of 51.61% and 69.05% and a positive and negative predictive value of 71.1% and 49.15% respectively.

Conclusion: King variceal prediction score is an appropriate tool for selection of the children with chronic liver disease for surveillance and is a useful tool in the screening of clinically significant varices in the children with chronic liver disease.

Keywords: Esophageal varices, chronic liver disease, children.

Resumen

Antecedentes: La hemorragia varicosa es una de las complicaciones graves de la hipertensión portal debida a la enfermedad hepática crónica en los niños, que puede poner en peligro su vida. Existe una herramienta útil limitada para seleccionar a los niños con enfermedad hepática crónica que se beneficiarán de la endoscopia superior para la evaluación de las vrices clínicamente significativas.

Materiales y métodos: Este estudio incluyó a todos los pacientes de ambos sexos, de menos de 18 años de edad, con diagnóstico de enfermedad hepática crónica (EPC), independientemente de su etiología. A todos los casos se les realizó una esofagogastroduodenoscopia (EGD) para evaluar las vrices esofágicas presentadas en la sala de Gastroenterología Pediátrica (GI) del Hospital Nemazee -un centro de referencia en el sur de Irán- afiliado a la Universidad de Ciencias Médicas de Shiraz. Se recogieron los datos demográficos de los pacientes, las etiologías y las complicaciones de la enfermedad hepática crónica con datos clínicos, bioquímicos y radiológicos. Se calculó el índice de predicción de varices de Kings y otros índices de predicción.

Resultados: Se recogieron datos de 104 pacientes; el 17,3% tenía la enfermedad de Wilson y el 16% atresia biliar. Veintisiete (27%) niños presentaban hemorragia gastrointestinal y, en total, 62 (59,6%) tenían vrices clínicamente significativas (grado II-III). La puntuación de predicción de varices de Kings (K-VaPS), la regla de predicción clínica (CPR), la regla de predicción de varices (VPR), la relación recuento de plaquetas/diámetro del bazo y la relación recuento de plaquetas/diámetro equivalente del bazo del adulto tuvieron una sensibilidad y especificidad óptimas del 51,61% y el 69,05%, el 43,55% y el 73,81%, el 51,61% y el 73,81%, el 53,33% y el 71,43%, el 51,61% y el 69,05%, respectivamente. La regla de predicción clínica (RPC) tuvo un AUROC favorable de 0,699 (0,59-0,80) en comparación con la puntuación de predicción de varices de Kings 0,646 (0,53-0,75). La puntuación de predicción de varices de Kings de 45,8 arrojó una sensibilidad y especificidad del 51,61% y 69,05% y un valor predictivo positivo y negativo del 71,1% y 49,15% respectivamente.

Conclusión: La puntuación de predicción de varices de King es una herramienta apropiada para la selección de los niños con enfermedad hepática crónica para su vigilancia y es una herramienta útil en el cribado de varices clínicamente significativas en los niños con enfermedad hepática crónica.

Palabras clave: Vrices esofágicas, enfermedad hepática crónica, niños.

Introduction

Cirrhosis is a diffuse process that histologically characterized by fibrosis and conversion of the normal liver architecture into structurally abnormal nodules, which lead to the disorganization of liver architecture¹. The progression of liver injury to cirrhosis may occur over weeks to years, it's also relatively uncommon in pediatric age groups². Cirrhosis was long thought to be irreversible and associated with limited life expectancy. Although, today it is considered as a dynamic condition, which can be reversed if adequately treated. Studies of the natural history of cirrhosis have found that the disease tends to present with a silent clinical course, followed by the onset of liver dysfunction and portal hypertension³.

In clinical practice severity of the disease and mortality risk is generally estimated on the basis of hypoprothrombinemia, hypoalbuminemia, MELD (Model for End-Stage Liver Disease)/PELD (Pediatric End-Stage Liver Disease) and Child-Pugh Turcotte scores and body mass index, considering this fact that low weight gain is characteristics of liver cirrhosis in infants[4]. The most common causes of cirrhosis in the first years of life are biliary atresia and genetic-metabolic diseases, whereas in older children, cirrhosis is most commonly caused by chronic viral hepatitis and autoimmune diseases^{5,6}.

As a result in 5-15% of cases, the condition is considered as cryptogenic. Cryptogenic cirrhosis in pediatric patients may result from the progression of fatty liver disease or from the effects of complex metabolic syndromes, such as mitochondriopathies. Chronic cholestasis, inborn errors of metabolism and chronic hepatitis are the main causes of cirrhosis in the children⁷.

There are many causes of portal hypertension including etiologies above the liver, within the liver, and below the liver. Suprahepatic abnormalities leading to portal hypertension include cardiac disease, hepatic vein etiology (Hepatic vein thrombosis, or Budd-Chiari syndrome), and inferior vena cava thrombosis or webs. Liver fibrosis can result from suprahepatic disease, and cirrhosis can also develop late in the disease course⁸.

Development of esophageal varices is almost universal, and the statistical risk of bleeding reaches 76% at 24 years of age⁹⁻¹³. Probability of bleeding is directly correlated with the size of varices as seen on endoscopy, from the absence of bleeding episode in children without varices or with grade I varices, to 85% prevalence of bleeding in patients with grade II or III varices, as reported by Lykavieris et al.⁴.

The currently accepted best available test for the diagnosis of varices is EGD. However, EGD has important limitations, including a lack of validated grading systems for variceal size and appearance, poor inter

observer variation, and the requirement for significant sedation or general anesthesia when it is performed in children¹⁴⁻¹⁶. Therefore, there has been considerable effort to find a noninvasive test for esophageal varices. Preliminary data suggests that laboratory tests such as platelet count, albumin and ultrasonographic parameters such as presence of splenomegaly, spleen size z score and platelet count to spleen size ratio and the clinical prediction rule (CPR) which calculated from platelet count, spleen size z-score, and albumin concentration may be useful as first-line tools for identification of adults and pediatric patients at risk of variceal development and thus reduce the number of unnecessary EGDs¹⁰. Kings prediction score is a useful tool in the selection of children with clinically significant varices eligible for a screening endoscopy using mentioned parameter in prediction of variceal grade¹⁷.

Materials and methods

This study include all Patients of either sex-aged less than 18 years old with diagnosis of chronic liver disease (CLD) independently of etiology. All cases underwent EGD for evaluation of esophageal varices presented in Pediatric Gastroenterology (GI) ward in Nemazee-Hospital-a referral center in south of Iran-affiliated to Shiraz University of Medical Science. EGD indications were suspicion of portal hypertension (PHT) based on persistent splenomegaly on the background of chronic liver disease or thrombocytopenia or gastrointestinal bleeding. Patients with portal vein thrombosis (PVT) were excluded from the study considering that the disease pathophysiology is different than that of CLD and PHT. At time of endoscopy grading of esophageal varices were recorded using Kings College Hospital three-size classification. Varices were considered CSV if they were grade II and III or if variceal bleeding was present. Patients were categorised for analysis purposes into clinically significant varices (CSV)+ve and CSV-ve groups.

Clinical data collected at the time of endoscopy included patient demographics, etiology of liver disease and complications such as hepatic encephalopathy, gastrointestinal bleeding, ascites, spontaneous bacterial peritonitis and other infections.

Laboratory data included alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum bilirubin, albumin, international normalized ratio (INR), haemoglobin (Hb), white cell count (WCC) and platelet count, serum creatinine, serum sodium (Na), Child-Turcotte-Pugh Classification (CHILD) score and Pediatric End-stage Liver Disease (PELD) score or Model for End-stage Liver Disease (MELD) score. All measurements were performed within 6 months of the EGD, Spleen size was measured by abdominal ultrasound. Spleen size values were expressed as spleen size z score (SSAZ). Equivalent adult

spleen size(EASS) was calculated as the mean adult spleen size(for gender) plus spleen size z score(SSAZ).

Females: $9.91(\text{cm}) + \text{SSAZ} \times 1.27(\text{cm})$
 Males: $11.29(\text{cm}) + \text{SSAZ} \times 1.49(\text{cm})$

Kings Variceal Prediction Score(K-VaPS) index and other prediction indices such as Varices Prediction Rule(VPR),Clinical Prediction Rule(CPR), AST-platelet ratio index(APRI),platelet count/spleen diameter ratio and platelet count/equivalent adult spleen diameter ratio which considered prediction of the presence of esophageal varices were calculated.

Variceal prediction indices

- Index 1**- Kings Variceal Prediction Score (K-VaPS):
 $(3 \times \text{albumin (g/L)}) - (2 \times \text{Equivalent Adult Spleen Size(EASS) (cm)})$
- Index 2**- Varices Prediction Rule (VPR):
 $(\text{albumin (g/dL)} \times \text{platelet count (x109/L)}) / 1000$
- Index 3**- Aspartate aminotransferase(ALT)-platelet ratio index (APRI) :
 $(\text{AST/Upper limit of normal}) / \text{platelet count (x109/L)} \times 100$
- Index 4**- Clinical Prediction Rule (CPR):
 $((0.75 \times \text{platelet count (x109/L)}) / (\text{Spleen Size Z Score(SSAZ)+5})) + (2.5 \times \text{albumin (g/dL)})$
- Index 5**- platelet count/spleen diameter ratio:
 $(\text{platelet count (x109/L)}) / \text{spleen size (mm)}$
- Index 6**- equivalent adult platelet count/spleen diameter ratio:
 $(\text{platelet count (x109/L)}) / \text{Equivalent Adult Spleen Size(EASS) (mm)}$

Statistical analyses

All statistical analysis were performed with the Statistical Pachege for Social Sciences(SPSS) version 18. Descriptive results were expressed as mean \pm SD (standard deviation) or number (percentage) of patients with a condition. When appropriate, either the Student t-test was used to compare quantitative data, and the Pearson chi-square test was applied for comparison of frequency data. All tests were two tailed and p values < 0.05 were considered significant. ROC curve analysis was used to calculate diagnostic accuracy as areas under the curve (AUROC) along with 95% confidence intervals. The diagnostic accuracy [sensitivity, specificity, positive and negative predictive values (PPV and NPV)] of these variables was calculated using the best cut-off as defined by the ROC curve analysis.

Results

Baseline characteristics

One hundred and four patients were consecutively included in our study, from which 51 were male (49%). The mean age of the patients was 6.43 ± 4.48 years. The mean duration of disease was 1.81 ± 2.45 years. the

mean Child and PELD/MELD scores were 9.39 ± 2.89 and 19.32 ± 16.22 respectively (**Table I**).

Table I: The mean amount of the clinical, biochemical and radiological data and different indices.

	Mean	Maximum	Minimum	St. deviation
Age (year)	6.43	18.00	0.25	4.48
Weight (Kg)	23.32	70.00	2.80	16.92
Duration (year)	1.81	16.00	0.08	2.45
Child score	9.39	15.00	5.00	2.89
PELD/MELD score	19.32	63.50	.00	16.22
Albumin	3.34	5.80	1.70	0.91
Total bilirubin	10.80	51.20	0.30	11.73
INR	2.84	14.00	1.00	2.60
AST	254.39	1770.00	12.00	325.89
ALT	184.08	3090.00	10.00	365.69
Creatinine	0.43	2.20	.10	0.30
WBC	9770.19	35400.00	1500.00	8650.00
Hb	10.01	17.20	3.60	2.46
Platelet	203250.00	1266000.00	6000.00	201772.00
Na	136.04	145.00	120.00	3.90
Spleen size (cm)	11.28	24.00	3.90	4.17
SSAZ	7.69	11.00	4.90	1.46
EASS	21.23	27.23	16.89	2.54
Index 1	57.56	133.4	5.02	27.69
Index 2	0.68	4.30	0.01	0.73
Index 3	6.22	90.30	0.12	11.95
Index 4	20.52	98.00	6.72	13.39
Index 5	2.19	26.37	0.04	3.07S
Index 6	0.947	7.44	0.02	1.00

Chronic liver disease etiologies

The most underlying chronic liver disease in this study were wilson disease (n:18),biliary atresia (n:16),cryptogenic cirrhosis (n:16),autoimmune hepatitis (n:14), tyrosinemia (n:9) and progressive familial intrahepatic cholestasis(PFIC) (n:8) (**Table II**).

Table II: The etiologies of the liver cirrhosis.

Ethiology	Number	Percent
Wilson disease	18	17.3
Biliary atresia	16	15.3
Cryptogenic Cirrhosis	16	15.3
Autoimmune hepatitis	14	13.4
Tyrosinemia	9	8.6
PFIC (progressive familial intrahepatic cholestasis)	8	7.6
GSD (glycogen storage disease)	3	2.8
INH (idiopathic neonatal hepatitis)	2	1.9
Alagille syndrome	2	1.9
Congenital hepatic fibrosis	1	0.9
Viral hepatitis	1	0.9
CF (cyclic fibrosis)	1	0.9
Other disease	13	12.5

Complications of chronic liver disease

Acute gastrointestinal bleeding was the indication of the first esophagogastroduodenoscopy(EGD) in 27 patients who presenting with hematemesis or melena. **Table III** shows the prevalence of different chronic liver disease complications. Encephalopathy was seen in 45.2% of cases as the most prevalent complication followed by ascites and GI bleeding. other complications included cyanosis, hepatorenal syndrome, hepatopulmonary

syndrome. Spontaneous bacterial peritonitis (SBP) was the least complication in our cases.

Table III: Prevalence of different complications of chronic liver disease .

Encephalopathy	45.2%
GI bleeding	26%
Ascites	37.5%
SBP	9.6%
Infection	10.6%
Other complications	26.0%

Table IV represent the relation between different complications and also sex and the EGD results. In CSV positive patients prevalence of GI bleeding was higher comparing with CSV negative cases but this relation was not statistically significant. Prevalence of other complications had an invert relation with CSV presentation in which in CSV positive cases other complications were less prevalent than those without complications, although this relation wasn't statistically significant ($p > 0.05$).

Table IV: The relation between different complications and sex and the endoscopy results.

		CSV negative %	CSV positive %	P-value
Sex	Male	45.1	54.9%	0.93
	Female	35.8	64.2	
Encephalopathy	No	43.9	56.1	0.42
	Yes	36.2	63.8	
GI bleeding	No	45.5	54.5	0.07
	Yes	25.9	74.1	
Ascites	No	44.6	55.4	0.25
	Yes	33.3	66.7	
SBP	No	41.5	58.2	0.48
	Yes	30.0	70.0	
Infection	No	39.8	60.2	0.71
	Yes	45.5	45.5	
Other complications	No	35.1	64.9	0.062
	Yes	55.6	44.4	

The relation between different criteria and the EGD results

As it showed in **table V** a subgroup analysis was carried out, evaluating the relation between different criteria that measured in our study and the EGD results. Out of 104 patients 62 (59.6%) cases were clinically significant varices (CSV) positive. By this detail that 32 cases had no varices, and prevalence of grade I, II and III varices were 10, 35 and 27; respectively. The CSV positive group had higher values of total bilirubin, INR, spleen size, Child score and PELD/MELD scores and lower platelet, albumin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) compared to the CSV negative group. There were significant relation between presence of CSV and disease duration ($p < 0.001$), albumin ($p = 0.02$), serum Na level ($p = 0.02$), platelet count ($p = 0.003$) and spleen size ($p = 0.01$). There was an significant relation

($p < 0.05$) between all indices and presence of CSV except index 3 (APRI index) (**Table V**).

Table V: Baseline clinical, biochemical and radiological data and different indices according to the presence or absence of clinically significant varices (CSV).

	Endoscopy	Mean	Std. Deviation	P- value
Age	CSV negative	6.38	5.02	0.92
	CSV positive	6.47	4.76	
Weight	CSV negative	23.32	17.37	0.99
	CSV positive	23.33	16.75	
Duration	CSV negative	1.01	1.22	< 0.001
	CSV positive	2.35	2.89	
Childscore	CSV negative	8.80	2.75	0.09
	CSV positive	9.79	2.94	
PELDscore	CSV negative	17.18	16.43	0.26
	CSV positive	20.77	16.05	
Albumin	CSV negative	3.59	0.87	0.02
	CSV positive	3.17	0.90	
Totalbilirubin	CSV negative	8.89	11.00	0.17
	CSV positive	12.09	12.12	
INR	CSV negative	2.64	1.94	0.52
	CSV positive	2.97	2.97	
AST	CSV negative	332.69	414.54	0.068
	CSV positive	201.35	238.22	
ALT	CSV negative	214.21	297.73	0.49
	CSV positive	163.67	406.42	
Creatinine	CSV negative	0.40	0.19	0.51
	CSV positive	0.44	0.35	
WBC	CSV negative	10430.95	7210.10	0.37
	CSV positive	9322.58	5409.74	
Hb	CSV negative	9.89	2.67	0.67
	CSV positive	10.10	2.33	
Platelet	CSV negative	285095.23	261934.53	0.003
	CSV positive	147806.45	122033.29	
Na	CSV negative	137.11	3.18	0.02
	CSV positive	135.32	4.19	
Spleen size	CSV negative	10.10	3.35	0.01
	CSV positive	12.08	4.49	
SSAZ	CSV negative	7.65	1.53	0.586
	CSV positive	7.72	1.42	
EASS	CSV negative	21.28	2.41	0.87
	CSV positive	21.19	2.64	
Index 1	CSV negative	65.32	27.61	0.012
	CSV positive	52.64	26.75	
Index 2	CSV negative	1.00	0.95	<0.001
	CSV positive	0.47	0.42	
Index 3	CSV negative	7.28	14.98	0.63
	CSV positive	5.50	9.43	
Index 4	CSV negative	26.02	17.69	0.001
	CSV positive	16.80	7.58	
Index 5	CSV negative	3.27	4.36	0.012
	CSV positive	1.46	1.35	
Index 6	CSV negative	1.30	1.35	0.01
	CSV positive	0.70	0.56	

Variceal prediction score indices

ROC analysis For the Kings variceal prediction score index demonstrated air under ROC curve (AUROC) of 0.646 (CI 0.53-0.75) and $p = 0.012$ with the optimal cut-off point of 45.8 and sensitivity and specificity of 51.61% and 69.05% respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 71.1% and 49.15%, respectively (**Table VI, figure 1**). This yielded a

diagnostic accuracy of 64%,so it can be considered as a suitable index in prediction of CSV in the children with chronic liver disease.

Table VI: Sensitivity, specificity, negative and positive predictive value and diagnostic accuracy of six indices.

Indices	Cut of point	P- value	Diagnostic accuracy	95% CI	Specificity %	Sensitivity %	PPV %	NPV %
1	45.8	0.012	0.64	0.53-0.75	69.05	51.61	71.1	49.15
2	0.325	0.001	0.68	0.58-0.69	73.81	51.61	74.4	50.8
3	3.19	0.63	0.47	0.35-0.59	52.38	51.61	61.5	46.9
4	13.84	0.001	0.69	0.59-0.80	73.81	43.55	71.0	46.9
5	1.19	0.002	0.68	0.57-0.79	71.43	53.33	73.3	50.8
6	0.615	0.004	0.66	0.55-0.77	69.05	51.61	71.1	49.1

Based on our study result,Varices Prediction Rule(VPR) with AUROC of 0.688 and p=0.001 and sensitivity and specificity 51.61% and 73.81% respectively (**Table VI, figure 2**), and Clinical Prediction Rule(CPR) with AUROC of 0.699 and p=0.001 and sensitivity and specificity 43.55% and 73.81%, respectively (**Table VI, figure 3**) were efficacious at predicting the presence of clinically significant varices.

In this results there was not a statically significant relation between the AST-Platelet Ratio Index and the incidence of CSV (P= 0.633).This index also has a worthless specificity (52.38%) and sensitivity(51.61%).In prediction of CSV based on area under ROC curve which was less than 0.5, it can not be considered as a suitable index in prediction of CSV in children with chronic liver disease (**table VI, figure 4**).

Figure 2: Area under ROC curve 0.688 of index 2 (varices prediction rule (VPR)).

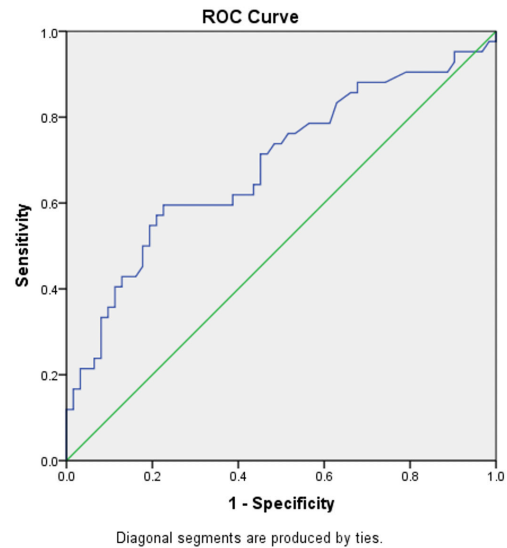


Figure 3: Area under ROC curve 0.699 of index 4 (Clinical Prediction Rule (CPR)).

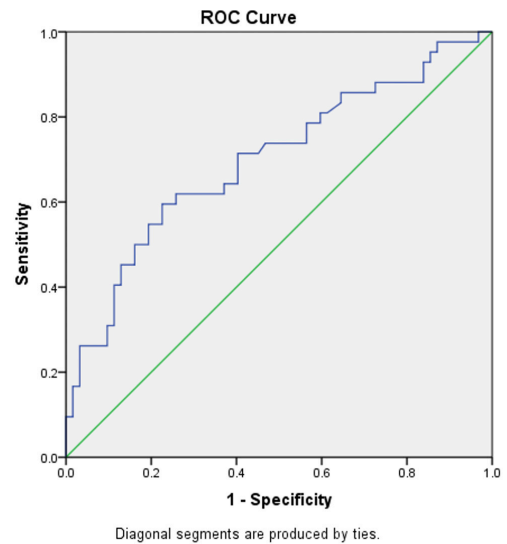


Figure 1: Area under curve 0.646 of index 1 (Kings Variceal Prediction Score).

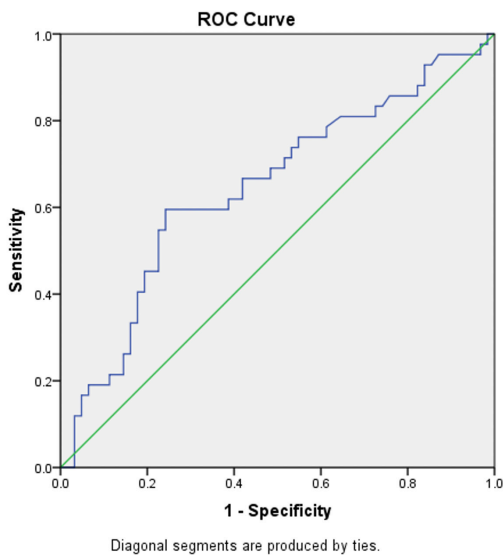
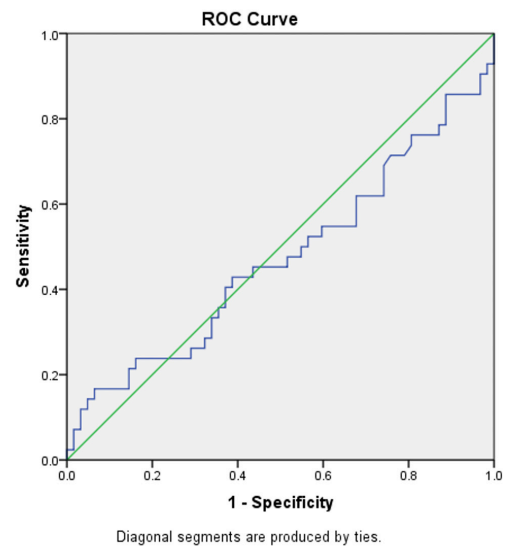


Figure 4: Area under ROC curve 0.472 of index 3 (AST-platelet ratio index (APRI)).



Other good indices for prediction of CSV were platelet count/spleen diameter ratio and platelet count/equivalent adult spleen diameter ratio with $p:0.002$ and $p:0.004$ respectively and sensitivity 53.33% and 51.61% and specificity 71.43% and 69.05% and AUROC 0.682 and 0.666, respectively (Table VI and figures 5 and 6).

Figure 5: Area under ROC curve: 0.682 of index 5 (Platelet Count/Spleen Diameter ratio).

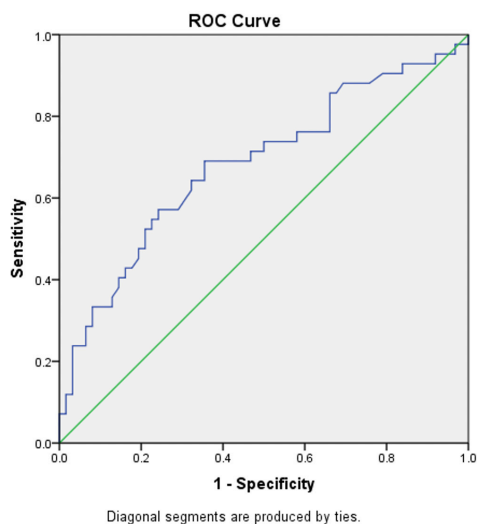
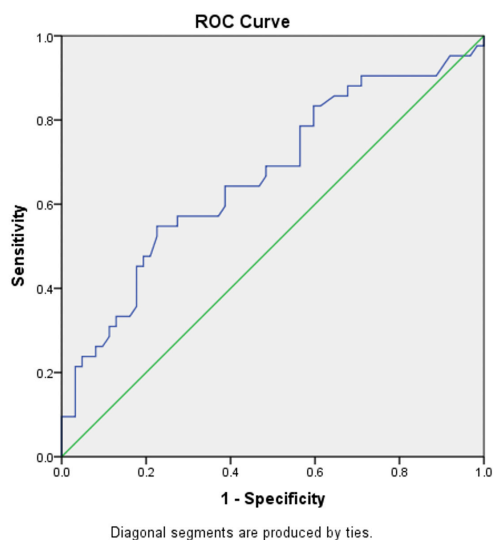


Figure 6: Area under ROC curve 0.666 of index 6(platelet count/ equivalent adult spleen diameter ratio).



Discussion

Portal hypertension is a key factor in the pathogenesis of cirrhosis outcomes. PHT is associated with development of a hyperdynamic circulation and complications such as ascitis, hepatic encephalopathy, and esophagogastric varices¹². About 50% of patients presenting with cirrhosis are reported to have varices, 24- 80% in cases who have PHT. Development of esophageal varices may occur in up

to 90% of patients with liver cirrhosis, being more common in Child-Pugh Class C patients compared to Child-Pugh Class A patients (85% versus 40%)¹³. Early diagnosis of varices before the first bleeding is essential as studies of primary prophylaxis clearly show that the risk of variceal hemorrhage can be reduced by 50% to about 15% for large esophageal varices. So early diagnosis and screening of varices should be warranted to improve the prognosis of liver cirrhosis-Considering the impact of upper GI bleeding due to esophageal varices(EV) rupture in the prognosis of cirrhotic patients, AASLD (American Association for the Study of Liver Disease) and the Baveno Consensus suggest that every patient diagnosed with cirrhosis should be investigated for esophageal varices(EV)¹⁴.

Endoscopy should be performed at 2-3 years intervals in the patients without varices and at 1-2 years intervals in the patients with small varices^{11,12}. A generalized screening program of periodic upper gastro-esophageal endoscopy in cirrhotic patients leads to high costs, and patient compliance may become reduced. However, at a given point in time, a variable proportion of patients will not have varices. Thus, screening all cirrhotic patients with upper GI endoscopy to detect the presence of varices implies a number of unnecessary endoscopies, which increase the workload of endoscopy units. Hence, the selection of patients who may be at a higher risk of having gastro-esophageal varices would be highly beneficial and cost-effective¹⁵.

Various non-invasive markers, such as model for end-stage liver disease (MELD), aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AST/ALT), AST to platelet ratio index (APRI), platelet count to spleen diameter (PC/SD), fibrosis-4-index (FIB-4), fibrosis index (FI) and King's score, have been demonstrated as a simple, non-invasive and easier practical alternative to predict the presence of esophageal varices in cirrhotic patients¹⁶⁻¹⁸.

In Eslam et al study platelet count was one of three markers that significantly predict presence of esophageal varices in cirrhotic patients¹¹. The present study showed same results in which platelet count beside spleen size, serum albumin level and Na level were simple markers that had significant relation with presence of esophageal varices¹¹.

Giannini et al have suggested that PC/SD (platelet count/spleen diameter ratio) could be an accurate predictor of esophageal varices in cirrhotic patients, and as the measurement of platelet and spleen size are part of the routine workup of these patients it could probably be the most cost effective non-invasive method for this²⁰. In our study equivalent platelet count/spleen diameter ratio amount had a significant relation with presence of clinically significant varices(CSV) in endoscopy. Considering the area under curve in ROC curve this index had good sensitivity and specificity in predicting CSV. Sanyal et al. were the first authors to raise the hypothesis that APRI

could be related to the presence of esophageal varices. They found a sensitivity of 68%, a specificity of 64%, a PPV of 51% and a NPV of 78%. We found values of 51.61%, 52.38%, 61.5% and 46.9% respectively, they proposed the cutoff point of 1.3 for APRI as a predictor of esophageal varices our cut off point for this index was 3.19²¹. Mattos et al performed a study that analysed the ability of APRI in predicting the existence of esophageal varices in a population of cirrhotic patients. APRI was not an independent factor for the prediction of esophageal varices. Its sensitivity, specificity and predictive values were insufficient for the index to be used for the screening of esophageal varices in cirrhotics²². Also in our study APRI index amount had not statically significant relation with the prevalence of esophageal varices with a worthless sensitivity and specificity in esophageal varices prediction.

Motto et al performed another study to investigate the platelet count squared/spleen diameter ratio (PS/SA), as a non-invasive predictor of esophageal varices in cirrhotics. In their study PS/SA had an excellent sensitivity to predict esophageal varices, allowing almost one fourth of patients without esophageal varices to spare endoscopy²³. Our study also showed a good sensitivity and specificity in prediction of esophageal varices. In Meyer et al study using a platelet count/spleen diameter ratio with a cut-off value of 0.909, yielded a negative predictive value of only 73% and a positive predictive value of 74%²⁴. In our study the sensitivity, specificity, negative predictive value and positive predictive value was 53.33%, 71.43%, 73.30% and 50.8% respectively with a cut-off value of 1.10. In Mosqueira et al study the PC/SD ratio had a sensitivity of 40%, specificity of 75%, PPV of 82%, NPV 30%. They concluded in their study that the PC/SD ratio was not an effective diagnostic test for esophageal varices²⁵.

Gana et al measured the ability of clinical prediction rule (CPR) to predict the presence of esophageal varices in children. Their study showed that noninvasive tests such as CPR and platelet count can assist in triaging children for EGD to identify esophageal varices²⁴. In our study CPR had the most sensitivity and specificity in predicting EV comparing to other indices. In Istrd et al study variceal prediction rule (VPR), CPR and APRI considered as suitable indices in prediction of esophageal varices with area under ROC curve of 0.75, 0.73-0.80 and 0.69-0.83 respectively[24]. In our study results were the same for VPR and CPR but not for APRI. Platelet count had significant relation with Presence of esophageal varices with p-value 0.002. In Gana et al study the best noninvasive predictors of esophageal varices of any size were as follows: platelet/spleen size ratio, CPR (AUROC: 0.80), and platelet count (AUROC:0.79). The positive predictive values for the CPR and platelet count were 0.87 and 0.86, the negative predictive values were 0.64 and 0.63, the positive likelihood ratios were 3.06 and 2.76, and the negative likelihood ratios were 0.64 and 0.63, respectively. Based on positive and negative predictive

values, the most accurate noninvasive tests were the CPR and platelet counts²⁶. Our study showed the same result and the CPR was the most accurate noninvasive test with sensitivity, specificity, negative predictive value and positive predictive value of 43.56%, 73.81%, 71.0% and 46.9% respectively the AUROC was 0.699. The CPR or platelet count therefore may be used as noninvasive tests for esophageal varices in a clinical or research setting to triage children to undergo EGD for confirmation and grading of varices²⁷.

Witters et al concluded in their study that King score can facilitate the selection of children with chronic liver disease undergoing an esophagogastroduodenoscopy (EGD) for the detection of clinically significant varices in a surveillance program¹⁷. In Timothy et al study a King's Score of greater than or equal to 16.7 predicted cirrhosis in 34% of patients (P <0.0001) with sensitivity 86%, specificity 80% and a high negative predictive value of 96%²⁷. In our study sensitivity 51.61%, specificity 69.05% and a high negative predictive value of 49.15% and positive predictive value of 71.1 with P-Value 0.012 and AUROC of 0.646. Based on our study results Kings Variceal Prediction Score amount has statistically significant relation with the incidence of CSV. This index has specificity and sensitivity based on area under ROC curve, so it can be considered as a suitable index in prediction of esophageal varices in children with chronic liver disease.

This study allowed us to prove that there is satisfactory cut-off value for Kings score to be used as a predictor of esophageal varices. A screening tool, in a context of a serious situation as the presence of esophageal varices, which is responsible for the most dramatic complication of cirrhosis, variceal bleeding, must have an excellent negative predictive value in order not to miss patients who could benefit from primary prophylaxis-The results of our study lead to the conclusion that Kings score is an appropriate substitute for endoscopy and can be used in the screening of esophageal varices among cirrhotic patients.

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Interests conflict








The researchers declare that they have no conflict of interest.

References

- Pinto RB, Schneider AC, da Silveira TR. Cirrhosis in children and adolescents: An overview. *World J Hepatol.* 2015 Mar 27;7(3):392-405.
- Dehghani SM, Imanieh MH, Haghighat M, Malekpour A, Falizkar Z. Etiology and complications of liver cirrhosis in children: report of a single center from southern Iran. *Middle East J Dig Dis.* 2013 Jan;5(1):41-6.
- Poordad FF. Presentation and complications associated with cirrhosis of the liver. *Curr Med Res Opin.* 2015 May;31(5):925-37.
- El-Shabravi MH, Kamal NM. Medical management of chronic liver diseases (CLD) in children (part II): focus on the complications of CLD, and CLD that require special considerations. *Paediatr Drugs.* 2011 Dec 1;13(6):371-83.
- Riahi-zhad M, Saneian H, Farghadani M, Parsai Arshad S. Doppler perfusion index in adolescents with non-alcoholic fatty liver disease. *Immunopathol Persa.* 2021;7(1):e07.
- Devictor D, Tissieres P, Afanetti M, Debray D. Acute liver failure in children. *Clin Res Hepatol Gastroenterol.* 2011;35(6-7):430-7.
- Imanieh MH, Dehghani SM, Khoshkhui M, Malekpour A. Etiology of Portal Hypertension in Children: A Single Center's Experiences. *Middle East J Dig Dis.* 2012 Oct;4(4):206-10.
- Bosch J, Vilaseca M, García-Calderó H, Lafoz E, García-Irigoyen O, Avila MA, et al. The anticoagulant rivaroxaban lowers portal hypertension in cirrhotic rats mainly by deactivating hepatic stellate cells. *Hepatology.* 2017 Jun;65(6):2031-44.
- Ripoll C, Groszmann R, Garcia-Tsao G, Grace N, Burroughs A, Planas R, et al. Portal Hypertension Collaborative Group. Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. *Gastroenterology.* 2007 Aug;133(2):481-8.
- Albreedy Am. Platelet Count To Spleen Diameter Ratio And To Spleen Area Ratio As Predictors For Esophageal Varices In Chronic Hepatitis C Patients With Liver cirrhosis. *J Egypt Soc Parasitol.* 2015 Dec;45(3):485-92.
- Eslam M, Ampuero J, Jover M, Abd-Elhalim H, Rincon D, Shatat M, et al. Predicting portal hypertension and variceal bleeding using non-invasive measurements of metabolic variables. *Ann Hepatol.* 2013 Jul-Aug;12(4):588-98.
- Hong WD, Dong LM, Jiang ZC, Zhu QH, Jin SQ. Prediction of large esophageal varices in cirrhotic patients using classification and regression tree analysis. *Clinics (Sao Paulo).* 2011;66(1):119-24.
- Tarzamni MK, Somi MH, Farhang S, Jalilvand M. Portal hemodynamics as predictors of high risk esophageal varices in cirrhotic patients. *World J Gastroenterol.* 2008 Mar 28;14(12):1898-902.
- Dib N, Konate A, Oberti F, Calès P. [Non-invasive diagnosis of portal hypertension in cirrhosis. Application to the primary prevention of varices]. *Gastroenterol Clin Biol.* 2005 Oct;29(10):975-87.
- Silkauskaitė V, Pranculis A, Mitraitė D, Jonaitis L, Petrenkiene V, Kupcinskis L, et al. Hepatic venous pressure gradient measurement in patients with liver cirrhosis: a correlation with disease severity and variceal bleeding. *Medicina (Kaunas).* 2009;45(1):8-13.
- Adami MR, Ferreira CT, Kieling CO, Hirakata V, Vieira SM. Noninvasive methods for prediction of esophageal varices in pediatric patients with portal hypertension. *World J Gastroenterol.* 2013 Apr 7;19(13):2053-9.
- Witters P, Hughes D, Karthikeyan P, Ramakrishna S, Davenport M, Dhawan A, et al. King's Variceal Prediction Score: A Novel Noninvasive Marker of Portal Hypertension in Pediatric Chronic Liver Disease. *J Pediatr Gastroenterol Nutr.* 2017 Apr;64(4):518-523.
- Ahmadvand H, Babaeenezhad E, Nasri M, Jafaripour L, Mohammadrezaei Khorramabadi R. Glutathione ameliorates liver markers, oxidative stress and inflammatory indices in rats with renal ischemia reperfusion injury. *J Renal Inj Prev.* 2019;8(2):91-7.
- Sezer OB, Çelik D, Tutar N, Özçay F. Can platelet count/spleen diameter ratio be used for cirrhotic children to predict esophageal varices? *World J Hepatol.* 2016 Nov 28;8(33):1466-70.
- Wang JH, Chuah SK, Lu SN, Hung CH, Chen CH, Kee KM, et al. Transient elastography and simple blood markers in the diagnosis of esophageal varices for compensated patients with hepatitis B virus-related cirrhosis. *J Gastroenterol Hepatol.* 2012 Jul;27(7):1213-8.
- Zambam de Mattos A, Alves de Mattos A, Daros LF, Musskopf MI. Aspartate aminotransferase-to-platelet ratio index (APRI) for the non-invasive prediction of esophageal varices. *Ann Hepatol.* 2013 Sep-Oct;12(5):810-4.
- Chawla S, Katz A, Attar BM, Gupta A, Sandhu DS, Agarwal R, et al. Platelet count/spleen diameter ratio to predict the presence of esophageal varices in patients with cirrhosis: a systematic review. *Eur J Gastroenterol Hepatol.* 2012 Apr;24(4):431-6.
- Schwarzenberger E, Meyer T, Golla V, Sahdala NP, Min AD. Utilization of platelet count spleen diameter ratio in predicting the presence of esophageal varices in patients with cirrhosis. *J Clin Gastroenterol.* 2010 Feb;44(2):146-50.
- Mosqueira JR, Montiel JB, Rodríguez D, Monge E. Evaluation of the diagnostic test of index platelet counts/size spleen, as a predictor of the presence of esophageal varices in cirrhosis. *Rev Gastroenterol Peru.* 2011 Jan-Mar;31(1):11-6.
- Gana JC, Turner D, Mieli-Vergani G, Davenport M, Miloh T, Avitzur Y, et al. A clinical prediction rule and platelet count predict esophageal varices in children. *Gastroenterology.* 2011 Dec;141(6):2009-16.
- Isted A, Grammatikopoulos T, Davenport M. Prediction of esophageal varices in biliary atresia: Derivation of the varices prediction rule, a novel noninvasive predictor. *J Pediatr Surg.* 2015;50(10):1734-8.
- Cross TJ, Rizzi P, Berry PA, Bruce M, Portmann B, Harrison PM, et al. King's Score: an accurate marker of cirrhosis in chronic hepatitis C. *Eur J Gastroenterol Hepatol.* 2009 Jul;21(7):730-8.

Investigating the effect of ORS with probiotics, zinc and vitamin A on children's diarrhea: a randomized clinical trial

Investigación del efecto de las SRO con probióticos, zinc y vitamina A en la diarrea infantil: un ensayo clínico aleatorizado

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Abstract

Background: Diarrhea is one of the leading causes of death in developing countries. Due to the interaction of diarrhea and malnutrition on each other, as well as the role of malnutrition in children's developmental and developmental disorders, improving diarrhea treatment programs plays an important role in children's health. Our aim in this study was to evaluate the effect of ORS with probiotics, zinc and vitamin A on children's diarrhea.

Methods: In this clinical trial study, children aged 9 months to 5 years were referred to Shahid Beheshti Hospital in Kashan with a complaint of acute watery diarrhea in 2017-2018. The children were randomly divided into five groups. In these groups, patients with zinc gluconate were treated with 20 mg of omental with ORS, vitamin A 20000 units with ORS, CFU probiotic with ORS, zinc gluconate, vitamin A and probiotic with ORS and finally ORS were treated only they got. Then, during the daily visit, the condition of the patients in terms of continuing diarrhea and the number of times diarrhea was asked to their mother during the last 24 hours and was recorded in the questionnaires. Then the results were entered in SPSS17 software and analyzed according to related statistical methods.

Results: All the intervention groups were similar and comparable in terms of gender characteristics ($p = 0.052$), age ($p = 0.871$) and weight ($p = 0.958$). The duration of diarrhea after intervention in the combined group decreased significantly ($P < 0.001$) and in the ORS group only increased significantly ($p = 0.013$). The frequency of diarrhea decreased significantly after intervention in all groups ($P < 0.001$). In the combined group, the number of diarrhea and the length of hospital stay decreased significantly.

Conclusion: The results of the present study showed that the group of children receiving zinc supplements, vitamin A, probiotics and ORS had a significant decrease in the number of times diarrhea and the duration of diarrhea and the duration of hospitalization.

Keywords: Children's diarrhea, probiotics, vitamin A, zinc, OR.

Resumen

Antecedentes: La diarrea es una de las principales causas de muerte en los países en desarrollo. Debido a la interacción de la diarrea y la malnutrición entre sí, así como el papel de la malnutrición en los trastornos del desarrollo de los niños, la mejora de los programas de tratamiento de la diarrea desempeña un papel importante en la salud de los niños. Nuestro objetivo en este estudio era evaluar el efecto de las SRO con probióticos, zinc y vitamina A en la diarrea infantil.

Métodos: En este estudio de ensayo clínico, los niños de 9 meses a 5 años fueron remitidos al Hospital Shahid Beheshti de Kashan con una queja de diarrea acuosa aguda en 2017-2018. Los niños fueron divididos aleatoriamente en cinco grupos. En estos grupos, los pacientes con gluconato de zinc fueron tratados con 20 mg de omental con SRO, vitamina A 20000 unidades con SRO, probiótico UFC con SRO, gluconato de zinc vitamina A y probiótico con SRO y, por último, sólo se trató con SRO. Luego, durante la visita diaria, se evaluó el estado de los pacientes en diarrea continua y el número de veces que tuvieron diarrea durante las últimas 24 horas y se registró en los cuestionarios. A continuación, los resultados se introdujeron en el programa informático SPSS17 y se analizaron según los métodos estadísticos correspondientes.

Resultados: Todos los grupos de intervención fueron similares y comparables en cuanto a las características de género ($p = 0,052$), edad ($p = 0,871$) y peso ($p = 0,958$). La duración de la diarrea tras la intervención en el grupo combinado disminuyó significativamente ($p < 0,001$) y en el grupo de SRO sólo aumentó significativamente ($p = 0,013$). La frecuencia de la diarrea disminuyó significativamente después de la intervención en todos los grupos ($p < 0,001$). En el grupo combinado, el número de diarreas y la duración de la estancia hospitalaria disminuyeron significativamente.

Conclusiones: Los resultados del presente estudio mostraron que el grupo de niños que recibió suplementos de zinc, vitamina A, probióticos y SRO tuvo una disminución significativa del número de veces de diarrea y de la duración de la misma, así como de la duración de la hospitalización.

Palabras clave: Diarrea infantil, probióticos, vitamina A, zinc, SRO.

Introduction

Diarrhea is one of the leading causes of death in developing countries, killing more than three million children a year^{1,2}. Most of these deaths are related to dehydration³. About 63% of all diarrhea in the world occurs in children under the age of five⁴. This is more common in disadvantaged areas and in children with malnutrition⁵. There are 70,000 deaths from diarrhea in the world each year⁶. According to statistics provided by the World Health Organization, the number of deaths due to diarrhea in children is much higher than deaths from AIDS and malaria⁷. According to the Department of Health, diarrhea is the second leading cause of death and disability among children. Most of the signs and symptoms of diarrhea syndrome are related to the pathology of the infection and the extent of the infection. Other symptoms depend on the complications (such as dehydration and electrolyte disturbance) and the nature of the infectious pathogen. The most common manifestations of gastrointestinal gastro intestinal infection in children are diarrhea, abdominal cramps, and vomiting. Fever is common in patients with inflammatory diarrhea⁸.

Due to the interaction of diarrhea and malnutrition on each other, as well as the role of malnutrition in children's developmental and developmental disorders, improving diarrhea treatment programs has an important role in children's health⁹. The duration of diarrhea depends on several factors, two of which are important and proven: malnutrition⁹ and decreased immunity⁹, and vitamin A deficiency can be associated with both factors. Vitamin A plays an important role in the visual process. But other roles have been mentioned, such as increasing the immune system and reducing the severity of infections, stopping some cancers, and linking some diseases such as visual impairment, skin diseases, increasing the severity of infections such as measles and diarrhea, respiratory and parasitic diseases to deficiency. It has been proposed¹⁰. Vitamin A deficiency is one of the most important problems in developing countries, so the World Health Organization recommends vitamin A supplements for children, and some researchers have suggested continuing to prescribe vitamin A supplements until the age of five¹¹. Despite the use of ORS, micronutrient deficiencies are still one of the leading causes of death in patients with diarrhea. In addition, micronutrient deficiencies increase the severity, duration, and chronicity of diarrhea in patients¹². Zinc is one of the most important micronutrients that is involved in neutralizing free radicals, the antioxidant system, and the proper functioning of the immune system¹³. It has been observed that serum zinc levels decrease in acute diarrhea¹⁴. Some studies have reported that zinc supplementation accelerates recovery, reduces the duration and severity of diarrhea, and reduces mortality in patients¹⁵. Oral zinc supplementation reduces the amount, frequency of bowel movements and the duration of diarrhea. This practice is associated with safety, efficiency and cost-effectiveness. Therefore,

supplementation is a simple and effective treatment for acute diarrhea control¹⁶. Co-administration of zinc and ORS simultaneously reduces treatment costs and the duration of acute diarrhea in children¹⁷. Probiotics are now used in various areas of prevention and treatment, especially in acute infectious diarrhea. The results of a systematic review of 56 studies in infants and children showed that probiotic use was safe and had a significant effect on reducing the duration and frequency of acute infectious diarrhea¹⁸. Yogurt has been known to be effective in treating diarrhea since ancient times, and many studies today have reported beneficial effects in the treatment of diarrhea¹⁹. In recent years, the use of probiotics to reduce the duration of treatment and the severity of infectious diarrhea in the clinical field has been proposed, and most studies have found the effects of lactobacilli and sucrose to be useful in the treatment of acute diarrhea²⁰. The aim of this study was to investigate the effect of ORS with probiotics, zinc and vitamin A on children's diarrhea.

Materials and methods

Study design

This study is an intervention and is a two-course clinical trial. The study population of all children with diarrhea with an age range of 9 months to 5 years referred to the children's subspecialty clinic of Shahid Beheshti Hospital in Kashan and the specialized clinic in 2017-2018 were studied with complaints of acute watery diarrhea.

Input and output criteria

The criteria for entering the study include children with acute gastroenteritis hospitalized in the pediatric ward of Shahid Beheshti Hospital and the age range of 9 months to 5 years. Criteria for withdrawal include bloody and infectious diarrhea, fever equal to or above 38 C, known chronic disease (cystic fibrosis, inflammatory bowel disease, and malabsorption), severe malnutrition (less than 3%), severe dehydration, or severe dehydration. Resistant vomiting, a history of taking supplements containing zinc in the past month, a history of taking supplements containing vitamin A and probiotics in the past month, and drug intolerance were excluded.

Sample size

The sample size was calculated using the sample size formula with 5% error parameters and 80% statistical power to compare a small variable in 5 groups independent of the previous study. The minimum sample size of 27 patients were obtained, including the loss of 20 percent in each of the study was 30.

The non-probabilistic sampling method was easy. And after applying entry and exit criteria, they were randomly divided into five groups. Group 1: This group received 20 mg of gluconate zinc in combination with ORS in 4

sachets, each of which could be dissolved in 250 ml of water, for 24 hours, Group 2: This group received vitamin A powder in the amount of 20,000 units with ORS in 4 sachets, each of which could be dissolved in 250 ml of water, for 24 hours. Group 3: The CFU 109 probiotic group received ORS with 4 sachets, each capable of dissolving in 250 ml of water, for 24 hours. Group 4: This group received 20 mg of gluconate zinc, 20,000 units of powdered vitamin A and 4 tablets of CFU 109 probiotic with ORS in 4 sachets, each of which can be dissolved in 250 ml of water, for 24 hours. Group 5: This control group, as the control group, received only ORS in 4 sachets, each of which could be dissolved in 250 ml of water, for 24 hours.

Gather information

Data collection was a questionnaire. A questionnaire containing demographic characteristics, nutritional status, history of zinc supplementation, vitamin A and probiotics was asked of the patient's parents, and since the follow-up period was up to three days, parents were asked to do so. According to the doctor's prescription, no additional supplement should be given to the patient. Water shortage and daily progression of the disease for each patient is completed by the pediatric assistant. and recorded in questionnaires.

Data analysis

After collecting the data, the data was entered into SPSS v17 software, Kolmogorov-Smir Now tests were used to check the normality of the data and to compare the mean between all groups, One Way ANOVA test was used for statistical analysis. ANCOVA statistical test was used to control the variable variables.

Moral considerations

The code of the ethics committee of this study is IR.KAUMS.REC.1395.114 of Kashan University of Medical Sciences and the registration number of IRCT20170101031212437N2.

Results

In this study, which was performed on 150 children hospitalized with diarrhea complaints, the frequency of sex included 59 males (39.3%) and 91 females (60.7%). The present findings, according to **table I**, showed that there was no significant relationship between gender and the groups studied and all groups were gender-equal and comparable (p=0.052). According to the One way ANOVA test, there was no significant difference in age in the studied groups and all groups were identical

Table I: Mean and standard deviation of treatment groups.

Therapeutic groups	Number	Average age group	The standard deviation of the age group	Average weight group	The standard deviation of the weight group	The average duration of diarrhea before the intervention	Critical deviation of the duration of diarrhea before the intervention	The average number of diarrhea times before the intervention	Critical deviation of the number of times diarrhea before the intervention	The average duration of diarrhea after the intervention	Critical deviation of the duration of diarrhea after the intervention
ORS * Zinc	30	2.80	1.23	14.77	3.71	2.30	0.92	5.93	1.05	0.65	0.12
ORS * Vitamin A.	30	2.48	1.15	14.20	3.69	2.47	0.82	6.23	1.07	0.50	0.09
ORS * Probiotics	30	2.58	1.15	14.13	3.43	2.52	0.82	5.93	1.01	0.57	0.10
ORS * Zinc * Vitamin A * Probiotic	30	2.62	1.19	14.53	3.36	2.83	0.65	6.00	1.02	0.35	0.06
ORS	30	2.53	1.24	14.47	3.39	2.33	0.71	5.80	1.03	0.73	0.13
Total	150	2.60	1.18	14.42	3.48	2.40	0.83	5.98	1.03	0.81	0.07

Table II: Frequency of duration and number of diarrhea before and after intervention according to treatment groups.

Therapeutic groups		Number	The average duration of diarrhea before and after the intervention	Standard criteria for the duration of diarrhea before and after the intervention	The average number of diarrhea times before and after the intervention	Critical deviation of the number of times diarrhea before and after the intervention
ORS * Zinc	Before intervention	30	2.30	0.92	5.93	1.05
	After the intervention	30	2.30	0.65	3.03	0.76
ORS * Vitamin A.	Before intervention	30	2.47	0.82	6.23	1.07
	After the intervention	30	2.43	0.50	3.03	0.76
ORS * Probiotics	Before intervention	30	2.07	0.87	5.93	1.01
	After the intervention	30	2.23	0.57	2.93	0.69
ORS * Zinc * Vitamin A * Probiotic	Before intervention	30	2.83	0.65	6.00	1.01
	After the intervention	30	2.13	0.35	2.40	0.77
ORS	Before intervention	30	2.33	0.71	5.93	1.03
	After the intervention	30	2.87	0.73	3.03	0.91

and comparable in terms of age ($p=0.871$). According to the One way ANOVA test, there was no significant relationship between weight and the studied groups and all groups were similar and comparable in terms of weight ($p=0.958$). According to the One Way ANOVA test, there was a significant difference between the duration of diarrhea before the intervention and the groups studied, so that the combined group had the highest dose of all substances and the probiotic group had the lowest duration of diarrhea before the intervention. ($p=0.006$). The present findings, according to the One way ANOVA test, showed that there was no significant difference in the number of diarrhea periods before the intervention in the studied groups and the number of diarrhea times before the intervention in the groups was similar and comparable ($p=0.588$). The present findings, according to the One way ANOVA test, showed a significant relationship between the duration of diarrhea after the intervention and the treatment groups studied, and in the combined group, the lowest duration of diarrhea was achieved after the intervention ($p<0.001$). Findings in **table II** showed that the duration of diarrhea after the intervention was significantly reduced ($P<0.001$) in the combined group and only significantly increased in the ORS group ($p = 0.013$) before the intervention. Findings in **table III** showed that the number of times diarrhea after the intervention decreased significantly compared to before the intervention in all groups. ($P<0.001$). The present findings indicate that there is a significant relationship between the length of hospital stay and the treatment groups studied, so that the combined group had the lowest and the vitamin A group had the longest hospital stay ($p<0.001$). The duration of diarrhea in both males and females in the ORS group is only the highest and in the combined group the lowest. According

to **table IV**, it can be shown that by eliminating the effect of age, sex and disruptive factors, a significant relationship remained between the duration of diarrhea after intervention with groups. ($p <0.001$). The frequency of diarrhea in both males and females in the ORS group is only the highest and in the combined group the lowest. According to **table V**, the significant relationship between the number of diarrhea recurrences after intervention with groups remained with the elimination of the effect of age on sex and disruptive factors. ($p <0.001$).

Discussion

Infectious diseases are considered the most important human threat in the last 10 days²¹⁻²⁵. The results of the present study showed that all the intervention groups were identical and comparable in terms of demographic characteristics of sex, age, weight and clinical characteristics, the number of times and duration of diarrhea before the intervention. The duration of diarrhea after the intervention decreased compared to before the intervention in the combined group and increased only in the ORS group. The frequency of diarrhea decreased after the intervention compared to before the intervention in all groups. In the variables after the intervention, including the duration of diarrhea, the number of times diarrhea and the duration of hospitalization, there is a significant relationship with the treatment groups studied. The combined group showed the shortest duration of diarrhea after the intervention, the lowest number of diarrhea times after the intervention, and the shortest duration of hospitalization. The ORS group alone had the longest duration of diarrhea after the intervention and the highest number of diarrhea times, and the vitamin

Table III: Comparison of different treatment groups with each other in terms of the duration of diarrhea and the frequency of diarrhea after the intervention.

Group	Groups	Significant duration of diarrhea after intervention	Significant frequency of diarrhea after the intervention
ORS * Zinc ORS * Vitamin A.	ORS * Vitamin A ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic ORS	0.9 0.99 0.001> 0.001>	1 0.99 0.02 0.001>
ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic	ORS * Zinc ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic ORS	0.90 0.66 0.001> 0.03	1 0.99 0.02 0.001>
ORS ORS * Zinc	ORS * Roy ORS * Vitamin A ORS * Zinc * Vitamin A * Probiotic ORS	0.99 0.66 0.001> 0.001>	0.99 0.99 0.07 0.001>
ORS * Vitamin A. ORS * Probiotics	ORS * Zinc ORS * Vitamin A. ORS * Probiotics ORS	0.001> 0.001> 0.001> <0.001	0.02 0.02 0.07 0.001>
ORS * Zinc * Vitamin A * Probiotic	ORS * Roy ORS * Vitamin A. ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic	<0.001 0.03 <0.001 <0.001	0.001> 0.001> 0.001> 0.001>

Table IV: Duration of diarrhea after intervention according to contextual variables.

References	Sum of squares	Degrees of freedom	Average of squares	F	Significant	Partial Eta Squared
Corrected model	52.790	12	4.399	13.512	0.001>	0.542
Intercept	10.843	1	10.843	33.305	0.001>	0.196
The duration of diarrhea before the intervention	0.528	1	0.528	1.621	0.205	0.012
Age	1.297	1	1.297	3.985	0.048	0.028
Weight	1.187	1	1.187	3.647	0.058	0.026
Gender	1.194	1	1.194	3.667	0.058	0.026
Group	48.946	4	12.237	37.585	0.001>	0.523

Table V: Number of diarrhea times after intervention according to contextual variables.

References	Sum of squares	Degrees of freedom	Average of squares	F	Significant	Partial Eta Squared
Corrected model	103.606	12	8.634	15.032	0.001>	0.568
Intercept	11.561	1	11.561	20.129	0.001>	0.128
The duration of diarrhea before the intervention	3.914	1	3.914	6.814	0.010	0.047
Age	0.790	1	0.790	1.376	0.243	0.010
Weight	0.253	1	0.253	0.440	0.508	0.003
Gender	3.474	1	3.474	6.049	0.015	0.042
Group	90.608	4	22.652	39.438	0.001>	0.535

A group had the longest hospital stay. Acute infectious diarrhea is still a major cause of morbidity in children. Additionally, the source of anxiety in affected families and children involved and because of the relative high cost to society and the family. Drugs used to treat diarrhea affect intestinal motility, ion transport, and intestinal bacteria to reduce the length of diarrhea^{26,27}. Probiotics have improved their reputation for treating diarrhea. But in most countries, microorganisms are still more of a food additive than a drug. For this reason, its safety and harmlessness aspects have been preferred in food industry research due to its effectiveness on clinical efficacy. In addition, the word "probiotic" is often incorrectly applied to certain categories of products that are used in most products²⁸. Probiotics are prescribed for diarrhea in many countries without specific indications. In this study, we did not conduct a quantitative or qualitative study of the amount and type of microbial probiotics, but because we intended to evaluate the effectiveness of probiotics on the clinical symptoms of diarrhea, we used probiotics available and prescribed by pediatricians. Other supplements included in the present study include vitamin A and zinc, which, in addition to some reports of therapeutic effects, were also a response to children's malnutrition. According to the National Food Administration in Mexico, 34% of children under the age of 5 are deficient in zinc and less than 5% are deficient in vitamin A, but children in urban areas are less at risk for nutritional deficiencies than children in rural areas²⁹. The findings of the study in the probiotic group with ORS showed a significant reduction in the number of times and a significant increase in the duration of diarrhea after the intervention. In the probiotic group, along with zinc and vitamin A, the effect of both duration and number of diarrhea was improved. In contrast to the present finding, Lactobacillus probiotics are less

associated with the length of diarrhea, and this effect has been reported in cocaine admitted to a hospital or clinic in both developed and developing countries³⁰. Another effective probiotic is the combination of *ST thermophilus* and *B bifidum*, which is effective in chronic diarrhea in the buttocks under 24 months. On the other hand, previous studies in streptococcal probiotic *Fecium* have shown an improvement in children's diarrhea and ineffectiveness in adult diarrhea³¹. It is noteworthy that most of the children involved had acute viral diarrhea. Some factors were distorted in similar studies but were not eliminated in their study. The results of the present study in the group treated with vitamin A or zinc with ORS showed a significant reduction in the number of times and no significant change in the duration of diarrhea after the intervention compared to before. In the probiotic group, along with zinc and vitamin A, the effect of both duration and number of diarrhea was improved. In addition to the present study, previous studies on the effect of vitamin A in different parts of the world showed an ineffective effect on diarrhea and increased risk of respiratory infections³². Our current study also showed a significant increase in hospital stay length in the vitamin A-only intervention group. A large number of previous trials that reported positive or negative effects of vitamin supplementation on diarrhea varied according to age, diet, and diet, and did not show any clear and definite effect on the overall prognosis of diarrhea³³. However, in the present study, we measured the effect of vitamin A in combination with ORS alone or with zinc and probiotics according to the main components of diarrhea assessment, ie duration and number of times. In contrast, in combination with the present results, it has been shown that zinc supplementation has a positive and effective effect on the prognosis of diarrhea³⁴. A study by Long et al.³⁵ found

that vitamin A supplementation was associated with an overall increase in acute diarrhea, fever, and infection among children living on the outskirts of Mexico City. However, it had no effect on diarrhea, fever or infection. However, in the present study, zinc had a significant effect on reducing the number of times diarrhea³⁶. Vitamin A supplementation, on the other hand, increases Th2 self-regulation. In contrast, zinc deficiency is associated with a decrease in Th1 immune response, and this is offset by a supplement that helps increase Th1³⁷. Deficiency of a significant effect of zinc supplementation in long-term study may be due to the reduction of diarrhea pathogens such as Salmonella and Typhoid after health education programs as well as the elimination of major microorganisms and their susceptible growth medium³⁸. Increased zinc self-regulation leads to Th1 stimulation and subsequent protection against these pathogens³⁹. Increased diarrhea indicates a relatively higher prevalence of gastrointestinal pathogens such as rotavirus.

References

- Bern C, Martines J, De Zoysa I, Glass R. The magnitude of the global problem of diarrhoeal disease: a ten-year update. *Bulletin of the world health organization*. 1992;70(6):705.
- Moradi G, Khazaei Z, Esmailnasab N, Roshani D, Zokaii M, Ghaderi E, et al. The relationship between maternal diseases during pregnancy and low birth weight: a nested case-control study in rural areas of Kurdistan province (West of Iran). *International Journal of Pediatrics*. 2017;5(8):5501-14.
- El-Khoury M, Banke K, Sloane P. Improved childhood diarrhea treatment practices in Ghana: a pre-post evaluation of a comprehensive private-sector program. *Global Health: Science and Practice*. 2016;4(2):264-75.
- Zhang S-X, Zhou Y-M, Xu W, Tian L-G, Chen J-X, Chen S-H, et al. Impact of co-infections with enteric pathogens on children suffering from acute diarrhea in southwest China. *Infectious diseases of poverty*. 2016;5(1):64.
- Niehaus MD, Moore SR, Patrick PD, Derr LL, Lortz B, Lima AA, et al. Early childhood diarrhea is associated with diminished cognitive function 4 to 7 years later in children in a northeast Brazilian shantytown. *The American journal of tropical medicine and hygiene*. 2002;66(5):590-3.
- Walker CLF, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. *The Lancet*. 2013;381(9875):1405-16.
- Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *The Lancet*. 2012;379(9832):2151-61.
- Organization WH. The treatment of diarrhoea: a manual for physicians and other senior health workers: World Health Organization; 2005.
- Gould LH, Walsh KA, Vieira AR, Herman K, Williams IT, Hall AJ, et al. Surveillance for foodborne disease outbreaks—United States, 1998–2008. *Morbidity and Mortality Weekly Report: Surveillance Summaries*. 2013;62(2):1-34.
- Long KZ, Rosado JL, DuPont HL, Hertzmark E, Santos JI. Supplementation with vitamin A reduces watery diarrhoea and respiratory infections in Mexican children. *British journal of nutrition*. 2007;97(2):337-43.
- Rodeheffer C, Von Messling V, Milot S, Lepine F, Manges AR, Ward BJ. Disease manifestations of canine distemper virus infection in ferrets are modulated by vitamin A status. *The Journal of nutrition*. 2007;137(8):1916-22.
- Kossmann J, Nestel P, Herrera M, Amin A, Fawzi W. Undernutrition in relation to childhood infections: a prospective study in the Sudan. *European journal of clinical nutrition*. 2000;54(6):463-72.
- Ross A, Caballero B, Cousins R, Tucker K, Ziegler T, Katherine Camacho Carr C. *Modern nutrition in health and disease (Modern Nutrition in Health & Disease (Shils))*. United States of America: Lippincott Williams & Wilkins; 2012.
- Arora R, Kulshreshtha S, Mohan G, Singh M, Sharma P. Estimation of serum zinc and copper in children with acute diarrhea. *Biological trace element research*. 2006;114(1-3):121-6.
- Al-Sonboli Na, Gurgel RQ, Shenkin A, Hart CA, Cuevas LE. Zinc supplementation in Brazilian children with acute diarrhoea. *Annals of tropical paediatrics*. 2003;23(1):3-8.
- Baqi AH, Black RE, El Arifeen S, Yunus M, Chakraborty J, Ahmed S, et al. Effect of zinc supplementation started during diarrhoea on morbidity and mortality in Bangladeshi children: community randomised trial. *Bmj*. 2002;325(7372):1059.
- Gregorio GV, Dans LF, Cordero CP, Pabello CA. Zinc supplementation reduced cost and duration of acute diarrhea in children. *Journal of clinical epidemiology*. 2007;60(6):560-6.
- Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. *Sao Paulo Medical Journal*. 2011;129(3):185.
- Boirivant M, Strober W. The mechanism of action of probiotics. *Current opinion in gastroenterology*. 2007;23(6):679-92.

Conclusion

The results of the present study showed that the group of children receiving zinc supplements, vitamin A, probiotics and ORS had a positive effect on reducing the number and duration of diarrhea. All groups also had a reduced effect on the number of times diarrhea.

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Interests conflict

The researchers declare that they have no conflict of interest.

20. Surawicz CM. Probiotics, antibiotic-associated diarrhoea and *Clostridium difficile* diarrhoea in humans. *Best Practice & Research Clinical Gastroenterology*. 2003;17(5):775-83.
21. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of *Brucella abortus* and *Brucella melitensis* in aborted bovine, ovine, caprine, buffaloes and camelid fetuses by application of conventional and real-time polymerase chain reaction. *The Thai Journal of Veterinary Medicine*. 2012a;42(1):13.
22. Dehkordi FS, Momtaz H, Doosti A. Application of Real-Time PCR for detection of *Aspergillus* species in aborted ruminant foetuses. *Bulgarian Journal of Veterinary Medicine*. 2012b;15(1):30-6.
23. Dehkordi FS. Prevalence study of *Coxiella burnetii* in aborted ovine and caprine fetuses by evaluation of nested and real-time PCR assays. *American Journal of Animal and Veterinary Sciences*. 2011a;6(4):180-6.
24. Safarpordehkordi F, Yahaghi E, Khodaverdi Darian E. Prevalence of antibiotic resistance in *Escherichia coli* isolated from poultry meat supply in Isfahan. *Iranian Journal of Medical Microbiology*. 2014;8(2):41-7.
25. Dehkordi FS, Tavakoli-Far B, Jafariaskari S, Momtaz H, Esmailzadeh S, Ranjbar R, Rabiei M. Uropathogenic *Escherichia coli* in the high vaginal swab samples of fertile and infertile women: virulence factors, O-serogroups, and phenotyping and genotyping characterization of antibiotic resistance. *New Microbes and New Infections*. 2020;38:100824.
26. Sharif A, Sharif M. The effect of bacterial and yeast probiotics on acute watery diarrhea in children. *Iranian Journal of Pediatrics*. 2014;24(S2):S40.
27. Farthing MJ. Novel targets for the pharmacotherapy of diarrhoea: a view for the millennium. *Journal of gastroenterology and hepatology*. 2000;15:G38-G45.
28. Drago L, De Vecchi E, Nicola L, Colombo A, Gismondo M. Microbiological evaluation of commercial probiotic products available in Italy. *Journal of chemotherapy*. 2004;16(5):436-67.
29. Rosado JL, Lopez P, Morales M, Munoz E, Allen LH. Bioavailability of energy, nitrogen, fat, zinc, iron and calcium from rural and urban Mexican diets. *British Journal of Nutrition*. 1992;68(1):45-58.
30. Szajewska H, Setty M, Mrukowicz J, Guandalini S. Probiotics in gastrointestinal diseases in children: hard and not-so-hard evidence of efficacy. *Journal of pediatric gastroenterology and nutrition*. 2006;42(5):454-75.
31. Kurugöl Z, Koturoğlu G. Effects of *Saccharomyces boulardii* in children with acute diarrhoea. *Acta Paediatrica*. 2005;94(1):44-7.
32. Grotto I, Mimouni M, Gdalevich M, Mimouni D. Vitamin A supplementation and childhood morbidity from diarrhea and respiratory infections: a meta-analysis. *The Journal of pediatrics*. 2003;142(3):297-304.
33. Fawzi WW, Mbise R, Spiegelman D, Fataki M, Hertzmark E, Ndossi G. Vitamin A supplements and diarrheal and respiratory tract infections among children in Dar es Salaam, Tanzania. *The Journal of pediatrics*. 2000;137(5):660-7.
34. Baqui AH, Black RE, Arifeen SE, Yunus M, Zaman K, Begum N, et al. Zinc therapy for diarrhoea increased the use of oral rehydration therapy and reduced the use of antibiotics in Bangladeshi children. *Journal of Health, Population and Nutrition*. 2004:440-2.
35. Long KZ, Montoya Y, Hertzmark E, Santos JI, Rosado JL. A double-blind, randomized, clinical trial of the effect of vitamin A and zinc supplementation on diarrheal disease and respiratory tract infections in children in Mexico City, Mexico. *The American journal of clinical nutrition*. 2006;83(3):693-700.
36. Rosado JL, Lopez P, Muñoz E, Martinez H, Allen LH. Zinc supplementation reduced morbidity, but neither zinc nor iron supplementation affected growth or body composition of Mexican preschoolers. *The American journal of clinical nutrition*. 1997;65(1):13-9.
37. Prasad AS, Beck F, Grabowski SM, Kaplan J, Mathog RH. Zinc deficiency: changes in cytokine production and T-cell subpopulations in patients with head and neck cancer and in noncancer subjects. *Proceedings of the Association of American Physicians*. 1997;109(1):68-77.
38. Velázquez FR, Garcia-Lozano H, Rodríguez E, Cervantes Y, Gómez A, Melo M, et al. Diarrhea morbidity and mortality in Mexican children: impact of rotavirus disease. *The Pediatric infectious disease journal*. 2004;23(10):S149-S55.
39. Schlaak J, Nieder P, zum Büschenfelde K-HM, Fleischer B. Human T helper cells reactive with somatic bacterial antigens belong to the Th1 subset. *Medical microbiology and immunology*. 1994;183(3):169-75.

Drug use evaluation of oral hypoglycemics in diabetic patients in a tertiary care hospital, India

Evaluación del uso de fármacos de hipoglucemiantes orales en pacientes diabéticos en un hospital de atención terciaria, India

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Abstract

Objective: To evaluate drug use of oral hypoglycemic in hospitalized diabetic patients in a tertiary care hospital.

Methodology: A retrospective study of 6 months duration was undertaken during 2017-2018. A total number of 110 patients case sheets were utilized for study from diabetics patients, department of Saphthagiri Institute of Medical Sciences & Research Centre (SIMSRC). Patients were included in study with any age with diagnosis of diabetes mellitus. Randomization was done by selecting alternative case sheets. The data's were collected in profoma, which includes name, age, gender, diagnosis, number of drugs prescribed, with dose and routes of drug administration and also condition of patient on discharge were recorded. blood transfusion and nutritional preparations were not included in the study. Source of data was collected from patient's case sheets obtained from record section. Ethical clearance was taken from institutional ethical committee. Drugs data on the utilization of oral hypoglycemics and patient's data were computed using MS Excel and statistical analysis was done by using SPSS (Statistical package for the social sciences).

Results: Out of 110 patients enrolled in the study from inpatient department, Majority of patients 34.5% belonged to age group of 51-60 years. the number of Female patients were high by 10.9%. 55.4% patients were females and 44.5% patients were males. In Diabetes mellitus patients the most common co-morbid conditions are Hypertension (47.4%), Ischemic Heart Disease (11.4%), Coronary Artery Disease (8%), Unstable Angina (6.8%), Asthma (4%), Chronic Kidney Disease (4%), Anemia (3.4%), Myocardial Infarction (3.4%), Liver Dysfunction (2.2%), Congestive Cardiac Failure (1.7%), COPD (1.7%), ESRD (1.1%) and hyperlipidemia, Infection (1.1%). Among these 15 co-morbid conditions Hypertension and Ischemic Heart Disease are comparatively high. Out of 110 prescriptions, the total number of drugs prescribed were 816. Number of appropriate prescriptions were 95.4% and Number of inappropriate prescriptions were 4.5%. Anti-diabetics were the commonest class of drugs prescribed accounting for 20.7% of the total drugs. Glimepiride + metformin was used most widely 54.2% as a combination therapy. Out of 173 Oral Hypoglycemic prescribed 69.9% were given as Twice a day, followed by 21.9% were given as Three times a day and Once daily in 5.2%.

Conclusion: This study gives an overview of the Evaluation Of Oral Hypoglycemics in the study area. The study showed that patients between the ages of 51 and 60 years were admitted more frequently than other age groups. The most common illness for which patients were hospitalized involves Type 2 DM, Hypertension, Ischemic Heart Disease, Coronary Artery Disease and Unstable Angina. In Diabetes mellitus patients the most common co-morbid condition is Hypertension. In this study Anti-diabetics were the commonest class of drugs prescribe. In monotherapy, Biguanides (Metformin) utilization was high and in combination therapy, Glimepiride + metformin was used most widely. The most frequency of treatment observed were given twice a day.

Keywords: Oral hypoglycemics, Diabetes mellitus, Metformin, Biguanides, Glimepiride, Hypertension, Evaluation.

Resumen

Objetivo: Evaluar el uso de fármacos hipoglucemiantes orales en pacientes diabéticos hospitalizados en un hospital de tercer nivel.

Metodología: Se realizó un estudio retrospectivo de 6 meses de duración durante 2017-2018. Un número total de 110 pacientes hojas de casos hojas se utilizaron para el estudio de los pacientes diabéticos, del departamento de Saphthagiri Institute of Medical Sciences & Research Centre (SIMSRC). Se incluyeron en el estudio pacientes de cualquier edad con diagnóstico de diabetes mellitus. La aleatorización se hizo seleccionando hojas de casos alternativos. Los datos se recogieron en un formulario que incluía el nombre, la edad, el sexo, el diagnóstico, el número de medicamentos prescritos, la dosis y las vías de administración de los mismos, así como el estado de salud de los pacientes. de los medicamentos, con la dosis y las vías de administración de los mismos, así como el estado del paciente al ser dado de alta. no se incluyeron en el estudio. La fuente de datos se recogió de las hojas de los casos de los pacientes obtenidas en la sección de registros. La autorización ética fue de ética del comité ético institucional. Los datos sobre la utilización de hipoglucemiantes orales y los datos de los pacientes se calcularon con MS Excel y el análisis estadístico se realizó con el SPSS (Statistical package for the social sciences).

Resultados: De los 110 pacientes inscritos en el estudio en el departamento de hospitalización, la mayoría de los pacientes, el 34,5%, pertenecían al grupo de edad de 51-60 años. El número de pacientes femeninos era elevado, un 10,9%. El 55,4% de los pacientes eran mujeres y el 44,5% eran hombres. En los pacientes con diabetes mellitus, las afecciones comórbidas más comunes son la hipertensión (47,4%), la cardiopatía isquémica (11,4%), la arteriopatía coronaria (8%) y la enfermedad inestable. coronaria (8%), angina inestable (6,8%), asma (4%), enfermedad renal crónica (4%), anemia (3,4%), infarto de miocardio (3,4%), disfunción hepática (2,2%). (2,2%), insuficiencia cardíaca congestiva (1,7%), EPOC (1,7%), enfermedad renal terminal (1,1%) e hiperlipidemia, infección (1,1%). Entre estas 15 condiciones de comorbilidad, la hipertensión y la cardiopatía isquémica son comparativamente altas. De las 110 prescripciones, el número total de medicamentos recetados fue de 816. El número de prescripciones apropiadas fue del 95,4% y el número de prescripciones inapropiadas fue del 4,5%. Los anti-diabéticos fueron la clase de fármacos más recetados, con un 20,7% del total de fármacos. La glimepirida y la metformina fueron los más utilizados. El 54,2% se utilizó como terapia combinada. De los 173 hipoglucemiantes orales prescritos, el 69,9% se administró dos veces al día, seguido del 21,9% se administraron tres veces al día y el 5,2% una vez al día.

Conclusión: Este estudio ofrece una visión general de la evaluación de los hipoglucemiantes orales en el área de estudio. El estudio mostró que los pacientes entre 51 y 60 años fueron ingresados con mayor frecuencia que otros grupos de edad. La enfermedad más común por la que los pacientes fueron hospitalizados son la DM tipo 2, la hipertensión, la cardiopatía isquémica, la arteriopatía coronaria y la angina inestable. En los pacientes con mellitus la enfermedad comórbida más común es la hipertensión. En este estudio, los anti-diabéticos fueron la clase de fármacos más prescritos. En monoterapia, la utilización de Biguanidas (Metformina) fue alta y en terapia combinada, Glimepirida + metformina fue la más utilizada. ampliamente. La mayor frecuencia de tratamiento observada se administró dos veces al día.

Palabras clave: Hipoglucemiantes orales, diabetes mellitus, metformina, biguanidas, glimepirida, hipertensión, evaluación.

Introduction

Diabetes mellitus (DM) is one of the oldest diseases known to man, which was the first reported in Egyptian literature about 3000 years ago¹. The name diabetes was first given by the Greek Physician Aretaeus (30-90CE). Avicenna, is the famous Arabian physician who first described the complications and progression of the disease². People living with type 2 DM are more vulnerable to various forms of both short and long-term complications, which often lead to their premature death. The world health organization (WHO) defines diabetes mellitus as "A metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in the insulin secretion, insulin action, or both."^{3,4} India has the largest population of diabetes in the world. The international diabetes federation (IDF) estimates the number of people with diabetes in India will reach 80million by the year 2025.⁵ The world health organization (WHO) has projected that the global prevalence of type-2 diabetes mellitus will more than double from 5 million in 1995 to 300 million by 2025. Between 1995 and 2025, there will be a 35% increase in worldwide prevalence of diabetes mellitus, from 4 to 5.4%.⁶

Diabetes prevalence is continuously growing all over the world. Type 2 diabetes constitute about 85% to 95% of the diabetic population in the developed countries and even higher in the developing countries. In 2003, 194 million people having age between 20 to 79 years are diabetic and a quarter of them belong to developing countries. There is a rapid increase in the prevalence of diabetes in Asian countries.⁷ Various classes of anti-diabetic drugs including insulin and oral hypoglycemic agents (OHA) are currently used in the treatment of diabetes, which acts by different mechanisms to reduce the blood glucose levels to maintain optimal glycemic control.⁸ There are several classes of oral drugs used to control blood glucose levels, including: Sulfonylureas, such as glipizide and glimepiride, are considered hypoglycemic agents because they stimulate the release of insulin from beta cells in the pancreas, thus reducing blood glucose levels.⁹ Glipizide 2.5 to 10mg PO before breakfast and evening meal, start with low dose.45 glimepiride 1 to 2 mg orally once a day.¹⁰

Diabetes mellitus requires ongoing medical care as well as patient and family education both to prevent acute illness and to reduce the risk of long term complications. Evaluation of drug use has become an integral part of the pharmacotherapy. Participation in drug utilization study programmes can directly improve the quality of patients' care, by preventing the use of unnecessary or irrational drug therapy and by preventing adverse drug reactions¹¹. Drug utilization studies provide physicians with feedback on their performance and assist the design of educational programmes that may improve

prescribing and drug use performance¹². Considering the fact that, India carries a huge diabetic population which is swelling further, medicine utilization studies might be one of the strategies to rationalize the medicine use in diabetics and to manage disease better in the community. Hence a medicine utilization study of oral hypoglycemic was carried out at the Medicine Outpatient Department (OPD) in tertiary care hospital. There were two aims of the study to assess the prescribing pattern of oral hypoglycemic drugs by using ADA guideline, and to correlate association of diabetes with demographic details of patients.

Materials and methods

This study was conducted for a period of 6 months, the study included 110 patients from IP department of Sapthagiri Institute of Medical Science, a tertiary care hospital in Bangalore.

The purpose and other details of the study were discussed with the patients. An oral consent was taken from all the participating patients, prior inclusion in the study. diabetes mellitus patients, irrespective of age and sex, who were prescribed at least one oral hypoglycemic were included in the present study. Diagnosed diabetic patients who do not receive pharmacological therapy, unable to reply verbal questions as well as mentally retarded and unconscious patients were excluded from the study. This is a retrospective and prospective observational study. The patients who satisfied the inclusion criteria was enrolled into the study with the help of patient consent form. The clinical pharmacist reviewed the patient case notes, medication chart, laboratory data and other relevant data. A structured data collection form was used to record all the necessary data including patient demographic details, patient medication history, co morbid conditions and reason for admission, medication details and lab investigation. The pattern of drug dosing was also recorded.

Result and discussion

This study was carried out with an aim to assess the Oral Hypoglycemics used in hospitalized patients of tertiary care hospital in Sapthagiri Institute of Medical Science And Research Centre, Bangalore. The duration of study was six months.

The patient were divided in six age group such as 30-40, 41-50, 51-60, 61-70, 71-80 and >80.

The majority of patients, 34 % were on age group 51-60 years, this may be due to fact that age is a risk factor for developing diabetes mellitus supported by Mandana Moradi et.al.¹³ (**Table I**)

Table I: Age Distribution Of Patients Observed (n=110).

Age distribution (in years)	Total No. of patients	IN percentage
30-40	11	10%
41-50	13	11.80%
51-60	38	34.50%
61-70	25	22.70%
71-80	17	15.40%
>80	6	5.40%

Out of 110 patients, 49 (44.5%) patients were males and 61 (55.4%) patients were females. the number of female patients were high by 10.9%.The study shows that female patients are more than male patients, however in earlier study female predominance were seen which is in agreement with our result supported by Syed Muhammad Ashar et.al.¹⁴ The reason for having diabetes more in females than in males could be because of lifestyle.

In Diabetes mellitus patients the most common co-morbid conditions are Hypertension, Ischemic Heart Disease, Coronary Artery Disease, Unstable Angina, Asthma, Chronic Kidney Disease, Anemia, Myocardial Infarction, Liver Dysfunction, Congestive Cardiac Failure, COPD, ESRD and hyperlipidemia, Infection. Among these 15 co-morbid conditions Hypertension and Ischemic Heart Disease are comparatively high (**Table II**).

Table II: Co-Morbid Conditions Of Patients (n=175).

Co-morbid conditions	No. of Patients	In Percentage
Hypertension	83	47.40%
IHD	20	11.40%
CAD	14	8%
Unstable angina	12	6.80%
Asthma	7	4%
CKD	7	4%
Anemia	6	3.40%
MI	6	3.40%
Liver dysfunction	4	2.20%
CCF	3	1.70%
Acute kidney injury	3	1.70%
COPD	3	1.70%
Infection	3	1.70%
ESRD	2	1.10%
Hyperlipidemia	2	1.10%

The total number of drugs prescribed were 816. Average number of drugs per prescription were 7.41. The risk of drug interaction may increase with increase in number of drugs per prescription which ultimately lead to prescribing errors and in hazardous to the health of patient. Anti-diabetic drugs were the most common drugs prescribed which accounts for 169 (20.7%) of total drugs (**Table III**).

Table III: Number Of Medications Prescribed In Study Population.

Total no of prescriptions	110
Total no of drugs prescribed	816
Average no of drugs per prescription	7.41
No. of appropriate prescriptions	105 (95.4%)
No. of inappropriate prescriptions	5 (4.5%)

In the present study 47.4% patient reported hypertension along with diabetes mellitus, these results were supported by Dashputra AV et al.¹⁵ this study indicates that hypertension is the commonest co-morbidity seen with diabetes mellitus. Anti-platelet were the second commonest drug prescribed which accounts for 69 (9.3%) antibiotics 53 (6.4%), Analgesic 45 (5.2%), Diuretics 37 (4.5%), Hypolipidemic 35 (4.2%), Anti-angina 31 (3.7%), Respiratory agent 14 (1.7%), Calcium channel blocker 12 (1.4%), Benzodiazepines 8 (0.9%), Antihistamine 8 (0.9%), Antihypertensive drugs 8 (0.9%), and others (PPIs, IV fluids, Corticosteroids, Antacid, Anti-emetic, Antifungal, Vitamins) 328 (40.1%) were prescribed (**Table IV**).

Table IV: Distribution Of Different Types Drugs Prescribed (n=816).

Drugs prescribed	Total No. of drugs	In Percentage
Anti-diabetic	169	20.70%
Anti-platelet	69	9.30%
Antibiotics	53	6.40%
Analgesic	45	5.20%
Diuretics	37	4.50%
Hypolipidemic	35	4.20%
Anti-angina	31	3.70%
Respiratory agent	14	1.70%
Calcium channel blocker	12	1.40%
Benzodiazepines	8	0.90%
Antihistamine	8	0.90%
Antihypertensive drugs	7	0.80%
Others*	328	40.10%

* PPIs, IV fluids, Corticosteroids, Antacid, Anti-emetic, Antifungal, Vitamins

Anti-diabetic drugs commonly prescribed as monotherapy were metformin (49.2%), Glimepiride (25.36%), Sitagliptin (15.21%), Glyburide (10.1%) and as combination therapy Glimepiride/metformin (54.2%), Glimepiride/metformin/voglibose (25.7%), Sitagliptin/metformin(20%). Biguanides (metformin) (49.2%) utilization was high as monotherapy in prescription, this may be due to its high advantages of no weight gain these results were supported by Ramachandran G et al [16]. In combination therapy Glimepiride/metformin combination was most widely used (54.2%) (**Table V**).

Table V: Evaluation Of Single Prescribed Oral Hypoglycemics (n=138).

Monotherapy	Number Of Prescription	In Percentage
Metformin	68	49.20%
Glimepiride	35	25.36%
Sitagliptin	21	15.21%
Glyburide	14	10.10%
Total	138	100.00%

Anti-platelet were the second commonest drug prescribed which accounts for 69 (9.3%) antibiotics 53 (6.4%), Analgesic 45 (5.2%), Diuretics 37 (4.5%), Hypolipidemic 35 (4.2%), Anti-angina 31 (3.7%), Respiratory agent 14 (1.7%), Calcium channel blocker 12 (1.4%), Benzodiazepines 8 (0.9%), Antihistamine 8 (0.9%), Antihypertensive drugs 8 (0.9%), and others (PPIs,

IV fluids, Corticosteroids, Antacid, Anti-emetic, Antifungal, Vitamins) 328 (40.1%) were prescribed (Table VI).

Table VI: Evaluation Of Combination Therapy Of Oral Hypoglycemics (n=35).

Combination therapy	N ^o of Prescription	In Percentage
Glimepiride/metformin	19	54.20%
Glimepiride/metformin/voglibose	9	25.70%
Sitagliptin/metformin	7	20%
Total	35	100

Out of 173 Oral Hypoglycemic prescribed 69.9% were given as Twice a day, followed by 21.9% were given as Three times a day and Once daily in 5.2%. This is based on the choice and course of drugs for the therapy (Table VII).

Table VII: Distribution of frequency of treatment observed (n=173).

Frequency of treatment	Number of patients prescribed with antibiotics	IN percentage
Once Daily	9	5.20%
Twice a day	121	69.90%
Three times a day	38	21.90%
Four a a day	5	2.80%

Conclusion

This observational study of evaluation of oral Hypoglycemics shows metformin was the most commonly prescribed anti-diabetic drug in Monotherapy followed by Glimepiride. Among Fixed drug combination therapy Glimepiride/metformin was the most commonly prescribed antidiabetic drug. The study showed that Majority of patients belonged to age group of 51-60 years. Hypertension was most common associated co-morbidity in diabetic patients. Incidence of diabetes has been found higher in female as compared to male and majority of the patients develop diabetes in the most productive years of their life. In this study, males were found to be more affected by type 2 diabetes mellitus than females. Most of the patients were prescribed two Oral Hypoglycemic. Average number of drugs per prescription was found to be 7.1. The most commonly drugs prescribed apart from antidiabetic were Anti-platelet drugs followed by Analgesics. It was observed that most prescribed Oral Hypoglycemic was Metformin, Glimepiride and Sitagliptin.

Interests conflict

The researchers declare that they have no conflict of interest.

References

- Ahmed AM. History of diabetes mellitus. Saudi medical journal. 2002 Apr 1;23(4):373-8.
- Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman medical journal. 2012 Jul;27(4):269.
- Monteiro C, Silvestre S, Duarte AP, Alves G. Assessment of suspected adverse drug reactions in elderly patients with diabetes mellitus based on a Portuguese spontaneous reporting database: analysis of reporting from 2008 to 2018. Expert Opinion on Drug Safety. 2021 Jun 1:1-9.
- Acharya KG, Shah KN, Solanki ND, Rana DA. Evaluation of antidiabetic prescriptions, cost and adherence to treatment guidelines: A prospective, cross-sectional study at a tertiary care teaching hospital. Journal of basic and clinical pharmacy. 2013 Sep;4(4):82.
- King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. Diabetes care. 1998 Sep 1;21(9):1414-31.
- Sierra GN. The global pandemic of diabetes. African Journal of Diabetes Medicine. 2009;17(11):4-8.
- Ashar SM, Hanif A, Jadoon A, ur Rehman M. Assessment of Drug Use Pattern Using WHO Prescribing Indicators in the Medication Therapy of Indoor Diabetic Patients. International Journal of Basic Medical Sciences and Pharmacy (IJBMSp). 2016 Jul 3;6(1).
- Agarwal AA, Jadhav PR, Deshmukh YA. Prescribing pattern and efficacy of anti-diabetic drugs in maintaining optimal glycemic levels in diabetic patients. Journal of basic and clinical pharmacy. 2014 Jun;5(3):79.
- Mukhtar Y, Galalain A, Yunusa U. A modern overview on diabetes mellitus: a chronic endocrine disorder. European Journal of Biology. 2020 Nov 23;5(2):1-4.
- Kumar A, Sharma AK, Dutt R. Reverse-Phase High-Performance Liquid Chromatography Method Development and Validation for Estimation of Glimepiride in Bulk and Tablet Dosage Form. International Journal of Pharmaceutical Quality Assurance. 2020 Jun 25;11(02):296-302.
- Baksaas I, Lunde PK. National drug policies: the need for drug utilization studies. Trends in pharmacological sciences. 1986 Jan 1;7:331-4.
- Parthasarathi G, Nyfort-Hansen K, Nahata MC, editors. A text book of clinical pharmacy practice: essential concepts and skills. Orient Blackswan; 2004.
- Moradi M, Mousavi S. Drug use evaluation of diabetes mellitus in nonhospitalized patients. Int J Pharm Pharm Sci. 2016; 8(8), 337-41.
- Ashar SM, Hanif A, Jadoon A, ur Rehman M. Assessment of Drug Use Pattern Using WHO Prescribing Indicators in the Medication Therapy of Indoor Diabetic Patients. International Journal of Basic Medical Sciences and Pharmacy (IJBMSp). 2016 Jul 3;6(1).
- Dashputra AV, Badwaik RT, Borkar AS, Date AP, Kalnawat NR. Pattern of antidiabetic drugs used in outpatient and hospitalized patients in a tertiary health institute of central India. Hypertension. 2014;89(59.3):68.
- Ramachandran G, Rohith V, Topno I. Evaluation of prescribing pattern of anti-diabetic drugs using WHO prescribing indicators in a tertiary care hospital in Puduchery: A cross-sectional study. The Pharma Innovation. 2015 Jul 1;4(5, Part B):76.

Designing a competency model for managers of health care networks in Iran

Diseño de un modelo de competencias para gestores de redes sanitarias en Irán

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Abstract

Objective: One of the basic pillars of the organizational development and excellence is the existence of competent managers at different levels of management. This study aimed to design a native model to determine the competencies of managers in the Iranian health care network.

Methods: The present study was a combined study using the quantitative-qualitative methodology. In the qualitative part, 14 experts of the country's health network were selected by purposive sampling method, and in the quantitative part, 184 managers of country's health networks were selected based on multi-stage cluster sampling method. The research tool is a semi-structured interview in the qualitative part of interviews and a researcher-made questionnaire in the quantitative part. To test and validate the appropriate model, the competency model of AMOS software was used.

Results: The results of qualitative part showed that the dimensions and subscales of competency model are as follows: basic competencies with two components of personality traits (19 indices) and individual skills (22 indices); Managerial competencies with two components of managerial abilities (11 indices) and managerial skills (16 indices). The results of quantitative part explained the competency model well by performing the first, second, and third-order confirmatory factor analysis of each of the main and sub-dimensions and indices.

Conclusion: The competency model designed in this study can be used in the field of selecting managers of health and treatment networks in the country by considering localization, educational needs assessment, redefining the performance evaluation system, optimizing the career path management system, etc.

Keywords: Manager, health network, competency model, confirmatory factor analysis.

Resumen

Objetivo: Uno de los pilares básicos del desarrollo y la excelencia organizacional es la existencia de gerentes competentes en los diferentes niveles de gestión. Este estudio tuvo como objetivo diseñar un modelo nativo para determinar las competencias de los gerentes en la red de atención médica iraní.

Métodos: El presente estudio fue un estudio combinado utilizando la metodología cuantitativa-cualitativa. En la parte cualitativa, se seleccionaron 14 expertos de la red de salud del país mediante el método de muestreo intencional, y en la parte cuantitativa, se seleccionaron 184 administradores de las redes de salud del país con base en el método de muestreo por conglomerados de etapas múltiples. La herramienta de investigación es una entrevista semiestructurada en la parte cualitativa de las entrevistas y un cuestionario elaborado por el investigador en la parte cuantitativa. Para probar y validar el modelo apropiado, se utilizó el modelo de competencia del software AMOS.

Resultados: Los resultados de la parte cualitativa mostraron que las dimensiones y subescalas del modelo de competencia son las siguientes: competencias básicas con dos componentes de rasgos de personalidad (19 índices) y habilidades individuales (22 índices); Competencias gerenciales con dos componentes de habilidades gerenciales (11 índices) y habilidades gerenciales (16 índices). Los resultados de la parte cuantitativa explicaron bien el modelo de competencias al realizar el análisis factorial confirmatorio de primer, segundo y tercer orden de cada una de las principales y subdimensiones e índices.

Conclusión: El modelo de competencias diseñado en este estudio puede ser utilizado en el campo de la selección de gerentes de redes de salud y tratamiento en el país considerando la localización, evaluación de necesidades educativas, redefiniendo el sistema de evaluación del desempeño, optimizando el sistema de gestión de carrera, etc.

Palabras clave: Gerente, red de salud, modelo de competencia, análisis factorial confirmatorio.

Introduction

Intense competition and rapid growth, and continuous technological changes put increasing pressure on organizations and their various methods to improve the productivity of human resources. Among these, the role of managers of organizations is very important¹. Because of their position, managers can bring valuable successes and reciprocal regrets to the institution under their supervision. They play an important role in the evolution and excellence of the organization via the strategic planning, resource allocation, organizing people, leadership and performance management, and evaluation and control. Organizations strive to compete with the most competent managers as a competitive advantage, identification, absorption, and retaining².

Therefore, World Health Organization has emphasized the importance of management and leadership in health care centers that the issuance of statements, emphasis on the words of management in naming the year, the publication of tens of volumes of guidelines for health system managers are among the cases confirming this³. Health care organizations with dynamic, complex, and vulnerable environments need managers who have the necessary competencies to direct the organizational behavior of health care team members. By efficient and effective management, health care organizations have led to a change in approach from the professional bureaucracy model to the managerial competency model⁴. To increase the independence and competence of managers and employees, health care organizations should develop measures related to human resource management (HRM)⁵.

The county health network, as the first staff organization of the Ministry of Health in the environmental layers, as the largest organization in charge of health in the country and also the second organization due to the number of manpower and organizational units, has characteristics which distinguish it from many organizations and these characteristics are mainly related to various health programs and sensitive and key prevention and treatment missions that all members of society need.

The existence of public hospitals in the county, several thousand comprehensive centers of rural and urban health services, many of which are 24 hours a day, maternity facilities, disease counseling centers, and more than several thousand health centers in all parts of the country confirms the importance of health system management system of the county. However, the system of selection and appointment of managers of the county health network is traditional and mainly emphasizes the responsibility and management of general practitioners. Not learning management principles and skills before or during management, intermittent withdrawal of physicians from the health system due to continuing education or preference to work in purely medical and private wards

and lack of a continuous monitoring and evaluation system, in addition to managerial weakness and waste of resources, has led to lack of motivation of other specialized forces. Due to the lack of forecasting and inclusion of management disciplines in compiling the conditions to obtain managerial positions in the health care network and by examining the biographies of managers on the website of medical universities, it can be seen that the number of managers with higher education history in health care management system in the network management system of the whole country is very limited while the vast majority of them were selected from general practitioners. Using a system of recruitment and selection of managers based on competence can greatly help the performance of the health system in meeting the challenges and address the issues arising from managerial weaknesses in this area. Therefore, identifying the key competencies for selecting, training, and developing health care network managers is absolutely essential.

Despite numerous studies in the field of identifying the competencies of managers and presenting different models and frameworks, most of them have not achieved a coherent and comprehensive framework of competencies⁶. Therefore, this study was conducted to design and compile a local competency model for county health network managers in Iran.

Research method

In the present study, which was conducted in 2021, a combined (quantitative-qualitative) methodology was used. The statistical population of qualitative section included expert faculty members, managers of the country's health care network, and the best and most knowledgeable experts of the country's health care network. The research sample was selected by the purposive sampling method who entered the study. 14 people, including 6 professors, 5 managers, and 3 experts participated in the study purposefully and according to the rule of theoretical saturation and voluntarily. Criteria to select university professors to enter the interview, included having books and articles in the field of educational management, managerial competencies, innovation and creativity in education and management, and history of giving lectures in scientific circles and meetings in the field of education and management in the country's health networks. The criterion to select the best managers and experts was the introduction of managers and experts and the sample introduced by the Deputy Minister of Education and training experts of the country's health networks. In addition to the purposiveness of the sampling method, the snowball technique was also used, and the interviewees were asked to identify people who can provide us with appropriate quality data in this regard. Since semi-structured interviews were used in the qualitative stage of this study, in order to analyze the data obtained from the interview, the three-step

coding method of Strauss and Corbin (1998) was used as open, axial, and selective coding. In qualitative data analysis, the following steps were followed: 1) data review, 2) data organization, 3) data coding, 4) data classification, 5) creation of subcategories, 6) creation of main categories or major axes, and 7) report compilation.

In the second stage of research, after conducting qualitative research and making a questionnaire, a quantitative method was used to test the proposed competency model of country's health care network managers. The purpose of this stage of the research is to determine complex patterns of relationships, test the extent of relationships among categories, and achieve levels of generalizability in the larger sample. In this stage, descriptive-analytical research method and structural equation modeling were used. The statistical population of quantitative research includes 905 managers of the country's health care network in 2021. In the present study, in the first step, the multi-stage cluster sampling method was used, and in the second step, the sampling method proportional to the volume was used. To determine the sample size, the Cochran sampling formula was used, and 184 samples were determined. After receiving the information of the questionnaire, due to non-response and distortion of some of them, 179 questionnaires were finally analyzed. A researcher-made questionnaire was used to collect data in a quantitative stage. The basis for making the questionnaire is the indices identified in the qualitative stage of the research. The questionnaire of the present study was designed and implemented according to the 5-point Likert scale. The final model was in the form of 90 indices in 3 dimensions of basic competencies, managerial competencies, specialized competencies so that the basic competencies include two components with personality traits (19 indices) and individual skills (22 indices); Managerial competencies with two components of managerial abilities (11 indices) and managerial skills (16 indices); Furthermore, the index of specialized competencies is with two components of specialized knowledge (15 indices) and specialized experience (7 indices). Descriptive and inferential statistical methods were used to analyze the data. In the descriptive statistics part, mean and standard deviation and in the inferential statistics part, first and second-order confirmatory factor analysis by helping AMOS software and also univariate and correlated t-test by helping SPSS25 software were used.

Analysis of findings

The results of the first stage of Delphi removed 14 indices from 104 indices, added 3 indices, merged 2 indices into 1, and also modified 7 indices. The second round was performed with 90 indices. In the second round, the average of all sub-indices was higher than 4 and no sub-index was removed or added, and the third round was repeated with the same 90 indices along with the average comments of members. Based on

this, the competency model of the country's healthcare network managers was extracted in three stages. The first stage consists of 3 general dimensions, which are: the dimension of basic competencies, the dimension of managerial competencies, and the dimension of specialized competencies. The second stage consists of 6 components: personality traits, individual skills, managerial abilities, managerial skills, specialized knowledge, and specialized experience, and the third stage of the model includes 90 competency indices of the country's health network managers, which are shown in **table I**. The result of qualitative analysis is presented.

After the findings of qualitative results, in the quantitative part, in order to explain and evaluate the validity of the competency measurement model of the country's health care network managers, the reliability index (Cronbach's alpha coefficient) and first, second and third-order confirmatory factor analysis was used, which is as follows. **Table II** shows the reliability of the dimensions and subscales of the competency model of the country's health care network managers using Cronbach's alpha coefficient index.

The results of the reliability coefficient using Cronbach's alpha coefficient in **table II** show that for the dimensions and subscales of the competency model of the country's health care network managers, the reliability rate is between 0.79, and 0.94, and the general model's reliability is 0.942 (equivalent to 94.2%) which indicates the appropriate reliability of the test, its dimensions, and subscales.

In the confirmatory factor analysis method, it is first necessary to study the validity of indices to determine that the selected indices have the necessary accuracy in measuring the subscales and dimensions of the model. In such a way that the factor load of each index with its component and dimension has a t-value higher than 1.96 at the significant level of 0.05 and 2.58 at the significant level of 0.01 and positive. In this case, this index has the necessary accuracy to measure that hidden structure or attribute.

All indices have an appropriate factor load on their latent variable, and these factor loads are significant with respect to the t-value at the 0.01 level. In other words, the t-value corresponding to each factor load is greater than its critical value (2.58) at the level of 0.01. As a result, it can be said that these indices have the necessary accuracy to measure the indices of each component, so they entered the final analysis.

Each of the personality traits, individual skills, managerial abilities, managerial skills, specialized knowledge, and specialized experience can act as a component for the dimensions of the competency model of the country's health network managers, so the second-order confirmatory factor analysis is performed (**Figure 1** and **table III**).

Table I: Results of qualitative research analysis.

Dimensions	Components	Number of items	Indices
Basic competencies	Personality characteristic	19	Commitment to work, honesty, good manners, determination in action, altruism, high work conscience, discipline, self-confidence, flexibility, confidentiality, responsibility, spirituality, confidence-building, insight and awareness, accuracy and speed, open to criticism, regularity.
	Individual skills	22	Verbal and writing skills, decision-making skills, performance evaluation skills, effective listening skills, communication skills, problem-solving skills, learning and personal development, ability to influence others, empowering others, analytical thinking, emotional intelligence, creative thinking, creativity and innovation, personal development, motivation skills, negotiation skills, coaching, critical thinking, learning skills, effective presentation, systematic thinking, self-awareness.
Managerial competencies	Managerial abilities	11	Planning, organizing, coordinating, monitoring, and controlling, human resource management, financial resource management, physical resource management, information resource management, legal resource management, research and development management, marketing management.
	Management skills	16	Strategic thinking, leadership, team building and networking, entrepreneurship, the delegation of authority, time management, project management, performance management, transformation management, knowledge management, risk management, future management, contingency management, quantitative management, crisis management, management systemic.
Specialized competencies	Professional knowledge	15	Health system management, health policy, health system development, health economics, health information technology, health research, health education, medical education, specialized language in health, health law, health performance statistics and analysis, health system monitoring and evaluation, specialized education, principles and generalities of health services, primary health services.
	Specialized experience	7	Health care, work experience in the health center, work experience in the hospital, management experience in health centers, management experience in the health center, management experience in hospital, management experience in the health system.

Table II: Results of the reliability scale of the competency model of the managers of the country's health care.

Dimension	Component	Number of indices	Reliability	Desired level	Result
Basic competencies	Personal characteristics	19	0.879	Greater than 0.70%	Confirmation
	Personal skills	22	0.920	Greater than 0.70%	Confirmation
Basic competencies		41	0.940	Greater than 0.70%	Confirmation
Managerial competencies	Managerial abilities	11	0.796	Greater than 0.70%	Confirmation
	Managerial skills	16	0.903	Greater than 0.70%	Confirmation
Managerial competencies		27	0.916	Greater than 0.70%	Confirmation
Specialized competencies	Specialized knowledge	15	0.822	Greater than 0.70%	Confirmation
	Specialized experience	7	0.899	Greater than 0.70%	Confirmation
Specialized competencies		22	0.855	Greater than 0.70%	Confirmation
General model		90	0.942	Greater than 0.70%	Confirmation

Figure 1: Model for measuring the competence of managers of the country's health care network in the standard mode.

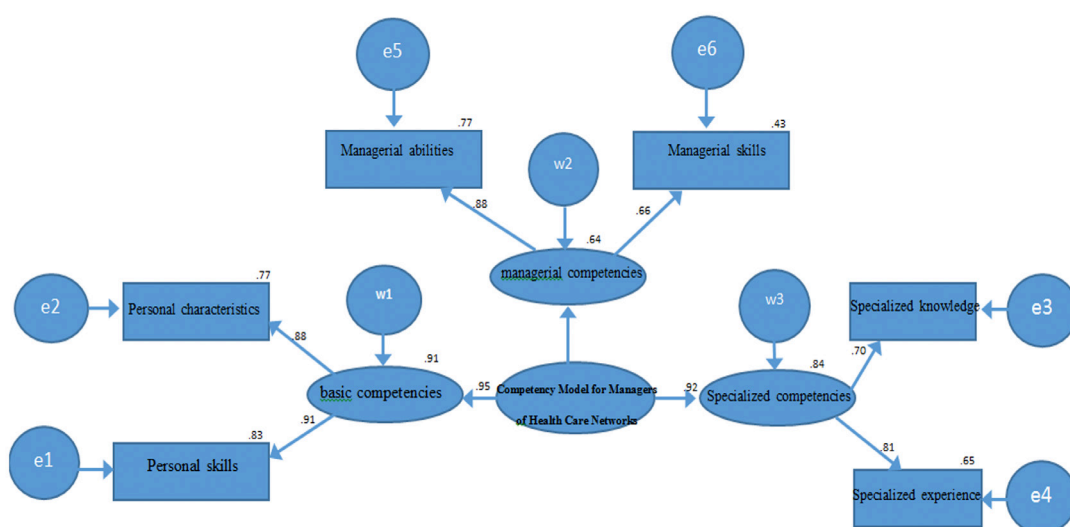


Table III: Results of the second-order confirmatory factor analysis of the competency model of the country's health care network managers.

Component	Factor load	t-value	Significance level	R ²
Personal characteristics	0.88	65.10	0.01	0.77
Personal skills	0.91	78.03	0.01	0.83
Managerial abilities	0.88	88.97	0.01	0.77
Managerial skills	0.66	116.98	0.01	0.43
Specialized knowledge	0.70	29.03	0.01	0.49
Specialized experience	0.81	38.63	0.01	0.65

Table IV: Results of the third-order confirmatory factor analysis of the competency model of the managers of the country's health care network.

Model dimensions	Factor load	t-value	Significance level	R ²
Basic competencies	0.95	35.11	0.01	0.91
Managerial competencies	0.80	37.42	0.01	0.64
Specialized competencies	0.92	34.97	0.01	0.84

Table V: Results of confirmatory factor analysis of the competency model of the country's health care network managers.

Measurement model	χ^2	df	χ^2/df	RMSEA	GFI	CFI	NFI
Competency model							
	Desired level accepted by fit indices		Less than 4	Less than 0.08	About 0.90 and greater		
	Result		Confirmed	Confirmed	Confirmed		

Table VI: Results of Friedman ranking to test dimensions and subscales of the competency model of the country's health care network managers.

Variable	Value of test statistic	Number	Degrees of freedom	Test error (sig.)	Test level
Subscales	64.143	179	5	<0.01	0.01
Dimensions	33.209	179	2	<0.01	0.01

As shown in **table III**, the values of factor load are desirable in the second-order factor analysis. On the other hand, the t-value corresponding to each factor load is more than its critical value (2.58) at the level of 0.01 and is significant. Furthermore, the coefficient of determination (R²) measures the relationship between the explained variance of a latent variable and its total value of variance. The value of this coefficient is between zero and 1, the larger the values, the more desirable. Values of 0.19, 0.33, and 0.67 are described as weak, moderate, and significant, respectively. According to **table III**, the values of R² are significant and desirable.

Since each of the components of personality traits, individual skills, managerial abilities, managerial skills, specialized knowledge, and specialized experience related to the dimensions of basic competencies, managerial competencies, and specialized competencies act from the competency model of health network managers of the country, so the third-order confirmatory factor analysis is performed (**Figure 1** and **table IV**).

Table IV shows that the factor load values are desirable in the third-order factor analysis. On the other hand, the t-value corresponding to each factor load is more than its critical value (2.58) at the level of 0.01 and is significant. Furthermore, according to **table III**, the values of R² are significant and desirable.

Table V shows the results of confirmatory factor analysis of the competency model of the managers of the country's health care network.

The results of confirmatory factor analysis (measurement model) of competency model of the managers of the country's health network in **table V** show that the ratio of chi-square to the degree of freedom (χ^2/df) in measuring the competency model of the managers of health network and its indices are less than the desired level and the acceptable value is 4 and also the value of the root index of estimating the variance of the approximation error (**RMSEA**) in the measurement model is less than the significant and acceptable level of 0.08, which indicates a suitable and good fit. Similarly, the values of goodness of fit index (**GFI**), comparative fit index (**CFI**) and normed fit index of Bentler-Bonnet (**NFI**) are about 0.90 and greater than the desired value of 0.90, which are considered appropriate and desirable values. Therefore, the measurement model of the competency model of the country's health care network managers and its dimensions are supported by the research data at the appropriate level of the theories used and is a suitable model to explain the competency of the country's health care network managers. Therefore, all indices and dimensions used in the research have the explanatory power for the competency model of health care network managers in the country and according to the validity results, fitness characteristics, reported reliability coefficients and factor, data collection tool has technical features (reliability and credibility) at a very good level.

Table VI shows the results of Friedman ranking test to examine the dimensions and subscales of the competency model of the managers of country's health care network.

Table VII: Distribution of the average dimensions and components of the competency model of the managers of the country's health care network.

Components	Number	Average	Standard deviation
Personal characteristics	179	4.06	0.98
Personal skills	179	3.84	1.07
dimension: basic competencies	179	3.95	0.81
Managerial abilities	179	3.51	0.97
Managerial skills	179	3.79	0.83
dimension: managerial competencies	179	3.97	0.82
Specialized knowledge	179	4.00	0.92
Specialized experience	179	3.94	0.91
dimension: Specialized competencies	179	3.65	0.67

Table VII: Results of ranking the dimensions and components of the competency model of the managers of the country's health care network.

Scale	Component		Dimensions	
	Average rank	Prioritization	Average rank	Prioritization
Personal characteristics	3.97	1		
Personal skills	3.60	4		
dimension of basic competencies			2.29	1
Managerial abilities	2.74	6		
Managerial skills	3.28	5		
dimension: managerial competencies			1.68	3
Specialized knowledge	3.73	2		
Specialized experience	3.67	3		
dimension: Specialized competencies			2.13	2

Table VI shows that the error value of the Chi-square test obtained is less than the significance level of 0.01 which results in an error level of less than 0.05. Therefore, the significance of Friedman test means that the ranking of dimensions and subscales of the competency model of the country's health network managers is significant, and the research sample has a different ranking of the dimensions and subscales of the competency model of the country's health network managers.

Table VII shows the distribution of average dimensions and components of the competency model of the managers of the country's health care network.

Table VII shows that among the dimensions and components of the competency model of the managers of country's health care network, the next dimension is "managerial competencies" with a value of 3.97 and the component of "personality traits" with a value of 4.06, respectively.

Table VIII shows the ranking results of the dimensions and components of the competency model of the managers of country's health care network.

Comparing the average rankings of the dimensions and components of the competency model of country's health care network managers in **table VIII** shows that the highest average rank (2.29) among the dimensions of model is attributed to the dimension of basic competencies in scoring, that is, the most important dimension of the competency model of the managers of country's health care network is the dimension of basic competencies. Similarly, the highest average rank (3.97) among the components of the model is attributed to

personality traits in scoring, that is, the most important component of the competency model of health care network managers is personality traits.

Discussion

Based on this study's results, the competency model of Iranian health care network managers with three dimensions of basic competencies, managerial competencies, and specialized competencies, six indices of personality traits, individual skills, managerial abilities, managerial skills, specialized knowledge, and specialized experience and 90 indices were designed and presented. Among the dimensions of the model, basic competencies and among the indices, personality traits were the most important. According to the results of study by Fanley et al.⁷, the main competencies of managers of health care organizations are as follows: quality evaluation based on outcomes, strengthening professional competencies, planning based on process management, project cost evaluation, informal communication style, and participatory leadership. The results of this study are consistent with the study of Alrich et al.⁸, and Zahedi et al.⁹.

Regarding basic competencies, flexibility, negotiation skills, systematic thinking and analytical thinking were identified as the most important and emphasized points. In the study of Andreja et al.¹⁰, in connection using competency models in leadership assessment in nursing, the index of flexibility in work was emphasized as one of the most important issues. In the study of Messium et al., communication skills, flexibility, lifelong learning, teamwork, and participation were identified as some of

the most important skills needed by new managers in the field of health¹¹. What is important is that the basic competencies that were mentioned in various studies should play a key role in the selection and appointment of managers, and it is necessary to continuously monitor and improve these competencies after employing people in managerial positions.

In terms of managerial competencies, planning and coordination, strategic management, systematic management, and contingency management were of the highest importance. According to the research results, the level of attention to various elements in strategic planning was moderate and high. In the study of Sadeghifar et al. among the community of hospital managers, the indices of creating a vision for the future / studying and predicting the future, evaluating strengths and weaknesses, as well as examining current threats and opportunities as components of strategic management, attracted the most attention¹². In studies conducted by Aung et al.¹³, Karmnad et al.¹⁴, Trayulasa and Rekltesib¹⁵, and Kansal and Jane¹⁶, indices of ability to plan, coordinate, communicate, have strategic thinking were emphasized as managerial competencies. Therefore, this study's results are consistent with the mentioned studies.

In the field of specialized competencies, having specialized education and knowledge in the fields of health system management, health policy, health economics, and monitoring and evaluation of the health system was of the highest importance. Moreover, having work experience and effective experience in the field of health services administration was emphasized by the participants in the study. The ACHE model¹⁷ also places great emphasis on the characteristic of professionalism as one of the main items of competence of health managers. In the study of Ranjbar et al.¹⁸, specialized knowledge and information and professional credibility, and in the research of Abolghasemi et al.¹⁹, technical and managerial knowledge were considered important and priority characteristics of specialized competencies of managers which is consistent with the findings of this study.

Conclusion

At present, in Iran, the election and appointment of health network managers is mainly based on a static model and

mainly based on fixed and evidence-based conditions. The transition from this approach to a competency-based approach is something which can be the source of positive and sometimes transformational changes in the health care delivery system. The competency model designed in this study can be used to select the managers of health and treatment networks in the country by considering localization, educational needs assessment, redefining the performance appraisal system, optimizing the career path management system, etc.

Study limitations

In this study, a survey (questionnaire tool) was used to validate the model; there were limitations associated using this tool in this research. The limited studies and previous records on the competencies of health managers in the country have limited the possibility of comparing the results of this study with previous studies.

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Author's Contribution

Study concept and design: Pourmenati, Masoudi Asl, Hesam, and Vahdat. Statistical analysis and interpretation of data: Pourmenati, Masoudi Asl, and Hesam. Drafting of the manuscript: Pourmenati, Masoudi Asl. Critical revision of the manuscript: Hesam, and Vahdat.

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There is no financial disclosure.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Yeganegi A. Examining the relationship between managers' competencies and management effectiveness: The case of communication company of Qazvin. *Journal of Development & Evolution Management*. 2010;1389(5):57-67.
2. Armstrong M. *Strategic human resource management*: pdf drive.com; 2019.
3. ROftEM W. Improving hospital performance in the Eastern Mediterranean Region Morocco: World Health Organization; 2009 [cited 2015 4 December].
4. Bode I, Maerker M. Management in medicine or medics in management? The changing role of doctors in German hospitals. *International Journal of Public Sector Management*. 2014.
5. Farr-Wharton R, Brunetto Y, Shacklock K. Professionals' supervisor-subordinate relationships, autonomy and commitment in Australia: a leader-member exchange theory perspective. *The International Journal of Human Resource Management*. 2011;22(17):3496-512.
6. Mousavi Z, Soltan Hosseini M. The Codification of Competency Model of Managers in Sport and Youth General Office of Isfahan Province (A Case Study). *New Trends in Sport Management*. 2018;5(19):95-109.
7. Fanelli S, Lanza G, Enna C, Zangrandi A. Managerial competences in public organisations: the healthcare professionals' perspective. *BMC health services research*. 2020;20(1):1-9.
8. Ulrich D, Kryscynski D, Ulrich M, Brockbank W. *Competencies for HR professionals who deliver outcomes*. 2017.
9. Zahedi S, Sheikh E. Strategic competency pattern of state middle managers in economics and industry sector. *Journal of Strategic Management Studies*. 2010;1(1):95-139.
10. Andreja K, Seljak J, Stare J. The use of competency models to assess leadership in nursing. *Iranian journal of public health*. 2013;42(9):988.
11. Messum D, Wilkes L, Jackson D. What employability skills are required of new health managers? *Asia Pacific Journal of Health Management*. 2015;10(1):28-35.
12. Sadeghifar J, Jafari M, Tofighi S, Ravaghi H, Maleki MR. Strategic planning, implementation, and evaluation processes in hospital systems: A survey from Iran. *Global journal of health science*. 2015;7(2):56.
13. Awang M, Mohammed AH, Rahman MSA, Abdullah S, Mod MZC, Sani SIA, et al. Facility management competencies in technical institutions. *Procedia-Social and Behavioral Sciences*. 2012;65:755-60.
14. Carmenado I, TurekRahoveanu A, AfonsoGallegos A. Project Management Competencies for Regional Development in Romania: Analysis from "Working with People" Model [Project Management Competencies for Regional Development in Romania: Analysis from "Working with People" Model] *Procedia Economics and Finance*. Vol. 8, 614-621. DOI: [https://doi.org/10.1016/S2212-5671\(14\).2014.00136-1](https://doi.org/10.1016/S2212-5671(14).2014.00136-1).
15. Trivellas P, Reklitis P. Leadership competencies profiles and managerial effectiveness in Greece. *Procedia Economics and Finance*. 2014;9:380-90.
16. Kansal J, Jain N. Development of competency model and mapping of employees competencies for organizational development: a new approach. 2019.
17. ACHE. *ACHE Healthcare Executive competencies Assessment Tool, A supplement to Healthcare Executives*. 2011:1-30.
18. Ranjbar M, Khaef Elahi A, Danaee Fard H, Fani A. Measuring competency model for managers in the health sector (structural equation modeling approach). *Journal of Mazandaran University of Medical Sciences*. 2014;23(109):104-13.
19. ABOLGHASEMI M, GHAREMANI M, KHORASANI A. *Designing an Efficient Model of Managers Competency of Science and Technology parks of Iranian public University*. 2016.

Intramammary lymph nodes, clinical characteristics and prevalence

Ganglios linfáticos intramamarios, características clínicas y prevalencia

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Abstract

Introduction: Intramammary lymph nodes are mostly benign findings; however the value of these nodes is still controversial. Here we aimed to study the prevalence and clinical significance of intramammary lymph nodes in 1000 patients undergoing routine screening mammography.

Methods: We performed a cross sectional study on 1000 patients attending a radiology clinic for screening mammography. The intramammary lymph node was diagnosed using mammography and confirmed by ultrasound exam.

Results: Of 1000 participants, 69 had intramammary lymph node, with the mean age of 50.3 ± 1.29 . In those with intramammary lymph node, 32 (46.4%) had the first time screening, 3 (4.3%) had discharge, 20 (29%) had pain, 8 (11.6%) had palpable mass, 45 (65.2%) had axillary lymph node, 11 (15.9%) had histological distortion, 16 (23.2%) had micro-calcification and 9 (13%) had mass in mammography. The prevalence of intramammary lymph nodes was highest in the 2nd breast quadrants, both in right and left breast.

Discussion: This is an observation of the prevalence and clinical characteristics on intramammary lymph nodes in an unselected patients attending for routine follow up. Future prospective studies may elucidate more findings of the value of these nodes.

Keywords: Intramammary lymph nodes, breast cancer, mammography.

Resumen

Introducción: Los ganglios linfáticos intramamarios son, en su mayoría, hallazgos benignos; sin embargo, el valor de estos ganglios sigue siendo controvertido. El objetivo de este trabajo es estudiar la prevalencia y la importancia clínica de los ganglios linfáticos intramamarios en 1.000 pacientes sometidas a una mamografía de cribado rutinaria.

Métodos: Realizamos un estudio transversal en 1000 pacientes que acudieron a una clínica de radiología para realizar una mamografía de cribado. El ganglio linfático intramamario se diagnosticó mediante mamografía y se confirmó mediante ecografía.

Resultados: De 1000 participantes, 69 tenían ganglio linfático intramamario, con una edad media de $50,3 \pm 1,29$ años. De las que tenían ganglio linfático intramamario, 32 (46,4%) tenían la primera exploración, 3 (4,3%) tenían secreción, 20 (29%) tenían dolor, 8 (11,6%) tenían masa palpable, 45 (65,2%) tenían ganglio linfático axilar, 11 (15,9%) tenían distorsión histológica, 16 (23,2%) tenían microcalcificación y 9 (13%) tenían masa en la mamografía. La prevalencia de los ganglios linfáticos intramamarios fue mayor en los segundos cuadrantes mamarios, tanto en la mama derecha como en la izquierda.

Discusión: Se trata de una observación de la prevalencia y las características clínicas de los ganglios linfáticos intramamarios en una paciente no seleccionada que acude a un seguimiento rutinario. Futuros estudios prospectivos podrán dilucidar más hallazgos sobre el valor de estos ganglios.

Palabras clave: Ganglios linfáticos intramamarios, cáncer de mama, mamografía.

Introduction

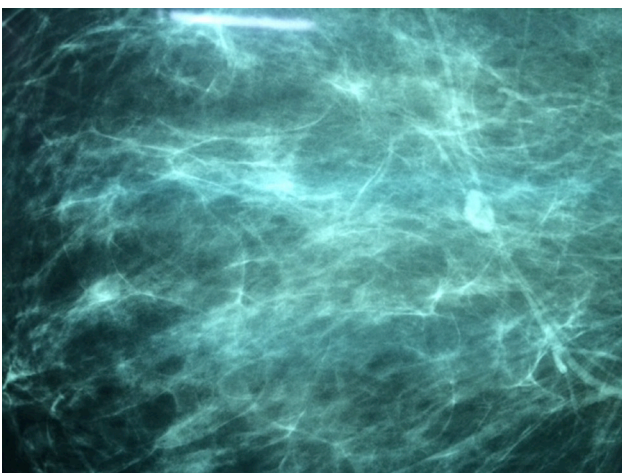
Breast cancer is one of the prevalent cancers among women. It has a high mortality rate especially in developing countries¹. Hence early diagnosis and management is of great clinical importance. Intramammary lymph nodes are mostly incidentally discovered during routine screening². While studies have shown the significance and value of axillary lymph nodes in the staging and outcome of breast cancer³⁻⁵, the value of intramammary lymph nodes is not known yet^{6,7}. Metastatic disease to the intramammary lymph nodes may be the first clinical and/or mammographic sign of breast cancer and may significantly affect prognosis^{8,9}. While some studies have shown the coincidence of intramammary lymph nodes with metastatic breast cancer^{10,11}, there are reports of the intramammary lymph node associated with, lymphoma, ovarian cancer, HIV infection and toxoplasmosis and non malignant lymphadenopathy¹²⁻¹⁷.

Here we aimed to study the prevalence and clinical significance of intramammary lymph nodes in 1000 patients undergoing routine mammography.

Materials and methods

We performed a cross-sectional study on 1000 healthy women age between 32 to 88 coming for routine screening. Patient's recruitment was from March 2017 to May 2019, in the radiology clinic of the imam hospital affiliated with Tehran University of medical science. Exclusion criteria were previous history of mastectomy or breast reconstruction surgery or any other breast surgery, breast cancer, or any other malignancy. Demographic and anthropometric data including age, history of screening, history of infection, breast feeding were recorded. The local ethics review committee of Tehran University of Medical Science approved the study

Figure 1: Intramammary Lymph node, MLO view.



protocol. Written informed consent was obtained. The mammographs were studied by one radiologist and one radiology registrar and the intramammary lymph nodes were reported by them. Then participants had been recalled and the intramammary lymph nodes nature were confirmed by ultrasound exam.

Mammography

Bilateral mammography was performed by digital mammography (Hologic, Lorad selenia, kv=24-34, mas=80) in mediolateral and craniocaudal views for all cases. Diagnostic criteria for intramammary lymph node are a well-defined iso to hyperdense mass with minimum diameter less than 1 cm and central radiolucent cleft (**Figure 1**). All intramammary lymph nodes were confirmed by ultrasound. (GE Logic 500, linear probe 13 Mhz) (**Figure 2**).

Data analysis

The statistical package SPSS 17 for windows (Chicago, Illinois, USA), was used for analysis. Kolmogorov-Smirnov test was employed to test the normality of the variables in each group. Variables distributed normally are presented as mean \pm standard error of mean (SEM).

Results

Of 1000 participants, 69 had intramammary lymph node, with the mean age of 50.3 ± 1.29 . The clinical

Figure 2: Intramammary lymph node, Ultrasound scan.



Table I: Presenting the characteristics of the intramammary lymph nodes in patients with positive intramammary lymph node.

	N. lymph nodes	Frequency(percent)
Number lymph node right	0	15(21.7%)
	1	45(65.2%)
	2	6(8.7%)
	3	2(2.9%)
	4	1(1.4%)
Number lymph node left	0	37(53.6%)
	1	18(26.1%)
	2	12(17.4%)
	3	1(1.4%)
	4	1(1.4%)
Central lymph node	yes	2(2.9%)
Right Breast (Number of nodes in each quadrant)	Left upper q (Q1)	1 (1.4%)
	Left lower q (Q2)	49 (71.0%)
	Right lower q (Q3)	1 (1.4%)
	Right upper (Q4)	0 (0%)
Left Breast (Number of nodes in each quadrant)	Right upper q (Q1)	0 (0%)
	Right lower q (Q2)	37 (53.6%)
	Left lower q (Q3)	2 (2.9%)
	Left upper q (Q4)	0(0%)

characteristics of patients with intramammary lymph nodes are demonstrated in the **table I**. In those with intramammary lymph node, 32 (46.4%) had the first time screening, 3 (4.3%) had discharge, 20 (29%) had pain, 8 (11.6%) had palpable mass, 45 (65.2%) had axillary lymph node, 11 (15.9%) had histological distortion, 16 (23.2%) had micro-calcification and 9 (13%) had mass in mammography. The prevalence of intramammary lymph nodes were highest in the 2nd breast quadrants, both in right and left breast.

Discussion

Intramammary lymph nodes are mostly benign findings, however they are important as they could be the site of primary tumor or metastasis. Here we showed that the prevalence and clinical characteristics of the intramammary lymph nodes in an unselected patients attending a radiology clinic for routine follow up, was 6.9%. We also showed that the second quadrant is the most common site of these nodes. Importantly none of these patients had retraction or other clinical signs of malignancy. On the other hand all of the 69 cases had typical benign reactive axillary lymph nodes on the same site.

This is the first report of the prevalence of intramammary lymph nodes in Iran. The prevalence of these nodes has been reported to be between 1-20 percent^{5,18}. However the value of these nodes is still controversial¹⁹. While some studies suggest a poor survival in those with intramammary nodes, others suggest the contrary²⁰.

We showed that the nearly 50% of those with intramammary lymph node, has concomitant axillary nodes. The appearance of intramammary and axillary lymph nodes was exactly the same in ultrasound exam. In consistent with our findings, in a meta analysis of 18 papers on these nodes, metastatic intramammary nodes were strongly correlated with axillary lymph nodes involvement²¹. Others also suggested axillary node dissection in the presence of intramammary lymph nodes^{12,22-23}. This shows the value of early biopsy and diagnosis in those with concomitant involvement. The second breast quadrant had the most number of lymph nodes. We could not find any study defining the value of breast quadrant in the predictive value of intramammary lymph nodes.

In conclusion, this is an observation of the prevalence and clinical characteristics on intramammary lymph nodes in an unselected patients attending for routine follow up. Future prospective studies may elucidate more findings of the value of these nodes. The principal limitation of the present study is its cross sectional nature which preclude the determination of the direction of causality. We also did not follow the patients to discover the nature of the nodes. However we took advantage of a relatively large sample size and close similarity between groups in most of the potentially confounding variables.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Harirchi I, Azary S, Montazeri A, Mousavi SM, Sedighi Z, Keshtrand G, et al. Literacy and breast cancer prevention: a population-based study from Iran. *Asian Pac J Cancer Prev* 2012; 13: 3927-30.
2. Schmidt WA, Boudousquie AC, Vetto JT, Pommier RF, Alexander P, Thurmond A, et al. Lymph nodes in the human female breast: a review of their detection and significance. *Hum Pathol* 2001; 32: 178-87.
3. Stranzl H, Peintinger F, Ofner P, Prettenhofer U, Mayer R, Hackl A. Regional nodal recurrence in the management of breast cancer patients with one to three positive axillary lymph nodes. Outcome of patients following tangential irradiation without a separate nodal field. *Strahlenther Onkol* 2004; 180: 623-8.
4. Shen J, Hunt KK, Mirza NQ, Krishnamurthy S, Singletary SE, Kuerer HM, et al. Intramammary lymph node metastases are an independent predictor of poor outcome in patients with breast carcinoma. *Cancer* 2004; 101: 1330-7.
5. Khalili SM, Janati Ataei P, Hazini A, Nasiri M, Kariman N, Ahmadi Doulabi M. Comparing the quality of life of women suffering from breast cancer receiving palliative care and ordinary care. *Immunopathol Persa* 2020;6(2):e22.
6. Jadusingsh IH. Intramammary lymph nodes. *J Clin Pathol* 1992; 45: 1023-6.
7. Egan RL, McSweeney MB. Intramammary lymph nodes. *Cancer* 1983; 51: 1838-42.
8. Lindfors KK, Kopans DB, Googe PB, McCarthy KA, Koerner FC, Meyer JE. Breast cancer metastasis to intramammary lymph nodes. *AJR Am J Roentgenol* 1986; 146: 133-6.
9. Sadr Z, Jamali Moghaddam M, Sabet Rouhani H, Sani'ee N, Biglari Abhari M. Study of family medicine role in breast cancer prevention: A systematic review. *J Prev Epidemiol*. 2021;6(2):e32. doi: 10.34172/jpe.2021.32.
10. Rivera AL, Diwan A, Muylaert S, Lucci A. Intramammary lymph node presenting as the primary breast mass in infiltrating lobular carcinoma. *Curr Surg* 2006; 63: 107-9.
11. Solorzano S, Seidler M, Mesurole B. Metastatic intramammary lymph node as a synchronous benign-appearing breast nodule detected in a patient with breast cancer. *AJR Am J Roentgenol* 2009; 192: W349.
12. Ohta K, Endo N, Kaizaki Y. Axillary and intramammary lymphadenopathy caused by Kikuchi-Fujimoto disease mimicking malignant lymphoma. *Breast Cancer* 2009.
13. Siriwardana HP, Teare L, Kamel D, Inwang ER. Toxoplasmosis presenting as a swelling in the axillary tail of the breast and a palpable axillary lymph node mimicking malignancy: a case report. *J Med Case Rep* 2011; 5: 348.
14. Susini T, Olivieri S, Molino C, Castiglione F, Tavella K, Viligiardi R. Ovarian cancer initially presenting as intramammary metastases and mimicking a primary breast carcinoma: a case report and literature review. *J Womens Health (Larchmt)* 2010; 19: 169-74.
15. Konstantinopoulos PA, Dezube BJ, March D, Pantanowitz L. HIV-associated intramammary lymphadenopathy. *Breast J* 2007; 13: 192-5.
16. Solomon SB, Gatewood OM, Brem RF. HIV Infection: Analysis of Mammographic Findings. *Breast J* 1999; 5: 112-5.
17. Rahimi H, Rezaei Borojerdi Z, Ataei Azimi S, Rashidian E, Jafarian A. Prognostic significance evaluation of B-cell lymphoma 2 (BCL2) and Ki-67 expression in diffuse large B-cell lymphoma patients. *Immunopathol Persa*. 2020;6(1):e07.
18. Nassar A, Cohen C, Cotsonis G, Carlson G. Significance of intramammary lymph nodes in the staging of breast cancer: correlation with tumor characteristics and outcome. *Breast J* 2008; 14: 147-52.
19. de Ferrater MB, Vidal-Sicart S, Zanon G, Martinez-Roman S, Sanjuan A, Fernandez PL, et al. Importance of intramammary node resection in breast cancer staging. *Clin Nucl Med* 2007; 32: 572-3.
20. Hogan BV, Peter MB, Shenoy H, Horgan K, Shaaban A. Intramammary lymph node metastasis predicts poorer survival in breast cancer patients. *Surg Oncol* 2010; 19: 11-6.
21. Abdullgaffar B, Gopal P, Abdulrahim M, Ghazi E, Mohamed E. The Significance of Intramammary Lymph Nodes in Breast Cancer: A Systematic Review and Meta-Analysis. *Int J Surg Pathol* 2012.
22. R, Degnim AC, Boughey JC, Nassar A, Jakub JW. A positive intramammary lymph node does not mandate a complete axillary node dissection. *Am J Surg* 2012; 203: 151-5.
23. Guth AA, Mercado C, Roses DF, Hiotis K, Skinner K, Diflo T, et al. Intramammary lymph nodes and breast cancer: a marker for disease severity, or just another lymph node? *Am J Surg* 2006; 192: 502-5.
24. Lee SK, Kim S, Choi MY, Kim J, Lee J, Jung SP, et al. The Clinical Meaning of Intramammary Lymph Nodes. *Oncology* 2012; 84: 1-5.

Preparation and implementation of standard therapeutic guidelines for poisoning cases in a tertiary care hospital, Mysuru, India

Preparación e implementación de pautas terapéuticas estándar para casos de intoxicación en un hospital de atención terciaria, Mysuru, India

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Abstract

Objective: The goal of the research is to prepare and implement the standard therapeutic guidelines for poisoning cases in a Tertiary Care Hospital, Mysuru, India. It also aims to identify common agents associated with the poisoning cases and to study the result outcomes and identify the types of poisons, route of administration, and outcomes of poisoning cases.

Methodology: A retro-prospective observational study was conducted in tertiary care hospital over 6 months. All necessary data were collected in a well-designed data collection form. Standard therapeutic guidelines were prepared with the reference of modern medical toxicology textbooks, patient poisoning treatment chart research articles, and other national guidelines.

Result: A total of 50 patients' poisoning case sheets were studied. The majority of patients with poisoning cases were found in the age group of 31-40 (32%), followed by the age group of 41-50(24%), age group of 0-15 (14%), age group of 21-30 (12%), age group of 51-60 (12%), and age group of 16-20(6%). Among them, a significant number of poisoning cases show the duration of hospital stay. The majority of patients in the study had a shorter stay in the hospital. We found 32(64%) of patients with poisoning had a shorter stay of 3-5 days in the hospital, followed by 16(32%) of patient's hospital stay was 6-8 days, 1(2%) patients for 0-2 days and 1(2%) patients for 9-11 days. The majority of patients with poisoning were married 33(66%) than unmarried 17(34%). Among patients with poisoning 9(18%) had health insurance and 41(82%) did not have health insurance. The pattern of poisoning in the study, the most common being OP 14(28%), paracetamol 6(12%), carbamate 5(10%), pyrethroid 4(8%), aluminium phosphide 4(8%), acetone 3(6%), eucalyptus 2(4%), snakebite 2(4%), benzodiazepines 1(2%), Ethanol 1(2%), HCL 1(2%), kerosene 1(2%), metformin 1(2%), metoprolol 1(2%), naphthalene 1(2%), phenytoin 1(2%), sulfuric acid 1(2%), organochlorine 1(2%). Among all the poisoning cases 50% of substances associated with poisoning were pesticides, 12% chemical poisons, 10% hydrocarbons, 10% analgesic antipyretics, 6% neurotoxic poisons, 4% organic poisons, 4% other drugs. 93.9% of poisoning were due to oral exposure, 2% eye exposure, 2% dermal exposure and inhalation exposure 2%. We also found that 84% were deliberate poisoning and 16% were accidental poisoning.

Conclusion: Prepared the Standard Therapeutic Guidelines for 60 substances/compounds associated with the poisoning. Standard therapeutic guidelines offer toxicological information services to health professionals and patients in identifying poisons, symptoms, antidotes, and management of poisoning cases. A total of 50 patient case sheets of poisoning cases were followed at Tertiary Care Hospital. OP compounds were the most common among poisons. Most of the middle age people were common victims of poisoning. Educational awareness, poison information, and standard therapeutic guidelines for poisoning cases will help to reduce the growth of public health problems.

Keywords: Standard therapeutic guidelines, Drug overdose, toxicology, Poisoning.

Resumen

Objetivo: El objetivo de la investigación es preparar y aplicar las directrices terapéuticas estándar para los casos de envenenamiento en un hospital de atención terciaria, Mysuru, India. También tiene como objetivo identificar los agentes comunes asociados a los casos de envenenamiento y estudiar los resultados e identificar los tipos de venenos, la vía de administración y los resultados de los casos de envenenamiento.

Metodología: Se realizó un estudio observacional retrospectivo en un hospital de atención terciaria durante 6 meses. Se recogieron todos los datos necesarios en un formulario de recogida de datos bien diseñado. Se prepararon directrices terapéuticas estándar con la referencia de libros de texto de toxicología médica modernos, artículos de investigación de la tabla de tratamiento de intoxicaciones de pacientes y otras directrices nacionales.

Resultado: Se estudiaron las fichas de casos de intoxicación de un total de 50 pacientes. La mayoría de los pacientes con casos de envenenamiento se encontraban en el grupo de edad de 31 a 40 años (32%), seguidos por el grupo de edad de 41 a 50 años (24%), el grupo de edad de 0 a 15 años (14%), el grupo de edad de 21 a 30 años (12%), el grupo de edad de 51 a 60 años (12%) y el grupo de edad de 16 a 20 años (6%). Entre ellos, un número significativo de casos de intoxicación muestra la duración de la estancia hospitalaria. La mayoría de los pacientes del estudio tuvieron una estancia hospitalaria más corta. Encontramos que 32(64%) de los pacientes con intoxicación tuvieron una estancia más corta de 3-5 días en el hospital, seguido por 16(32%) de la estancia hospitalaria del paciente fue de 6-8 días, 1(2%) pacientes de 0-2 días y 1(2%) pacientes de 9-11 días. La mayoría de los pacientes con intoxicación estaban casados 33(66%) que los solteros 17(34%). Entre los pacientes con intoxicación, 9 (18%) tenían seguro médico y 41 (82%) no tenían seguro médico. El patrón de envenenamiento en el estudio, el más común fue OP 14(28%), paracetamol 6(12%), carbamato 5(10%), piretroide 4(8%), fosforo de aluminio 4(8%), acetona 3(6%), eucalipto 2(4%), mordedura de serpiente 2(4%), benzodiazepinas 1(2%), etanol 1(2%), HCL 1(2%), queroseno 1(2%), metformina 1(2%), metoprolol 1(2%), naftalina 1(2%), fenitoína 1(2%), ácido sulfúrico 1(2%), organoclorados 1(2%). Entre todos los casos de intoxicación, el 50% de las sustancias asociadas a la intoxicación eran pesticidas, el 12% venenos químicos, el 10% hidrocarburos, el 10% antipiréticos analgésicos, el 6% venenos neurotóxicos, el 4% venenos orgánicos, el 4% otros fármacos. 93 El 9% de las intoxicaciones se debieron a la exposición oral, el 2% a la exposición ocular, el 2% a la exposición dérmica y el 2% a la exposición por inhalación. También se encontró que el 84% fueron intoxicaciones deliberadas y el 16% fueron intoxicaciones accidentales.

Conclusión: Se elaboraron las Guías Terapéuticas Estándar para 60 sustancias/compuestos asociados a la intoxicación. Las guías terapéuticas estándar ofrecen servicios de información toxicológica a los profesionales de la salud y a los pacientes en la identificación de los venenos, los síntomas, los antidotos y el manejo de los casos de envenenamiento. Se hizo un seguimiento de un total de 50 hojas de casos de intoxicación en el Hospital de Atención Terciaria. Los compuestos OP fueron los más comunes entre los venenos. La mayoría de las personas de mediana edad fueron víctimas habituales de envenenamiento. La concienciación educativa, la información sobre venenos y las directrices terapéuticas estándar para los casos de envenenamiento ayudarán a reducir el crecimiento de los problemas de salud pública.

Palabras clave: Directrices terapéuticas estándar, sobredosis de drogas, toxicología, envenenamiento.

Introduction

Deliberate self-harm and self-injurious behaviors are major public health problems globally¹, particularly amongst young people². According to the World Health Organization (WHO) above 800,000 individuals end it all and 10-20 million individuals endeavor purposeful self-harm worldwide consistently³. It is estimated the Asian mainland contributes approximately 60% of worldwide suicides⁴.

Poisoning is a health concern in both created and developing countries. Yearly, numerous people are inebriated either purposefully or accidentally, a condition that brings about a significant expansion in the morbidity and mortality rate^{5,6}.

The medical management of poisoning crises is troublesome and, to date, there are no obvious proof-based rules for the best management of the greater part of the poisoning, with the accessibility of countless synthetic substances and medications, intense poisoning is a typical medical crisis in any country.⁷ The specific incidence of this issue in our nation stays questionable however it is estimated that around 10-15 million cases of poisoning are accounted for each year, of which, above 50,000 pass on.⁸ Cases of poisoning might be treated in

many spots, for example at the location of the accident, during transport, in an emergency clinic. The kind of care that can be given will rely upon whoever connects with the patient and in what conditions. Certain individuals from the local area, like firemen, policemen, teachers, may as often as possible be quick to be confronted with poisoning cases.^{7,8}

In rural areas, nurses and primary health care workers, and even agronomists and veterinaries, may have to deal with poisoned persons. They all need at least some basic training in first aid as well as decontamination and measures for their protection. General practitioners or family doctors are often the first medically qualified persons consulted. They must be able to give appropriate initial.⁸

Treatment and may need to contact their local poison information center. Most patients with serious poisoning, if they survive, will sooner or later reach a hospital, ideally one with a wide range of medical facilities, including intensive care. In some places, specialized treatment services have been established offering the best possible conditions for the management of poisoning. These services also have the advantage of ready access to a wide range of related medical facilities.

Most cases of poisoning, however, will be treated through a country's normal health service facilities, usually at a general hospital, far from a poison information center, and without access to a specialized clinical toxicology unit.⁹

In an emergency, the relevant medical personnel at general hospitals and other health service facilities where poisoning cases are treated must have rapid access to toxicological information and experience. Here, the poison information center plays a key role through its telephone advice service. Ideally, centers should circulate information to general hospitals and other health service facilities regularly.^{10,11}

This information should be adapted to suit local needs and should include general advice on the diagnosis and management of poisoning cases commonly expected to be treated at the particular hospital or facility, as well as information on new developments in patient management and on new types of poisoning.¹²

Death due to poisoning has been known since time immemorial. Poisoning is a major problem all over the world, although its type and the associated morbidity and mortality vary from country to country. According to the legal system of our nation, all poisoning passing cases are recorded as unnatural demise and a medico-legal autopsy is routine. Toxicology is characterized by the investigation of the impacts of substance specialists on biological materials. Current toxicology is a multidisciplinary science and legal toxicology is needed to decide any exogenous substance specialist present in biological specimens made accessible regarding medico-legal investigations.¹³

Organophosphorus poisoning happens ordinarily in southern India, where ranchers structure a significant extent of the populace who regularly use organophosphorus compounds like parathion as insecticides. Accordingly, because of the easy openness of these compounds, an enormous number of self-destructive cases are experienced in this region.¹⁴ Furthermore, snakebite is a typical intense medical crisis looked at by rustic populaces in tropical and subtropical countries with heavy rainfall and humid climate.¹⁵ Some 35,000-50,000 individuals pass on every year from snakebite, which is a typical reason for morbidity and mortality in India.¹⁶

Organophosphorus (OP) compounds have been generally utilized for years and years in horticulture for crop assurance and nuisance control, thousands of these compounds have been screened and more than 100 of them have been advertised for these purposes¹⁷. Operations comprise a heterogeneous class of synthetic substances explicitly intended for the control of nuisances, weeds, or plant diseases. Their application is as yet the best and acknowledged means for the assurance of plants from bothers, and has contributed significantly to upgraded agricultural productivity and crop yields¹⁸.

There is a need, especially for the people that have high frequencies for certain methods of drug use, to understand the factors involved in poisoning and how to effectively design prevention programs to reduce their occurrence and adverse outcomes. Also for effective management of an acutely poisoned victim and to familiarize the physicians about various steps required in the effective management of patients with acute poisoning.

Materials and methods

This is an observational, retrospective study. This study was conducted in the Departments of Clinical Pharmacy, over 6 months from September 2019 to March 2020. The approval for this study was obtained from The Institutional Ethics Committee (IEC) of Farooqia College of Pharmacy, Mysore at Clinical Pharmacy Department for conducting our project work based on our presentation given for the same to the committee members. Modern Medical Toxicology textbook, Patient case sheets, Research articles, and National guidelines.

Study Procedure

Standard therapeutic guidelines were prepared with the reference of modern medical toxicology textbooks, patient poisoning treatment chart research articles, and other national guidelines.

- The data collection form was designed to collect and document the data.
- All the needful and applicable information was collected in a distinctive form.
- Data abstracted from patients' medical records including age, gender, date and time of the admission and discharge, marital status, insurance coverage, chief complaint, and vitals.
- This investigation was used to assess the circumstances of the poisoning including accidental or intentional. The rate of hospitalization and the outcome of poisoning events were examined. This study has evaluated the length of stay and the casualty rates that have occurred and the outcome of the case were examined.
- Finally, all the data were collected to generate graphical representation, tables using MS Excel.

Result and discussion

The medical management of poisoning emergencies needs evidence-based standard therapeutic guidelines for the best management of most of the poisoning. Prepared the Standard therapeutic guidelines for 60 substances/chemicals associated with the poisoning. Standard therapeutic guidelines offer toxicological information services to health professionals and patients in identifying poisons, symptoms, antidotes, and management of poisoning cases.

A total of 50 patients' case sheets of poisoning cases were studied. All necessary data were collected in a well-designed data collection form. We mainly focused on the poisoning cases. As it is the need of the hour issue. The majority of patients with poisoning cases were found in the age group of 31-40 years (32%), followed by the age group of 41-50 years (24%), age group of 0-15 years (14%), age group of 21-30 years (12%), age group of 51-60 years (12%) and age group of 16-20 years (6%).

Among them, a significant number of poisoning cases show the duration of hospital stay. The majority of patients in the study had a shorter stay in the hospital. We found 32 (64%) of patients with poisoning had a shorter stay of 3-5 days in the hospital, followed by 16 (32%) of patient's hospital stay was 6-8 days, 1 (2%) patients for 0-2 days and 1 (2%) patients for 9-11 days. The majority of patients with poisoning were married 33 (66%) than unmarried 17 (34%). Among patients with poisoning 9 (18%) had health insurance and 41 (82%) did not have health insurance. **Table I.**

Table I: demography of study pateints.

No of pateint	% of pateint	
GENDER		
MALE	30	6000%
FEMALE	20	40
Age details		
0-15	7	14
16-20	3	6
21-30	6	12
31-40	16	32
41-50	12	24
51-60	6	12
Duration of hospital stay		
0-2 day	1	2
3-5 day	32	64
6-8 day	16	32
9-11 day	1	2
Marital status		
Married	33	66
Unmarried	17	34

The pattern of poisoning in this study, the most common being OP in 14(28%) patients, Paracetamol 6(12%), Carbamate 5(10%), Pyrethroid4(8%), Aluminium phosphide 4(8%), Acetone 3(6%), Eucalyptus 2(4%), Snake bite 2(4%), Benzodiazepines1(2%), Ethanol 1(2%), Hcl 1(2%), Kerosene 1(2%), Metformin 1(2%), Metoprolol 1(2%), Naphthalene 1(2%), Phenytoin 1(2%), Sulfuric acid 1(2%), Organochlorine 1(2%). The results are presented in **table II.**

Among all the poisoning cases 50% of substances were associated with poisoning of pesticides, 10% of substances were hydrocarbons, 12% were chemical poisons, 10% were analgesic-antipyretics, 6% were neurotoxic poisons, 4% were organic poisons, 4% were corrosive poisons, 4% were other drugs. The results are presented in **table III.**

Table II: Pattern of poisoning.

Name of a substance/poison	Number of people	% of patient
Organophosphate	14	28
Paracetamol	6	12
Carbamate	5	10
Pyrethroid	4	8
Aluminium phosphide	4	8
Acetone	3	6
Eucalyptus	2	4
Snake bite	2	4
HCL	1	2
Sulfuric acid	1	2
Metoprolol	1	2
Naphthalene	1	2
Phenytoin	1	2
Metformin	1	2
Benzodiazepine	1	2
Ethanol	1	2
Kerosene	1	2
Organochlorine	1	2

Table III: Types of poison.

Type of poisons	% substance
Pesticides	50%
Hydrocarbons	10%
Analgesic-Antipyretics	10%
Chemical Poisons	12%
Neurotoxic Poisons	6%
Organic Poisons	4%
Corrosive Poisons	4%
Other Drugs	4%

Among all the poisoning 46 (93.9%) were due to oral exposure, 1 (2%) were due to eye exposure, 1 (2%) were dermal exposure, 1 (2%) were inhalation exposure. The results are presented in **table IV** among all the poisoning, 42(84%) were deliberate poisoning, 8(16%) were accidental poisoning. Among all the patients, 46(92%) patients survived, 4(8%) patients expired.

Table IV: Pattern for the route of administration.

Route of administration	% substance
Oral exposure	93.90%
Dermal exposure	2%
Eye exposure	2%
Inhalation exposure	2%

The pattern of poisoning in the study, the most common being OP 14(28%), Paracetamol 6(12%), Carbamate 5(10%), Pyrethroid 4(8%), Aluminium phosphide 4(8%), Acetone 3(6%), Eucalyptus 2(4%), Snakebite 2(4%), Benzodiazepines 1(2%), Ethanol 1(2%), HCL 1(2%), Kerosene 1(2%), Metformin 1(2%), Metoprolol 1(2%), Naphthalene 1(2%), Phenytoin 1(2%), Sulfuric acid 1(2%), Organochlorine 1(2%). Among all the poisoning cases 50% of substances associated with poisoning were pesticides, 12% chemical poisons, 10% hydrocarbons, 10% analgesic antipyretics, 6% neurotoxic poisons, 4% organic poisons, and 4% other drugs. 46(93.9%) of poisoning were due to oral exposure, 1(2%) eye exposure, 1(2%) dermal exposure, and 1(2%) inhalation exposure. We also found that 84% were deliberate poisoning and 16% were accidental poisoning.

Conclusion

Poisoning and drug overdose (DO) are important health problems in developing countries. These emergencies are associated with high mortality and morbidity. The medical management of poisoning emergencies needs evidence-based standard therapeutic guidelines for the best management of most of the poisoning. The relevant medical personnel at general hospitals and other health service facilities where poisoning cases are treated must have rapid access to toxicological information.

The medical management of poisoning emergencies needs evidence-based standard therapeutic guidelines for the best management of most of the poisoning. Prepared the Standard Therapeutic Guidelines for 60 substance/compounds associated with the poisoning concerning modern medical toxicology textbooks, patient poisoning treatment chart research articles, and other national guidelines. Standard therapeutic guidelines offer toxicological information services to health professionals

and patients in identifying poisons, symptoms, antidotes, and management of poisoning cases. OP compounds were the most common among poisons. Most of the middle age people were common victims of poisoning. Among them, a significant number of poisoning cases show the duration of hospital stay. The majority of patients in the study had a shorter stay in the hospital. We found 32 (64%) of patients with poisoning had a shorter stay of 3-5 days in the hospital, followed by 16 (32%) of patient's hospital stay was 6-8 days, 1 (2%) patients for 0-2 days and 1 (2%) patients for 9-11 days. Among all the poisoning cases 50% of substances associated with poisoning were pesticides, 12% chemical poisons, 10% hydrocarbons, 10% analgesic antipyretics, 6% neurotoxic poisons, 4% organic poisons, and 4% other drugs. The overall case-fatality report in our study was 8%, there were 4 mortalities among which the poisons used were OP (2) and carbamate (2).

Interests conflict

The researchers declare that they have no conflict of interest.

References

- Hawton K, James A. Suicide and deliberate self-harm in young people. *BMJ* 2005; 330(7496):891-4.
- Cooper J, Kapur N, Webb R, Lawlor M, Guthrie E, Mackway-Jones K. Suicide after deliberate self-harm: A four-year cohort study. *American Journal of Psychiatry* 2005;162:297-303.
- Paiman A, Ali TS, Asad N, Syed IA. Psychosocial factors of deliberate self-harm in Afghanistan: a hospital based, matched case-control study. *Eastern Mediterranean health journal* 2019; 25(11):798.
- Chen YY, Chien-Chang Wu K, Yousuf S, Yip PS. Suicide in Asia: opportunities and challenges. *Epidemiologic reviews* 2012; 34(1):129-44.
- Lall SB, Al Wahaibi SS, Al Riyami MM, Al Kharusi K. Profile of acute poisoning cases presenting to health centres and hospitals in Oman. *EMHJ-Eastern Mediterranean Health Journal* 2003; 9 (5-6): 944-54
- Lamminpää A. Hospitalizations Due To Poisonings In Finland-1978-1984. *Journal of Toxicology: Clinical Toxicology* 1991; 29(1):111-29.
- Lam RPK, Lau EHY, Yip WL, Leung JKS, Tsui, MSH. Traditional Chinese medicine poisoning in the emergency departments in Hong Kong: Trend, clinical presentation and predictors for poor outcome. *World Journal of Emergency Medicine* 2021; 12(2):143.
- Kadu SS, Burungale SU, Swami AA. Pattern of Acute Organophosphorus Poisoning at a Tertiary Care Hospital of Western Maharashtra. *International Journal of Clinical and Biomedical Research* 2021; 7(2): 23-7.
- Chan YC, Chan CK, Ng CH, Ng SH, Lau KK, Tse ML. Hong Kong Poison Information Centre: Annual report 2016. *Hong Kong Journal of Emergency Medicine* 2017; 24(5):244-54.
- World Health Organization. Improving the availability of poisons centre services in Eastern Africa: highlights from a feasibility study for a subregional poison centre in the Eastern Africa Subregion, including a toolkit on setting up a poisons information service. *World Health Organization* 2015.
- World Health Organization. Guidelines for establishing a poison centre 2020.
- Rotella JA, Greene SL, Koutsogiannis Z, Gaudins A, Hung Leang Y, Kuan K, Wong A. Treatment for beta-blocker poisoning: a systematic review. *Clinical Toxicology* 2020; 58(10), 943-83.
- Islam MN, Islam N. Retrospective study of 273 deaths due to poisoning at Sir Salimullah Medical College from 1988 to 1997. *Legal Medicine* 2003; 5:S129-S131.
- Kanchan T, Menezes RG. Suicidal poisoning in Southern India: gender differences. *Journal of Forensic and Legal Medicine* 2008;15(1):7-14.
- Banejee RN. Poisonous snakes and their venoms, symptomatology and treatment. *Progress in Clinical Medicine, Second Series. India: Heinemann* 2003: 136-79.
- Warrell DA. Guidelines for the clinical management of snake bites in the Southeast Asian region. *Southeast Asian Journal of Tropical Medicine and Public Health* 1999
- Mansour MK, El-Kashoury AA, Rashed MA, Koretem KM. Oxidative and biochemical alterations induced by profenofos insecticide in rats. *Nat Sci* 2009; 7(2):1-15.
- Bolognesi C. Genotoxicity of pesticides: a review of human biomonitoring studies. *Mutation Research/Reviews in Mutation Research* 2003; 543(3), 251-272.

ORIGINAL

Anthropometric profile in 1.350 well being and beauty professionals

Perfil antropométrico en 1.350 profesionales del bienestar y la belleza

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Abstract

Introduction: Obesity and overweight are two important public health problems that affect more and more people, and not only in the developed world. The aim of this work is to assess the anthropometric profile of workers who deal with people's well-being and beauty.

Material and methods: A descriptive, cross-sectional study of 1,350 wellness and beauty workers in which the anthropometric profile is assessed using scales such as body mass index, waist to height ratio, conicity index, body roundness index and body shape index. Scales estimating body fat percentage such as CUN BAE, ECORE-BF, Deuremberg formula or relative fat mass.

Results: The percentage of obesity in women ranges between 13.1% if we apply the criteria of the body mass index and 33.7% if we apply the body fat percentage with CUN BAE. In men these percentages are 8.1% and 29.7% respectively.

Conclusions: The prevalence of high values of anthropometric parameters in wellness and beauty workers is lower than those found in other workers who also act on people's wellbeing, such as health workers.

Keywords: Obesity, overweight, body fat.

Resumen

Introducción: La obesidad y el sobrepeso son dos importantes problemas de salud pública que cada vez afectan a más personas y no sólo del mundo desarrollado. El objetivo de este trabajo es valorar el perfil antropométrico de trabajadores que se ocupan del bienestar y de la belleza de las personas.

Material y métodos: Estudio descriptivo y transversal en 1.350 trabajadores del bienestar y de la belleza en los que se valora el perfil antropométrico mediante escalas como el índice de masa corporal, el índice cintura/altura, el índice de conicidad, índice de redondez corporal o el índice forma del cuerpo. También se incluyen escalas que estiman el porcentaje de grasa corporal como CUN BAE, ECORE-BF, Formula de Deuremberg o la masa grasa relativa.

Resultados: El porcentaje de obesidad oscila en las mujeres entre el 13,1% si aplicamos los criterios del índice de masa corporal y el 33,7% si lo que aplicamos es el porcentaje de grasa corporal con CUN BAE. En los varones estos porcentajes son del 8,1% y 29,7% respectivamente.

Conclusiones: La prevalencia de valores elevados de los parámetros antropométricos en los trabajadores del bienestar y la belleza son inferiores a los encontrados en otros trabajadores que también actúan sobre el bienestar de las personas como son los sanitarios.

Palabras clave: Obesidad, sobrepeso, grasa corporal.

Introduction

Overweight and obesity are two major health problems that have cohabited with us for many years and considering their current prevalence it seems that the efforts that have been made to control them have not been effective.

The World Health Organization (WHO) in 2016 issued a report on the global prevalence of overweight and obesity¹, the results of which were very worrying:

The global prevalence of obesity in the last 40 years has tripled and more than 1250 million adults are overweight and 650 million obese. In adolescents, 18% are overweight. According to the WHO, obesity causes more deaths than malnutrition and is no longer a problem exclusive to developed countries.

Unfortunately, the increase in the prevalence of overweight or obesity worldwide seems irreversible. By 2030 a large increase is expected almost everywhere in the world with figures as high as 65.8% in Oceania, 45.5% in Asia, 44.5% in North America, 42.1% in Africa and 35.2% in South America².

Obesity can lead to major health problems including lung disease, metabolic syndrome, cardiovascular disease, diabetes mellitus, cancer, liver disease, gynaecological disorders, as well as venous and periodontal disease³⁻⁶ and even psychosocial problems⁷. Other conditions such as gout, high blood pressure (HBP), skin problems and osteoarthritis are also more common in people with excess fat. People with obesity also have a higher surgical risk.

The aim of this study is to find out the anthropometric profile of people working in the health and beauty care environment.

Methods

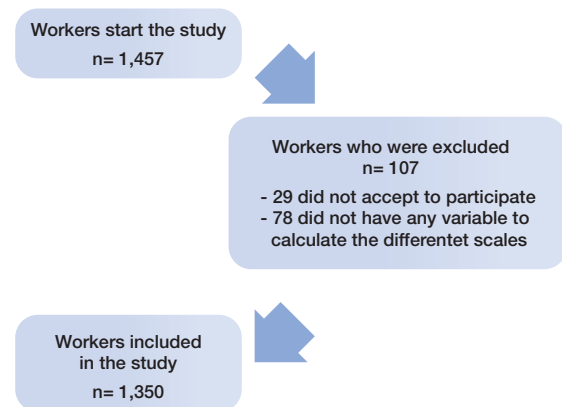
A retrospective and cross-sectional study was carried out in 1,457 workers of beauty between January 2019 and December 2019. Of these, 107 were excluded (29 for not accepting to participate and 78 for not having some of the parameters needed to calculate the different scales, thus a total of 1,350 workers were finally included in the study. (See Flowchart in **figure 1**)

Workers were selected from among those who attended periodic occupational medical examinations.

Inclusion criteria

- Aged between 18 and 69 years old.
- Accept to participate in the study.

Figure 1: Flow chart of the study participants.



All anthropometric measurements and clinical tests were carried out by the health personnel of the different occupational health units participating in the study, after homogenizing the measurement techniques.

Weight and height were determined with a scale-height rod using a SECA 700 scale and a SECA telescopic height rod 220. Waist and hip circumference was measured with a SECA 20. Values were considered to be high when >88 cm in women and >102 cm in men⁸. The cut-off point for the waist to height ratio is 0.50.

Blood pressure (BP) was measured with OMRON M3 automatic sphygmomanometer and after 10 minutes of rest. Three measurements were made at one minute intervals, obtaining the mean value of the three. An individual was considered to have hypertension if they presented blood pressure values over 140 mm Hg systolic BP⁹.

Lipid profile values were classified as following: high cholesterol >200 mg/dl, high LDL >130 mg/dl, and high triglycerides >150 mg/dl. Uric acid was considered high when values were >5.60 in women and 7.00 in men. If an individual was taking medication for any of these, they were also classified as having altered values. Basal blood glucose results were classified based on the recommendations of the American Diabetes Association⁹, whereby it was considered that the individual presented diabetes if values were >126 mg/dl in two different determinations, if they also presented HbA1c \geq 6.5% or if the individual was receiving hypoglycemic treatment.

An individual was considered a smoker if they had regularly consumed at least 1 cigarette/day in the last month, or had stopped smoking less than a year ago.

Social class was obtained from the 2011 National Classification of Occupations (NCO-11) based on the proposal made by the social determinants group of the Spanish Society of Epidemiology¹⁰. We opted for

classification in three categories: Class I. Directors/managers, university professionals, athletes, and artists. Class II. Intermediate occupations and self-employed workers without employees. Class III. Unskilled workers. People in social class I and II are considered white collar and those in social class III are considered blue collar.

BMI is calculated by dividing weight by height in meters squared. Obesity is considered to be over 30.

We have used 4 formulas to estimate the percentage of body fat:

- CUN BAE¹¹ (Clínica Universidad de Navarra Body Adiposity Estimator) The formula is:

$$-44.988 + (0.503 \times \text{age}) + (10.689 \times \text{gender}) + (3.172 \times \text{BMI}) - (0.026 \times \text{BMI}^2) + (0.181 \times \text{BMI} \times \text{gender}) - (0.02 \times \text{BMI} \times \text{age}) - (0.005 \times \text{BMI}^2 \times \text{gender}) + (0.00021 \times \text{BMI}^2 \times \text{age}).$$

Where male sex equals 0 and female sex equals 1.

The CUN BAE cut-off points for obesity are from 25% in men and 35% in women.

- ECORE-BF¹² (Equation Córdoba for Estimation of Body Fat) It is calculated by the formula: $-97.102 + 0.123 (\text{age}) + 11.9 (\text{gender}) + 35.959 (\text{LnIMC})$.

Being male is valued as 0 and female as 1. The same cut-off points as CUN BAE are proposed.

- Deuremberg fat mass index¹³.

$$\text{Fat mass \%} = 1.2 \times (\text{BMI}) + 0.23 \times (\text{Age in years}) - 10.8 \times (\text{gender}) - 5.4$$

Women are given a value of 0 and men a value of 1. Obesity is considered to be 25% or more in men and 32% or more in women.

- The normalized weight-adjusted index¹⁴ (NWA) is calculated by the formula : $(\text{weight}/10) - (10 \times \text{height}) + 10]$ weight is expressed in kg and height in meters.

- Visceral adiposity index (VAI)¹⁵

Female:

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

Male:

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

- Body roundness index (BRI)¹⁶

$$BRI = 364.2 - 365.5 \times \sqrt{1 - [(WC/(2\pi))/ (0.5 \times \text{Height})]^2}$$

- Body Surface Index (BSI)¹⁷ and Body Surface Area (BSA).

w is weight and h is height

- Relative fat mass¹⁸

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

- Conicity index¹⁹

$$\frac{\text{waist circumference (in metres)}}{0,109} \times 1 \sqrt{\frac{\text{Weight (in kilogram)}}{\text{Height (in metres)}}$$

- Body shape index²⁰ (ABSI)

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

- Metabolic Score for Visceral Fat (METS-VF)²¹

$$\text{METS-VF} = 4.466 + 0.011 * (\text{Ln}(\text{METS-IR}))^3 + 3.239 * (\text{Ln}(\text{WHtr}))^3 + 0.319 * (\text{Sex}) + 0.594 * (\text{Ln}(\text{Age}))$$

where METS-IR = $(\ln ((2 \times \text{fasting plasma glucose}) + \text{triglyceride}) \times \text{body mass index}) / (\ln (\text{HDL-cholesterol}))$.

Statistical analysis

A descriptive analysis of the categorical variables was performed, 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 association analysis was performed using the 2 test (with correction of Fisher’s exact statistic when conditions required it) and Student’s t test for independent samples. Statistical analysis was performed with the SPSS 27.0 program, with an accepted statistical significance level of 0.05.

Ethical considerations and aspects

The study was approved by the Clinical Research Ethics Committee. All procedures were performed in accordance with 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

Table I shows the anthropometric, clinical, analytical and socio-demographic characteristics of the study participants. Sixty-nine percent are women, the average age is about 35 years. The majority group is between 30 and 39 years old. 31.9% are smokers (slightly higher percentage in women). The values of all clinical and analytical parameters are higher in men.

The mean values of all the anthropometric scales analysed in this study (BMI, WtHR, Body Surface index, NVAI, BRI, ABSI, VAI, CI and METS-VF) show higher values in men. The scales assessing body fat percentage (CUN BAE, ECOPE-BF, RFM and Deuemberg formula) show higher values in women as women have a higher amount of body fat. The complete data can be found in **table II**.

Table I: Characteristics of the population.

	Women (n=932) mean (SD)	Men (n=418) mean (SD)	Total (n=1350) mean (SD)	p-value
Age (years)	35.1 (8.9)	34.4 (8.7)	34.9 (8.9)	0.159
Height (cm)	163.1 (6.1)	176.2 (6.5)	167.1 (8.7)	<0.0001
Weight (kg)	64.3 (13.9)	77.5 (11.7)	68.4 (14.6)	<0.0001
Waist circumference (cm)	73.6 (10.7)	83.8 (9.5)	73.7 (11.4)	<0.0001
Systolic blood pressure (mmHg)	112.7 (13.5)	124.8 (13.2)	116.4 (14.5)	<0.0001
Diastolic blood pressure (mmHg)	70.0 (9.3)	74.4 (10.3)	71.3 (9.8)	<0.0001
Total cholesterol (mg/dl)	181.4 (34.0)	184.5 (35.3)	182.4 (34.4)	0.121
HDL-cholesterol (mg/dl)	58.1 (8.3)	53.6 (8.9)	56.7 (8.8)	<0.0001
LDL-cholesterol (mg/dl)	107.0 (32.8)	109.6 (32.8)	107.8 (32.8)	0.184
Triglycerides (mg/dl)	81.5 (38.1)	109.7 (75.4)	90.2 (54.1)	<0.0001
Glycaemia (mg/dl)	85.9 (12.4)	90.7 (12.6)	87.4 (12.6)	<0.0001
AST (U/L)	18.4 (9.5)	24.8 (9.4)	21.1 (9.9)	<0.0001
ALT (U/L)	18.7 (10.5)	28.6 (18.0)	21.9 (14.2)	<0.0001
GGT (U/L)	17.6 (11.3)	31.7 (28.0)	22.2 (19.6)	<0.0001
	%	%	%	p-value
< 30 years	271 (29.1)	154 (36.8)	425 (31.5)	0.027
30-39 years	407 (43.6)	154 (36.8)	561 (41.5)	
40-49 years	187 (20.1)	84 (20.1)	271 (20.1)	
50-69 years	67 (7.2)	67 (6.3)	93 (6.9)	
Blue collar	587 (63.0)	148 (35.4)	735 (54.4)	<0.0001
White collar	345 (37.0)	270 (64.6)	615 (45.6)	
Non smokers	614 (65.9)	306 (73.2)	920 (68.1)	0.004
Smokers	318 (34.1)	112 (26.8)	430 (31.9)	

Table II: Mean values of overweight and obesity indicators.

	Women n=932 Mean (SD)	Men n=418 Mean (SD)	p-value
Body mass index	24.2 (5.1)	25.0 (3.5)	0.005
Waist to height ratio	0.45 (0.06)	0.48 (0.05)	<0.0001
CUN BAE	33.0 (7.2)	22.4 (5.5)	<0.0001
ECORE-BF	33.0 (7.1)	22.5 (5.1)	<0.0001
Relative fat mass	30.9 (5.6)	21.5 (4.5)	<0.0001
Deuremberg formula	31.7 (6.7)	21.7 (4.7)	<0.0001
Body fat index	26.1 (8.0)	20.6 (6.8)	<0.0001
Body surface index	49.2 (8.1)	55.5 (6.3)	<0.0001
Normalized weight adjusted index	0.12 (1.4)	0.13 (1.1)	0.922
Body roundness index	2.6 (1.2)	3.0 (0.9)	<0.0001
Body shape index	0.069 (0.01)	0.074 (0.01)	<0.0001
Visceral adiposity index	2.4 (1.3)	5.9 (5.3)	<0.0001
Conicity index	1.1 (0.1)	1.2 (0.1)	<0.0001
METS-VF	5.2 (0.8)	5.9 (0.7)	<0.0001

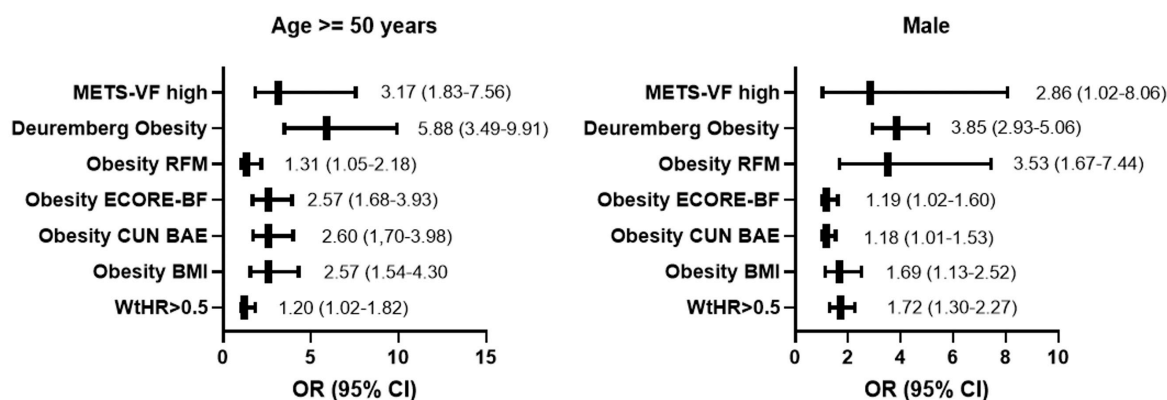
Table III: Prevalence of elevated values of overweight and obesity indicators.

	Women n=932 % (IC 95%)	Men n=418 % (IC 95%)	p-value
Waist to height ratio >0,5	16.8 (15.2-18.4)	25.8 (24.0-27.6)	<0.0001
Overweight BMI	18.7 (17.1-20.3)	36.8 (35.0-38.6)	<0.0001
Obesity BMI	13.1 (11.6-14.7)	8.1 (6.9-9.3)	
Overweight CUN BAE	25.5 (23.9-27.1)	34.9 (33.1-36.7)	0.002
Obesity CUN BAE	33.7 (32.1-35.3)	29.7 (27.9-31.5)	
Overweight ECOPE-BF	26.4 (24.8-28.0)	38.3 (36.5-40.1)	<0.0001
Obesity ECOPE-BF	33.2 (31.6-34.8)	28.7 (26.9-30.5)	
RFM obesity	38.8 (37.2-40.4)	20.6 (18.8-22.4)	<0.0001
Overweight Deuremberg formula	37.3 (35.7-38.9)	40.7 (38.9-42.5)	<0.0001
Obesity Deuremberg formula	51.0 (49.4-52.6)	22.0 (20.2-23.8)	
METS-VF alto	0.9 (0.5-1.3)	1.9 (1.1-2.7)	0.086

The prevalence of high values, indicating overweight or obesity, of the different scales analysed in this study show in most cases higher values in men (WTHR, BMI, CUN BAE, ECORE-BF and METS-VF). Only RFM and Deuremberg formula show higher prevalences in women. The prevalence of obesity according to BMI is 8.1% in men and 13.1% in women. All data are presented in **table III**.

In the multivariate analysis using binary logistic regression, the covariates age, male sex, being blue collar and being a smoker were established as covariates. Of these, only age and sex increase the risk of having high values for the different scales. The complete data can be found in **figure 2**.

Figure 2: Multivariate análisis with Logistic binary regression.



Discussion

The anthropometric profile found in the people working in aesthetics and beauty of the people analysed in this study shows a prevalence of obesity that is not too high in any of the scales used.

No hemos encontrado ningún estudio que valore el perfil antropométrico o cardiovascular de los trabajadores del bienestar y de la belleza por ello no podemos comparar nuestros resultados con los obtenidos por otros autores. Sin embargo si podemos establecer comparaciones con otros colectivos que también se encargan del bienestar de las personas como es el personal sanitario. Un estudio realizado en trabajadores sanitarios de atención primaria de España²² mostró que los valores de IMC eran superiores a los encontrados por nosotros, aunque la edad media de los profesionales era casi 10 años mayor que la nuestra. Datos similares al estudio español se encontraron en trabajadores hospitalarios de Portugal²³.

As strengths of the study we would highlight the large sample size (more than 1300 people) and the large

number of scales used to assess overweight and obesity, specifically¹⁴.

As weaknesses we find that the estimation of body fat has not been carried out with objective methods such as bioimpedance but with indirect estimators.

The absence of studies of this type in this group of workers makes our work pioneering and could constitute a starting point for future research, as well as a reference with which to compare new work that may be carried out.

Conclusion

The anthropometric profile of beauty-related workers is better than that of workers in other productive sectors.

Interests conflict

The researchers declare that they have no conflict of interest.

References

- World Health Organization 2020. Obesity and Overweight. Available at: <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight> (acces 7 october 2021).
- Ampofo AG, Boateng EB. Beyond 2020: Modelling obesity and diabetes prevalence. *Diabetes Res. Clin. Pract* 2020; 167:108362
- Russell L, Allen B. Obesity and You. *South Med J* 2008;101(4):337.
- Danielsson G, Eklof B, Grandinetti A, Kistner RL. The influence of obesity on chronic venous disease. *Vasc Endovasc Surg.* 2002;36(4):271-6.
- Björntorp P. Obesity: a chronic disease with alarming prevalence and consequences. *J Intern Med.* 1998;244:2679.
- Arteaga A. Overweight and obesity as an universal health problema. *REV. MED. CLIN. CONDES* 2012; 23(2) 145-53
- Cárdenas-García LJ, Alquicira-Sahagún RA, Martínez-Maraver MC, Robledo-Dominguez A. Obesidad y su asociación con factores emocionales: estudio comparativo entre alumnos universitarios de nuevo ingreso. *Aten Fam.* 2014;21(4):121-125.
- Luengo Pérez LM, Urbano Gálvez JM, Pérez Miranda M. Validación de índices antropométricos alternativos como marcadores del riesgo cardiovascular. *Endocrinol Nutr.* 2009;56(9):439-46.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2010;33(Suppl 1):S62-9.
- 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
- 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.
- 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.
- 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.
- Doménech-Asensi G, Gómez-Gallego C, Ros-Berruezo 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;35:359-67
- Amato M, Giordano C, Galia M, Criscimanna A, Vitabile S, BSC, Midiri M, et al. Visceral Adiposity Index A reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care.* 2010;33(4):920-2
- Rico-Martín S, Calderón-García JF, Sánchez-Rey P, Franco-Antonio C, Martínez Alvarez M, Sánchez Muñoz-Torrero JF. Effectiveness of body roundness index in predicting metabolic syndrome: A systematic review and meta-analysis. *Obes Rev.* 2020;21(7): e13023
- Shirazu I, Sackey 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
- 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.
- Andrade MD, Freitas MC, Sakumoto AM, Pappiani C, Andrade SC, Vieira VL. Association of the conicity index with diabetes and hypertension in Brazilian women. *Arch Endocrinol Metab.*2016; 60(5):436-42.
- Bertoli S, Leone A, Krakauer NY, Bedogni G, Vanzulli A, Redaelli VI. 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.
- Feng Y, Yang X, Li Y, Wu Y, Han M, Qie R, Huang S, Wu X, Zhang Y, Liu D, Hu F, Zhang M, Yang Y, Shi X, Lu J, Zhao Y, Hu D. Metabolic Score for Visceral Fat: A reliable indicator of visceral obesity for predicting risk for hypertension. *Nutrition.* 2021 Aug 10;93:111443.
- Herruzo Caro B, Martín García JJ, Molina Recio G, Romero Saldaña M, Sanz Pérez JJ, Moreno Rojas R. Promoción de la salud en el lugar de trabajo. Hábitos de vida saludable y factores de riesgo cardiovascular en trabajadores de ámbito sanitario en atención primaria. *Rev Asoc Esp Espec Med Trab* 2017; 26(1): 9-21.
- Basei CE, Avancini PR, Manfoia WC. Metabolic syndrome in workers in a university hospital. *Rev Port Cardiol* 2012; 31: 629-36.

ORIGINAL

Sociodemographic variables influencing the prevalence of insulin resistance in the Italian population

Variables sociodemográficas que influyen en la prevalencia de resistencia a la insulina en población italiana

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Abstract

Introduction: Insulin resistance (IR) is a very common pathology that is usually related to different cardiometabolic disorders such as obesity or non-alcoholic fatty liver disease. Its frequency is increasing worldwide. The aim of this study was to determine the prevalence of IR in the Italian population and to determine the influence of certain sociodemographic variables such as age, sex and social status on its occurrence.

Methods: Descriptive and cross-sectional study in 20774 Italian workers with a mean age of 40.1 years. The risk of developing insulin resistance was assessed with three scales: Metabolic score-insulin resistance (METS-IR), triglyceride-glucose index (T&G index) and triglyceride/HDL-c ratio. The sociodemographic variables analyzed were age, sex and social class.

Results: The prevalence of IR ranged from 11.3% (METS-IR) to 28% (TGA index) in men and 6.3% (METS-IR) to 18% (Triglycerides/HDL). The sociodemographic variable that most increased the risk of presenting IR was age 50 years and older, with OR ranging from 1.92 (95% CI 1.74-2.13) using the METS-IR scale to 2.61 (95% CI 2.43-2.81) if the TyG index was used.

Conclusion: The Italian population shows a low prevalence of high risk values for insulin resistance. The variables that most increase this risk are age, sex and social class.

Keywords: Insulin resistance, social class, gender.

Resumen

Introducción: La resistencia a la insulina (RI) es una patología muy frecuente que suele relacionarse con diferentes alteraciones cardiometabólicas como la obesidad o el hígado graso no alcohólico. Su frecuencia va en aumento en todo el mundo. El objetivo de este estudio fue determinar la prevalencia de IR en la población italiana determinado también la influencia que tienen determinadas variables sociodemográficas como la edad, el sexo y la clase social en su aparición.

Metodología: Estudio descriptivo y transversal en 20774 trabajadores italianos con una edad media de 40,1 años. Se valora el riesgo de presentar resistencia a la insulina con tres escalas: Score metabólico- resistencia a la insulina (METS-IR), índice triglicéridos-glucosa (índice TyG) y cociente triglicéridos/HDL-c. las variables sociodemográficas analizadas son la edad, el sexo y la clase social.

Resultados: La prevalencia de RI osciló entre 11,3% (METS-IR) y 28% (índice TyG) en hombres y 6,3% (METS-IR) y 18% (Triglicéridos/HDL). La variable sociodemográfica que más incrementó el riesgo de presentar RI fue la edad a partir de los 50 años con OR que van de 1,92 (IC 95% 1,74-2,13) aplicando la escala METS-IR a 2,61 (IC 95% 2,43-2,81) si se emplea el índice TyG.

Conclusión: La población italiana muestra una baja prevalencia de valores de alto riesgo de resistencia a la insulina. Las variables que más aumentan este riesgo son la edad, el sexo y la clase social.

Palabras clave: Resistencia a la insulina, clase social, género.

Introduction

Insulin resistance is a very common pathology that often accompanies obesity¹, prediabetes, type 2 diabetes, polycystic ovary syndrome², cardiovascular disease and other metabolic disorders, such as hypertension and nonalcoholic fatty liver disease. Insulin resistance has also been associated with an increased risk of developing various cancers, Alzheimer's disease, mental disorders and other chronic disorders³.

Some authors estimate that up to 45% of the population in the United States and other countries currently have insulin resistance^{4,5}. In studies of obese women, they found that more than 70% are insulin resistant and among people with type 2 diabetes, the figure rises to more than 80%⁶.

Genetic, environmental and lifestyle risk factors are known to contribute to the development of insulin resistance⁷. Although some people may be genetically more prone to develop insulin resistance, perhaps the greatest impact has been the change in our food environment in recent decades. There is greater availability of cheap hypercaloric food and beverages, and this may have led to whole populations adopting an unhealthy lifestyle characterized by the consumption of high levels of sugar and other refined carbohydrates. Carbohydrates are broken down into large amounts of glucose that we may not need for energy, and some of it is stored in our cells.

The importance of this health problem has led us to carry out this study whose objective is to determine the prevalence of insulin resistance in the Italian population, assessing the sociodemographic variables that influence it.

Methods

A retrospective and cross-sectional study was carried out in 20.774 Italian workers between January 2019 and December 2020. The workers were selected based on their attendance to periodic occupational medical examinations.

Selection criteria:

- Belongs to one of the participating companies.
- Accepts participating in the study.

Of the 22.689 workers initially included in the study, 1.749 were excluded due to not having data from all the necessary variables to calculate the insulin resistance scales; and 166 did not give permission to participate in the study. The final number of workers included in the study was 20.774.

All anthropometric and analytical determinations were performed by health professionals from the different

occupational health units that participated in the study, after standardizing the measurement techniques.

Weight and height were determined with a height bar scale (model: SECA 700 to which a SECA 220 telescopic height bar was added). Body mass index (BMI) was calculated by dividing weight by height in squared meters.

Blood glucose, total cholesterol and triglycerides: These were determined by peripheral venipuncture and after fasting for at least 12 hours. Automated enzymatic methods were used. HDL were determined by precipitation with Cl2Mg dextran sulfate.

Three scales were used to assess insulin resistance.

- Metabolic score for Insulin resistance (METS-IR)⁸ whose formula is

$\text{Ln} [(2 * \text{glucose}) + \text{Triglycerides}] * \text{BMI} / (\text{Ln}[\text{HDLc}])$ High risk is considered to be values from 50

- Triglyceride glucosa index⁹ (TyG index) whose formula is

$\text{Ln} [\text{triglycerides (mg/dL)} * \text{glucose (mg/dL)} / 2]$ The cut-off points for high values are set at 8.7 for women and 8.8 for men.

- Atherogenic index Triglycerides/HDL-c¹⁰ The cut-off points for high values are set at 2.2 for women 3.1 for men.

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. A bivariate association analysis was performed using the χ^2 test (with a correction with the Fisher's exact statistical test, when conditions required so) and a Student's t-test for independent samples. For the multivariate analysis, binary logistic regression was used with the Wald method, with the calculation of the Odds-ratio and the Hosmer-Lemeshow goodness-of-fit test was performed. Correlation and agreement between the scales were determined with Pearson's correlation index and Cohen's Kappa index respectively. Statistical analysis was performed with the SPSS 27.0 program, and a p value of <0.05 was considered as statistically significant.

Considerations and ethical aspects

The study was approved by the Clinical Research Ethics Committee. 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.

The anthropometric, analytical, clinical and sociodemographic characteristics of the population are presented in **table I**. Most of the variables, with the exception of LDL cholesterol, show more unfavorable values in men. The majority of the patients were between 30 and 49 years of age and belonged mainly to the most disadvantaged social class (social class III). All data are shown in **table I**.

The mean values of the three insulin resistance scales increase in value with increasing age. This situation is observed in both sexes and the differences observed are statistically significant. There is also an increase in the values of the three scales as one descends in social class in both sexes, although the differences are only

statistically significant in women. The complete data can be found in **table II**.

The prevalence of high values of the three scales follows a pattern similar to that observed with the mean values, i.e., there is an increase in prevalence as age increases and as one moves down the social scale. This situation is seen in both men and women and in all cases the differences are statistically significant. The mean prevalence of insulin resistance ranged from 11.5% in men and 6.3% in women when using the METS-IR scale to 28.0% with the TyG index scale in men and 18.8% with the Triglycerides/HDL-c scale in women. The complete data are available in **table III**.

Table I: Characteristics of the population.

	Women (n=8.500) mean (SD)	Men (n=12.274) mean (SD)	Total (n=20.774) mean (SD)	p-value
Age (years)	39.5 (10.9)	40.5 (11.1)	40.1 (11.0)	<0.0001
Height (cm)	161.9 (6.5)	174.7 (7.0)	169.4 (9.3)	<0.0001
Weight (kg)	66.2 (14.0)	81.3 (14.8)	75.1 (16.2)	<0.0001
BMI (kg/m ²)	25.3 (5.2)	26.6 (4.5)	26.1 (4.8)	<0.0001
Waist circumference (cm)	74.7 (10.5)	86.2 (11.2)	81.5 (12.3)	<0.0001
Waist to height ratio	0.46 (0.06)	0.49 (0.06)	0.48 (0.06)	<0.0001
Systolic blood pressure (mmHg)	117.3 (15.7)	128.2 (15.7)	123.7 (16.6)	<0.0001
Diastolic blood pressure (mmHg)	72.5 (10.5)	77.7 (11.1)	75.6 (11.1)	<0.0001
Total cholesterol (mg/dl)	190.9 (35.6)	192.7 (39.1)	191.9 (37.7)	0.001
HDL-c (mg/dl)	56.8 (8.8)	50.4 (8.6)	53.0 (9.2)	<0.0001
LDL-c (mg/dl)	116.2 (34.5)	118.1 (36.7)	117.3 (35.8)	<0.0001
Triglycerides (mg/dl)	89.7 (46.5)	123.5 (83.5)	110.7 (72.7)	<0.0001
Glycaemia (mg/dl)	87.7 (14.1)	93.4 (22.2)	91.1 (19.5)	<0.0001
	%	%	%	p-value
18-29 years	21.3	18.9	19.9	<0.0001
30-39 years	29.2	27.9	28.4	
40-49 years	29.0	29.2	29.1	
50-59 years	17.2	20.1	18.9	
60-69 years	3.4	3.9	3.7	
Social class I	6.8	5.0	5.8	<0.0001
Social class II	23.4	14.7	18.3	
Social class III	69.8	80.2	76.0	

Table II: Mean values of indicators of insulin resistance according sociodemographic variables by sex.

Men	n	TG/HDL		TyG index		METS-IR	
		Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
18-29 years	2317	1.8 (1.2)	<0.0001	8.2 (0.5)	<0.0001	34.7 (7.4)	<0.0001
30-39 years	3430	2.4 (1.8)		8.4 (0.5)		38.0 (7.9)	
40-49 years	3580	2.9 (2.4)		8.6 (0.6)		40.6 (8.7)	
50-59 years	2465	3.2 (2.3)		8.7 (0.6)		42.4 (8.6)	
60-69 years	482	3.3 (2.1)		8.8 (0.6)		43.3 (7.9)	
Social class I	619	2.6 (2.2)	0.113	8.5 (0.5)		38.7 (7.6)	0.078
Social class II	1808	2.6 (2.5)		8.5 (0.6)		38.8 (8.0)	
Social class III	9847	2.6 (2.0)		8.5 (0.6)		39.3 (8.8)	
Women	n	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
18-29 years	1811	1.4 (0.7)	<0.0001	8.0 (0.4)	<0.0001	32.7 (7.7)	<0.0001
30-39 years	2478	1.5 (0.7)		8.1 (0.4)		34.1 (8.5)	
40-49 years	2462	1.7 (1.0)		8.2 (0.5)		35.9 (8.2)	
50-59 years	1461	2.0 (1.3)		8.4 (0.5)		37.7 (8.3)	
60-69 years	288	2.2 (1.3)		8.5 (0.5)		40.0 (8.5)	
Social class I	578	1.4 (0.8)	0.025	8.1 (0.4)		32.5 (6.8)	0.001
Social class II	1987	1.6 (1.0)		8.1 (0.5)		33.9 (8.0)	
Social class III	5935	1.7 (1.0)		8.2 (0.5)		35.8 (8.6)	

Table III: Prevalence of high values of indicators of insulin resistance according sociodemographic variables by sex.

		TG/HDL high		TyG index high		METS-IR high	
Men	n	% (95% CI)	p-value	% (95% CI)	p-value	% (95% CI)	p-value
18-29 years	2317	9.8 (9.1-10.5)	<0.0001	10.4 (9.8-11.0)	<0.0001	4.4 (3.7-5.2)	<0.0001
30-39 years	3430	20.0 (19.6-20.4)		21.6 (21.2-22.0)		8.4 (8.0-8.8)	
40-49 years	3580	29.3 (28.9-29.7)		31.6 (31.2-32.0)		13.5 (13.0-13.9)	
50-59 years	2465	35.8 (35.3-36.3)		39.2 (38.7-39.8)		17.7 (17.2-18.2)	
60-69 years	482	40.5 (39.0-42.0)		45.2 (43.7-46.7)		17.6 (16.0-19.1)	
Social class I	619	23.3 (21.4-25.2)		24.2 (22.3-26.2)		9.4 (8.5-10.3)	
Social class II	1808	22.7 (22.0-23.4)		23.1 (22.4-23.8)		9.4 (8.7-10.1)	
Social class III	9847	25.2 (25.0-25.5)		27.7 (27.5-27.9)		11.8 (11.6-12.0)	
Total	12274	25.3 (25.0-25.6)		28.0 (27.7-28.3)		11.3 (11.0-11.6)	
Women	n	% (95% CI)	p-value	% (95% CI)	p-value	% (95% CI)	p-value
18-29 years	1811	9.6 (8.9-10.3)	<0.0001	5.3 (4.6-6.0)	<0.0001	4.0 (3.4-4.6)	<0.0001
30-39 years	2478	13.2 (12.7-13.7)		8.2 (7.7-8.8)		5.3 (4.8-5.8)	
40-49 years	2462	19.5 (19.0-20.0)		13.3 (12.8-13.9)		6.3 (5.8-6.8)	
50-59 years	1461	30.3 (29.6-31.0)		25.5 (24.8-26.2)		7.8 (7.2-8.4)	
60-69 years	288	36.8 (35.0-38.6)		31.9 (30.1-33.8)		12.5 (10.7-14.3)	
Social class I	578	10.4 (9.5-11.3)		7.4 (6.5-8.3)		2.6 (1.9-3.3)	
Social class II	1987	15.9 (15.3-16.5)		11.4 (10.8-12.0)		5.0 (4.4-5.6)	
Social class III	5935	19.4 (19.1-19.7)		13.9 (13.6-14.2)		7.0 (6.7-7.3)	
Total	8500	18.0 (17.6-18.4)		12.6 (12.2-13.0)		6.3 (5.9-6.7)	

The degree of correlation between the three scales shows a very high value between TyG index and Triglycerides/HDL and somewhat lower between METS-IR and the other two scales. The specific data are presented in **table IV**. Something similar can be observed with Cohen's kappa concordance index (see **table V**).

In the multivariate analysis using binary logistic regression, age 50 years and older, social class II-III and male were established as covariates.

Figure 1 shows that the variable that most increases the risk of presenting insulin resistance with the three scales used is age over 50 years (with OR ranging from 2.61 (95% CI 2.43-2.81) in the case of the T&G index to 1.92 (95% CI

1.74-2.13) in the case of METS-IR) followed by male sex. The variable with the least influence was social class.

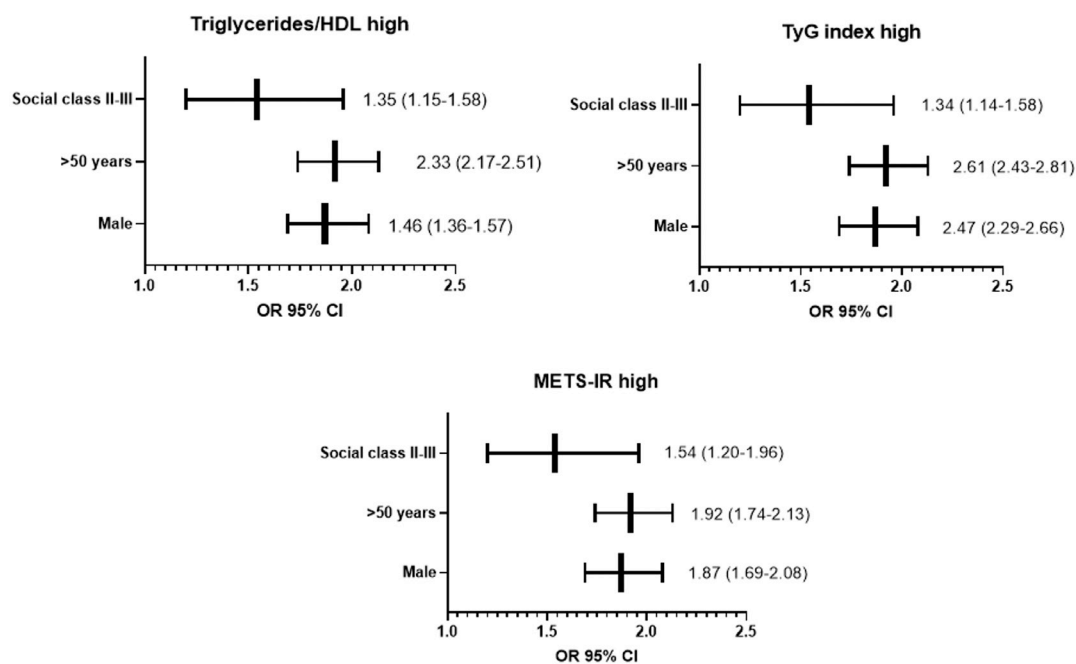
Table IV: Pearson's correlation coefficient of different scales of insulin resistance.

	TG/HDL	TyG index	METS-IR
TG/HDL	1	0.831	0.553
TyG index		1	0.572
METS-IR			1

Table V: Kappa Cohen index of different scales of insulin resistance.

	TG/HDL	TyG index	METS-IR
TG/HDL	1	0.757	0.315
TyG index		1	0.289
METS-IR			1

Figure 1: Binary Logistic regression analysis.



Discussion

The prevalence of insulin resistance is higher in men and varies according to the scale applied, ranging from 11.5% to 28% in men and 6.3% to 18.8% in women.

The sociodemographic variables that most increase the risk of insulin resistance are age 50 years and older, followed by male sex and social classes II-III.

The prevalence of insulin resistance varies from country to country. A Danish population study showed a prevalence of 15.5%¹¹, while the highest prevalence rates were reported in other countries reaching 23.3%, 39.1% and 46.5% in Thailand, Texas-USA and Venezuela¹²⁻¹⁴ respectively. A study from Lebanon with people of a similar mean age to our study reported one of the highest prevalence rates compared to other countries, reaching 44.6%¹⁵.

In our study, belonging to the male sex increases the risk of presenting insulin resistance between 1.46 and 2.47 times, being this figure lower than that reported in a Lebanese study which was 3.9 times¹⁶. Similar figures were obtained in another study carried out in the USA¹⁷. However, Naja et al¹⁵ showed no differences by sex.

In our study, the most disadvantaged social classes have a higher prevalence of insulin resistance; these data are

consistent with those found by Lawlor¹⁸ in Scotland, Goodman in the USA¹⁹ and Buitrago-López, although the latter was conducted in children²⁰.

We have found that age increases the prevalence of insulin resistance, which is similar to data obtained several decades ago in a systematic review²¹.

The strengths of the study include the large sample size (more than 20,000 people) and the large number of scales used and sociodemographic variables analyzed.

As a main limitation, we can point out that the study was carried out in the working population between 18 and 70 years of age, so that it cannot be extrapolated to the entire population.

Conclusión

The prevalence of high-risk values of insulin resistance in the Italian population can be considered low. The variables that most increase this risk are, in order, age, sex and social class.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Kahn BB, Flier JS. Obesity and insulin resistance. *J Clin Invest.* 2000;106(4):473-481.
2. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. *Clin Epidemiol.* 2013;6:1-13.
3. Facchini FS, Hua N, Abbasi F, Reaven GM. Insulin resistance as a predictor of age-related diseases. *J Clin Endocrinol Metab.* 2001 Aug;86(8):3574-8.
4. Van der Aa MP, Fazeli Farsani S, Knibbe CA, de Boer A, van der Vorst MM. Population-Based Studies on the Epidemiology of Insulin Resistance in Children. *J Diabetes Res.* 2015;2015:362375.
5. Bermudez V, Salazar J, Martínez MS, Chávez-Castillo M, Olivar LC, Calvo MJ, et al. Prevalence and Associated Factors of Insulin Resistance in Adults from Maracaibo City, Venezuela. *Adv Prev Med.* 2016;2016:9405105.
6. Kocelak P, Chudek J, Olszanecka-Glinianowicz M. Prevalence of metabolic syndrome and insulin resistance in overweight and obese women according to the different diagnostic criteria. *Minerva Endocrinol.* 2012 Sep;37(3):247-54.
7. Wilcox G. Insulin and insulin resistance. *Clin Biochem Rev.* 2005;26(2):19-39.
8. Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. *Eur J Endocrinol.* 2018;178(5):533-44.
9. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord.* 2008;6(4):299-304
10. López-González AA, Rivero YI, Vicente-Herrero MT, Queimadelos M, Monroy MN, Núñez-Fernández C. The influence of tobacco consumption, physical activity, diet and age on the values of different atherogenic indexes in Spanish Mediterranean population. *Medicina Balear* 2014; 29 (2); 23-31
11. Friedrich N, Thuesen B, Jørgensen T, Juul A, Spielhagen C, Wallaschofski H, et al. The association between IGF-I and insulin resistance: a general population study in Danish adults. *Diabetes Care.* 2012 Apr;35(4):768-73.

12. Do HD, Lohsoonthorn V, Jiamjarasrangi W, Lertmaharit S, Williams MA. Prevalence of insulin resistance and its relationship with cardiovascular disease risk factors among Thai adults over 35 years old. *Diabetes Res Clin Pract.* 2010;89(3):303-8.
13. Qu H, Li Q, Rentfro AR, Fisher-Hoch SP, McCormick JB. The definition of insulin resistance using HOMA-IR for Americans of Mexican descent using machine learning. *PLoS One.* 2011;6(6):e21041.
14. Bermudez V, Salazar J, Martínez MS, Chávez-Castillo M, Olivar LC, Calvo MJ, et al. Prevalence and associated factors of insulin resistance in adults from Maracaibo city, Venezuela. *Adv Prev Med.* 2016;2016:1-13
15. Naja F, Nasreddine L, Hwalla N, Moghames P, Shoaib H, Fattat M, et al. Association of *H. pylori* infection with insulin resistance and metabolic syndrome among Lebanese adults. *Helicobacter.* 2012;17(6):444-51.
16. Fahed M, Abou Jaoudeh MG, Merhi S, Mosleh JMB, Ghadih R, Al Hayek S, et al. Evaluation of risk factors for insulin resistance: a cross sectional study among employees at a private university in Lebanon. *BMC Endocr Disord.* 2020 Jun 10;20(1):85.
17. Cnop M, Havel PJ, Utzschneider KM, Carr DB, Sinha MK, Boyko EJ, et al. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. *Diabetologia.* 2003 Apr;46(4):459-69.
18. Lawlor DA, Ebrahim S, Davey Smith G; British women's heart and health study. Socioeconomic position in childhood and adulthood and insulin resistance: cross sectional survey using data from British women's heart and health study. *BMJ.* 2002 Oct 12;325(7368):805.
19. Goodman E, Daniels SR, Dolan LM. Socioeconomic disparities in insulin resistance: results from the Princeton School District Study. *Psychosom Med.* 2007 Jan;69(1):61-7.
20. Buitrago-Lopez A, van den Hooven EH, Rueda-Clausen CF, Serrano N, Ruiz AJ, Pereira MA, et al. Socioeconomic status is positively associated with measures of adiposity and insulin resistance, but inversely associated with dyslipidaemia in Colombian children. *J Epidemiol Community Health.* 2015 Jun;69(6):580-7.
21. Muller DC, Elahi D, Tobin JD, Andres R. The effect of age on insulin resistance and secretion: a review. *Semin Nephrol.* 1996 Jul;16(4):289-98.

ORIGINAL

Relationship between blood pressure levels and body mass index values in 41,093 ukrainians people

Relación entre los niveles de presión arterial y los valores del índice de masa corporal en ucranianos

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Abstract

Introduction: Arterial hypertension and excess weight are two important public health problems that are increasingly affecting the world population, both in developed and developing countries. The aim of this study is to relate blood pressure values to body mass index (BMI) values in a group of people from Ukraine.

Material and methods: Cross-sectional study in 41,093 Ukrainians in which the relationship between blood pressure and BMI was assessed. BMI is classified according to WHO criteria into 8 types ranging from underweight to type IV obesity.

Results: There is a direct relationship between blood pressure values and BMI values in such a way that as BMI increases, blood pressure values increase in parallel. Age after 50 years, male sex, belonging to social class III and obesity increase the risk of presenting arterial hypertension.

Conclusions: There is a relationship between BMI and blood pressure values in the Ukrainian population.

Keywords: Hypertension, body mass index, obesity, social class.

Resumen

Introducción: La hipertensión arterial y el exceso de peso son dos importantes problemas de salud pública que cada vez afectan más a la población mundial, tanto en los países desarrollados como los que están en vías de desarrollo. El objetivo de este estudio es relacionar los valores de tensión arterial con los valores de índice de masa corporal (IMC) en un colectivo de personas de Ucrania.

Material y métodos: Estudio transversal en 41.093 ucranianos en los que se valora la relación existente entre la presión arterial y el IMC. El IMC se clasifica según los criterios de la OMS en 8 tipos que van de bajo peso a obesidad tipo IV.

Resultados: Existe una relación directa entre los valores de tensión arterial y los valores de IMC de manera que a medida que se incrementa el IMC aumentan paralelamente los valores de tensión arterial. La edad a partir de 50 años, el sexo masculino, pertenecer a la clase social III y la obesidad incrementan el riesgo de presentar hipertensión arterial.

Conclusiones: Existe relación entre los valores de IMC y los valores de tensión arterial en población ucraniana.

Palabras clave: Hipertensión, índice de masa corporal, obesidad, clase social.

Introduction

Arterial hypertension (HT) refers to sustained systolic and/or diastolic blood pressure. This pathology is considered the most common chronic disease, affecting 42.6% of the Spanish adult population¹. It is the leading cause of morbidity and causes the greatest number of circulatory system consultations, and is considered the most important risk factor for cardiocerebrovascular disease, being frequently associated with other risk factors such as age, sex, obesity, smoking, sedentary lifestyle, alcohol and dyslipidemias^{2,3}.

Obesity is a chronic disease that has greatly increased in prevalence in recent decades and has become an important public health problem. It is defined as excess body weight due to the accumulation of adipose tissue, although the most commonly used formula is the body mass index (BMI), the quotient between weight in kilograms and height in meters squared. A value higher than 30 is indicative of obesity⁴.

Different studies, both cross-sectional^{5,6} and longitudinal⁷, have shown a positive relationship between obesity and blood pressure. Excess weight increases the risk of HT by up to six times, as does a BMI above 27. Every 10 kg of weight gain increases systolic blood pressure (SBP) by 2-3 mmHg and diastolic blood pressure (DBP) by 1-3 mmHg⁸.

It is very important to know this association between blood pressure and BMI in order to establish preventive programs and treatment strategies based on changes in dietary and hygienic habits, so that the influence of a decrease in BMI on the decrease in blood pressure figures can be demonstrated⁹.

Therefore, the aim of this study was to determine the relationship between BMI and SBP and DBP values in a large group of workers.

Materials and methods

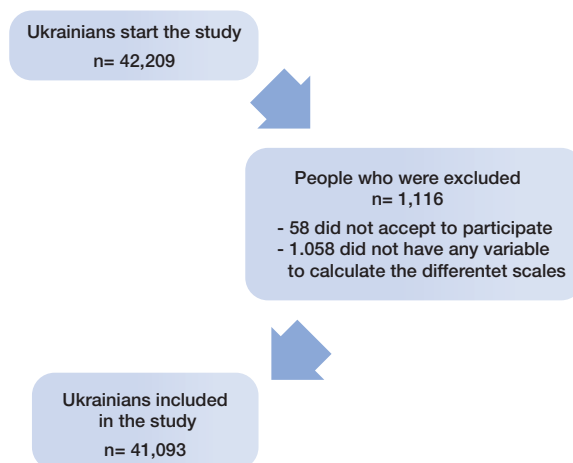
Study design

A retrospective and cross-sectional study was carried out in 421,625 Spanish workers between January 2019 and June 2020. The workers were selected based on their attendance to periodic occupational medical examinations. 418,343 (246,061 men and 172,282 women) finally entered the study. The workers finally included in the study and the reasons for exclusion are presented in the flow chart. (See **figure 1**)

Inclusion criteria:

- Belongs to one of the participating companies.
- Agree to participate in the study and consent to the use of the data for epidemiological purposes.

Figure 1: Flow chart of the study participants.



- Not less than 18 years of age and not more than 69 years of age.
- Have the parameters to calculate body mass index (BMI) or the presence of hypertension.

The anthropometric, clinical and analytical measurements were carried out by the healthcare professionals of the different occupational health units that participated in the study, after standardizing the measurement techniques.

To measure weight (in kilograms) and height (in cm), a height bar scale (model: SECA 700) with an added SECA 220 telescopic height bar was used. BMI is calculated by dividing weight by height in meters squared and was classified according to SEEDO criteria¹⁰.

Blood pressure was measured with a calibrated OMRON M3 automatic sphygmomanometer after 10 minutes of rest. Three measurements were taken at one-minute intervals, obtaining the mean value of the three. The JNC-7 criteria were used to classify blood pressure¹¹.

An individual was considered a smoker if he/she 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 12 months ago.

The social class was determined from the 2011 National Classification of Occupations (CNO-11) and based on the proposal made by the Spanish Society of Epidemiology¹². We opted for classification into 3 categories: Class I. Directors/managers, university professionals, athletes 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. A bivariate association analysis was performed using the χ^2 test (with a correction with the Fisher's exact statistical test, when conditions required so) and a Student's t-test for independent samples. For the multivariate analysis, binary logistic regression was used with the Wald method, with the calculation of the Odds-ratio and the Hosmer-Lemeshow goodness-of-fit test was performed. Statistical analysis was performed with the SPSS 27.0 program and a p value of <0.05 was considered as statistically significant.

Considerations and ethical aspects

All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 2013 Declaration of Helsinki. All patients signed written informed consent documents prior to participation in the study.

Results

The anthropometric, clinical, and analytical characteristics of the sample are presented in **table I**. A third of all

workers of both sexes were smoker. All parameters show more unfavorable values in males. The majority of workers (75.9%) belong to social class III.

The **table II** shows that in both men and women the SBP and DBP values increase as the BMI values increase. In both sexes the differences observed for SBP and DBP are statistically significant.

The **table III** shows a prevalence of arterial hypertension (sum of AHT 1 and 2) that increases with increasing BMI. This trend is observed in both men and women. The prevalence of HT is higher in men.

In the multivariate analysis using binary logistic regression, the covariates established were male sex, age over 50 years, belonging to social classes II or III, and being obese. The variables that most increased the risk of presenting arterial hypertension were age over 50 years (OR 3.59 95% CI 3.53-3.65) and obesity (OR 3.29 95% CI 3.23-3.35). The complete data can be found in **figure 2**.

Table I: Sociodemographic, anthropometric, analytical and clinical characteristics of workers.

	Women n=16,923 Mean (SD)	Men n=24,170 Mean (SD)	Total n=41,093 Mean (SD)	p-value
Age	39.6(10.8)	40.6 (11.1)	40.2 (11.0)	<0.0001
Height	161.8 (6.5)	174.6 (7.0)	169.4 (9.3)	<0.0001
Weight	66.2 (14.0)	81.4 (14.7)	75.1 (16.2)	<0.0001
BMI	25.3 (5.2)	26.7 (4.5)	26.1 (4.8)	<0.0001
Waist circumference	74.8 (10.6)	86.2 (11.1)	81.5 (12.2)	<0.0001
SBP	117.4 (15.7)	128.2 (15.5)	123.7 (16.5)	<0.0001
DBP	72.6 (10.4)	77.8 (11.0)	75.6 (11.0)	<0.0001
Total cholesterol	190.6 (35.8)	192.6 (38.9)	191.8 (37.7)	<0.0001
HDL-c	56.8 (8.7)	50.3 (8.5)	53.0 (9.1)	<0.0001
LDL-c	116.1 (34.8)	118.0 (36.7)	117.2 (35.9)	<0.0001
Triglycerides	89.1 (46.2)	123.7 (86.4)	109.5 (74.6)	<0.0001
Glycemia	87.8 (15.1)	93.3 (21.3)	91.0 (19.2)	<0.0001
	Percentage	Percentage	Percentage	p-value
18-29 years	20.7	18.8	19.6	<0.0001
30-39 years	29.7	27.6	28.4	
40-49 years	29.6	30	29.9	
50-59 years	16.8	19.7	18.5	
≥60 years	3.2	3.9	3.6	
Social class I	6.9	4.9	5.7	<0.0001
Social class II	23.4	14.9	18.4	
Social class III	69.7	80.3	75.9	
Non smokers	67.2	66.6	66.9	<0.0001
Smokers	32.8	33.4	33.2	

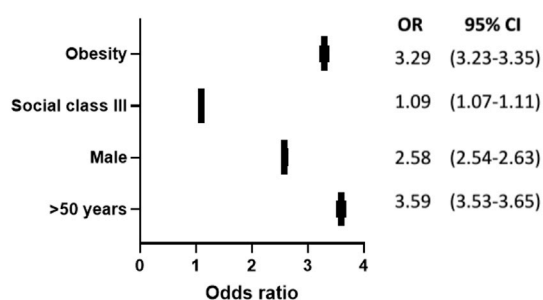
Table II: Mean values of systolic and diastolic blood pressure according body mass index values by sex.

	Men					Women				
	n	SBP		DBP		n	SBP		DBP	
		Mean (SD)	p-value	Mean (SD)	p-value		Mean (SD)	p-value	Mean (SD)	p-value
Underweight	240	118.0 (13.8)	<0.0001	70.3 (9.6)	<0.0001	560	108.6 (13.0)	<0.0001	67.7 (9.0)	<0.0001
Normal	9,153	123.4 (13.8)		73.8 (9.9)		8,866	113.8 (13.9)		70.3 (9.5)	
Overweight I	4,819	127.4 (14.3)		77.4 (10.2)		2,281	118.8 (15.0)		73.4 (10.1)	
Overweight II	5,220	130.6 (15.1)		80.0 (10.5)		2,481	121.4 (15.7)		75.1 (10.3)	
Obesity I	3,606	134.8 (16.1)		82.8 (10.8)		1,846	125.0(16.4)		77.3 (10.5)	
Obesity II	863	138.9 (17.0)		85.2 (11.2)		632	128.5 (17.3)		79.6 (11.1)	
Obesity III	252	143.2 (18.2)		87.9 (11.7)		240	132.1 (18.1)		81.8 (11.2)	
Obesity IV	17	149.4 (19.3)		91.4 (12.4)		17	136.0 (21.1)		84.2 (12.8)	

Table III: Prevalence of values of blood pressure according body mass index values by sex.

	Men								p-value
	Underweight	Normal weight	Overweight I	Overweight II	Obesity I	Obesity II	Obesity III	Obesity IV	
	n=240	n=9,153	n=4,819	n=5,220	n=3,606	n=863	n=252	n=17	
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	
Normal	49.5 (49.1-49.9)	31.5 (31.4-31.6)	20.8 (20.7-20.9)	14.4 (14.3-14.5)	9.2 (9.0-9.4)	5.7 (5.5-6.0)	3.8 (3.4-4.2)	1.2 (0.8-1.6)	<0.0001
Prehypertension	42.5 (42.1-42.9)	53.5 (53.4-53.6)	55.3 (55.2-55.3)	52.9 (52.8-53.0)	46.2 (46.0-46.5)	38.8 (38.6-39.0)	30.4 (30.0-30.8)	22.4 (21.7 (23.1)	
Hypertension I	6.8 (6.5-7.1)	12.7 (12.6-12.8)	19.6 (19.5-19.7)	25.5 (25.4-25.6)	32.4 (32.2-32.6)	37.5 (37.3-37.7)	39.9 (39.5-40.3)	36.2 (35.5-36.9)	
Hypertension II	1.2 (1.0-1.4)	2.3 (2.2-2.3)	4.4 (4.3-4.4)	7.2 (7.1-7.3)	12.2 (12.0-12.4)	18.0 (17.8-18.2)	25.9 (25.5-30.3)	40.2 (39.4-41.0)	
	Women								p-value
	n=560	n=8,866	n=2,281	n=2,481	n=1,846	n=632	n=240	n=17	
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	
Normal	74.4 (74.2-74.6)	61.4 (61.3-61.5)	46.0 (45.9-46.1)	38.7 (38.5-38.9)	28.8 (28.6-29.0)	21.4 (21.1-21.7)	14.4 (14.0-14.8)	13.1 (12.1-14.2)	<0.0001
Prehypertension	22.7 (22.5-22.9)	32.3 (32.2-32.4)	41.3 (41.2-41.4)	44.3 (44.1-44.5)	47.8 (47.6-48.0)	47.2 (46.9-48.5)	45.8 (45.3-46.3)	36.6 (35.4-37.8)	
Hypertension I	2.5 (2.3-2.7)	5.3 (5.2-5.4)	10.3 (10.2-10.5)	13.7 (13.5-13.9)	18.0 (17.8-18.2)	23.3 (23.0-23.6)	27.0 (26.4-27.6)	29.7 (28.5-30.9)	
Hypertension II	0.4 (0.3-0.5)	1.1 (1.0-1.1)	2.4 (2.3-2.5)	3.3 (3.2-3.4)	5.3 (5.2-5.5)	8.2 (7.9-8.5)	12.8 (12.3-13.3)	20.6 (19.4-21.8)	

Figure 1: Binary logistic regression.



Discussion

The most outstanding results of our study are the increase in the prevalence of arterial hypertension parallel to the increase in BMI, from a prevalence of 2.9% in women and 8% in men with low weight to a prevalence of 60.3% in women and 76.4% in men with type IV obesity. Another interesting fact is that obesity increases the risk of presenting arterial hypertension more than 3 times.

Obesity and the excess distribution of visceral fat produce various alterations at the hormonal, inflammatory and endothelial levels. These alterations stimulate a series of mechanisms that induce hypertension and increase cardiovascular morbidity¹³. Most hypertensive patients are overweight or obese. A study conducted in Finland found that more than 85% of hypertension occurs in subjects with a BMI > 25 kg/m²¹⁴. In the same way that obese subjects have a tendency to develop hypertension, hypertensive subjects appear to be prone to weight gain. Thus, the relationship between obesity and hypertension becomes a “two-way street”, as there is evidence that future weight gain is significantly higher in hypertensive patients than in normotensive subjects¹⁵.

In 2017, a large global analysis was published regarding BMI trends in different counties between 1975 and

2016. During that period, no changes were detected in the BMI of European children, but increased in Central Latin America, Polynesia and Micronesia for these. The prevalence of obesity was greater than 20% in several countries in Polynesia and Micronesia, the Middle East and North Africa, the Caribbean, and the United States¹⁶. For what we believe it is interesting to describe the results of our study population.

Different studies, some older, such as those of Brown et al¹⁷ in the North American population, and other more recent ones, such as those of Hossain¹⁸ in Bangladesh or those of Landi et al¹⁹ in almost 8,000 Italian adults, found an association between BMI and blood pressure values similar to that obtained by us. A Canadian study²⁰ conducted in almost 20,000 persons with an age range similar to ours and another conducted in an exclusively female North American working population²¹ also with ages similar to ours also found a positive association between BMI values and blood pressure figures. The same occurs with a study published on the Chinese population, in a sample of 15,296 participants over 15 years of age. It also showed a correlation between BMI and VAI (Visceral adiposity index with prehypertension and hypertension, BFP (Percentage of body fat) with prehypertension and abdominal obesity with hypertension²². A recent Pakistani study²³ conducted in a young population (mean age 33.5 years) also found a relationship between BMI and arterial hypertension.

Strengths and limitations

The strengths of the study include the large sample size in both men and women and the inclusion of the effect of social class in the multivariate analysis. The most important limitations of the study are that the study population is a working population between 18 and 69 years of age, which means that persons aged 70 years and older are not represented, and that the study was carried out in the Ukrainian population, which could make it difficult to extrapolate the results to other geographical settings.

Conclusion

There is a close relationship between BMI values and systolic and diastolic blood pressure values in this group of workers.

Interests conflict

The researchers declare that they have no conflict of interest.

References

- Menéndez E, Delgado E, Fernández-Vega F, Prieto MA, Bordiú E, Calle A, et al. Prevalence, Diagnosis, Treatment, and Control of Hypertension in Spain. Results of the Di@bet.es Study. *Rev Esp Cardiol*. 2016 Jun;69(6):572-8.
- Martins D, Tareen N, Pan D, Norris. The relationship between body mass index and pulse pressure in older adults with isolated systolic hypertension. *Am J Hypertens*. Executive summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of high blood cholesterol in adults (Adult treatment panel III). *JAMA*; 285:2486-97.2002;15 :538-43.
- Busquets Cortés C, Aguiló Juanola MC, González San Miguel HM, Siquier Homar PJ, López Roig C, López-González AA. Are risk factors and cardiovascular risk scales controlled in hypertensive patients under treatment? *Academic Journal of Health Sciences* 2021; 36(4):125-135
- Montero JC. Epidemiología de la obesidad en siete países de América Latina. *Form contin nutr obes* 2002; 342:1-8.
- Van den Hoogen PCW, Feskens EJM, Nagelkerke NJD y col. The relation between blood pressure and mortality due to coronary heart disease among men in different parts of world. *N Eng J Med* 2000; 342:1-8.
- Bender R, Jockel KH, Richter B, Spraul M, Berger M. Body weight, blood pressure and mortality in a cohort of obese patients. *Am J Epidemiol* 2002;156 (3): 239-45.
- Eberhardt R, Coffman JD. Cardiovascular Morbidity and Mortality in peripheral arterial disease. *Curr brg targets Cardiovascular Heematol Disord* 2004 Sep; 4(3): 209-17.
- Girerd X, Giral P. Risks ratification for the prevention of cardiovascular complications of hypertension. *Curr Med Des Opin*. 2004 Jul;20 (7): 1137-42.
- Douketis JD, Sharma AM. Obesity and Cardiovascular disease: pathogenic mechanisms and potential benefits of weight reduction. *Seminary Vascular Medicine* 2005. Feb; 5(1): 25-33
- Salas-Salvadó J, Rubio MA, Barbany M, Moreno B and Grupo Colaborativo de la SEEDO. Consenso SEEDO 2007 para la evaluación del sobrepeso y la obesidad y el establecimiento de criterios de intervención terapéutica. *Med Clin (Barc)* 2007;128(5):184-96
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. *JAMA* 2003;289(19):2560-71.
- 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
- Poulter NR, Prabhakaran D, Caulfield M. Hypertension. *Lancet*. 2015;386(9995):801-12.
- Kastarinen MJ, Nissinen AM, Vartiainen EA, Jousilahti PJ, Korhonen HJ, Puska PM, Tuomilehto J. Blood pressure levels and obesity trends in hypertensive and normotensive Finnish population from 1982 to 1997. *J Hypertens* 2000; 18: 255-62.
- Julius S, Valentini M, Palatini P. Overweight and hypertension: a 2-way street? *Hypertension* 2000; 35: 807-13.
- NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: A pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017; 390(10113): 2627-42.
- Brown CD, Higgins M, Donato KA, Rohde FC, Garrison R, Obarzanek E, et al. Body mass index and the prevalence of hypertension and dyslipidemia. *Obes Res*. 2000 Dec;8(9):605-19
- Hossain FB, Adhikary G, Chowdhury AB, Shawon MSR. Association between body mass index (BMI) and hypertension in south Asian population: evidence from nationally-representative surveys. *Clin Hypertens*. 2019 Dec 15;25:28.
- Landi F, Calvani R, Picca A, Tosato M, Martone AM, Ortolani E, et al. Body Mass Index is Strongly Associated with Hypertension: Results from the Longevity Check-up 7+ Study. *Nutrients*. 2018 Dec 13;10(12):1976.
- Aronow WS. Association of obesity with hypertension. *Ann Transl Med*. 2017 Sep; 5(17): 350.
- Huang Z, Willett WC, Manson JE, et al. Body weight, weight change, and risk for hypertension in women. *Ann Intern Med* 1998;128:81-8.
- Hu L, Huang X, You C, Li J, Hong K, Li P, Wu Y, Wu Q, Bao H, Cheng X. Prevalence and Risk Factors of Prehypertension and Hypertension in Southern China. *PLoS One*. 2017 Jan 17;12(1):e0170238. doi: 10.1371/journal.pone.0170238. eCollection 2017.
- Ahmed H, Thaver IH. Hypertension and obesity in community of Nain-Sukh. *J Pak Med Assoc*. 2020 Apr;70(4):482-487.

The epidemiological and preventive situation in Spain of causal human papilloma virus cancers

Situación epidemiológica y preventiva en España de los cánceres causados por el virus del papiloma humano

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Abstract

The epidemiological circumstances in Spain of the oncogenic action of the human papilloma virus –3,376 cancers/year– and the primary and secondary preventive actions recommended and in application in Spain of these oncological pathologies are presented and discussed.

Keywords: Cancer, epidemiology, prevention, papilloma, virus.

Resumen

Se presentan y discuten las circunstancias epidemiológicas en España de la acción oncogénica del virus del papiloma humano –3.376 cánceres/año– y las acciones preventivas primarias y secundarias recomendadas y en aplicación en España de estas patologías oncológicas.

Palabras clave: Cáncer, epidemiología, prevención, virus del papiloma.

Epidemiology

Data for the year 2021 from the Cancer Observatory (CaOb) of the Spanish Cancer Association (SCA)¹ report that during the reference year, 285,530 cancers were diagnosed in Spain, 165,848 in men and 119,682 in women.

The human papillomavirus (HPV) maintains a causal relationship with all cervical cancers, with 90% of anal cancers, with 70% of vaginal cancers, with 40% of vulva and penis cancers, and with 30% of the oro-pharynx².

The SCA CaOb registers for the year 2021 the incidence numbers in Spain of these cancers with the possibility of being HPV dependent which are summarized in **table I**. There are no data on the incidence of anal cancer in Spain: Spanish data available add cancer colon, rectum and anus³, but the estimate of the Catalan Institute of Oncology⁴ is that between 350 and 400 are diagnosed per year.

Table I

Cancer	Cases
Cérvix	1.958
Oro-pharynx	1.203
Vulva	1.025
Penis	513
Anus	375
Vagina	151

Taking into consideration all these figures and relating them, the data expressed in **table II** are concluded, such as the causal HPV cancers that have been diagnosed in Spain in 2021.

Table II

Cáncer	Cases HPV +
Cervix	1.958
Oro-pharynge	360
Vulva	410
Penis	205
Anus	338
Vagina	105

A total of 3,376 cancers caused by HPV infection have been diagnosed in 2021 in Spain. This is a firm etiological relationship, neither estimated nor speculative, which places HPV as the second identified external cause of cancer, after smoking and slightly above sunlight and other types of radiation⁵.

What is the trend of this incidence?

If the figures for 2012 are consulted 1, the global figures are 250,383 cancers diagnosed in Spain, 143,320 in men and 107,064 in women. For causal HPV cancers, the result is expressed in **table III**, except for anal cancer for the reasons mentioned above.

Table III

Cancer	Cases
Cervix	1.883
Oro-pharynge	1.065
Vulva	1.080
Penis	491
Vagina	139

If we apply the HPV causality percentages to these numbers, as was done previously for 2021, the result is detailed in **table IV**.

Table IV

Cancer	Cases
Cervix	1.883
Oro-pharynge	319
Vulva	432
Penis	196
Vagina	97

Comments

A 14% increase in the total number of cancers, which in the case of those caused by HPV infection lead to a significant increase in cases of cervical and oropharyngeal cancer, and with similar figures, with slight variations, for the other cancers. Based on the following considerations, prevention work seems to be a priority, as a second preventive oncological action, behind the much-needed social, political and medical fight against smoking, the first cause of cancer identified⁶: 8 million smokers in Spain, with 52,000 deaths caused.

Prevention

Primary

Understood as the procedure that eliminates the cause of cancer, the primary prevention of the cancers in question will be to avoid HPV infection.

Knowing that HPV transmission occurs basically through sexual contact⁷, the use of a male condom will be the first measure to be proposed and adopted, given the

evidence that its use⁸ considerably reduces the risk of contagion, although not totally, by 70%.

The most effective, efficient and safe way to prevent infection by HPV is vaccination against it. Currently there is a nonavalent vaccine –Gardasil9®– which guarantees according to its summary products characteristics⁹ a greater than 97% prevention capacity for each of the HPV cancers that originate, under highly secure application conditions.

The coverage of HPV vaccination in Spain¹⁰, applied to girls aged 11-14 within the Public Health program, is 79%, with a range that ranges from 71% in Madrid to 91% in La Rioja and without including the data for Asturias, the Balearic Islands and the Canary Islands. The coverage in preventive-care recommendation in women between 15 and 55 years of age is 4%, with a very slight tendency to increase annually¹¹.

Comments

Establishing sex education programs and facilitating access to condoms in some simple way are two political-social actions that we consider very necessary. The beginning of sexual relations in Spain is located around 15-16 years¹². This legislative and educational action would aim not only to avoid and / or control sexually transmitted diseases, but also to avoid the personal, family and medical drama that almost it is always an unwanted pregnancy in adolescents, which in Spain represent 3% of deliveries, an increasing figure¹³.

The level of vaccination coverage against HPV is satisfactory, at a level that allows to achieve herd immunity¹⁴. However, in line with the most current recommendations in application in neighboring countries, two actions should be recommended:

- Active rescue of unvaccinated women up to 26 years of age.
- Incorporation of men into vaccination programs.

The efficacy of Gardasil9® is documented without gender difference and from 9 years of age, with no upper limit⁹. Capturing 30% of unvaccinated women to offer them the undoubted benefits of vaccination is a task of great health impact, as well as incorporating boys into HPV vaccination, in order to cut off the main source of HPV transmission to women and to protect them from causal HPV cancers^{15,16}. The SCA is preparing a document of position¹⁷ that will be forwarded to the Ministry of Health, requesting that children be vaccinated against HPV, in which it is recalled that more than 50 countries in the world have already made this decision.

Secondary

In Spain, secondary preventive regulations related to recommendations for the early diagnosis (screening) of

cancer, issued by the Ministry of Health¹⁸ (Order SCB / 480/2019), include cervical, female breast and colon cancer, for be the only three that meet the conditions dictated and published by the European Union in the year 2000¹⁹, which have not been modified.

The current recommendation in Spain 18 on the prevention of cervical cancer is specified as follows:

- Target population: women between the ages of 25 and 65.
- Primary screening test and interval between examinations:
 - 25-34 years: Cytology every 3 years.
 - 35-65 years: Determination of high-risk HPV (HPV-HR).
 - If HPV-HR Negative: Repeat HPV- HR test at 5 years.
 - If HPV-HR positive: Triage with cytology. If HPV-HR positive and cytology negative: repeat HPV-HR one year.
- The Autonomous Communities and Cities have 5 years to initiate the change in the program and 5 more years to achieve coverage close to 100% of the population.

The current situation in Spain can be summarized as follows²⁰:

- They do not communicate news about updating programs: Balearic Islands, Valencian Community, Asturias, Cantabria, and Extremadura.
- Budgeting and looking for options: Canary Islands.
- With poblational screening pilot programs: Galicia and Andalusia.
- Trying to agree on strategies: Catalonia, Madrid.
- Resuming previous programs suspended by the pandemic: La Rioja.
- Poblational screening trying to improve them: Castilla y León and the Basque Country.
- Screened with local initiatives: Aragón.
- Evolving to poblational screening: Castilla La Mancha, Murcia, Navarra.

There are no public application programs for secondary prevention of the other HPV-dependent cancers in progress or in the project.

Comments

- The criterion that cervical cancer is not an oncological priority for Public Health can be accepted. It is the breast and the prostate, more incidents in women and men, respectively, the colon, more population incident, and the lung, the one with the highest mortality. Tumors with low incidence but very high mortality could be added to the list, cancers of the central nervous system (glioblastomas) or of the pancreas¹, of

which we do not know their oncogenic history and, consequently, we do not have at the moment of preventive or diagnostic capacity early^{21,22}. Cervical cancer occupies the 22nd place in the cancer incidence classification in 2021¹, 1,958 cases, which have caused 676 deaths, also number 22 on the list.

Comparing 2012 with 2021, a slight increase in its frequency is observed, bad news and even more so if we remember that it is a cancer that the World Health Organization has declared the first with a certain possibility of being eradicated²³, as has been the case of our socio-sanitary world infections such as polio or smallpox. The joint application of highly effective strategies of primary prevention –vaccination against HPV– and secondary – redesigned poblational screening– does it, it should make it possible. If we do not do it –and it is also a warning from the WHO²³– cervical cancer will present a 30% increase in its incidence by 2030.

- In the registries that record it, anal cancer shows a consolidated tendency to increase its incidence and mortality²⁴, both in women and in men. Maintaining anal sex is a circumstance that increases the risk, but not doing so does not eliminate it²⁵. High-quality information highlights that anal cytology and / or HPV determination, followed by high-resolution anoscopy, offer very good efficacy in preventive control and in the early diagnosis of anal cancer²⁶, a cancer with an established and detectable oncogenic history, very similar to that of cervical cancer, low and high grade intraepithelial lesions of the anus²⁷. All this information will make it feasible and necessary in the near future incorporate into clinical practice and Public Health policies regulated strategies for the secondary prevention of anal cancer, reinforcing the primary prevention that vaccination against HPV has already demonstrated⁹.
- One in three oro-pharyngeal cancers is causal HPV: its natural history and oncogenic process have not been established, although its relationship is, in addition to HPV infection, smoking, alcoholism and poor oral hygiene²⁸. The calls for attention in the medical literature follow one another, demanding attention to this pathology, which still does not receive, in general terms, the necessary investigative and healthcare attention²⁹, to correct the increasing trend that the comparison 2012 - 2021 shows
- Preventive procedures for cancers of the vulva and vagina, which are causative HPV in a high proportion, are well established. The Spanish Association of Cervical Pathology and Colposcopy has done, does and will surely do a great job in promoting clinical practice guidelines in this regard^{30,31}. The impact that this educational work

is going to have will be reflected in the incidence rates of these two cancers recorded in the registries. The aforementioned data points to a slight decrease and, therefore, to an initial success of this initiative.

In short, and as described and proposed very recently³², it is

urgent to establish adequate preventive mechanisms in our environment for the prevention of HPV-dependent cancers, a group of cancers that represent a serious health problem.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Available in <https://observatorio.contraelcancer.es/Access> 03.12.2021.
2. Li Y, Xu C. Human Papillomavirus-Related Cancers. *Adv Exp Med Biol.* 2017; 1018: 23-4.
3. Available in https://seom.org/images/Cifras_del_cancer_en_España_2021.pdf Access 03.12.2021.
4. Instituto Catalán de Oncología: Presented in EUROGIN 2018.
5. Available in <https://www.cancer.org/es/cancer/causas-del-cancer.html> Access 04.12.2021.
6. Available in <https://observatorio.contraelcancer.es/informes/informe-dinamico-tabaco> Access 04.12.2021.
7. Kjaer SK, Chackerian B, van den Brule AJ, Svare EI, Paul G, Walbomers JM, et al. High-risk human papillomavirus is sexually transmitted: evidence from a follow-up study of virgins starting sexual activity (intercourse). *Cancer Epidemiol Biomarkers Prev.* 2001; 10: 101-6.
8. Pierce Campbell CM, Lin H-Y, Fulp W, Papenfuss MR, Salmerón JJ, Quiterio MM, Lazcano-Ponce E, et al. Consistent condom use reduces the genital human papillomavirus burden among high-risk men: the HPV infection in men study. *J Infect Dis* 2013; 208:373-84.
9. Available in https://cima.aemps.es/cima/dochtml/ft/1151007002/FT_1151007002.html Access 04.12.2021.
10. Available in <https://www.mscbs.gob.es/profesionales/saludPublica/prevPromocion/vacunaciones/calendario-y-coberturas/coberturas/docs/Tabla11.pdf> Access 04.12.21.
11. Ramírez M, de la Fuente J, Andía D, Hernández JJ, Fiol G, Tomé A. Cobertura de vacunación VPH en mujeres entre 15-55 años en España. Tendencia temporal en el periodo 2007-2020. Presented to XXXIII Congreso de la Asociación Española de Patología Cervical y Colposcopia. Málaga. 11-13 November 2021.
12. Available in https://www.mscbs.gob.es/profesionales/saludPublica/prevPromocion/promocion/saludJovenes/estudioHBSC/docs/HBSC2018/HBSC2018_ConductaSexual.pdf Access 04.12.21.
13. Available in https://sego.es/mujeres/Embarazo_adolescencia.pdf Access 04.12.2021.
14. Marra F, Cloutier K, Oteng B, Marra C, Ogilvie G. Effectiveness and cost effectiveness of human papillomavirus vaccine: a systematic review. *Pharmacoeconomics* 2009; 27: 127-47.
15. Laprise JF, Chesson HW, Markowitz LE, Drolet M, Martin D, Bénard E, et al. Effectiveness and Cost-Effectiveness of Human Papillomavirus Vaccination Through Age 45 Years in the United States. *Ann Intern Med.* 2020; 172: 22-9.
16. Dilley S, Miller KM, Huh WK.: Human papillomavirus vaccination: Ongoing challenges and future directions. *Gynecol Oncol.* 2020; 156: 498-502.
17. Cortés J, Gil A, Martínón, F, Bosch FX, Fernández- Marcos A, Ramón y Cajal JM. Asociación Española contra el Cáncer: La vacunación frente al virus papiloma humano en varones. Situación y propuestas. In press.
18. BOLETÍN OFICIAL DEL ESTADO Núm. 101. Sábado 27 de abril de 2019 Sec. I. Pág. 43021. Available in <https://boe.es/boe/dias/2019/04/27/pdfs/BOE-A-2019-6277.pdf> Access 04.12.2021
19. Recommendations on cancer screening in the European Union. Advisory Committee on Cancer Prevention. *Eur J Cancer.* 2000; 36: 1473-8.
20. Andía D.: Situación actual del cribado de cáncer de cérvix en España. Presented at XXXIII Congreso de la Asociación Española de Patología Cervical y Colposcopia. Málaga. 11-13 Noviembre 2021.
21. Tan AC, Ashley DM, López GY, Malinzak M, Friedman HS, Khasraw M. Management of glioblastoma: State of the art and future directions. *CA Cancer J Clin.* 2020; 70: 299-312.
22. Cooperman AM, Iskandar ME, Wayne MG, Steele JG. Prevention and Early Detection of Pancreatic Cancer. *Surg Clin North Am.* 2018; 9 8:1-12.
23. Ghebreyesus TA, Director. WHO Executive Meeting. Intercontinental Hotel, Geneva, 19 May 2018.
24. Heer E, Hackl M, Ferlitsch M, Waldhoer T, Yang L. Trends in incidence of anal cancer in Austria, 1983-2016. *Wien Klin Wochenschr.* 2020; 132: 438-43.
25. Heywood W, Smith AM. Anal sex practices in heterosexual and male homosexual populations: a review of population-based data. *Sex Health.* 2012; 9: 517-26.
26. Bull-Henry K, Morris B, Buchwald UK. The importance of anal cancer screening and high-resolution anoscopy to gastroenterology practice. *Curr Opin Gastroenterol.* 2020; 36: 393-401.
27. Limoges-Gonzalez M, Al-Juburi A.J.. Anal Intraepithelial Neoplasia. *Clin Gastroenterol.* 2017; 51: 203-7.
28. Chimenos-Küstner E, Marques-Soares MS, Schemel-Suárez M. Aetiopathology and prevention of oropharyngeal cancer. *Semergen.* 2019; 45: 497-503.
29. You EL, Henry M, Zeitouni AG. Human papillomavirus-associated oropharyngeal cancer: review of current evidence and management. *Curr Oncol.* 2019; 26: 119-23.
30. Available in https://www.aepcc.org/wp-content/uploads/2019/01/AEPCC_Guia_VIN_ok.pdf Access 05.12.2021 .
31. Available in https://www.aepcc.org/wp-content/uploads/2016/03/AEPCC_revista05-ISBN.pdf Access 05.12.2021.
32. Ghebre R, Berry-Lawhorn JM, D'Souza G. State of the Science: HPV-Related Malignancies. *Am Soc Clin Oncol Educ Book.* 2021; 41: 1-12.

The role of environmental factors and molecular genetics diagnosis in treatment of breast cancer in Iran, Qom (2019-2020)

El papel de los factores ambientales y el diagnóstico de genética molecular en el tratamiento del cáncer de mama en Irán, Qom (2019-2020)

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Abstract

Cancer is one of the leading causes of death and disability worldwide, especially in developing countries. Development is considered. In most cases, cancer is not because of the person's innate biology, but because of the environment in which the person lives are created. In this study, the available evidence on the role of environmental factors and how they affect the incidence of cancer has been reviewed. BRCA1 and BRCA2 are the two most important high-risk genes for hereditary breast cancer. A significant proportion of familial breast cancer is caused by mutations in the CHEK2 gene. Other gene susceptibility alleles are also uncommon causes of breast cancer. More than 1000 mutations in BRCA1 and BRCA2 have been found, and molecular techniques for detecting mutations in these genes are now well established. Mutations in BRCA1 and BRCA2 generate genomic instability, which leads to changes in other important genes, such as tumor suppressor genes and/or oncogenes. In the near future, there is the possibility of personalizing treatment plans for individual women. The discovery of miRNAs as gene expression regulators establishes them as a novel candidate for diagnostic and prognostic markers, as well as therapeutic targets. Information related to crime victims Cancer patients during the years 2019 to 2020 in Iran in Qom city. It was recorded that it has been collected and has been analyzed and analyzed. In this review the PARS codes. They are used as diagnostic codes for breast cancer are ICD of 10 C50. The number of registered breast cancers during these three years was 399. The number of registered breast cancers during these three years has been 399.

Keywords: Cancer, breast, molecular genetics, diagnosis, treatment.

Resumen

El cáncer es una de las principales causas de muerte y discapacidad en todo el mundo, especialmente en los países en desarrollo. Se considera el desarrollo. En la mayoría de los casos, el cáncer no se debe a la biología innata de la persona, sino al entorno en el que vive. En este estudio, se ha revisado la evidencia disponible sobre el papel de los factores ambientales y cómo afectan la incidencia del cáncer. BRCA1 y BRCA2 son los dos genes de alto riesgo más importantes para el cáncer de mama hereditario. Una proporción significativa de cáncer de mama familiar es causada por mutaciones en el gen CHEK2. Otros alelos de susceptibilidad genética también son causas poco frecuentes de cáncer de mama. Se han encontrado más de 1000 mutaciones en BRCA1 y BRCA2, y las técnicas moleculares para detectar mutaciones en estos genes están ahora bien establecidas. Las mutaciones en BRCA1 y BRCA2 generan inestabilidad genómica, lo que conduce a cambios en otros genes importantes, como los genes supresores de tumores y / o los oncogenes. En un futuro próximo, existe la posibilidad de personalizar los planes de tratamiento para mujeres individuales. El descubrimiento de los miARN como reguladores de la expresión génica los convierte en un nuevo candidato para marcadores de diagnóstico y pronóstico, así como dianas terapéuticas. Información relacionada con víctimas de delitos Pacientes con cáncer durante los años 2019 a 2020 en Irán en la ciudad de Qom. Se registró que se ha recogido y ha sido analizado y analizado. En esta revisión los códigos PARS. Se utilizan como códigos de diagnóstico para el cáncer de mama son ICD de 10 C50. El número de cánceres de mama registrados durante estos tres años fue de 399. El número de cánceres de mama registrados durante estos tres años ha sido de 399.

Palabras clave: Cáncer, seno, genética molecular, diagnóstico, tratamiento.

Introduction

Breast cancer is one of the most common cancers women. The risk of developing this cancer in a lifetime is 10% for women. This cancer in developing countries Found about 10% of all cancers and 23% of cancers Women make up more than 15% of healthy women At least one person with breast cancer in relatives Have first degree and experimental data show that the risk of breast cancer in these women is doubled This cancer is the second deadliest cancer among women. after lung cancer Breast cancer is one of the most common and worrying women's health problems in the world¹. Today, many efforts are made to increase the rate Mortality from breast cancer through procedures reduce early detection. If diagnosed This cancer can be treated in a timely manner It largely prevented breast cancer. Proper screening, however, can slow the progression of cancer Stop, but usually in advanced types of cancer, Treatment is ineffective. Overall cancer result combination of different factors including: hereditary mutations and is an environmental factor, the main cause of cancer, Defects in genes are more monotonous or occurs spontaneously in somatic cells². Although genetic factors play a role in the development of cancer. According to research, as much as environmental factors are not decisive, significant and rapid changes in updates Cancer can only be exposed to change over the past few decades.

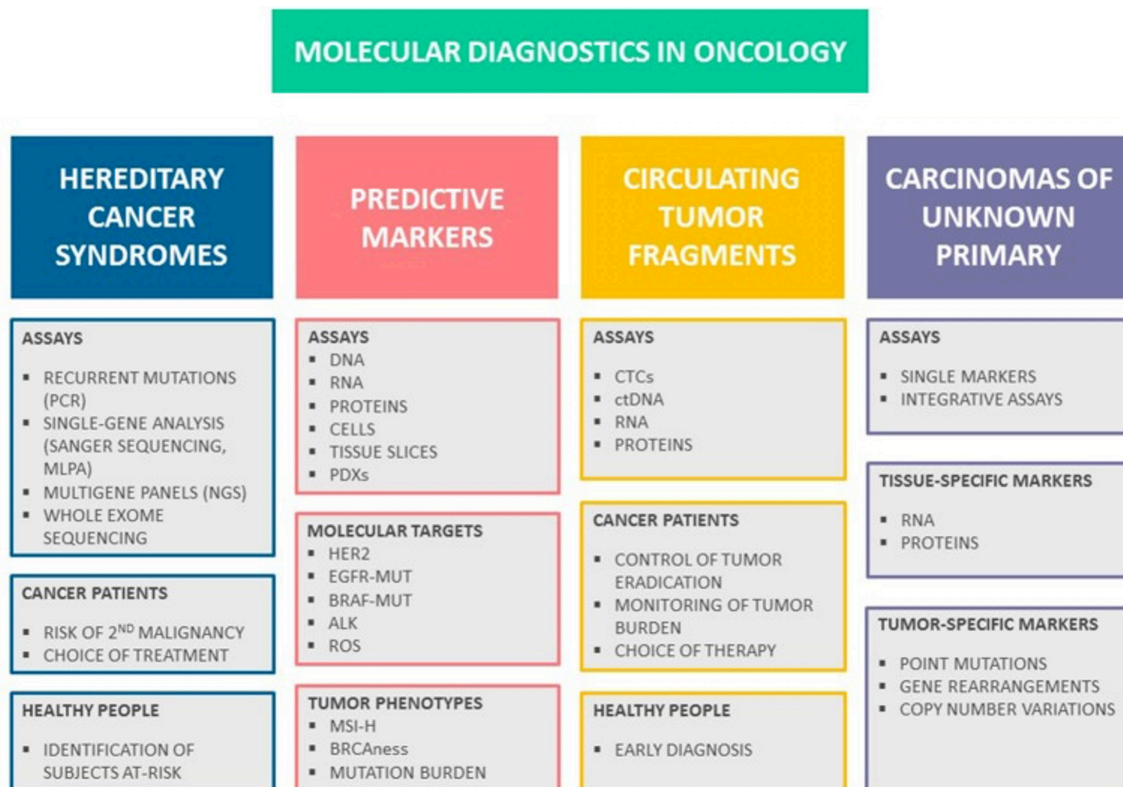
Population is attributed to environmental factors Numerous environments are known to cause Cancer in humans. However, such assumptions are often without Being able to provide convincing evidence or proof of acceptance or their rejection has been delayed for several years or decades. This has led to serious criticisms of environmental epidemiology³.

There are several major avenues in cancer medicine, which utilize molecular-based assays. Testing for hereditary cancer syndromes is now routinely used both for identification of persons at-risk and for personalization of systemic treatment.

Although the genes responsible are often cancerous Breast families have not yet been discovered, about half of Familial cancers due to mutations in the reproductive lineage (Tumor suppressor genes) Tumor suppressor genes It often occurs that their role is to maintain correctness and (TSGs) The whole is the genome⁴. These genes include the following:

- a. BRCA2, BRCA Genes
- b. Related to the family cancer syndrome TSGs
Other ATM and PTEN, rare TP like 53
- c. Other low to medium risk genes such as
2 RAD50, NBS1, PALB2, BRIP1 Such as
(mismatch)
- d. awkward open repair genes of the pair

Figure 1: Molecular diagnostics in oncology.



BRCA2 and BRCA1 genes, respectively 13 are located and the component q is 12-17 and 13 q are 12-chromosome 21 Conventional genes are considered tumor suppressors because Existence of a copy of a defective gene inherited for It is enough to be prone to cancer, even if it is a loss A healthy allele is needed to make a tumor. These genes are proteins large companies encrypt multiple jobs that are spatial Multiple linkages for protein-protein interactions It has three main functional areas and is in BRCA. Gene 1 Participates in several protein complexes. Not yet clear BRCA does not know which of the many functions 1 Its specific role as a gene predisposes to breast and ovarian cancer^{5&6}.

Materials and methods

In a general definition, the environment refers to all non-genetic factors and lifestyle factors such as usage tobacco, biological agents such as hepatitis viruses, drugs, Nutrition includes occupational exposure and other factors. but in A more limited definition, the environment includes all non-genetic factors that a person is not able to directly control them or in other words, it does not depend on the direct choice of the individual. Information related to crime victims Cancer patients during the years 2019 to 2020 in Qom. It was recorded that it has been collected and has been analyzed and analyzed. In this review the PARS codes They are used as diagnostic codes for breast cancer. ICD of 10 C50. The number of registered breast cancers during two years was 399.

Findings

As the most susceptible BRCA and 2 BRCA1 genes Breast cancer is known and several They have cellular functions that include such a vital role in Is homologous. DNA repair proteins DNA plays a vital role in the repair of BRCA and 2 BRCA1 Broken dots have this process. The homologous recombination process is repaired. Thus, inherited mutations in each of these genes are associated with Lack of heterorigocytes, cells into instability Chromosomal and greatly increase the likelihood of change. BRCA and 2 BRCA carriers of mutations in genes 1, 10-20 times more likely to get cancer DNA (They have breasts because of their ability to repair) Two strands of DNA damaged through the repair process Broken down into BRCA and 2 BRCA, genes 1. They belong to the tumor suppressor gene family. Perform this Genes in normal cells, providing stability and help prevent uncontrolled DNA growth Is cellular^{7&8}. As the second most influential gene locus on BRCA gene 2 13 is a length of 10 kb q chromosome 12 There is a genome. This gene has 21 DNA exons Which encodes a 3411 amino acid protein BRCA does. More than 300 types of mutations in gene 2 It has been identified that most of these mutations are of the type C-terminal is the final codon The region is protected with

BRCA in protein 2 Is banded to recombine DSS and 1 ssDNA.) Homolog is required⁹.

Unexplained weight loss, anorexia, fever, fatigue (fatigue Excess), pain, and skin changes are signs of onset Cancers are 4. Along with general symptoms, changes in habits Intestine or bladder function, wound that does not heal, patches White inside the mouth or white spots on the tongue, bleeding or unusual discharge, tightening or mass formation in the breast or other parts of the body, indigestion or difficulty swallowing, any changes New in the skin, annoying cough or hoarseness and ... from Signs and symptoms of certain cancers¹⁰. The incidence of cancer in the world is increasing and the death rate Cancer due to cancer in West Asian countries, including Iran It has an ascent. About 8 million new cancers in the world every year 5 million people die / add to cancer each year and they do. This is while 65% of them are in countries It is developing and, in the meantime, the main burden of cancer in Asia and Southeast Asia. In Iran, about 90 thousand annually Case (140 people per 100,000 population) New infection Cancer is registered and currently 400 thousand people in the country About 30,000 people are diagnosed with cancer each year 6. In other words, 450 patients die annually, shortening the life of the Iranian people for a thousand years^{11&12}.

Based on scientific evidence and documents, the most important risk factors cancer has its roots in high-risk lifestyles and behaviors They are often preventable. International Research Institute, more than 100 human carcinogens IARC cancer. These agents are divided into 4 carcinogenic groups for Humans, potentially carcinogenic to humans, potentially carcinogenic to humans and the possibility of carcinogenesis for humans are classified¹³. Physical activity and nutritional factors people's lifestyle It is the third most important cause of cancer. Diet Inadequate, overweight, and inactivity are contributing factors While research is underway to better understand. They are cancerous the role of these factors in the development of cancer is progressing, new findings show that each of these factors. They can affect the risk of cancer¹⁴. What conclusions about the relationship between exposure to pollutants Environmental problems and cancer in humans' Intrinsic properties associated with the toxicity of these compounds and aspects The methodology of epidemiological research is used. In other words, it can be said that the assessment of exposure and also, the Achilles heel research methodology of all studies Concerning the relationship between environmental pollutants Has been with cancer. Strong design combination of studies, evaluation Advanced exposure rate with better understanding of the mechanism of the disease and the use of exposure biomarkers can reinforce evidence Lead epidemiologically¹⁵.

Results

The median incidence of breast cancer is in the population of tens of thousands, the trend is increasing. 9-11.3-32, respectively 9.3-31- during 31 years 91 out of tens of thousands of women had a female population of 21.9. The median incidence of IT in women is 11.31, respectively. During these three years, breast cancer has been the first most common cancer in women. The average age of the cancer victim was 9.1 years. More than 1. % of the median incidence in the age group of 91 to 33 years. Which is 11 years less than the global hemisphere. Unfortunately, in our country, the peak prevalence of breast cancer among women in the fourth and fifth decades of life Many Pashtuns are a decade lower than the world average. That's why you can watch women Under 31 years of age should be examined for one to two years, and from this age onwards Visit. In fact, from the age of forty onwards, in addition to examinations, mammography (breast imaging) should be performed. Do it annually so that by repeating these tests regularly, breast cancer can be detected in the early stages and advocated for the treatment of rabies. BRCA and 2 BRCA More than 1000 mutations in 1. It is reported that most of them are cut off from this Proteins lead. Today, genetic testing techniques To BRCA and 2 molecular BRCA to find mutations Extensive syntax is used and a variety of techniques are used for A study of the activity of defective proteins has also been developed. Causes instability of BRCA genome and BRCA mutation in 1 It may be due to changes in other key genes Contains tumor suppressor genes or oncogenes^{16&17}.

Compared to diffuse breast cancers, cancer Breast families have special characteristics. Studies The latter using comparative genomic hybridization Comparative genomic Hybridization Along with (DNA microarray) DNA microarray analysis Characteristics of FISH and IHC Safety - Tissue Chemistry Genetics and phenotype show specific immunity for these tumors Data¹⁸ Molecular pathology and biology Together BRCA and 2 BRCA mutation-induced tumors in 1.

BRCA is no longer different. Mutation-related tumors 1 Aggressive features, including early onset, high grade (PR) and progesterone receptor (ER) tumor, estrogen receptor Negative and show high proliferation rate¹⁹. Cell proliferation is an important feature of cancer and protein. A good indicator of this is non-histone nuclear Ki67 It can also be used as a Ki process. Painting 67A reliable indicator of reproductive activity and as a marker Usefulness of treatment, through multiple measurements on Consecutive tissue samples are used during treatment²⁰.

Breast tumors include a heterogeneous group of cells. There is a small part of them called stem cells They form. These cells due to their ability to proliferate in the process of tumor formation, (self-renewal) and self-renewal They are effective. Loss of self-regulatory process regulation an increase in stem cells leads to this problem Probably involved in the early stages of cancer. MiRNAs are capable of simultaneously regulating several target genes They are a good candidate for regulating the process of self-renewal Stem cells and deciding the fate of the cell has done²¹.

Conclusion

In most cases, cancer is not because of the individual's innate biology, but because it is created by the environment in which the person lives. So that a significant share of cancer deaths Especially among men because of smoking. the countries to reduce this mortality, we must focus on prevention Start smoking among working youth and individuals Encourage a smoker to quit. In countries with income Down, especially in Asia and sub-Saharan Africa, A high proportion of cancers are caused by infection. For some cancers in the body, being overweight is a risk Is considered an invoice. Support and training on Sun protection for all members of the community, Family, health care system, schools, workshops, Organizations and mass media are essential. From the case points the focus of such studies is to assess the extent of exposure and Also research methodology on the impact of pollutants Environmental and occupational on the incidence and prevalence of cancer in society It is a problem. DNA and repair of BRCA and 2 BRCA genes 1 A number of breast cancers have a high rate of instability They show a genome. Breast cancer is a heterogeneous disease and has been for years It is believed that tumors that are characteristic They have different biological, clinical outcomes and responses. They have different treatments. Breast cancer based on receptor status is in the tumor. With (ER, PR, HER growth hormone 2) using these markers, four functional groups can be used identified tumors: a. Negative HER Hormone receptor positive and Negative (HER triple tumor b) Negative hormone receptor and negative) With or without HER expression c) Tumors with overexpression Hormone receptor .

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Wiechmann L, Kuerer HM. The molecular journey from ductal carcinoma in situ to breast cancer. *Cancer*.2008; 112: 2130.
2. Berjis K, Ghiasi M, Sangy S. "Health need assessment in female adolescents, in Qom: A cross sectional study." *Journal of education and health promotion* vol. 8 39. 15 Feb. 2019, doi: 10.4103/jehp.jehp_11_18.
3. Cotran RS, Kumar V, Robbins SL, eds. *Pathologic Basis of Disease*, 5th Ed. Philadelphia: W.B. Saunders,1994
4. DeVita VT, Lawrence TS, Rosenberg SA, eds. *Cancer Principles & Practice of Oncology*, 8th Ed. Philadelphia: Lippincott Williams & Wilkins. 2008
5. The World Health Organization histological typing of breast tumors, 2nd ed. The World organization. *Am J Clin Pathol* . 1982; 78: 806.
6. Antoniou AC, Easton DF Models of genetic susceptibility to breast cancer. *Oncogene* 2006; 25: 5898.
7. Zabetian Hoseini M, Nassiri MR, Aslaminejad A, Ghafarzadegan K, Mouseghi A, Ghowati S, et al. Measurement of human progesterone receptor A expression in normal and breast cancer tissue using realtime PCR technique. *Iran J Obstet Gynecol Infertil* 2012;15(1):51-9. (Persian).
8. Rohlfis EM, Puget N, Graham ML, Weber BL, Garber JE, Skrzynia C, et al. An Alu-mediated 7.1 kb deletion of BRCA1 exons 8 and 9 in breast and ovarian cancer families that results in alternative splicing of exon 10. *Genes Chromosomes Cancer* 2000; 28(3):300-7.
9. Casilli F, Di Rocco ZC, Gad S, Tournier I, Stoppa-Lyonnet D. Rapid detection of novel BRCA1 rearrangements in high-risk breast-ovarian cancer families using multiplex PCR of short fluorescent fragments. *Hum Mutat* 2002; 20(3):218-26.
10. Schouten JP, McElgunn CJ, Waaijer R, Zwijnenburg D, Diepvens F, Pals G. Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. *Nucleic Acids Res* 2002; 30(12):e57.
11. Miryousefiata F, Sangy S. Assessing the Correct Understanding of Families about the Occurrence of Marital Cancer (Statistical Population: Denmark, Sweden and Iran), *J. Med. Chem. Sci.*, 2021, 4(1) 60-74 DOI: 10.26655/JMCHEMSCI.2021.1.8 URL: http://www.jmchemsci.com/article_120965.htm
12. Venkitaraman AR. Cancer susceptibility and the functions of BRCA1 and BRCA2. *Cell* 2002; 108(2):171-82.
13. Scully R, Livingston DM. In search of the tumor-suppressor functions of BRCA1 and BRCA2. *Nature* 2000; 408(6811):429-32.
14. Kurian AW. BRCA1 and BRCA2 mutations across race and ethnicity: distribution and clinical implications. *Curr Opin Obstet Gynecol* 2010; 22(1):72-8.
15. Antoniou A, Cunningham A, Peto J, Evans DG, Lalloo F, Narod SA. The BOADICEA model of genetic susceptibility to breast and ovarian cancers: updates and extensions. *Br J Cancer* 2008; 98(8):1457-66.
16. World Health Organization. A review of human carcinogens. Part B: Biological agents: World Health Organization, International Agency for Research on Cancer; 2012. 320-400.
17. Miryousefiata F, Alsadat Miryousefiata F. The effect of Familact probiotic supplement in patients with diabetes (Evaluation of Blood Glucose Parameters, Lipid Profile). *ACADEMIC JOURNAL OF HEALTH SCIENCES*. 2021; 36 (3): 52-63. doi: 10.3306/AJHS.2021.36.03.52 www.medicinabaleaer.org
18. Esposito K, Ciardiello F, Giugliano D. Unhealthy diets: a common soil for the association of metabolic syndrome and cancer. *Endocrine* 2014;46(1): 39-42.
19. Baan R, Straif K, Grosse Y. Carcinogenicity of alcoholic beverages. *Lancet Oncol* 2007;8(4): 292-3.
20. Boffetta P, Hashibe M, La Vecchia C . The burden of cancer attributable to alcohol drinking. *Int J Cancer* 2006;119(4): 884-7.
21. SangyS, Miryousefi Ata F, Miryousefiata F. Study of Thymus and T-cell Development and Tumor Immunology .Budapest International Research in Exact Sciences. 2021; 3,(3) :162-170 DOI: <https://doi.org/10.33258/birex.v3i3.2081>

ORIGINAL

Relationship between different scales related to cardiovascular risk and Finrisk test values in workers

Relación entre diferentes escalas relacionadas con el riesgo cardiovascular y valores del test de Finrisk en trabajadores

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Abstract

Introduction: Cardiovascular diseases are the main cause of death in developed countries and one of the risk factors most closely related to them is diabetes. The aim is to study the relationship between the values of a test that determines the risk of suffering diabetes mellitus and the values of different scales related to cardiovascular risk.

Methods: Cross-sectional study in 59,042 workers in which the values of the Finrisk test were related to the values of some cardiovascular risk scales such as the body shape index, conicity index, visceral adiposity index, Cholindex and hypertriglyceridemic waist among others.

Results: All the scales included in this study increase their values in parallel to the increase in the values of the Finrisk test. This situation occurs in both women and men.

Conclusion: There is a relationship between the values of the Finrisk test and all the scales analyzed in this study.

Key words: Finrisk test, diabetes mellitus, cardiovascular diseases.

Resumen

Introducción: Las enfermedades cardiovasculares son la principal causa de muerte en los países desarrollados y uno de los factores de riesgo que más se relaciona con ellas es la diabetes. El objetivo es estudiar la relación entre los valores de un test que determina el riesgo de sufrir diabetes mellitus y los valores de diferentes escalas relacionadas con el riesgo cardiovascular.

Material y métodos: Estudio transversal en 59,042 trabajadores en los que se relacionan los valores del test de Finrisk con los valores de algunas escalas de riesgo cardiovascular como el índice de forma del cuerpo, índice de conicidad, índice de adiposidad visceral, Cholindex y cintura hipertriglicéridémica entre otros.

Resultados: Todas las escalas incluidas en este estudio van incrementando su valor paralelamente al incremento de los valores del test de Finrisk. Esta situación se produce tanto en las mujeres como en los hombres.

Conclusión: Existe una relación entre los valores del test de Finrisk y todas las escalas analizadas en este trabajo.

Palabras clave: Test Finrisk, diabetes mellitus, enfermedades cardiovasculares.

Introduction

Cardiovascular diseases (CVD) cause great morbidity and mortality both in the developed and undeveloped countries. In recent years 80 percent of deaths from CVD have occurred in countries with medium or low income, and the number is growing¹. The cardiovascular risk (CVR) is defined as the likelihood of an event in a given period, usually 10 years, for its determination generally scales are based on cohort studies are used. Determining the CVR it is based on clinical guidelines that address cardiovascular prevention.

In the occurrence of CVD is influenced by different factors such as tobacco consumption, obesity, dyslipidemia and diabetes. The risk of diabetes can be determined with different scales among which we highlight the FINRISK (FINnish Diabetes Risk Score) questionnaire for being perhaps the most widely used. FINRISK has been successfully implemented as a practical screening instrument to assess diabetes risk and to detect undiagnosed type 2 diabetes in European populations²⁻⁴. However it has also become evident that it is not universally applicable among all ethnic groups and populations^{5,6}.

There are many indexes that help predict CVD from classic Body Mass Index (BMI), waist circumference and waist to height ratio to the most recent Body Adiposity Index (BAI)^{7,8}. There are other indices that could perhaps be useful in predicting these CVD among which are the Body Shape Index (ABSI) at some authors they have linked to an increased risk of cardiovascular mortality⁹, the Visceral Adiposity Index (VAI) which has been linked with visceral fat levels¹⁰, type 2 diabetes¹¹ and coronary artery disease¹², Cholesterol Index (CI) which has been linked with high coronary risk¹⁴ and Hypertriglyceridemic waist (HTGW) has been associated with type 2 diabetes¹⁵, coronary artery disease¹⁶ and even acute myocardial infarction¹⁷.

An analysis of the scientific literature shows that previous indexes have not been used too much in cardiovascular prevention but perhaps can provide valuable information on the assessment of CVR.

For all these reasons, and trying to improve cardiovascular prevention, this study presents the main objective is to determine what relationship exists between FINRISK test values and the values of these indices.

Materials and Methods

Subjects and study protocol

A cross-sectional study with adult workers (ages, 20-69 years) was performed. All subjects were belong

to different productive sectors. Participants in the study were systematic selected during their work health periodic examination between January 2018 and December 2019. Every day each worker was assigned a number and half of the examined workers were randomly selected using a random number table. Thus, from a total population of 130487 workers, 65200 of them were invited to participate in the study. 4402 (6.8%) refused to participate and 1756 (2.8%) they are excluded to be diabetic and not being able to perform the FINRISK test, being the final number of participants 59042 (90.4%), with 25510 women (43.2%) and 33532 men (56.8%). The mean of age of participants in the study was 39.70 years (SD±10.25). All participants were informed of the purpose of this study before they provided written informed consent to participate. Following the current legislation, members of the Health and Safety Committees were informed as well. The study protocol was in accordance with the Declaration of Helsinki and was approved by the relevant research ethics committee. After acceptance, a complete medical history, including family and personal history and FINRISK questionnaire, was recorded. The following inclusion criteria were considered: age between 18 and 70 (working age population), no diabetic, agreement to participate in the study and to be gainfully employed. Subjects who did not meet any of the inclusion criteria and those who refused to participate were excluded from the study.

Measurements and calculations

All anthropometric measurements were made in the morning, after an overnight fast, at the same time (9 a.m.), and according to the recommendations of the International Standards for Anthropometric Assessment (ISAK)¹⁸. Furthermore, all measurements were performed by well trained technicians or researchers to minimize coefficients of variation. Each measurement was made three times and the average value was calculated. Weight and height were determined according to recommended techniques mentioned above. Body weight was measured to the nearest 0.1 kg using an electronic scale (Seca 700 scale, Secagmbh, Hamburg). Height was measured to the nearest 0.5 cm using a stadiometer (Seca 220 (CM) Telescopic Height Rod for Column Scales, Secagmbh, Hamburg). BMI was calculated as weight (kg) divided by height (m) squared (kg/m²). Criteria to define overweight were the ones of the World Health Organization (WHO)¹⁹ which considers obesity when BMI ≥ 30 kg/m². Abdominal waist was measured using a flexible steel tape (Lufkin Executive Thinline W 606). The plane of the tape was perpendicular to the long axis of the body and parallel to the floor. Waist circumference was measured at the level of the umbilicus and superior iliac crest. The measurement was made at the end of a normal expiration while the subject stood upright, with feet together and arms hanging freely at the sides. Waist circumference (WC) was measured using a tapeline at the level midway between the lateral lower rib margin and

iliac crest. Waist-to-height ratio (WtHR) was calculated by dividing WC by height in cm.

Venous blood samples were taken from the antecubital vein with suitable vacutainers without anticoagulant to obtain serum. Blood samples were taken following a 12 h overnight fast. Participants were seated at rest for at least 15 minutes before blood samples were taken. Serum was obtained after centrifugation (15 min, 1,000 g, 4°C) of blood samples. Serum was stored at -20°C and analysis were performed within 3 days. Concentrations of glucose, cholesterol and triglycerides were measured in serum by standard procedures used in clinical biochemistry laboratory using a clinical system Beckman Coulter SYNCHRON CX@9 PRO (Beckman Coulter, Brea, CA, USA).

Blood pressure was determined after a resting period of 10 minutes in the supine position using an automatic and calibrated sphygmomanometer OMRON M3 (OMRON Healthcare Europe, Spain). As indicated for the anthropometrical measures, blood pressure was measured three times with a one-minute gap between each measurement and an average value was calculated.

FINRISK questionnaire value 8 items: age, BMI, waist circumference, physical activity, dietary consumption of fruits, vegetables, and berries, Use of antihypertensive medication, previously measured high blood glucose and family history of diabetes. The maximum achievable score is 26. Less than 7 points is considered low risk, 7-11 point slightly elevated risk, 11-14 points moderate risk, 15-20 points high risk and 21-26 points very high risk.

Real Body shape index (ABSI)⁹ was calculated using the equation:

$$- \text{Waist circumference (cm)} / \text{BMI}^{2/3} \text{ weight}^{1/2} \text{ (kg)}$$

Theoretical ABSI is set based on sex and age. The ratio between real and theoretical ABSI is called ABSI relative risk (ABSI RR). ABSI RR <1 is considered abnormal.

Conicity index(CI)¹⁴ was calculated using the equation:

$$- \text{Waist circumference (m)} / (0,109 \sqrt{\text{weight (kg)/height (m)}})$$

The cut-off to consider high CI were 1.18 for women and 1.25 for men.

Visceral Adiposity Index (VAI)²⁰ was calculated using the equations:

$$\text{Women (Waist circumference } / (39.68 + (1.89 \text{ BMI})) \times (\text{triglycerides} / 1.03) \times (1.31 / \text{HDL-C})$$

$$\text{Men (Waist circumference } / (36.58 + (1.89 \text{ BMI})) \times (\text{triglycerides} / 0.81) \times (1.52 / \text{HDL-C})$$

The cut-off to consider optimal VAI²¹ were < 30 years (≥ 2.52) 30-42 years (≥ 2.23) 43-51 years (≥ 1.92) 52-65 years (≥ 1.93) ≥ 66 years (≥ 2.00)

Cholindex13 was calculated using the equations:

- LDL-C-HDL-C (if triglycerides <400 mg/dl) or LDL-C-HDL-C+TG/5 (if triglycerides ≥ 400 mg/dl)

The cut-off to consider high Cholindex was 80 mg/dl

We believe that there are Hypertriglyceridemic waist (HTGW)¹⁵ when:

- Waist circumference ≥ 88 cm in women and ≥ 102 cm in men and triglycerides ≥ 150 mg/dl.

Statistical analyses

All the data were tested for their normal distribution (Kolmogorov-Smirnov test). Results are expressed as means and standard deviations (SD) and, when required, in percentages. Student t test for unpaired data was used to evaluate differences in anthropometric and biochemical characteristics between genders. Chi-square test was used for the difference of proportions. The existence of significant bivariate correlations between parameters such as ABSI, CI, VAI and Cholindex and FINRISK questionnaire was ascertained by determining Pearson or Spearman correlation coefficients. Statistical analysis was carried out using IBM SPSS Statistics 27.0 software (SPSS/IBM, Chicago, IL, USA). Significance was accepted at $p < 0.05$.

Results

Age and anthropometrical and clinical characteristics of the participants in the study as a whole and categorized by gender are shown in **table I**. Significant differences between men and women were found in all parameters analyzed with higher values of age, anthropometric characteristics (height, weight, body mass index, waist circumference, and waist to height ratio), systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides in men.

The mean values for the different indices according FINRISK questionnaire are shown in **table II**. The ABSI, VAI and Cholindex values in women are worsening in parallel with FINRISK test values, the same applies to men. The Conicity index values behave differently in men and women, in men also they are getting worse with increasing the value of the FINRISK test, however in women no clear relationship with the test was observed.

The prevalence of normal and altered values of the different indices according FINRISK questionnaire values are shown in **table III**. In women, the prevalence of high

VAI, HTGW and high Cholindex is increasing in parallel with the increase in the value of the FINRISK test, in men we can observe the same with high VAI, HTGW, high CI and high Cholindex. ABSI altered shows no clear relationship with the FINRISK questionnaire values in women and men. In women this relationship was not seen with the high CI.

The Pearson correlations between parameters such as ABSI, CI, VAI and Cholindex and FINRISK questionnaire was -0.087 ABSI, 0.242 CI, 0.398 VAI and, 0.329 Cholindex, p-value <0.01.

Discussion

Tanto los valores medios como la prevalencia de valores elevados de todas las escalas analizadas en este estudio van aumentando a medida que lo hacen los valores del test de Finrisk, esta situación se puede apreciar tanto en las mujeres como en los hombres.

Sólo hemos encontrado un estudio que relacione los valores del test de Finrisk con escalas relacionadas con el riesgo cardiovascular como hemos hecho nosotros, aunque no empleando las mismas escalas. Este estudio

Table I: Anthropometric, clinical and analytical characteristics of participants in the study.

Characteristics ¹	Women (n=25,510)	Men (n=33,532)	Total (n=59,042)	p value ¹
Age (years)	39.30 ± 10.10	40.01 ± 10.35	39.70 ± 10.25	<0.0001
Weight (kg)	161.32 ± 6.51	173.94 ± 7.04	168.49 ± 9.25	<0.0001
Height (cm)	64.87 ± 12.94	81.06 ± 13.75	74.06 ± 15.62	<0.0001
BMI (kg/m ²)	24.94 ± 4.84	26.78 ± 4.16	25.98 ± 4.56	<0.0001
Waist circumference (cm)	75.24 ± 9.66	88.37 ± 9.54	82.69 ± 11.59	<0.0001
WtHR	0.47 ± 0.06	0.51 ± 0.06	0.49 ± 0.06	<0.0001
Systolic BP (mmHg)	114.36 ± 14.94	124.91 ± 15.36	120.35 ± 16.06	<0.0001
Diastolic BP (mmHg)	70.29 ± 10.34	75.77 ± 10.74	73.40 ± 10.91	<0.0001
Total cholesterol (mg/dl)	192.78 ± 36.39	196.74 ± 38.63	195.03 ± 37.73	<0.0001
HDL-C (mg/dl)	55.03 ± 9.17	50.68 ± 7.53	52.56 ± 8.56	<0.0001
LDL-C (mg/dl)	120.39 ± 36.92	121.82 ± 37.18	121.20 ± 37.07	<0.0001
Triglycerides (mg/dl)	86.98 ± 43.77	123.24 ± 85.76	107.58 ± 72.99	<0.0001

BMI, Body mass index. WtHR, waist-to-height-ratio. Systolic BP, Systolic blood pressure. Diastolic BP, Diastolic blood pressure. HDL-C, high-density lipoprotein cholesterol. LDL-C, low-density lipoprotein cholesterol.

1. Data are expressed as means ± standard deviation.
2. Statistical significance was estimated by independent t-test

Table II: Mean values of the different indices according FINRISK test.

		n ²	ABSI		CI		VAI		Cholindex	
			Mean (SD)	p value ¹	Mean (SD)	p value ¹	Mean (SD)	p value ¹	Mean (SD)	p value ¹
Women	Low	19,057	0.090 (0.080)	<0.0001	1.08 (0.08)	<0.0001	2.14 (1.09)	<0.0001	60.75 (40.78)	<0.0001
	Slightly raised	4,777	0.091 (0.012)		1.14 (0.14)		3.01 (1.94)		77.08 (41.26)	
	Moderate	1,017	0.088 (0.011)		1.12 (0.13)		3.33 (2.10)		84.26 (40.31)	
	High	643	0.088 (0.012)		1.15 (0.14)		4.15 (2.83)		88.81 (41.27)	
	Very high	16	0.084 (0.090)		1.11 (0.11)		6.06 (3.74)		99.66 (45.81)	
Men	Low	22,465	0.094 (0.070)	0.010	1.17 (0.07)	<0.0001	2.53 (1.63)	<0.0001	66.36 (39.56)	<0.0001
	Slightly raised	8,117	0.094 (0.090)		1.23 (0.11)		4.48 (3.96)		84.35 (43.70)	
	Moderate	1,856	0.093 (0.080)		1.24 (0.10)		5.17 (4.26)		89.74 (44.86)	
	High	960	0.093 (0.090)		1.25 (0.11)		6.28 (5.67)		90.37 (49.95)	
	Very high	134	0.092 (0.080)		1.25 (0.10)		7.14 (5.56)		99.63 (46.40)	

- ABSI, Body shape index. CI, Conicity index.
1. Statistical significance was estimated by independent t-test
 2. Number of participants in the study.

Table III: Cataloging the various indices according on the value of FINRISK test by sex.

	Women					Men					p value
	Low	Slightly raised	Moderate	High	Very high	Low	Slightly raised	Moderate	High	Very high	
High VAI	37.7	66.0	74.6	84.9	93.8	48.7	79.6	86.3	88.2	94.0	<0.0001
Normal VAI	62.3	34.0	25.4	15.1	6.3	51.3	20.4	13.7	11.8	6.0	
HTGW absence	99.9	90.1	85.1	71.2	43.8	98.3	76.6	67.6	57.2	44.0	<0.0001
HTGW presence	0.1	9.9	14.9	28.8	56.3	1.7	23.4	32.4	42.8	56.0	
ABSI Relative Risk altered	89.9	76.7	85.3	81.0	100.0	82.8	74.2	81.6	76.3	84.3	<0.0001
Normal ABSI Relative Risk	10.1	23.3	14.7	19.0	0.0	17.2	25.8	18.4	23.8	15.7	
High Conicity index	11.2	35.1	28.0	39.5	37.5	14.5	41.0	47.7	48.6	48.5	<0.0001
Normal Conicity index	88.8	64.9	72.0	60.5	62.5	85.5	59.0	52.3	51.4	51.5	
High Cholindex	31.0	46.8	51.4	60.2	75.0	34.9	51.9	57.5	54.4	68.7	<0.0001
Normal Cholindex	69.0	53.2	48.6	39.8	25.0	65.1	48.1	42.5	45.6	31.3	

VAI, Visceral Adiposity Index. HTGW, Hypertriglyceridemic waist. ABSI, Body Shape Index.

realizado en población Española determinó los valores de diferentes parámetros antropométricos, clínicos (índice de masa corporal, perímetro de cintura, índice cintura altura, tensión arterial), analíticos (perfil lipídico y glucemia) y escalas relacionadas con riesgo cardiovascular (índices aterogénicos, síndrome metabólico, REGICOR, SCORE, edad del corazón y edad vascular) en más de 68.000 personas y al igual que nosotros observó como todas las escalas aumentaban sus valores a medida que lo hacían los valores del test de Finrisk.

Entre las fortalezas de este estudio destacaremos el gran tamaño de la muestra que supera las 59.000 personas y la variedad de escalas que se han tenido en cuenta.

Como limitación principal es que se ha realizado en

población laboral por lo que se han excluido personas menores de 18 y mayores de 69 años lo que impide extrapolar los resultados a la población general.

Conclusiones

Existe una relación directa entre los valores del test de Finrisk y los valores de todas las escalas relacionadas con el riesgo cardiovascular analizadas en este trabajo, de manera que a medida que se incrementan los valores del test lo hacen también los valores de todas las escalas.

Interests conflict







The researchers declare that they have no conflict of interest.

References

1. Leeder S. A race against time: the challenge of cardiovascular disease in developing economies. Columbia University, New York. 2004.
2. Saaristo T, Peltonen M, Keinänen-Kiukaanniemi S, Vanhala M, Saltevo J, Niskanen L, Oksa H, Korpi-Hyövälti E, Tuomilehto J. FIN-D2D Study Group. National type 2 diabetes prevention programme in Finland: FIN-D2D. *Int J Circumpolar Health*. 2007;66:101-12
3. Soriguer F, Valdes S, Tapia MJ, Esteve I, Ruiz de Adana MS, Almaraz MC, et al. Validation of the FINRISK (FINnish Diabetes Risk SCore) for prediction of the risk of type 2 diabetes in a population of southern Spain. *Pizarra Study. Med Clin (Barc)* 2012;138:371-6.
4. Tankova T, Chakarova N, Atanassova I, Dakovska L. Evaluation of the Finnish Diabetes Risk Score as a screening tool for impaired fasting glucose, impaired glucose tolerance and undetected diabetes. *Diabetes Res Clin Pract*. 2011;92:46-52.
5. Makrilakis K, Liatis S, Grammatikou S, Perrea D, Stathi C, Tsiligros P, Katsilambros N. Validation of the Finnish diabetes risk score (FINRISK) questionnaire for screening for undiagnosed type 2 diabetes, dysglycaemia and the metabolic syndrome in Greece. *Diabetes Metab*. 2011;37:144-51
6. Hippisley-Cox J, Coupland C, Robson J, Sheikh A, Brindle P. Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. *BMJ*. 2009;338:b880.
7. Lopez AA, Cespedes ML, Vicente T, Tomas M, Bannasar-Very M, Tauler P, et al. Body adiposity index utilization in a Spanish Mediterranean population: comparison with the body mass index. *PLoS One*. 2102;7(4):e35281
8. Bannasar-Very M, Lopez-Gonzalez AA, Tauler P, Cespedes ML, Vicente-Herrero T, Yañez A, et al. Body adiposity index and cardiovascular health risk factors in Caucasians: a comparison with the body mass index. *PLoS One*. 2013;8(5):e63999.
9. Krakauer NY, Krakauer JC. A new Body Shape Index predicts mortality hazard independently of Body Mass Index. *Plos One*. 2012;7(7):e39504
10. Mohammadreza B, Farzad H, Davoud K, Fereidoun A. Prognostic significance of the Complex "Visceral Adiposity Index" vs simple anthropometric measures: Tehran lipid and glucose study. *CardiovascDiabetol*. 2012;11:20
11. Al-Daghri NM, Al-Attas OS, Wani K, Alnaamil AM, Sabico S, Al-Ajlan A, et al. Sensitivity of various indices in identifying cardiometabolic disease in Arab adults. *CardiovascDiabetol*. 2015;14:101
12. Patil VC, Parale GP, Kulkarni PM, Patil HV. Relation of anthropometric variables to coronary artery disease risk factors. *Indian Journal of Endocrinology and Metabolism*. 2011; 15(1):31-7.
13. Akpınar O, Bozkurt A, Acartürk E, Seydaoglu G. A new index (CHOLINDEX) in detecting coronary artery disease risk. *AnadolukardiyolDerg*. 2013; 13:315-9.
14. Gondin-Pitanga FJ, Lessa I. Anthropometric indexes of obesity as an instrument of screening for high coronary risk in adults in the city of Salvador-Bahia. *Arquivos Brasileiros de Cardiologia*. 2005;85(1):26-31
15. Amini M, Esmailzadeh A, Sadeghi M, Mehvarfar N, Amini M, Zare M. The association of hypertriglyceridemic waist phenotype with type 2 diabetes mellitus among individuals with first relative history of diabetes. *JRMS*. 2011; 16(2):156-64.
16. Arsenault BJ, Lemieux I, Despres JP, Wareham NJ, Kastelein JJP, Khaw KT, et al. The hypertriglyceridemic-waist phenotype and the risk of coronary artery disease: results from the EPIC-Norfolk Prospective Population Study. *CMAJ*. 2010;182(13):1427-32
17. Egeland GM, Igland J, Nygard O, Sulo G, Tell GS. Hypertriglyceridemic-waist phenotype is a usefull global assessment tool for predicting acute myocardial infarction. *J Cardiovasc Dis Diagn*. 2015;3:4
18. Bioelectrical impedance analysis in body composition measurement: National Institutes of Health Technology Assessment Conference Statement. *Am J Clin Nutr*. 1996;64:524S-532S.
19. Organization WH. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation. 2000. Ginebra:WHO
20. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral Adiposity Index. A reliable indicator of visceral function associated with cardiometabolic risk. *Diabetes Care*. 2010; 33(4):920-2
21. Amato MC, Giordano C, Pitrone M, Galluzzo A. Cut-off points of the visceral adiposity index (VAI) identifying a visceral adipose dysfunction associated with cardiometabolic risk in a Caucasian Sicilian population. *Lipids in Health and Disease*. 2011; 10:183-90.
22. López-González ÁA, García-Agudo S, Tomás-Salvá M, Vicente-Herrero MT, Queimadelos-Carmona M, Campos-González I. FINRISK Test: Relationship between cardiovascular risk parameters and scales in Spanish Mediterranean population. *Rev Med Inst Mex Seguro Soc*. 2017 May-Jun;55(3):309-16.

Prevalence of overweight and obesity in spanish working population along the Covid-19 pandemic. Adiposity indicators and related variables

Prevalencia de sobrepeso y obesidad en población laboral española durante la pandemia Covid-19. Indicadores de adiposidad y variables relacionadas

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Abstract

Introduction: Obesity is a multifactorial and complex disease, being the Body Mass Index (BMI) the standardized method used to define and evaluate overweight or obesity in epidemiological studies, however and compared to adiposity indicators, this method presents low sensitivity and shows a high inter-individual variability.

Methods: A descriptive cross-sectional study was performed in 815 workers, aged between 18 and 66 years with data collected along regular health surveillance examinations of participating companies from March 2020 to June 2021. The following variables were collected: socio-demographic: age, sex, cultural level and social class; occupational variables: type of work and role; anthropometric variables: weight, height and BMI; and adiposity indicators: visceral fat, body fat, waist circumference and waist/height, and waist/hip indices, establishing interrelationships between them.

Results: Significant differences were found between obesity prevalence and gender, being higher in men and increasing with age. As well, the prevalence was higher in workers with elementary education as the highest degree obtained. In women, it was observed an inverse correlation between social class level and obesity prevalence. In men with non-manual jobs (white collar) and women with manual jobs (blue collar), the prevalence established was higher. It is worth highlighting the association between BMI, body fat and waist/height index.

Conclusions: The average BMI results of the workers were found to be overweight, showing higher values in men (27.49) than in women (26.33) and a relation to age and occupations. The BMI shows concordance with all the indicators of adiposity, with body and visceral fat and the waist/height index standing out.

Keywords: Obesity, Visceral adiposity, Anthropometry, body mass index.

Resumen

Introducción: La obesidad es una enfermedad multifactorial y compleja, siendo el Índice de Masa Corporal (IMC) el método estandarizado utilizado para definir y evaluar el sobrepeso u obesidad en los estudios epidemiológicos, sin embargo y en comparación con los indicadores de adiposidad, este método presenta una baja sensibilidad y muestra una alta variabilidad interindividual.

Métodos: Se realizó un estudio descriptivo transversal en 815 trabajadores, con edades comprendidas entre los 18 y los 66 años con datos recogidos a lo largo de los exámenes periódicos de vigilancia de la salud de las empresas participantes desde marzo de 2020 hasta junio de 2021. Se recogieron las siguientes variables: sociodemográficas: edad, sexo, nivel cultural y clase social; ocupacionales: tipo de trabajo y rol; antropométricas: peso, talla e IMC; e indicadores de adiposidad: grasa visceral, grasa corporal, perímetro de cintura y cintura/altura, e índices de cintura/cadera, estableciendo interrelaciones entre ellos.

Resultados: Se encontraron diferencias significativas entre la prevalencia de obesidad y el género, siendo mayor en los hombres y aumentando con la edad. Asimismo, la prevalencia fue mayor en los trabajadores con estudios primarios como máxima titulación obtenida. En las mujeres se observó una correlación inversa entre el nivel de clase social y la prevalencia de obesidad. En los hombres con trabajos no manuales (cuello blanco) y en las mujeres con trabajos manuales (cuello azul), la prevalencia establecida fue mayor. Cabe destacar la asociación entre el IMC, la grasa corporal y el índice cintura/altura.

Conclusiones: Los resultados del IMC promedio de los trabajadores se encontraron con sobrepeso, mostrando valores más altos en los hombres (27,49) que en las mujeres (26,33) y una relación con la edad y las ocupaciones. El IMC muestra concordancia con todos los indicadores de adiposidad, destacando la grasa corporal y visceral y el índice cintura/altura.

Palabras clave: Obesidad, Adiposidad visceral, Antropometría, Índice de masa corporal.

Introduction

Obesity is a multifactorial and complex disease. Its world prevalence has doubled since 1980 and almost a third of the world's population is estimated to be overweight or obese; likewise, it is currently considered a global and progressing epidemic, affecting more than 2 billion people¹.

Obesity rates have been increasing along all ages and in both genders, regardless of geographic location, ethnic origin or socioeconomic level, although its prevalence increases with age and differs according to sex, varying between men and women².

Body Mass Index (BMI) is a standard method generally used to define and evaluate overweight or obesity in epidemiological studies, however, this method presents low sensitivity and shows a high inter-individual variability compared with adiposity indicators for any BMI given due to differences by age, sex and ethnicity. As well, obesity is related with an increased cardiometabolic risk, which is highly dependent on body fat location such as visceral, subcutaneous, and ectopic deposits within muscular tissue or the liver³.

This background suggest that obesity might have a greater incidence in the population, thus requiring a more urgent attention than epidemiological studies suggest. An exclusive relying on BMI to assess its prevalence might difficult future interventions to prevent and control obesity.

The aim of this study is to estimate the prevalence of obesity in a sample of Spanish working population, taking into account BMI values and additional indicators such as adiposity, their interrelationships, and social and labor variables in order to establish additional preventive actions in the workplace.

Method

Study Design

A descriptive cross-sectional study performed in a sample of Spanish working population composed by 815 participants (481 males and 334 females), aged between 18 and 66 years who attended the regular health surveillance examinations of the participating companies from March 2020 to June 2021. Participation was voluntary and under an informed consent to use the results for epidemiological purposes.

The Ethics Committee for Clinical Research of the Health Area of the Balearic Islands (IB 4383/20) approved the current study.

Instruments and Procedure

In order to determine weight and height, it was used a SECA 700 scale divided into fractions of 50 grams, with a

maximum capacity of 200 kg. Height was measured with a telescopic measuring meter SECA 220 incorporated in the scale with a measuring range of 60 to 200 cm divided on millimetric scale. BMI was calculated as the weight in kilograms divided by the squared height in meters. The BMI ranges defined by the WHO and included in this study were as follows: normal weight BMI < 25; overweight 25 \geq BMI < 30; obese class I 30 \geq BMI < 40; obese class II 40 \geq BMI.

The hip and waistline perimeters were determined with a SECA 20 measuring tape, with a measuring range from 1 cm to 200 cm, divided on a millimetric scale. The ranges considered for the waistline perimeter were: Normal in men < 94 cm and in women < 80 cm. The hip perimeter was measured to determine the waistline/hip index only. The TANITABC-420MA analyzer was used to determine the body composition, estimating the percentage of body fat and visceral fat.

The following adiposity indicators (AI) have been calculated:

- Waist circumference (WC): considered normal in men when below 94 cm and in women below 80 cm.
- Waist to hip ratio (WHR): considered normal in men when below 0.94 and in women when below 0.84.
- Waist to height ratio (WHtR): considered normal when below < 0.5 for both genders.
- Total body fat percentage (TBF%): considered normal in men when below 10% and in women when below 20%.
- Visceral fat (VF): considered normal when below < 10 for both genders.

The social and labor variables included in the study were the following:

- Age: Individuals were classified in different age ranges: between 18 to 39 years, between 40 to 50 years and between 51 to 66 years.
- Gender: A categorical variable, with individuals classified as female or male.
- Social class and type of work: Determined on the basis of the National Classification of Occupations of the year 2011 (CNO-11) and on the basis of the proposal made by the Group of Social Determinants from the Spanish Society of Epidemiology⁵. For the statistical analysis, a reduced classification with three categories was used from the original seven categories:
 - Class I. Directors/managers, college professionals, sportsmen and artists.
 - Class II. Intermediate occupations and self-employed persons without employees.
 - Class III. Unskilled workers.
- Type of work: manual (blue collar) and not manual (white collar), as simplified from the previous authors⁵.

- Study level: according to the current education system in Spain classified in three categories:
 - Elementary school: consisting of six basic levels, from first to sixth grade in primary school.
 - Intermediate: compulsory secondary education, with two cycles. The first cycle ranged from the first to third course, and the second cycle consisting of the fourth course.
 - Superior: completed university degrees or superior vocational education, in any of the forms established and in accordance with the legislation in force when they were completed.
- Workplace characteristics: manual handling of loads (MHL) and vehicle driving (at least 1/3 of the working day) and sedentary work (seated at least 50% of the working day) were included.

Statistical Analysis

A descriptive analysis of the categorical and quantitative variables was carried out by using descriptive statistics with means and standard deviations (SD) for continuous variables and percentage for categorical variables. A bivariate association analysis was performed using the 2-test (corrected with the Fisher exact test, if required) and Student's *t*-test for independent samples. The Cohen Kappa test was used to assess the concordance between the different scales.

Data were analyzed using Statistical Package for the Social Sciences version 27 (SPSS Inc, Chicago) and considering a *p*-value < 0.05 as statistically significant.

Results

The characteristics of the population sample are shown in **table I**. The average age of the population is 48 years old in both genders, with a global BMI value of overweight and being higher in men (27.49) than in women (26.33). As well, significant differences between all adiposity indicators (AI) were found between genders, taking into account the different reference values in some of the AI according to gender: with an almost normal waistline in men (94.6 cm) and high in women (84.5 cm). The waistline/height ratio was within the normal boundaries in both genders (men = 0.55 and women = 0.53). The waistline/hip ratio was normal in men (0.92) and slightly normal in women (0.85). Total body fat was high in both genders (24.7 in men and 36.08 in women). Visceral fat was high in men (11.35) and normal in women (7.5).

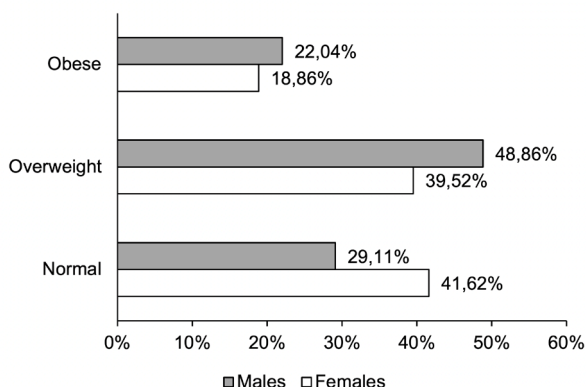
There are significant differences in the prevalence of overweight and obesity by gender, with higher percentages in men (**Figure 1**).

There were no significant differences in the educational level between men and women. Regarding the social class and type of work, social class III and manual work was predominant in both genders, being higher in men with statistically significant differences. There are significant differences observed in the characteristics of the workplace between genders: vehicle driving with manual handling of loads was predominant in male population, while women were majorly sedentary.

Table I: Characteristics of the Study Population. Comparison between genders.

Variable	Male (N = 481)	Female (N = 334)	P
Anthropometric and adiposity variables: mean (SD)			
Age	48.25 (8.35)	48.89 (8.16)	0.277
Weight	82.79 (13.93)	67.97 (11.98)	<0.0001
Height	173.42 (6.81)	160.72 (5.98)	<0.0001
BMI	27.49 (4.01)	26.33 (4.47)	<0.0001
Waist	94.61 (10.96)	84.35 (11.43)	<0.0001
Waist/height	0.55 (0.06)	0.53 (0.07)	<0.0001
Hip	106.22 (58.83)	99.00 (10.13)	0.027
Waist/Hip	0.92 (0.07)	0.85 (0.06)	<0.0001
Total body fat	24.70 (6.58)	36.08 (7.78)	<0.0001
Visceral fat	11.35 (4.53)	7.53 (2.65)	<0.0001
BMI classification (%)			
Normal	29.11	41.62	0.001
Overweight	48.86	39.52	
Obesity	22.04	18.86	
Study level (%)			
Elementary	49.06	41.92	0.116
Intermediate	32.43	35.63	
Superior	18.50	22.46	
Social class and type of work (%)			
Class I	3.33	2.40	<0.0001
Class II	20.58	36.83	
Class III	76.09	60.78	
Type of work (%)			
Non-manual work	23.91	39.22	<0.0001
Manual work	76.09	60.78	
Workplace characteristics (%)			
Sedentary work (seated > 50% working day)	25.16	41.92	<0.0001
Driving of vehicles and MHL (at least 1/3 of the working day)	71.93	53.29	<0.0001

SD = Standard deviation. Abbreviations: BMI, Body mass index; MHL, Manual handling of loads.

Figure 1: Percentage of overweight and obesity prevalence by gender.

The prevalence of overweight/obesity in relation to social, cultural and work variables are included in **table II**.

BMI values differ significantly between genders; normal weight was predominant in women aged between 18 and 50 years, while they were majorly overweight aged above 50. In men, BMI increases with age, with normal parameters until aged 39, then, predominantly overweighted. In men, the prevalence of obesity increases progressively in with age, while in women the relationship is not linear, being more frequent in the 40 to 50 years interval.

In women, overweight and obesity levels were more prevalent in people with elementary studies, while in men

and although obesity is predominant among those in elementary studies, a high percentage of overweight in men with higher education still stands out.

In both genders, overweight is more prevalent in social class II workers. In women, obesity increases with the social class, unlike in men, on which it was found a higher percentage of obese workers belonging to the social class I and its prevalence declined as the class increased.

Regarding the type of work, there were also significant differences within gender. There was a higher obesity prevalence in women with manual jobs (blue-collar), while in men, obesity was higher in white-collar workers. Overweight was more frequent in non-manual workers for both genders, with a higher prevalence in men.

Among men, both overweight and obesity predominate in jobs with a sedentary behavior during more than 50% of the working day; however, obesity is higher in those who perform other tasks that do not involve sedentary behavior. In both sedentary and non-sedentary jobs, the prevalence of overweight or obesity was higher in men than in women.

Overweight and obesity were most often associated with work that does not require motor vehicle driving or MHL in men; nevertheless, in women there is a higher percentage of obesity among MHL drivers and

Table II: Prevalence of overweight/obesity in relation to social, cultural and work variables.

Age (years)	Females				Males			
BMI Classification	18-39	40-50	51-66	P < 0.0001	18-39	40-50	51-66	P < 0.0001
Normal	56.00	40.60	37.75		45.57	32.8	19.72	
Overweight	34.00	37.59	43.05		40.51	44.97	55.4	
Obesity	10.00	21.80	19.21		13.92	22.22	24.88	
Study level								
BMI Classification	Elementary	Intermediate	Superior	P < 0.0001	Elementary	Intermediate	Superior	P < 0.0001
Normal	35.71	46.22	45.33		24.58	32.69	34.84	
Overweight	42.86	37.82	36.00		49.15	46.79	51.68	
Obesity	21.43	15.97	18.67		26.27	20.51	13.48	
Social class								
BMI Classification	Class I	Class II	Class III	P < 0.0001	Class I	Class II	Class III	P < 0.0001
Normal	50.00	39.84	42.36		37.50	18.18	31.69	
Overweight	37.50	43.09	37.44		37.50	57.58	46.99	
Obesity	12.50	17.07	20.20		25.00	24.24	21.31	
Type of work								
BMI Classification	Non manual	Manual		P < 0.0001	Non manual	Manual		P < 0.0001
Normal	40.46	42.36			20.87	31.69		
Overweight	42.75	37.44			54.78	46.99		
Obesity	16.79	20.2			24.35	21.31		
Workplace characteristics: sedentary								
BMI Classification	Seated < 50%	Seated ≥ 50%		P < 0.0001	Seated < 50%	Seated ≥ 50%		P < 0.0001
Normal	43.30	39.29			32.22	19.83		
Overweight	37.11	42.86			46.67	55.37		
Obesity	19.59	17.86			21.11	24.79		
Workplace characteristics: MHL and vehicle driving								
BMI Classification	MHL only	MHL + driving		P < 0.0001	MHL only	MHL + driving		P < 0.0001
Normal	37.18	45.51			25.93	30.35		
Overweight	44.23	35.39			50.37	48.27		
Obesity	18.59	19.10			23.70	21.39		

Abbreviations: BMI, Body mass index; MHL, Manual handling of loads

higher overweight prevalence among non-drivers MHL workers. It is worth highlighting the presence of statistical significance in these results.

Additionally, the concordance between BMI and adiposity indicators (AI) was studied by using the Cohen's kappa statistic. The results are shown in **table III** and **table IV**, which illustrate that the BMI is the index that presents higher concordance with the rest of the AI. Within the total population studied, the relationship between BMI and AI found was moderate for the total body fat and visceral fat and strong with the waist to height ratio. In women, it was moderate with the total body fat and strong with the waist to height ratio; and in men, it was shown a moderate relationship between BMI and the waist to height ratio and strong between the BMI and the visceral fat and the total body fat.

Regarding the relationship between the different adiposity indicators, the concordance was variable. Global data showed that the total body fat has a moderate level of agreement with the waist to height ratio (0.46), as well between the waist to height ratio and the waist to hip ratio (0.49). In women, the findings were similar, with moderate concordance between the total body fat and the waist to height ratio (0.55) and between the waist to height ratio and the waist to hip ratio (0.49). In men, there was a strong relationship between the visceral fat and the waist to height ratio (0.62); and moderate between the visceral

fat and the total body fat (0.56), the waist to height ratio and the total body fat (0.41), and between the waist to height ratio and the waist to hip ratio (0.47). For the rest of the parameters analyzed, the level of agreement were either poor or weak and none of them presented and almost perfect level of agreement.

Discussion

Through the last years, obesity and the actions taken on its associated risk factors have been an important part of health promotion programs in Spain and other developed countries; however, the prevalence is still variable. Studies based on BMI criteria in the USA show a prevalence of obesity around 27.7% in working population⁶, while epidemiologic studies in Spain (Aragon) show different numbers, with overweight rate around 38.6% and obesity at 18.4%, with higher incidence in men than in women⁷.

Along the present study, the prevalence rates found were higher for both overweight and obesity in men (48.50% and 22.04%, respectively) and in women (39.52% and 18.86%, respectively). It is worth highlighting that the data of this study was collected during the COVID-19 pandemic, which had its impact in the workers lifestyle such as changes in eating habits and the decrease of physical activity.

The influence of social, cultural and personal variables

Table III: Concordance between BMI and adiposity indicators. Global results and by gender.

Concordance: Global results				
BMI	Visceral fat	Body fat	Waist to height ratio	Waist to hip ratio
	0.471	0.574	0.610	0.281
Concordance: Females				
BMI	Visceral fat	Body fat	Waist to height ratio	Waist to hip ratio
	0.177	0.510	0.723	0.380
Concordance: Males				
BMI	Visceral fat	Body fat	Waist to height ratio	Waist to hip ratio
	0.664	0.624	0.544	0.251

Value of Kappa (level of agreement): < 0.20 Poor; 0.21 – 0.40 Weak; 0.41 – 0.60 Moderate; 0.61 – 0.80 Strong; 0.81 – 1.00 almost perfect.

Table IV: Concordance between adiposity indicators. Global results and by gender.

Concordance: Global results	Visceral fat	Body fat	Waist to height ratio	Waist to hip ratio
Visceral fat	1	0.311	0.360	0.165
Body fat		1	0.462	0.207
Waist to height ratio			1	0.490
Waist to hip ratio				1
Concordance: Females				
Visceral fat	1	0.070	0.130	0.118
Body fat		1	0.546	0.224
Waist to height ratio			1	0.493
Waist to hip ratio				1
Concordance: Males				
Visceral fat	1	0.556	0.616	0.329
Body fat		1	0.411	0.200
Waist to height ratio			1	0.465
Waist to hip ratio				1

Value of Kappa (level of agreement): < 0.20 Poor; 0.21 – 0.40 Weak; 0.41 – 0.60 Moderate; 0.61 – 0.80 Strong; 0.81 – 1.00 almost perfect.

is generally accepted in obesity related studies, but still showing contradictory results. Epidemiologic studies performed in USA between 1990 and 2006 show that the association between obesity and the aforementioned variables is dynamic and complex, and therefore, population programs and health policies are needed to facilitate preventive interventions⁸. Our results highlight the influence of age, gender, social class and cultural level on obesity, which is in agreement with other authors in terms of age and gender, but not totally in terms of social class and cultural level⁹.

Non-manual workers have been emphasized in some studies as people with higher risk of obesity, especially in sedentary administrative work. In our study, gender differences were observed, with obesity being more prevalent in men who performed sedentary work contrasting with women. These results differ as well in studies carried out in workers¹⁰ in Portugal which, while showing differences in the type of work, vary according to the regional location of the studied population¹¹.

In obesity, anthropometric measures such as body mass index (BMI) and waistline circumference are widely used as suitable adiposity indices, although there are still limitations in the estimation of body fat. BMI does not take into account variabilities in body composition by gender and age, and new studies are increasingly including the waistline circumference, and the relationship between the BMI and body fat as indicators¹².

In our study, the level of agreement between BMI and diverse adiposity indicators was established, being the waistline/height index and body fat the most consistent indicators with the BMI in relation to the classification of overweight and obesity. The correlation between other adiposity indicators such as the visceral fat and BMI was not entirely clear in women; however, it was strong in men.

Other authors highlight the importance of taking into account the body fat location, as there are individuals

classified as non-obese based entirely on BMI (BMI < 30), but still with high body fat values, and recommend the inclusion of body fat composition measures in common medical practice for both diagnosis and therapeutic decision-making¹³.

Our results are consistent with other authors who reaffirm that anthropometric measures are simple, economic and non-invasive tools, useful for diagnosing obesity and assessing the risk of morbidity and mortality. Some of them are easy to obtain, such as abdominal perimeter¹⁴. Still, the most commonly used parameters are BMI, waistline circumference, the ratios between waist to hip and waist to height, visceral fat and body fat¹⁵.

A high amount of visceral adipose tissue leads to a higher mortality rate rather than the absolute increase in body fat^{16,17}. All the variables related to obesity have been incorporated in our work, including body fat, visceral fat and the waistline to height ratio, being the last one used as well in other studies^{18,19}, but with less importance than the rest of the indicators.

Conclusions

The average BMI results of the workers were found to be overweight, showing higher values in men (27.49) than in women (26.33) and a relation to certain ages and occupations. In both genders it increases with age, but in women it is more frequent in the interval between 40-50 years old. In both genders, overweight's prevalence is higher in non-manual workers. The BMI shows the highest concordance with all the indicators of adiposity, with a moderate relationship with body fat and visceral fat and a strong relationship with the waist/height index.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Caballero B. Humans against Obesity: Who Will Win? *Adv Nutr.* 2019 Jan 1;10(suppl_1):S4- S9. doi: 10.1093/advances/nmy055. PMID: 30721956; PMCID: PMC6363526.
2. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. *Metabolism.* 2019 Mar;92:6-10. doi: 10.1016/j.metabol.2018.09.005. Epub 2018 Sep 22. PMID: 30253139
3. Daud A, Shahadan SZ. Association Between Body Mass Index and Cardiometabolic Risks Among Malay Obese Adults. *Clin Nurs Res.* 2019 Feb;28(2):202-216. doi: 10.1177/1054773817724041. Epub 2017 Aug 6. PMID: 28782381.
4. World Health Organization. Body mass index – BMI. 2020. Available at: <https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi>
5. Domingo-Salvany A, Bacigalupe A, Carrasco JM, Espelt A, Ferrando J, Borrell C. Propuestas de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011. *Gac Sanit [Internet].* 2013 Jun [citado 2021 Sep 07] 27(3):263-272. Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213-1112013000300013&lng=es. <https://dx.doi.org/10.1016/j.gaceta.2012.12.009>

6. Luckhaupt SE, Cohen MA, Li J, Calvert GM. Prevalence of obesity among U.S. workers and associations with occupational factors. *Am J Prev Med.* 2014 Mar;46(3):237-48. doi: 10.1016/j.amepre.2013.11.002. PMID: 24512862.
7. Ramón Arbués E, Martínez Abadía B, Gracia Tabuenca T, Yuste Gran C, Pellicer García B, Juárez-Vela R, et al. Prevalencia de sobrepeso/obesidad y su asociación con diabetes, hipertensión, dislipemia y síndrome metabólico: estudio transversal de una muestra de trabajadores en Aragón, España. *Nutr Hosp.* 2019 Mar 7;36(1):51-59. doi: 10.20960/nh.1980. PMID: 30834762.
8. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. *Epidemiol Rev.* 2007;29:6-28. doi: 10.1093/epirev/mxm007. Epub 2007 May 17. PMID: 17510091.
9. De Silva AP, De Silva SH, Haniffa R, Liyanage IK, Jayasinghe KS, Katulanda P, Wijeratne CN, Wijeratne S, Rajapakse LC. A cross sectional survey on social, cultural and economic determinants of obesity in a low middle income setting. *Int J Equity Health.* 2015 Jan 17;14:6. doi: 10.1186/s12939-015-0140-8. PMID: 25595202; PMCID: PMC4300585.
10. Narisada A, Suzuki K. Association between procrastination, white-collar work and obesity in Japanese male workers: a cross-sectional study. *BMJ Open.* 2019 Nov 18;9(11):e029931. doi: 10.1136/bmjopen-2019-029931. PMID: 31740465; PMCID: PMC6887083.
11. Alves L, Stringhini S, Barros H, Azevedo A, Marques-Vidal P. Inequalities in obesity in Portugal: regional and gender differences. *Eur J Public Health.* 2017 Aug 1;27(4):775-780. doi: 10.1093/eurpub/ckx041. PMID: 28407055.
12. Pasco JA, Nicholson GC, Brennan SL, Kotowicz MA. Prevalence of obesity and the relationship between the body mass index and body fat: cross-sectional, population-based data. *PLoS One.* 2012;7(1):e29580. doi: 10.1371/journal.pone.0029580. Epub 2012 Jan 13. PMID: 22253741; PMCID: PMC3258232.
13. Gómez-Ambrosi J, Silva C, Galofré JC, Escalada J, Santos S, Millán D, et al. Body mass index classification misses subjects with increased cardiometabolic risk factors related to elevated adiposity. *Int J Obes (Lond).* 2012 Feb;36(2):286-94. doi: 10.1038/ijo.2011.100. Epub 2011 May 17. PMID: 21587201.
14. Fang H, Berg E, Cheng X, Shen W. How to best assess abdominal obesity. *Curr Opin Clin Nutr Metab Care.* 2018 Sep;21(5):360-365. doi: 10.1097/MCO.0000000000000485. PMID: 29916924; PMCID: PMC6299450.
15. Gažarová M, Galšneiderová M, Mečiarová L. Obesity diagnosis and mortality risk based on a body shape index (ABSI) and other indices and anthropometric parameters in university students. *Rocz Panstw Zakl Hig.* 2019;70(3):267-275. doi: 10.32394/rpzh.2019.0077. PMID: 31515986.
16. Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. *Obes Rev.* 2010 Jan;11(1):11-8. doi: 10.1111/j.1467-789X.2009.00623.x. Epub 2009 Jul 28. PMID: 19656312.
17. Swainson MG, Batterham AM, Tsakirides C, Rutherford ZH, Hind K. Prediction of whole-body fat percentage and visceral adipose tissue mass from five anthropometric variables. *PLoS One.* 2017 May 11;12(5):e0177175. doi: 10.1371/journal.pone.0177175. PMID: 28493988; PMCID: PMC5426673.
18. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obes Rev.* 2012 Mar;13(3):275-86. doi: 10.1111/j.1467-789X.2011.00952.x. Epub 2011 Nov 23. PMID: 22106927.
19. Tsatsoulis A, Paschou SA. Metabolically Healthy Obesity: Criteria, Epidemiology, Controversies, and Consequences. *Curr Obes Rep.* 2020 Jun;9(2):109-120. doi: 10.1007/s13679-020-00375-0. PMID: 32301039.

ORIGINAL

Effect of a *Coriolus versicolor*-based vaginal gel on cervical epithelialization and vaginal microbiota in HPV-positive women: EPICERVIX pilot study

Eficacia de un gel vaginal basado en Coriolus versicolor sobre la epitelización cervical y la microbiota vaginal en mujeres positivas al VPH: Estudio piloto EPICERVIX

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Abstract

Objectives: A *Coriolus versicolor*-based vaginal gel (Papilocare®) has been shown to speed up the cervicovaginal mucosa epithelialization and a tendency to improve the composition of the microbiota in healthy women. The study aimed to evaluate the effects of this gel on cervical epithelialization and composition of vaginal microbiota in HPV-positive women with normal cytology and colposcopy.

Methods: A total of 21 HPV-positive women with negative Papanicolaou smear and normal colposcopy were once-daily treated with Papilocare® for 21 days. At baseline and the end of treatment, degree of epithelialization of the cervix mucosa was evaluated by colposcopy (and rated by the five-point Likert scale), and vaginal microbiota composition was analysed by next-generation sequencing.

Results: At the end of treatment, cervix epithelialization was improved in 52.6% of women. The treatment produced a statistically significant reduction in phylogenetic diversity. Moreover, abundance in *Proteobacteria* phylum was reduced (38.5% vs 93.6% at baseline) while increased in *Firmicutes* phylum (44.6% vs 2.1%). A significant increase and reduction in the proportion of *Lactobacillus* spp. Beij. (*Lactobacillaceae* family), including *L. crispatus* and *L. iners*, and *Gardnerella vaginalis* was reported, respectively.

Conclusions: The application of the *Coriolus versicolor*-based vaginal gel significantly improved ectocervix epithelialization and the vaginal microbiota composition among HPV-positive women without cervical lesions, which could support its use for preventing HPV-associated cervix lesions.

Keywords: Cervix epithelialization, human papillomavirus, *Lactobacillus*, Papilocare, vaginal microbiota, *Coriolus versicolor*.

Resumen

Objetivos: Un gel vaginal basado en *Coriolus versicolor* (Papilocare®) ha mostrado acelerar la epitelización de la mucosa cervicovaginal y una tendencia a mejorar la composición de la microbiota en mujeres sanas. El estudio fue diseñado para evaluar los efectos de este gel sobre la mucosa cervicovaginal y la composición de la microbiota de mujeres VPH positivas con citología y colposcopia normales.

Métodos: Un total de 21 mujeres fueron tratados una vez al día con Papilocare® durante 21 días. En el momento basal y al final del tratamiento, se evaluó el grado de epitelización de la mucosa cervical mediante colposcopia (y se cuantificó mediante una escala Likert de cinco puntos) y se analizó la composición de la microbiota vaginal mediante tecnologías nuevas de secuenciación.

Resultados: Al final del tratamiento, la epitelización de la mucosa cervical mejoró en el 52.6% de las mujeres. El tratamiento produjo una reducción estadísticamente significativa en la diversidad filogenética. Además, se redujo la abundancia de *Proteobacteria* phylum (38.5% vs 93.6% en el momento basal), mientras que se incrementó la de *Firmicutes* phylum (44.6% vs 2.1%). Se observó un aumento y disminución significativa de las proporciones de *Lactobacillus* spp. Beij. (familia *Lactobacillaceae*), incluyendo *L. crispatus* and *L. iners*, y de *Gardnerella vaginalis*, respectivamente.

Conclusiones: La aplicación del gel vaginal basado en *Coriolus versicolor* mejoró significativamente la epitelización del ectocérvix y la composición de la microbiota vaginal en mujeres VPH positivas sin lesiones cervicales, lo que podría apoyar su uso para prevenir las lesiones de cérvix asociadas al VPH.

Palabras clave: Epitelización cérvix, papilomavirus humano, *Lactobacillus*, Papilocare, microbiota vaginal, *Coriolus versicolor*.

Introduction

Human papillomavirus (HPV) is the most common viral infection of the reproductive tract and is mainly transmitted through sexual contact. There is clear evidence linking HPV infection and different types of cancers, including the anus, vulva, vagina, penis and oropharynx^{1,2}. More than 100 types of HPV have been reported, and at least 14 are considered as cancer-causing or high-risk types. Specifically, HPV 16 and 18 account for 70% of all cervical cancers and pre-cancerous lesions worldwide^{3,4}. Despite extensive research, the underlying mechanisms of the HPV life cycle and HPV-induced carcinogenesis have not been fully identified. It is generally accepted that several cofactors, including viral genotype, host immune status, vaginal microbiota and ectocervix histological structure⁵⁻⁷, may regulate a balance between infection and virus clearance. This is crucial for cervical cancer development in HPV-infected women⁸⁻¹¹. Although HPV vaccines are available, they do not protect against all HPV types or established infections^{1,12}, so a more in-depth understanding of the pathological mechanisms of HPV is needed to identify new tools for preventing the infection and development of associated cancers. Regarding vaginal microbiota, several studies have reported an association between abnormalities in its composition (dysbiosis) and the existence of HPV¹³⁻¹⁶. Vaginal dysbiosis has been characterized by a decrease in *Lactobacillus* spp. Beij. (*Lactobacillaceae* family), with a concomitant increase in diversity and anaerobic bacteria abundance, including species of *Gardnerella* Chavan (*Bifidobacteriaceae* family)¹⁷⁻¹⁹.

Considering the histological structure of the ectocervix, it has been reported that a well epithelialized cervix with squamous epithelium and limited or non-existent transformation zone with cellular activity prevents integrative colonization of HPV with oncogenic potential²⁰. Consequently, promoting ectocervix squamous cell epithelialization, which may function as a barrier, seems a plausible approach to hinder HPV integration and prevent infection. In this sense, a non-hormonal vaginal gel based on *Coriolus versicolor* L. (*Polyporaceae* family), Papilocare® (Procure Health, Castelldefels, Barcelona, Spain), has recently been approved in Spain. Its components possess hydrating properties, act as moisturizer and lubricant, enhance and accelerate the repair of atrophic or injured epithelium of the cervicovaginal mucosa, as well as display immunomodulatory effects and restore the balance of the microbiota²¹⁻²⁶. Furthermore, *Coriolus versicolor*, traditionally used in Chinese medicine, has been reported to have antimicrobial, antiviral and anti-tumour properties²⁷. Remarkably, in an open-label prospective pilot study, 21 asymptomatic healthy women were treated with this vaginal gel for 12 consecutive days, and it significantly improved cervical epithelialization while a tendency to improve the dysbiosis status was observed²⁸. These encouraging results prompted us to

evaluate the *Coriolus versicolor*-based vaginal gel in HPV-positive women with normal cytology and colposcopy for a longer period (21 days), by assessing its impact on cervical epithelialization and modulation of vaginal microbiota composition.

Methods

Study design

An observational, non-comparative, open-label, prospective pilot EPICERVIX study included HPV-positive women with negative Papanicolaou smear and normal colposcopy who received treatment with Papilocare® between July 2016 and January 2017 in the Department of Gynaecology at the Obstetrics & Gynaecology Institute (Madrid, Spain). The study was performed under conditions of routine daily practice and in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. Approval of the study protocol by the institutional review board was not required since studies with a medical device class 1 (not a drug) already marketed and used within approval indications are exempted, according to Spanish law (<http://sid.usal.es/docs/F3/LYN14832/14832.pdf>).

Participants

Inclusion criteria to participate in the study included: sexually active women; aged 25 years or over; attending a routine gynaecological monitoring visit; with diagnosis of HPV by polymerase chain reaction (PCR)-based HPV deoxyribonucleic acid (DNA) detection within three months prior to the consultation; a normal Papanicolaou smear and normal colposcopy findings; and eligible for the prescription of the vaginal gel. Exclusion criteria were: clinically relevant disorders of the immune system or treatment with immunosuppressant agents; abnormal vaginal bleeding (without diagnosis) within the six months prior to the consultation; symptomatic vulvovaginal infection; history of gynaecologic cancer; use of vaginal contraceptives or other vaginal hormonal treatments; scheduled surgery preventing compliance with treatment; participation in another clinical trial; fertile women not using effective contraceptive methods; pregnant or breastfeeding; and contraindication for the use of Papilocare® or known allergies to some of its components.

Study procedures

Women who gave consent to participate in the study and met the inclusion criteria were advised on appropriate use of the vaginal gel Papilocare® according to the patient information leaflet. The gel contains *Coriolus versicolor* as the main component together with niosomes of hyaluronic acid (a moisturizing agent), beta-glucan (an immunomodulator agent), Bioecolia® (a probiotic agent), phytosomes of *Centella asiatica* L. (*Apiaceae* family) (a tissue regenerating agent), *Azadirachta indica* A. Juss.

(*Meliaceae* family) extract (Neem) (an antioxidant/anti-inflammatory agent), and *Aloe vera* L. (*Asphodelaceae* family) (a re-epithelialization agent). Patients were encouraged to apply Papilocare® once a day before bedtime for 21 consecutive days. The use of douches or vaginal deodorants was not permitted, but sexual activity with or without condom was not limited. Participants found to be eligible, after acceptance for inclusion in the trial, visited the clinic on day 0 (baseline/visit 1) and on day 21 (visit 2). Degree of epithelialization was evaluated colposcopically and samples were obtained to determine the composition of the vaginal microbiota.

Cervical epithelialization

The epithelialization degree of the cervical mucosa was evaluated by the investigator by standard colposcopy and rated using a five-point Likert scale, where five was no ectopy, four: mild (<25% of the external os), three: moderate (25%–50% of the external os), two: severe (>50% of the external os) and one: severe ectopy and bleeding.

Characterization of microbiota

DNA from study samples was isolated as reported elsewhere²⁹. Amplicon fragments were PCR-amplified from the total DNA in duplicate with the Phusion high-fidelity DNA polymerase. A single round of PCR was performed using "fusion primers", targeting 16S rRNA V1-4 region with multiplexing on the Illumina MiSeq machine. PCR products were verified visually by running a high-throughput Invitrogen 96-well-E-gel. The PCR reactions from the same samples were pooled in one plate, then cleaned and normalized using the high-throughput Invitrogen SequalPrep 96-well Plate kit. Samples were then pooled to make one library to be quantified fluorometrically before sequencing. For taxonomic analysis, sequences were selected to estimate the total bacterial diversity of the DNA samples in a comparable manner and were trimmed to remove barcodes, primers, chimeras, plasmids, mitochondrial DNA; in addition to any non-16S bacterial reads and sequences < 150 bp. MG-RAST (metagenomics analysis server)³⁰, with the Ribosomal Database Project (RDP) for analyses of all sequences. The pipeline uses bar coded sequence readings, divides them into individual communities by bar code, makes taxonomic assignments to RDP database with external programmes³¹ and predicts phylogenetic diversity, with a minimum e-value of 1e-5, minimum identity of 60% and a minimum alignment length of 15 measured in base pairs for RNA databases. Each value expressed the percentage relative frequency of readings with predicted proteins and rRNA genes defined for the particular taxonomic level. The output file was also evaluated with SPSS 17.0 Software Package (SPSS Inc., Chicago, Ill, USA) and the Statistical Analysis of Metagenomic Profiles (STAMP) software 2.1.3³².

The composition of bacterial communities was evaluated by calculating three major ecological parameters,

including the Chao1 richness index for abundance data (an estimate of a total community)³³, the Pielou's evenness index (to show how evenly individuals in the community were distributed over different operational taxonomic units (OUT)³⁴, and the Shannon biodiversity index (a combined parameter of richness and evenness)³⁵. The Shannon biodiversity index was categorized as less than two (low diversity), two to three (normal), and more than three (high diversity). Furthermore, a two-dimensional scatterplot was generated by principal coordinates analysis (PCoA) to visualize whether the experimental groups in the input phylogenetic tree had significantly different microbial communities. This method enables visualization of dissimilarities of the data in terms of distance³⁶.

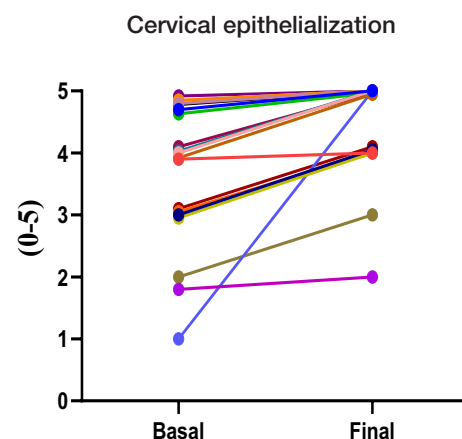
Statistical analysis

Calculation of sample size was unnecessary since the study was exploratory. Quantitative variables were expressed as mean and standard deviation (SD) while categorical variables appeared as frequencies and percentages. Paired samples of continuous data were compared to the Wilcoxon signed-rank test. Data were evaluated using the Power Analysis and Sample Size software programme, version 2011.

Results

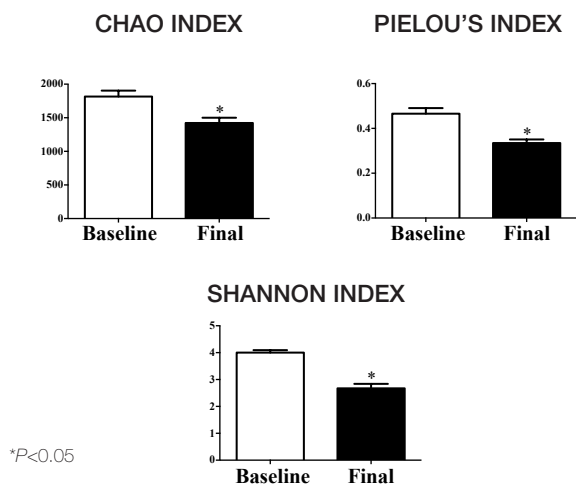
A total of 21 patients participated in the study, with a mean age of 38.9 years (range 25-59 years). Microbiota analysis was performed on all women, but cervical epithelialization was analysed in 19 of them. Treatment with the *Coriolus versicolor*-based vaginal gel revealed a beneficial effect on re-epithelialization of the cervix, with median score of 5 (range: 2-5) at the final visit as compared to 4 (range: 2-5) at the onset of the study ($P<0.01$) (Figure 1) and an overall improvement of 18%. Cervix epithelialization improved in 52.6% of women and a score of 5 (no ectopy) was observed in 66.7%, while only 38.1% of the patients had that value at the beginning of the study.

Figure 1: Degree of epithelialization of the cervix mucosa rated by the 5-point Likert scale.



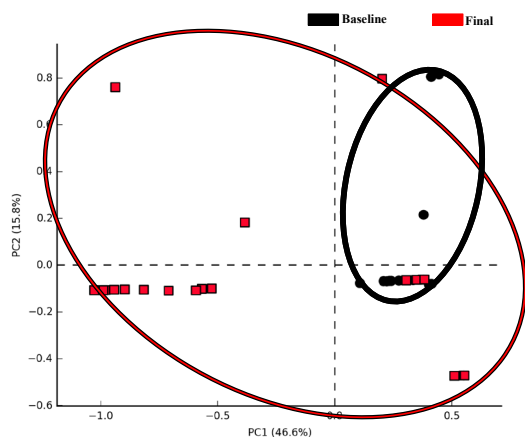
Microbial richness, evenness and diversity, analysed with the Chao, Pielous's and Shannon indices, were significantly decreased at the final visit in comparison with baseline (Figure 2).

Figure 2: Estimate of the phylogenetic diversity of the vaginal microbiota at baseline and after 21 days of treatment with Papilocare® using Chao richness, Pielou evenness and Shannon diversity.



In the PCoA analysis, the composition of vaginal microbial communities clearly differed at the time points evaluated (baseline and end of study) (Figure 3).

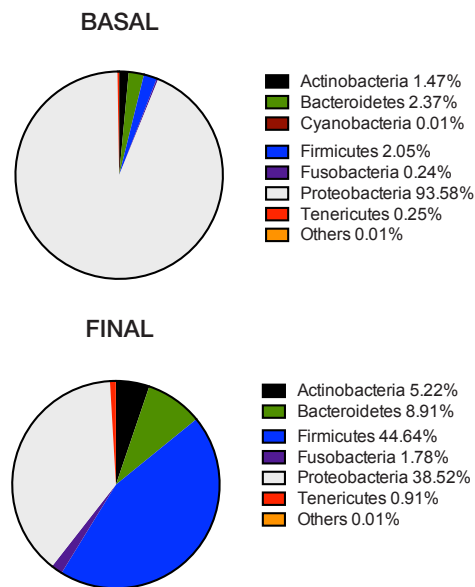
Figure 3: Principal component analysis plot based on Bray-Curtis distances.



Moreover, there was a notable change of abundance in the most representative phyla. At baseline, the predominant phylum was *Proteobacteria* (93.6%) with a lower proportion of bacteria belonging to the phyla *Actinobacteria*, *Bacteroidetes* and *Firmicutes* (1.5%, 2.4% and 2.1%, respectively). At the end of the treatment, a statistically significantly ($P < 0.005$) higher proportion of the phyla *Firmicutes* (44.6%), to which *Lactobacilli* belongs,

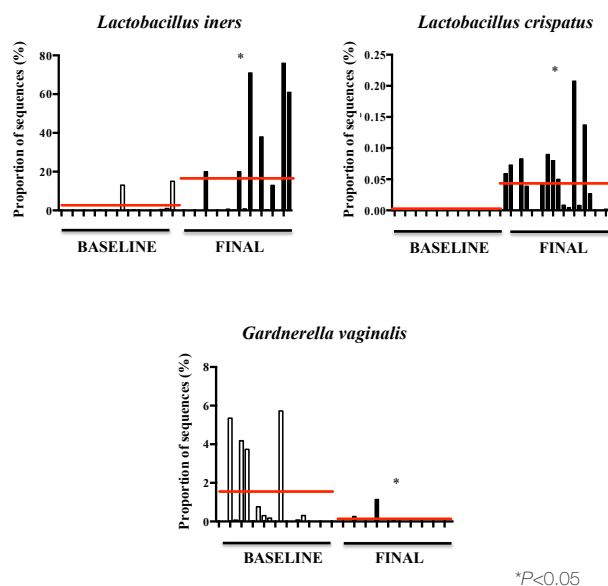
was observed, together with a decrease in the phylum *Proteobacteria* (38.5%), which includes a large number of potential pathogens (Figure 4).

Figure 4: Proportions of the different phyla of bacteria in the ectocervix samples at baseline and at the end of the study after 21 days of treatment with Papilocare®



Finally, at the end of treatment, statistically significant increases ($P < 0.05$) in comparison with baseline were documented for *L. iners* and *L. crispatus*. However, other species, such as *Gardnerella vaginalis* decreased significantly (Figure 5).

Figure 5: Individual proportions of *Lactobacillus iners* and *crispatus* and *Gardnerella vaginalis* at baseline and after 21 days of treatment with Papilocare®



Discussion

This study performed on HPV-positive women revealed that once-daily vaginal application of Papilocare® for 21 consecutive days had a favourable effect on cervix epithelialization and vaginal microbiota. These findings, although obtained in a small study population, are clinically relevant since the moisturizing, repairing and epithelizing properties of the vaginal gel, as well as its effect restoring the balance of vaginal microbiota could contribute to prevent the clinical course of HPV-associated lesions.

The cervix has a very unstable histological structure with permanent confrontation of the scaly vaginal strata and the cylindrical endocervical glandular epithelium. Below this glandular epithelium there is a lining consisting of 'reserve' cells that retain the ability to grow and differentiate into mature forms of squamous or glandular epithelium. This process has been called metaplasia and generates an area identified in the cervix as a 'transformation zone'. This is a common process in sexually active women, especially in those using hormonal contraceptives or intra-uterine devices and in women who have given birth. The reserve cells in the metaplastic process of re-epithelialization fulfil this condition and are perfect targets for the anchoring of HPV^{37,38} since HPV needs to integrate into mitotically active cells²⁰. Thus, the preservation of a well epithelized cervical neck and an extended transformation zone would prevent the integrative colonization of HPV. Therefore, the reported effects of Papilocare® in repairing, stimulating squamous epithelialization and remodelling the transformation zone may have an important indirect role in reducing the susceptibility of the cervix to HPV infection. Moreover, and although it has not been explored in this study, *Corioli* *versicolor* has been reported to have immunostimulatory properties that mediate the clearance of oral HPV³⁹ and might control the proliferation of malignancies⁴⁰.

Moreover, the vaginal microbiota plays a significant role in the health and disease of the female reproductive tract. Next-generation sequencing techniques based upon analysis of bacterial 16S rRNA genes enable in-depth study of the vaginal microbial community structure, which is not possible with standard culture-based microbiological techniques. There is emerging evidence that increased diversity of vaginal microbiota together with reduced relative abundance of *Lactobacillus* spp. is involved in HPV acquisition and persistence⁷. Actually, a recent study of women with low- and high-grade cervical dysplasia and invasive cervical carcinoma, revealed that elevated vaginal pH and decreased *Lactobacillus* dominance were associated with severity of the cervical neoplasm⁴¹. Furthermore, a dysbiotic, non-*Lactobacillus*-dominant and highly diverse vaginal microbiota has been linked to the increasing severity of precancerous cervical intraepithelial neoplasia (CIN)¹⁶. Interestingly, the HPV-positive women recruited to the study presented a

dysbiotic vaginal microbiota dominated by *Proteobacteria* and with a reduced abundance of *Firmicutes*. The results in this study revealed that treatment with Papilocare vaginal gel led to a shift towards the vaginal microbiota composition found in healthy women, with a reduction in microbial abundance, evenness and diversity. Moreover, the treatment significantly reduced the abundance of species associated with HPV infection such as *Gardnerella vaginalis*⁴² and increased the proportion of *Lactobacillus* spp. Currently, *Lactobacillus* depletion is a well-known feature of vaginal dysbiosis and abnormal vaginal microbiome⁴³. These results are in accordance with our previous study in which gel-treatment of asymptomatic healthy women improved vaginal dysbiosis²⁸.

These results should be interpreted considering the exploratory pilot nature of the study, the single-centre and open label design and especially the short-term use of the vaginal gel product. Nevertheless, HPV-positive women without cytological and colposcopy abnormalities were carefully selected and, to the best of our knowledge, this is the first study to assess cervical re-epithelialization and changes in the vaginal microbiota associated with the use of a natural hydrating and moisturizing gel; whose components have proven anti-inflammatory, epithelizing and immunomodulatory effects, together with the capacity to preserve the vaginal microbiota balance. These encouraging preliminary findings provide the basis for designing an investigational plan involving clinical trials and observational studies, which is currently underway. Subsequently, confirmatory data will support its potential use in HPV-positive patients. In addition, this product will have the advantage of an easy and convenient administration protocol.

In conclusion, Papilocare® significantly improved cervix epithelialization among HPV-positive women without cervical lesions. The higher abundance of specific species of the genus *Lactobacillus* after the treatment suggests a restoration of the altered microbiota composition in these women. These results might account for the mechanisms of action of Papilocare® underlying its positive effects on repairing cervical lesions.

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Authors' Contributions

Conceptualization, S.G., L.S., J.C., A.R.N and J.G.; methodology, T.V., J.G-M., F.A., R.M. and M.E.R.C.; validation, A.R.N. and J.G.; resources, J.C., L.S. and J.G.; writing-original draft preparation, M.E.R.C., J.G. and A.R.N.; writing-review and editing, T.V., J.G. and A.R.N.; supervision and funding acquisition, J.C., J.G.

and A.R.N. All authors have read and agree with the published version of the manuscript.

Interests conflict

J.C., S.G. and L.S. have been speakers at Procure Health events in several conferences. The remaining authors have no conflict of interest to declare.

References

1. Facts C. American Cancer Society. Cancer Facts & Figures 2009. Atlanta: American Cancer Society; 2009.
2. Krzowska-Firych J, Lucas G, Lucas C, Lucas N, Pietrzyk Ł. An overview of Human Papillomavirus (HPV) as an etiological factor of the anal cancer. *J Infect Public Health*. 2019; 12(1): 1-6.
3. Bruni L, Barrionuevo-Rosas L, Albero G, Serrano B, Mena M, Gómez D, et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). human papillomavirus and related diseases in the world. Summary report 27 July 2017. 2018.
4. Bosch FX, Lorincz A, Munoz N, Meijer CJ, Shah KV. The causal relation between human papillomavirus and cervical cancer. *J Clin Pathol*. 2002; 55(4): 244-65.
5. Wang SS, Hildesheim A. Chapter 5: Viral and host factors in human papillomavirus persistence and progression. *J Natl Cancer Inst Monogr*. 2003; (31): 35-40.
6. Doeberitz M, Vinokurova S. Host factors in HPV-related carcinogenesis: cellular mechanisms controlling HPV infections. *Arch Med Res*. 2009; 40(6): 435-42.
7. Mitra A, MacIntyre DA, Marchesi JR, Lee YS, Bennett PR, Kyrgiou M. The vaginal microbiota, human papillomavirus infection and cervical intraepithelial neoplasia: what do we know and where are we going next? *Microbiome* 2016; 4(1): 58.
8. Syrjanen K. Mechanisms and predictors of high-risk human papillomavirus (HPV) clearance in the uterine cervix. *Eur J Gynaecol Oncol*. 2007; 28(5): 337-51.
9. Moscicki AB, Schiffman M, Burchell A, Albero G, Giuliano AR, Goodman MT, et al. Updating the natural history of human papillomavirus and anogenital cancers. *Vaccine* 2012; 30 Suppl 5: F24-33.
10. Bodily J, Laimins LA. Persistence of human papillomavirus infection: keys to malignant progression. *Trends Microbiol*. 2011; 19(1): 33-9.
11. Tota JE, Chevarie-Davis M, Richardson LA, Devries M, Franco EL. Epidemiology and burden of HPV infection and related diseases: implications for prevention strategies. *Prev Med*. 2011; 53 Suppl 1: S12-21.
12. Arbyn M, Xu L, Simoons C, Martin-Hirsch PP. Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors. *Cochrane Database Syst Rev*. 2018; 5: CD009069.
13. Gillet E, Meys JF, Verstraelen H, Bosire C, De Sutter P, Temmerman M, et al. Bacterial vaginosis is associated with uterine cervical human papillomavirus infection: a meta-analysis. *BMC Infect Dis*. 2011; 11: 10.
14. Kyrgiou M, Mitra A, Moscicki AB. Does the vaginal microbiota play a role in the development of cervical cancer? *Transl Res*. 2017; 179: 168-82.
15. Audirac-Chalifour A, Torres-Poveda K, Bahena-Roman M, Tellez-Sosa J, Martinez-Barnette J, Cortina-Ceballos B, et al. Cervical Microbiome and Cytokine Profile at Various Stages of Cervical Cancer: A Pilot Study. *PLoS one* 2016; 11(4): e0153274.
16. Mitra A, MacIntyre DA, Lee YS, Smith A, Marchesi JR, Lehne B, et al. Cervical intraepithelial neoplasia disease progression is associated with increased vaginal microbiome diversity. *Sci Reports* 2015; 5: 16865.
17. Fredricks DN, Fiedler TL, Marrazzo JM. Molecular identification of bacteria associated with bacterial vaginosis. *N Engl J Med*. 2005; 353(18): 1899-911.
18. Gao W, Weng J, Gao Y, Chen X. Comparison of the vaginal microbiota diversity of women with and without human papillomavirus infection: a cross-sectional study. *BMC Infect Dis*. 2013; 13: 271.
19. Lee JE, Lee S, Lee H, Song YM, Lee K, Han MJ, et al. Association of the vaginal microbiota with human papillomavirus infection in a Korean twin cohort. *PLoS one* 2013; 8(5): e63514.
20. Hwang LY, Ma Y, Shiboski SC, Farhat S, Jonte J, Moscicki AB. Active squamous metaplasia of the cervical epithelium is associated with subsequent acquisition of human papillomavirus 16 infection among healthy young women. *J Infect Dis*. 2012; 206(4): 504-11.
21. Chu KK, Ho SS, Chow AH. *Coriolus versicolor*: a medicinal mushroom with promising immunotherapeutic values. *J Clin Pharmacol*. 2002; 42(9): 976-84.
22. Møller MS, Goh YJ, Viborg AH, Andersen JM, Klæenhammer TR, Svensson B, et al. Recent insight in α -glucan metabolism in probiotic bacteria. *Biologia* 2014; 69: 713-21.
23. Shukla S, Bharti AC, Hussain S, Mahata S, Hedau S, Kailash U, et al. Elimination of high-risk human papillomavirus type HPV16 infection by 'Praneem' polyherbal tablet in women with early cervical intraepithelial lesions. *J Cancer Res Clin Oncol*. 2009; 135(12): 1701-9.
24. Bylka W, Znajdek-Awizen P, Studzinska-Sroka E, Danczak-Pazdrowska A, Brzezinska M. *Centella asiatica* in dermatology: an overview. *Phytother Res*. 2014; 28(8): 1117-24.

25. Chen J, Geng L, Song X, Li H, Giordan N, Liao Q. Evaluation of the efficacy and safety of hyaluronic acid vaginal gel to ease vaginal dryness: a multicenter, randomized, controlled, open-label, parallel-group, clinical trial. *J Sex Med.* 2013; 10(6): 1575-84.
26. Radha MH, Laxmipriya NP. Evaluation of biological properties and clinical effectiveness of Aloe vera: A systematic review. *J Tradit Complement Med.* 2015; 5(1): 21-6.
27. Saleh MH, Rashedi I, Keating A. Immunomodulatory Properties of *Coriolus versicolor*: The Role of Polysaccharopeptide. *Front Immunol.* 2017; 8: 1087.
28. Palacios S, Losa F, Dexeus D, Cortes J. Beneficial effects of a *Coriolus versicolor*-based vaginal gel on cervical epithelialization, vaginal microbiota and vaginal health: a pilot study in asymptomatic women. *BMC Women's Health* 2017; 17(1): 21.
29. Rodríguez-Nogales A, Algieri F, Garrido-Mesa J, Vezza T, Utrilla MP, Chueca N, et al. Differential intestinal anti-inflammatory effects of *Lactobacillus fermentum* and *Lactobacillus salivarius* in DSS mouse colitis: impact on microRNAs expression and microbiota composition. *Mol Nutr Food Res.* 2017; 61(11).
30. Meyer F, Paarmann D, D'Souza M, Olson R, Glass EM, Kubal M, et al. The metagenomics RAST server - a public resource for the automatic phylogenetic and functional analysis of metagenomes. *BMC bioinformatics* 2008; 9: 386.
31. Wang Q, Garrity GM, Tiedje JM, Cole JR. Naive bayesian classifier for rapid assignment of rRNA sequences into the new bacterial taxonomy. *Appl Environ Microbiol.* 2007; 73(16): 5261-7.
32. Parks DH, Tyson GW, Hugenholtz P, Beiko RG. STAMP: statistical analysis of taxonomic and functional profiles. *Bioinformatics* 2014; 30(21): 3123-2134.
33. Chao A. Nonparametric estimation of the number of classes in a population. *Scand J Statist.* 1984: 265-70.
34. Pielou EC. The measurement of diversity in different types of biological collections. *J Theor Biol.* 1966; 13: 131-44.
35. Shannon C. A mathematical theory of communication. *J Bell Syst Tech.* 1948; 27(3): 379-423.
36. Caporaso JG, Kuczynski J, Stombaugh J, Bittinger K, Bushman FD, Costello EK, et al. QIIME allows analysis of high-throughput community sequencing data. *Nat Methods* 2010; 7(5): 335-6.
37. Schiffman M, Wentzensen N. Human papillomavirus infection and the multistage carcinogenesis of cervical cancer. *Cancer Epidemiol Biomarkers Prev.* 2013; 22(4): 553-60.
38. Rocha-Zavaleta L, Yescas G, Cruz RM, Cruz-Talonia F. Human papillomavirus infection and cervical ectopy. *Int J Gynaecol Obstet.* 2004; 85(3): 259-66.
39. Donatini B. Control of oral human papillomavirus (HPV) by medicinal mushrooms, *Trametes versicolor* and *Ganoderma lucidum*: a preliminary clinical trial. *Int J Med Mushrooms.* 2014; 16(5): 497-8.
40. Mao XW, Green LM, Gridley DS. Evaluation of polysaccharopeptide effects against C6 glioma in combination with radiation. *Oncology* 2001; 61(3): 243-53.
41. Laniewski P, Barnes D, Goulder A, Cui H, Roe DJ, Chase DM, et al. Linking cervicovaginal immune signatures, HPV and microbiota composition in cervical carcinogenesis in non-Hispanic and Hispanic women. *Sci Rep.* 2018; 8(1): 7593.
42. Murta EF, Souza MA, Araujo Junior E, Adad SJ. Incidence of *Gardnerella vaginalis*, *Candida sp* and human papilloma virus in cytological smears. *Sao Paulo Med J.* 2000; 118(4): 105-8.
43. Mendling W. Vaginal microbiota. *Adv Exp Med Biol.* 2016; 902: 83-93.

Evaluation the effectiveness of the cognitive rehabilitation therapy model for improvement executive functions in high- functions autistic children, by using neuroimaging, neuropsychological and molecular genetics technique

Evaluación de la eficacia del modelo de terapia de rehabilitación cognitiva para la mejora de las funciones ejecutivas en niños autistas de altas funciones, mediante el uso de técnicas de neuroimagen, neuropsicológicas y de genética molecular

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Abstract

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized mainly by difficulty in social communication and impaired executive performance. Executive functions are cognitive multi-dimensional capabilities required for complex behaviors. In recent years, serious efforts have been made better to understand certain executive deficiencies in children with ASD. Herein, we used a D-KEFS-based training program to increase the executive performance of autistic children on the Wisconsin card sorting test (WCST). Also, we evaluated children's brain activity using electroencephalography (EEG) during the training course and their expression profile of BDNF, CREB1, and FOXP2 genes, which are associated with neural development.

Methods: Twenty autistic children referred to clinics and mental counseling centers were enrolled in this non-randomized before-after trial compared to twenty normal children. The WCST as pre and post-test was used to evaluate the training program's effectiveness on executive functions. Blood samples were obtained for gene expression, and all subjects were evaluated with a five-minute closed-eye EEG. The D-KEFS training program was conducted for patients for five weeks.

Results: improvement of executive functions after the training program and increase in expression level of BDNF and CREB1 genes in autistic subjects showed in results. Also theta and bdelta waves were increased in cortical areas of children with autism after five weeks training.

Conclusion: The study results showed that cognitive rehabilitation therapy might improve executive functions in children with ASD, probably through gene expression and neural activity alterations.

Key words: Autism spectrum disorder (ASD), cognitive rehabilitation therapy (CRT), Delis-Kaplan executive function system (D-KEFS), Wisconsin Card Sorting Test (WCST), BDNF, CREB1, FOXP2, gene expression, electroencephalography (EEG).

Resumen

Antecedentes: El trastorno del espectro autista (TEA) es un trastorno del neurodesarrollo caracterizado principalmente por la dificultad en la comunicación social y el deterioro de las funciones ejecutivas. Las funciones ejecutivas son capacidades cognitivas multidimensionales necesarias para los comportamientos complejos. En los últimos años, se han hecho serios esfuerzos para comprender mejor ciertas deficiencias ejecutivas en los niños con TEA. En este caso, utilizamos un programa de entrenamiento basado en el D-KEFS para aumentar el rendimiento ejecutivo de los niños autistas en la prueba de clasificación de tarjetas de Wisconsin (WCST). Además, evaluamos la actividad cerebral de los niños mediante electroencefalografía (EEG) durante el curso de entrenamiento y su perfil de expresión de los genes BDNF, CREB1 y FOXP2, asociados al desarrollo neuronal.

Métodos: Veinte niños autistas remitidos a clínicas y centros de asesoramiento mental se inscribieron en este ensayo no aleatorio de antes y después en comparación con veinte niños normales. Se utilizó el WCST como pre y post test para evaluar la eficacia del programa de entrenamiento en las funciones ejecutivas. Se obtuvieron muestras de sangre para la expresión génica, y todos los sujetos fueron evaluados con un EEG de ojos cerrados de cinco minutos. El programa de entrenamiento D-KEFS se llevó a cabo para los pacientes durante cinco semanas.

Resultados: se observó una mejora de las funciones ejecutivas tras el programa de entrenamiento y un aumento del nivel de expresión de los genes BDNF y CREB1 en los sujetos autistas. También las ondas theta y bdelta aumentaron en las áreas corticales de los niños con autismo después de cinco semanas de entrenamiento.

Conclusión: Los resultados del estudio mostraron que la terapia de rehabilitación cognitiva podría mejorar las funciones ejecutivas en los niños con TEA, probablemente a través de la expresión de genes y las alteraciones de la actividad neuronal.

Palabras clave: Trastorno del espectro autista (TEA), terapia de rehabilitación cognitiva (TRC), sistema de función ejecutiva Delis-Kaplan (D-KEFS), test de clasificación de tarjetas de Wisconsin (WCST), BDNF, CREB1, FOXP2, expresión génica, electroencefalografía (EEG).

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder diagnosed by symptoms based on (1) deficits in communication and social connections and (2) repetitive, stereotyped behaviors¹. This condition has been considered a spectrum due to vast, heterogeneous manifestations. For instance, cognitive and verbal disabilities are more severe and profound in some patients than others, and therefore, some have better intellectual and communication abilities^{2,3}. In other words, autistic children are known as non-verbal children. ASD often interferes with the development of social and communication skills¹.

In the year 2019, the prevalence of autism has been estimated at 1 in 160 children, globally⁴. Generally, ASD is four times more frequent in males than females⁵. The ASD prevalence increased in recent decades; for instance, it was increased in the united states from 5-4 per thousand in 1990 to one in 50 in 2013⁶.

Generally, ASD is associated with cognitive and psychological problems, such as mental retardation, attention deficit-hyperactivity disorder (ADHD), irritability, and anxiety. Inability to understanding and recognizing emotions is one of the most prominent features of ASD and is probably one of the main problems in their social relationships⁷. These problems make it very difficult to be present in the community as an active, self-reliant, and successful person, which poses serious challenges for their parents, teachers, and caregivers¹.

The exact underlying etiopathogenesis of ASD is still unclear, but several mechanisms have been proposed in recent years, including genetic and neurologic alterations⁸. Mounting evidence argues that a single factor does not cause ASD, but the interaction between environment and genetic factors may be responsible^{7,9-11}. Today, ASD is considered a deficit in neurobiological development, strengthened by evidence stressed on its biological background and proposed etiopathogenesis related to neonatal period^{10,12-14}. The cognitive and behavioral defects of ASD can be seen in 18-24-month-olds, but a definite diagnosis can be made at the age of three, which means that these traits are evident in the early years of life⁹.

Several genetic factors have been introduced in ASD, including alterations in X, 7, 12, and 22 chromosomes. Point mutations in genes, including GluR6, PTEM, WNT2, and FMR1, in addition to epigenetic modifications, alter gene expression¹⁵. For instance, ASD has been reported in 15-60% of patients with fragile X syndrome, which is attributed to the *fmr1* gene deletion or variants¹⁵. Further, neurobiological evidence demonstrated abnormal frontal lobe function, the executive function's main structure¹⁶⁻¹⁸. Also, ADS cognitive function deficits in ASD, often attributed to anterior cingulate cortex (ACC)

function, a region responsible for storing information and impulse control¹⁹. Although cognitive functions are not attributed to a single region, various regions are involved in different executive functions.

Treatment options for ASD symptoms are very limited and mainly designed to better control the disease, but well-designed educational interventions may improve these symptoms and increase their communications²⁰. Accordingly, cognitive rehabilitation therapy improves the executive functions of autistic children effectively¹⁵. Cognitive rehabilitation is a complex method design to increase understanding, comprehension, attention, learning, recall, and problem-solving in individuals with neuropsychological disorders, such as ASD²¹.

In recent years, grave attempts have been made to improve individual executive performance in ASD children²², but most research focused on communication issues, and executive functions' promotion was less considered²³. Although previous studies have examined the differences between autistic children, efforts continue to provide a novel treatment strategy focused on executive functions in ASD children. This study aimed to evaluate educational interventions' effectiveness to increase executive functions in autistic children, and its influence on underlying neurobiology.

Materials and methods

Subjects

We designed this non-randomized controlled before-and-after study on twenty children diagnosed with autism (study group) and twenty matched non-autistic healthy children at the age between 6-12 years-old (control group) in Tehran, Iran in 2018, aiming evaluation the cognitive rehabilitation intervention on psychoneurological and genetic profiles of executive functions. The study protocol was approved by Informed consent from parents or legal guardians was obtained.

The inclusion criteria for cases was the Intelligence Quotient (IQ) score >70. The exclusion criteria were as followed: **1.** History of any narcotic, recreational drugs, or alcohol consuming abuse in both the study and control groups and their parents. **2.** Any mental or intellectual problem in both study and control groups. The IQ test was obtained to exclude subjects with intellectual problems in control and subjects with IQ scores less than or equal to 70 in the study group. **3.** Any psychologic problems in the control group were screened with a non-structured psychiatric interview performed by the study psychiatrist. **4.** Any physical problem or disability, which can be a potential confounding factor. **5.** Coincide ASD and ADHD. **6.** Significant experienced physical or emotional trauma in the last four months due to the gene expression profile's potential effect.

Delis-Kaplan Executive Function System (D-KFES) training programs

The training program was planned to improve executive functions based on D-KFES in the study group. The training program duration was five weeks, including playing sessions for 15 minutes per day. The playing session was done in a quiet room with minimal auditory and visual disturbance in the examiner's presence.

This program consisted of three types of tests; Trail Making Test, to improve the flexibility of thinking; Color-Word Test, improve the ability of fast respond; and Sorting Test to improve the planning, memory, attention, and problem-solving abilities.

The Delis-Kaplan Executive Function System (D-KEFS) is a standard assessment tool to evaluate a wide range of verbal and non-verbal executive functions. D-KEFS includes nine independent subtests that comprehensively assess children and adults' executive functions.

Wisconsin Card Sorting Test (WCST)

The WCST is a neuropsychological assessment tool used to measure problem-solving skills, classification, abstract thinking, concept formation, and cognitive flexibility, all attributed to the frontal lobe function. Both healthy subjects and patients (before and after the intervention) were assessed with WCST¹. An expert trainer explained the method for each participant to perform the test. Participants must match the number of shown cards to one of four card categories. The matching can be done by shape, color, or number. After 10 consecutive correct matchings, the rule of matching changes and shift to a new rule of matching. After each matching set was completed, it was called the "completing set." The matching rules change up to 5 sessions. We measured three outcomes of WCST in this study: the number of preserved errors (PE), the number of completing sets (NOC), and the total of errors (ΣE).

Gene expression analysis in blood

We used peripheral blood samples from subjects and stored in EDTA tubes at 4°C. RNA extracted from blood by using commercial RNA extraction kits and cDNA synthesized from RNA samples. The expression of FOXP2, CREB1, and BDNF as target genes and the GAPDH gene as a reference gene was examined with Real-time polymerase chain reaction (Real time PCR).

Table I: Primer sequences used for Real time PCR assessment.

Forward Primer BDNF	5'CTGTAGTCGCCAAGGTGGTT3'
Reverse Primer BDNF	5'AAGTGCTAGGAAGAGCCGTG3'
Forward primer GAPDH	5'AAGGGCCCTGACAACCTTT3'
Reverse primer GAPDH	5'CTCCCCTCTCAAGGGTCT3'
Forward primer FOXP2	5'TGGCATTAAACATGGAGGGC3'
Reverse primer FOXP2	5'TTTGGAAGTGTGGAGGAGGT3'
Forward primer CREB1	5'CCCGAAGAAACCCGAAGTCT3'
Reverse primer CREB1	5'GGCCGCGCACGGAAAC3'

RNA extraction, cDNA synthesis and Real time PCR procedure were conducted based on previous study²⁴. Primer sequences of genes were presented in **table I**.

Electroencephalography (EEG)

The EEG recording was used to evaluate the training program (intervention) impact on cortical activities. We compared the EEG results with gene expression results for a possible relationship between EEG pattern and gene expression. Twenty-one channels of EEG were recorded with a Negar amplifier in an isolated faraday room using Ag/AgCl electrodes in the linked-ear montage. The sampling rate was 256 Hz and a 40 Hz low-pass filter was applied. EEG was recorded using a nineteen channel Electrocap® and electrodes impedance was kept under 10 k Ω . Linked-ear montage was used for recording. EEG cancellation was minimized in this montage. Five minutes of EEG was recorded in eyes closed condition. Artifact rejection was performed by using z-score based algorithm, applied by Neuroguide software (www.appliedneuroscience.com). The algorithm works based on amplitude and frequency. The acceptable z-scores were selected between -1.96 and +1.96 by 95% accuracy. The average of signal remaining was 184 seconds after the automatic artifact rejection. Finally 60 artifact free signal segments with length of 3 seconds. The selection was performed from entire signals and the test-retest and split half tests for all EEG channels were remained over 0.9.

Statistical analysis

We used SPSS software v. 22.0 (IBM Corp. USA). The level of statistical significance is considered a p-value of less than 0.05. Descriptive data are expressed as mean \pm SD (range), and the level of statistical significance was set at $P < 0.05$. One-way ANOVA analysis was used for multiple group comparisons, statistical differences. Pearson correlation test was used for assessments of relations between variables.

Results

In the present study, 20 children (15 boys and 5 girls) with the confirmed diagnosis of ASD (the study group) and 20 sociodemographically matched non-psychiatric children were enrolled as the study population with age range of 8 ± 4 years and 8 ± 2 years, respectively. Also, the IQ score was 91 ± 4 in the study group and 108 ± 10 in the control group. There was no statistically significant difference regarding sex, age, and IQ score. Data were presented in **table II**.

Table II: Demographic data and IQ score of the study population.

Group	Patient	Control	p-value
Age	8 ± 4.3	8 ± 2.5	0.44
Gender	Male	15 boys	0.58
	Female	5 girls	
IQ score	91 ± 4	108 ± 10	0.33

Table III: The results of Wisconsin test in control and study (before and after the training program).

No. of Comparisons	Group	Number of completed sets (NOC)		Preserved error (PE)		Total of errors (ΣE)	
		Mean	p-value	Mean	p-value	Mean	p-value
1	Control Study (before)	2.9	0.01	12.2	0.02	31.3	0.01
		1.9		27.6		60.4	
2	Control Study (after)	2.9	0.01	12.2	0.02	31.3	0.29
		2.2		20.3		52.3	
3	Study (before) Study (after)	1.9	0.04	27.6	0.18	60.4	0.03
		2.2		20.3		52.3	

Table IV: Results of BDNF, CREB1 and FOXP2 genes expression comparison between control and Autistic children (before and after the training program) groups.

Gene	Comparisons	Ratio (fold change)*	p-value
BDNF	Autistic children (before) vs. Control	0.55	0.01
	Autistic children (after) vs. Control	0.89	0.03
	Autistic children (before) vs. Autistic children (after)	0.66	0.04
CREB1	Control vs. Autistic children (before)	0.62	0.02
	Control vs. Autistic children (after)	0.78	0.04
	Autistic children (before) vs. Autistic children (after)	0.54	0.04
FOXP2	Control vs. Autistic children (before)	0.89	0.09
	Control vs. Autistic children (after)	0.95	0.24
	Autistic children (before) vs. Autistic children (after)	0.93	0.21

* by 2- $\Delta\Delta CT$ method.

WCST results

We used WCST to examine higher-level cognitive abilities in the control and the study group (before and after the intervention). The result of the WCST is summarized in **table III**. The results of WCST showed that all three outcomes (i.e., NOC, PE, and ΣE) were significantly lower in the study group before the treatment compared to the control group ($p < 0.01$). However, the ΣE in the study group significantly decreased after the training program, compared to before the training program ($p = 0.03$, **table III**).

Gene expression

mRNA level of FOXP2, CREB1, and BDNF genes evaluated by using Real-time PCR. The results of gene expression comparison including fold changes and statistical analysis presented in **table IV**.

EEG study

The frequency band analysis of EEG results showed low frequency of Delta, Theta and Alpha in ASD group compared with control group. After the treatment increase in frequency of Delta, Theta and Alpha were observed in ASDs. Correlation study between the gene expression results and EEG studies show a significant correlation between theta

frequency and expression of BDNF and CREB1 among the study group. Data were presented in **table V**.

Discussion

The global incidence of ASD was progressed in recent decades⁴, and a better understanding of the disease's neurobiological complexities seems indispensable, aiming to improve the treatment interventions⁵. Typically, ASD is a heterogeneous disease, with a complex interaction between environmental and genetic factors^{20,25,26}. Hence, there is no definite treatment, and current strategies mainly aim to control the condition and increase the quality of life and communication with the environment. In the present study, we explored the cognitive rehabilitation strategy's effects based on the D-KEFS, and assessed the outcome with psychological, electrophysiological and molecular assessments.

Figure 1: Fourier analysis of three groups, first line from the above is ASDs before treatment, second line refer to ASDs after treatment and last line from the above is referring to normal children.

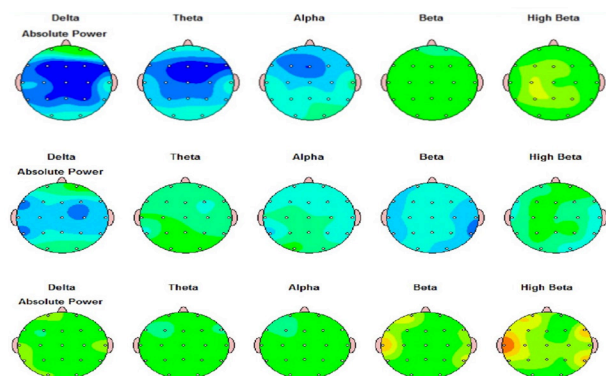


Table V: Correlation study of gene expression results and EEG frequency band.

Waves	CREB1	FOXP2	BDNF
Alpha	R: 0.15 p value: 0.34	R: 0.41 p value: 0.07	R: 0.18 p value: 0.63
Beta	R: 0.28 p value: 0.39	R: 0.18 p value: 0.33	R: -0.18 p value: 0.53
Theta	R: 0.78 p value: 0.002	R: 0.12 p value: 0.43	R: 0.44 p value: 0.02
Delta	R: 0.29 p value: 0.19	R: 0.21 p value: 0.17	R: -0.32 p value: 0.2
High Beta	R: 0.35 p value: 0.16	R: 0.42 p value: 0.09	R: -0.27 p value: 0.11

Executive functions are high-cognitive and metacognitive functions that carry a set of higher abilities, consisted of self-control, inhibition, self-initiation, strategic planning, cognitive flexibility, and impulse control. These functions are compromised in neuropsychological and neurodevelopmental disorders, including ASD. Cognitive rehabilitation is shown might be effective in such diseases. Kenworthy et al. revealed that early educational rehabilitation in autistic children could improve sociability, flexibility, and problem solving²⁷. Rezaei et al. demonstrated that emotional control education might increase social cognition and executive reaction in children with ASD²⁸. Studies have shown that D-KEFS-based training programs, designed to increase cognitive and behavioral performance, can increase the executive performance in schizophrenic and ADHD patients (ref). However, the program's effectiveness in children with autism has not been studied. Hence, neuropsychological tests are widely recognized as reliable and valid tools for executive assessment.

Previously, Brady et al. explored the executive functions in autistic adolescents using D-KEFS and revealed that despite the normal and acceptable executive functions in this group, their performance significantly differed compared to non-autistic, matched control²⁹. Boyer et al. examined adolescents' planning skills with ADHD using all D-KEFS subtests and showed that only 1% of the study subjects had impaired planning functionality³⁰. Herein, we applied WCST in the present study to evaluate the D-KEFS-based training program's effectiveness. The WCST results showed that the training program could improve the executive function in children with ASD compared to matched control groups and results before the training program. The EEG showed only modest alterations in cortical activities than before the training program.

Different brain regions, including the prefrontal area and parietal cortex, are involved in various cognitive functions (such as attention, perception, unconscious processing, working memory, and decision making). Solomon et al. studied the connection between brain regions and executive functions in ASD using functional magnetic resonance imaging (fMRI) studies. Their study demonstrated that functional connectivity between frontoparietal regions was lower than matched controls. Just et al. studied regions associated with inhibition in autistic adolescents compared to matched controls and found that these areas were hypoactive in autistic subjects¹⁹.

In recent decades, studies are shifted toward the neurobiological basis of cognitive disorders. Mounting evidence emphasized the role of environmental factors, such as pollutions, infectious disease, and alcohol or substance abuse during the neonatal period. Several hypotheses about the neurobiology of ASD have been

proposed, such as inflammatory or immune system responses, consequently affecting the cognitive and behavioral functions^{6,20,31,32}. Other hypotheses.

With the advantage of microarray and DNA sequencing methods, exploring the connection between genes and diseases emerged. Up to now, several genetic candidates have been introduced for ASD, but they are not currently used in routine clinical settings^{2,33-37}. Abbasi et al. showed that NRG1 expression is associated with working memory, inhibition, and consciousness in autistic children³⁸. Numerous genes are proposed in the brain's cognitive functions, such as BDNF, CREB1, and FOXP2. The BDNF is a known factor implicate in neuroplasticity. The CREB1 is a member of transcription factors associated with learning and memory, and the FOXP2 is a known genetic factor involved in language development and verbal communication skills in humans. We explored the training program's effectiveness on BDNF, CREB1, and FOXP2 gene expression.

Previous reports demonstrated the association between cognitive disorders and candidate genes' expression status, such as BDNF^{12,29,39-42}. However, the rehabilitation program's effect on gene expression is not well-studied. Although these genes' expression was lower in the study group before and after the intervention compared to healthy subjects, the expression level significantly increased after the intervention. This observation may be correlated with improved executive functions in the study group.

Our study could be considered as pilot study for a potential treatment for Autistic children with cognitive disabilities. There were several limitations in present study including lack of samples, short training time and lack of comprehensive cognition testings.

Conclusion

We evaluated cognitive rehabilitation's effectiveness in autistic children with psychologic tests in conjugation with genetic and electrophysiological assessments. The results showed that improvement with cognitive training program might be associated with modifications in genes and neural activity, which indicates a strong influence of the environment on patients with ASD's neurobiology. Our results can help signify the educational program's role in disease management.

Author Contributions

Fazlollah Shahraki, was the study designer. He was involved in clinical and laboratory data collection and analysis of data. he was also participated in writing the manuscript.

Peyman Hassani-Abharian was the head of the research team. He was involved in clinical and laboratory data collection, data analysis and editing the manuscript.

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Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Fletcher-Watson S, McConnell F, Manola E, McConachie H. Interventions based on the Theory of Mind cognitive model for autism spectrum disorder (ASD). *Cochrane database of systematic reviews*, 2014.
2. Gross C. Defective phosphoinositide metabolism in autism. *Journal of neuroscience research*. 2017; 95: 1161-73.
3. Jiujiang M, Kelley E, Hall L. Restricted, repetitive behaviors in autism spectrum disorder and obsessive-compulsive disorder: a comparative review. *Child Psychiatry & Human Development*. 2017; 48: 944-59.
4. Elsabbagh M, Divan G, Koh YJ, Kim YS, Kauchali S, Marcín C, et al. Global prevalence of autism and other pervasive developmental disorders. *Autism research*. 2012; 5: 160-79.
5. Christensen DL, Baio J, Braun KV, Bilder D, Charles J, Constantino J, et al, Lee LC 2018. Prevalence and characteristics of autism spectrum disorder among children aged 8 years-autism and developmental disabilities monitoring network, 11 sites, United States, 2012. *MMWR Surveillance Summaries*. 2016; 65: 1.
6. Ghaffari MA, Mousavinejad E, Riahi F, Mousavinejad M, Afsharmanesh MR. Increased serum levels of tumor necrosis factor-alpha, resistin, and visfatin in the children with autism spectrum disorders: a case-control study. *Neurology research international*, 2016.
7. Gepner B, Deruelle C, Grynfeldt S. Motion and emotion: A novel approach to the study of face processing by young autistic children. *Journal of autism and developmental disorders*. 2001; 31: 37-45.
8. Zhang R, Zhang H-F, Han J-S, Han S-P. Genes related to oxytocin and arginine-vasopressin pathways: associations with autism spectrum disorders. *Neuroscience bulletin*. 2017; 33: 238-46.
9. Ronemus M, Iossifov I, Levy D, Wigler M. The role of de novo mutations in the genetics of autism spectrum disorders. *Nature Reviews Genetics*. 2014; 15:133-41.
10. Girault JB, Piven J. The neurodevelopment of autism from infancy through toddlerhood. *Neuroimaging Clinics*. 2020; 30: 97-114.
11. Olsson NC, Flygare O, Coco C, Görling A, Råde A, Chen Q, et al. Social skills training for children and adolescents with autism spectrum disorder: a randomized controlled trial. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2017; 56: 585-92.
12. Bishop D. Genes, cognition and communication: insights from neurodevelopmental disorders. *Annals of the New York Academy of Sciences*. 2009; 1156: 1.
13. Barkoski JM, Busgang S, Bixby B, Bennett D, Schmidt R, Barr DB, et al. Prenatal phenol and paraben exposures in relation to child neurodevelopment including autism spectrum disorders in the MARBLES study. *Environmental research*. 2019; 179: 108719.
14. Mc Partland JC, Jeste SS. Connectivity in context: emphasizing neurodevelopment in autism spectrum disorder. *Biological psychiatry*. 2015; 77: 772-4.
15. Jacquemont ML, Sanlaville D, Redon R, Cormier-Daire V, Lyonnet S, Amiel J, et al. Array-based comparative genomic hybridisation identifies high frequency of cryptic chromosomal rearrangements in patients with syndromic autism spectrum disorders. *Journal of medical genetics*. 2006; 43: 843-9.
16. Carper R A, Moses P, Tigue ZD, Courchesne E. Cerebral lobes in autism: early hyperplasia and abnormal age effects. *Neuroimage*. 2002; 16: 1038-51.
17. Fujii E, Mori K, Miyazaki M, Hashimoto T, Harada M, Kagami S. Function of the frontal lobe in autistic individuals: a proton magnetic resonance spectroscopic study. *The Journal of Medical Investigation*. 2010; 57, 35-44.
18. Scott-Van Zeeland AA, Abrahams BS, Alvarez-Retuerto AI, Sonnenblick LI, Rudie JD, Ghahremani D. Altered functional connectivity in frontal lobe circuits is associated with variation in the autism risk gene CNTNAP2. *Science translational medicine*. 2010; 2: 56ra80-56ra80.
19. Just MA, Cherkassky VL, Keller TA, Minshew NJ. Functional and anatomical cortical underconnectivity in autism: evidence from an fMRI study of an executive function task and corpus callosum morphometry. *Cerebral cortex*. 2007; 17: 951-61.
20. Theoharides T, Tsilioni I, Patel A, Doyle R. Atopic diseases and inflammation of the brain in the pathogenesis of autism spectrum disorders. *Translational psychiatry*. 2016; 6: e844-e844.
21. Wolters G, Stapert S, Brands I, Van Heugten C. Coping styles in relation to cognitive rehabilitation and quality of life after brain injury. *Neuropsychological rehabilitation*. 2010; 20: 587-600.
22. Chan AS, Cheung MC, Han YMY, Sze SL, Leung WW, Man HS, et al. Executive function deficits and neural discordance in children with autism spectrum disorders. *Clinical Neurophysiology*. 2009; 120:1107-15.
23. Mazzocco MM, Myers GF. Complexities in identifying and defining mathematics learning disability in the primary school-age years. *Annals of dyslexia*. 2003; 53: 218-53.

24. Haghhighatfard A, Andalib S, Amini Faskhodi M, Sadeghi S, Ghaderi AH, Moradkhani S, Rostampour J, Tabrizi Z, Mahmoodi A, Karimi T. Gene expression study of mitochondrial complex I in schizophrenia and paranoid personality disorder. *The World Journal of Biological Psychiatry*. 2017;1-14.
25. Yui K, Tanuma N, Yamada H, Kawasaki Y. Decreased total antioxidant capacity has a larger effect size than increased oxidant levels in urine in individuals with autism spectrum disorder. *Environmental Science and Pollution Research*. 2017; 24: 9635-44.
26. Frustaci A, Neri M, Cesario A, Adams JB, Domenici E, Bernardina BD, et al. Oxidative stress-related biomarkers in autism: systematic review and meta-analyses. *Free Radical Biology and Medicine*. 2012; 52: 2128-41.
27. Kenworthy L, Anthony LG, Naiman DQ, Cannon L, Wills MC, Luong-Tran C, et al. Randomized controlled effectiveness trial of executive function intervention for children on the autism spectrum. *Journal of Child Psychology and Psychiatry*. 2014; 55: 374-83.
28. Rezaei A, Kazemi MS. The Effect of Emotional Regulation Training on Social Cognition and Executive Functions of Children with Autism Spectrum Disorder. *Quarterly Journal of Child Mental Health*. 2017; 4: 82-91.
29. Brady DI, Saklofske DH, Schwean VL, Montgomery JM, Thome KJ, McCrimmon AW. Executive functions in young adults with autism spectrum disorder. *Focus on Autism and Other Developmental Disabilities*. 2017; 32: 31-43.
30. Boyer BE, Geurts HM, Van der Oord S. Planning skills of adolescents with ADHD. *Journal of attention disorders*. 2018; 22: 46-57.
31. Xu N, Li X, Zhong Y. Inflammatory cytokines: potential biomarkers of immunologic dysfunction in autism spectrum disorders. *Mediators of inflammation*, 2015.
32. Fantuzzi G. Adipose tissue, adipokines, and inflammation. *Journal of Allergy and Clinical Immunology*. 2005; 115: 911-9.
33. Kushima I, Aleksic B, Nakatochi M, Shimamura T, Okada T, Uno Y, et al. Comparative analyses of copy-number variation in autism spectrum disorder and schizophrenia reveal etiological overlap and biological insights. *Cell reports*. 2018; 24: 2838-56.
34. Wang ET, Taliaferro JM, Lee JA, Sudhakaran IP, Rossoll W, Gross C, et al. Dysregulation of mRNA localization and translation in genetic disease. *Journal of Neuroscience*. 2016; 36: 11418-26.
35. Mokhtari B, Karimzadeh F. A review on the Autism with the most approach on the critical biomarkers. *Razi Journal of Medical Sciences*. 2018; 24: 35-46.
36. Shen L, et al. in *Reviews on Biomarker Studies in Psychiatric and Neurodegenerative Disorders*, Springer 2019; 207-33.
37. Bjørklund G, Meguid NA, El-Ansary A, El-Bana MA, Dadar M, Aaseth GJ, et al. Diagnostic and severity-tracking biomarkers for autism spectrum disorder. *Journal of Molecular Neuroscience*. 2018; 66: 492-511.
38. Abbasy S, Shahraki F, Haghhighatfard A, Ghasemzadeh-Qazvini M, Towfigh-Rafiei S, Noshadrad E, et al. Neuregulin1 types mRNA level changes in autism spectrum disorder, and is associated with deficit in executive functions. *EBioMedicine*. 2018; 37: 483-8.
39. Ricci S, Businaro R, Ippoliti F, Vasco V R Lo, Massoni F, Onofri E, et al. Altered cytokine and BDNF levels in autism spectrum disorder. *Neurotoxicity research*. 2013; 24: 491-501.
40. Ferrer A, Labad J, Salvat-Pujol N, Barrachina M, Costas J, Urretavizcaya M, et al. BDNF genetic variants and methylation: effects on cognition in major depressive disorder. *Translational psychiatry*. 2019; 9: 1-10.
41. Post RM. Role of BDNF in bipolar and unipolar disorder: clinical and theoretical implications. *Journal of psychiatric research*. 2007; 41: 979-90.
42. Najmabadi H, Hu H, Garshasbi M, Zemojtel T, Abedini SS, Chen W, et al. Deep sequencing reveals 50 novel genes for recessive cognitive disorders. *Nature*. 2011; 478: 57-63.

ORIGINAL

The study of gestational diabetes as a silent disease

El estudio de la diabetes gestacional como enfermedad silenciosa

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Abstract

Many of the deaths associated with diabetes are due to cardiovascular complications. Deaths from diabetes are premature and occur when patients are economically active in society. Gestational diabetes is a silent condition that affects both the mother and the foetus throughout pregnancy. Gestational diabetes is a silent condition that affects both the mother and the foetus throughout pregnancy. This study examines the gestational diabetes as a silent disease. In women with a history of gestational diabetes, diabetes prevention to early detection and control of diabetes, need to be given training on follow ups the after delivery. The follow ups, are including postpartum diabetes screening and lifestyle changes (exercise and diet compliance).

Key words: Self-regulation model, gestational diabetes, silent diabetes.

Resumen

Muchas de las muertes asociadas con la diabetes se deben a complicaciones cardiovasculares. Las muertes por diabetes son prematuras y ocurren cuando los pacientes son económicamente activos en la sociedad. La diabetes gestacional es una condición silenciosa que afecta tanto a la madre como al feto durante el embarazo. La diabetes gestacional es una condición silenciosa que afecta tanto a la madre como al feto durante el embarazo. Este estudio examina la diabetes gestacional como una enfermedad silenciosa. En las mujeres con antecedentes de diabetes gestacional, es necesario capacitar desde la prevención de la diabetes hasta la detección temprana y el control de la diabetes sobre el barbecho después del parto. Los barbechos incluyen exámenes de detección de diabetes posparto y cambios en el estilo de vida (ejercicio y cumplimiento de la dieta).

Palabras clave: Modelo de autorregulación, diabetes gestacional, diabetes silenciosa.

Introduction

During the study of deaths due to diabetes in four provinces of the country (East Azerbaijan, Bushehr, Chaharmahal Bakhtiari and Semnan) in 1999, 272 people per ten thousand people were estimated. In other words, diabetes was the 16th leading cause of death in men and the 9th leading cause of death in women¹. Decreased insulin secretion, decreased glucose uptake due to insulin resistance, and increased glucose uptake to varying degrees are involved in each type of diabetes. Diabetes causes premature and late changes that result in disability, cost of treatment, and ultimately increase mortality. Diabetes is the fifth leading cause of death in the world and the number one cause of chronic renal failure, non-traumatic amputation and blindness in many societies².

According to studies in India, if an adult low-income family lives with an adult with diabetes, 25% of the total family income is earmarked for diabetes care. In an American family with one child with diabetes, 10% of family income is allocated to diabetes control³. The total cost of health care for a person with diabetes in the United States is two to three times higher than for those without the disease. In 1997, for example, the cost of treating diabetes in the United States was estimated at \$ 44 billion⁴. A recent analysis of health care costs in the Pacific West and at the World Health Organization shows that 16% of hospital expenditures were for people with diabetes⁵. The cost of diabetes affects everyone and everywhere. These costs are not just financial expenses. Imperceptible costs such as pain, anxiety, discomfort, headache and, in general, a

decrease in quality of life, which generally affect the lives of patients and their families, are almost incalculable. The direct costs of patients and their families are: medical care, medicines, insulin and other necessities. Patients may also incur certain other costs, such as an increase in car insurance, life, and medical services. In most countries, the most expensive forms of diabetes treatment are hospital expenses, late complications of diabetes such as heart attacks and kidney failure, and problems with diabetic foot^{6&7}. In general, the direct costs of diabetes account for 15% - 2.5% of the total health budget⁸. The quality of people's daily work activities decreases with diabetes, and some of them even lose the ability to work. Illness, absenteeism, disability, premature retirement, or premature death cause a decline in productivity and a loss of productivity⁹. Estimating the costs of declining productivity in society is not easy, although in many cases these costs are estimated to be equal to or even higher than the direct costs of diabetes care. Indirect costs of diabetes in the United States, for example, were \$ 54 billion in 1997, while direct costs of the disease were \$ 44 billion in the same year¹⁰. The total estimated indirect costs of diabetes in 25 Latin American countries indicate that these costs are five times the direct costs of diabetes health care. This situation may be due to limited access to high quality care services, high incidence of complications, disability and premature death. In the same way, the problems caused by the decrease of household income will be more due¹⁰. Pain, anxiety, discomfort, and other factors that reduce the quality of life are called intangible costs, which are very high.

Literature of Review

The articles reviewed in this study include two Persian articles and one English article. By searching for terms such as: postpartum diabetes, self-regulation, postponement, in Iran Doc, Magiran, SID databases and searching for terms such as, screening, diabetes, type 2 diabetes, follow up, postpartum, procrastination, Gestational diabetes was obtained in PubMed, science direct, ProQuest, ISI databases in the period 2016-2005. The following studies are sorted by the closest time. Coppola et al. (2013) conducted a cross-sectional study of 6770 pregnant women at Pugliese-Ciaccio Hospital in Caucasian, southern Italy. The statistical population of this study included women who participated in gestational diabetes screening from January 2004 to December 2011. The aim of this study was to "accurately determine the predictive factors in performing postpartum glucose tolerance test in women with a history of gestational diabetes". Out of 6770 pregnant women, 1159 (17.1%) were diagnosed as gestational diabetes. All of these women were included in the study, except those who, according to the American Diabetes Association, had pre-pregnancy diabetes. Demographic characteristics included age, level of education, number of deliveries,

history of gestational diabetes, family history of diabetes, pre-pregnancy weight, and previous diagnosis of polycystic ovary syndrome based on Rotterdam criteria. After January 2011, women at the hospital were given verbal and written counseling on the importance of follow-up at 35 to 40 weeks of gestation. In this study, the rate of women's participation in postpartum glucose tolerance test was reported on the two dates mentioned above (2011-2011 and 2011 onwards) and also in this study, predictive factors in performing this test were determined. Out of 1159 women diagnosed with gestational diabetes, 374 (32.3%) participated in postpartum screening. There was a significant increase in referral rate following counseling. Also, interestingly, the previous diagnosis of polycystic ovary syndrome was determined as the most important predictor of postpartum follow-up. Explain that these women may be more eager to seek medical advice because they often experience undesirable clinical problems such as irregular menstruation, infertility, and hirsutism. In addition, these women are often treated with metformin and antidiabetic drugs and may be more aware of the risk of type 2 diabetes or more closely associated with the health care system. Other prognostic factors included a previous history of gestational diabetes, higher education, and insulin therapy during pregnancy. Also, there was no significant difference between body mass index, family history of type 2 diabetes and number of deliveries with the rate of participation¹¹.

Overall, the data of this study showed that the intervention as a counseling is an effective, inexpensive, and simple tool in increasing the rate of oral glucose tolerance test for women with a history of gestational diabetes. However, despite counseling, some women still do not participate. Polycystic ovary syndrome was also a strong predictor of women's participation in the postpartum diabetes test. Finally, the authors of this article write that further studies are needed to determine whether their findings are common in other populations¹². Butorn et al. (2014) in a cohort study examined the relationship between education level and gestational diabetes. In this study, 7511 pregnant women were studied and the prevalence of gestational diabetes at 4 educational levels was analyzed. Odds Ratio was calculated for better interpretation and analysis. The results of this study showed that people with the lowest level of education (elementary) compared to people with higher education are three times more likely to develop gestational diabetes (OR = 3.07). And there is a significant and direct relationship between education level and the incidence of gestational diabetes¹³.

Lubner et al. (2006) conducted a study to determine the predictors of postpartum diabetes in women with gestational diabetes. The aim of this study was to identify the risk factors for postpartum diabetes and women with a history of gestational diabetes from 1989 to 1999 were followed up. In this study, 302 subjects were present in the study and their glucose tolerance

was assessed at 9 months, 2 years, 5 years, 8 years and 11 years after delivery. The results showed that the risk of postpartum diabetes in women with BMI = 30 is significantly higher risk so that the risk in this group is 1.5 times lower than people with BMI (P = 0.04). Smith et al. (2005) examined the extent of physical activity and postpartum psychosocial activity in women with a history of gestational diabetes. This study was performed on 226 subjects living in Sydney with a mean age of 33.4 years. The results showed that only 33.6% of women had adequate physical activity and exercise after childbirth. Among physical activities, walking was the most rewarding activity. On the other hand, the most important barriers to postpartum sports activities were caring for the baby or infant (49.1% of the subjects) and not having enough time (37.6% of the subjects). In addition, women's self-efficacy for physical activity was low. Among the psychological-social support, verbal support was also reported as the most common support received by women (39% of the subjects). More than half of the women stated that they had not received any support in the field of housework¹⁴.

Discussion

1. Complications of Diabetes

Symptoms of diabetes are due to high blood sugar levels above 180 mg, which cause glucose to enter the urine. Increased volume and frequency of urination, thirst, weakness and fatigue, overeating, blurred vision and itchy skin and vagina are the most common early symptoms of diabetes. Chronic complications of diabetes fall into three main categories: large vessel complications, small vessel complications, and neurological complications. Complications of large vessels (macrovascular) are seen in the form of atherosclerosis of the coronary arteries, cerebrovascular disease and peripheral vascular disease. Complications of small vessels (microangiopathy) include diabetic nephropathy and retinopathy, which are the most common and major late complications. Neuromuscular complications of diabetes are mostly manifested in the form of mononeuropathy of one or more nerve trunks, symmetrical peripheral polyneuropathy, diabetic neuropathy of the autonomic nerves and diabetic myopathy. According to a study conducted at the Endocrinology Research Center in Isfahan in 1996, the prevalence of complications among people with diabetes was as follows:

- 34% of ischemic heart disease
- 50% hypertension
- 12% heart failure
- 44% retinopathy
- 5% cataract
- 27% bacteriuria
- 10% nephropathy (Statistics of 1379 Dialysis and Kidney Transplant Center in Iran show that 22.4%

- of cases have led to dialysis due to diabetes)
- 72% neuropathy
- 60% depression
- 2.5% diabetic foot
- 37% hypercholesterolemia
- 37% hypertriglyceridemia¹⁴

2. Incidence and prevalence of diabetes

The prevalence of diabetes has increased significantly in the last two decades. Although the prevalence is seen in both types of diabetes, the increase in the prevalence of type 2 diabetes has been far greater than in type 1 diabetes. In the 21st century, the prevalence of type 2 diabetes and impaired glucose tolerance (IGT) has become epidemic due to decreased physical activity and weight gain and obesity¹⁵.

The incidence of type 1 diabetes is lower than that of type 2 diabetes, and is generally between 3 and 35 per 100,000 people per year. The incidence of type 1 diabetes in Canada and the United States is reported to be between 8 and 20 per 100,000 people. In general, type 1 diabetes is rare and more common in residents of Japan, China, the Philippines, as well as Asian Indians, African blacks, and Eskimos. Type 1 diabetes is difficult to diagnose per 100,000 people in a year, and therefore many studies are incomplete in terms of defining indicators and their results should be considered with caution.

The prevalence of type 2 diabetes in the general population is between 1 to 4% and in people over 40 years between 5 to 10%. Given the growing prevalence of type 2 diabetes in the world, the World Health Organization declared it a latent epidemic and since 1993 has called on all countries to fight diabetes¹⁵.

A study conducted by the Endocrine Research Center of Shahid Beheshti University of Medical Sciences showed that the prevalence of type 2 diabetes in people over 30 years of age is about 7.6% in women and 7.1% in men. The results of this study also showed that the prevalence of renal glucose intolerance is 14.6% and 8.9% in men.

In a study in Tehran, the prevalence of gestational diabetes was reported to be 4.7%, and in another study in villages around Tehran, the results showed that 12.7% of pregnant women after consuming 50 g of oral glucose, serum sugar above 140 Mg / dL.

3. Classification of types of diabetes

The types of diabetes are divided according to its pathological process. The most common types of diabetes are types 1 and 2, which differ in etiology, epidemiology and many other dimensions. In addition to type 1 and type 2 diabetes, diabetes may appear for other reasons such as genetic disorders, some diseases, etc. Gestational diabetes is different from type 1 and type 2 diabetes because it is diagnosed for the first time in a

pregnant woman. The effects on the mother and fetus are similar to those who already have diabetes and then become pregnant, and may become completely normal after termination of pregnancy. There are three ways to diagnose type 2 diabetes today:

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

Normal plasma glucose levels in the fasting state and 2 hours after eating 75 g of glucose are 100 and 140 mg/dL, respectively. The American Diabetes Association prefers fasting plasma glucose levels because it is more practical, more proportionate, and more reproducible. If fasting plasma is between 100. 125 It is called "fasting diabetes disorder". If the glucose concentration is between 140 and 200 two hours after glucose consumption, it is called "glucose tolerance disorder". In these two groups, the incidence of diabetes is higher. Although two-thirds of them may not always have the symptoms of diabetes, they are more likely to have cardiovascular complications. Lifestyle changes can reduce the risk of developing diabetes in these groups¹⁵. Hemoglobin A1C is closely related to blood sugar levels, but is not currently used as a diagnostic test for diabetes because its normal nature cannot rule out impaired glucose tolerance or mild diabetes.

4. Epidemiology and etiology of diabetes

The etiology and epidemiology of the two types of diabetes are quite different. **Table I** lists some of these differences^{16&17}.

5. Type 1 diabetes

Type 1 diabetes is divided into two types, types A1 and B1. Type A1 results from immunological destruction of beta cells, leading to insulin deficiency. People with type B1 do not have immunological characteristics, but for unknown reasons have insulin deficiency and are highly

susceptible to diabetic ketoacidosis. It seems that in type 1 diabetes, genetics is a contributing factor that plays an important role in causing the disease along with environmental factors. The predisposing gene in this type of diabetes is located on chromosome¹⁸.

Due to the fact that most new cases (incidence rates) of type 1 diabetes are seen in spring and autumn, and its prevalence has increased with the change of school and exposure to new viruses, and also due to the fact that in some epidemics Viral cases of type 1 diabetes have also increased. It seems that special attention has been paid to the role of viral agents in the etiology of this type of diabetes. An increase in cases of type 1 diabetes has been reported in epidemics of coxsackie, mumps, hepatitis and rubella^{19&20}.

Some sources have suggested that the pathogens of type 1 diabetes are immunoglobulin antibodies that act against the islets of Langerhans. These antibodies are present in 60 to 90% of patients' blood at the beginning of the disease, but are seen in only 10% of patients after ten years²¹. In general, the etiological factors of type 1 diabetes can be expressed as the fact that in most patients with insulin-dependent diabetes there is a genetic predisposing factor that predisposes the pancreatic beta cells to a virus or chemical or immunological factors. Favorable. After beta cell damage, antigens bleed into the bloodstream, producing antibodies that invade the cell and cause further cell damage²¹.

6. Type 2 diabetes

It is the most common type of diabetes that develops slowly and gradually in old age and does not tend to cause ketoacidosis. Genetic and control factors are involved in causing this disease. The disease typically begins in a person with a normal carbohydrate metabolism and progresses to glucose intolerance with increased insulin compensation. This finding suggests that the major disorder in type 2 diabetes may not be due to decreased beta cell activity, but in this type of diabetes, the disturbance of peripheral tissue responses to the effects of insulin and glucose is of particular importance²².

Table I: Comparison of type 1 and type 2 diabetes.

	Type 1 diabetes	Type 2 diabetes
The genetic locus	chromosome 6	probably chromosome 11
The onset of the disease	rapid	acute
Disease age	less than 40 years	more than 40
Weight	Normal	low
Ketoacidosis	common/uncommon	low
Plasma insulin	normal decrease	normal
plasma glucagon	high suppressive	resistant to suppression
insulin resistance	Rare	available
Common anti-beta	antibodies Common	not available
Acute complications	hyperosmolar	coma ketoacidosis
Insulin therapy	Insulin therapy responds	resistant
Treatment with sulfonyl urea	does not work	It works

Genetic predisposing factors play a much stronger role in type 2 diabetes than in type 1 diabetes. If one of the monozygotic twins develops type 2 diabetes, the chance of becoming infected is almost 100%. While the same condition in type 1 diabetes has a 50% chance of developing²³. Long-term studies have shown that about 50% of first-degree relatives of patients with type 2 diabetes develop diabetes by the age of 80²⁴. Despite the role of genetic factors, the most important risk factors for type 2 diabetes are overweight and obesity. In a society, there is a strong and direct relationship between obesity and the prevalence of diabetes. Sedentary lifestyle also appears to play an independent role in increasing the risk of type 2 diabetes. Numerous studies have shown that the prevalence of type 2 diabetes is higher in rural communities than in urban communities, one of the main reasons being inactivity in urban communities.

7. Prevention and screening in diabetes

Diabetes is a debilitating disease with chronic and costly complications that affects most organs of the body. The need for measures to diagnose, prevent and closely monitor diabetes in order to prevent or delay acute and chronic complications has been proven by numerous studies.

7.1. Type 1 diabetes

The cause of this disease is autoimmune and screening and early detection of this type of diabetes is not recommended and performed except in some communities for the following reasons:

1. Uncertainty of a specific limit of any antibody (standard titer specified) that causes the disease.
2. If antibodies can be identified by testing and finding antibodies, a solution to prevent and delay the clinical onset of type 1 diabetes has not been found to date; Because such measures must focus on the immune system, these studies are still in the early stages of the world.
3. Due to the very low prevalence of type 1 diabetes, screening it will not be cost effective (10% -5% of all diabetics).
4. In type 1 diabetes, the symptoms appear quickly and clearly. Therefore, severe symptoms of the disease are the reason for the patient to see a doctor who therefore does not need screening²⁵.

7.2. Type 2 diabetes

Early prevention and cognition and timely and correct treatment of type 2 diabetes are important in the world for the following reasons:

In this type of diabetes, hyperglycemia develops gradually. These people are often asymptomatic or have no severe symptoms, and as a result, in many cases, the disease is not diagnosed (at any given time, at least 50% of people with diabetes are unaware of

their disease. Undiagnosed). During this period, there is asymptomatic and metabolic disorders due to high plasma glucose. These people are at risk for macro and microvascular complications and usually see a doctor when they become aware of a chronic complication of diabetes such as diabetic foot, gangrene of the foot, heart attack or stroke, or kidney failure. Diagnosing glucose intolerance before diabetes and taking steps to control risk factors, including weight loss (through diet modification and increased physical activity), can prevent or at least delay the onset of diabetes. Proper control of blood sugar after early diagnosis of diabetes prevents the occurrence or progression of complications. On the other hand, detection of impaired glucose tolerance or diabetes is possible by performing a simple and non-invasive test such as measuring fasting glucose (twice) or oral glucose tolerance test (OGTT). Considering the progressive and latent course of diabetes, the existence of a cheap and efficient diagnostic method for early diagnosis of the disease and finally the possibility of controlling and preventing the progression of the disease with its early diagnosis, generally confirm the need for screening²⁶.

8. Gestational Diabetes

Any amount of glucose intolerance that first develops or manifests during pregnancy is called gestational diabetes. Gestational diabetes is the most important medical complication and common metabolic disorder in pregnant women. Gestational diabetes is defined as the varying severity of carbohydrate intolerance that first begins or is diagnosed during pregnancy. This definition applies to treatment regardless of whether or not insulin is used (27, 28). As the pregnancy progresses, the increased tissue resistance to insulin increases the demand for insulin. In most pregnancies, this requirement is met, resulting in a balance between insulin resistance and insulin production. But if resistance overcomes, the pregnant woman becomes hyperglycemic, and in these conditions, blood glucose levels rise during pregnancy, and the symptoms of diabetes become apparent in a pregnant woman who has not had diabetes. This condition often occurs in the last half of pregnancy; Insulin resistance progressively increases until delivery. The prevalence of gestational diabetes is reported to be between 1-14% in different parts of the world. A review article conducted in 2014 in 12 provinces of Iran has estimated the prevalence of gestational diabetes at 5.88%^{27&28}.

Gestational diabetes as a silent disease affects the phenomenon of pregnancy, adversely affects the mother and fetus and leads to adverse pregnancy outcomes, the most common of which are fetal macrosomia, birth defects, cesarean section, poly Hydramnios, preeclampsia, and neonatal metabolic disorders (hypoglycemia, hyperglycemia, hyperbilirubinemia), respiratory distress syndrome, and late-onset complications include

maternal type 2 postpartum diabetes²⁹. Although in most women with a history of gestational diabetes, glucose intolerance returns to normal within a few weeks after delivery, insulin resistance or impaired insulin secretion have been reported in these women³⁰.

9. Risk factors for gestational diabetes

The most important risk factors for gestational diabetes are: Age over 30 years, obesity, family history of gestational or type 2 diabetes, history of macrosomic (large) childbirth, and history of stillbirth.

9.1. Guidelines for diagnosing gestational diabetes

9.2. Pregnancy tips

In 2013, the World Health Organization and the International Diabetes Association (IADPSG) officially recommended a two-hour GTT test with 75 g of glucose for screening and diagnosing gestational diabetes^{31&32}. For all pregnant women, a fasting blood sugar test should be requested at the first pregnancy visit and its interpretation is as follows:

Table II: Interpretation of fasting blood sugar test at the first visit.

Fasting blood sugar mg/dl	≤92	Normal
Pre-diabetic	125-93 mg/dl	
Abnormal	≥126	

If fasting blood sugar is between 93 and 125 mg/dL, the person is considered pre-diabetic and proper diet and exercise are recommended. If the fasting blood sugar is 126 or more, the test is repeated, and if the second test is equal to more than 126, the person is diabetic and should be treated. For all non-diabetic pregnant women (normal and pre-diabetic) for screening for gestational diabetes, a two-hour oral glucose tolerance test with 75 g of glucose (OGTT) is required at 28-24 weeks of gestation and is interpreted according to the following guidelines:

Table III: Interpretation of oral glucose tolerance test at 24-48 weeks of gestation.

Fasting blood sugar	≥92	
Blood sugar 1 hour after consuming 75 grams of glucose (mg/dl)	≥180	abnormal
Blood sugar 2 hours after consuming 75 grams of glucose (mg /dl)	≥153	

If at least one of the above results is abnormal, definitive diagnosis of gestational diabetes and necessary action and follow-up are necessary.

9.3. Recommendations after pregnancy

For all women with gestational diabetes, in order to detect stable diabetes, in the 6th to 12th week after delivery, oral glucose tolerance test with 75 g of glucose (fasting and two-hour sampling) should be requested and its interpretation is as follows³¹:

Table IV: Interpretation of oral glucose tolerance test, 6-12 weeks postpartum.

Fasting blood sugar (mg/dl)	99≥	normal
	-125 100	Pre-diabetic
	≥126	
Blood sugar 2 hours after glucose intake (mg/dl)	<140	Normal
	140-199 ≥200	Pre-diabetic Diabetic

9.4. Importance of postpartum follow-up

After childbirth, glucose intolerance persists in about 30% of women with gestational diabetes. Also, women with gestational diabetes are seven times more likely to develop type 2 diabetes, even with mild glucose intolerance, than women with pregnancies with normal glucose tolerance³¹. The prevalence of type 2 diabetes following gestational diabetes has been reported from 3 to 70%. The incidence of this infection increases significantly in the first 5 years after delivery and at a slower rate up to 10 years after delivery³².

More than half of women with gestational diabetes develop type 2 diabetes within the next 20 years³³. Overall, women with a history of gestational diabetes are 7 to 10 times more likely to develop type 2 diabetes³⁴. In women with a history of gestational diabetes, in order to diagnose and control diabetes early or to prevent diabetes, it is necessary to provide training on postpartum follow-up. This includes screening for postpartum diabetes and lifestyle changes (exercise and diet)³⁴.

The American Diabetes Association recommends that women diagnosed with gestational diabetes should be screened for type 2 diabetes 6-12 weeks postpartum and then repeated every three years. It is done to prevent the complications of diabetes. With the diagnosis of pre-diabetes, it is recommended to follow a diet, do more physical activity, to prevent type 2 diabetes, as well as periodic blood sugar tests. If the blood sugar level is normal, it is necessary that because of the high risk of developing diabetes due to a history of gestational diabetes, diet and physical activity, do not become obese and repeat diagnostic tests every three years³⁵. In fact, the primary goal of treatment in women with a history of gestational diabetes is behavioral changes in lifestyle, including changes in diet and physical activity, which modulate the onset and severity of type 2 diabetes in later life³⁶. However, the cooperation of women with a history of postpartum diabetes in timely referral for screening for

postpartum diabetes is weak and most of them do not refer for screening^{36,37}. Studies in the United States and Canada have shown that women refer to postpartum glucose measurements in 45-20% of cases³⁶.

10. Self-regulatory model

According to the results of a study in Iran, the participation rate of women with a history of gestational diabetes for postpartum screening for diabetes was 48.7%³⁷. There are barriers to postnatal diabetes screening in women with a history of gestational diabetes, including stress, time pressure, problems adjusting to maternal role^{38&39}, and chronic self-management deficits. Studies have shown that daily management of diabetes requires behavioral self-regulation and self-regulation is a significant predictor of physical activity and diet^{40&41}.

Self-regulation is the process by which people set their goals, control their emotions and thoughts, and improve their strategies. In self-regulation, a person evaluates his behavior and if it fits his standards, his behavior is evaluated well and makes him happy, and if this behavior does not fit the standards, he tries to achieve the standards by changing the behavior. Then re-evaluates to see if it has been able to reduce or eliminate the behavior gap from the standards. When there is no gap between behavior and standards, then it stops the process or sends it out of its mind^{42&43}. Miller, Brown, and Frederick designed a seven-step self-regulating model. In this model, self-regulatory behavior slips due to failure or defect in each of these stages, these seven stages include: acceptance, evaluation, commissioning, review, planning, implementation and measurement. For many people, taking action and maintaining a lifestyle change is the most difficult aspect of self-care programs and they delay it⁴⁴. Procrastination is defined as a form of failure in self-regulation when a person voluntarily delays despite expecting a bad delay. In short, despite the expectation of a bad result, the relevant action is not performed. New research has shown that procrastination has been associated with negative physical health outcomes, in particular it has been shown that procrastination has been associated with less healthy behaviors, such as nutrition and healthy activity. Part of the poor health experience by procrastinators may be due to their tendency to delay their health problems^{45&46}.

Due to the high prevalence of type 2 diabetes in women with a history of gestational diabetes, one of the midwives' duties is to inform women with gestational diabetes during pregnancy and after delivery and to encourage them to be screened for diabetes. In the postpartum period and to prevent the occurrence of type 2 diabetes or delay its onset, lead them to a healthier lifestyle (diet and physical activity)⁴⁷. However, various studies have shown that women's participation in diabetes screening, diet and physical activity is not desirable and many studies have been conducted by women with a history of gestational diabetes to follow these postpartum follow-ups. Interventions are considered necessary because one of the reasons for the non-participation of these women in postpartum follow-up is lack of self-regulation and procrastination, and self-regulatory strategies provide the basis for purposeful action. This study aims to investigate the effect of self-regulatory model education on postpartum follow-up (including diabetes testing, exercise and physical activity, as well as diet) in women with a history of gestational diabetes. It is hoped that the results and achievements of this study will be a small step towards promoting the health of mothers in Iran.

Conclusion

In conclusion, Gestational diabetes is a silent condition that affects both the mother and the foetus throughout pregnancy. After gestational diabetes, the prevalence of type 2 diabetes has been observed to range from 30 to 70%. Women with a history of gestational diabetes should receive instruction on follow ups after delivery to help with diabetes prevention, early detection, and control. The follow ups, are including postpartum diabetes screening and lifestyle changes (exercise and diet compliance. Training according to the self-regulatory model improves the physical activity and nutritional status of women with a history of gestational diabetes and it is recommended that this model in the programs of the Ministry of Health and at different levels of Use clinical centers and provide training packages based on this model to the health team, especially midwives, nurses, health workers and even doctors.

Interests conflict

The researchers declare that they have no conflict of interest.

References

1. Beaglehole R, Bonita R, Horton R, Adams C, Alleyne G, Asaria P, et al. Priority actions for the non-communicable disease crisis. *The Lancet*. 2011;377(9775):1438-47.
2. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *The Lancet*. 1997;349(9064):1498-504.
3. Currie SL. Applying the Theory of Planned Behaviour to persons with prediabetes and diabetes: An examination of intention and behaviour for healthy eating and physical activity: Library and Archives Canada=Bibliothèque et Archives Canada; 2011.
4. Didarloo A, Shojaeizadeh D, Ardebili HE, Niknami S, Hajizadeh E, Alizadeh M. Factors influencing physical activity behavior among iranian women with type 2 diabetes using the extended theory of reasoned action. *Diabetes & metabolism journal*. 2011;35(5):513-22.
5. Ghazanfari Z, Niknami S, Ghofranipour F, Hajizadeh E, Montazeri A. Development and psychometric properties of a belief-based Physical Activity Questionnaire for Diabetic Patients (PAQ-DP). *BMC medical research methodology*. 2010;10(1):104.
6. Group UPDS. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ: British Medical Journal*. 1998;703-13.
7. Morris AP, Voight BF, Teslovich TM, Ferreira T, Segre AV, Steinthorsdottir V, et al. Large-scale association analysis provides insights into the genetic architecture and pathophysiology of type 2 diabetes. *Nature genetics*. 2012;44(9):981.
8. Gray A, Raikou M, McGuire A, Fenn P, Stevens R, Cull C, et al. Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41). *Bmj*. 2000;320(7246):1373-8.
9. Redekop WK, Koopmanschap MA, Stolk RP, Rutten GE, Wolffenbuttel BH, Niessen LW. Health-related quality of life and treatment satisfaction in Dutch patients with type 2 diabetes. *Diabetes care*. 2002;25(3):458-63.
10. Norris SL, Engelgau MM, Narayan KV. Effectiveness of self-management training in type 2 diabetes. *Diabetes care*. 2001;24(3):561-87.
11. Panzram G. Mortality and survival in type 2 (non-insulin-dependent) diabetes mellitus. *Diabetologia*. 1987;30(3):123-31.
12. Macintosh MC, Fleming KM, Bailey JA, Doyle P, Modder J, Acolet D, et al. Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study. *Bmj*. 2006;333(7560):177.
13. Abolhasani F, Tehrani M, Reza M, Tabatabaei O, Larjani B. Burden of diabetes and its complications in Iran in year 2000. *Iranian Journal of Diabetes and Metabolism*. 2005;5(1):35-48.
14. Lopes-Virella MF, Carter RE, Gilbert GE, Klein RL, Jaffa M, Jenkins AJ, et al. Risk factors related to inflammation and endothelial dysfunction in the DCCT/EDIC cohort and their relationship with nephropathy and macrovascular complications. *Diabetes care*. 2008;31(10):2006-12.
15. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabetic medicine*. 1997;14(S5).
16. HR AM, Azizi F. The assessment of relation between lipid distribution and weight change with diabetes incidence in a group of Tehran, district 13 population. *پژوهش در پزشکی*. 2008;32(2):105-13.
17. Borch-Johnsen K, Neil A, Balkau B, Larsen S. Glucose tolerance and mortality: comparison of WHO and American Diabetes Association diagnostic criteria. *The Lancet*. 1999;354(9179):617.
18. Puavilai G, Chanprasertyotin S, Sriphrapradaeng A. Diagnostic criteria for diabetes mellitus and other categories of glucose intolerance: 1997 criteria by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (ADA), 1998 WHO consultation criteria, and 1985 WHO criteria. *Diabetes research and clinical practice*. 1999;44(1):21-6.
19. Group UHS. Risk of hypoglycaemia in types 1 and 2 diabetes: effects of treatment modalities and their duration. *Diabetologia*. 2007;50(6):1140-7.
20. Gill G, Woodward A, Casson I, Weston P. Cardiac arrhythmia and nocturnal hypoglycaemia in type 1 diabetes—the 'dead in bed'syndrome revisited. *Diabetologia*. 2009;52(1):42.
21. DeWitt DE, Hirsch IB. Outpatient insulin therapy in type 1 and type 2 diabetes mellitus: scientific review. *Jama*. 2003;289(17):2254-64.
22. Canavan RJ, Unwin NC, Kelly WF, Connolly VM. Diabetes-and nondiabetes-related lower extremity amputation incidence before and after the introduction of better organized diabetes foot care. *Diabetes care*. 2008;31(3):459-63.
23. Horikawa Y, Oda N, Cox NJ, Li X, Orho-Melander M, Hara M, et al. Genetic variation in the gene encoding calpain-10 is associated with type 2 diabetes mellitus. *Nature genetics*. 2000;26(2):163.
24. Sladek R, Rocheleau G, Rung J, Dina C, Shen L, Serre D, et al. A genome-wide association study identifies novel risk loci for type 2 diabetes. *Nature*. 2007;445(7130):881-5.
25. Barker JM. Type 1 diabetes-associated autoimmunity: natural history, genetic associations, and screening. *The Journal of Clinical Endocrinology & Metabolism*. 2006;91(4):1210-7.
26. Association AD. Screening for type 2 diabetes. *Diabetes care*. 2003;26:S21.
27. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. *American journal of obstetrics and gynecology*. 1982;144(7):768-73.
28. Bellamy L, Casas J-P, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *The Lancet*. 2009;373(9677):1773-9.
29. Ju H, Rumbold AR, Willson KJ, Crowther CA. Borderline gestational diabetes mellitus and pregnancy outcomes. *BMC Pregnancy and Childbirth*. 2008;8(1):31.
30. Xiong X, Saunders L, Wang F, Demianczuk N. Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes. *International Journal of Gynecology & Obstetrics*. 2001;75(3):221-8.
31. Bennett WL, Ennen CS, Carrese JA, Hill-Briggs F, Levine DM, Nicholson WK, et al. Barriers to and facilitators of postpartum follow-up care in women with recent gestational diabetes mellitus: a qualitative study. *Journal of Women's Health*. 2011;20(2):239-45.
32. Group NDD. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes*. 1979;28(12):1039-57.

33. Alberti KGMM, Zimmet Pf. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabetic medicine*. 1998;15(7):539-53.
34. Hoffman L, Nolan C, Wilson JD, Oats JJ, Simmons D. Gestational diabetes mellitus-management guidelines-The Australasian Diabetes in Pregnancy Society. *Medical Journal of Australia*. 1998;169(2):93-7.
35. Clark HD, Keely E. Getting mothers with gestational diabetes to return for postpartum testing: What works and what does not. *Diabetes Management*. 2012;2(1):33-9.
36. Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, Pi-Sunyer X, et al. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. *The Journal of Clinical Endocrinology & Metabolism*. 2008;93(12):4774-9.
37. Carson MP, Frank MI, Keely E. Original research: postpartum testing rates among women with a history of gestational diabetes—systematic review. *Primary care diabetes*. 2013;7(3):177-86.
38. Nielsen KK, Kapur A, Damm P, De Courten M, Bygbjerg IC. From screening to postpartum follow-up—the determinants and barriers for gestational diabetes mellitus (GDM) services, a systematic review. *BMC pregnancy and childbirth*. 2014;14(1):41.
39. Keely E, Clark H, Karovitch A, Graham I. Screening for type 2 diabetes following gestational diabetes family physician and patient perspectives. *Canadian Family Physician*. 2010;56(6):558-63.
40. Jayne RL, Rankin SH. Application of Leventhal's self-regulation model to Chinese immigrants with type 2 diabetes. *Journal of Nursing Scholarship*. 2001;33(1):53-9.
41. Ginis KAM, Latimer AE, Arbour-Nicitopoulos KP, Bassett RL, Wolfe DL, Hanna SE. Determinants of physical activity among people with spinal cord injury: a test of social cognitive theory. *Annals of Behavioral Medicine*. 2011;42(1):127-33.
42. Anderson ES, Wojcik JR, Winett RA, Williams DM. Social-cognitive determinants of physical activity: the influence of social support, self-efficacy, outcome expectations, and self-regulation among participants in a church-based health promotion study. *HEALTH PSYCHOLOGY-HILLSDALE THEN WASHINGTON DC-*. 2006;25(4):510.
43. Teixeira PJ, Carraça EV, Marques MM, Rutter H, Oppert J-M, De Bourdeaudhuij I, et al. Successful behavior change in obesity interventions in adults: a systematic review of self-regulation mediators. *BMC medicine*. 2015;13(1):84.
44. Wenzel V, Weichold K, Silbereisen RK. The life skills program IPSY: Positive influences on school bonding and prevention of substance misuse. *Journal of adolescence*. 2009;32(6):1391-401.
45. Bandura A. Social cognitive theory of self-regulation. *Organizational behavior and human decision processes*. 1991;50(2):248-87.
46. Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. *The lancet*. 2006;366(9503):2112-7.
47. Sirois FM, Melia-Gordon ML, Pychyl TA. "I'll look after my health, later": An investigation of procrastination and health. *Personality and Individual Differences*. 2003;35(5):1167-84.

Las sedes de la Real Academia de Medicina de las Islas Baleares (1830-2022)

The headquarters of the Royal Academy of Medicine of the Balearic Islands (1830-2022)

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Resumen

El 18 de marzo de 1831 quedó constituida la Real Academia de Medicina y Cirugía de Palma de Mallorca, que se instaló en el edificio de la extinguida Universidad Literaria.

Las disponibilidades económicas de la recién fundada Academia fueron, en general, muy escasas. No obstante su labor científica ha sido ingente a lo largo de sus casi 200 años de historia.

Las sedes académicas variaron de lugar en la capital balear, hasta que el arriendo de una vivienda en la calle Morey 8, el 16 de agosto de 1948, proporcionó tranquilidad y bienestar a la Corporación. Décadas después, el 2 de agosto de 1994, el presidente José Tomás Monserrat informó haber recibido una solicitud de desahucio del local por parte de su propietario.

La Junta directiva dio los pasos para buscar una solución. Afortunadamente, se consiguió del Govern Balear el actual edificio, sito en la calle Can Campaner 4. En noviembre de 1996 –hace ahora 25 años– se trasladó la Corporación académica a la nueva sede.

Palabras clave: Real Academia de Medicina de Baleares; historia; sedes corporativas.

Summary

On March 18, 1831, the Royal Academy of Medicine and Surgery of Palma de Mallorca was established. Installed in the building of the extinct Literary University, the economic resources of the newly founded Academy were, in general, very scarce. However, his scientific work has been enormous throughout its almost 200 years of history.

The locations of the Academy varied from place to place in the Balearic capital, until the lease of a house at Calle Morey 8, on August 16, 1948, provided tranquility and well-being to the Corporation. Decades later, on August 2, 1994, the President José Tomás Monserrat reported having received a request for eviction.

The directive board of the Academy took steps to find a solution. Fortunately, the current building was obtained from the Govern Balear. Located at Calle Can Campaner 4, in November 1996 –25 years ago now– the Royal Academy moved to the new headquarters.

Key words: Royal Academy of Medicine of the Balearic Islands; history; corporate headquarters.

Introducción

Las Reales Academias desempeñan un importante papel en el desarrollo social, científico, económico y cultural español. El fomento de la Medicina española empezó a resurgir gracias al afán renovador del médico liberal Pedro Castelló Ginesta cuando, en 1827, organizó la Junta Superior Gubernativa de Medicina y Cirugía como el organismo central para dirigir y promover las actividades científicas.



Pedro Castelló Ginesta (1770-1850)

Un escrito dirigido al Presidente de esta Junta Superior fue la Real Cédula que el rey Fernando VII, en San Ildefonso, firmó el 31 de agosto de 1830, dando a conocer el Reglamento general para el régimen literario e interior de las Reales Academias de Medicina y Cirugía del Reino, que decía así:

“Deseoso de fomentar en mis dominios el estudio teórico y práctico de la Ciencia de Curar proporcionando a los que se dediquen a este tan noble como útil y apreciable Facultad todos los medios de adelantar, de instruirse y de extender la esfera de sus conocimientos, he creído a propósito, para el logro de tan importante objeto, fundar Academias en varios puntos bajo un nuevo plan”

La Real Cédula del 15 de enero de 1831 señalaba los distintos distritos médicos y sus respectivas Academias. Se publicaba, a continuación, el Reglamento General.

En base al nuevo ordenamiento, la Real Academia de Medicina y Cirugía de Palma de Mallorca quedó constituida el 18 de marzo de 1831.

Las *Reales Academias de Medicina* fueron, en un principio, diez, ubicadas en *Madrid*, para Castilla la Nueva; *Valladolid* para Castilla la Vieja; *Santiago*, para Galicia y Asturias; *Sevilla*, para su Reino, el de Córdoba y Provincia de Extremadura; *Cádiz*, para la suya; *Granada* para su Reino, el de Jaén y el de Murcia; *Valencia*, *Barcelona*, *Zaragoza* y *Palma de Mallorca*, para las Islas Baleares.

Por su origen y estatutos la Real Academia de Medicina y Cirugía de Palma de Mallorca tuvo un talante bien distinto al de su predecesora, la Academia Médico-Práctica de Mallorca (1788-1800). Democrática esta última, pudiendo pertenecer a ella todos los médicos de la Isla, fue la primera oficial, real, selectiva. Los socios de la recién creada institución fueron considerados como criados de la Real Casa. *“Tendrán un uniforme particular de un frac azul turquí, cerrado con nueve botones dorados, espada y hebillas doradas, escarapela roja con presillas de oro”*. Entre sus obligaciones, figuraba realizar los exámenes de reválida de médicos, parteras y bachilleres en Medicina.

La Junta Superior Gubernativa comisionó a D. Miquel Noguera de Superna (1774-1833) para organizar la Real Academia y se le encomendó su instalación en el edificio del local de la extinguida Universidad Literaria.



Miguel Noguera de Superna (1774-1833)



Figura 1: Imagen del patio del antiguo Seminario, primera sede de la Real Academia de Medicina.



Figura 2: Claustro del convento jesuita de Monti-Sión, segundo local social académico.

Las disponibilidades económicas de la recién fundada Real Academia, al ser muy escasas, tuvieron que contentarse con entrar de prestado en el edificio del Real Seminario Conciliar (**Figura 1**), bajo unas condiciones mezquinas, según consta en un oficio dirigido por su vicerrector, Juan Herrera, el 7 de junio de 1831 al vicepresidente de la Real Academia de Medicina:

“No teniendo en el edificio de este Real Seminario Conciliar pleno dominio, no puedo conceder a V. pleno derecho para tener las Sesiones en él como me pide en su oficio de 17 del mes próximo pasado y sólo se extienden mis facultades a la concesión de poder ocupar algunas de las salas de él, interín no se necesiten para los Catedráticos las aulas y academias; por cuya razón, siempre que V. desee ocuparlas por los objetos que indica, deberá ser con la circunstancia de dejarlas a libre disposición de los Catedráticos cuando éstos las necesiten para los alumnos, sirviéndose contestar si desea admitir esta concesión bajo las condiciones que llevo expuestas”.

Al aplicar el Decreto del 4 de julio de 1835, la regente doña María Cristina, en nombre de su hija la reina Isabel II, de supresión de la Compañía de Jesús en España, “*por convenir a la prosperidad y bien del Estado*”, se apresuró la Real Academia de Medicina a instalarse en el Colegio de los Padres Jesuitas de la calle Monti-Sion (**Figura 2**), también de forma modesta, en unas habitaciones del ex-convento. En este lugar permanecerá la Corporación hasta entrado el siglo XX.

Estos decepcionantes avatares iniciales de la Real Academia contrastan con la ingente labor científica realizada, desde su fundación, por los Académicos que supieron engrandecerla con una dignidad jamás puesta en entredicho.

Las sedes académicas desde la Guerra civil

Al principio de la Guerra Civil (1936-39) la Real Academia ocupaba un espacio en el Museo Provincial de Bellas Artes, en el Estudio General (**Figura 3**) I. En los primeros meses de la contienda, sufrió el edificio un bombardeo de la aviación republicana. El destrozo provocó la necesidad de buscar otro asentamiento, provisional, lográndolo en la calle San Francisco n.º 1, hasta tanto se pudiera ocupar otro local asignado en la calle Concepción, dependiente del Hospital Provincial.



Figura 3: Fachada del Estudio General Luliano.

Felizmente, el 16 de agosto de 1948 se firmó el contrato de arriendo de una vivienda situada en la calle Morey n.º 8, primer piso, segunda puerta (**Figura 4**). Formalizaron la escritura su propietario D. Francisco Pizá Alabern y el presidente de la Real Academia Dr. José Sampol Vidal. Empezaba una época de tranquilidad, bonanza y bienestar que se prolongaría hasta la convocatoria de la Junta de Gobierno de 2 de agosto de 1994, en que el presidente Dr. José Tomás Monserrat informó que el motivo del requerimiento urgente y en época vacacional,



Figura 4: Vista del palmesano carrer de Morey.

se basaba en haber recibido una solicitud de desahucio del local social por parte de su propietario, tramitado por el Juzgado n.º 2 de esta capital.

El requerimiento interesaba se dictare sentencia declarando resuelto el contrato de arrendamiento de la referida vivienda y proceder al desalojo de la misma y la imposición de costas al propio demandado.

Admitida a trámite la demanda, habiéndose solicitado por parte de la Real Academia una sentencia absolutoria, se celebró el juicio el 1 de febrero de 1995.

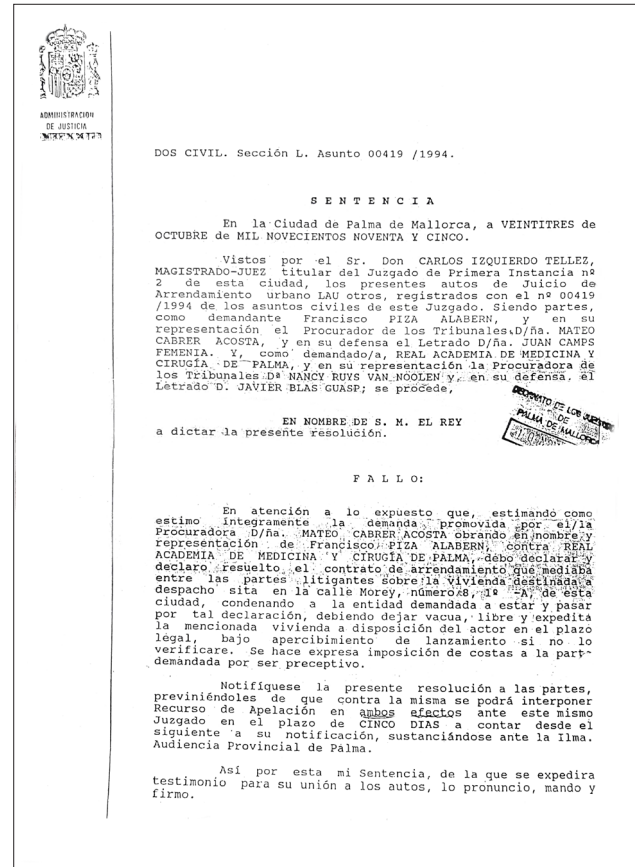
El acta de la sesión inaugural del Curso académico 1995, presidida por el entonces presidente de la Comunidad Sr. Gabriel Cañellas Fons dice que, una vez abierto el acto:

“Nuestro Sr. presidente, en breves palabras, trazó la orientación que, en su criterio, tenía que tomar la Real Academia, e hizo pública petición de un local adecuado para la RR.AA. de esta capital y agradeció enormemente las atenciones recibidas de las Corporaciones públicas de la Comunidad”.

En la posterior sesión de gobierno de 4 de julio de 1995 se comentó, con extrañeza, que en los momentos actuales de verano, todavía no se haya fallado el pleito del contrato de arriendo de nuestro local social, pues según informe de nuestro letrado, debería haberse resuelto ya. Mientras tanto las gestiones continuaban.

El fallo, emitido el 23 de octubre de 1995, declaró resuelto el contrato de arrendamiento y condenó a la entidad demandada a dejar vacua, libre y expedita la vivienda en el plazo legal, bajo apercibimiento de lanzamiento si no lo verificare (Figura 5).

Figura 5: Fallo del 23 e octubre de 1995.



El problema generado para la centenaria institución académica era mayúsculo. La Junta directiva corporativa acordó y dio los pasos para darle solución.

Así, el presidente Dr. Tomás Monserrat en la junta de gobierno del 14 noviembre de 1995 pudo extenderse en explicar, con satisfacción, la visita que había efectuado a un local de la calle de Can Campaner, con el conseller de Sanitat, Dr. Bartolomé Cabrer, el Director Gral. de Sanidad Dr. Ginés Martínez Pina, el de Acción Social Dr. José M.ª Fiol, junto al coordinador de la consellería D. Domingo Lull, el aparejador Sr. Rullán, el maestro de obras y otros operarios al mejor objeto de poder ubicar el mobiliario y la biblioteca corporativos a las obras que se estaban realizando. Se trataba del antiguo convento de las Reparadoras, edificio con doble entrada por las calles de la Rosa y Campaner. El presidente lo señalaba como el próximo local social de la Academia. Con vistas a la mejor adaptación posible a las necesidades académicas se calculaban unos gastos de nueve millones de pesetas.

El mes siguiente, el 5 de diciembre de 1995, la presidencia dio cuenta de la sentencia dictada el 23 de octubre anterior en sentido contrario a la corporación. En cumplimiento al acuerdo unánime se ordenó al letrado de la Academia, D. Joaquín Blas Guasp interponer recurso sobre la misma. Por unanimidad se acordó, de ser posible, firmar cuanto antes un contrato con el Govern Balear.

En enero de 1996, el secretario Dr. Santiago Forteza, informaba en junta de la visita efectuada con el presidente Tomás Monserrat al presidente Sr. Cristobal Soler en su despacho del Consolat de Mar, de la que extrajeron, aparte de su calurosa acogida, una inmejorable impresión tanto en lo referente al futuro local como en la dotación presupuestaria y de personal auxiliar de secretaría.

El Dr. Bartolomé Cabrer Barbosa, académico numerario y conseller de Sanidad, oficialmente manifestó el ofrecimiento del nuevo local social –la antigua residencia convento de las Reparadoras–, recientemente adquirido por el Govern Balear.

En la sesión ordinaria de 22 octubre 1996, se aceptó el presupuesto a la Casa Mobeltrans para el traslado del mobiliario a la nueva sede ascendía a unas setecientas mil pesetas. Asimismo, si por cuestiones técnicas dicho traslado tuviese que realizarse en dos fechas separadas, se acordó autorizar al propietario de la sede actual académica a que ocupe por separado la primera parte del mismo que quedare desocupada, antes del desalojo total del piso.

El presidente Tomás Monserrat comunicó la previsión de que, a fines del mes actual, el local se encontrara listo para la instalación de la biblioteca y de la secretaría y señaló la inminencia de la firma del convenio entre la conselleria y la Real Academia; para una mejor redacción se había entregado un ejemplar de los estatutos corporativos.

El 12 de noviembre de 1996 el Secretario General por orden del Excmo. Señor Presidente Dr. Tomás participaba a los académicos que la junta se reuniría el día 19 de noviembre de 1996, a las 19'30, en sesión ordinaria de Gobierno. “Esta Junta tendrá lugar en el nuevo local social, iglesia de las monjas Reparadoras, calle Campaner nº 4, bajos, de esta Ciudad”.

El edificio

Se trata de un ejemplo de la arquitectura neogótica en Mallorca, convertida en un privilegiado salón de actos. El edificio y sus anexos pertenecían a las monjas Reparadoras que, principalmente, se dedicaban a la adoración del Santísimo Sacramento, a la catequesis y a los ejercicios espirituales.

La congregación había sido fundada por la baronesa Emilia, hija de los condes Oultremont y Lierneux de Presle, parientes de sangre del Papa Pío IX. Ya viuda, la baronesa Emilia tuvo una revelación de la Virgen, que le pidió verse reemplazada aquí en la tierra, por almas que profesasen a su Divino Hijo, amor y respeto especialísimo con el fin de “la reparación para Jesús con María”.



Figura 6: Visión general del salón de actos.

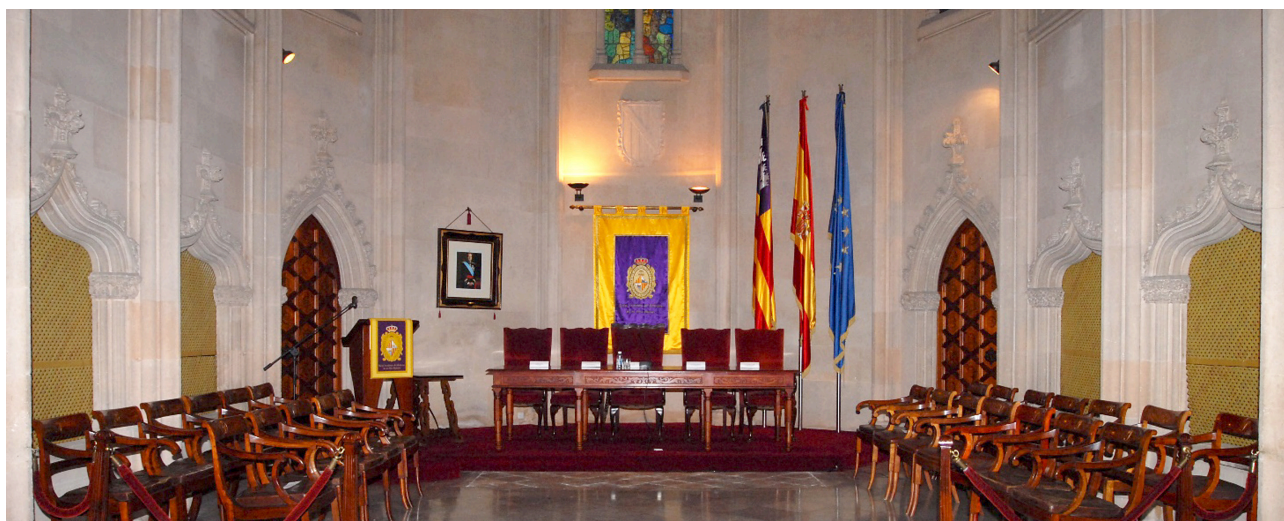


Figura 7: Presidencia de la sala de actos académica, en la antigua Iglesia de las monjas Reparadoras.

El salto a Mallorca de las Reparadoras se produjo el 22 de febrero de 1906. En principio se instalaron en la casa solariega de la familia del historiador D. Alvaro Campaner. En 1920 se proyectó un nuevo templo, a cargo del arquitecto Guillem Forteza, que escogió para el diseño el estilo neogótico. El proyecto fue ejecutado por Antonio Jiménez y por el maestro de obras Joan Comas. Miquel Sacanell realizó el artesanado.

Se accede por la calle Campaner a través de un portal de medio punto, blasonado con una cruz y un cáliz, emblema de la Congregación. El templo consta de ábside y de una nave. La cubierta se realizó de madera policromada. Se inauguró, solemnemente, el 1 de junio de 1924. Pronto se cumplirá un siglo.

Como señaló Bartomeu Bestard, cronista oficial de la Ciudad de Palma, "las Reparadoras ya no habitan en la calle Campaner, el edificio gestionado por la Conselleria de Sanitat, se ha convertido en un privilegiado salón de actos con gran empaque en la ciudad" (Figura 6 y 7).

25 aniversario en la sede de Can Campaner

El acta de la sesión ordinaria del 19 de noviembre de 1996, comienza con:

"Una vez realizado el traslado de nuestro mobiliario y enseres al nuevo local de la calle Can Campaner nº 4, esta es la primera vez que celebramos esta Junta en el domicilio indicado, habiendo abandonado definitivamente el anterior de la calle Morey nº 8. En esta nueva ubicación el Excmo. Sr. Presidente Dr. D. José Tomás Monserrat, abrió la sesión a las 19'30 horas, asistiendo a la misma los Muy Il'tres. Sres. Académico Numerarios que se citan al margen".

Los académicos presentes en esa primera sesión fueron Forteza, Tejerina, Román, Tomás, Miró, Anguera, Muntaner, Bujosa. A continuación, la presidencia mostró la "satisfacción personal y colectiva por tener una nueva sede social que desea definitiva". Y continuó:

"Creo que vivimos hoy unos momentos importantes y trascendentes en la casi doble centenaria historia de la Real Academia. Me siento obligado, por creer

que es de justicia, dar las gracias y manifestar mi gratitud a todas las personas y entidades que han hecho posible la vivida realidad ahora presente, de categoría fabulosa.

Hace un año estábamos pendientes de cumplimentar una sentencia judicial de desahucio obligado del anterior local social, ocupado por nuestra corporación durante casi medio siglo. Hoy vivimos la otra cara de la moneda, otra distinta realidad, nos encontramos en un salón de actos maravilloso y amplio, poseyendo un lugar reservado de dimensiones no soñadas para poder ubicar el archivo, la biblioteca y la secretaría y realizar cómodamente las Juntas de Gobierno.

Mi agradecimiento abarca, en primer lugar, a todos los Muy Il'tres. Sres. académicos numerarios por el esfuerzo realizado a lo largo de este curso, en favor de la Institución. Gracias, también, a la Junta de Gobierno, de un modo singular al vicepresidente y secretario, que por sus funciones reglamentarias, han llevado la parte más activa en la preparación y realización de proyectos, entrevistas, solicitudes, inventarios, visitas, inspecciones, etc. Gracias igualmente al M. H. Sr. Presidente de CAIB y a sus antecesores en el cargo, por su interés y amable acogida, así como a los anteriores y a los actuales Sres. consellers de Educación y Sanidad, por su apoyo y munificencia presupuestaria.

Creo que es de obligada y de estricta justicia, señalar de un modo especial, la gran ayuda recibida del M.I.Sr. Dr. D. Bartolomé Cabrer Barbosa, académico numerario y también recordar a los que llevaron a término las ideas, proyectos, reformas, adecuaciones, decorados e iluminación y, de un muy singular modo, a D. Domingo Llull por su colaboración inapreciable. Gracias a todos."

En la siguiente sesión ordinaria, celebrada el 12 de diciembre, a propuesta del Dr. Tejerina, vicepresidente de la Corporación, se acordó por unanimidad que constara en acta la satisfacción por la consecución de este nuevo local social "que tanto satisface nuestras necesidades".

Bibliografía recomendada

Bestard, Bartomeu. "Las Reparadoras, salón de solemnidades". Diario de Mallorca, 20/04/2008.

Piña Homs, Román. *Historia de la Universidad de Mallorca, grandezas y miserias de una élite intelectual. Siglos XV-XX*. Palma, Editorial Leonard Muntaner.

Rodríguez Tejerina, José M^º. "La Real Academia de Medicina y Cirugía de Palma de Mallorca a los ciento cincuenta años de su fundación (1831-

1981)". *Comunicaciones, II Congreso Nacional de RR.AA.* Palma de Mallorca, 1981, p.33-46

Tomás Monserrat, José. "La Real Academia de Medicina y Cirugía de Palma de Mallorca y la Ciencia Médica del siglo XIX. Nota para el estudio de su contribución". *Comunicaciones, II Congreso Nacional de RR. AA.* Palma de Mallorca, 1981, p.53-67.

Ozonoterapia, respaldo científico y uso como terapia complementaria en la COVID-19

Ozone therapy, scientific support and use as complementary therapy in COVID-19

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Resumen

La pandemia originada por el coronavirus SARS-CoV2 (COVID-2019) ha infectado a más de 246 millones de personas, con un 2 % de letalidad. Hasta la fecha, no existen terapias con una eficacia probada bajo estudios clínicos y solo pocas vacunas clínicamente aprobadas. A pesar de la gran variedad de fármacos bajo investigación, el arsenal farmacológico para enfrentar esta enfermedad se encuentra muy restringido. En este contexto, hay un acercamiento a métodos de tratamientos complementarios y tradicionales. La ozonoterapia hoy cuenta con un amplio respaldo de estudios toxicológicos, moleculares, preclínicos y clínicos, con un ritmo de aparición de 4 artículos diarios en la base de datos MedLine de PubMed en los últimos meses. Existe un amplio número de trabajos que han soportado los mecanismos por los cuales el ozono médico, puede ser usado como terapia complementaria en esta infección. En la actualidad hay 23 ensayos clínicos inscritos en bancos de ensayos clínicos públicos, 7 de ellos con resultados. Por otra parte, han aparecido 28 artículos científicos con resultados de su uso en las fases de prevención, tratamiento del paciente infectado y tratamiento de convalecientes. Los principales resultados indican que el ozono: disminuye los índices de inflamación, disminuye el tiempo de respiración asistida, mejora la saturación de oxígeno y negativiza la PCR en períodos más cortos. No obstante, son necesarios estudios clínicos controlados más amplios para ratificar estos resultados.

Palabras clave: Ozono, ozonoterapia, COVID-19, SARS Cov2.

Summary

The pandemic caused by the SARS-CoV2 coronavirus (COVID-2019) has infected more than 246 million people, with a 2% fatality rate. To date, there are no therapies with proven efficacy under clinical studies and only few clinically approved vaccines. Despite the great variety of drugs under investigation, the pharmacological arsenal to face this disease is very restricted. In this context there is an approach to complementary and traditional treatment methods. Today ozone therapy has extensive support from toxicological, molecular, preclinical and clinical studies, with a rate of appearance of 4 articles per day in PubMed's MedLine database in the recent months. There is a large number of studies that have supported the mechanisms by which medical ozone can be used as a complementary therapy in this infection. There are currently 23 clinical trials registered in public clinical trial banks, 7 of them with results. In addition, 28 scientific articles have appeared with results of its use in the phases of prevention, treatment of the infected patient and treatment of convalescents. The main results of the studies indicate that ozone: reduces inflammation indices, decreases assisted breathing time, improves oxygen saturation and makes PCR negative in shorter periods. However, larger controlled clinical studies are needed to confirm these results.

Key words: Ozone, ozone therapy, COVID-19, SARS Cov2.

Hasta octubre de 2021, la pandemia originada por el coronavirus SARS-CoV2 (COVID-2019) se ha extendido por más 223 países o territorios. Ha infectado a más de 246 millones de persona y ha causado más de 5 millones de muertes, con un 2 % de letalidad. Esto representa una amenaza sin precedentes para la salud y la economía mundial. Un tratamiento específico eficaz aún no está disponible para pacientes con infección por COVID-19. Las experiencias en el manejo anterior de infecciones virales respiratorias han proporcionado información sobre el tratamiento de la COVID-19. Numerosas terapias potenciales, incluida la terapia de soporte, agentes inmunomoduladores, terapia antiviral y transfusión de plasma de convalecientes, se han aplicado tentativamente en contextos clínicos. Varias de estas terapias han proporcionado beneficios, pero los estudios clínicos controlados no han demostrado la real eficacia de la mayoría de los más de 350 fármacos en estudio. A la par se está trabajando en más de 150 tipos de vacunas, aproximadamente el 25% de ellas en las distintas fases de ensayos en humanos¹. No obstante, el desarrollo de una vacuna efectiva y segura está aún lejano².

Los enfoques tradicionales de descubrimiento de fármacos consumen mucho tiempo y los métodos de prueba y error suelen ser ineficaces. Debido a los requisitos regulatorios para evaluar la seguridad y la eficacia, el tiempo necesario para desarrollar un nuevo fármaco toma, como promedio, de una a dos décadas. Un enfoque racional para superar las altas tasas de fracaso, el tiempo y los costos involucrados en la investigación y el desarrollo, es reutilizar los medicamentos existentes, en función de la similitud de los mecanismos para los cuales van dirigidos con la patogenia de la enfermedad. Además, los medicamentos reutilizados tienen la ventaja de reducir los costos y el tiempo de desarrollo, ya que los datos farmacocinéticos, toxicológicos y de seguridad están previamente disponibles. Tomando la reutilización como estrategia principal, se están realizando muchos ensayos controlados aleatorios de medicamentos conocidos, en pacientes con la COVID-19.

Los corticosteroides y los inhibidores de la interleucina-6 probablemente confieren importantes beneficios en pacientes con COVID-19 grave. Los inhibidores de la quinasa Janus parecen tener beneficios prometedores, pero la certeza es baja. La azitromicina, hidroxiquina, lopinavir-ritonavir e interferón beta no parecen tener ningún beneficio importante. Sigue siendo incierto si el remdesivir, la ivermectina y otros fármacos confieren algún beneficio importante para el paciente. Los glucocorticoides probablemente reducen la mortalidad y la ventilación mecánica en pacientes con COVID-19 en comparación con la atención estándar. La efectividad de la mayoría de las intervenciones es incierta porque la mayor parte de los ensayos controlados aleatorios hasta ahora han sido pequeños y tienen limitaciones importantes³.

De acuerdo con la revisión sistemática en tiempo real sobre la COVID-19 / Intervenciones farmacológicas, luego del análisis de 101 ensayos clínicos que involucraron a 67 491 pacientes, tomando en consideración el criterio "mortalidad", se pudo concluir que los corticosteroides probablemente reducen la mortalidad. La colchicina puede reducir la mortalidad. Aún no hay evidencia convincente de que cualquiera de los otros tratamientos tenga un beneficio en este resultado, en comparación con el cuidado estándar o entre sí. Por otro lado, la administración de Hidroxiquina, Interferón beta, Lopinavir-ritonavir, Remdesivir, Azitromicina, Vitamina D, Vitamina C, Anticoagulantes, Inhibidores de la interleucina 6 e Inhibidores de la enzima convertidora de angiotensina no la reducen. Los efectos de Favipiravir, Hidroxiquina más Azitromicina, Ivermectina, factor estimulante de colonias de granulocitos humanos recombinantes, doxiciclina más ivermectina, son muy inciertos¹.

Las dosis altas de corticosteroides están estrechamente asociadas con eventos adversos como infecciones secundarias, aclaramiento viral retardado y aparición de resistencia viral. La Organización Mundial de la Salud desaconsejó la administración rutinaria de corticosteroides, excepto para indicaciones como enfermedad pulmonar obstructiva crónica exacerbada y shock séptico. La colchicina inhibe la polimerización de la tubulina y la generación de microtúbulos y, posiblemente, los efectos sobre las moléculas de adhesión celular, las quimiocinas inflamatorias y el inflammasoma. Reduce la reacción inflamatoria excesiva al inhibir la síntesis de TNF-alfa e Interleucina-6. La colchicina no tiene una ventana terapéutica amplia, el tratamiento con este medicamento debe manejarse bien. No puede administrarse con antibióticos macrólidos o en caso de disfunción renal o hepática. En este contexto diferentes países se han acercado a métodos de tratamientos complementarios y tradicionales. Están en estudio diversos compuestos de origen natural, tanto en la prevención como en el tratamiento de la COVID-19⁴, lo que confirma la necesidad de estrategias terapéuticas o complementarias en el enfrentamiento de esta enfermedad

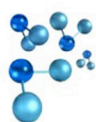
La ozonoterapia, como método complementario⁵ también ha tenido un amplio respaldo como propuesta terapéutica. En la actualidad se registran 25 trabajos de revisión bibliográfica que justifican su uso. Los trabajos han sido escritos por 100 autores de 12 nacionalidades, fundamentalmente de Italia (39%), España (15%), Irán (15%) y Estados Unidos (13%). Los principales mecanismos apoyados son: modulación de Nrf2-NF-κB, modulación de la liberación de citocinas, mejora del estado de hipoxia, mejora del flujo sanguíneo, liberación de óxido nítrico, modulación del estrés oxidativo, efecto citoprotector y regulador del microbiota intestinal⁶⁻⁹. Todas las hipótesis se basan en estudios previos moleculares, preclínicos, y clínicos que soportan el uso del ozono médico desde el punto de vista científico. De hecho, la biblioteca

especializada del ISCO3 (www.isco3.org) contiene en la actualidad 3672 estudios sobre el uso médico del ozono, de los cuales 753 (20 %) son estudios básicos y 2497 (68 %) son estudios clínicos. Mientras que la palabra clave *ozone therapy* en la base de datos PubMed de Biblioteca Nacional de Medicina de los EE.UU. da como resultado 4024 documentos relacionados con la ozonoterapia de los cuales 301 son ensayos clínicos, 207 ensayos controlados aleatorios, 55 de revisión sistemática y 33 estudios de meta-análisis, que apoyan el uso del ozono en la medicina. El número de artículos sobre este tema en 2020 y 2021 llegó a alcanzar una media de 4 artículos indexados por día. Por otra parte, en ClinicalTrials.gov (base de datos de los estudios clínicos en los Institutos Nacionales de Salud de EEUU) hay 61 estudios registrados para ozonoterapia (de los cuales: terminados 3, completados 25, activos no reclutados 3 y reclutando 13).

Sobre el uso del ozono en la COVID-19, actualmente hay 23 ensayos clínicos en bases de datos de ensayos clínicos públicos, 7 de ellos con resultados. España, Italia, China, Cuba e Irán tienen un historial de 3 ensayos clínicos registrados por país. Además, Turquía y Brasil tienen 2 ensayos clínicos en curso. Bajo ensayos clínicos, hay 999 pacientes con la COVID-19 (Figura 1). La vía de administración mayormente propuesta es la auto hemoterapia mayor y en segundo lugar la insuflación rectal⁹⁻¹⁷.

Hasta el momento se han publicado 28 artículos científicos con resultados, sobre la aplicación de ozono en los pacientes con la COVID-19. Los artículos que reportan una intervención en los pacientes COVID-19 suman 25. En esquemas de prevención se han tratado 444 sujetos mientras que en esquema de intervención se han involucrado 395 pacientes. Los estudios que han involucrados pacientes convalecientes de la COVID-19 agrupan 189 pacientes. El 57% de los manuscritos están indexados en la base de datos MedLine. Las vías de administración más utilizadas para la intervención en pacientes con la COVID-19 son: la auto hemoterapia mayor y la solución salina ozonizada¹⁸. Italia, España y China concentran la mayoría de los autores en este tema. Los países que han creado las redes de investigación más internacionalizadas son Italia y España. Los principales resultados de los estudios indican que el ozono: disminuye los índices de inflamación, disminuye el tiempo de respiración asistida, mejora la saturación de oxígeno y negativiza la PCR en períodos más cortos (Figura 2). Uno de los estudios con resultados ya publicados tuvo lugar en Ibiza (Islas baleares, España). Los datos preliminares permitieron concluir que, en los pacientes tratados con auto hemoterapia, el tiempo para la mejoría clínica era significativamente más corto y también el tiempo para la disminución la proteína C reactiva, ferritina, dímero D y la lactato deshidrogenasa¹⁷. No obstante, son necesarios estudios clínicos controlados más amplios para ratificar estos resultados.

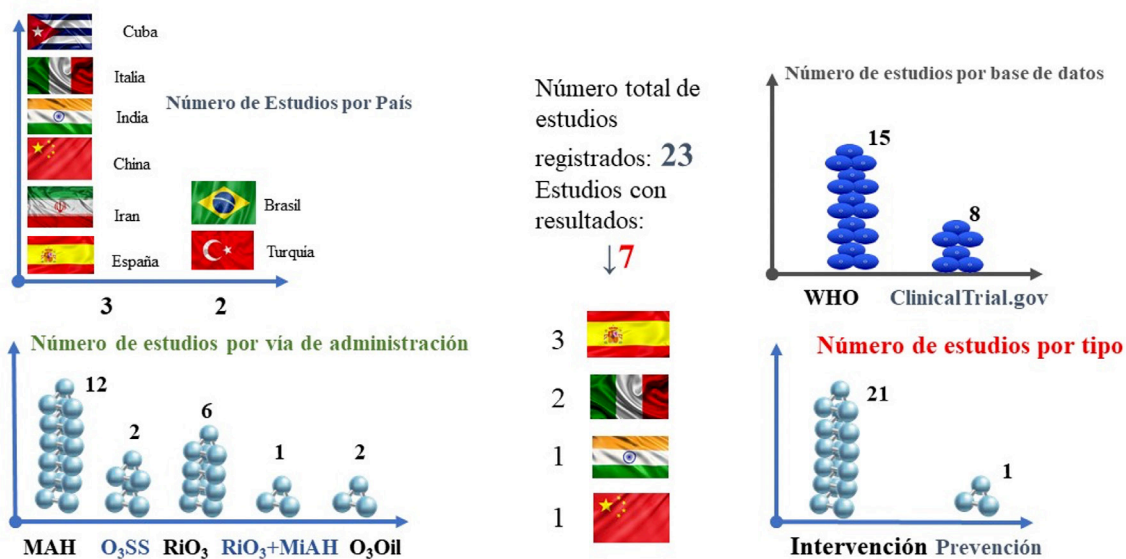
Figura 1: Ozono y la COVID-19. Estado actualizado de los ensayos clínicos en curso. Leyenda: MAH, Auto hemoterapia mayor; MIAH, Auto hemoterapia menor; SSO3 Solución salina ozonizada; RIO3, insuflación rectal; O3 Oil, aceite ozonizado; WHO, Organización mundial de la salud.



Artículos a texto completo disponibles en: <https://isco3.org/library/>

Actualización: Octubre 2021

Número total de pacientes inscritos en grupos de Terapia con O₃: 999



Fuentes: ClinicalTrials.gov [U.S. National Library of Medicine], International Clinical Trials Registry Platform (ICTRP) [WHO]

A pesar de este cúmulo de estudios sobre las potencialidades del ozono médico como terapia complementaria, se sigue tildando al ozono de “biocida” (sustancias que están destinadas a destruir, contrarrestar, neutralizar, impedir la acción o ejercer un control de otro tipo sobre cualquier organismo considerado nocivo para el ser humano) o a la ozonoterapia de “pseudociencia” (falso tratamiento que es presentado como científico). Ello denota un total desconocimiento del concepto de ozono médico definido en la Declaración de Madrid sobre la ozonoterapia⁵, donde se definen aspectos básicos como el tipo de equipo, calificación y preparación del personal que lo ejecuta y protocolos de actuación seguros. Por otra parte, ignora el cúmulo de artículos científicos que contienen los resultados de los hallazgos moleculares, preclínicos y clínicos sobre este tema.

De esta forma el ozono médico queda marginado al concepto de medicamento huérfano (medicamentos no desarrollados ampliamente por la industria farmacéutica por razones financieras, ya que van destinados a un reducido grupo de pacientes, y que, sin embargo, responden a necesidades de salud pública). De hecho, la mayor parte de las investigaciones en ozonoterapia la realiza el sector privado, ya que son escasos los fondos públicos para soportar estos estudios. En materia de costos vale la pena aclarar que la mayor parte de

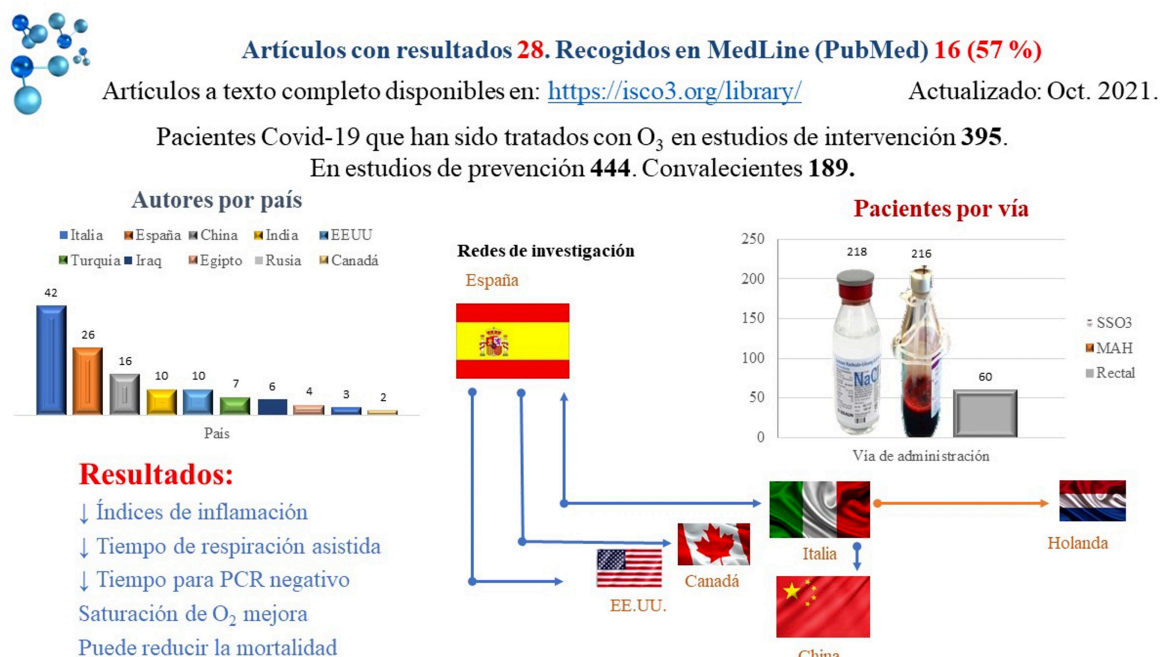
la ozonoterapia se aplica en consultorios privados y esto incide en el costo del tratamiento al paciente. Sin embargo, si este proceder fuera introducido en el sector público, los ahorros de recursos, medicamentos y tiempos de estadías hospitalarias, tendrían una gran repercusión en términos de economía sanitaria, tal y como lo han demostrado algunos estudios en esta dirección^{19,20}.

Se puede decir que en la actualidad existen las premisas científicas para llevar a cabo estudios clínicos más amplios, que permitan la introducción de la ozonoterapia en el tratamiento complementario de patologías de gran incidencia en la población, como enfermedades infecciosas, la diabetes y sus complicaciones, el control del dolor, enfermedades donde incide la hipoxia, entre otras. En particular en el caso de la COVID-19, los resultados preliminares son alentadores, en el sentido que cuando se aplica siguiendo los protocolos correctos, por personal entrenado, con los equipos certificados; las mejorías que se han reportado, permiten la recuperación más acelerada de los pacientes.

Conflicto de intereses

El autor declara no tener ningún conflicto de interés.

Figura 2: Ozono y la COVID-19, Actualización de los estudios clínicos publicados. Leyenda: SSO3, solución salina ozonizada; MAH, autohemoterapia mayor.



Referencias

1. Siemieniuk RA, Bartoszko JJ, Ge L, Zeraatkar D, Izcovich A, Kum E, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ*. Jul 30 2020;370:m2980.
2. Tu YF, Chien CS, Yarmishyn AA, Lin YY, Luo YH, Lin YT, et al. A Review of SARS-CoV-2 and the Ongoing Clinical Trials. *Int J Mol Sci*. Apr 10 2020;21(7).
3. Hans-Christoph D. Dexamethason senkt die 28-Tage-Mortalität. *InFo Neurologie*. 2020;22(9):29-31.
4. Luo H, Tang QL, Shang YX, Liang SB, Yang M, Robinson N, et al. Can Chinese Medicine Be Used for Prevention of Corona Virus Disease 2019 (COVID-19)? A Review of Historical Classics, Research Evidence and Current Prevention Programs. *Chin J Integr Med*. Apr 2020;26(4):243-50.
5. ISCO3. *Madrid Declaration on Ozone Therapy*. 3 ed. Madrid, Spain: ISCO3; 2020.
6. Martínez-Sánchez G, Schwartz A, Di-Donna V. Potential Cytoprotective Activity of Ozone Therapy in SARS-CoV-2/COVID-19. *Antioxidants (Basel)*. 2020;9(389).
7. Gavazza A, Marchegiani A, Rossi G, Franzini M, Spaterna A, Mangiaterra S, et al. Ozone Therapy as a Possible Option in COVID-19 Management. *Front Public Health*. 2020;8:417.
8. Tommaso-Ranaldi G, Rocco-Villani E, Franza L. Rationale for ozone-therapy as an adjuvant therapy in COVID-19: a narrative review. *Med Gas Res*. 2020;10(3):134-8.
9. Zheng Z, Dong M, Hu K. A preliminary evaluation on the efficacy of ozone therapy in the treatment of COVID-19. *J Med Virol*. May 21 2020;92(11):2348-50.
10. Franzini M, Valdenassi L, Ricevuti G, Chirumbolo S, Depfenhart M, Bertossi D, et al. Oxygen-ozone (O₂-O₃) immunocellular therapy for patients with COVID-19. Preliminary evidence reported. *Int Immunopharmacol*. Aug 8 2020;88:106879.
11. Fernandez-Cuadros ME, Albaladejo-Florin MJ, Alava-Rabasa S, Usandizaga-Elio I, Martinez-Quintanilla Jimenez D, et al. Effect of Rectal Ozone (O₃) in Severe COVID-19 Pneumonia: Preliminary Results. *SN Compr Clin Med*. Aug 3 2020:1-9.
12. Wu J, Cherie T, Hongzhi Y, Youwei W, Yutao T, Wenwei S, et al. Recovery of One ICU-Acquired COVID-19 Patient Via Ozonated Autohemotherapy. *The Innovation SSRN*. DOI: 10.1016/j.xinn.2020.100060. 2020.
13. Razzaq HA, Hasan MS, Al-Dhalemy MF, Al-Silaykhee WM, Alhmadi HB, Majeed ZA. Utilization of Ozone as a Complementary Therapy for COVID-19 Patients. *International Journal of Psychosocial Rehabilitation*. 2020;24(7):10577-88.
14. Peña-Lora D, Albaladejo-Florin MJ, Fernández-Cuadros ME. Uso de Ozonoterapia en paciente anciana con neumonía grave por COVID-19. *Revista Española de Geriátria y Gerontología*. 2020;55(6):362-4.
15. Schwartz A, Narros RM. COVID-19 Dermatological manifestations. Presentation of two cases. *Ozone Therapy Global Journal*. 2020;10(1):27-38.
16. Brownstein D, Richard NG, Rowen R, Drummond JD, Taylor-Eason PA, Brownstein H, et al. A Novel Approach to Treating COVID-19 Using Nutritional and Oxidative Therapies. *Science, Public Health Policy, and The Law. Clinical and Translational Research*. 2020;2(4).
17. Hernandez A, Vinals M, Pablos A, Vilas F, Papadakos PJ, Wijeyesundera DN, et al. Ozone therapy for patients with COVID-19 pneumonia: Preliminary report of a prospective case-control study. *Int Immunopharmacol*. Dec 5 2020;90:107261.
18. Schwartz A, Martínez-Sánchez G, Menassa de Lucía A, Mejía Viana S, Alina Mita C. Complementary Application of the Ozonized Saline Solution in Mild and Severe Patients with Pneumonia Covid-19: A Non-randomized Pilot Study. *JPPR*. 2021;9(2):126-42.
19. Rodríguez VB, Abreu-Casas D, Rodríguez-Paz NJ, Prieto-Jiménez IL, Álvarez-Rosell N. Efectividad de la ozonoterapia en el tratamiento del dolor por hernia de disco intervertebral [Effectiveness of ozone therapy in the treatment of pain due to intervertebral disc herniation]. *Rev. Chil. Neurocirugía*. 2019;45:8-19.
20. Martínez-Sánchez G, Al-Dalain SM, Menendez S, Re L, Giuliani A, Candelario-Jalil E, et al. Therapeutic efficacy of ozone in patients with diabetic foot. *Eur J Pharmacol*. Oct 31 2005;523(1-3):151-61.

CASE REPORT

Linfoma de orbita. Presentación de una pequeña serie

Orbital lymphoma. Presentation of a small series

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Resumen

El linfoma orbitario es el tumor maligno más frecuente que afecta a la órbita y a sus anexos. La mayoría de los linfomas de los anexos oculares son Linfomas No Hodgkin (LNH) de células B y los más frecuentes son los linfomas extranodales de zona marginal de tejido linfoide asociados a mucosa (MALT). Los linfomas del globo ocular y sus anexos pueden afectar cualquier estructura: intraocular, órbita, párpados, conjuntiva y glándula lagrimal. La mayoría se presenta con una proptosis indolora de 5 a 7 meses de evolución, con pocos signos de inflamación. Como tienden a moldearse alrededor de las estructuras orbitarias, la afectación de la visión y la diplopía son poco frecuentes. La biopsia dará el diagnóstico de certeza y es necesaria para la tipificación del tumor. En el presente trabajo se reportan cuatro pacientes con diagnóstico de LNH de órbita y que de forma general presentaron proptosis en el debut de la enfermedad.

Palabras clave: Linfoma orbitario, linfoma No Hodgkin, linfoma extranodal.

Abstract

Orbital lymphoma is the most common malignant tumor affecting the orbit and its attachments. The majority of ocular adnexal lymphomas are B-cell Non-Hodgkin's lymphomas (NHL), and the most common are mucosa-associated extranodal marginal zone lymphoid tissue (MALT) lymphomas. Lymphomas of the eyeball and its annexes can affect any structure: intraocular, orbit, eyelids, conjunctiva, and lacrimal gland. Most present with painless proptosis lasting 5 to 7 months, with few signs of inflammation. As they tend to mold around orbital structures, vision impairment and diplopia are rare. The biopsy will give the diagnosis of certainty and is necessary for the typing of the tumor. In the present work, four patients with a diagnosis of NHL of the orbit and who generally presented proptosis at the onset of the disease are reported.

Key words: Orbital lymphoma, Non-Hodgkin lymphoma, extranodal lymphoma.

Introducción

El linfoma orbitario es el tumor maligno más frecuente que afecta a la órbita y a sus anexos (párpados, conjuntiva, glándula lagrimal). Se puede presentar de manera intraocular y en ocasiones de forma bilateral. En su mayoría son linfomas No Hodgkin (LNH) de células B y los más frecuentes son los linfomas extranodales de la zona marginal, fundamentalmente del tipo MALT (Tumor linfoide asociado a mucosas) entre un 35-80% de los casos, seguidos por el linfoma difuso de células grandes B¹. En Cuba representan el 25,6 % de todos los tumores orbitarios, y ocupan el primer lugar en cuanto a la incidencia de tumores primarios en esta localización, incluyendo tanto benignos como malignos².

Los linfomas de órbita afectan principalmente a pacientes entre los 50 y los 70 años^{1,3}. Son los tumores de órbita malignos más frecuentes en los adultos, y en los chicos son extremadamente raros. Tienen una leve preponderancia en mujeres¹. Los linfomas del globo ocular y sus anexos pueden afectar cualquier estructura: intraocular, órbita, párpados, conjuntiva y glándula lagrimal⁴⁻⁶.

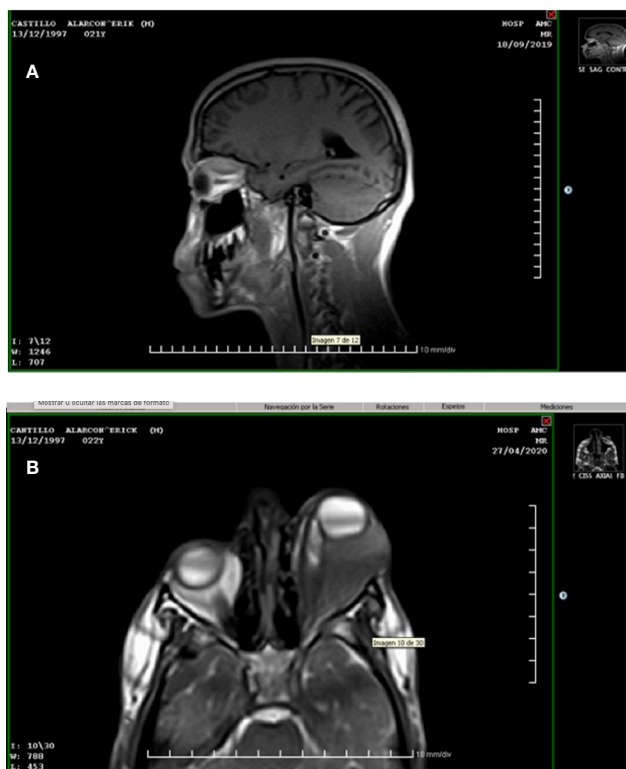
En el presente trabajo se reportan cuatro pacientes con diagnóstico de LNH de órbita y que de forma general presentaron proptosis en el debut de la enfermedad.

Presentación de casos

Caso 1

Varón de 21 años de edad, con antecedentes de pseudotumor orbitario izquierdo en enero del 2019. Acude a consulta por recidiva de la proptosis en septiembre de ese mismo año. Se realizó Resonancia Magnética Nuclear (RMN) y se comprobó un engrosamiento del musculo recto superior izquierdo interpretándose como una recidiva del pseudotumor. Se impone nuevamente tratamiento esteroideo. Pasados tres meses ocurre una nueva recidiva. Esta vez hay afectación severa de las funciones visuales. Se aplica tratamiento con metilprednisolona consiguiendo regresión del exoftalmos y mejoría de las funciones visuales. Se le realiza biopsia con incisión transpalpebral que informa la presencia de tejido inflamatorio inespecífico. En abril del 2020 acude nuevamente el paciente con dolor intenso, exoftalmos severo, agudeza visual (AV) de percepción luminosa. En esta oportunidad es valorado con neurocirugía se realiza cirugía transcraneal con extracción parcial del tumor y biopsia. Esta vez se informa un LNH de alto grado células B. Fue remitido a oncología donde se realizó quimioterapia con una remisión parcial de la lesión seguida de radioterapia.

Figura 1: (A) Infiltración a nivel del recto superior del OI que se aprecia en corte sagital de RMN realizada en la primera recidiva de la enfermedad. (B) Exoftalmo severo provocado por la progresión de la lesión.

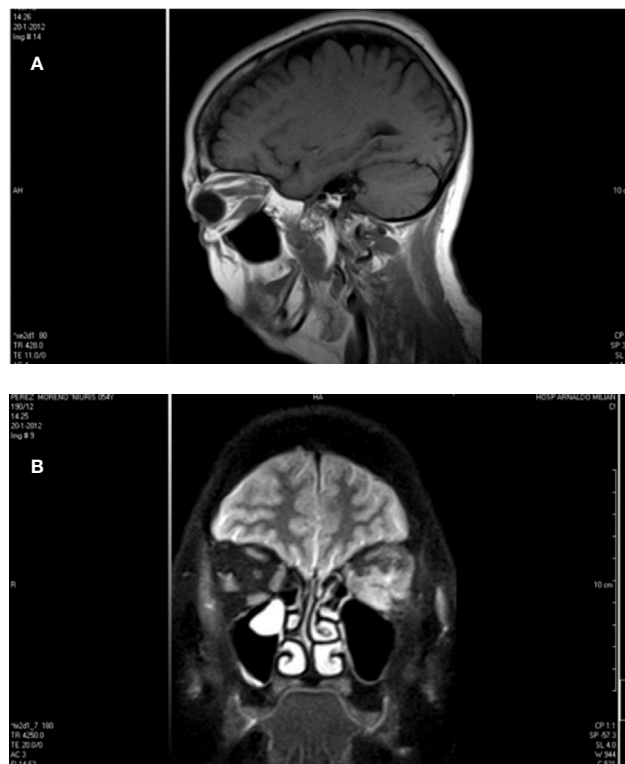


Caso 2

Mujer de 52 años de edad, con diagnóstico de un Síndrome de Tolosa Hunt en el 2010 por lo que realizó

tratamiento con esteroides e Inmuran por 2 años, sin que existiera mejoría del cuadro. Se mantuvo bajo seguimiento por neurología con una conducta expectante. A pesar del tratamiento mantuvo edema de párpados en su ojo izquierdo (OI), discreta quemosis, ptosis palpebral, limitación de la musculatura extrínseca de ese mismo ojo. En la exploración de las funciones visuales se constató AV ojo derecho (OD) 100 VAR; OI 98 VAR. Visión de colores (VC) OD 21/21; OI 18/21. Se realizan nuevas imágenes de cráneo y órbita donde aparece una lesión en el cono orbitario de mayores dimensiones que en estudios previos. Ante el empeoramiento de las funciones visuales así como el resultado de las neuroimágenes se remite a neurocirugía. Se decide realizar biopsia por incisión que informa como resultado LNH de células B. Fue remitida a oncología, se realizó el estudio de extensión, objetivándose localización única en la órbita izquierda. Se indicó tratamiento con quimioterapia y actualmente la paciente se encuentra estable sin recidivas.

Figura 2: RMN cráneo y órbita. Gran tumefacción de músculos rectos y nervio óptico. (A) vista sagital (B) Vista coronal.



Caso 3

Varón de 70 años de edad. Acude a consulta en el año 2018 por aumento de volumen y desviación del OI desde hace 1 año. Al examen oftalmológico se constata para ambos ojos AV 100 VAR, sin embargo VC OD 20/21; OI 1/21. Tensión ocular (TO) OD 16 mmHg; OI 23 mmHg. Exoftalmometría: Base: 108mm OD: 16mm; OI: 22mm. Defecto pupilar aferente relativo OI. En posición primaria de la mirada una esotropía e Hipertropía OI, que alterna al Cover test así como limitación de la abducción OI.

Se realiza ciclo de esteroides. Se indica una perimetría computarizada 32D donde aparece una reducción concéntrica a 25°, además una RMN de cráneo y órbita que informa presencia de un engrosamiento del músculo recto superior y recto externo izquierdo, y una imagen hipointensa hacia la porción lateral del nervio óptico izquierdo que lo comprime hacia la línea media y ensancha el agujero de conjunción de ese lado. Es valorado en conjunto con neurocirugía. Es sometido a cirugía y como resultado de la biopsia informan un LNH de células B tipo MALT. Se impone tratamiento con quimioterapia. A los 2 años del diagnóstico presenta recidiva de la enfermedad. Esta vez aparece en estudio de RMN infiltración de senos perinasales izquierdos, grasa retroocular, así como partes del lóbulo frontal. Se impone nuevo tratamiento con quimioterapia y radioterapia con una evolución favorable.

Figura 3: RMN de órbita en la recidiva de la enfermedad. gruesa imagen de forma redondeada de contornos irregulares que se introduce desde el seno maxilar izquierdo, fosa nasal izquierda, etmoidales posteriores, con cambios de la intensidad de señal del cono orbitario insinuándose la grasa retro ocular, así como partes del lóbulo frontal (A) Vista axial, (B) Vista coronal.



Caso 4

Varón de 71 años de edad, que acude a consulta en el año 2020 por aumento de volumen del OI desde hace 2 meses así como dolor ocular y visión borrosa al mirar al lado izquierdo. Al examen oftalmológico se constata una mejor agudeza visual corregida (MAVC) OD 80 VAR; OI 62 VAR. VC: AO 21/21. Exoftalmometría Base

100mm, OD 15mm; OI 19mm. Limitación de todos los movimientos oculares OI. Además se encontró discreto edema de párpados y una lesión palpable a nivel de la órbita izquierda, en el reborde orbitario superior interno, dura y no movable. Se indican neuroimágenes y se informa en RMN contrastada de órbita una masa de aspecto tumoral de localización intra y extraconal izquierda que involucra los músculos recto superior y medio así como la inserción del nervio óptico. A nivel de la órbita derecha similares características pero de menor tamaño. Ambas imágenes tienen realce homogéneo tras la administración de contraste. Es valorado en conjunto con neurocirugía. El estudio de extensión mostró lesión intraabdominal en íntimo contacto con el colon descendente y polo superior del riñón izquierdo además de una masa en el mediastino anterior y medio. Se realiza biopsia incisional de tejido retrororbitario apareciendo proceso un linfoma No Hodgkin de células del manto. Se indicó tratamiento con quimioterapia con una respuesta excelente al tratamiento.

Figura 4: TAC de cráneo y órbita. Lesión infiltrativa en ambas órbitas.



Discusión

Los linfomas oculares (LO) y de los anexos oculares (LAO) tienen una incidencia de 7-8% de todos los tumores extra ganglionares^{3,5}. La proliferación celular anormal del tejido linfóide ocurre generalmente en los ganglios linfáticos, pero en la cuarta parte de los casos, puede existir afectación extraganglionar (piel, tubo digestivo, sistema nervioso central, pulmón, anexos oculares, tiroides y otros sitios)⁷.

La mayoría de los linfomas de órbita se presentan con una proptosis indolora de 5 a 7 meses de evolución, con pocos signos de inflamación. Pueden ser uni o bilaterales: la afectación bilateral ocurre en el 10%-25% de los pacientes^{8,9}. Si bien se sabe y está ampliamente descrito que el linfoma es una enfermedad indolora y que normalmente no está asociada a signos inflamatorios, en varios estudios se ha documentado una incidencia del 5% al 28% de dolor y también se han observado casos con presentación inflamatoria.^{1-3,10,11}

Como tienden a moldearse alrededor de las estructuras orbitarias, la afectación de la visión y la diplopía son poco frecuentes, a pesar del gran tamaño que algunos

linfomas tienen. La ptosis mecánica puede presentarse en los linfomas que afectan la glándula lagrimal o los párpados. Cuando afectan el saco lagrimal, se pueden observar con epifora, edema en el ángulo cantal medial o dacriocistitis. Cuando invaden músculos extraoculares pueden tener diplopía, dolor y edema, además de proptosis. La bilateralidad al momento de la presentación es el único factor predictivo significativo en el desarrollo de linfoma sistémico.^{3,5,8}

Después de la evaluación clínica es fundamental realizar imágenes para evaluar la lesión y su extensión y así planear la biopsia. La biopsia dará el diagnóstico de certeza y es necesaria para la tipificación del tumor. La tomografía computada (TC) de órbita demuestra una lesión irregular o bien circunscrita e hiperdensa que moldea las estructuras que lo rodean sin erosionar hueso.^{3,8,9}

Para el diagnóstico de certeza se debe realizar una biopsia con toma de una adecuada cantidad de tejido para análisis anatomopatológico e inmunohistoquímica. No se recomienda la biopsia por aspiración con aguja fina.^{3,9,11,12}

El linfoma de órbita puede ser enmascarado por un pseudotumor orbitario tanto clínica como radiológicamente. La similitud en la presentación clínica de ambas entidades puede ser un reto para el diagnóstico. Las características de la lesión en el caso de un linfoma atípico pueden ser muy semejantes a la de un pseudotumor, incluso en las imágenes radiológicas. El examen histopatológico es confirmatorio. La biopsia

por incisión y la inmunohistoquímica juegan un papel muy importante en estos casos para resolver el dilema diagnóstico.^{11,12,13}

La radioterapia es el tratamiento de primera línea de los linfomas de bajo grado, con la cual se ha logrado un control excelente de la enfermedad. En otros casos, como ocurre con el LDCG-B, de mayor agresividad se utiliza la combinación de la radioterapia con quimioterapia. El esquema más utilizado comprende el uso de ciclofosfamida, doxorubicina, vincristina y prednisona, asociados al Rituximab en los linfomas de células B (R-CHOP).^{3,5,8,9,12,13}

Los pacientes de la serie que se presenta tuvieron un comienzo insidioso de su enfermedad, como signo común presentaron proptosis y hubo afectación de la agudeza visual en diferente grado durante su evolución. De forma general presentaron una buena respuesta al tratamiento, solo uno presentó recidiva.

Los linfomas que afectan a la órbita son padecimientos infrecuentes, aunque no por eso dejan de ser importantes ya que son predominantemente malignos. El diagnóstico y manejo integral y oportuno de ellos puede darle un buen pronóstico al paciente y evitar complicaciones, ya que responden en general de forma adecuada al tratamiento.

Conflicto de intereses

El autor declara no tener ningún conflicto de interés.

Bibliografía

- Olsen TG, Holm F, Mikkelsen LH, Rasmussen PK, Coupland SE, Esmali B, Finger PT, Graue GF, Grossniklaus HE, Honavar SG, Khong JJ, McKelvie PA, Mulay K, Sjö LD, Vemuganti GK, Thuro BA, Heegaard S. Orbital Lymphoma-An International Multicenter Retrospective Study. *Am J Ophthalmol*. 2019 Mar;199:44-57
- Abreu Perdomo FA, Ortiz Ramos DL, Santos Silva D, González García JL, Fernández González O, Caballero García J. Características clínicas y patológicas de los tumores orbitarios. *Revista Cubana de Oftalmología* 2018; 31(2): 1-12.
- Di Nisio LA, Zárate J, Weil D. Linfomas orbitarios. *Oftalmología Clínica y Experimental* 2017;10(3): 88-93.
- Cabrera PC, Santana AJ, Rodríguez BD, Olivera MO, Miranda RM. Linfoma no Hodgkin con infiltración ocular: a propósito de un caso. *AMC (ISSN 1025-0255)* 2016 Mar.-Abr; 20(2)
- Hindsø TG, Esmali B, Holm F, Mikkelsen LH, Rasmussen PK, Coupland SE. International multicenter retrospective cohort study of ocular adnexal marginal zone B-cell lymphoma. *Br J Ophthalmol*. 2020 Mar;104(3):357-62
- Saakyan SV, Amiryán AG, Andreeva TA, Sklyarova NV, Zhiiltsova MG, Zakharova GP. [Non-Hodgkin lymphoma (a case of simultaneous ocular and orbital involvement)]. *Vestn Oftalmol*. 2015 May-Jun;131(3):82-9.
- Fernández Águila JD, Valladares Urquiza Y, Rodríguez Pino MY, Villares Álvarez I. Linfoma primario del Sistema Nervioso Central. Presentación de un caso. *Medisur* 16.2 (2018): 344-51.
- Seresirikachorn K, Norasetthada L, Ausayakhun S, Apivatthakakul A, Tangchittam S, Pruksakorn V, Wudhikam K, Wiwatwongwana D. Clinical presentation and treatment outcomes of primary ocular adnexal MALT lymphoma in Thailand. *Blood Res*. 2018 Dec;53(4):307-13.
- Abreu Perdomo FA, Saborit Martínez Y, Ortiz Ramos DA, Jiménez Galainena JJ, Nazario Dolz M. Características clínico-patológicas y tratamiento del linfoma orbitario." *Revista Cubana de Oftalmología* 2019;32.4
- Ferlini MA, Soto Taborda T, Herrera Rodríguez AA. Linfoma MALT: un diagnóstico diferencial de edema periorbitario. *Revista Médica Sinergia* 2020; 5(5): 414
- Vallinayagam M, Krishnamoorthy J, Vijayakumar L, Suryawanshi D. Bilateral Primary Orbital Non Hodgkin's Lymphoma Masquerading As Myositic Pseudotumor In An Elderly Patient." *The Official Scientific Journal of Delhi Ophthalmological Society* 2017; 28.2: 40-2.
- Verdijk RM. Lymphoproliferative tumors of the ocular adnexa. *The Asia-Pacific Journal of Ophthalmology* 6.2 (2017): 132-42.
- Toledo MC. Linfoma orbitario de células del manto. *Acta Médica* 2021; 22.1

CASE REPORT

Dificultad en el aprendizaje; la punta del iceberg

*Learning disability; the tip of the iceberg***Unai Díaz-Moreno Elorz¹** , **Montserrat Pons Rodríguez²** , **Jorge Roldán Busto³** , **Fernando Ferragut Agut⁴** , **María Ángeles Ruiz Gómez²** , **Ana B. Marín Quiles³** 

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Received: 30 - XII - 2021**Accepted:** 28 - II - 2022**doi:** 10.3306/AJHS.2022.37.02.177**Resumen**

Niño de 6 años y 9 meses derivado a consulta de neuropediatría por dificultades en el aprendizaje. Lo definían como un niño despistado desde siempre, pero últimamente había bajado notablemente el rendimiento escolar. Se inició protocolo estudio con cita de seguimiento. Al mes siguiente, se presentó en urgencias por un episodio de desorientación visuoespacial y episodios de desconexión del medio. Se le realizó EEG y RM con hallazgos compatibles con adrenoleucodistrofia ligada al X (ADL-X) en fase muy avanzada, confirmándose posteriormente genéticamente. A pesar de que el trasplante de progenitores hematopoyéticos (TPH) se ofrece en estadios más tempranos de la enfermedad, ante la falta de alternativas terapéuticas, se realizó TPH, en espera de ver evolución.

Palabras clave: Adrenoleucodistrofia, dificultades de aprendizaje, rendimiento escolar.

Abstract

A boy aged 6 years and 9 months was referred to neuropediatrics for learning difficulties. He was defined as a child who had always been absent-minded, but lately his school performance had dropped significantly. A study protocol was initiated with a follow-up appointment. The following month, he presented to the emergency department for an episode of visuospatial disorientation and episodes of disconnection from the environment. EEG and MRI were performed with findings compatible with X-linked adrenoleukodystrophy (ADL-X) in a very advanced stage, which was later confirmed genetically. Although hematopoietic stem cell transplantation (HSCT) is offered in earlier stages of the disease, given the lack of therapeutic alternatives, HSCT was performed, awaiting evolution.

Key words: Adrenoleukodystrophy, learning difficulties, school performance.

Descripción del caso

Niño de 6 años y 9 meses derivado por su pediatra a consultas de neuropediatría tras objetivar, desde el colegio, dificultades en el aprendizaje tras el reinicio de las clases después de la pandemia COVID19.

El paciente no presentaba antecedentes personales de interés, su desarrollo psicomotor había sido normal hasta el momento, y su rendimiento académico óptimo (destacaba en la clase). Los padres refieren que el abuelo materno realizó un intento autolítico en su juventud. No refieren otros antecedentes de interés.

Los padres referían que desde siempre había sido un niño despistado, y que le costaba orientarse espacialmente. Por este motivo, habían acudido a un optometrista compartimental con mejoría franca de la clínica. Además,

referían que siempre había sido un niño torpe pero que últimamente presentaba caídas frecuentes.

En este momento, la exploración física del niño era completamente normal, por lo que se dio una nueva cita en 2 meses, con informes psicopedagógicos escolares.

Al mes acudió a urgencias por desorientación visuoespacial; No se sabía colocar los zapatos en el pie correcto, no sabía reconocer el entorno donde se encontraba... Además, los padres referían episodios de desconexión del medio con mirada perdida, en los últimos 4 días. (2-3 episodios por día).

En la exploración física, presentaba lenta respuesta a órdenes verbales y dificultad para el procesamiento de información visual, a pesar órdenes repetidas, siendo el resto exploración normal.

En la RM craneal se visualizaba afectación de la sustancia blanca periventricular posterior, con zonas de realce periférico por desmielinización activa. También existía afectación del esplenio del cuerpo caloso, tálamos posteriores, vía cortico-espinal en el tronco encefálico, lemniscos laterales y pirámides bulbares (**Figura 2**).

Destaca, en la analítica, una ACTH >1250.00 pg/ml (1,00-46,00 pg/ml) con cortisol normal 7,70 µg (1,73-14,82 µg /dl).

Se solicitaron ácidos grasos de cadena muy larga (AGCML) en plasma, que mostraron elevación del Ácido hexacosanoico (C26:0): 3,830 µmol/L (Normal < 0,980) y Ácido lignocérico (C24:0): 92,6 µmol/L (Normal < 78,8).

Se solicitó secuenciación del gen ABCD1, que mostró una mutación 1073 C>G (p. Ser358*) que provoca un codón stop prematuro en la posición 358 de la proteína. La mutación había sido previamente descrita y se terminó

Figura 1: Electroencefalograma.

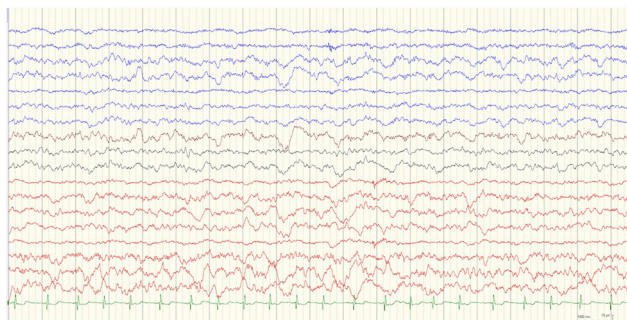
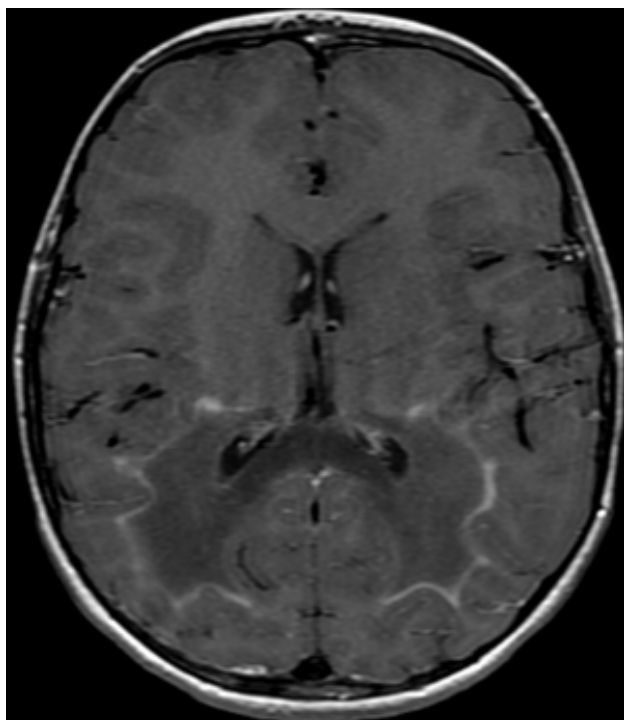


Figura 2.



de confirmar el diagnóstico. Se completó estudio de segregación familiar, encontrando la misma mutación en la madre del paciente, actualmente asintomática.

Se inició tratamiento sintomático, y, a pesar de no ser a priori candidato a trasplante de progenitores hematopoyéticos, debido a lo avanzada que se encontraba la enfermedad, se encontró rápidamente un donante en el Hospital Vall D'Hebrón. Tras consensuarlo con los padres, y dado que era la única medida potencialmente terapéutica que podría alterar de alguna manera el curso natural de la enfermedad, se realizó trasplante el 18 de junio de 2021, quedando a la espera de ver la evolución posterior.

Discusión del caso

Las dificultades del aprendizaje son uno de los motivos de derivación más frecuente a las consultas de neuropediatría. La mayoría de las ocasiones, encontramos una causa orgánica que las justifique. Sin embargo, hay ciertas enfermedades que hay que conocer y en las que se debería pensar ante un deterioro cognitivo, conductual y neurológico rápidamente progresivo. La ALD-X es una enfermedad de causa genética rara (1/20.000 nacidos vivos), localizada en el cromosoma Xq28, producida por mutaciones en el gen ABCD1.

Este gen codifica una proteína transmembrana peroxisomal (ALDP) que se encuentra implicada en el transporte de los ésteres de coA-AGCML desde el citosol al peroxisoma, lo que da lugar a una disminución de la degradación de los AGCML y resulta en un acúmulo de los mismos. El acúmulo de AGCML en las células gliales produce una desestabilización de la vaina de mielina y deterioro de la función axonal. Además, este acúmulo de AGCML afecta a la corteza suprarrenal –provocando insuficiencia suprarrenal primaria, como en el caso de nuestro paciente– y las células de Leydig.¹

Existe una marcada variabilidad fenotípica, incluso, intrafamiliar. No existe una clara correlación entre el genotipo y el fenotipo.

En el 40-45% de los casos, se presenta como una adrenomieloneuropatía (afectación espinal) en hombres alrededor de los 30 años y en mujeres portadoras en edad posmenopáusica. Sin embargo, en el 30-35% de los casos su forma de presentación es en la infancia. A partir de los 3 años, presentan un amplio espectro de signos y síntomas, entre los que se destaca el deterioro cognitivo y neurológico progresivo. En general, comienzan con trastornos del comportamiento y del rendimiento escolar, y se instaura rápidamente una tetraparesia espástica con afectación bulbar y pérdida de habilidades adquiridas seguida de deterioro visual y auditivo, que progresa a un estado vegetativo con un desenlace fatal y

devastador en 3-5 años.^{2,3} En la RM cerebral, se observa desmielinización de la sustancia blanca, generalmente, bilateral y de predominio periventricular posterior. Las lesiones se cuantifican según el método de Loes y col.⁴ Un Loes 0 corresponde a un SNC normal, mientras que un Loes 34 a la máxima afectación posible. A partir de un Loes 9 se considera enfermedad avanzada. Nuestro paciente tenía un Loes 12.

La insuficiencia suprarrenal aparece en el 70% de los pacientes y, en general, suele ser la presentación inicial, años o, incluso, décadas antes de la aparición de los síntomas neurológicos. Es el único signo en un 10% de los pacientes con ADL-X. Es importante realizar siempre una evaluación analítica de la función suprarrenal porque, en la mayoría de los casos, puede existir alteración de esta, aunque no presente clínica, lo que precisa tratamiento sustitutivo, como ocurre con nuestro paciente.

El diagnóstico bioquímico se establece determinando un acumulo de la concentración plasmática de AGCML, fundamentalmente, el ácido hexacosanoico (C26:0) y tetracosanoico (C24:0), así como la relación de ellos con el ácido behénico (C22).

El 99.9% de los hombres afectados de la enfermedad presentarán niveles elevados de C:26 y C:24 por separado, considerándose esta elevación patognomónica de la enfermedad. No ocurre lo mismo en el caso de las mujeres, ya que el 15-20% de las mismas pueden tener niveles normales de ACGML, confirmando el diagnóstico mediante pruebas genéticas.

El diagnóstico definitivo se obtiene mediante secuenciación Sanger del gen ABC1. En el caso de nuestro paciente, se detectó una mutación que codificaba un codón de parada prematuro que impedía la formación completa de la proteína.

La misma mutación se encontró en su madre, y estamos pendientes de resultados de los abuelos maternos. Como opciones terapéuticas, tenemos por un lado las medidas sintomáticas (Antioxidantes para la inflamación crónica y el estrés oxidativo que presentan estos pacientes) y por otro lado terapias que pueden detener o modificar el curso natural de la enfermedad, como son la terapia génica y el trasplante alogénico de progenitores hematopoyéticos (TPH).

El TPH ha demostrado detener la progresión de la forma cerebral infantil, pero, por un mecanismo todavía desconocido, no impide la aparición de adrenomielseuropatía a partir de la tercera década de la vida. Además, tiene un alto riesgo de complicaciones (inmunosupresión, enfermedad injerto contra huésped...), y la clínica neurológica empeora en los primeros 6-9 meses tras el mismo, por lo que en la mayoría de centros los pacientes con LOE > 9 no serían candidatos al mismo.

Se ha llevado a cabo un ensayo clínico con 20 pacientes afectados de ADL con terapia génica; Esta consiste en extraer células CD 34+ del propio paciente e inocular el gen ABCD1 salvaje a través de un vector del HIV a las mismas. Posteriormente, se reintroducen en el paciente. Esta terapia ha mostrado resultados prometedores en ensayos clínicos, deteniendo la progresión de la enfermedad a los 18-24 meses⁵.

Una forma de aplicar estos tratamientos modificadores de la enfermedad de forma óptima (antes de la aparición de síntomas), sería incluir esta enfermedad en el programa de cribado neonatal, como ya se ha hecho en EE.UU. y se está empezando a hacer en Holanda⁶⁻⁸.

Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses.

Bibliografía

- Berger J, Forss-Petter S, Eichler FS. Pathophysiology of X-linked adrenoleukodystrophy. *Biochimie*, 2014;98:135-42.
- Huffnagel IC, Laheji FK, Aziz-Bose R, Tritos NA, Marino R, Linthorst GE, et al. The natural history of adrenal insufficiency in X-linked adrenoleukodystrophy: An international collaboration. *Journal of Clinical Endocrinology and Metabolism*, 2019;104: 118-26.
- Turk BR, Theda C, Fatemi A, Moser AB. X-linked adrenoleukodystrophy: Pathology, pathophysiology, diagnostic testing, newborn screening and therapies. *Int J Dev Neurosci*. 2020;80(1):52-72.
- Loes DJ, Fatemi A, Melhem ER, Gupte N, Bezman L, Moser HW, Raymond GV. Analysis of MRI patterns aids prediction of progression in X-linked adrenoleukodystrophy. *Neurology*. 2003 Aug 12;61(3):369-74.
- Engelen M, Kemp S, de Visser M, van Geel BM, Wanders RJ, Aubourg P, Poll-The BT. X-linked adrenoleukodystrophy (X-ALD): clinical presentation and guidelines for diagnosis, follow-up and management. *Orphanet J Rare Dis*. 2012 Aug 13;7:51.
- Barendsen RW, Dijkstra IME, Visser WF, Alders M, Blik J, Boelen A, et al. Adrenoleukodystrophy Newborn Screening in the Netherlands (SCAN Study): The X-Factor. *Front Cell Dev Biol*. 2020 Jun 17;8:499. doi: 10.3389/fcell.2020.00499. Erratum in: *Front Cell Dev Biol*. 2021 Jan 28;9:631655.
- Tang H, Matteson J, Rinaldo P, Tortorelli S, Currier R, Sciortino S. The Clinical Impact of CLIR Tools toward Rapid Resolution of Post-Newborn Screening Confirmatory Testing for X-Linked Adrenoleukodystrophy in California. *Int J Neonatal Screen*. 2020 Aug 5;6(3):62.
- Matteson J, Sciortino S, Feuchtbaum L, Bishop T, Olney RS, Tang H. Adrenoleukodystrophy Newborn Screening in California Since 2016: Programmatic Outcomes and Follow-Up. *Int J Neonatal Screen*. 2021 Apr 17;7(2):22.



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