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Becas **RELYENS-GRUP MED** de rotación externa para MIR, Beca de rotación externa internacional para MIR, Becas de Innovación, Premios de investigación, Premio Camilo José Cela de Humanidades Médicas, Premio *Fundació Mutual Mèdica* al mejor proyecto de tesis doctoral y Certamen Banco Santander de casos clínicos para MIR.

El jurado calificador de los premios y becas convocados por la *Fundació Patronat Científic* del COMIB, reunido el día 7 de noviembre del presente, acordó la concesión de las siguientes becas y premios:

BECAS RELYENS-GRUP MED DE ROTACIÓN EXTERNA PARA MIR

Dos becas para estancias en hospitales nacionales, dotadas cada una de 1.500 euros.

- Joan Siquier Padilla, residente de la especialidad de Cardiología en el Hospital Universitario Son Espases, para una estancia de tres meses en el Servicio de Cardiología y Unidad UCI Coronaria e Insuficiencia Cardíaca del Hospital Universitari de Bellvitge en Barcelona.
- Bernat Mas Matas, residente de la especialidad de Dermatología en el Hospital Universitario Son Llàtzer, para una estancia de dos meses en el Servicio de Dermatología Pediátrica del Hospital Sant Joan de Déu en Barcelona.

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- Natasha Woods Kreisler, residente de la especialidad de Pediatría y Áreas Específicas en el Hospital Universitario Son Espases, para una estancia de un mes y medio en el Servicio de Gastroenterología, Hepatología y Nutrición Pediátrica del *Hospital for Sick Children (SickKids)* en Toronto, Canadá.

BECAS DE INNOVACIÓN

Dos becas para estancias en centros sanitarios extranjeros, dotadas cada una con 3.000 euros.

- Carla Soldevila Verdeguer, FEA de Cirugía General y del Aparato Digestivo en el Hospital Universitario Son Espases, para una estancia de cuatro semanas en la Unidad de Carcinomatosis Peritoneal del *Mount Sinai Hospital* en Toronto, Canadá.
- Olga Claramonte Bellmunt, FEA de Cirugía General y del Aparato Digestivo en el Hospital Universitario Son Llàtzer, para una estancia de tres meses en el Servicio Cirugía Hepato-Biliar en el *Centre Hépatobiliaire. Hopital Paul Brousse* en Villejuif, Francia.

Desierta la adjudicación de las dos becas para estancias en centros sanitarios nacionales.

PREMIOS DE INVESTIGACIÓN

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“Premio Damià Carbó”

Al trabajo científico titulado “*Effects of six months treatment with liraglutide among patients with psoriasis and obesity, beyond metabolic control?*”, presentado por Joana Nicolau, Antoni Nadal, Pilar Sanchis, Cristina Nadal y Lluís Masmiquel.

“Premio Mateu Orfila”

Desierta la adjudicación.

“Premio Metge Matas”

Al artículo “*The coexistence of low albumin levels and obesity worsens clinical outcomes among subjects admitted for sars-cov-2 infection*”, cuyos autores son Joana Nicolau, Irene Rodríguez, Andrea Romano, Keyla Dotres, Antelm Pujol y Lluís Masmiquel.

PREMIO CAMILO JOSÉ CELA DE HUMANIDADES MÉDICAS

Un premio dotado de 1.500 euros concedido al trabajo titulado “La compasión me ha hecho ser más persona y mejor médico”, firmado por María Belén González Gragera.

PREMIO FUNDACIÓ MUTUAL MÈDICA AL MEJOR PROYECTO DE TESIS DOCTORAL

Un premio dotado de 2.000 euros al proyecto titulado “Deterioro cognitivo en la diabetes mellitus tipo 2: relación con las características clínicoepidemiológicas y papel de la dieta con especial referencia a la ingesta de fitato”, presentado por Antelm Pujol Calafat.

CERTAMEN BANCO SANTANDER DE CASOS CLÍNICOS PARA MIR

Tras la exposición de los cinco casos clínicos seleccionados como finalistas, el jurado, reunido el día 14 de noviembre del presente, acordó conceder:

- El primer premio, dotado de 1.000 euros, al caso titulado “Cuando la piel revela el diagnóstico: el rol decisivo del dermatólogo en una paciente con insuficiencia respiratoria grave”, cuya autora es Verónica Fernández Tapia.
- El segundo premio, dotado de 500 euros, al caso titulado “Neumonía necrotizante por SAMS ¿productor de PLV? A propósito de un caso”, cuya autora es Noelia Plaza Mendoza.

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ORIGINAL

Variables associated with overweight and obesity in Spanish healthcare workers

Variables asociadas al sobrepeso y obesidad en trabajadores sanitarios españoles

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Abstract

Introduction: Obesity is a multifactorial chronic disease that, due to the continuous increase in its prevalence worldwide and its high associated morbidity and mortality, is currently considered the pandemic of the 21st century. The objective of this study is to assess how various sociodemographic variables and health habits are associated with the prevalence of excess weight, as determined by five different scales, in a large cohort of healthcare workers.

Methodology: A dual study design —longitudinal-retrospective and cross-sectional— was conducted among healthcare workers divided into four categories (physicians, nurses, healthcare technicians, and auxiliary staff). The study evaluated the association of age, sex, professional category, smoking habits, physical activity, and adherence to the Mediterranean diet with obesity, as determined by five different scales: Body Mass Index (BMI), Waist-to-Height Ratio (WtHR), Body Adiposity Index (BAI), Clínica Universidad de Navarra Body Fat Estimator (CUN BAE), and the Visceral Fat Metabolic Score (METS-VF).

Results: All the variables analyzed in the study were associated with high values on the five overweight-obesity scales, with age showing the strongest association (as reflected in odds ratio values).

Conclusions: The healthcare worker profile at the highest risk of obesity, according to any of the five scales, is an older male, working as auxiliary nursing staff or porter, who smokes, is sedentary, and has low adherence to the Mediterranean diet.

Key words: Obesity, Mediterranean diet, physical activity, healthcare worker, smoking, CUN BAE.

Resumen

Introducción: La obesidad es una enfermedad crónica multifactorial que debido al incremento continuo de su prevalencia en todo el mundo y a su elevada morbilidad asociada es considerada en la actualidad como la pandemia del siglo XXI. El objetivo de este estudio es evaluar cómo las variables sociodemográficas y los hábitos de salud están asociados con la prevalencia de exceso de peso, determinada mediante cinco escalas diferentes, entre los trabajadores sanitarios de todas las regiones de España.

Metodología: Un estudio doble: longitudinal-retrospectivo y transversal en trabajadores sanitarios divididos en cuatro categorías (médicos, enfermeras, técnicos sanitarios y personal auxiliar) evaluó la asociación de la edad, el sexo, la categoría profesional, el tabaquismo, la actividad física y la adherencia a la dieta mediterránea con la presencia de obesidad determinada con cinco escalas diferentes: índice de masa corporal (IMC), índice cintura/altura (WtHR), índice de adiposidad corporal (BAI), Clínica Universitaria de Navarra Estimator de grasa corporal (CUN BAE) y puntuación metabólica para grasa visceral (METS-VF).

Resultados: Todas las variables analizadas en el estudio se asociaron con la presencia de valores altos de las cinco escalas de sobrepeso-obesidad, siendo la edad la que mostró una mayor asociación (reflejada en los valores de odds ratio).

Conclusiones: El perfil de trabajador sanitario con mayor riesgo de presentar obesidad con cualquiera de las cinco escalas sería un varón, de edad avanzada, auxiliar de enfermería o celador, fumador, sedentario y con baja adherencia a la dieta mediterránea.

Palabras clave: Obesidad, dieta mediterránea, actividad física, trabajador sanitario, consumo de tabaco, CUN BAE.

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Introduction

Obesity is a chronic, multifactorial disease characterized by an abnormal or excessive accumulation of body fat that can harm health¹. It is recognized as one of the most critical public health issues worldwide² due to its high prevalence³ and severe consequences in terms of morbidity and mortality⁴. According to the World Health Organization (WHO), in 2022, 43% of adults aged 18 years and older were overweight, and 16% were obese⁵. These figures have continued to rise, highlighting the need for a comprehensive understanding of the epidemiological, pathophysiological, diagnostic, and complication-related aspects of obesity⁶.

The prevalence of obesity has alarmingly increased in recent decades, affecting individuals of all ages, genders, and socioeconomic levels. This phenomenon has been termed the "global obesity pandemic"⁷. In regions such as North America and Europe, over 25% of the adult population is estimated to be obese⁸. In developing countries, epidemiological transitions have led to a rapid increase in obesity prevalence, coexisting with issues of undernutrition⁹. Moreover, childhood obesity has grown significantly, with nearly 39 million children under the age of 5 being overweight or obese in 2020. Childhood obesity constitutes a major risk factor for its persistence into adulthood, further contributing to the global healthcare burden¹⁰.

Obesity results from a chronic imbalance between caloric intake and energy expenditure, regulated by a complex neurohormonal system involving the hypothalamus, adipose tissue, the gastrointestinal system, and endocrine signals¹¹. Adipose tissue plays a central role in the pathophysiology of obesity¹², functioning not only as an energy storage depot but also as an active endocrine organ that secretes adipokines such as leptin¹³, adiponectin¹⁴, and resistin¹⁵. These molecules regulate metabolism, inflammation, and insulin sensitivity¹⁶. In obesity, adipose tissue expands and becomes dysfunctional, resulting in a state of chronic low-grade inflammation and insulin resistance¹⁷.

Additionally, the distribution of body fat significantly impacts metabolic risk, with visceral fat being more harmful than subcutaneous fat. The accumulation of visceral fat is associated with metabolic dysfunction¹⁸, lipotoxicity¹⁹, and an increased production of inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6)²⁰.

Obesity is associated with a wide range of complications affecting nearly all body systems. Major complications include:

1. Metabolic: Insulin resistance, type 2 diabetes mellitus, dyslipidemia, and metabolic syndrome²¹.
2. Cardiovascular: Hypertension, coronary artery disease, heart failure, and stroke²².

3. Respiratory: Obstructive sleep apnea syndrome and restrictive lung disease²³.

4. Musculoskeletal: Osteoarthritis and chronic musculoskeletal pain, which can be disabling²⁴.

5. Oncological: Increased risk of cancers such as breast, colon, endometrial, and prostate cancer²⁵.

6. Psychological: Anxiety disorders, depression, and social stigmatization are common among individuals with obesity²⁶.

These complications underscore the importance of early identification and effective interventions for patients with obesity.

Diagnosing obesity extends beyond quantifying excess weight and includes evaluating body composition and fat distribution. Key diagnostic methods include:

1. Body Mass Index (BMI): The most widely used method for classifying obesity, calculated by dividing weight in kilograms by the square of height in meters (kg/m^2). While useful for initial classification, it does not differentiate between fat and lean mass or assess fat distribution²⁷.

2. Waist-to-Height Ratio (WtHR): This metric relates waist circumference to height, offering better evaluation of metabolic risk associated with abdominal fat²⁸.

3. Body Adiposity Index (BAI): Estimates body fat percentage based on the ratio of hip circumference to height. Although more specific than BMI, its use is limited due to the need for validation across diverse populations²⁹.

4. CUN-BAE (Clinica Universidad de Navarra Body Adiposity Estimator): A method using equations based on BMI, age, and sex, shown to be a reliable tool for estimating body fat in clinical settings³⁰.

5. METS-VF (Metabolic Syndrome Visceral Fat Index): Combines clinical and biochemical measures to estimate visceral fat volume and its impact on metabolic risk, particularly useful for identifying individuals at high cardiometabolic risk³¹.

An integrative approach combining these metrics with advanced methods such as bioelectrical impedance analysis³², dual-energy X-ray absorptiometry (DXA)³³, and magnetic resonance imaging (MRI)³⁴ enables a more accurate evaluation of obesity. This facilitates risk stratification, personalization of therapeutic interventions, and effective treatment monitoring.

Study Objective

The objective of this study is to analyze how different sociodemographic variables (age, sex, and socioeconomic status) and health behaviors (smoking, physical activity, and adherence to the Mediterranean diet) are associated with various scales used to evaluate overweight and obesity in a specific cohort of healthcare workers.

Methods

Study Design and Sample

This study utilized a mixed-methods approach, incorporating both a retrospective longitudinal study and a cross-sectional descriptive study. A total of 44,939 healthcare workers from various regions of Spain participated, including 14,305 men (31.8%) and 30,634 women (68.2%). The participants were selected from individuals undergoing mandatory annual medical check-ups provided by their employers during the study period. The longitudinal study covered the years 2010 to 2019.

Inclusion Criteria:

- Aged between 18 and 69 years.
- Employed by one of the participating companies.

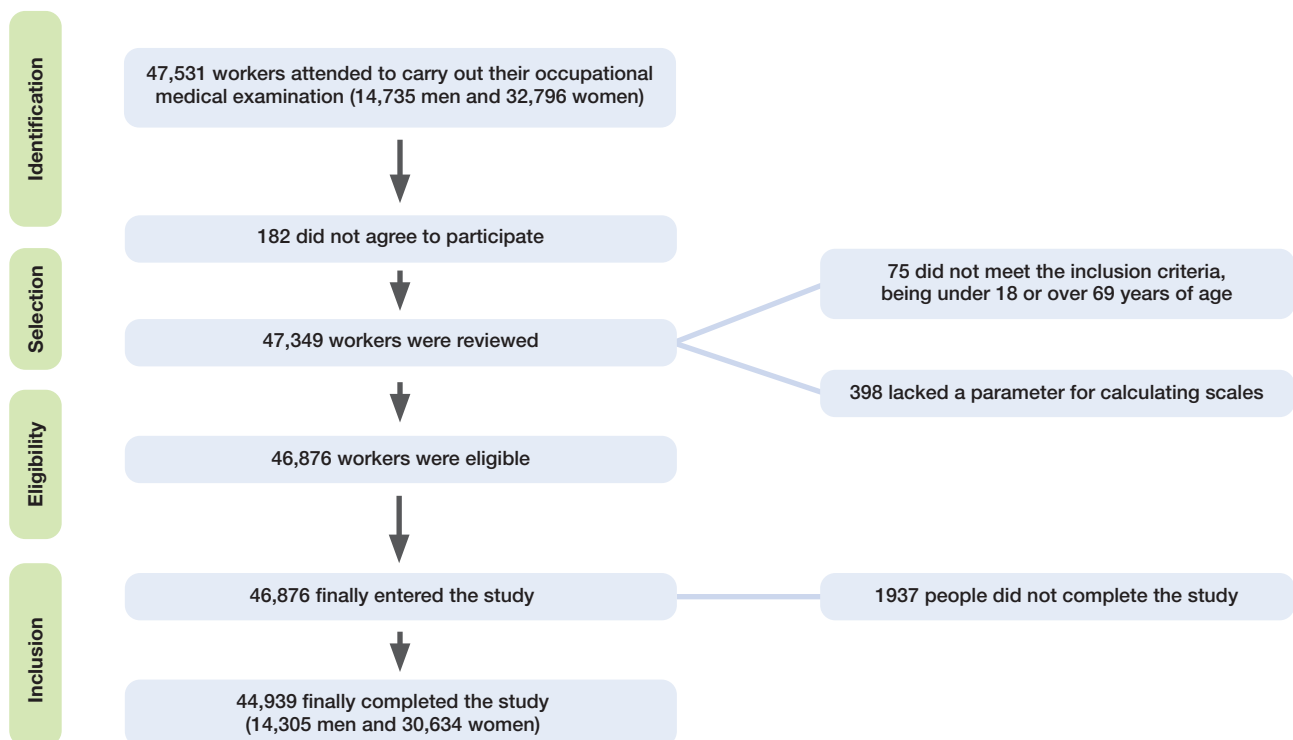
- Provided informed consent to participate in the study.
- Authorized the use of their data for epidemiological purposes.

Exclusion Criteria:

- Aged under 18 or over 69 years.
- Not employed by a participating company.
- Did not provide informed consent to participate in the study.
- Did not authorize the use of their data for epidemiological purposes.

The flow chart of the study participants is presented in **figure 1**.

Figure 1: Presents the flowchart detailing the selection and inclusion process for study participants.



Data Collection Procedures

Data collection was conducted by occupational health teams from the collaborating companies using the following methods:

- **Medical History:** Sociodemographic information (age, sex, occupation) and health-related data such as smoking status, physical activity levels, adherence to the Mediterranean diet, and stress levels were recorded.
- **Physical and Clinical Measurements:** Data collected included height, weight, waist circumference, hip circumference, and blood pressure (systolic and diastolic).

- **Laboratory Tests:** Biochemical analyses included lipid profiles, liver function tests, and fasting blood glucose levels.

To minimize bias, all measurements adhered to standardized protocols:

- **Height and Weight:** Measured using a SECA 700 scale and SECA 220 stadiometer, with participants wearing only underwear.
- **Circumferences:** Waist circumference was measured using a SECA measuring tape placed between the

lowest rib and the iliac crest, while hip circumference was measured at the widest part of the buttocks, with participants standing upright and relaxed.

- Blood Pressure: Measured using an OMRON-M3 sphygmomanometer after 10 minutes of rest in a seated position, ensuring participants had not consumed food, beverages, or tobacco in the prior hour. Three measurements were taken at one-minute intervals, with the average recorded.

Blood samples were obtained via venipuncture after a 12-hour fast, refrigerated, and processed in reference laboratories within 72 hours. Laboratory analyses included:

- Triglycerides, total cholesterol, and glucose levels: Determined using enzymatic methods.
- HDL cholesterol: Measured by precipitation.
- LDL cholesterol: Calculated using the Friedewald formula, provided triglyceride levels were below 400 mg/dL.

Obesity scales

- BMI is calculated by dividing weight by height in meters squared. Obesity is considered to be over 30.

- Waist-to-height ratio (WtHR) is considered high from 0.5

- BAI was calculated using the equation $((\text{hip circumference})/(\text{height}^{1.5})) - 18$, as proposed by Bergman et al³⁵. The resulting values were categorized as low, normal, high, or very high based on the criteria established by Gallagher et al³⁶ for the White population.

- CUN BAE (Clínica Universidad de Navarra Body Adiposity Estimator)³⁷ 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

- Metabolic score for visceral fat (METS-VF)³⁸ $\text{METS-VF} = 4.466 + 0.011 \times (\text{Ln}(\text{METS-IR}))^3 + 3.239 \times (\text{Ln}(\text{WtHR}))^3 + 0.319 \times (\text{Sex}) + 0.594 \times (\text{Ln}(\text{age}))$. Man = 1 woman = 0 $\text{METS-IR} = \text{Ln} [(2 \times \text{glycaemia}) + \text{Triglycerides}] \times \text{BMI} / \text{Ln}[\text{HDLc}]$ High risk is considered as from 7,18.

Operational Definitions

- Professional Categories: Healthcare workers were classified into four groups: physicians, nurses, health technicians (e.g., laboratory, pathology, radiology), and nursing assistants/orderlies.

- Smoking: Defined as consuming at least one cigarette per day in the previous 30 days or having quit within the preceding year.

- Mediterranean Diet Adherence: Assessed using the PREDIMED questionnaire, with high adherence defined as a score of 9 or higher³⁹.

- Physical Activity: Measured using the International Physical Activity Questionnaire (IPAQ), evaluating frequency, duration, and intensity⁴⁰.

Statistical Analysis

Descriptive analysis of categorical variables was performed using frequencies and distributions. The Kolmogorov-Smirnov test assessed the normality of quantitative variables, followed by the calculation of means and standard deviations. Bivariate analysis included Student's t-test for comparing means and the chi-square test for proportions. Variables associated with obesity scales were analyzed using a binary logistic regression model, with model fit evaluated using the Hosmer-Lemeshow test. Stratified analysis was conducted to identify potential confounding factors, but no significant confounding was found. Concordance between scales was assessed using Cohen's kappa coefficient. Statistical analysis was performed using SPSS version 29.0, with a significance level of 0.05.

Ethical Considerations

The study complied with the ethical principles outlined in the Declaration of Helsinki and was approved by the Ethics and Research Committee of the Balearic Islands (CEI-IB) under code IB 4383/20. All participants provided signed informed consent, and their data were anonymized in accordance with Spain's Organic Law 3/2018 on Data Protection.

Results

The anthropometric, clinical, analytical, sociodemographic, and health-related data for the 44,939 workers included in the study are presented in **table I**. The participants' mean age was slightly over 41 years, with lower values consistently observed in the female group. The population's mean age predominantly ranged from 30 to 49 years.

Adherence to the Mediterranean diet was reported by 45.8% of men and 37.9% of women. Regular physical activity was practiced by 47.5% of men and 38.9% of women. Smoking prevalence was 16.1% in men and 15% in women.

Tables II and III present the mean values and prevalence of high values for the various scales assessing overweight and obesity, stratified by sociodemographic variables and health behaviors. The results indicate that both the mean values and the prevalence of high values on the overweight-obesity scales increase progressively with age and decrease as socioeconomic status declines. These values are higher among smokers, sedentary individuals, and those with low adherence to the Mediterranean diet. In contrast, all values are lower in women. The observed differences are consistently statistically significant ($p < 0.001$).

Table I: Characteristics of the population.

	Men n=14,305	Women n=30,634	p-value
	Mean (SD)	Mean (SD)	
Age (years)	41,1 (10,6)	40,4 (10,5)	<0.001
Height (cm)	176,0 (7,5)	162,6 (6,0)	<0.001
Weight (kg)	81,2 (14,5)	63,7 (13,3)	<0.001
Waist circumference (cm)	89,7 (12,6)	76,7 (11,8)	<0.001
Hip circumference (cm)	101,7 (8,8)	99,3 (10,7)	<0.001
Systolic blood pressure (mmHg)	128,2 (13,1)	116,1 (13,8)	<0.001
Diastolic blood pressure (mmHg)	79,9 (10,6)	74,8 (10,1)	<0.001
Total cholesterol (mg/dL)	191,8 (37,2)	187,8 (34,6)	<0.001
HDL-c (mg/dL)	48,9 (11,2)	59,3 (12,8)	<0.001
LDL-c (mg/dL)	165,2 (46,2)	144,8 (38,9)	<0.001
Triglycerides (mg/dL)	111,0 (73,2)	81,7 (47,0)	<0.001
Glucose (mg/dL)	93,6 (18,2)	88,9 (12,4)	<0.001
AST (U/l)	24,1 (17,2)	18,2 (8,0)	<0.001
ALT (U/l)	29,0 (36,7)	17,3 (13,7)	<0.001
GGT (U/l)	30,2 (28,8)	18,1 (18,1)	<0.001
	N (%)	N (%)	p-value
< 30 years	2400 (16.8)	5984 (19.5)	<0.001
30-39 years	4200 (29.4)	8304 (27.1)	
40-49 years	4512 (31.5)	10128 (33.0)	
50-59 years	2449 (17.1)	5150 (16.8)	
60-69 years	744 (5.2)	1120 (3.6)	
Physicians	5064 (35.4)	5024 (16.4)	<0.001
Nurses	4008 (28.0)	12752 (41.6)	
Health Technicians	1728 (12.1)	4128 (13.5)	
Nursing assistants or orderlies	3505 (24.5)	8782 (28.5)	
Non-smokers	12001 (83.9)	26094 (85.0)	<0.001
Smokers	2304 (16.1)	4592 (15.0)	
No physical activity	7512 (52.5)	18744 (61.1)	<0.001
Yes physical activity	6793 (47.5)	11942 (38.9)	
Non Mediterranean diet	7771 (54.2)	19213 (62.1)	<0.001
Yes Mediterranean diet	6534 (45.8)	11413 (37.9)	

HDL High density lipoprotein. LDL Low density lipoprotein. AST Aspartate Aminotransferase. ALT Alanine Aminotransferase. GGT Gamma-glutamyl transpeptidase. SD Standard deviation.

Table II: Mean values of obesity scales according sociodemographic variables and healthy habits by sex.

Men	n	BMI		WtHR		BAI		CUN BAE		METS-VF	
		Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
< 30 years	2400	24.1 (4.1)	<0.001	0.46 (0.06)	<0.001	23.9 (4.3)	<0.001	19.7 (6.6)	<0.001	5.6 (0.8)	<0.001
30-39 years	4200	25.4 (4.0)		0.49 (0.06)		25.1 (3.7)		23.1 (5.6)		6.1 (0.6)	
40-49 years	4512	26.6 (3.9)		0.52 (0.06)		25.7 (3.4)		26.0 (5.3)		6.5 (0.6)	
50-59 years	2449	28.0 (4.1)		0.55 (0.08)		27.6 (4.6)		29.4 (5.4)		6.9 (0.6)	
60-69 years	744	28.3 (4.4)		0.56 (0.06)		27.7 (5.1)		30.3 (4.9)		7.1 (0.4)	
Physicians	5064	25.9 (3.7)	<0.001	0.50 (0.06)	<0.001	24.7 (5.2)	<0.001	23.6 (6.2)	<0.001	6.1 (0.7)	<0.001
Nurses	4008	25.7 (4.2)		0.50 (0.07)		25.3 (3.6)		24.6 (6.0)		6.2 (0.7)	
Health Technicians	1728	26.3 (4.9)		0.51 (0.09)		25.7 (3.9)		24.9 (7.6)		6.3 (0.9)	
Nursing assistants or orderlies	3505	27.2 (4.7)		0.53 (0.08)		26.5 (4.5)		26.6 (6.6)		6.6 (0.8)	
Non-smokers	12001	25.8 (4.3)	<0.001	0.50 (0.07)	<0.001	25.3 (4.2)	<0.001	24.6 (6.4)	<0.001	6.2 (0.8)	<0.001
Smokers	2304	26.2 (4.3)		0.51 (0.07)		25.7 (4.2)		25.0 (6.5)		6.4 (0.8)	
No physical activity	7512	27.3 (4.7)	<0.001	0.53 (0.08)	<0.001	26.6 (4.4)	<0.001	26.5 (6.9)	<0.001	6.6 (0.8)	<0.001
Yes physical activity	6793	25.0 (3.5)		0.49 (0.06)		24.7 (3.6)		23.1 (5.5)		6.1 (0.7)	
Non Mediterranean diet	7771	27.0 (4.6)	<0.001	0.52 (0.07)	<0.001	26.1 (4.4)	<0.001	26.0 (6.3)	<0.001	6.6 (0.8)	<0.001
Yes Mediterranean diet	6534	25.6 (3.7)		0.49 (0.07)		25.2 (3.8)		23.8 (5.8)		6.2 (0.8)	
Women	n	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
< 30 years	5984	22.3 (3.6)	<0.001	0.43 (0.05)	<0.001	27.9 (4.6)	<0.001	28.9 (5.7)	<0.001	4.7 (0.8)	<0.001
30-39 years	8304	23.2 (4.8)		0.45 (0.07)		28.9 (5.3)		31.6 (6.4)		5.2 (0.8)	
40-49 years	10128	24.8 (4.8)		0.48 (0.07)		30.8 (5.4)		35.2 (5.9)		5.8 (0.8)	
50-59 years	5150	25.9 (5.1)		0.51 (0.08)		32.2 (5.7)		38.1 (6.1)		6.2 (0.8)	
60-69 years	1120	26.1 (5.5)		0.53 (0.07)		32.3 (6.0)		39.3 (6.0)		6.4 (0.7)	
Physicians	5024	22.1 (3.2)	<0.001	0.44 (0.05)	<0.001	28.0 (4.3)	<0.001	30.3 (5.7)	<0.001	5.0 (0.9)	<0.001
Nurses	12752	23.4 (4.3)		0.46 (0.07)		29.2 (5.2)		32.3 (6.1)		5.3 (0.9)	
Health Technicians	4128	25.2 (5.2)		0.49 (0.08)		31.1 (5.7)		35.2 (7.2)		5.7 (0.9)	
Nursing assistants or orderlies	8782	25.9 (5.6)		0.51 (0.08)		31.9 (5.9)		36.7 (6.9)		6.0 (0.9)	
Non-smokers	26094	24.0 (4.7)	<0.001	0.47 (0.07)	<0.001	29.9 (5.4)	<0.001	33.5 (6.8)	<0.001	5.5 (0.9)	<0.001
Smokers	4592	24.4 (5.6)		0.48 (0.08)		30.5 (6.1)		34.3 (7.1)		5.7 (0.9)	
No physical activity	18744	24.8 (5.3)	<0.001	0.48 (0.08)	<0.001	30.9 (5.8)	<0.001	34.6 (7.3)	<0.001	5.7 (0.9)	<0.001
Yes physical activity	11942	23.0 (3.7)		0.45 (0.06)		28.7 (4.8)		32.2 (5.9)		5.3 (0.9)	
Non Mediterranean diet	19213	24.5 (5.3)	<0.001	0.48 (0.08)	<0.001	30.3 (5.7)	<0.001	34.1 (7.0)	<0.001	5.7 (0.8)	<0.001
Yes Mediterranean diet	11413	23.5 (3.8)		0.46 (0.07)		29.2 (5.9)		32.8 (6.0)		5.4 (0.8)	

BMI Body mass index. WtHR Waist to height ratio. BAI Body adiposity index. CUN BAE Clínica Universidad de Navarra-Body adiposity Estimator. METS-VF Metabolic score for visceral fat. SD Standard deviation.

Table III: Prevalence of high values of obesity scales according sociodemographic variables and healthy habits by sex.

	n	BMI obesity		WtHR high		BAI obesity		CUN BAE obesity		METS-VF high	
		%	p-value	%	p-value	%	p-value	%	p-value	%	p-value
Men											
< 30 years	2400	9.1	<0.001	20.9	<0.001	5.8	<0.001	16.8	<0.001	2.1	<0.001
30-39 years	4200	10.3		37.7		10.2		26.9		6.9	
40-49 years	4512	14.4		54.8		14.5		52.7		12.8	
50-59 years	2449	29.4		76.4		20.3		77.5		42.1	
60-69 years	744	32.3		83.9		22.5		82.8		48.4	
Physicians	5064	12.0	<0.001	41.9	<0.001	16.8	<0.001	32.9	<0.001	8.4	<0.001
Nurses	4008	13.7		45.0		9.9		46.4		13.3	
Health Technicians	1728	16.7		50.0		8.5		47.2		19.4	
Nursing assistants or orderlies	3505	22.6		63.7		12.3		56.2		27.4	
Non-smokers	12001	15.6	<0.001	48.9	<0.001	10.5	<0.001	37.5	<0.001	14.6	<0.001
Smokers	2304	15.8		49.4		14.2		46.6		16.4	
No physical activity	7512	21.7	<0.001	62.9	<0.001	22.1	<0.001	58.1	<0.001	23.3	<0.001
Yes physical activity	6793	9.2		34.3		7.3		30.8		8.1	
Non Mediterranean diet	7771	20.9	<0.001	60.0	<0.001	20.5	<0.001	52.8	<0.001	21.5	<0.001
Yes Mediterranean diet	6534	10.1		37.8		8.3		34.2		9.8	
Women											
< 30 years	5984	4.5	<0.001	11.0	<0.001	1.9	<0.001	15.2	<0.001	0.5	<0.001
30-39 years	8304	6.9		19.1		4.6		26.0		1.3	
40-49 years	10128	13.1		31.8		5.1		44.2		2.2	
50-59 years	5150	18.3		51.0		7.1		63.7		9.3	
60-69 years	1120	18.6		55.7		7.9		74.3		12.9	
Physicians	5024	2.2	<0.001	11.5	<0.001	9.2	<0.001	19.4	<0.001	0.6	<0.001
Nurses	12752	7.5		19.1		4.2		29.9		1.6	
Health Technicians	4128	17.2		38.0		3.4		46.5		3.9	
Nursing assistants or orderlies	8782	17.9		47.0		6.9		56.5		6.4	
Non-smokers	26094	10.6	<0.001	27.5	<0.001	3.9	<0.001	37.4	<0.001	3.0	<0.001
Smokers	4592	12.2		33.4		5.1		41.5		3.8	
No physical activity	18744	13.8	<0.001	34.7	<0.001	10.3	<0.001	44.3	<0.001	4.5	<0.001
Yes physical activity	11942	6.2		18.4		3.2		28.1		0.9	
Non Mediterranean diet	19213	13.3	<0.001	33.0	<0.001	10.0	<0.001	41.9	<0.001	4.0	<0.001
Yes Mediterranean diet	11413	7.0		19.6		4.2		31.3		1.3	

BMI Body mass index. WtHR Waist to height ratio. BAI Body adiposity index. CUN BAE Clínica Universidad de Navarra-Body adiposity Estimator. METS-VF Metabolic score for visceral fat.

Table IV: Multinomial logistic regression.

	BMI obesity	WtHR high	BAI obesity	CUN BAE obesity	METS-VF high
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Women	1	1	1	1	1
Men	1.92 (1.80-2.04)	3.64 (3.47-3.82)	8.46 (7.90-9.03)	1.65 (1.57-1.73)	5.86 (5.01-6.73)
< 30 years	1	1	1	1	1
30-39 years	1.36 (1.20-1.52)	1.75 (1.56-1.95)	1.19 (1.14-1.25)	2.24 (1.97-2.51)	1.77 (1.55-1.99)
40-49 years	2.35 (2.08-2.62)	3.98 (3.55-4.41)	1.34 (1.21-1.47)	5.38 (4.75-6.02)	3.89 (3.69-4.20)
50-59 years	3.96 (3.47-4.46)	7.45 (6.64-8.27)	1.79 (1.60-1.99)	7.89 (7.01-8.77)	7.81 (6.91-8.72)
60-69 years	4.41 (3.81-5.02)	12.47 (11.01-13.93)	2.45 (2.05-2.86)	11.21 (10.01-12.42)	14.20 (12.99-15.42)
Physicians	1	1	1	1	1
Nurses	1.14 (1.10-1.18)	1.33 (1.24-1.43)	1.17 (1.13-1.21)	1.21 (1.13-1.29)	1.32 (1.17-1.48)
Health Technicians	1.68 (1.55-1.81)	2.15 (2.03-2.27)	1.64 (1.50-1.78)	1.78 (1.69-1.88)	1.91 (1.70-2.12)
Nursing assistants or orderlies	2.85 (2.60-3.11)	3.38 (3.16-3.60)	1.84 (1.68-2.00)	2.48 (2.33-2.63)	3.94 (3.50-4.39)
Non-smokers	1	1	1	1	1
Smokers	1.17 (1.12-1.22)	1.18 (1.13-1.24)	1.14 (1.10-1.18)	1.33 (1.21-1.45)	1.25 (1.19-1.32)
Yes physical activity	1	1	1	1	1
No physical activity	2.52 (2.36-2.69)	2.87 (2.74-3.01)	2.16 (2.02-2.31)	2.58 (2.47-2.69)	3.94 (3.57-4.31)
Yes Mediterranean diet	1	1	1	1	1
Non Mediterranean diet	1.90 (1.71-2.10)	2.02 (1.84-2.21)	1.72 (1.55-1.89)	1.98 (1.85-2.12)	2.87 (2.60-3.15)

BMI Body mass index. WtHR Waist to height ratio. BAI Body adiposity index. CUN BAE Clínica Universidad de Navarra-Body adiposity Estimator. METS-VF Metabolic score for visceral fat. OR Odds ratio.

Table IV presents the results of the multinomial logistic regression analysis, showing that all variables included in the model are associated with the presence of high values on the overweight-obesity scales. Among all variables, the strongest association (highest odds ratio values) is observed for age, followed by professional category and physical activity.

The Pearson correlation index is very high among all the scales assessing excess weight, whereas Cohen's

kappa concordance coefficient values are low, except for the pairs BMI and BAI, WtHR and CUN-BAE, and BAI and METS-VF. Full data can be found in **table V**.

Table VI presents the results of the retrospective longitudinal study, showing the prevalence of high values on the overweight-obesity scales during the pre (2010) and post (2019) periods. The differences in prevalence between these periods increased with age and decreased with socioeconomic status. These

differences were more pronounced among smokers, individuals who do not engage in regular physical activity, and those with low adherence to the Mediterranean diet.

In all cases, the prevalence differences were smaller among women. In all cases the differences observed show statistical significance ($p < 0.001$).

Table V: Pearson and kappa Cohen coefficient.

<i>Pearson</i>	BMI	WtHR	BAI	CUN BAE	METS-VF
BMI	1	0.896	0.855	0.955	0.816
WtHR		1	0.820	0.904	0.937
BAI			1	0.835	0.774
CUN BAE				1	0.906
METS-VF					1
<i>kappa Cohen</i>	BMI obesity	WtHR high	BAI obesity	CUN BAE high	METS-VF high
BMI obesity	1	0.467	0.552	0.331	0.404
WtHR high		1	0.220	0.706	0.151
BAI obesity			1	0.150	0.553
CUN BAE high				1	0.100
METS-VF high					1

BMI Body mass index. WtHR Waist to height ratio. BAI Body adiposity index. CUN BAE Clínica Universidad de Navarra-Body adiposity Estimator. METS-VF Metabolic score for visceral fat.

Table VI: Differences in the prevalences of high values of overweight and obesity scales between the pre and post periods by sex.

	n	BMI obesity			WtHR high			BAI obesity			CUN BAE obesity			METS-VF high		
		% pre-post	difference %	p-value	% pre-post	difference %	p-value	% pre-post	difference %	p-value	% pre-post	difference %	p-value	% pre-post	difference %	p-value
Men																
<30 years	2400	8.6-9.1	5.3	<0.001	19.6-20.9	6.1	<0.001	5.4-5.8	7.3	<0.001	15.3-16.8	8.9	<0.001	1.9-2.1	7.3	<0.001
30-39 years	4200	9.4-10.3	8.7		34.7-37.7	7.9		9.2-10.2	9.9		23.5-26.9	12.8		6.2-6.9	9.9	
40-49 years	4512	12.4-14.4	13.8		48.3-54.8	11.8		12.5-14.5	13.5		44.6-52.7	15.3		11.2-12.8	12.4	
50-59 years	2449	24.4-29.4	17.1		65.5-76.4	14.3		16.7-20.3	17.8		62.6-77.5	19.2		35.9-42.1	14.8	
60-69 years	744	25.7-32.3	20.3		69.5-83.9	17.2		17.9-22.5	20.4		64.3-82.8	22.4		39.3-48.4	18.9	
Physicians	5064	11.2-12.0	6.7	<0.001	39.3-41.9	6.1		15.5-16.8	7.7	<0.001	29.7-32.9	9.8		7.7-8.4	7.9	
Nurses	4008	12.5-13.7	8.8		41.4-45.0	7.9		9.0-9.9	9.1		41.3-46.4	10.9		12.1-13.3	8.9	
Health Technicians	1728	14.7-16.7	11.8		43.1-50.0	13.8		7.5-8.5	11.8		39.5-47.2	16.3		17.1-19.4	11.8	
Nursing assistants or orderlies	3505	19.0-22.6	15.9		54.0-63.7	15.3		10.3-12.3	16.6		45.0-56.2	19.9		22.6-27.4	17.5	
Non-smokers	12001	14.1-15.6	9.9	<0.001	44.5-48.9	8.9	<0.001	9.5-10.5	9.7	<0.001	32.7-37.5	12.8	<0.001	13.1-14.6	10.1	<0.001
Smokers	2304	13.8-15.8	12.8		43.2-49.4	12.6		12.5-14.2	12.3		39.0-46.6	16.3		14.3-16.4	12.9	
No physical activity	7512	17.4-21.7	19.9	<0.001	50.1-62.9	20.3	<0.001	17.3-22.1	21.5	<0.001	44.4-58.1	23.5	<0.001	18.2-23.3	21.8	<0.001
Yes physical activity	6793	8.7-9.2	5.3		32.1-34.3	6.3		6.8-7.3	6.9		28.7-30.8	6.9		7.5-8.1	7.9	
Non Mediterranean diet	7771	17.0-20.9	18.6	<0.001	48.7-60.0	18.9	<0.001	16.4-20.5	20.0	<0.001	41.5-52.8	21.4	<0.001	17.1-21.5	20.5	<0.001
Yes Mediterranean diet	6534	18.8-10.1	6.7		35.0-37.8	7.4		7.7-8.3	7.5		31.6-34.2	7.6		9.0-9.8	8.6	
Women																
<30 years	5984	4.4-4.5	2.8	<0.001	10.6-11.0	3.3	<0.001	1.8-1.9	3.9	<0.001	14.5-15.2	4.5	<0.001	0.5-0.5	5.7	<0.001
30-39 years	8304	6.5-6.9	6.1		17.9-19.1	6.4		4.3-4.6	6.3		24.2-26.0	6.8		1.2-1.3	8.2	
40-49 years	10128	11.9-13.1	8.9		28.8-31.8	9.5		4.6-5.1	9.9		39.8-44.2	9.9		2.0-2.2	10.3	
50-59 years	5150	15.6-18.3	14.8		44.2-51.0	13.4		6.1-7.1	13.4		55.0-63.7	13.6		7.8-9.3	15.9	
60-69 years	1120	15.5-18.6	16.9		46.3-55.7	16.9		6.4-7.9	18.9		61.2-74.3	17.6		10.4-12.9	19.7	
Physicians	5024	2.1-2.2	3.1	<0.001	11.1-11.5	3.6	<0.001	8.8-9.2	4.8	<0.001	18.4-19.4	4.9	<0.001	0.6-0.6	5.6	<0.001
Nurses	12752	7.1-7.5	5.2		18.3-19.1	4.4		3.9-4.2	6.1		27.8-29.9	6.9		1.5-1.6	7.9	
Health Technicians	4128	15.5-17.2	8.9		35.0-38.0	7.9		3.1-3.4	9.9		41.7-46.5	10.3		3.4-3.9	12.8	
Nursing assistants or orderlies	8782	15.3-17.9	14.3		41.2-47.0	12.3		5.8-6.9	15.3		48.1-56.5	14.8		5.4-6.4	15.8	
Non-smokers	26094	9.7-10.6	8.6	<0.001	25.3-27.5	7.9	<0.001	3.6-3.9	8.6	<0.001	33.8-37.4	9.6	<0.001	2.7-3.0	10.9	<0.001
Smokers	4592	10.9-12.2	10.8		30.3-33.4	9.3		4.6-5.1	10.5		36.8-41.5	11.3		3.3-3.8	13.1	
No physical activity	18744	11.3-13.8	18.3	<0.001	29.0-34.7	16.5	<0.001	8.7-10.3	15.8	<0.001	36.1-44.3	18.6	<0.001	3.6-4.5	20.4	<0.001
Yes physical activity	11942	5.9-6.2	5.4		17.4-18.4	5.3		3.0-3.2	6.2		26.4-28.1	6.1		0.8-0.9	7.9	
Non Mediterranean diet	19213	10.9-13.3	17.8	<0.001	28.0-33.0	15.3	<0.001	8.6-10.0	14.1	<0.001	34.7-41.9	17.5	<0.001	3.2-4.0	19.5	<0.001
Yes Mediterranean diet	11413	6.5-7.0	6.5		18.3-19.6	6.4		3.9-4.2	6.9		29.0-31.3	7.2		1.2-1.3	8.6	

BMI Body mass index. WtHR Waist to height ratio. BAI Body adiposity index. CUN BAE Clínica Universidad de Navarra-Body adiposity Estimator. METS-VF Metabolic score for visceral fat.

Discussion

In our study, we observed associations between sociodemographic factors (age, sex, socioeconomic status) and lifestyle factors (tobacco use, physical activity, and adherence to the Mediterranean diet) with the prevalence of overweight, assessed using indicators such as BMI, waist-to-height ratio, BAI, CUN-BAE, and METS-VF. These indicators provide a comprehensive perspective on the distribution and impact of excess weight in various contexts, including healthcare workers, who are exposed to occupational and personal factors that may influence their nutritional and metabolic status.

Age is one of the most consistently associated factors with overweight in our research. This finding aligns with previous studies that have shown a linear relationship, where increasing age is generally linked to higher levels of body fat up to a certain point, followed by stabilization or decline in advanced ages due to muscle loss and metabolic changes⁴¹. In the context of healthcare workers, this association may be influenced by the nature of their work, which often involves irregular shifts, variable physical demands, and high levels of stress⁴². Additionally, indicators such as METS-VF⁴³ and CUN-BAE⁴⁴, which provide more specific information on visceral adipose tissue and fat distribution, have proven particularly sensitive in detecting age-related changes. Several recent studies suggest that healthcare workers over 40 years of age are at higher risk of developing visceral obesity compared to their younger counterparts, which may increase their susceptibility to metabolic diseases^{45,46}.

Sex also plays a critical role in the prevalence and distribution of excess weight, as evidenced by the results obtained in this study. Various authors have demonstrated that women tend to present higher levels of general and subcutaneous adiposity compared to men, who are more prone to visceral fat accumulation, which is more closely associated with metabolic complications^{47,48}. In the healthcare sector, women represent a significant proportion of the workforce and are exposed to factors that may exacerbate this tendency, such as long shifts and additional responsibilities outside of work. Recent research has shown that the CUN-BAE indicator may be particularly useful in assessing adiposity in women, as it incorporates sex- and age-specific factors in its calculations⁴⁹. On the other hand, BMI and waist-to-height ratio, while widely used, may underestimate metabolic risk in men due to their inability to differentiate between lean and fat mass⁵⁰.

Socioeconomic status (SES) is a key social determinant in the development of overweight. In our research, this may be due to its influence on access to healthy foods, opportunities for physical activity, and perceived stress levels⁵¹. Among healthcare workers, the impact of SES could be mediated by professional categorization. For

example, technical or auxiliary workers may be more exposed to factors that promote obesity, such as less flexible schedules and reduced access to workplace wellness programs⁵².

According to our results, tobacco use is associated with high values on overweight and obesity scales. Some authors have traditionally considered tobacco as a protective factor against weight gain due to its appetite-suppressing effects⁵³. However, this relationship is complex and depends on factors such as the duration and intensity of smoking, as well as the potential for weight gain after quitting⁵⁴. Among healthcare workers, tobacco may interact with other lifestyle factors to influence overweight. For instance, a study conducted on nurses and doctors showed that smokers had lower BMI but higher levels of visceral fat, which could increase their risk of cardiovascular diseases⁵⁵.

Physical activity is one of the most important protective factors against overweight, as highlighted in our results. In the case of healthcare workers, physical activity may be limited by long working hours and associated fatigue. A study conducted in the Valencian Community on 647 healthcare workers that evaluated physical activity both at work and outside of it found lower activity levels among women. Additionally, higher professional categories were associated with higher levels of physical activity—two findings that align with our results⁵⁶.

Adherence to the Mediterranean diet, according to our findings, has been consistently associated with a lower risk of overweight and metabolic diseases. This dietary pattern, characterized by high consumption of fruits, vegetables, legumes, whole grains, fish, and olive oil, and low consumption of red meat and ultra-processed foods, appears to have a protective effect against visceral fat accumulation and chronic inflammation⁵⁷. Among healthcare workers, adherence to the Mediterranean diet may be compromised by a lack of time to prepare healthy meals and the availability of unhealthy food options in hospital settings⁵⁸. Recent studies have shown that higher adherence to this diet is associated with a lower prevalence of overweight according to indicators such as BAI⁵⁹ and CUN-BAE⁶⁰, underscoring the importance of promoting this dietary pattern in intervention programs targeting this population.

The strengths of this study include the large sample size (nearly 45,000 healthcare workers), making it one of the largest studies evaluating obesity in healthcare workers. Another strength is the use of numerous validated scales to assess overweight, addressing not only anthropometric profiles but also the estimation of body and visceral fat. Finally, we should highlight the inclusion of a wide range of variables, both sociodemographic and health-related, in the study.

One limitation of the study is the exclusion of unemployed individuals, retirees, those under 18, and those over 69 years of age. Although this exclusion reduces the generalizability of the results to the broader population, we believe that the large sample size partially mitigates this effect. Another limitation is the lack of information on potential confounding factors, such as the presence of comorbidities or the use of pharmacological treatments, due to the unavailability of these data.

Conclusion

Age, sex, professional category, tobacco use, physical activity, and adherence to the Mediterranean diet are all associated with the presence or absence of excess weight, assessed using different scales such as BMI, waist-to-height ratio, BAI, CUN-BAE, and METS-VF.

Conflict of Interest

The authors declared that there is no conflict of interest

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ORIGINAL

The relationship between attitudes of parents towards childhood vaccines and vaccine confidence: a cross-sectional study in Turkish Society

La relación entre las actitudes de los padres hacia las vacunas infantiles y la confianza en las vacunas: un estudio transversal en la sociedad turca

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Abstract

Introduction and objectives: This study examines the relationship between parents' attitudes towards childhood vaccines and vaccine confidence during the coronavirus pandemic in Turkish society.

Material and methods: This cross-sectional study was conducted by using an online form with 1.031 parents in Turkish society. This cross-sectional study was conducted between 10 November and 10 December 2020 by using an online form with 1.031 parents in Turkish society. Snowball sampling was applied. Parents were recruited through social media tools and websites such as WhatsApp, Instagram, Twitter, and Facebook.

Results: It was found that 86.8% of the parents had their children vaccinated in the vaccination schedule. There was a strong correlation between the Vaccination Confidence Scale and the Parent Attitudes about Childhood Vaccines Scale ($r = .610$; $p \leq 0.001$).

Conclusions: It was predicted that the study results could be beneficial for health professionals working in primary health care as well as social workers working on this subject.

Key words: Vaccination, Vaccine confidence, Parental attitudes, Childhood vaccines, Society.

Resumen

Introducción y objetivos: Este estudio examina la relación entre las actitudes de los padres hacia las vacunas infantiles y la confianza en las vacunas durante la pandemia de coronavirus en la sociedad turca.

Materiales y métodos: Este estudio transversal se realizó mediante un formulario en línea con 1.031 padres de la sociedad turca. Este estudio transversal se realizó entre el 10 de noviembre y el 10 de diciembre de 2020 mediante el uso de un formulario en línea con 1.031 padres de la sociedad turca. Se aplicó muestreo de bola de nieve. Los padres fueron reclutados a través de herramientas de redes sociales y sitios web como WhatsApp, Instagram, Twitter y Facebook.

Resultados: Se encontró que el 86,8% de los padres vacunaron a sus hijos en el calendario de vacunación. Hubo una fuerte correlación entre la Escala de Confianza en la Vacunación y la Escala de Actitudes de los Padres sobre las Vacunas Infantiles ($r = 0,610$; $p \leq 0,001$).

Conclusiones: Se predijo que los resultados del estudio podrían ser beneficiosos para los profesionales de la salud que trabajan en la atención primaria de salud, así como para los trabajadores sociales que trabajan en este tema.

Palabras clave: Vacunación, Confianza en las vacunas, Actitudes de los padres, Vacunas infantiles, Sociedad.

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Introduction

The primary purpose of health services is to ensure that people continue to live healthy and prevent diseases. One of the most important public health practices in maintaining health and preventing communicable diseases is immunization studies. The immune response caused by the administration of antigen to the body against a microorganism is called immunization, and the process applied to obtain this response is called vaccination^{1,2}. Despite being recognized as one of the most successful public health measures, vaccination is perceived as unsafe and unnecessary by an increasing number of parents³. The issue of vaccine rejection has been debated around the world for many years, and has recently become more and more on the agenda. The efficacy, safety, necessity, and importance of vaccines are some of the main topics discussed. Vaccination is very important for children to grow and develop in a healthy way. In recent years, reservations expressed by families for different reasons may affect vaccine acceptance⁴. Parents' ignorance of vaccine rejection is one of the most important reasons for this^{2,5}. Studies emphasize that informing families by healthcare professionals is the most reliable source and increases vaccination rates^{4,6}.

The return on investment of childhood vaccination programs is quite high⁴. Thanks to the Expanded Immunization Program implemented by the World Health Organization (WHO) since 1974, deaths of millions of people have been prevented by administering diphtheria, whooping cough, measles, polio, tetanus and tuberculosis vaccines^{3,7-9}. The vaccination rate in Turkey was 98% in 2016, whereas this rate decreased to 96% in 2017. While measles was seen in 84 children in 2017 across the country, it reached 716 in 2018 and 2.905 in 2019. According to the data of the Ministry of Health in Turkey in April 2018, the number of families who reject vaccines has exceeded 20,000^{10,11}. The World Health Organization has gathered the factors that prevent vaccination under three main headings. These factors are: contextual effect; individual and group effects; and vaccines and vaccination effects¹². Some of these include not trusting the vaccine content; side effects of the vaccine; family's perception of the disease; not getting enough information about vaccines; religious reasons; and the pharmaceutical industry¹³.

For example, in anti-vaccine discourses, the relation of mercury in the vaccine with autism has been put forward, and such a relationship has not been shown in many scientific studies. Vaccines that have been applied in the world for about twenty years and in our country for the last ten years to reduce vaccine rejection do not contain mercury. However, the hesitation of the parents about this still continues^{1,14,15}. Anti-vaccination actions play a role in terms of lowering vaccine acceptance rates and increasing vaccine-preventable disease outbreaks and epidemics³. The reoccurrence

of vaccine-preventable outbreaks, including measles and pertussis, can be given as an evidence¹⁶. For this reason, the World Health Organization has included vaccine rejection among the ten global problems it determined for 2019¹⁷. In the world, the primary problem in vaccination in underdeveloped countries is related to the inadequacy of the necessary technical infrastructure and the number of healthcare personnel below the need, while in developed and developing countries, it is related to the fact that parents are not informed about the vaccines adequately and accurately and that the necessity of vaccination is not explained. Among the reasons why children are not fully vaccinated on time are the socioeconomic structure of the family, the education level of the parents, the number of children, the distance to the health institution, insufficient or wrong information, lack of trust in vaccines, and the risk of vaccines to cause immunosuppressive diseases^{18,19}.

There is frequent public distrust among parents against the vaccine. It is an undeniable fact that midwives and nurses, as health professionals, have important responsibilities in informing the public about vaccines and the importance of vaccination. In the fight against vaccine rejection, it is inevitable to carry out scientific studies in order to increase social trust in vaccination and to offer solutions in the light of these researches. In the literature review, studies on this subject are very limited. The coronavirus pandemic is also an important process to raise awareness on this issue. Therefore, the study was conducted to determine the relationship between the attitudes of parents towards childhood vaccines and vaccine confidence during the coronavirus pandemic in Turkish society.

Materials and methods

Design, Data Collection and Sample

This cross-sectional study was conducted between 10 November and 10 December 2020 by using an online form with 1.031 parents in Turkish society. Snowball sampling was applied. Parents were recruited through social media tools and websites such as WhatsApp, Instagram, Twitter, and Facebook. A participation link with an informed consent were shared with participants to invite participants to study.

Inclusion criteria in the study

Having at least one child

Measurements

Data collection tools

The data of the study were collected using the "Parent Information Form", "Vaccination Confidence Scale" and "Parent Attitudes about Childhood Vaccines Scale" prepared by the researchers by scanning the literature.

The Parent Information Form, consists of 15 questions which are related to parents' socio-demographic characteristics, such as gender, age, educational status, income perception, employment status, and their opinions about childhood vaccinations, the decision to have childhood vaccinations, the effect of the COVID-19 pandemic on childhood vaccination, and the decision to have a possible coronavirus vaccine⁷.

The Vaccination Confidence Scale (VCS): This 8-item scale, which was developed by Gilkey et al.²⁰ with 0.77 coefficient alpha, was adapted to the Turkish language by Özdemir and Kadioğlu²¹. The scale items are scored between 0 (strongly disagree) and 10 (strongly agree) and consist of three subscales: benefits of vaccination, harms of vaccination, and trust in healthcare providers. The total score that can be obtained from the scale varies between 0-80: 0-40 is obtained from the 'benefits of vaccination' subscale, whereas 0-20 is obtained from the 'harms of vaccination' subscale and 0-20 from the 'trust in healthcare providers' subscale. A high score is interpreted as a high perception of vaccine trust. The Cronbach alpha coefficient of the Turkish form of the scale was 0.70, and it was, a similar way, 0.69 in this study. The low coefficient alphas can be explained by the low number of items in the scale²⁰.

The Parent Attitudes about Childhood Vaccines Scale (PACV): The scale, which was developed by Opel et al.²²⁻²⁴ and whose validity and reliability were studied, was adapted to Turkish by Bulun and Acuner²⁵. The answers to the scale questions, which consist of 15 questions in total, include three different response formats. Three questions are closed-ended (Yes/No/I don't know), 10 questions are the 5-item Likert type (Strongly Agree/Agree/Not Sure/Disagree/Strongly Disagree), and two questions are the scoring type (from 0 to 10). While scoring the scale items, the hesitant responses were scored as 2, the unstable responses were scored as 1, and the unhesitant responses were scored as 0, and the scores from each item were added without any weighting to determine the total score. In the scale, there is a simple linear transformation table that can be used according to the situation where the answers given to the first two questions are "Yes", "No" or "Don't know" and where there can be one or two missing data in the last 13 questions. The lowest score that can be obtained from the scale is 0, whereas the highest score is 100. High scores in the scale indicate vaccine hesitancy. The Cronbach alpha score was calculated as 0.74 for the original scale, 0.84 for the Turkish version. The Cronbach alpha score calculated for the whole scale in this study was 0.85.

Ethical considerations

This study was approved by the Scientific Research Council of Bartın University (Reference number: 2020-SBB-0213 / Date: 5 November 2020). Participation in the study was on a voluntary basis. Electronic informed

consent was presented on the first page of the online forms. On the first page of the survey, the participants were electronically asked whether they were willing to participate and informed that they could withdraw from the survey at any time.

Statistical analysis

The values of Skewness and Kurtosis were examined in order to test the compliance of the study data to normal distribution. Descriptive statistics were given in terms of number, percentage and standard deviation. Chi-square test was used for the comparison of categorical variables, ANOVA for data conforming to normal distribution in group comparisons, and Mann-Whitney U analysis for data not compatible with normal distribution. Pearson's correlation was used to evaluate the relationship between the Vaccine Confidence Scale and its subscales, and the Parent Attitudes About Childhood Vaccines Scale and its subscales. Since all the questions were mandatory in the prepared survey, there is no missing data in the data. SPSS 22.0 was used for analysis, and $p \leq 0.05$ was accepted as the level of significance.

Results

The characteristics of the parents regarding their socio-demographic characteristics are given in **table I**. 86.13% of the participants were mother parents and the mean age was 37.41 (± 9.08), whereas the average age of the fathers was 44.62 (± 9.96). 52.96% of the parents do not work, 39.57% have university or higher education, 41.9% have two children, and 60.8% defined their income as equal to their expenses.

The differences between the Vaccine Confidence Scale and its subscales, and the PACV scale scores according to some socio-demographic characteristics of the parents are given in **table II**. Statistical differences were found between the age groups of the participants in terms of the Vaccine Confidence Scale ($F = 3.515$; $p = 0.015$), benefits subscale ($F = 5.675$; $p = 0.001$) and PACV scores ($F = 7.371$; $p = <0.001$). According to the Post-hoc analysis, this difference is due to the fact that the scores obtained by the parents under the age of 29 from the Vaccine Confidence Scale are lower than those of the 30-39 and 50-and-older age groups and that the scores obtained by the parents under the age of 29 from the benefits subscale were lower than those of all the other age groups. On the other hand, the PACV score of the participants aged 29 and under is higher than all other age groups, and the PACV score of the 30-39 age group is lower than the 40-49 age group. A statistical difference was found in terms of number of children parents have, Vaccine Confidence Scale ($F = 5.520$; $p = 0.004$), benefits subscale ($F = 7.251$; $p = 0.001$), trust subscale ($F = 0.772$; $p = 0.023$) and PACV scores ($F = 8.594$; $p = <0.001$). According to the Post-hoc analysis, the reason for the

difference was that the scores of the parents with three children and more from the benefits subscale were lower than those with one or two children and that

the trust subscale and the Vaccine Confidence Scale scores of the same group were lower than those with 2 children.

Table I: Socio-demographic Characteristics of the Parents.

Variables	Parents -1.031		Mother -888		Father -143		Statistics	
	Number	%	Number	%	Number	%	X ²	p
Age Group								
29 and younger	198	19.2	187	21.1	11	7.7	78.525	<.001
30-39	347	33.7	317	35.7	30	21		
40-49	353	34.2	300	33.8	53	37.1		
50 and older	133	12.9	84	9.5	49	34.3		
Mean (±SD). Min.-Max.	38.41 (±9.53). 18-70		37.41 (±9.08). 18-70		44.62 (±9.96). 21-69			
Employment Status								
Unemployed	546	52.96	509	57.3	37	25.9	19.319	<.001
Healthcare worker / Healthcare graduate	187	18.14	176	19.8	11	7.7		
Not a health worker	298	28.9	203	22.9	95	66.4		
Education status								
Elementary school or literate	401	38.89	336	37.8	65	45.5	27.119	<.001
High School	222	21.53	188	21.2	34	23.8		
University or higher	408	39.57	364	41.0	44	30.8		
Number of Children								
One	340	33.0	296	33.3	44	30.8	8.96	0.011
Two	432	41.9	383	43.1	49	34.3		
Three and more	259	25.1	209	23.5	50.0	35.0		
Mean (±SD). Min.-Max.	2.04 (±1.04). 1-9		2.01 (±0.99). 1-9		2.26 (±1.28). 1-9			
Economic condition								
Income less than expenses	232	22.5	205	23.1	27	18.9	1.817	<.001
Income equal to expenses	627	60.8	539	60.7	88	61.5		
Income more than expenses	172	16.7	144	16.2	28	19.6		

X²: Pearson Chi-Square Test; SD: Standard deviation

Table II: Comparison of the Average Scores of the Parents from the PACV and Vaccine Confidence Scale According to Their Socio-demographic Characteristics.

Variables	Parents		Benefits of Vaccination	Harms of Vaccination	Trust in Healthcare Providers	Vaccination Confidence Scale	PACV
	Number	%	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)
Age Group							
29 and younger	198	19.2	27.96 (±10.25)	8.60 (±4.85)	15.27 (±5.09)	51.83 (±13.00)	32.68 (22.62)
30-39	347	33.7	30.85 (±8.13)	8.07 (±4.68)	15.89 (±4.29)	54.82 (±11.39)	24.94 (19.87)
40-49	353	34.2	30.01 (±8.04)	8.39 (±4.38)	15.26 (±4.28)	53.65 (±10.60)	28.80 (20.00)
50 and older	133	12.9	31.06 (±7.58)	8.44 (±3.74)	15.57 (±3.83)	55.08 (±10.06)	24.79 (18.39)
F / p value			5.675 / 0.001	.674 / 0.568	1.467 / 0.222	3.515 / 0.015	7.371 / <0.001
Post hoc LCD			(a) < (b); (a) < (c); (a) < (d)			(a) < (b); (a) < (d)	(a) > (b); (a) > (c); (a) > (d); (b) < (c)
Employment Status							
Unemployed	546	52.96	30.01 (8.58)	8.32 (4.46)	15.53 (4.40)	53.86 (11.25)	28.61 (20.90)
Healthcare worker / Healthcare graduate	187	18.14	30.49 (8.77)	7.99 (4.60)	15.78 (4.44)	54.25 (11.86)	26.66 (20.59)
Not a health worker	298	28.9	29.80 (8.34)	8.56 (4.50)	15.33 (4.37)	53.68 (11.21)	26.79 (19.62)
F / p value			.381 / 0.683	.917 / 0.400	.607 / 0.545	.148 / 0.862	1.084 / .339
Education status							
Elementary school or literate	401	38.89	29.94 (±8.30)	8.37 (±4.25)	15.30 (±4.35)	53.61 (±11.18)	28.60 (±19.68)
High School	222	21.53	29.63 (±9.16)	8.14 (±4.69)	15.65 (±4.76)	53.42 (±11.84)	27.27 (±21.70)
University or higher	408	39.57	30.35 (±8.43)	8.39 (±4.64)	15.65 (±4.24)	54.39 (±11.22)	27.13 (±20.59)
F / p value			0.558 / 0.572	.248 / 0.780	.808 / 0.446	.716 / 0.489	.597 / 0.551
Number of Children							
One	340	33	29.96 (±9.29)	8.02 (±4.56)	15.56 (±4.62)	53.53 (11.81)	26.09 (20.88)
Two	432	41.9	31.02 (±7.75)	8.26 (±4.61)	15.85 (±4.16)	55.13 (10.44)	26.30 (19.31)
Three and more	259	25.1	28.49 (±8.57)	8.85 (±4.20)	14.90 (±4.45)	52.24 (11.94)	32.26 (21.24)
F / p value			7.251 / 0.001	2.637 / 0.072	0.772 / 0.023	5.520 / 0.004	8.594 / <0.001
Post hoc LCD			(a) > (c); (b) > (c)		(b) > (c)	(b) > (c)	(a) < (b); (a) < (c)
Economic condition							
Income less than expenses	232	22.5	29.37 (±8.67)	8.35 (±4.34)	15.38 (±4.65)	53.09 (±12.52)	30.16 (20.20)
Income equal to expenses	627	60.8	30.03 (±8.46)	8.35 (±4.59)	15.50 (±4.33)	53.89 (±11.15)	27.34 (20.31)
Income more than expenses	172	16.7	30.94 (±8.62)	8.20 (±4.40)	15.75 (±4.30)	54.90 (±10.25)	25.87 (21.29)
F / p value			1.683 / 0.186	.079 / 0.924	.359 / 0.699	1.247 / 0.288	2.468 / 0.085

F: Analysis of variance; SD: Standard deviation; PACV: The Parent Attitudes about Childhood Vaccines Scale.

Table III: Parents' Attitudes towards Vaccines.

Variables	Parents (1.031)		Mother (888)		Father (143)		Statistics	
	Number	%	Number	%	Number	%	X ²	p
Do you find it necessary to vaccinate your child?								
Yes	861	83.51	740	83.3	121	84.6	0.154	0.926
No	71	6.89	62	7	9	6.3		
I am indecisive	99	9.6	86	9.7	13	9.1		
Have your child had all the vaccinations recommended by the Ministry of Health?								
Yes	895	86.81	774	87.2	121	84.6	2.366	0.506
S/he missed some vaccinations	73	7.08	63	7.1	10	7		
No, never	22	2.13	19	2.1	3	2.1		
I don't know/ I don't remember	41	3.98	32	3.6	9	6.3		
Has there been any change in your decision to vaccinate your child during the coronavirus pandemic?								
Yes	163	15.81	140	15.8	23	16.1	0.009	0.923
No	868	84.19	748	84.2	120	83.9		
Would you like to get the possible coronavirus vaccine?								
Yes	396	38.41	323	36.4	73	51	11.897	0.003
No	162	15.71	141	15.9	21	14.7		
I am indecisive	473	45.88	424	47.7	49	34.3		

X²: Pearson Chi-Square Test**Table IV:** Parents' Attitudes towards Vaccines and the comparison of PACV and Vaccine Confidence Scale Scores (N=1.031).

	Mother n (%) or Mean Rank	Father n (%) or Mean Rank	Statistics U	p
Vaccination Confidence Scale	888 (86.13)	143 (13.87)		
Benefits of Vaccination	518.8	498.64	61009.500	0.452
Harms of Vaccination	521.24	483.48	58842.000	0.158
Trust in healthcare providers	507.58	568.27	56017.000	0.023
PACV	524.81	461.29	55668.000	0.017
Parents who do not consider it necessary or hesitate to vaccinate their child				
Vaccination Confidence Scale	148 (16.7)	22 (15.4)		
Benefits of Vaccination	87.11	74.66	1389.500	0.268
Harms of Vaccination	87.31	73.3	1359.500	0.212
Trust in healthcare providers	84.92	89.39	1542.500	0.690
PACV	87.52	71.89	1328.500	0.163
Parents who do not have all the Ministry of Health vaccinations for their children, missed some vaccinations or have no knowledge				
Vaccination Confidence Scale	114 (12.8)	22 (15.4)		
Benefits of Vaccination	69.08	65.5	1188.000	0.696
Harms of Vaccination	69.5	63.3	1139.500	0.498
Trust in healthcare providers	67.26	74.91	1113.000	0.403
PACV	69.32	64.23	1160.000	0.577
Parents who have a change in their decision to vaccinate your child during the coronavirus pandemic				
Vaccination Confidence Scale	748 (84.2)	120 (83.9)		
Benefits of Vaccination	85.44	61.07	1128.500	0.022
Harms of Vaccination	86.63	53.85	962.500	0.002
Trust in healthcare providers	80.43	91.59	1389.500	0.292
PACV	84.49	66.83	1261.000	0.095
Parents who are indecisive or unwilling to get a possible coronavirus vaccine				
Vaccination Confidence Scale	565 (63.6)	70 (49.0)		
Benefits of Vaccination	319.79	303.51	18761.000	0.483
Harms of Vaccination	322.04	285.36	17490.500	0.114
Trust in healthcare providers	310.76	376.44	15684.000	0.005
PACV	322.93	278.2	16989.000	0.053
	310.4	379.33	15482.000	0.003

U= Mann-Whitney U; PACV: The Parent Attitudes about Childhood Vaccines Scale

Table III presents the parents' views on vaccines. 83.51% of the participants thought that it was necessary to vaccinate their children, 86.81% had their children vaccinated in the vaccination schedule, 84.19% stated that the COVID-19 pandemic did not change the decision to vaccinate their child, and 38.41% would have possible coronavirus vaccination. Probable coronavirus vaccination decisions are statistically more common in fathers compared to mothers ($X^2 = 11.897$; $p = 0.003$). Although there is not seen **table III**, the most common reasons for parents not having their children vaccinated or being indecisive are: "I believe vaccines have serious side effects." (18.2%); "I believe that vaccines can be harmful to my child." (14.8%); and "Some scientists' negative opinions and public statements about the vaccine." (14.0%).

Parents' views on vaccines and comparison of PACV and Vaccine Confidence Scale scores are presented in **table IV**. Perception of harms ($U = 56017.000$; $p = 0.023$) and trust ($U = 55668.000$; $p = 0.017$) were found statistically higher in mothers than fathers. There was a difference between the parents in terms of the Vaccination

Confidence Scale, benefits subscale and PACV scores in the parents who changed their decision to vaccinate their child during the coronavirus pandemic. It was statistically calculated that the perception of benefits ($U = 1128.500$; $p = 0.022$) and vaccine confidence ($U = 962.500$; $p = 0.002$) were higher in mothers compared to fathers and that mothers' attitudes towards childhood vaccinations were lower ($U = 1146.000$; $p = 0.027$). Parents who did not want to have a possible coronavirus vaccine or were indecisive were found to have a statistically higher perception of harms compared to fathers ($U = 15684.000$; $p = 0.005$), and lower PACV scores ($U = 15482.000$; $p = 0.003$).

The relationship between the parents' attitudes towards childhood vaccines and the Vaccination Confidence Scale scores is given in **table V**. The PACV scale total score was strongly correlate with the Vaccination Confidence Scale total score, the benefits subscale, and the trust subscale. At the same time, a medium correlation was found between the total score of the PACV scale and the harms subscale of the Vaccination Confidence Scale.

Table V: The Relationship between Parents' Attitudes towards Childhood Vaccines and Vaccine Confidence Scale Scores.

Variables	M	SD	1	2	2a	2b
1. Converted score PACV	27.73	20.48				
2. Vaccination Confidence Scale	53.88	11.34	-.610** [-.36- -.31]			
2a. Benefits of vaccination subscale	30.03	8.54	-.729** [-.32- -.29]	.886** [.65-.69]		
2b. Harms of vaccination subscale	8.33	4.50	.442** [-.09- -.11]	.071** [-.00- -.05]	-.307** [-.69- -.47]	
2c. Trust in healthcare providers subscale	15.52	4.40	-.609** [-.14- -.12]	.785** [-.29- -.32]	.655** [.18-1.36]	-.244** [-.31- -.19]

**Pearson Correlation is significant at the 0.01 level (2-tailed); Strong correlation, between ± 0.50 and ± 1 ; Medium correlation, between ± 0.30 and ± 0.49 ; Small correlation, below ± 0.29 .

Discussion

Vaccine rejection is becoming an important public health problem by threatening the health of our children as well²⁶⁻²⁸. This study aims to examine the relationship between the attitudes of parents towards childhood vaccines and vaccine confidence during the coronavirus pandemic. The majority of the parents participating in the study were mothers. In other studies conducted with parents, mothers are also at a high rate^{7,29}. In the study, the proportion of parents who had university or higher education and who stated that their income was equal to their expenses was high. A statistically significant difference was found between the mother and father participants in terms of socio-demographic variables, and it is thought that this may be due to the difference in the number of participants in both groups.

In the study, while the age of the parents and the number of children are among the factors affecting attitudes towards

vaccines, the education level is not. In other studies, it was found that the higher the education level of the mother is, the higher the vaccination rate is^{30,31}. Kaydırak et al.⁷ found that the most important variable affecting the parents' approach to vaccination is the education level of the mother and father. In the study of Özceylan et al.⁵, vaccine rejection and hesitation were associated with high income group and high education level. The results of the studies are not similar to the study.

Almost all of the parents stated that they considered it necessary to vaccinate their children, that they had their children vaccinated in the vaccination schedule, and that the COVID-19 pandemic did not change the decision to vaccinate their child. Adisa et al.³⁰ found that the rate of those, who believed that vaccination could prevent all childhood fatal diseases, stated that the vaccine was the best for children, and that the number of those, who had

their children vaccinated, was quite high. In the study of Vasantha et al.³² it was stated that the majority of the mothers had their children vaccinated and had a positive attitude towards vaccines. In the study of Wani et al.³³, mothers believe that vaccination is important and almost all of them argue that it is important to comply with the vaccination schedule. The study results are similar.

In the study, the most common reasons the parents used for not having their children vaccinated or being indecisive were those: "I believe vaccines have serious side effects", "I believe vaccines can be harmful to my child", and "some scientists' negative opinions and public statements about the vaccine". In the study conducted by Sandhofer et al.³⁴ in Australia, fear of vaccines' side effects, suspicion of vaccine efficacy and distrust in the pharmaceutical industry were among the reasons for vaccine rejection. In another study by Chan et al.³⁵ religious beliefs were stated as the cause of vaccine rejection. In the study by Lim et al.³⁶, believing in alternative treatment, doubting the vaccine content, social media, family influence, long waiting in the clinic, and religious and personal beliefs are among the reasons for vaccine rejection. It is an indisputable fact that social media is one of the most effective factors in the increase of vaccine opposition with the widespread use of the internet recently. In recent years, the internet and social media have become a determining factor in issues that affect all areas of daily life such as health which concerns all members of society.

In order to ensure herd immunity in the society, at least 67% of the individuals should be vaccinated^{37,38}. According to an online research conducted in Australia, 85.8% of the society stated that they would get the coronavirus vaccine³⁷. According to the study conducted in Poland, 74.6% of the society is of the opinion that vaccination against the coronavirus is mandatory, and only 8% says that vaccines are not safe³⁹. According to the results of online surveys in France, 26% of the society stated that they would not accept to be vaccinated if the coronavirus vaccine was developed.⁴⁰ As a result of the research conducted with the participation of 7 countries in Europe, it was seen that 73.9% of the society was willing to get the coronavirus vaccine³⁸. In a study conducted with pregnant women in Vietnam, 60.4% stated that they were willing to be vaccinated, whereas 82.6% were willing to pay for the COVID-19 vaccine. Among the reasons for refusing the vaccine, it was stated that 66.9% of pregnant women were worried about the safety of the vaccine and that 45.2% thought that the preventive effect of the vaccine was low⁴¹. In a study conducted in China, it was reported that 96.2% of individuals with depression and anxiety disorders were more willing to get the COVID-19 vaccine and to pay for the COVID-19 vaccine⁴². More than 95% of healthcare workers in Asia also stated that they were willing to get vaccinated⁴³. In the study, only 38.4% of parents

reported that they would have their children had a possible coronavirus vaccine. This situation shows that it is important to increase the acceptability of the vaccine in our country. In order to increase the sustainability and reliability of global vaccination programs, priority populations should be identified and communication, intersectoral collaboration and home care services should be increased⁴⁴. The results of the study confirm that it is important to establish national and international vaccination programs with interdisciplinary cooperation of nurses, midwives and social workers.

Immunization programs will be more successful only with the participation of nurses, midwives, doctors, social workers, the press, and local politicians, and vaccination acceptance rates in the community will increase⁴⁵. Social workers especially need to be trained to develop macro-level programs and to provide necessary collaborations with institutions in the community⁴⁶. Thus, working together with this professional group of nurses and midwives will enable the development of effective social programs to increase the trust of parents with vaccine insecurity⁴⁷. There are differences in attitudes towards harms of vaccination between parents. Mothers rely more on the vaccine and think it is beneficial. Wani et al.³³ found that the majority of mothers believed that vaccines were beneficial. In addition, the study found that mothers had more confidence in healthcare providers. It has been emphasized in different studies that healthcare workers are the most effective and reliable source of information about vaccination services and that their attitudes towards vaccines have a strong influence on the success of vaccination^{48,49}. The study results support the literature. In increasing vaccination rates, it is important to identify the reasons for vaccination hesitation and to develop specific strategies to increase the confidence. Healthcare professionals have a key role in addressing vaccine hesitation by providing advice to parents who are hesitant about vaccination acceptance.

In our study, a high degree of correlation was found between parents' attitudes towards childhood vaccines, and Vaccine Confidence Scale scores. A strong association was found between the benefits subscale and the trust subscale. These results support that healthcare providers have good communication with parents and establishing trust is one of the most effective ways to overcome hesitation about vaccination.

Conclusion

Society immunity is very important to protect the society from diseases and to improve health. Vaccine refusal and vaccine rejection have led to a decline in vaccination rates in the population. In this study, it was found that the parents considered it necessary to vaccinate their children at a very high rate and had their children vaccinated in the vaccination schedule. In addition, a

high degree of correlation was found between parents' attitudes towards childhood vaccines and Vaccination Confidence Scale scores. It is important to organize regular and continuous education programs for parents and to inform them about benefits of vaccination in order to strengthen and develop positive attitude towards vaccination during these trainings. In this context, the study results are an important resource for health professionals working in primary health care as well as social workers working on this subject.

Limitations

This study has some limitations. First, the proportion of the father parents who agreed to participate in the study was significantly lower than that of the mother parents. Secondly, only those individuals, who could fill in online forms, who were at least literate, and who had an electronic device to fill in the form, participated in the study.

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Declaration of Interest Statement

The authors declare no conflicts of interests.

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Ethical considerations

This study was approved by the Scientific Research Council of Bartın University (Reference number: 2020-SBB-0213 / Date: 5 November 2020). Participation in the study was on a voluntary basis. Electronic informed consent was presented on the first page of the online forms. On the first page of the survey, the participants were electronically asked whether they were willing to participate and informed that they could withdraw from the survey at any time.

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ORIGINAL

Factors affecting Ventilator-associated Pneumonia in Stroke patients

Factores que afectan la neumonía asociada a la ventilación en pacientes con accidente cerebrovascular

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Abstract

Background: Stroke leads to many complications in the patient. These complications include disability, decreased mental health, and decreased quality of life. Ventilator-associated pneumonia (VAP) is one of the complications of ICU hospitalization.

Objectives: Due to the prevalence of stroke, this study aimed to determine the prevalence of factors affecting VAP in stroke patients admitted to the ICU.

Methods: This study was part of a registry data set with 140 patients with, and the data of patients who met the inclusion criteria were included in the study. The patients were also divided into two groups with VAP(N=40) and patients without a diagnosis of VAP(N=100). The used tool included a part of the data extracted from the registry tool, which includes the demographic characteristics of the patients and checklist form. data analysis was performed using SPSS version 16 software and descriptive and analytical tests including ANOVA, independent t-test, and regression analysis.

Results: Result showed of the 140 patients admitted to the ICU with a diagnosis of stroke, 30% of patients had chronic cardiovascular disease, 20% had leukemia/myeloma, and 32.1% had chronic respiratory disease as underlying diseases. also, variables such as gender (P=0.001, Exp=3.71), Cigarette Smoking Status (P=0.006, Exp=2.97), BMI (P=0.019, Exp=2.44), Chronic Renal Failure (P=0.047, Exp=2.71), Diabetic (P=0.001, Exp=4.04) and Leukemia/Myeloma (P=0.033, Exp=2.97) were associated with the incidence of VAP. Also, the mortality rate in stroke patients who had VAP was higher than other patients (P=0.003, Exp=3.75).

Conclusions: Given the high mortality rate in patients with VAP, preventive measures are recommended to reduce VAP in patients hospitalized in the ICU, especially patients with stroke.

Key words: Stroke, Ventilator-associated pneumonia, Prevalence.

Resumen

Antecedentes: El accidente cerebrovascular conlleva numerosas complicaciones en los pacientes. Estas complicaciones incluyen discapacidad, deterioro de la salud mental y una disminución en la calidad de vida. La neumonía asociada al ventilador (NAV) es una de las complicaciones de la hospitalización en la UCI.

Objetivos: Debido a la prevalencia del accidente cerebrovascular, este estudio tuvo como objetivo determinar la prevalencia de los factores que afectan la NAV en pacientes con accidente cerebrovascular ingresados en la UCI.

Métodos: Este estudio formó parte de un conjunto de datos de registro con 140 pacientes, y se incluyeron en el estudio los datos de aquellos que cumplieron con los criterios de inclusión. Los pacientes también se dividieron en dos grupos: pacientes con NAV (N=40) y pacientes sin diagnóstico de NAV (N=100). La herramienta utilizada incluyó una parte de los datos extraídos de la herramienta de registro, que incluye las características demográficas de los pacientes y un formulario de lista de verificación. El análisis de datos se realizó utilizando el software SPSS versión 16 y pruebas descriptivas y analíticas, incluidas ANOVA, t-test independiente y análisis de regresión.

Resultados: Los resultados mostraron que de los 140 pacientes ingresados en la UCI con diagnóstico de accidente cerebrovascular, el 30% tenía enfermedad cardiovascular crónica, el 20% tenía leucemia/mieloma y el 32.1% presentaba enfermedad respiratoria crónica como enfermedades subyacentes. Además, variables como el género (P=0.001, Exp=3.71), el estatus de fumador (P=0.006, Exp=2.97), el IMC (P=0.019, Exp=2.44), la insuficiencia renal crónica (P=0.047, Exp=2.71), la diabetes (P=0.001, Exp=4.04) y la leucemia/mieloma (P=0.033, Exp=2.97) se asociaron con la incidencia de NAV. Asimismo, la tasa de mortalidad en pacientes con accidente cerebrovascular que presentaron NAV fue mayor que en otros pacientes (P=0.003, Exp=3.75).

Conclusiones: Dada la alta tasa de mortalidad en pacientes con NAV, se recomiendan medidas preventivas para reducir la incidencia de NAV en pacientes hospitalizados en la UCI, especialmente en aquellos con accidente cerebrovascular.

Palabras clave: Accidente cerebrovascular, Neumonía asociada al ventilador, Prevalencia.

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Background

Stroke is one of the most common neurological diseases in the world. Stroke is one of the most common causes of death in the world. In fact, impaired blood supply is known to be one of the most important factors affecting organ dysfunction and is the most important cause of cell and organ death^{1,2}. Stroke is one of the main causes of emergency admission of patients to the hospital, which threatens the patient with numerous complications if there is a delay in referral and lack of appropriate treatment³.

Stroke is a cerebrovascular accident that results in a sudden decrease in the blood supply to the brain due to disruption of the blood vessels supplying the brain. In this situation, the lack of oxygen causes brain tissue to be damaged or even destroyed. Stroke is divided into two types: ischemic and hemorrhagic, with most strokes being ischemic^{1,4,5}.

The etiology of ischemic stroke is related to an embolic or thrombotic event that disrupts blood flow in the brain. In fact, the ischemic type is caused by the blockage of cerebral vessels caused by plaque or clot in the large arteries of the brain. While the hemorrhagic type is caused by a sudden increase in blood pressure and rupture of the vessel wall and the entry of blood into the brain tissue, which is more dangerous than the ischemic type⁶⁻⁸. Stroke may be caused by diseases such as fibromuscular dysplasia, atherosclerotic disease, inflammatory conditions, or arterial dissection. Also, other factors such as the use of certain drugs such as oral contraceptives, systemic diseases, diabetes, smoking, and hypertension are effective in causing stroke^{9,10}.

In stroke patients, differential diagnosis is very important for rapid and accurate diagnosis and symptom management. For differential diagnosis, especially in ischemic patients, diseases such as complicated migraine, syncope, metabolic abnormalities, hyperglycemia, hypoglycemia, movement disorders, Wernicke encephalopathy, drug toxicity, intracranial hemorrhage, seizure, intracranial abscess, and sepsis should be considered^{9,11}. Stroke management includes blood pressure, temperature, glucose, nutrition, DVT prophylaxis, depression screening, cerebellar/cerebral edema, seizures, cardiac evaluation, antiplatelet treatment, antithrombotic treatment, and statins^{9,12,13}.

Stroke leads to many complications in the patient. These complications include disability, decreased mental health, and decreased quality of life¹⁴. Ventilator-associated pneumonia (VAP) is one of the complications of ICU hospitalization. VAP is highly prevalent in ICU patients and is one of the causes of mortality in these patients^{15,16}. Given the importance of stroke and the importance of identifying factors affecting the survival rate of these patients, conducting research on the prevalence and factors affecting the development of VAP is an important priority^{17,18}.

Objectives

Due to the prevalence of stroke, this study aimed to determine the prevalence of factors affecting VAP in patients admitted to the ICU.

Methods

This study is part of a registry data. Iran ICU Registry (IICUR) is a Persian ICU-based registry which was launched in 2018 through a collaboration with The Australian and New Zealand ICU (ANZICS). IICUR was approved by Ethics Committee of Shiraz University of Medical Sciences (Ethic Number IR.SUMS.REC.1397.559), and recognized by Iran Ministry of Health as the first and single registry of adult ICU in Iran.

This study was part of a registry data set with 140 patients, and the data of patients who met the inclusion criteria were included in the study. The patients were also divided into two groups with VAP and patients without a diagnosis of VAP. In fact, the data of 40 patients with a diagnosis of stroke and VAP (case group) extracted from the registry data that met the inclusion criteria were compared with the data of 100 patients with stroke and without a diagnosis of VAP (control group).

The inclusion criteria were admission of the patient with a diagnosis of stroke, patients with a minimum age of 18 years, hospitalization in the ICU, dependence and connection to a ventilator, at least 48 hours after the patient was intubated and connected to a ventilator, and the absence of pneumonia during the patient's admission to the ICU.

The used tool included a part of the data extracted from the registry tool, which includes the demographic characteristics of the patients, including M(Sd), Age, Nationality, BMI, as well as questions about Cigarette Smoking Status, Water pipe Smoking Status, Current dependency Drug Status, Chronic Conditions, Pregnancy Status, Cardiac Arrest in last 24 Hours. The criteria for diagnosing VAP were based on the CDC's definition and consistent with the methodology of previous studies. To diagnose VAP, leukopenia, leukocytosis, temperature, purulent discharge, chest x-ray, and abnormal chest sounds were evaluated.

Data analysis was performed using SPSS version 16 software and descriptive and analytical tests including ANOVA, independent t-test, and regression analysis.

Results

The findings showed that 140 patients with stroke were studied and of these patients, 40 patients were diagnosed with VAP and 100 patients were not VAP.

Table I: Comparison of variables studied in patients with VAP and No-VAP Group.

Variable		No-VAP(N=100)	VAP (N=40)	Total
Gender	Male	31 (31)	25 (62.5)	71 (50.7)
	Female	69 (69)	15 (37.5)	69 (49.3)
	P-Value	0.001		
Current dependency Drug Status	Yes	0 (0)	8 (20)	8 (5.7)
	No	100 (100)	32 (80)	132 (94.3)
	P-Value	0.000		
Pregnancy Status	Yes	1 (1)	0 (0)	1 (0.7)
	No	99 (99)	40 (100)	139 (99.3)
	P-Value	0.529		
Cardiac Arrest in last 24 Hours	Yes	12 (12)	7 (17.5)	19 (13.6)
	No	88 (88)	33 (82.5)	121 (86.4)
	P-Value	0.394		
Water pipe Smoking Status	Yes	5 (5)	2 (5)	7 (5)
	No	95 (95)	38 (95)	133 (95)
	P-Value	1.00		
Cigarette Smoking Status	Yes	44 (44)	28 (70)	72 (51.4)
	No	56 (56)	12 (30)	68 (48.6)
	P-Value	0.006		
BMI		38 (38)	24 (60)	62 (44.3)
		62 (62)	16 (40)	78 (55.7)
	P-Value	0.019		
Age	M(SD)	68.36 (5.45)	79.7 (2.22)	71.6 (7)
	P-Value	0.000		
Duration of Nasogastric Tube (Days)	M(SD)	10.26 (7.14)	19.22 (4)	13.34 (4.26)
	P-Value	0.026		
Length of stay in the ICU(Days)	(Days), M(SD)	12.92 (2)	13.1 (5.53)	11.07 (6.82)
	P-Value	0.000		

Table II: Comparison of variables studied in patients with VAP and No-VAP Group.

Variable		No-VAP(N=100)	VAP (N=40)	Total
Comorbidities, N (%)	Hepatic Failure			
	Yes	0 (0)	2 (5)	2 (1.4)
	No	100 (100)	38 (95)	138 (98.6)
	P-Value	0.024		
	Chronic Respiratory disease			
	Yes	30 (30)	15 (37.5)	45 (32.1)
	No	70 (70)	25 (62.5)	95 (67.9)
	P-Value	0.75		
	Chronic Renal Failure			
	Yes	5 (5)	6 (15)	11 (7.9)
	No	95 (95)	34 (85)	129 (92.1)
	P-Value	0.047		
	Immunosuppressed			
	Yes	8 (8)	5 (12.5)	13 (9.3)
	No	92 (92)	35 (87.5)	127 (90.7)
	P-Value	0.83		
	Leukemia/Myeloma			
	Yes	13 (13)	15 (37.5)	28 (20)
	No	87 (87)	25 (62.5)	112 (80)
	P-Value	0.03		
	Chronic Cardiovascular			
	Yes	26 (26)	16 (40)	42 (30)
	No	74 (74)	24 (60)	98 (70)
	P-Value	0.104		

According to the findings, there was a relationship between gender, current drug dependency status, cigarette smoking status and age with the rate of VAP. So that VAP was reported more in women, people with a history of drug dependency, with a history of smoking and older age (**Table I**).

The findings in **table II** showed of the 140 patients admitted to the ICU with a diagnosis of stroke, 30% of patients had chronic cardiovascular disease, 20% had leukemia/myeloma, and 32.1% had chronic respiratory disease as underlying diseases. Also result showed the VAP incidence status in terms of the individual's underlying

diseases. According to the findings, a significant relationship was observed between underlying diseases, including Hepatic Failure ($P=0.02$), Chronic Renal Failure ($P=0.04$), and Leukemia/Myeloma ($P=0.03$), and the incidence of VAP. (Table II).

The findings in table III showed the results of the association between the variables examined in the study

and the incidence of VAP. According to the findings, variables such as gender ($P=0.001$, $\text{Exp}=3.71$), Cigarette Smoking Status ($P=0.006$, $\text{Exp}=2.97$), BMI ($P=0.019$, $\text{Exp}=2.44$), Chronic Renal Failure ($P=0.047$, $\text{Exp}=2.71$), Diabetic ($P=0.001$, $\text{Exp}=4.04$) and Leukemia/Myeloma ($P=0.033$, $\text{Exp}=2.97$) were associated with the incidence of VAP. Also, the mortality rate in stroke patients who had VAP was higher than other patients ($P=0.003$, $\text{Exp}=3.75$).

Table III: Relationship between the variables studied and the incidence of VAP.

Variable	Exp(B)	VAP		
		95.0% Confidence Interval for B		P-value
		Lower Bound	Upper Bound	
Gender	3.71	1.72	7.99	.001
Cigarette Smoking Status	2.97	1.35	6.49	.006
BMI	2.44	1.15	5.18	.019
Deaths	3.752	1.577	8.925	.003
Duration of Nasogastric Tube	.938	.870	1.010	.092
Length of stay in the ICU	0.29	0.18	0.47	0.000
Chronic Respiratory disease	.850	.307	2.359	.756
Chronic Renal Failure	2.719	.477	15.514	.047
Immunosuppressed	.858	.210	3.509	.831
Leukemia/Myeloma	2.978	1.089	8.143	.033
Chronic Cardiovascular	2.423	.947	6.196	.10
Diabetic	4.04	1.74	9.36	0.001

Discussion

Result showed, smoking use was one of the factors affecting the development of VAP. In studies conducted, smoking and alcohol consumption were found to be one of the factors affecting the development of pneumonia²³⁻²⁶. In the meta-analysis study by Li et al., smoking was also identified as one of the factors of VAP in brain trauma patients (OR: 2.13)²⁷. In the study by Chang et al., smoking was associated with the development of VAP with $P=0.003$ in cerebral hemorrhage patients [28], which is consistent with this study. On the other hand, in the study by Xu et al., smoking was present in 17.8% of patients in the VAP group and 79% of patients in the No VAP group ($P=0.76$). Also, alcohol consumption was present in 15.5% of patients in the VAP group and 84.5% of patients in the No VAP group ($P=0.31$)²⁹, which is inconsistent with the results of this study.

According to the findings, the rate of deaths in ICU in patients with VAP was higher than in patients with No VAP. In the Kasuya et al. cohort study, 31 patients with VAP and 80 patients without VAP were examined in patients admitted to the ICU and it was observed that 28% of the patients had VAP. Also, according to the findings, in the No VAP group, 6% of the patients had deaths in ICU and 13% of them had deaths in hospital. Also, in the VAP group, 19% of the patients had deaths in ICU and 19% had deaths in hospital³⁰, which is consistent with the results of this study. Also, regarding the findings consistent with the results of this study, in the study of Xue et al., 42% of patients diagnosed with cerebral hemorrhage admitted to the ICU had VAP and their mortality rate was reported

to be 18%³¹. On the other hand, in a meta-analysis study by Melsen et al., which analyzed 52 articles with a sample size of 17,347 patients, it was shown that there was no significant association between mortality in acute respiratory distress syndrome patients or trauma patients with VAP³², which is contrary to the results of this study.

According to the results of this study, in VAP patients, the age and duration of ICU stay were reported to be higher than in No VAP patients. In the study by Jitpratoom et al., which investigated the factors affecting the development of pneumonia in stroke patients, 342 patients were included in the study. According to the findings, 54 (15.8%) of the patients were in the pneumonia group and 288 patients were in the non-pneumonia group. According to the findings, in the pneumonia group, the prevalence of UTI was 33%, respiratory failure was 50%, sepsis was 80%, and brain edema was 15%. While in the non-pneumonia group, UTI was 5%, respiratory failure was 5%, sepsis was 6%, and brain edema was 1%³³.

There was a relationship between chronic diseases and VAP. So that in people with diabetes, chronic renal failure and leukemia/myeloma, the rate of VAP was higher. In the study of Jiménez-Trujillo et al. in type 2 diabetes, the incidence of VAP was reported in 7952 patients, 13.6%, and the mortality rate was higher in diabetic patients³⁴. Also, in the study of Ana et al. in 245221 hospitalized patients, VAP was observed in 2752 patients and there was a relationship between diabetes and VAP³⁵. Also, in the study of Karatas et al., which examined 1152

patients with mechanical ventilation, it was shown that VAP was reported in 15.4% of patients. Also, factors such as cerebrovascular disease, organ failure, enteral nutrition, diabetes, pulmonary diseases, reintubation were reported as factors affecting the development of VAP³⁶, which is consistent with the results of this study.

Conclusions

Given the high mortality rate in patients with VAP, preventive measures are recommended to reduce VAP in patients hospitalized in the ICU, especially patients with stroke.

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Footnotes

Authors' Contribution: ARK, AV conceived the study, performed data analysis, and wrote the manuscript; ARK, AV, collected data and wrote the manuscript; ARK, AV, interpreted the results and wrote the manuscript, ARK, AV, designed the study, wrote, and edited the manuscript.

Conflict of Interests Statement: The authors declared no conflict of interests.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after its publication.

Ethical Approval: The current study was conducted after obtaining approval by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS. REC.1397.559).

<https://ethics.research.ac.ir/ProposalCertificateEn.php?id=30114&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&Letter-Print=true>

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ORIGINAL

Correlation of Radiological Imaging Techniques with Histopathological Findings in Parotid Tumors

Correlación de las técnicas de imagen radiológica con los hallazgos histopatológicos en los tumores parotídeos

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Abstract

Objective: This study aims to evaluate the diagnostic value of CT and MRI in differentiating between benign and malignant parotid tumors by comparing their findings with histopathological results.

Materials and methods: This retrospective study included 91 patients with parotid gland masses who underwent surgery between 2012 and 2021. Imaging was performed using high-resolution CT and MRI, with contrast and non-contrast sequences evaluated by radiologists. Pathological diagnoses were compared to preoperative radiological findings to assess diagnostic accuracy.

Results: A total of 91 patients were included in the study, with 50 females (54.9%) and 41 males (45.1%). Pleomorphic adenoma was the most common diagnosis, found in 46 patients (65.2% females, 34.8% males). Warthin tumor was present in 14 patients, predominantly males (85.7%). CT scans correctly identified 60 benign and 15 malignant lesions, with a sensitivity of 75%, specificity of 84.5%, and a negative predictive value (NPV) of 92.3%. MRI scans accurately diagnosed 60 benign and 14 malignant lesions, with a sensitivity of 70%, specificity of 84.5%, and an NPV of 90.9%. Hyperintensity on MRI T2 sequences was seen in 89.1% of pleomorphic adenoma cases, while only 31.7% of other pathologies exhibited hyperintensity. A statistically significant difference in hyperintensity was observed between pleomorphic adenoma and other pathologies ($p < 0.001$).

Conclusion: Radiological imaging methods (MRI and CT) are highly valuable tools for surgeons in the preoperative period, aiding in diagnosis, determining the size and location of the lesion, identifying associated pathologies, and planning the surgical approach. While they may not be sufficient for providing a definitive diagnosis, these imaging techniques are extremely helpful in distinguishing between benign and malignant lesions.

Key words: Parotid, tumor, radiology, pathology, sensitivity, specificity.

Resumen

Objetivo: Este estudio tiene como propósito evaluar el valor diagnóstico de la tomografía computarizada (TC) y la resonancia magnética (RM) en la diferenciación entre tumores parotídeos benignos y malignos, comparando sus hallazgos con los resultados histopatológicos.

Materiales y métodos: Este estudio retrospectivo incluyó a 91 pacientes con masas en la glándula parótida que se sometieron a cirugía entre 2012 y 2021. Las imágenes fueron obtenidas mediante TC de alta resolución y RM, evaluándose secuencias con y sin contraste por radiólogos. Los diagnósticos patológicos se compararon con los hallazgos radiológicos preoperatorios para determinar la precisión diagnóstica.

Resultados: Un total de 91 pacientes participaron en el estudio, de los cuales 50 eran mujeres (54,9%) y 41 hombres (45,1%). El adenoma pleomórfico fue el diagnóstico más frecuente, encontrado en 46 pacientes (65,2% mujeres, 34,8% hombres). El tumor de Warthin estuvo presente en 14 pacientes, predominantemente hombres (85,7%). Las TC identificaron correctamente 60 lesiones benignas y 15 malignas, con una sensibilidad del 75%, especificidad del 84,5% y un valor predictivo negativo (VPN) del 92,3%. Las RM diagnosticaron con precisión 60 lesiones benignas y 14 malignas, con una sensibilidad del 70%, especificidad del 84,5% y un VPN del 90,9%. En las secuencias T2 de la RM, se observó hiperintensidad en el 89,1% de los casos de adenoma pleomórfico, mientras que solo el 31,7% de otras patologías presentaron hiperintensidad. Se encontró una diferencia estadísticamente significativa en la hiperintensidad entre el adenoma pleomórfico y otras patologías ($p < 0,001$).

Conclusión: Los métodos de imagen radiológica (TC y RM) son herramientas de gran valor para los cirujanos durante el periodo preoperatorio, ya que facilitan el diagnóstico, determinan el tamaño y la localización de la lesión, identifican patologías asociadas y ayudan a planificar el abordaje quirúrgico. Aunque estas técnicas de imagen no sean suficientes para proporcionar un diagnóstico definitivo, son extremadamente útiles para distinguir entre lesiones benignas y malignas.

Palabras clave: Parótida, tumor, radiología, patología, sensibilidad, especificidad.

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Introduction

Parotid gland tumors represent a significant portion of head and neck tumors, accounting for approximately 2-6.5% of all cases¹⁻⁴. These tumors exhibit a wide histological diversity, ranging from benign to malignant forms, making accurate diagnosis crucial for appropriate treatment planning⁴. Benign tumors often require less invasive surgical approaches, while malignant tumors necessitate more extensive surgical interventions, following oncological principles to ensure complete resection and minimize recurrence risks^{5,6}. Thus, distinguishing between benign and malignant parotid tumors preoperatively is of utmost importance for guiding the treatment strategy.

Various radiological imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), are commonly employed in the preoperative evaluation of parotid masses⁷. These imaging modalities provide vital information regarding tumor size, location, involvement of surrounding structures, and potential malignancy. In particular, CT scans offer detailed anatomical views and are useful for assessing the extent of bony involvement and calcifications. Meanwhile, MRI, with its superior soft tissue contrast, can better delineate tumor margins, infiltration into adjacent tissues, and perineural invasion, which are crucial factors in determining malignancy⁸⁻¹⁰.

Despite the advances in radiological imaging, histopathological examination remains the gold standard

for definitive diagnosis. Techniques such as fine needle aspiration biopsy (FNAB) and frozen section analysis during surgery provide valuable insights into the tumor's nature, aiding in surgical decision-making^{7,11}. However, radiological imaging plays an essential role in preoperative planning by helping surgeons evaluate the tumor's characteristics and choose the most appropriate surgical approach^{5,7,12}.

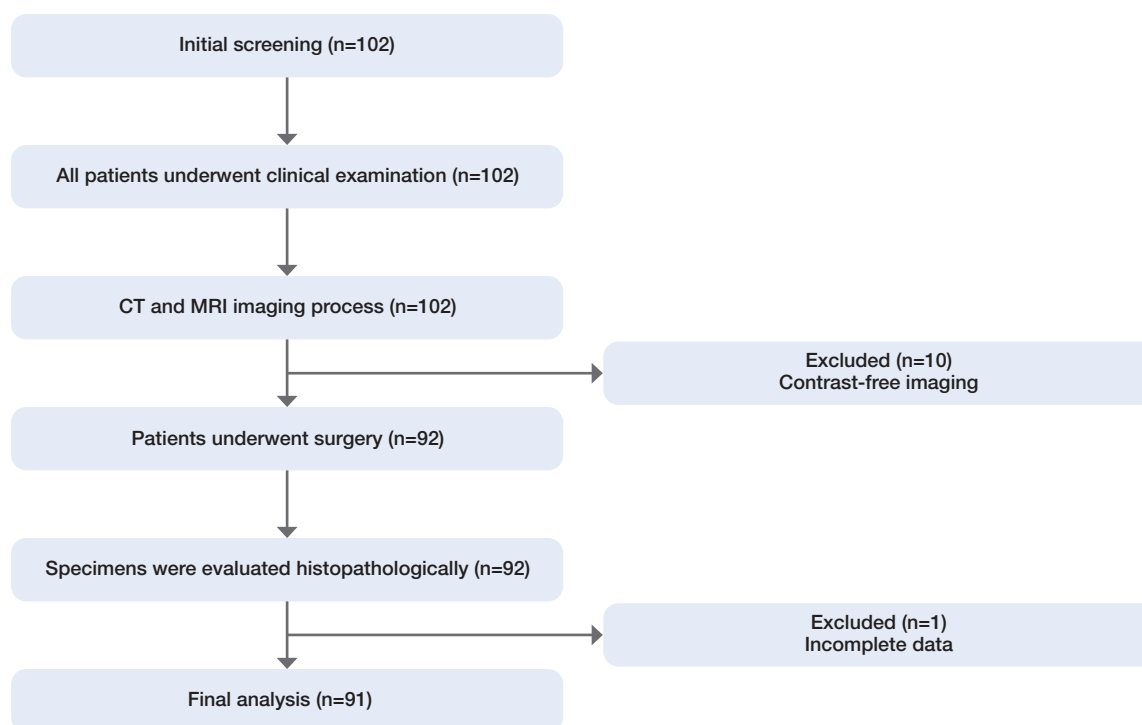
This study aims to evaluate the diagnostic value of CT and MRI in differentiating between benign and malignant parotid tumors by comparing their findings with histopathological results.

Materials and methods

Patients and design

This retrospective study was conducted at the Department of Otorhinolaryngology, Dicle University Faculty of Medicine, between 2012 and 2021. A total of 91 patients who underwent surgical intervention due to the presence of a parotid gland mass were included in the study. The selection criteria for inclusion in the imaging analysis were based on the availability of high-quality preoperative imaging studies in our hospital's system. Patients with missing or incomplete retrospective data, or those whose data could not be evaluated, and patients underwent contrast-free imaging, were excluded from the study (**Figure 1**).

Figure 1: Flow chart of patients selection.



Ethical approval

Ethical approval were obtained from Dicle University non-interventional Local ethical committee (no: 329, date: 30.06.2021).

Imaging techniques and equipment

The imaging studies were conducted using a 64-slice high-resolution CT scanner (Brilliance CT 64, Philips Medical Systems, Cleveland, OH) and MRI scanners with varying field strengths, including 1 Tesla (T) (Expert; Siemens, Erlangen, Germany), 1.5T, and 3T (Achieva; Philips Medical Systems, Best, Netherlands). The CT scans were acquired after the administration of intravenous contrast, and images were obtained during the venous phase. MRI studies included both contrast-enhanced sequences and non-contrast sequences such as T1-weighted, T2-weighted, and diffusion-weighted imaging (DWI). The MRI protocol aimed to provide a comprehensive assessment of the parotid masses by evaluating tissue characteristics with and without contrast.

Image evaluation

All imaging studies were reviewed retrospectively using the hospital's picture archiving and communication system (PACS) (Infiniti, Korea). Both CT and MRI images were evaluated by a radiologist with expertise in head and neck imaging. For CT, contrast-enhanced images were used to assess the characteristics of the mass, while for MRI, both contrast-enhanced and non-contrast images (T1W, T2W, and DWI sequences) were evaluated to provide a detailed overview of the mass, including its size, shape, internal structure, and relationship with adjacent tissues. Venous-phase images were specifically analyzed to identify any abnormal vascularity or enhancement patterns.

Pathological examination

Following surgical resection, the parotid gland specimens were immediately fixed in 10% formalin solution and sent to the pathology laboratory for further analysis. An expert pathologist performed a detailed histopathological examination of the specimens. The pathological evaluation was conducted according to standard histopathological techniques, and the final diagnosis for each specimen was recorded.

Correlation of radiological and pathological findings

The radiological findings from both CT and MRI were compared with the final histopathological diagnosis obtained from the resected specimens. Preliminary radiological diagnoses were made based on the imaging characteristics and were documented before surgery. After surgery, the histopathological results were accessed via the hospital's information system and compared with the preoperative radiological diagnoses. The accuracy of the imaging techniques in predicting the pathological nature of the parotid masses was then assessed.

Statistical analysis

Statistical Package for Social Sciences for Windows, version 24.0 (SPSS, Inc., Chicago, USA), was used for appropriate statistical analyses. Descriptive values are presented as count (n), percentage (%), mean, standard deviation (SD), and median. The normality of data distribution was assessed using various graphical and analytical tests, including the Kolmogorov-Smirnov test. For comparing two independent samples with normal distribution, the independent samples t-test was applied, while the Mann-Whitney U test was used for non-normally distributed independent samples. The chi-square test was employed for analyzing categorical variables. A sankey diagram has been created to illustrate the comparison and relationship of predictive ability. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 91 patients with parotid gland masses were included in our study, consisting of 50 female patients (54.9%) and 41 male patients (45.1%). The average age of the female patients was 45.14 years, while the average age of the male patients was 46.56 years.

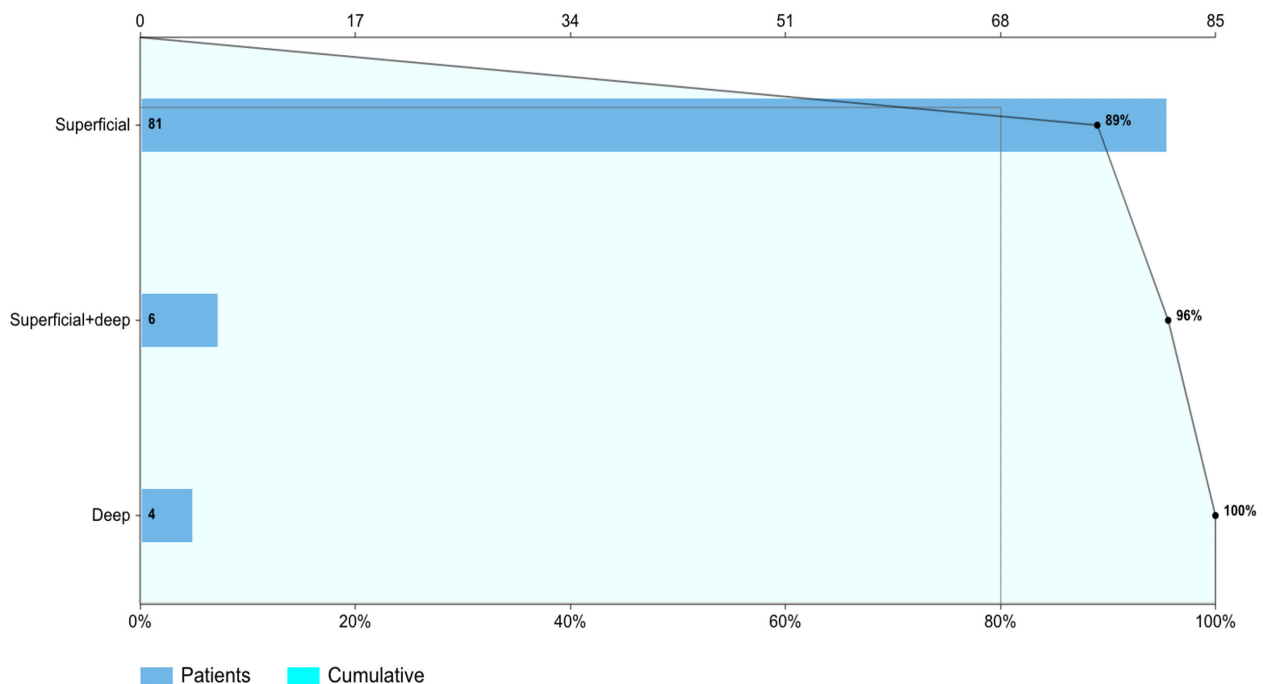
The most common diagnosis was pleomorphic adenoma, observed in 46 patients, with 30 females (65.2%) and 16 males (34.8%). Warthin tumor was present in 14 patients, predominantly in males (12 males, 85.7%; 2 females, 14.3%). Mucoepidermoid carcinoma was diagnosed in 6 patients, with 4 females (66.7%) and 2 males (33.3%). Squamous cell carcinoma was seen in 5 patients (3 females, 60%; 2 males, 40%). Adenoid cystic carcinoma and lipoma were each identified in 4 patients, with an equal gender distribution (50% in both sexes). Two cases of inflammatory processes were noted, with 1 female and 1 male affected. Lymphoma was identified in 1 male patient, while metastatic lymphadenopathy was observed in 2 females (**Table I**).

When examining the anatomical localization of parotid gland masses, it was observed that 81 (89.01%) were superficially located, 6 (6.59%) were both deep and superficial, and 4 (4.40%) were deeply located (**Figure 2**).

When parotid gland masses were categorized by age groups and malignancy characteristics, benign masses were most frequently observed in patients aged 31-50 years (n=28, 30.77%). It was noted that the incidence of malignant masses increased with age, with the highest prevalence of malignancy occurring in patients over 70 years (n=8, 8.79%). When analyzed by gender and malignancy characteristics, benign masses were found in 38 (41.76%) of the 50 female patients and malignant masses in 12 (13.19%). Similarly, among the 41 male patients, 33 (36.26%) had benign masses, while 8 (8.79%) had malignant masses.

Table I: Comparison of pathological findings according to gender.

	Female (n) (%)	Male (n) (%)	Total (n)
Pleomorphic adenoma	30 (65.2%)	16 (34.8%)	46
Warthin Tumor	2 (14.3%)	12 (85.7%)	14
Mucoepidermoid Carcinoma	4(66.7%)	2(33.3%)	6
Squamous Cell Carcinoma	3(60%)	2(40%)	5
Adenoid Cystic Carcinoma	2(50%)	2(50%)	4
Lipoma	2(50%)	2(50%)	4
Inflammatory Process	1(50%)	1(50%)	2
Lymphoma	0	1(100%)	1
Metastatic Lymphadenopathy	2(100%)	0	2
Basal Cell Carcinoma	1(100%)	0	1
Ductal Adenocarcinoma	1(100%)	0	1
Myoepithelioma	1(100%)	0	1
Hemangioma	0	1(100%)	1
Granulomatous Lymphadenitis	1(100%)	0	1
Basal Cell Adenoma	1(100%)	0	1
Simple Cyst	0	1(100%)	1
Total	50(54.9%)	41(45.1%)	91

Figure 2: Pareto chart of the anatomical localization of parotid gland masses.

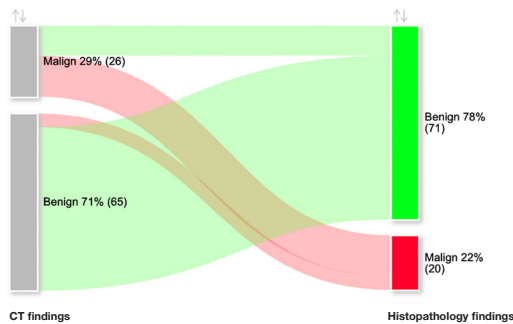
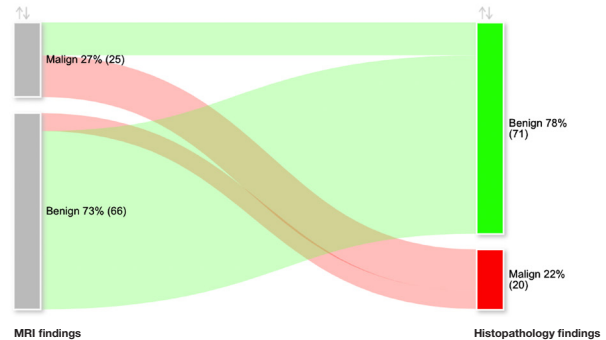
In the histopathological definitive diagnosis, a total of 91 cases were evaluated based on CT findings. Of these, 26 lesions were diagnosed as malignant, with 15 correctly identified as malignant by CT and 11 incorrectly classified as benign. Among the 65 benign lesions, 60 were correctly identified as benign on CT, while 5 were misclassified as malignant. Overall, CT had a sensitivity of 75.00% and a specificity of 84.50% in detecting malignancy. The positive predictive value (PPV) was 57.69%, while the negative predictive value (NPV) was 92.30% (**Table II, Figure 3**).

In the histopathological definitive diagnosis, 91 cases were evaluated based on MRI findings. Of the 25 malignant lesions, 14 were accurately identified as malignant by MRI, while 11 were incorrectly classified as benign. Among the 66 benign lesions, 60 were correctly identified as benign, with 6 misclassified as malignant by MRI. The performance of MRI in detecting malignancy demonstrated a sensitivity of 70.00% and a specificity of 84.50%. The PPV was 56.00%, while the NPV was 90.90% (**Table II, Figure 4**).

Table II: Predictive performance of the CT and MRI.

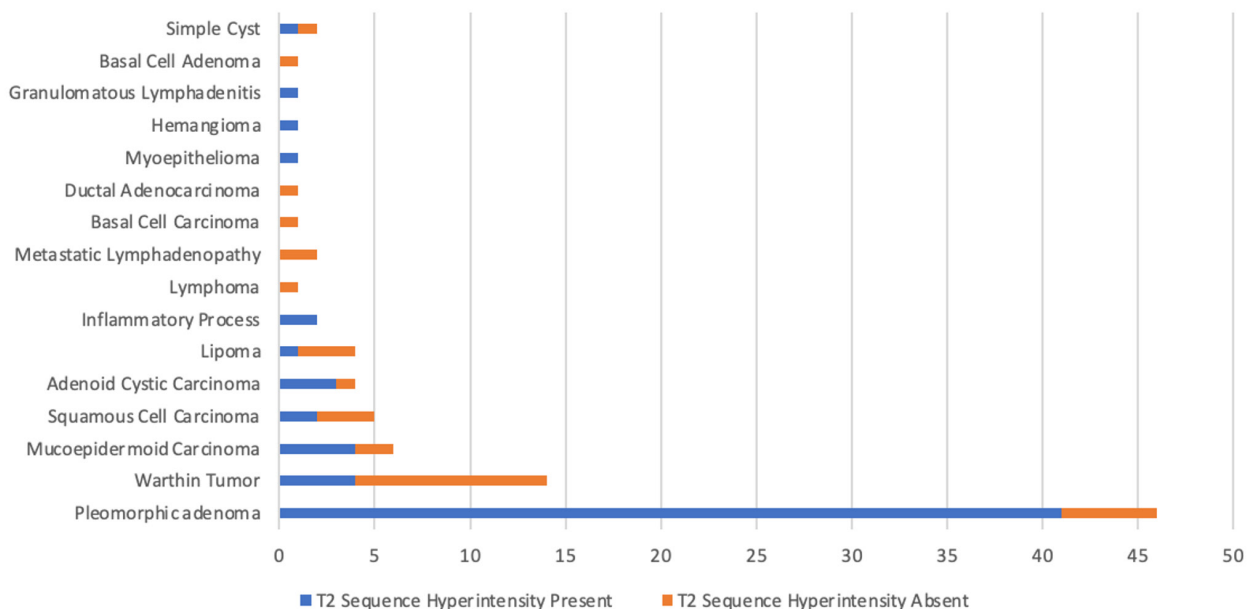
	Sensitivity	Specificity	PPV	NPV
CT predictive value	75%	84.50%	57.7%	92.3%
MRI predictive value	70%	84.5%	56%	90.9%

CT: Computed Tomography, MRI: Magnetic Resonance Imaging.

Figure 3: Sankey diagram to illustrate and compare the CT findings with histopathology findings.**Figure 4:** Sankey diagram to illustrate and compare the MRI findings with histopathology findings.

When examining the hyperintensities in the MRI T2 sequence based on the patients' pathological diagnoses, hyperintensity was observed in 41 out of 46 patients (89.1%) diagnosed with pleomorphic adenoma, while 5 patients (10.9%) did not show hyperintensity. In patients diagnosed with Warthin tumor, hyperintensity was present in 4 out of 14 cases (28.6%), and absent in the remaining 10 cases (71.4%). In 41 out of 46 patients (89.1%)

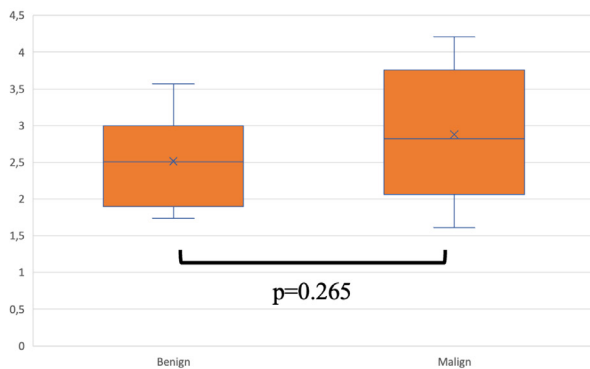
diagnosed with pleomorphic adenoma, hyperintensity was observed on the MRI T2 sequence, while in the remaining 45 patients with other diagnoses, hyperintensity was present in 19 cases (31.7%) (**Figure 5**). A comparison of hyperintensity on MRI T2 sequences between patients with pleomorphic adenoma and those with other diagnoses revealed a statistically significant difference between two groups ($p < 0.001$) (**Table III**).

Figure 5: Hyperintensities in the MRI T2 sequence based on the patients' pathological diagnoses.**Table III:** Comparison of hyperintensity on MRI T2 sequences between patients with pleomorphic adenoma and those with other diagnoses.

$p < 0.001$	Pleomorphic adenoma	Other pathologies	Total
T2 Sequence Hyperintensity present	41 (%88.3)	19 (%31.7)	60
T2 Sequence Hyperintensity absent	5 (%10.9)	26 (%49.5)	31
Total	46 (%50.5)	45 (%49.5)	91

In parotid gland masses, the average size of benign tumors was 2.54 ± 0.86 cm, while the average size of malignant tumors was 2.73 ± 1.20 cm. When evaluating the impact of tumor size in distinguishing between benign and malignant parotid masses, no statistically significant difference was found between the two groups ($p=0.265$) (Figure 6).

Figure 6: Comparison of tumour size.



Discussion

Our goal was to assess the diagnostic accuracy of CT and MRI in differentiating between benign and malignant parotid tumors by comparing imaging findings with histopathological results. Our key findings indicate that CT demonstrated a sensitivity of 75% and a specificity of 84.5% in detecting malignancies, while MRI showed a sensitivity of 70% and a specificity of 84.5%. Additionally, the PPV for CT and MRI were 57.7% and 56%, respectively, while the NPV were 92.3% and 90.9%. These results highlight the reliability of both imaging techniques in ruling out malignancy, with CT providing a slightly higher predictive value for malignant lesions.

Parotid tumors, which are salivary gland tumors, have been reported with varying incidences across different age groups. Tian et al., in their study of 6,982 patients with parotid tumors, reported a female-to-male ratio of 0.9:1¹³. Fomete et al. found a ratio of 1.8:1¹⁴, while Waldron et al. reported a ratio of 1.6:1¹⁵. The ratios observed in our study are consistent with these findings, indicating no significant gender predominance in parotid tumors. In our study, 54.9% of the patients were female and 45.1% were male, resulting in a female-to-male ratio of 1.2:1.

In 89% of our patients, the lesion was located in the superficial lobe, in 4.4% it was in the deep lobe, and in 6.6% it involved both the superficial and deep lobes. Similarly, Çomoğlu et al., in their study of 369 patients with parotid tumors, found that 81% of the lesions were located in the superficial lobe, 7% in the deep lobe, and 12% involved both lobes¹⁶. It is expected that the majority of lesions originate from the superficial lobe, as it constitutes the larger portion of the parotid gland.

Benign parotid tumors are more common than malignant ones, with pleomorphic adenoma being the most frequently observed parotid tumor. In a study by Chidzonga et al. involving 121 patients with parotid tumors, pleomorphic adenoma was found in 67.7% of cases¹⁷. In the same study, the most common malignant tumors were adenoid cystic carcinoma (7.4%) and adenocarcinoma (5%). Similarly, Galdirs et al., in a review of nine previous studies, identified pleomorphic adenoma as the most frequent histological type, accounting for 42% of cases¹⁸. In this study, the most common malignant tumors were adenoid cystic carcinoma (ACC) and mucoepidermoid carcinoma. The frequency of these tumors varied by region, with ACC being predominant in the United States (71%) and mucoepidermoid carcinoma more common in Brazil (52%). In Germany, ACC accounted for 32.6% of cases, while mucoepidermoid carcinoma represented 31.4%¹⁸. In Nigeria, ACC was seen in 20% of cases, and mucoepidermoid carcinoma in 19.2%. In our study, pleomorphic adenoma was the most common tumor, observed in 50.55% of cases, consistent with the literature. Among malignant tumors, mucoepidermoid carcinoma was the most frequent (6.59%), followed by squamous cell carcinoma (5.49%) and adenoid cystic carcinoma (4.4%). The higher frequency of squamous cell carcinoma in our study, which differs from other studies, may be due to the fact that many of these tumors were infiltrating lesions from the skin, rather than primary parotid tumors, with malignancies spreading from adjacent skin tissue into the parotid gland.

Liu et al. recommended CT as an effective radiological tool for the differential diagnosis of primary salivary gland tumors¹⁹. However, when determining the location of a parotid gland tumor based on anatomical criteria in CT images, the anatomical landmarks used as references were not always visible, depending on the tumor's location²⁰. However, when assessing the location of a parotid gland tumor using anatomical criteria on CT images, the reference anatomical landmarks were not always visible due to the tumor's location. MRI provides direct visualization of parotid gland tumors and is particularly useful for confirming soft tissue boundaries. Additionally, ultrasound (US) is the best method for confirming the fascia around the parotid glands and measuring tumor distance. Cheng et al. reported that US is especially helpful in identifying benign parotid tumors²¹. Unlike CT, MRI offers the advantage of clearer soft tissue visualization without radiation exposure.

In distinguishing between benign and malignant tumors, various studies have reported different sensitivities and specificities for CT. Motoori et al. found a sensitivity of 40% and a specificity of 71%²², while Kim et al. reported 92% and 61%, respectively²³. Vogl et al. observed a sensitivity of 100% and a specificity of 89%²⁴, and Park et al. found a sensitivity of 43% and a specificity of 94%²⁵. Zhang et al., in their study of 83 patients with parotid

tumors, reported a sensitivity of 67% and a specificity of 78% for detecting malignant lesions using CT²⁶. A meta-analysis that compiled these data concluded that the overall sensitivity and specificity of CT for distinguishing malignant from benign parotid tumors were 70% and 73%, respectively²⁷. In our study, we found that the sensitivity of CT for detecting malignancy in parotid tumors was 75%, and the specificity was 84.5%. Additionally, we determined a negative predictive value of 92.3% and a positive predictive value of 57.69%. These findings are consistent with the literature, demonstrating the utility of CT in preoperative evaluation, though it may have limitations in accurately identifying all malignant lesions.

Several studies have investigated the predictive value of MRI in differentiating between benign and malignant tumors^{22,26,27}. In a 2005 study by Motori et al., the sensitivity and specificity of MRI were reported as 60% and 100%, respectively²². Zheng et al., in a 2018 study, found values of 82% and 94%²⁸, while Yuan et al. reported a sensitivity of 57% and a specificity of 81% (29). In 2017, Milad et al. conducted a study that recorded 100% sensitivity and 92% specificity³⁰. Lam et al., in their 2015 study, reported a sensitivity of 50% and a specificity of 97%³¹. A meta-analysis incorporating these studies concluded that the overall sensitivity and specificity of MRI in distinguishing benign from malignant parotid tumors were 80% and 90%, respectively²⁷. In our study, we found that the sensitivity of MRI for detecting malignancy in parotid gland tumors was 70%, and the specificity was 84.5%. Additionally, we determined a negative predictive value of 90.9% and a positive predictive value of 56%. These results align with existing literature, confirming the effectiveness of MRI in distinguishing between benign and malignant lesions, though its predictive accuracy may vary depending on the study.

Limitations

This study has several limitations that should be acknowledged. First, the retrospective nature of the study may have introduced selection bias, as only patients with available preoperative CT and MRI scans were included. This may limit the generalizability of the findings to a broader population of patients with parotid gland masses. Second, the sample size of 91 patients, while sufficient for analysis, is relatively small compared to larger multicenter studies, which may reduce the power of the results. Furthermore, imaging quality and

interpretation were based on retrospective reviews, and variations in imaging protocols or radiologist expertise may have influenced the outcomes. Third, the study focused solely on the diagnostic performance of CT and MRI, without including other imaging modalities such as ultrasound or PET scans, which may provide additional diagnostic value. Lastly, histopathological analysis remains the gold standard for diagnosis, and although imaging can aid in preoperative planning, it is still limited in providing definitive diagnoses, especially in distinguishing between certain benign and malignant tumors. Future studies with larger sample sizes, prospective designs, and multimodal imaging comparisons are needed to further validate the findings.

Conclusions

Our study demonstrates that both CT and MRI are valuable tools for the preoperative evaluation of parotid gland tumors, aiding in distinguishing between benign and malignant lesions. CT showed a sensitivity of 75% and specificity of 84.5%, while MRI demonstrated a sensitivity of 70% and specificity of 84.5%. Both modalities had high negative predictive values, making them reliable for ruling out malignancy. Radiological imaging methods (MRI and CT) are highly valuable tools for surgeons in the preoperative period, aiding in diagnosis, determining the size and location of the lesion, identifying associated pathologies, and planning the surgical approach. While they may not be sufficient for providing a definitive diagnosis, these imaging techniques are extremely helpful in distinguishing between benign and malignant lesions.

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No

Conflict of interest

No

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ORIGINAL

The Influence of Shift Work on Sociodemographic Characteristics, Anthropometric Parameters, Lifestyle Behaviors, and Its Relationship with Cardiovascular Risk Factors

Influencia del trabajo por turnos en las características sociodemográficas, los parámetros antropométricos, los hábitos de vida y su relación con los factores de riesgo cardiovascular

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Abstract

Introduction: Cardiovascular diseases are recognized as a major public health problem worldwide due to the high morbidity and mortality they cause. Their development is influenced by various risk factors, including dyslipidemia, arterial hypertension (HTN), and hyperglycemia.

Objective: This study assesses the association between sociodemographic variables, health habits, and shift work with the aforementioned cardiovascular risk factors (CRFs).

Methods: A cross-sectional, observational, and descriptive study was conducted, involving 53,053 workers from various occupational sectors across several regions of Spain. The sample included 31,753 men (17,527 of whom worked shifts) and 21,300 women (11,281 worked shifts). The relationship between shift work and CRFs was examined, along with its association with sex, age, social class, educational level, smoking, alcohol consumption, sedentary behavior, and an unhealthy diet.

Results: The three CRFs were more prevalent among shift workers. All variables related to unhealthy lifestyles showed a significantly higher prevalence among shift workers, with high statistical significance ($p < 0.001$). Additionally, all variables, particularly age and physical activity, were associated with the prevalence of CRFs. Men had a higher risk than women, with odds ratios (OR) ranging from 1.47 (95% CI 1.41-1.52) for dyslipidemia to 2.42 (95% CI 2.30-2.45) for HTN.

Conclusions: The profile of a worker at the highest risk of developing these CRFs is a shift worker, male, older, of low socioeconomic status, a smoker, sedentary, with low adherence to the Mediterranean diet, and a regular alcohol intake.

Key words: Cardiovascular risk factors, shift work, physical activity, Mediterranean diet, alcohol consumption, tobacco use.

Resumen

Introducción: Las enfermedades cardiovasculares son consideradas como un enorme problema de salud pública a nivel mundial debido a la elevada morbimortalidad que ocasionan. En su génesis se encuentran diferentes factores de riesgo entre los que destacaríamos la dislipemia, la hipertensión arterial (HTA) y la hiperglucemia.

Objetivo: Este estudio valora la asociación entre variables sociodemográficas, hábitos de salud y trabajo a turnos con los factores de riesgo cardiovascular (FRCV) antes mencionados.

Metodología: Se realizó un estudio observacional, transversal y descriptivo en el que participaron 53.053 trabajadores de diversos sectores laborales de varias comunidades autónomas españolas. Se incluyeron 31.753 hombres (17.527 de ellos trabajaban a turnos) y 21.300 mujeres (11.281 trabajaban a turnos). Se examinó la relación entre el trabajo a turnos y los FRCV, así como su asociación con el sexo, la edad, la clase social, el nivel educativo, el tabaquismo, el consumo de alcohol, el comportamiento sedentario y la dieta poco saludable.

Resultados: Los tres FRCV mostraron una mayor prevalencia entre los trabajadores por turnos. Todas las variables relacionadas con hábitos de vida poco saludables revelaron una prevalencia significativamente mayor entre los trabajadores por turnos, con alta significación estadística ($p < 0,001$). Igualmente todas las variables, pero especialmente la edad y la actividad física se asociaron con la prevalencia de los FRCV. Los hombres presentaban un riesgo mayor que las mujeres, con una OR que oscilaba entre 1,47 (IC 95% 1,41-1,52) para dislipemia y 2,42 (IC 95% 2,30-2,45) para HTA.

Conclusiones: El perfil de trabajador con mayor riesgo de presentar estos FRCV es un trabajador a turnos, varón, con edad avanzada, de estatus socioeconómico bajo, fumador, sedentario, con baja adherencia a la dieta mediterránea y consumidor habitual de alcohol.

Palabras clave: Factores de riesgo cardiovascular, trabajo a turnos, actividad física, dieta mediterránea, consumo de alcohol, consumo de tabaco.

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Introduction

Cardiovascular diseases are the leading cause of mortality worldwide¹, accounting for an extremely high number of deaths each year globally, a figure that continues to rise². Among the most important modifiable risk factors are dyslipidemia, hypertension, and hyperglycemia, which are key components of metabolic syndrome⁴ and significantly contribute to the development of atherosclerosis⁵ and other vascular disorders⁶.

Dyslipidemia, defined as abnormal blood lipid levels, affects a large proportion of the adult population, with variations depending on region, age, and sex⁷. This condition, particularly elevated levels of LDL-C and triglycerides, accelerates the formation of atherosclerotic plaques⁸ by promoting endothelial dysfunction⁹ and vascular inflammation¹⁰.

Hypertension affects millions of people worldwide¹¹. Its prevalence increases with age¹² and is linked to factors such as excessive sodium intake¹³, obesity¹⁴, and physical inactivity¹⁵. This "silent killer"¹⁶ contributes to the development of cardiovascular diseases by damaging the endothelium¹⁷ and increasing arterial stiffness¹⁸.

Hyperglycemia, often associated with type 2 diabetes, also affects a significant portion of the global adult population¹⁹. Its impact includes accelerating vascular damage —both microvascular and macrovascular²⁰— through mechanisms such as oxidative stress²¹, chronic inflammation²², and the formation of advanced glycation end-products²³.

These three factors are deeply interconnected, and their interaction amplifies cardiovascular risk. For instance, insulin resistance in hyperglycemia often coexists with hypertension and dyslipidemia, highlighting the need to address these factors comprehensively rather than in isolation²⁴.

Managing these conditions requires a multifaceted approach that combines lifestyle modifications²⁵ and pharmacological treatments. Dietary interventions, such as adopting the Mediterranean diet²⁶, and regular physical activity²⁷ have been shown to reduce cardiovascular risk. Similarly, pharmacological advancements, including PCSK9 inhibitors²⁸, GLP-1 receptor agonists²⁹, and SGLT2 inhibitors³⁰, have revolutionized the treatment of these pathologies.

Despite progress, significant challenges persist in the diagnosis and management of these conditions, particularly in vulnerable population.

This study aims to evaluate the associations between shift work, sociodemographic variables such as age, sex, social class, and educational level, as well as health-related behaviors like smoking, physical activity, adherence to the Mediterranean diet, and alcohol consumption, with different cardiovascular risk factors, including dyslipidemia, hypertension, and hyperglycemia.

Methods

Participants

This study was an observational, cross-sectional, descriptive analysis involving 53,053 workers from nearly all labor sectors across various regions of Spain. The sample comprised 31,753 men (17,527 of whom were shift workers) and 21,300 women (11,281 of whom were shift workers). Participants were selected from among those undergoing annual periodic medical examinations as part of occupational health assessments conducted by the participating companies. The selection period extended from January 2019 to June 2020.

Inclusion Criteria:

- Age between 18 and 69 years.
- Employment under a formal contract with one of the participating companies.
- Provision of informed consent to participate in the study.
- Authorization for the use of their data for epidemiological research purposes.

Figure 1 presents the flowchart outlining the selection process and the distribution of workers after applying the inclusion criteria.

Determination of Variables

The data required for this investigation were collected by personnel working in the occupational health departments of the participating companies. Data collection methods included a detailed anamnesis. Information on sociodemographic characteristics (such as age, sex, socioeconomic status, and education level) as well as lifestyle habits (including tobacco use, alcohol consumption, adherence to the Mediterranean diet, and physical activity) was obtained through comprehensive clinical history assessments.

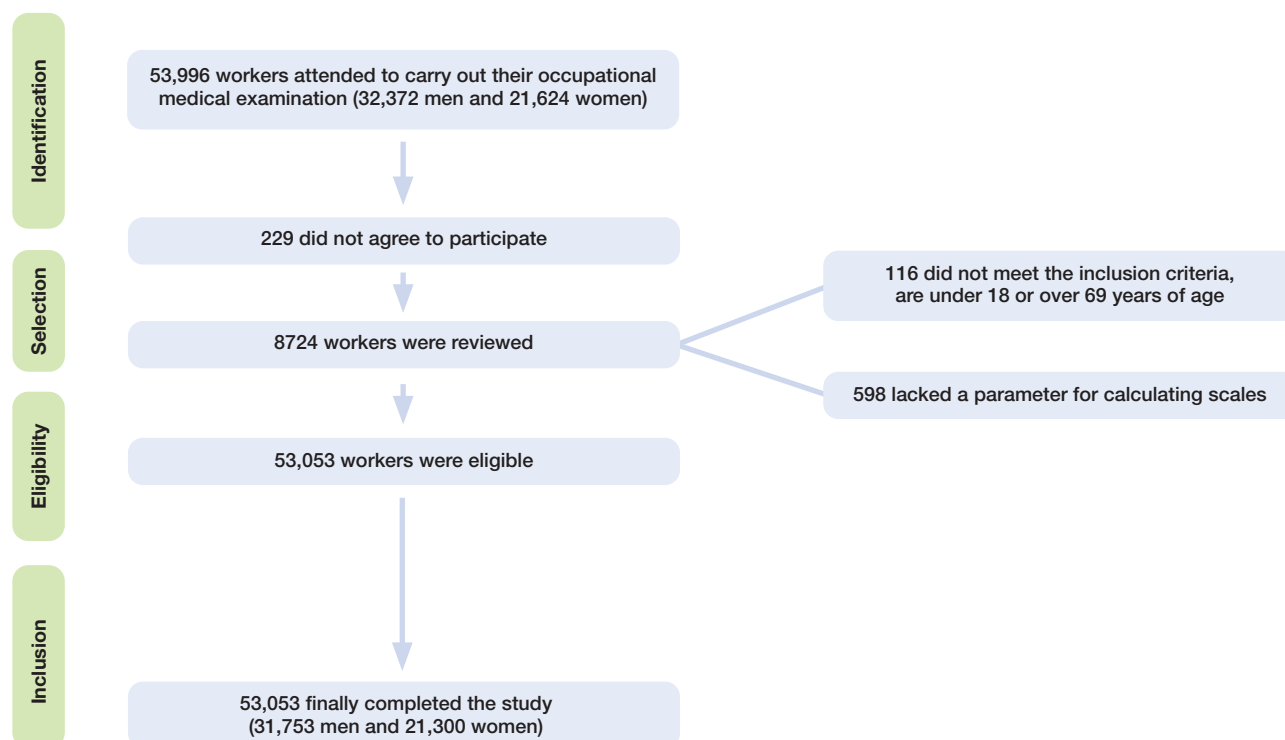
- Clinical and Anthropometric Measurements: These included height, weight, waist circumference, and systolic and diastolic blood pressure.
- Analytical Measurements: These comprised blood glucose levels and lipid profiles.

To minimize potential biases, measurement methodologies were standardized across all variables.

Anthropometric Measurements

Participants' height and weight were measured while standing upright, dressed only in undergarments, with arms relaxed at their sides and maintaining proper alignment of the head and chest. Measurements were recorded in kilograms and millimeters using a SECA-type scale and measuring device, adhering to international standards established for ISAK anthropometric evaluation.

Abdominal waist circumference was determined using a SECA model measuring tape, positioned horizontally

Figure 1: displays the data from the workers' flowchart after applying the inclusion criteria.

at the midpoint between the last rib and the iliac crest while participants stood in a relaxed posture. Similarly, hip circumference was measured at the widest part of the buttocks, ensuring the tape was parallel to the floor.

Clinical Measurements

Blood pressure was assessed using an OMRON-M3 blood pressure monitor. Participants were required to remain seated and at rest for at least ten minutes before measurements were taken. Appropriate cuff sizes were used to ensure accurate readings. Three consecutive blood pressure readings were recorded at one-minute intervals, and the average value was used for analysis. Individuals were classified as hypertensive if their systolic blood pressure exceeded 140 mmHg, their diastolic blood pressure exceeded 90 mmHg, or if they were undergoing antihypertensive treatment.

Analytical Measurements

Venous blood samples were collected following a 12-hour fasting period. Samples were processed and stored at refrigerated temperatures for no more than 48 to 72 hours before analysis, which was conducted in reference laboratories using standardized methodologies. Blood glucose, triglycerides, and total cholesterol levels were determined using enzymatic assays, while HDL cholesterol was measured using precipitation methods. LDL cholesterol levels were calculated using the Friedewald formula³¹ when triglyceride levels were below 400 mg/dL. For triglyceride levels exceeding this threshold, LDL cholesterol was measured directly.

All analytical results were expressed in mg/dL. Participants were identified as dyslipidemic if their lipid levels exceeded the reference laboratory thresholds or if they were receiving treatment for dyslipidemia. Hyperglycemia was considered to be glycemia values above 100 mg/dL or if the person was under treatment.

Gender was classified into two binary categories: male and female. Age was calculated as the difference between the date of birth and the date of the medical examination. Educational attainment was categorized into three levels based on the highest level completed: primary education, secondary education, and university education.

Social class was determined following the guidelines of the Spanish Society of Epidemiology, which relies on occupational categories outlined in the 2011 National Classification of Occupations (NCO-11)³². Participants were grouped into three social classes:

- Social Class I: University-educated professionals, executives, professional athletes, and artists.
- Social Class II: Intermediate-level professionals and skilled self-employed workers.
- Social Class III: Workers with lower levels of qualifications.

Smoking status was defined as having used tobacco products within the previous 30 days or not having abstained from smoking for at least one year.

Adherence to the Mediterranean diet was assessed through a validated 14-item questionnaire. Each affirmative response was awarded one point, with a total score of nine or higher indicating strong adherence to the Mediterranean dietary pattern³⁴.

Physical activity levels were evaluated using the International Physical Activity Questionnaire (IPAQ), a self-reported tool designed to assess activity levels over the previous seven days³⁴.

Alcohol consumption was measured using standard drinking units (SDUs), which provide a widely accepted method for estimating alcohol intake across various care settings. One SDU in Spain corresponds to 10 grams of pure alcohol, equivalent to approximately one glass of wine (100 mL), champagne (100 mL), or beer (200 mL), or half a serving of spirits (25 mL). Weekly consumption thresholds for significant health risks were defined as more than 35 SDUs for men and more than 20 SDUs for women³⁵.

When workers are expected to work beyond the standard nine-to-five shift, this is known as shift work. Working evenings, splitting shifts, alternating shift patterns, and consistently working early or late hours could all be part of this³⁶.

Statistical Analysis

Quantitative variables were analyzed using Student's t-test to compare means and standard deviations. For prevalence rates of categorical variables, the Chi-square (χ^2) test was applied. Variables related to cardiovascular risk factors were examined using a multinomial logistic regression model, with goodness-of-fit assessed through the Hosmer-Lemeshow test. A stratified analysis was conducted to identify potential confounding factors, although none of the variables analyzed exhibited such effects. All analyses were performed using SPSS software, version 28.0. Statistical significance was set at a p-value less than 0.05.

Results

Table I summarizes the anthropometric, clinical, analytical, and sociodemographic characteristics of the participants, disaggregated by sex and shift work status. Across all parameters, individuals engaged in shift work displayed less favorable clinical, analytical, and anthropometric profiles compared to those without shifts. These adverse findings were more pronounced in men, with the exception of HDL cholesterol. Notably, all observed differences between shift and non-shift workers were statistically significant, except for height.

Table I: Characteristics of the population.

	Non shift work Men n=14226 Mean (SD)	Shift work Men n=17527 Mean (SD)	p-value	Non shift work Women n=10019 Mean (SD)	Shift work Women n=11281 Mean (SD)	p-value
Age (years)	41.2 (10.9)	41.3 (10.5)	0.089	40.0 (10.5)	40.2 (10.3)	0.199
Height (cm)	173.8 (7.1)	173.7 (7.1)	0.219	161.0 (6.6)	161.2 (6.6)	0.015
Weight (kg)	81.5 (14.6)	84.5 (14.4)	<0.001	63.6 (12.8)	68.6 (12.8)	<0.001
Waist (cm)	89.5 (10.5)	90.8 (10.2)	<0.001	74.7 (9.7)	77.6 (10.9)	<0.001
Systolic BP (mmHg)	125.3 (15.7)	126.9 (16.0)	<0.001	114.8 (15.5)	116.1 (15.6)	<0.001
Diastolic BP (mmHg)	75.9 (10.7)	77.2 (11.0)	<0.001	70.3 (10.6)	71.6 (10.8)	<0.001
Total cholesterol (mg/dL)	197.3 (38.4)	201.2 (38.6)	<0.001	192.3 (36.6)	196.9 (37.3)	<0.001
HDL-cholesterol (mg/dL)	50.4 (7.8)	49.7 (7.7)	<0.001	55.0 (9.1)	54.5 (9.2)	<0.001
LDL-cholesterol (mg/dL)	120.9 (37.3)	123.8 (37.6)	<0.001	119.6 (36.9)	123.5 (37.5)	<0.001
Triglycerides (mmHg)	129.3 (93.7)	136.8 (95.5)	<0.001	87.5 (46.8)	93.6 (51.7)	<0.001
Glucose (mg/dL)	91.9 (26.4)	93.3 (26.4)	<0.001	86.6 (19.0)	87.8 (17.6)	<0.001
	%	%	p-value	%	%	p-value
18-29 years	16.4	13.8	<0.001	18.6	17.5	0.135
30-39 years	29.3	29.8		31.0	31.3	
40-49 years	29.0	31.3		29.6	30.6	
50-59 years	20.9	20.9		17.9	17.5	
60-69 years	4.4	4.2		2.9	3.1	
Social class I	6.8	8.2	<0.001	11.6	14.6	<0.001
Social class II	20.7	26.6		27.6	37.0	
Social class III	72.5	65.2		60.8	48.4	
Elementary school	69.5	63.8	<0.001	53.7	43.2	<0.001
High school	24.4	28.9		36.2	44.2	
University	6.1	7.3		10.1	12.6	
Non-smokers	67.9	66.0	<0.001	66.3	69.1	<0.001
Smokers	32.1	34.0		33.7	30.9	
Non physical activity	55.2	67.9	<0.001	40.8	60.7	<0.001
Yes physical activity	44.8	32.1		59.2	39.3	
Non Mediterranean diet	58.2	71.5		42.0	63.1	
Yes Mediterranean diet	41.8	28.5		58.0	36.9	
Non alcohol consumption	70.4	63.2	<0.001	85.3	83.5	<0.001
Yes alcohol consumption	29.6	36.8		14.7	16.5	

SD Standard deviation.

The most prevalent age group for both sexes ranged between 30 and 49 years. A significant proportion of workers, regardless of shift status, belonged to the lowest socioeconomic strata (Social Class III) and had completed only elementary education. Smoking prevalence was higher among men with shift work and women without shifts. Greater adherence to the Mediterranean diet and higher physical activity levels were observed among non-shift workers of both sexes. Conversely, alcohol consumption was significantly elevated among shift workers.

Tables II and III present the prevalence of dyslipidemia, hypertension, and hyperglycemia in both male and female workers, stratified by shift work status and according to various sociodemographic variables (age,

social class, and educational level) as well as health-related behaviors (smoking, physical activity, adherence to the Mediterranean diet, and alcohol consumption).

The prevalence of all three cardiovascular risk factors shows a progressive increase with advancing age and lower socioeconomic status. Higher prevalence rates are also observed among smokers, sedentary individuals, workers with low adherence to the Mediterranean diet, and those who regularly consume excessive amounts of alcohol. Across all risk factors analyzed, prevalence rates are consistently lower in women compared to men.

In all cases, the differences observed are statistically significant ($p < 0.001$).

Table II: Prevalence of cardiovascular risk factors according to shift or not shift work and according to different sociodemographic variables and healthy habits in men.

Men	Non shift work				Shift work			
	n	Dyslipidemia %	Hypertension %	Glucose high %	n	Dyslipidemia %	Hypertension %	Glucose high %
18-29 years	2329	26.8	9.0	7.6	2425	32.1	11.8	8.0
30-39 years	4174	48.0	12.4	13.4	5228	55.6	18.1	13.9
40-49 years	4130	68.4	24.7	22.7	5477	71.5	28.9	24.2
50-59 years	2972	75.6	37.7	34.9	3666	77.8	41.2	37.2
60-69 years	621	79.2	46.9	47.2	731	82.1	49.0	49.0
Social class I	972	51.5	15.5	17.2	1438	57.5	20.2	17.4
Social class II	2942	57.3	22.4	18.9	4669	62.8	26.9	19.3
Social class III	10312	60.6	23.7	22.9	11420	65.4	27.4	23.5
Elementary school	9874	61.0	25.1	23.1	11169	65.0	27.9	24.1
High school	3478	56.7	21.7	18.7	5070	62.7	26.9	19.5
University	874	54.2	16.1	17.3	1288	58.3	20.6	17.7
Non-smokers	9656	54.7	21.4	21.2	11567	62.8	25.8	21.8
Smokers	4570	59.0	22.6	22.7	5960	63.7	27.2	22.9
Non physical activity	7851	80.2	30.4	26.1	11899	77.8	33.2	29.9
Yes physical activity	6375	29.8	12.2	12.8	5628	32.0	13.0	13.9
Non Mediterranean diet	8275	78.5	29.4	25.4	12536	76.8	32.1	28.1
Yes Mediterranean diet	5951	28.5	12.3	12.7	4991	28.5	13.1	13.1
Non alcohol consumption	8996	46.6	15.7	12.7	12332	57.5	23.4	15.4
Yes alcohol consumption	5230	76.5	33.5	37.2	5195	77.3	34.5	37.3

$p < 0.001$ in all cases.

Table III: Prevalence of cardiovascular risk factors according to shift or not shift work and according to different sociodemographic variables and healthy habits in women.

Women	Non shift work				Shift work			
	n	Dyslipidemia %	Hypertension %	Glucose high %	n	Dyslipidemia %	Hypertension %	Glucose high %
18-29 years	1869	23.1	1.4	3.3	1975	28.7	3.0	4.0
30-39 years	3103	33.7	3.6	6.5	3530	38.2	4.8	7.0
40-49 years	2965	50.4	10.6	12.8	3450	57.4	13.1	13.9
50-59 years	1791	74.5	23.7	22.8	1974	78.5	24.5	23.5
60-69 years	291	79.0	31.3	33.8	352	83.2	32.7	39.8
Social class I	1164	33.2	2.0	6.6	1644	40.8	3.9	8.2
Social class II	2763	43.3	7.6	9.0	4175	49.5	9.6	9.9
Social class III	6092	48.4	12.1	14.3	5462	54.9	15.0	15.0
Elementary school	5377	49.7	12.6	13.7	4871	57.3	15.7	14.3
High school	3628	42.3	7.6	10.2	4984	47.6	9.3	11.7
University	1014	32.4	1.7	7.2	1426	40.2	4.0	8.2
Non-smokers	6638	42.9	8.0	10.7	7794	49.4	10.3	11.6
Smokers	3381	46.5	10.5	12.0	3487	51.2	11.8	12.8
Non physical activity	4090	66.8	16.4	15.8	6842	72.4	18.4	22.7
Yes physical activity	5929	26.2	3.4	5.0	4439	26.5	3.6	5.3
Non Mediterranean diet	4206	66.4	15.9	15.2	7115	71.5	18.0	21.9
Yes Mediterranean diet	5813	24.3	3.7	5.4	4166	26.3	3.7	5.5
Non alcohol consumption	8361	40.7	5.9	4.3	9619	47.6	8.3	4.5
Yes alcohol consumption	1658	68.5	28.9	45.9	1662	68.8	29.2	51.3

$p < 0.001$ in all cases.

The multinomial logistic regression analysis (**Table IV**) establishes the following reference categories for independent variables: female sex, age below 30 years, Social Class I, university-level education, non-smoking status, regular physical activity, high adherence to the Mediterranean diet, and no habitual alcohol consumption. The results indicate that all the

analyzed variables are significantly associated with the prevalence of the three cardiovascular risk factors. Among these, age, physical activity, and adherence to the Mediterranean diet demonstrate the strongest associations, as reflected by the highest odds ratio values. In all cases, the observed differences are statistically significant ($p < 0.001$).

Table IV: Multinomial logistic regression.

	Dyslipidemia OR (95% CI)	Hypertension OR (95% CI)	Glucose high OR (95% CI)
Women	1	1	1
Men	1.47 (1.41-1.53)	2.42 (2.30-2.55)	1.57 (1.48-1.66)
18-29 years	1	1	1
30-39 years	1.25 (1.10-1.41)	1.38 (1.24-1.52)	1.53 (1.37-1.70)
40-49 years	2.01 (1.77-2.26)	2.34 (2.11-2.58)	2.21 (1.99-2.44)
50-59 years	3.50 (3.09-3.92)	4.37 (3.92-4.83)	3.65 (3.27-4.04)
60-69 years	6.34 (5.55-7.13)	6.11 (5.37-6.86)	5.92 (5.17-6.67)
Social class I	1	1	1
Social class II	1.15 (1.12-1.18)	1.16 (1.11-1.22)	2.31 (2.14-2.49)
Social class III	1.39 (1.30-1.49)	1.64 (1.52-1.76)	3.10 (2.33-3.88)
University	1	1	1
High school	1.36 (1.30-1.43)	1.20 (1.14-1.26)	2.19 (2.01-2.37)
Elementary school	1.18 (1.14-1.23)	1.61 (1.50-1.73)	3.15 (2.40-3.91)
Non-smokers	1	1	1
Smokers	1.13 (1.10-1.17)	1.13 (1.10-1.17)	1.16 (1.11-1.22)
Yes physical activity	1	1	1
Non physical activity	2.93 (2.73-3.14)	1.97 (1.77-2.18)	3.88 (3.08-4.69)
Yes Mediterranean diet	1	1	1
Non Mediterranean diet	2.77 (2.58-2.97)	1.57 (1.43-1.71)	2.91 (2.22-3.61)
Non alcohol consumption	1	1	1
Yes alcohol consumption	1.40 (1.35-1.46)	1.27 (1.20-1.34)	4.46 (4.20-4.73)
Non shift work	1	1	1
Yes shift work	1.19 (1.16-1.23)	1.23 (1.18-1.29)	1.33 (1.20-1.46)

OR Odds ratio. $p < 0.001$ in all cases.

Discussion

Both the prevalence of dyslipidemia, hypertension, and hyperglycemia have been associated with shift work, sociodemographic variables, and health habits in our study.

As we will see, some authors align with our findings and have reported that the prevalence of dyslipidemia varies according to sociodemographic and behavioral factors. Aging is closely linked to an increase in total cholesterol and LDL levels due to physiological changes in lipid metabolism³⁷. Reduced lipoprotein activity³⁸ and increased hepatic cholesterol synthesis in older individuals contribute to these changes³⁹. Additionally, men tend to develop dyslipidemia at younger ages compared to women⁴⁰, who generally experience a rise in lipid levels post-menopause, likely due to the decline in estrogen levels⁴¹. These findings underscore the importance of addressing dyslipidemia differently based on sex and age.

Socioeconomic status plays a critical role in the prevalence of dyslipidemia, as suggested by our results. Similar findings have been reported by other researchers, who attribute this to individuals with lower educational and economic levels often consuming diets high in saturated and processed fats, which promote the development of dyslipidemia⁴².

Moreover, the stress associated with economic insecurity may contribute to altered lipid profiles⁴³, promoting systemic inflammation and endothelial dysfunction⁴⁴. In contrast, individuals with higher socioeconomic status generally have greater access to health information and nutritious foods, facilitating better lipid management.

According to our findings, smoking is a factor associated with the exacerbation of dyslipidemia. Other studies with similar results have observed that smoking increases triglyceride levels while reducing HDL cholesterol, fostering a pro-atherogenic environment⁴⁵. This may be mediated by various mechanisms, including RNA-containing vesicles⁴⁶. Conversely, we also observed that regular physical activity is associated with improvements in lipid profiles. As noted by some researchers, physical exercise increases HDL cholesterol levels and reduces triglycerides⁴⁷. The Mediterranean diet, also associated in our study with a lower prevalence of dyslipidemia, may achieve this by improving LDL and HDL cholesterol levels, thereby reducing the risk of atherosclerosis⁴⁸.

Alcohol consumption, another parameter linked to dyslipidemia in our study, presents a complex relationship. While moderate alcohol intake has been

associated with higher HDL cholesterol levels⁴⁹, excessive consumption contributes to elevated triglycerides and dyslipidemia⁵⁰.

Hypertension was associated in our research with all the variables analyzed, including sociodemographic factors, health habits, and shift work.

Several authors have demonstrated that hypertension is more prevalent with aging, as arterial stiffness and endothelial dysfunction increase with age⁵¹. Men are at greater risk for hypertension at younger ages, but women surpass men in prevalence as they age, particularly after menopause, since sex hormones have a protective role in younger women, while their decline post-menopause elevates the risk of hypertension⁵².

Socioeconomic status has also been linked to hypertension prevalence, consistent with our findings. Studies supporting our results explain that individuals with fewer economic resources often consume diets high in sodium and low in potassium, increasing their risk of developing hypertension⁵³. Additionally, chronic stress associated with economic insecurity can contribute to elevated blood pressure⁵⁴.

Health habits showed a significant association with hypertension prevalence, as indicated by our findings. Excessive salt consumption⁵⁵ and physical inactivity⁵⁶ are widely recognized as key factors favoring hypertension. Conversely, regular physical activity, such as aerobic exercise, helps reduce blood pressure by improving cardiovascular function and reducing arterial stiffness⁵⁷. The Mediterranean diet, with its low sodium and high potassium content, has been shown to be effective in preventing and managing hypertension⁵⁸. Excessive alcohol consumption is strongly associated with hypertension, as it increases vascular resistance and promotes vasoconstriction⁵⁹.

Hyperglycemia, particularly in the context of type 2 diabetes, is a major risk factor for cardiovascular disease and, according to our findings, is associated with shift work as well as all the sociodemographic variables and health habits analyzed.

Our results align with previous research showing that the prevalence of type 2 diabetes increases significantly with age, largely due to reduced insulin sensitivity⁶⁰ and changes in glucose metabolism⁶¹. While both men and women can develop type 2 diabetes, men are at higher risk at younger ages, whereas women, particularly after menopause, experience a greater increase in risk⁶².

Low socioeconomic status is associated with a higher risk of hyperglycemia and type 2 diabetes, as reflected in our results. Various researchers attribute this to factors such as limited access to healthy foods⁶³, chronic stress⁶⁴, and reduced availability of healthcare^{65,66}.

Healthy lifestyles, on the other hand, have been positively associated with reduced hyperglycemia prevalence, according to our data. Some studies have demonstrated that smoking decreases insulin sensitivity and increases the risk of insulin resistance⁶⁷. Physical activity, conversely, enhances insulin sensitivity and helps maintain healthy glucose levels⁶⁸. The Mediterranean diet, rich in antioxidants and healthy fats, has been shown to prevent and control type 2 diabetes⁶⁹. Regarding alcohol consumption, excessive intake can disrupt glucose metabolism, while moderate amounts may have protective effects on insulin resistance in some studies⁷⁰.

Shift work, particularly night shifts, has been linked to various health problems, including an increased risk of dyslipidemia, hypertension, and diabetes, as observed in this study. Circadian rhythm disruption, sleep disturbances, and occupational stress negatively impact metabolic regulation, promoting dyslipidemia⁷¹, hypertension⁷², and hyperglycemia⁷³. Chronic exposure to shift work is also associated with increased risk of obesity and altered dietary patterns, which can contribute to the development of these risk factors⁷⁴.

Strengths and Limitations

One of the primary strengths of this study lies in its substantial sample size, encompassing over 53,000 participants. This extensive sample provides a robust basis for generalizing the findings to a broader population, significantly improving the statistical power and reliability of the results. Furthermore, the sample's diverse origin, including individuals from various autonomous communities and professional sectors, enhances its representativeness of the Spanish population. In the group of shift workers, all participants followed a rotating schedule that included day, evening, and night shifts. The consistency of the findings with those reported in studies from other countries supports the generalizability of our results to other populations and validates observations derived from smaller samples.

Another notable strength of this study is its investigation of multiple variables linking shift work to cardiovascular risk factors, such as dyslipidemia, hypertension, and hyperglycemia, with analyses stratified by sex. This approach addresses a significant gap in the literature, as few existing studies examine these associations comprehensively, and those that do often present contradictory findings.

However, the study's cross-sectional design constitutes its primary limitation. While associations between shift work and obesity-related variables can be identified, causal relationships cannot be established. Additionally, the "healthy worker effect" poses a methodological challenge in shift work research; individuals with cardiovascular risk factors may be less likely to engage in or remain in shift work, potentially leading to an underestimation of the observed associations. The lack of data on the duration

of shift work also precludes the ability to explore the relationship between exposure length and cardiovascular risk factors. Another limitation is the omission of workplace location as a variable, which might influence the findings due to differences across companies or job roles. Lastly, in assessing dietary habits, the study only considers adherence to the Mediterranean diet, lacking information on the consumption of fast food, snacks, pastries, and similar items, which could offer additional insights.

Conclusion

Dyslipidemia, hypertension, and hyperglycemia are key risk factors for cardiovascular diseases, with their prevalence and severity being influenced by various sociodemographic and lifestyle factors. Age, sex, and socioeconomic status are critical determinants of the risk for these conditions, alongside behaviors related to tobacco use, physical activity, diet, and alcohol consumption. Furthermore, shift work poses an additional challenge to metabolic health by disrupting biological rhythms and promoting unhealthy lifestyle patterns. It is essential to adopt comprehensive approaches that include interventions targeting these factors.

Author Contributions

Conceptualization: Á.A.L.-G. and J.I.R.-M.; Data collection and analysis: J.T. and P.J.T.L. Data curation: J.T. Methodology: E.M.-A.R. and P.J.T.L. Validation: C.M.S.; Formal analysis: Á.A.L.-G.; Investigation: J.T.; Draft: J.T.; P.J.T.L., C.M.S. and E.M.-A.R.; Revision: J.I.R.-M. and Á.A.L.-G. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The research team is dedicated to consistently adhering to the ethical guidelines for health sciences research

established at both national and international levels, specifically following the Declaration of Helsinki. The primary focus is on ensuring participant anonymity and the confidentiality of their data. Ethical approval for the study was granted by the Ethics and Research Committee of the Balearic Islands (CEI-IB) under reference number IB 4383/20. Participation in the study was entirely voluntary, with participants providing both written and verbal consent after being thoroughly informed about the study's objectives. To facilitate this process, participants received an information sheet explaining the study's purpose, along with an informed consent form. To maintain confidentiality, the data collected were coded in such a way that only the project coordinator could link the data back to individual participants, making re-identification impossible. The identities of the participants will not be disclosed in any study report, nor will any identifying information be revealed by the researchers. The research team guarantees that all study participants have the right to access, correct, delete, and oppose their data as per their rights. The team also commits to full compliance with Organic Law 3/2018, of 5 December, on the Protection of Personal Data and Guarantee of Digital Rights and Regulation (EU) 2016/679 of the European Parliament and the Council of 27 April 2016 on Data Protection (RGPD).

Informed Consent Statement

Informed consent was obtained from all participants involved in this study.

Data Availability Statement

The study data are securely stored in a database that meets all security requirements at the ADEMA-Escuela Universitaria. The Data Protection Officer is Ángel Arturo López González.

Conflicts of Interest

The authors declare no conflicts of interest.

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ORIGINAL

Efecto protector del fitato sobre las complicaciones vasculares en pacientes con diabetes mellitus tipo 2 de alto riesgo cardiovascular

Protective effect of phytate on vascular complications in patients with type 2 diabetes mellitus at high cardiovascular risk

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Resumen

Introducción: El fitato, componente importante de la dieta mediterránea, tiene propiedades antioxidantes, antiinflamatorias y de inhibición de la formación de productos avanzados de la glicación (AGEs) y de la calcificación vascular. Nuestro objetivo es investigar la relación entre el consumo de fitato, los niveles de AGEs, los niveles del receptor de productos finales de glicación avanzada (RAGEs), IL-1 β , IL-6, HbA1c y complicaciones vasculares en 101 pacientes con diabetes tipo 2.

Material y Métodos: Se evaluaron 101 pacientes (49 hombres, edad media 69 $\pm$ 8 años) desde 2012, con un seguimiento promedio de 5 años. El consumo de fitato se determinó mediante encuesta validada, y los niveles de IL-1 β , IL-6, Adiponectina, RAGEs por luminex y AGEs por ELISA. Se definió un objetivo vascular compuesto por ictus, enfermedad coronaria, estenosis aórtica o insuficiencia cardíaca.

Resultados: El 38% presentó complicaciones vasculares. Los pacientes con complicaciones tenían mayor presión arterial (77 $\pm$ 18 vs. 66 $\pm$ 14 mmHg; $p=0.002$), menor filtrado glomerular (61 $\pm$ 23 vs. 77 $\pm$ 22 ml/min; $p=0.001$), niveles más bajos de HDL (38 $\pm$ 11 vs. 46 $\pm$ 14 mg/dL; $p=0.002$), más triglicéridos (173 $\pm$ 75 vs. 140 $\pm$ 82 mg/dL; $p=0.005$) y mayor cociente albuminuria/creatinina (152 $\pm$ 271 vs. 25 $\pm$ 49 mg/g; $p<0.001$). El consumo de fitato fue menor en pacientes con complicaciones (0.35 $\pm$ 0.20 vs. 0.41 $\pm$ 0.17; $p=0.046$), con niveles significativamente más bajos de adiponectina y mayores de IL-1 β , AGEs y HbA1c. No hubo correlación significativa entre consumo de fitato e IL-6 o RAGEs. Se encontró una mayor probabilidad de estar libre de eventos cardiovasculares a los 5 años con un consumo de fitato >250 mg/día ($p=0.037$).

Conclusión: Un consumo adecuado de fitato (>0.25 g/d) podría tener un efecto protector en complicaciones vasculares en pacientes con diabetes.

Palabras clave: Fitato, complicaciones vasculares, diabetes tipo 2, riesgo cardiovascular.

Abstract

Introduction: Phytate, an important component of the Mediterranean diet, has antioxidant and anti-inflammatory properties and inhibits the formation of advanced glycation end products (AGEs) and vascular calcification. Our objective was to investigate the relationship between phytate consumption, AGEs, RAGEs, IL-1 β , IL-6, HbA1c levels, and vascular complications in 101 patients with type 2 diabetes.

Materials and Methods: A total of 101 patients (49 men, mean age 69 $\pm$ 8 years) were evaluated since 2012, with an average follow-up of 5 years. Phytate consumption was determined through a validated survey, and levels of IL1, IL6, Adiponectin, RAGEs by luminex, and AGEs by ELISA were measured. A composite vascular outcome was defined as stroke, coronary disease, aortic stenosis, or heart failure.

Results: 38% presented vascular complications. Patients with complications had higher blood pressure (77 $\pm$ 18 vs. 66 $\pm$ 14 mmHg; $p=0.002$), lower glomerular filtration rate (61 $\pm$ 23 vs. 77 $\pm$ 22 ml/min; $p=0.001$), lower HDL levels (38 $\pm$ 11 vs. 46 $\pm$ 14 mg/dL; $p=0.002$), higher triglycerides (173 $\pm$ 75 vs. 140 $\pm$ 82 mg/dL; $p=0.005$), and a higher albumin/creatinine ratio (152 $\pm$ 271 vs. 25 $\pm$ 49 mg/g; $p<0.001$). Phytate consumption was lower in patients with complications (0.35 $\pm$ 0.20 vs. 0.41 $\pm$ 0.17; $p=0.046$), with significantly lower adiponectin and higher levels of IL-1 β , AGEs, and HbA1c. No significant correlation was found between phytate consumption and IL-6 or RAGE concentration. A higher probability of being free from cardiovascular events over 5 years was observed with phytate consumption >250 mg/day ($p=0.037$).

Conclusion: Adequate phytate intake (>0.25 g/d) may have a protective effect against vascular complications in patients with diabetes.

Key words: Phytate, vascular complications, diabetes type 2, cardiovascular risk.

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Introducción

La diabetes tipo 2 (DM2) es un trastorno endocrino caracterizado por niveles elevados de glucosa en la sangre y alteraciones en el metabolismo de carbohidratos, proteínas y grasas. Las principales preocupaciones en los pacientes con DM2 son las complicaciones microvasculares y macrovasculares. Las guías de práctica clínica recomiendan un enfoque de tratamiento que se centre en el control metabólico, y no únicamente en el control de la glucosa¹. La mayoría de las personas con DM2 tienen un riesgo cardiovascular elevado o muy elevado².

La alimentación juega un papel fundamental tanto en la prevención como en el tratamiento diversas enfermedades. De hecho, llevar una dieta equilibrada y mantener una actividad física regular podría evitar hasta el 80% de los casos de enfermedad cardíaca coronaria, el 90% de los casos de diabetes tipo 2 y el 30% de todos los tipos de cáncer³. La evidencia científica respalda de forma constante la dieta mediterránea como una opción protectora para la salud cardiovascular⁴. De hecho, la Asociación Americana de Diabetes en sus Standards of Care de 2024 sugiere la dieta mediterránea como el patrón alimentario a recomendar y seguir para las personas que viven con la DM2⁵. Además, los componentes de la dieta mediterránea actuarían de forma conjunta para reducir el riesgo cardiovascular, gracias a sus propiedades antiinflamatorias y sus efectos sobre el microbioma⁶.

La dieta mediterránea se distingue por un consumo elevado de alimentos vegetales como frutas, verduras, panes, cereales, legumbres, frutos secos, semillas y aceite de oliva⁷. De forma más específica, ciertos alimentos incluidos en la dieta mediterránea han sido investigados de manera individual. Varios estudios han demostrado que un mayor consumo de legumbres y frutos secos es beneficioso para la prevención de enfermedades cardiovasculares^{8,9}. Los frutos secos se consideran un factor protector frente a enfermedades cardiovasculares, especialmente en lo que respecta a la enfermedad coronaria y la incidencia y mortalidad por accidente cerebrovascular^{9,10}. Un aumento en la ingesta de legumbres y cereales integrales mejora el control glucémico y reduce los niveles de HbA1c^{11,12}. Tanto las legumbres como los cereales integrales son ricos en fitato, lo que podría explicar, en parte, los beneficios observados en la literatura científica. Sanchis et al. 2018 mencionaron que la evidencia observacional sugiere que en la región mediterránea el consumo de fitato es más bajo en pacientes con DM2 en comparación con sujetos no diabéticos (datos no publicados)¹³.

En su forma tradicional, la dieta Mediterránea implica la ingesta de alrededor de 1 gramo de fitato al día, junto con una cantidad adecuada de otros minerales y componentes bioactivos. Por otro lado, dietas como la

europaea o americana pueden aportar hasta 2 gramos de fitatos diarios¹⁴. Es importante que el consumo de altas dosis de fitatos se acompañe de un contenido adecuado de minerales¹⁵.

El fitato se considera un nutraceutico, es decir, un compuesto que puede ayudar a tratar o prevenir enfermedades y trastornos a través de diversas funciones bioactivas¹⁵. Desde el descubrimiento de la molécula de fitato, las investigaciones han demostrado que puede apoyar funciones fisiológicas esenciales, así como ofrecer propiedades antioxidantes, antiinflamatorias, anticancerígenas, antidiabéticas, neuroprotectoras y antimicrobianas. Además, tiene la capacidad de prevenir la pérdida de masa ósea y reducir la calcificación patológica, como la calcificación vascular y la litiasis renal¹⁵. La FDA clasifica el fitato como Generalmente Reconocido como Seguro (GRAS, por sus siglas en inglés)¹⁶.

De hecho, nuestro grupo de investigación, mostró en un ensayo cruzado aleatorizado 'in vitro' e 'in vivo' que el consumo de fitato inhibe la glicación de proteínas en pacientes con DM2 reduciendo los productos finales de glicación avanzada (AGEs) y el receptor de productos finales de glicación avanzada (RAGE)¹³. Ambos juegan un papel fundamental en la calcificación vascular. Otros trabajos como el de Fernández-Palomeque et al. 2015, en un estudio transversal en una población de 188 personas mayores, encontraron que los sujetos con mayores niveles de fitato en orina tenían menor calcificación mitral¹⁰. Sanchis et al. 2016, en un estudio transversal prospectivo realizado entre 69 pacientes con enfermedad renal crónica, se objetivó que el consumo de fitato se asoció negativamente con la calcificación aórtica abdominal¹⁷.

El objetivo de nuestro trabajo es investigar la relación entre el consumo de fitato mediante encuesta validada, los niveles de AGEs, RAGEs, IL-1 β , IL-6, HbA1c y las complicaciones vasculares en una cohorte de 110 pacientes con diabetes mellitus tipo 2 de alto o muy alto riesgo cardiovascular.

Materiales y métodos

Sujetos y diseño del estudio

Este fue un estudio unicéntrico, observacional y prospectivo que entre el 2012 y el 2014 en consultas externas del Departamento de Endocrinología y Nutrición del Hospital Universitario de Son Llàtzer, un centro público de atención terciaria que cubre a 250,000 residentes de áreas urbanas y rurales en las Islas Baleares (España). Se reclutaron de forma consecutiva a 110 pacientes con diabetes de alto y muy alto riesgo cardiovascular: pacientes con factores de riesgo cardiovascular (edad superior a 50 años, hipertensión, dislipidemia, tabaco u obesidad) o lesión en órgano diana (retinopatía diabética, microalbuminuria, enfermedad renal crónica)¹.

Se excluyeron pacientes con esperanza de vida inferior a 1 año, procesos malignos e infecciosos graves intercurrentes.

Obtención de muestras

Las muestras de sangre se recolectaron por la mañana (después de 12 horas de ayuno), se dejaron reposar durante 30 minutos a temperatura ambiente y luego se separó el suero mediante centrifugación. La mayoría de las determinaciones en sangre y orina se realizaron por potenciometría, fotometría, espectrometría de absorción molecular o inmunoquimioluminiscencia utilizando un analizador automatizado (Architect ci16200, Abbott, Chicago, IL, EE. UU.) La hemoglobina glucosilada se determinó por cromatografía líquida de alta resolución (ADAMS A1C HA-8180V, Menarini, Florencia, Italia). Los niveles de adiponectina, interleucina-6 (IL-6), interleucina-1beta (IL-1 β) y receptor de productos avanzados de glicación (RAGE) se midieron mediante un ensayo multiplex optimizado basado en esferas magnéticas para la plataforma Luminex® (LXSAHM, Bio-Techne R&D Systems, S.L.U.). Los AGE en muestras de suero se midieron utilizando el Kit de ELISA Competitiva OxiSelect™ AGEs de Cell Biolabs, que permite una detección y cuantificación rápida de los AGE circulantes. La cuantificación se determinó utilizando una curva estándar de AGE-BSA.

Durante el año 2020 se revisaron los datos disponibles en la última observación clínica realizada con periodicidad mínima anual en nuestro centro y además se revisaron los datos disponibles en historia electrónica de salud de la comunidad autónoma donde constan los informes de alta de ingresos hospitalarios o pruebas complementarias realizadas en otros centros así como el estatus vital. En el seguimiento se han perdido 9 pacientes que no acudieron a los seguimientos y de los que no se dispone de la información mínima electrónica. Por tanto, nuestra muestra final es de 101 pacientes de alto o muy alto riesgo (49 hombres y edad media 69 +/- 8 años) evaluados inicialmente desde el año 2012 y con un seguimiento medio de 4.5 +/- 0.7 años.

Se consideró como objetivo vascular final compuesto la presencia de ictus, enfermedad coronaria (IAM o ingreso por angor inestable), estenosis aórtica grave, insuficiencia cardíaca y muerte cardiovascular.

Estimación del consumo de fitatos

El consumo de fitatos se determinará utilizando un Cuestionario de Frecuencia Alimentaria (FFQ) semicuantitativo de 137 ítems, previamente validado en la población española¹⁸ Los alimentos se agruparán en categorías (leche y productos lácteos, cereales y productos de grano, verduras, legumbres, huevos, carne y pescado, productos cárnicos, aceites y grasas, 'comida rápida', productos enlatados, frutas, frutos secos, bebidas). El FFQ utilizado en este estudio pide a

los participantes que estimen la frecuencia de consumo de cada alimento como diaria, semanal, mensual o rara vez/nunca. El FFQ considera 10 fuentes clave de fitatos (granos enteros, legumbres y frutos secos), el tamaño de la porción de cada alimento y la concentración de fitatos en cada uno de ellos. Todos los cuestionarios completados serán revisados por un profesional de la salud para verificar su exactitud y completitud. Se especificarán porciones medianas y unidades (rebanadas, vasos, cucharaditas, etc.) para cada alimento.

La ingesta de nutrientes se calculará a partir de los Cuestionarios de Frecuencia Alimentaria utilizando una tabla de composición de alimentos¹⁹ que incluye más de 800 alimentos.

Consideraciones éticas

El Comité de Investigación del Hospital Son Llàtzer y el Comité Ético de Investigación de las Islas Baleares [CEI-IB] (IB1933/12 PI) aprobaron el estudio, validado el 22 de febrero de 2018. El número del ensayo clínico es U1111-1201-5736, que es el Número Universal del Ensayo (UTN).

Análisis estadístico

Los datos se presentan como medias (desviaciones estándar) o frecuencia (porcentajes).

Las comparaciones entre grupos se analizaron mediante la prueba t de muestras independientes o la prueba U de Mann-Whitney para las variables continuas, y la prueba de Chi cuadrado o la prueba exacta de Fisher para las variables categóricas.

Las diferencias intragrupo (antes vs. después) se evaluaron utilizando muestras pareadas t o la prueba pareada de Wilcoxon para las variables continuas, y la prueba de McNemar para las variables dicotomizadas. Las asociaciones bivariadas fueron evaluadas por los coeficientes de correlación de Pearson o Spearman.

El punto óptimo de corte de la variable consumo de fitato con respecto a la presencia de complicaciones CV se determinó mediante la curva COR y el índice de Youden. La curva Kaplan-Meier se utilizó para estudiar la presencia de complicaciones CV en función de la ingesta de fitato (> y < a 250 mg/día).

Un valor de p de dos colas inferior a 0,05 se consideró estadísticamente significativo. Los análisis estadísticos se realizaron utilizando SPSS versión 23.0 (SPSS Inc., Chicago, IL, EE. UU.).

Resultados

Características basales de nuestra muestra de pacientes

La media de edad de nuestros pacientes es de 69.4 ($\pm$ 8) siendo el 51.9% mujeres y presentando un índice

de masa corporal de $31.3 \text{ kg/m}^2 (\pm 6)$. El 64.4% de los pacientes presentaba una DM2 de más de 10 años de evolución. El 93% de los pacientes presentaban hipertensión arterial y el 53,8% presentan enfermedad renal crónica grado 3. La **tabla I**, muestra también el consume de tóxicos en nuestra muestra de pacientes.

Comparación de las variables entre los grupos sin complicaciones vasculares y con complicaciones vasculares

Treinta y ocho pacientes (38%) presentaron alguna de las complicaciones vasculares. En cuanto a los factores clásicos de riesgo, los pacientes con complicaciones vasculares presentaban mayor presión arterial (77 ± 18 vs.

$66 \pm 14 \text{ mmHg}$; $p=0.002$), menor filtrado glomerular (61 ± 23 vs. $77 \pm 22 \text{ ml/min}$; $p=0.001$), niveles más bajos de HDL (38 ± 11 vs. $46 \pm 14 \text{ mg/dL}$; $p=0.002$), mayores niveles de triglicéridos (173 ± 75 vs. 140 ± 82 ; $p=0.005$) y mayor cociente albuminuria/creatinina (152 ± 271 vs. $25 \pm 49 \text{ mg/g}$; $p<0.001$) en comparación con los que no presentaron complicaciones. El consumo de fitato fue menor en los pacientes con complicaciones vasculares (0.35 ± 0.20 vs. 0.41 ± 0.17 ; $p=0.046$). En estos pacientes también se observaron niveles más bajos de adiponectina (0.27 ± 0.09 vs. $0.32 \pm 0.12 \text{ micorg/mL}$; $p=0.047$). Por el contrario, se detectaban niveles más elevados de IL-1 β (1.4 ± 0.5 vs. $1.2 \pm 0.2 \text{ U/mL}$; $p=0.046$), AGEs (9.1 ± 4.1 vs. 7.4 ± 3.8 ; $p=0.048$) y HbA1c 7.9 ± 1.4 vs. $7.4 \pm 1.4 \%$; $p=0.028$).

Tabla I: Características basales de los pacientes (n=101) proporcionadas con medias (desviaciones estándar) o frecuencia (porcentajes).

CARACTERÍSTICAS BASALES (n = 101)		
Edad (años)	69,4	$\pm 8,0$
Género (femenino)	54	(51,9%)
IMC (kg/m^2)	31,3	$\pm 6,0$
Circunferencia de cintura (cm)	109	± 11
Presión arterial sistólica (mmHg)	146	± 19
Presión arterial diastólica (mmHg)	76,3	$\pm 10,8$
Frecuencia cardíaca (latidos/min)	77,5	$\pm 13,4$
Tiempo de diagnóstico de diabetes mellitus tipo 2		
Menos de 5 años	9	(8,7%)
Entre 5 y 10 años	28	(26,9%)
Más de 10 años	67	(64,4%)
Comorbilidades y tóxicos frecuentes		
Hipertensión arterial	93	(89,4%)
Enfermedad cardiovascular previa	48	(46,2%)
Estadio de enfermedad renal crónica		
2 (eGFR 89-60 ml/min/1.73 m^2)	13	(12,5%)
3a (eGFR 59-45 ml/min/1.73 m^2)	26	(25,0%)
3b (eGFR 44-30 ml/min/1.73 m^2)	30	(28,8%)
Tabaco (actual o pasado)	40	(38,5%)
Alcohol (actual o pasado)	13	(12,5%)

Tabla II: Comparación de las variables entre los grupos sin complicaciones vasculares y con complicaciones vasculares. Las diferencias se evaluaron con t-student para muestras independientes o el test U de Mann Whitney.

	SIN COMPLICACIONES VASCULARES (n = 62)	CON COMPLICACIONES VASCULARES (n = 38)	p-value
	Media $\pm$ SD	Media $\pm$ SD	
Edad (años)	68.8 ± 8.7	70.6 ± 6.7	0.347
IMC (kg/m^2)	30.7 ± 5.0	32.5 ± 7.4	0.215
Circunferencia cintura (cm)	108 ± 11	112 ± 12	0.149
PA sistólica (mmHg)	141 ± 14	155 ± 21	<0.001
PA diastólica (mmHg)	75 ± 11	79 ± 10	0.059
Frecuencia cardíaca (latidos/min)	77 ± 12	78 ± 16	0.616
Filtrado glomerular CDK-EPI (ml/min)	77 ± 22	61 ± 23	0.001
Glucosa sangre (mg/dL)	160 ± 64	176 ± 85	0.547
Urea sangre (mg/dL)	42 ± 15	52 ± 22	0.027
Creatinina sangre (mg/dL)	1.0 ± 0.3	1.3 ± 0.5	0.001
Colesterol total mg/dl	183 ± 190	157 ± 32	0.377
Colesterol HDL, mg/dl	46 ± 14	38 ± 11	0.002
Colesterol LDL, mg/dl	87 ± 26	88 ± 25	0.891
Triglicéridos (mg/dL)	140 ± 82	173 ± 75	0.005
Albumina sangre (g/dL)	5 ± 4	4 ± 0	0.011
Fosfatasa alcalina (u/L)	78 ± 23	84 ± 22	0.087
25 OH Vit D3 (ng/ml)	30 ± 15	26 ± 13	0.129
Coc, Alb/creat orina (mg/g)	25 ± 49	152 ± 271	<0.001
Microalbuminuria (mg/dL)	6 ± 20	21 ± 34	<0.001
Fitatos_consumidos gr/día	0.41 ± 0.17	0.35 ± 0.20	0.046
Adiponectina (micorg/mL)	0.32 ± 0.12	0.27 ± 0.09	0.047
IL1 beta (picog/mL)	1.2 ± 0.2	1.4 ± 0.5	0.046
IL6 (picog/mL)	1.5 ± 0.7	1.9 ± 1.3	0.099
RAGE (picog/mL)	960 ± 280	1076 ± 455	0.508
AGEs (U/mL)	7.4 ± 3.8	9.1 ± 4.1	0.048
HbA1c (%)	7.4 ± 1.4	7.9 ± 1.4	0.028

Cálculo de punto óptimo de ingesta de fitato asociado a presentación de complicaciones vasculares

Se calculó el punto óptimo de corte asociado a prestar complicaciones vasculares mediante el índice Youden resultando ser una ingesta de fitato superior a 250 mg/día presentando una sensibilidad del 38% y una especificidad del 91%. El área bajo la curva fue de 0,621 (0,497-0,745); $p=0,046$. (Figura 1).

Cálculo de ingesta de fitato en los grupos sin versus con complicaciones vasculares

El grupo sin complicaciones cardiovasculares presenta un consumo de fitato de diario de 408 mg/día (± 165) significativamente superior al del grupo con complicaciones vasculares presenta un consumo de 348 mg/día (± 200) (p -valor=0.046). (Figura 2).

Cálculo de ingesta de fitato asociado a presentación de complicaciones vasculares en función del tiempo

Al evaluar la asociación entre el consumo de fitato y la aparición de un evento cardiovascular en función del tiempo, se encontraron diferencias significativas entre un consumo mayor y menor de 250 mg/día de fitato ($p=0.037$). También, el grupo de mayor consumo de fitato presentaba menor probabilidad de sufrir estenosis aórtica grave ($p=0.001$). (Tabla III).

Probabilidad de estar libre de evento cardiovascular para un consumo estimado de fitato mayor y menor a 250 mg/día

Al analizar la relación entre el consumo de fitato y la aparición de eventos cardiovasculares a lo largo del tiempo, se observaron diferencias significativas entre quienes consumían más de 250 mg/día de fitato y aquellos con un consumo menor ($p=0.037$). Así la probabilidad de estar libre de evento CV a los 5 años fue del 73.7 % y del 36.2% para un consumo superior e inferior a 250 mg/día de fitato, respectivamente. (Figura 3).

Figura 1: Curva COR del fitato con respecto a complicaciones vasculares.

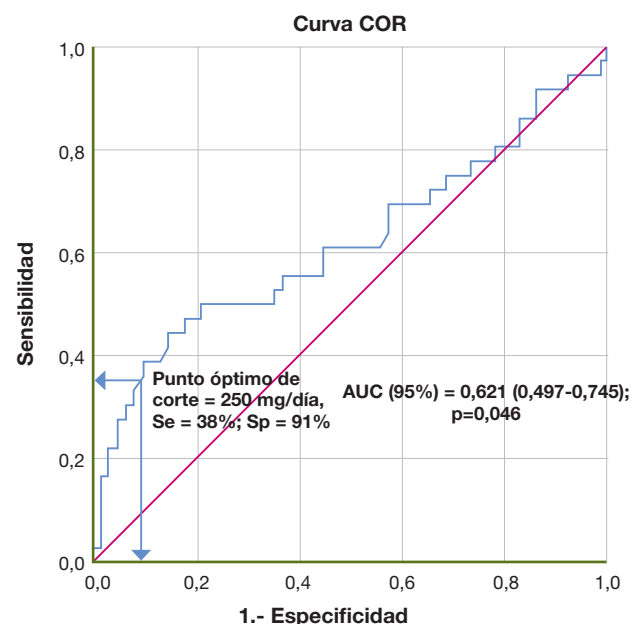


Figura 2: Fitato consumidos por los pacientes con y sin complicaciones vasculares.

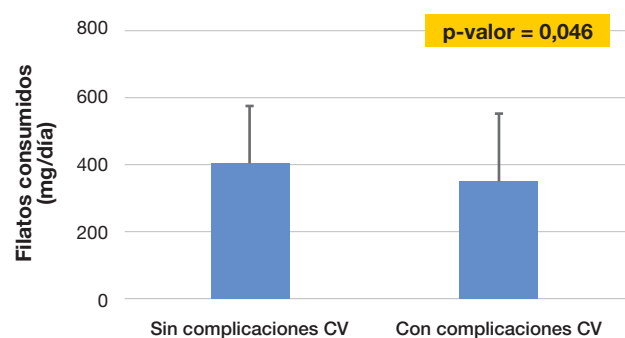


Figura 3: Curva Kaplan-Meier asociada a la probabilidad de estar libre de evento cardiovascular para un consumo estimado de fitato mayor y menor a 250 mg/día. Las diferencias entre grupos se evaluaron usando log Rank (Mantel-Cox).

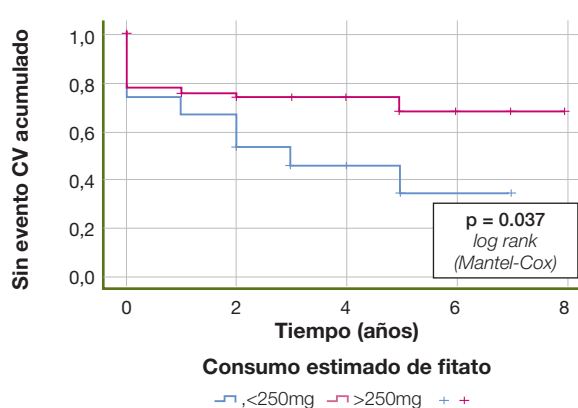


Tabla III: Eventos cardiovasculares en función de la ingesta de fitato.

	Fitato <250 mg/día (n=19)	Fitato ≥250 mg/día (n=82)	Todos (N=101)	p-valor
Exitus	4 (21,1%)	15 (18,3%)	19 (18,8%)	0,752
ICTUS	4 (21,1%)	8 (9,8%)	12 (11,9%)	0,232
E. Coronaria	4 (21,1%)	13 (15,9%)	17 (16,8%)	0,734
I.C.	6 (31,6%)	13 (15,9%)	19 (18,8%)	0,188
ERT	3 (15,8%)	5 (6,1%)	8 (7,9%)	0,170
EAO grave	4 (21,1%)	0 (0,0%)	4 (4,0%)	0,001
I.C.	6 (31,6%)	13 (15,9%)	19 (18,8%)	0,188
Objetivo vascular compuesto	13 (68,4%)	25 (30,5%)	38 (37,6%)	0,037

Discusión

En este trabajo reportamos que los pacientes que presentan mayor número de complicaciones vasculares asimismo presentan menor consumo de fitato. Concretamente, al evaluar la asociación entre el consumo de fitato y la aparición de un evento cardiovascular en función del tiempo, se encontraron diferencias significativas entre un consumo mayor y menor de 250 mg/día de fitato siendo el primer trabajo que propone un punto de corte óptimo para obtener beneficios mediante el consumo de fitato. Así la probabilidad de estar libre de evento CV a los 5 años fue del 73.7 % y del 36.2% para un consumo superior e inferior a 250 mg/día de fitato, respectivamente. Además, las personas que consumen más de 250 mg/día de fitato presentan significativamente mayores niveles de adiponectina y menores de IL-1 β , HbA1c y AGEs. Sin diferencias en IL-6 ni RAGEs.

El fitato podría reducir las complicaciones vasculares a través de varios mecanismos. El fitato puede disminuir el estrés oxidativo al actuar como un quelante del hierro, lo que impide la formación de radicales hidroxilo impulsados por el hierro y disminuye la peroxidación de lípidos^{15,20}. El fitato previene la deposición de hidroxapatita en los vasos sanguíneos, que es un componente clave de la calcificación vascular²¹. El mecanismo de acción del fitato incluye su capacidad para quelar iones de calcio, inhibiendo así la cristalización de las sales de calcio, que son precursores de la calcificación vascular^{15,21}. Además, desempeña un papel clave en la secreción de insulina al regular la homeostasis del calcio^{15,22,23}. Se ha documentado que el fitato inhibe la amilasa, lo que podría ralentizar la digestión y absorción de carbohidratos²⁴. El fitato también influye en el metabolismo lipídico. Investigaciones han mostrado que su suplementación reduce la actividad de la lipasa, el colesterol total, las lipoproteínas de baja densidad (LDL), los lípidos hepáticos totales y los triglicéridos hepáticos, mientras que aumenta los niveles de lipoproteínas de alta densidad (HDL)²⁵. El fitato influye en la composición de la microbiota intestinal, promoviendo el crecimiento de bacterias beneficiosas que producen ácidos grasos de cadena corta (AGCC) como el propionato. Se ha demostrado que estos AGCC mejoran la salud metabólica al fortalecer la integridad de la barrera intestinal y reducir la inflamación sistémica²⁶. Además, el fitato tiene propiedades antioxidantes y antiinflamatorias, que pueden contribuir a sus efectos protectores contra las enfermedades cardiovasculares¹⁵.

El fitato tiene un perfil de acción pleiotrópico, pero destaca especialmente por su capacidad para inhibir la calcificación vascular. Este sería el principal, pero no el único mecanismo, por el cual el fitato reduciría el riesgo cardiovascular. La calcificación vascular es un factor de riesgo significativo para las enfermedades cardiovasculares, especialmente en poblaciones con afecciones como el envejecimiento, la diabetes y la enfermedad renal². Estudios epidemiológicos sugieren

que una mayor ingesta dietética de fitato está asociada con una menor incidencia de calcificación cardiovascular. Fernández-Palomeque et al. con un diseño de estudio transversal encontró una correlación inversa entre los niveles urinarios de fitato y la calcificación del anillo mitral en una población anciana, lo que sugiere que una mayor ingesta de fitato está asociada con una reducción de la calcificación vascular¹⁰. Además, Sanchis et al. realizaron un estudio en pacientes con enfermedad renal crónica (ERC) y encontraron que una mayor ingesta dietética y excreción urinaria de fitato estaban asociadas con puntuaciones más bajas de calcificación de la aorta abdominal¹⁷. Además, estudios en animales han demostrado que el fitato dietético puede reducir significativamente la calcificación aórtica relacionada con la edad²¹.

El consumo de fitato también podría mejorar el control metabólico incidiendo en los niveles de glucosa en personas con diabetes al mejorar la sensibilidad a la insulina y reducir los productos avanzados de glicación (AGEs). Un ensayo cruzado aleatorizado demostró que el consumo diario de suplementos de fitato redujo significativamente los niveles circulantes de AGEs y de hemoglobina glucosilada (HbA1c) en pacientes con diabetes mellitus tipo 2¹³. Los AGEs contribuyen a la resistencia a la insulina y a diversas complicaciones relacionadas con la diabetes (entre ellas la calcificación vascular). Al disminuir los AGEs, el fitato ayuda a mejorar el control metabólico. Además, se ha demostrado que el fitato mejora la sensibilidad a la insulina. Esto se logra mediante mecanismos como la promoción de la diferenciación de adipocitos y el aumento de la captación de glucosa estimulada por insulina, lo cual está mediado por la regulación al alza de factores de transcripción clave y sustratos del receptor de insulina¹⁵.

En nuestro trabajo, que las personas que consumen más de 250mg de fitato diarios presentan mayores niveles de adiponectina. La adiponectina, una adipocina secretada por el tejido adiposo, tiene implicaciones significativas para el riesgo cardiovascular a través de sus efectos sobre la sensibilidad a la insulina y la calcificación vascular. La adiponectina mejora la sensibilidad a la insulina al promover la captación de glucosa y la oxidación de ácidos grasos en los tejidos periféricos. Activa las vías de la proteína quinasa activada por AMP (AMPK) y el receptor activado por proliferadores de peroxisomas alfa (PPAR α), lo que mejora la respuesta a la insulina y reduce la producción hepática de glucosa²⁷. Los niveles elevados de adiponectina se asocian con una menor resistencia a la insulina, lo que es un factor clave para reducir el riesgo cardiovascular²⁸. A la vez, la adiponectina también desempeña un papel protector contra la calcificación vascular. Inhibe la diferenciación osteoblástica de las células musculares lisas vasculares (VSMCs) a través de la vía de señalización AdipoR1/p38 MAPK, reduciendo así la formación de nódulos calcificados. Además, la adiponectina antagoniza los

efectos estimulantes de las citoquinas proinflamatorias como el TNF-alfa en la calcificación de las VSMCs, mitigando aún más la calcificación vascular²⁷. Se ha demostrado que la adiponectina de alto peso molecular (HMMW) inhibe la calcificación vascular en receptores de aloinjertos renales, lo que sugiere su posible papel terapéutico en la prevención de eventos cardiovasculares²⁹. De hecho, nuestro grupo de investigación mostró que la suplementación con 380mg/ tres veces al día de fitato en forma de suplemento durante 12 semanas en un ensayo cruzado aleatorizado aumentó los niveles de adiponectina en suero en pacientes con diabetes mellitus tipo 2³⁰. Este estudio también observó una reducción simultánea en los niveles de HbA1c. Por tanto, los resultados reportados en este trabajo están en la misma línea de los reportados previamente.

A la vez, observamos que las personas que consumen más de 250mg de fitato diarios presentan menores niveles de IL-1 β . Esta es una citocina proinflamatoria que juega un papel crucial en la patogénesis de la aterosclerosis y otras enfermedades cardiovasculares. Es producida por la activación del inflammasoma NLRP3, que participa en la respuesta inflamatoria dentro de las placas ateroscleróticas. Los niveles elevados de IL-1 β contribuyen a la formación, progresión y desestabilización de las placas ateroscleróticas, lo que aumenta el riesgo de infarto de miocardio (IM) y otros eventos cardiovasculares³¹. La evidencia clínica respalda el papel de la IL-1 β en el riesgo cardiovascular. El ensayo CANTOS demostró que el canakinumab, un anticuerpo monoclonal contra la IL-1 β , redujo significativamente la incidencia de eventos cardiovasculares recurrentes en pacientes con antecedentes de IM, destacando el potencial terapéutico de dirigir la IL-1 β para reducir el riesgo cardiovascular. Además, un estudio realizado por Silvain et al. encontró que los niveles elevados de IL-1 β al ingreso estaban asociados de forma independiente con un mayor riesgo de mortalidad por todas las causas y por causas cardiovasculares en pacientes con IM agudo³². La IL-1 β también promueve la inflamación vascular al aumentar el reclutamiento y activación de leucocitos dentro de las placas ateroscleróticas, lo que agrava aún más la inestabilidad de las placas y el riesgo de eventos trombóticos³¹. El papel de esta citocina en la inflamación y la aterogénesis subraya su importancia como objetivo para intervenciones terapéuticas en enfermedades cardiovasculares. En cultivos celulares, el fitato influye en la respuesta inmunitaria, particularmente en el contexto de la inflamación mediada por IL-1 β . Según Weglarz et al., el fitato puede modular la liberación de citoquinas proinflamatorias como IL-8 e IL-6 a partir de células epiteliales del colon estimuladas con IL-1 β y lipopolisacáridos (LPS). Específicamente, el fitato redujo la secreción de IL-8 de manera dependiente de la dosis y reguló a la baja la secreción de IL-6 cuando las células fueron estimuladas por la acción combinada de LPS e IL-1 β ³³. Además, Markiewicz et al. demostraron que el hidrolizado de fitato (hPA120) modula la respuesta

inmunitaria de los colonocitos frente a las bacterias intestinales, afectando la secreción de citocinas, incluida IL-1 β . El estudio encontró que hPA120 disminuyó la expresión de marcadores proinflamatorios como NFkB1 y TNFR en colonocitos sanos, lo que sugiere un posible efecto antiinflamatorio³⁴. Por tanto, nuestro trabajo sería el primero en mostrar en humanos que el consumo de fitato en dosis superiores a 250mg diarios podría modular la respuesta inflamatoria al reducir la secreción y actividad de IL-1 β . Esta modulación puede contribuir a los efectos antiinflamatorios y cardioprotectores generales del fitato, dado el papel establecido de la IL-1 β en la promoción de la inflamación vascular y la aterosclerosis.

También observamos que el consumo de >250 mg/día de fitato consigue una mejoría significativa de la HbA1c hecho que concuerda con resultados obtenidos previamente en otros estudios. La ingesta de fitato está asociada con una reducción en los niveles de HbA1c. Un ensayo cruzado aleatorizado demostró que los pacientes con diabetes mellitus tipo 2 (DM2) que consumieron suplementos de fitato (380 mg de fitato, 3 veces al día) durante tres meses tuvieron niveles significativamente más bajos de HbA1c en comparación con aquellos que no consumieron fitato^{13,30}.

Se ha demostrado que la ingesta de fitato tiene varios efectos beneficiosos sobre los biomarcadores relacionados con la diabetes y la inflamación IL-6, los productos avanzados de glicación (AGEs) y el receptor de productos avanzados de glicación (RAGEs). Sin embargo, en esta cohorte, no hemos detectado una relación significativa entre el consumo de fitato y los niveles de IL-6 ni RAGEs. Un ensayo cruzado aleatorizado demostró que los pacientes con diabetes mellitus tipo 2 (DM2) que consumieron suplementos de fitato (380 mg de fitato, 3 veces al día) durante tres meses no encontró diferencias significativas en los niveles de IL-6 entre los pacientes que consumieron fitato y aquellos que no lo hicieron³⁰. Esto sugiere que, aunque el fitato tiene efectos beneficiosos en otros biomarcadores, su impacto en IL-6 puede ser limitado o variable. Respecto a los AGEs, un ensayo cruzado aleatorizado confirmó que los pacientes con DM2 que consumieron fitato tenían niveles más bajos de AGEs circulantes¹³. Aunque los estudios que vinculan directamente la ingesta de fitato con los niveles de RAGE son limitados, la reducción de AGEs debida al consumo de fitato sugiere un posible efecto en las vías mediadas por RAGE. La unión de AGEs a RAGEs desencadena vías de estrés inflamatorio y oxidativo, por lo que la reducción de AGEs podría mitigar teóricamente estos efectos³⁵.

Los pacientes con complicaciones vasculares presentan un perfil de mayor riesgo, con marcadores de inflamación, disfunción metabólica y enfermedad renal elevados, lo que explica su mayor propensión a desarrollar estas complicaciones. Encontramos que los pacientes con complicaciones vasculares, además de

un menor consumo de fitatos, presentan un mal control de marcadores clásicos de riesgo de enfermedad cardiovascular como son: mayor presión arterial, menor filtrado glomerular, niveles más bajos de HDL, mayores niveles de triglicéridos y mayor cociente albuminuria/creatinina en comparación con los que no presentaron complicaciones. El fitato por sus capacidades descritas como protector frente a la calificación vascular, propiedades antioxidantes y antiinflamatorias, podría mitigar el riesgo asociado a la alteración de la presión arterial y función renal que presentan esta muestra de pacientes. Además, Pujol et al., comenta el fitato mejora el metabolismo de lípidos y carbohidratos, lo que puede contribuir a mejores perfiles lipídicos generales, incluyendo el colesterol HDL y los triglicéridos¹⁵. Por tanto, una dieta mediterránea y no solo eso, una dieta mediterránea con ingesta de más de 250mg/día de fitato, sería una recomendación dietética que podría ejercer un efecto protector en pacientes con alto o muy alto riesgo cardiovascular.

Este estudio presenta varias limitaciones que deben considerarse al interpretar los resultados. En primer lugar, la muestra es relativamente pequeña, con solo 101 pacientes incluidos, lo que puede limitar la capacidad de generalizar los hallazgos a una población más amplia. Aunque este tamaño de muestra es adecuado para un estudio preliminar, sería necesario replicar los resultados en estudios con un mayor número de participantes para obtener conclusiones más robustas. Otra limitación importante es el diseño observacional del estudio. Este tipo de diseño no permite establecer una relación causal directa entre el consumo de fitato y la reducción de complicaciones vasculares, ya que solo se pueden observar correlaciones. Existen otros factores no controlados que podrían haber influido en los resultados, por lo que no se puede afirmar con certeza que el fitato sea la única variable responsable de los efectos observados. Además, la estimación del consumo de fitato se basó en cuestionarios de frecuencia alimentaria, que dependen de la memoria y precisión de los participantes. Este método puede dar lugar a una subestimación o sobreestimación

del consumo real de fitato, lo que introduce una fuente de variabilidad en los resultados. Otra limitación es la falta de correlación significativa entre el consumo de fitato y ciertos biomarcadores clave, como los RAGEs o IL-6, a pesar de haber encontrado asociaciones significativas con adiponectina, AGEs e IL-1 β . Esto sugiere que podrían estar influyendo otros factores no medidos que afectan los resultados observados. El tiempo de seguimiento, con una media de cinco años, puede no ser suficiente para captar completamente los efectos a largo plazo del consumo de fitato sobre las complicaciones vasculares, lo que limita la interpretación de los hallazgos en términos de prevención a largo plazo. Finalmente, el hecho de que sea un estudio unicéntrico, realizado en un único centro hospitalario en las Islas Baleares, limita la diversidad de la muestra. Esto significa que los resultados pueden no ser aplicables a otras poblaciones con diferentes características geográficas, socioeconómicas o culturales. Estudios multicéntricos, que incluyan participantes de diversas áreas, serían necesarios para confirmar la validez de estos hallazgos en otras poblaciones. En resumen, aunque este estudio ofrece resultados prometedores sobre el potencial efecto protector del fitato en las complicaciones vasculares de pacientes con diabetes tipo 2, necesitamos más estudios que confirmen los hallazgos.

Conclusiones

El consumo adecuado de fitato (>0.25 g/d) podría tener un efecto protector sobre la aparición de complicaciones vasculares en los pacientes con diabetes de alto y muy alto riesgo cardiovascular. Encontramos un efecto significativo en los niveles de adiponectina, AGEs, IL-1 β y HbA1c. Sin embargo, en esta cohorte, no hemos detectado una relación significativa entre el consumo de fitato y los niveles de IL-6 y RAGEs.

Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses.

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ORIGINAL

Dieciséis millones y medio de turistas al año y el indicador de consumo de antibióticos en las Illes Balears

Sixteen and a half million tourists a year and the indicator of antibiotic consumption in the Balearic Islands

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Resumen

Introducción: La Unión Europea ha aprobado unos objetivos de reducción del consumo de antibióticos para combatir la resistencia a los mismos. El consumo se calcula en DHD (dosis diaria definida por cada 1.000 habitantes/día). El objetivo de este artículo es estimar el impacto de la población flotante en los datos de consumo y proponer alternativas de cálculo del indicador ajustado a la población real.

Material y Método: Se recalculó el consumo de antibióticos en las Illes Balears empleando dos "poblaciones ficticias", utilizando el indicador de presión humana publicado por IBESTAT (Instituto de Estadística de las Illes Balears) y teniendo en cuenta la estancia media de los turistas extranjeros y nacionales, ponderando por el peso de los mismos.

Resultados: El consumo recalculado con población IBESTAT es de 16,25 DHD (receta oficial 8,60; mutuas 0,34; receta privada 6,09; consumo total comunitario 15,02 y consumo hospitalario público 1,23) con un descenso respecto a los valores oficiales del 23,26%. En el segundo escenario el consumo fue de 16,57 (receta oficial 8,77; Mutuas 0,34; receta privada 6,20; consumo total comunitario 15,32 y consumo hospitalario público 1,25) con un descenso del 21,76%. En ambos casos supondría prácticamente alcanzar el objetivo 2030 de reducción para las Illes Balears.

Discusión: Conocer la población real que estamos tratando es fundamental para estimar consumos, parametrizar las intervenciones ligadas a esos consumos e identificar espacios de reducción y mejora. En comunidades autónomas que reciben mucha población flotante durante el año, está justificado ajustar el denominador poblacional para corregir una sobreestimación del indicador.

Palabras clave: Agentes antibacterianos, Resistencia Antimicrobiana, Reglamento Sanitario Internacional, Prescripción de antibióticos, Administración de antibióticos.

Abstract

Introduction: The European Union has approved targets for reducing antibiotic consumption to combat antibiotic resistance. Consumption is calculated in DHD (defined daily dose per 1,000 inhabitants/day). The objective of this article is to estimate the impact of the floating population on consumption data and to propose alternatives for calculating the indicator adjusted to the real population.

Material and Method: The consumption of antibiotics in the Balearic Islands was recalculated using two "fictitious POPULATIONS", using the human pressure indicator published by IBESTAT (Statistics Institute of the Balearic Islands) and taking into account the average stay of foreign and national tourists, ponderated by their weight.

Results: The recalculated consumption with the IBESTAT population is 16.25 DHD (official prescription 8.60; mutual insurance 0.34; private prescription 6.09; total community consumption 15.02 and public hospital consumption 1.23) with a decrease compared to the official values of 23.26%. In the second scenario, consumption was 16.57 (official prescription 8.77; mutual insurance 0.34; private prescription 6.20; total community consumption 15.32 and public hospital consumption 1.25) with a decrease of 21.76%. In both cases it would mean practically reaching the 2030 reduction objective for the Balearic Islands.

Discussion: Knowing the real population we are treating is essential to estimate consumption, parameterize the interventions linked to that consumption and identify spaces for reduction and improvement. In autonomous communities that receive a large floating population during the year, it is justified to adjust the population denominator to correct an overestimation of the indicator.

Key words: Anti-Bacterial Agents, Drug Resistance, Microbial, International Health Regulations, Antibiotic prescription, Antibiotic stewardship.

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Introducción

La Comisión Europea y todos los estados miembros han identificado la resistencia a los antimicrobianos (RAM) como una de las tres principales amenazas prioritarias para la salud¹.

Se estima que más de 35.000 personas mueren cada año en la UE como consecuencia directa de una infección debida a bacterias resistentes a los antibióticos². En términos comparativos, se considera que debido a las RAM mueren el equivalente de las personas que fallecen por la gripe, la tuberculosis y el VIH/SIDA juntos.

Además, esta situación está empeorando con una tendencia creciente en los últimos años³. Preocupa también que esta tendencia es especialmente significativa en entornos sanitarios donde el 70% de los casos de infecciones por bacterias resistentes a los antibióticos fueron infecciones relacionadas con la asistencia sanitaria.

También se identifica un problema a corto y medio plazo con la investigación en nuevos antibióticos. La OMS en sus informes anuales sobre investigación y desarrollo tiene registrados, para el periodo 2017-2023⁴, un total de 128 nuevas moléculas. En ese mismo periodo, únicamente se han aprobado 16 nuevos antibióticos, la mayoría de los cuales tienen un beneficio clínico limitado. Destaca del informe que los estudios de nuevos antimicrobianos contra patógenos considerados prioritarios han pasado de 31 en 2017⁵ a 43 en 2023⁶. Hace falta ver cuántos de ellos acabarán demostrando su eficacia y siendo aprobados finalmente.

En la base de este problema se encuentra el uso inadecuado de los antibióticos. Pese a que la información dirigida a los ciudadanos ha incidido sobre esta preocupación y sobre la concienciación en hacer un buen uso de los antimicrobianos, estudios recientes siguen identificando que la mitad de la población europea desconoce que los antibióticos son ineficaces contra los virus y que un 10% sigue utilizándolos sin receta médica⁷.

También se ha identificado la necesidad de continuar con programas de actualización en la utilización de antibióticos entre los profesionales sanitarios prescriptores. Se estima que hasta un 70% de las prescripciones en atención primaria podrían ser inadecuadas. Esto supone 23 millones de prescripciones al año en la UE, con un ahorro potencial de 114 millones de euros⁸. Numerosos estudios han identificado la existencia de prescripción inadecuada de antibióticos en otros ámbitos como hospitales de agudos^{9,10}, servicios de urgencias¹¹, áreas de rehabilitación¹², o centros sociosanitarios. Todos ellos inciden en la necesidad de desarrollar estrategias para mejorar este problema, entre ellas, los programas de formación a prescriptores.

Desde el punto de vista del impacto económico, las RAM generan un gasto sanitario adicional en la UE de unos 1.500 millones de euros¹³. Otros estudios sitúan los costes para España en unos 150 millones de € al año^{14,15}.

El medio ambiente y las actuaciones en salud animal también tienen impacto en las RAM. Diversas facetas y diversos sectores implicados hacen que desde la UE se haya propuesto abordar las RAM desde el concepto de «Una sola salud» (*One Health*), abarcando la salud humana, la salud animal, la fitosanidad y el medio ambiente. Además, la diversidad de esta amenaza hace que no se pueda abordar desde un sector de forma independiente ni desde cada país por separado¹⁶.

El problema de las RAM es, por tanto, real, de una gran magnitud que requiere ser considerado como un problema ecológico que trasciende lo puramente sanitario.

Con todas estas consideraciones, si nos centramos en la salud humana, la principal medida a implementar es reducir la utilización inadecuada.

Para ello es necesario implementar estrategias que ayuden a la toma de decisiones de los prescriptores: guías clínicas actualizadas y accesibles, contemplando las resistencias en los entornos locales; test de diagnóstico rápido en el punto de atención, incluyendo atención primaria y urgencias (*Streptococo* grupo A, PCR, test COVID y gripe)^{17,18}; ayudas a la prescripción^{19,20,21} desde receta electrónica; programas de prescripción diferida²², presentaciones en envases ajustados a la pauta prescrita para evitar sobrantes²³, y la implementación de los PROA (Programas de Optimización de uso de Antibióticos) en hospitales y atención primaria^{24,25,26,27}.

En este contexto la UE ha aprobado unos objetivos recomendados para todos los países miembros que abarcan distintos aspectos²⁸. En el objetivo concreto de reducción de consumos la propuesta es que, en el año 2030, el consumo total de antibióticos en el ser humano, medido como dosis diaria definida (DDD) por cada 1.000 habitantes al día, en los sectores comunitario y hospitalario juntos, se reduzca en un 20% en comparación con el año de referencia 2019.

Esta propuesta contempla también que al menos el 65 % del consumo total de antibióticos en el ser humano pertenezca al grupo «antibióticos de acceso» definido en la clasificación AWaRe de la OMS. Y se complementa con otros objetivos como son la reducción de incidencia de septicemias provocadas por *Staphylococcus Aureus* resistente a la Meticilina (SARM) en un 15%, la incidencia total de septicemias por *Escherichia Coli* resistente a la Cefalosporina de tercera generación en un 10%, la incidencia total de septicemias por *Klebsiella Pneumoniae* resistente al Carbapenem en un 5% comparados con las incidencias de los datos de 2019.

Además, propone establecer indicadores que evalúen la consecución de los objetivos recomendados, y es en ese punto concreto dónde se sitúa nuestro trabajo.

La reducción propuesta a España es del 27% (3% anual), que, a su vez, desde la Agencia Española del Medicamento y Productos Sanitarios (AEMPS) se ha trasladado a las distintas CCAA. En nuestro caso, teniendo en cuenta el punto de partida de los consumos del año 2019, supone un descenso del 2,6% anual.

La forma de calcular los consumos se realiza con el cálculo de las DHD (dosis diaria definida (DDD) por cada 1.000 habitantes al día) que se puede entender como el número de personas por cada mil en tratamiento antibiótico cada día del año.

El denominador para estimar este cálculo es, en España, el dato oficial del padrón anual. En ese contexto, la pregunta de investigación que nos hemos planteado es cómo puede afectar a ese denominador poblacional recibir al año 16.5 millones de turistas. Nuestro análisis se dirige a estimar el impacto de la población flotante que recibimos en las Illes Balears, recalcular las DHD del consumo de antibióticos y relacionarlo con los objetivos de reducción de consumos hasta 2030.

Material y método

Para el cálculo de las DHD (Dosis por mil habitantes día) la UE y la AEMPS utiliza la siguiente fórmula:

$$DHD = [(N^{\circ} DDD * 1.000_{\text{habitantes}}) / (\text{población} * 365_{\text{días}})]$$

Siendo “Nº DDD” el Σ de DDD por envase prescrito y “POBLACIÓN” la población empadronada reconocida por el INE para cada territorio.

El resultado se interpreta como el número de personas de un territorio que consumen antibióticos por día y por mil personas.

Para recalcular los datos de consumo de antibióticos en las Illes Balears, se ha estimado una “POBLACIÓN ficticia” calculada a partir del indicador de presión humana publicado por IBESTAT (Instituto de estadística de las Illes Balears), ambos para el mismo año 2022²⁹.

Esta población la hemos calculado para dos escenarios distintos. En el primer caso se han calculado en base a la media de la población máxima y de la población mínima estimada para cada mes de 2022 y para el año completo por IBESTAT.

En el segundo escenario, hemos estimado la población teniendo en cuenta la estancia media de los turistas extranjeros, la estancia media de los turistas nacionales, ponderando por el peso de los mismos en el total de turistas, para cada mes y para el año completo de 2022.

Resultados

En la **tabla I** se detallan los datos de consumo de antibióticos del año 2022 en DHD del SNS y de las CCAA publicados en la página web del PRAN de la AEMPS³⁰. El consumo medio para España es de 22,81 DHD, mientras que en las Illes Balears es de 21,18 DHD. Las Illes Balears se han situado, en los últimos años, siempre por debajo de la media nacional de consumo. Destaca, sin embargo, que tanto en consumo hospitalario como, sobre todo, en consumo de recetas privadas, nos situamos por encima de la media estatal.

La población de Baleares para el año 2022 según los datos del padrón del INE es de 1.176.659 habitantes.

En la **tabla II** se detallan los valores de población máxima y mínima del indicador de presión humana estimados por IBESTAT teniendo en cuenta la población flotante que cada día se encuentra en la CA. Este indicador se construye mediante la suma de las estimaciones diarias de población residente y población estacional.

En la **tabla III**, se presentan las diferencias entre los datos de padrón y de las estimaciones de población flotante. Según estas estimaciones, se observan incrementos máximos del 75,28% y mínimos del 2,51% sobre el padrón en función de los distintos meses del año.

Para calcular las nuevas DHD, en primer lugar, hemos obtenido las DDD a partir de los datos oficiales y seguidamente hemos sustituido el denominador de padrón por el recalculado, contemplando dos escenarios posibles. En el primero, hemos utilizado la población media anual a partir de las cifras mensuales de población estimadas por IBESTAT, que es de 1.533.404 habitantes. En el segundo escenario, hemos tenido en cuenta la estancia media de los turistas extranjeros y la estancia media de los turistas nacionales y ponderando por el peso de los mismos en el total de turistas, la cifra obtenida de este modo es de 1.503.946 habitantes. Los resultados de estas estimaciones y del recalcado de las DHD para el año 2022 en las Illes Balears son los que se ofrecen en la **tabla IV**.

El consumo recalculado en el primer escenario es de 16,25 DHD para el consumo global desagregado de la siguiente manera: receta oficial 8,60; mutuas 0,34; receta privada 6,09; consumo total comunitario 15,02 y consumo hospitalario público 1,23. Esto supone un descenso respecto a los valores oficiales del 23,26%. En el segundo escenario, los resultados obtenidos son los siguientes: receta oficial 8,77; Mutuas 0,34; receta privada 6,20; consumo total comunitario 15,32 y consumo hospitalario público 1,25, para un consumo global de 16,57. En este caso, el descenso sobre los valores oficiales sería del 21,76%. Con ello, en ambos casos supondría prácticamente cumplir el objetivo 2030 para las Illes Balears que es de 16,81 DHD.

Tabla I: Consumo de antibióticos sector comunitario, sector hospitalario y total por CCAA y SNS. Año 2022. Fuente: elaboración propia a partir de datos publicados por la AEMPS.

2022	Consumo TOTAL [A+B]	Consumo sector hospitalario [A]	Consumo sector comunitario [B]	Receta Oficial [B1]	Mutuas [B2]	Receta Privada [B3]
Andalucía	23,24	0,95	22,29	15,44	1,14	5,71
Aragón	22,41	1,50	20,91	13,90	0,92	6,10
Asturias	23,52	1,60	21,92	16,10	0,81	5,02
Canarias	22,23	1,20	21,03	14,14	0,66	6,24
Cantabria	25,02	1,68	23,34	17,72	0,75	4,87
Castilla La Mancha	26,20	1,43	24,77	19,07	1,02	4,68
Castilla y León	25,27	1,70	23,57	16,71	1,29	5,57
Cataluña	21,38	1,31	20,07	11,37	0,29	8,40
Comunidad Valenciana	25,16	1,33	23,83	15,40	0,75	7,67
Extremadura	26,77	1,56	25,21	18,30	1,37	5,54
Galicia	24,19	1,83	22,36	15,62	1,00	5,74
Illes Balears	21,18	1,60	19,58	11,21	0,44	7,93
La Rioja	24,34	2,17	22,17	15,12	0,77	6,27
Madrid	20,98	1,30	19,68	11,14	0,92	7,62
Murcia	25,14	1,24	23,90	16,66	1,10	6,14
Navarra	19,40	1,22	18,18	14,34	0,46	3,39
País Vasco	19,08	1,48	17,60	12,73	0,22	4,66
SNS	22,81	1,26	21,55	14,16	0,82	6,56

Tabla II: Estimaciones de población máxima y mínima del indicador de presión humana las Illes Balears. Datos mensuales año 2022. Fuente IBESTAT.

	máximo	mínimo
ENERO	1.225.976	1.213.311
FEBRERO	1.257.325	1.226.873
MARZO	1.351.174	1.254.217
ABRIL	1.544.446	1.365.717
MAYO	1.735.446	1.527.479
JUNIO	1.859.370	1.732.215
JULIO	2.032.116	1.861.339
AGOSTO	2.062.428	1.861.786
SEPTIEMBRE	1.861.473	1.696.411
OCTUBRE	1.698.376	1.373.916
NOVIEMBRE	1.366.053	1.245.402
DICIEMBRE	1.241.861	1.206.980

Tabla III: Diferencias entre los datos de padrón y de las estimaciones de población flotante. Datos mensuales año 2022. Fuente: elaboración propia a partir de datos IBESTAT.

2022	diferencia máxima respecto a padrón	diferencia mínima respecto a padrón	diferencia promedio respecto a padrón	incremento máximo respecto a padrón	incremento mínimo respecto a padrón	incremento promedio respecto a padrón
ENERO	49.317	36.652	42.985	4,19%	3,11%	3,65%
FEBRERO	80.666	50.214	65.440	6,86%	4,27%	5,56%
MARZO	174.515	77.558	126.037	14,83%	6,59%	10,71%
ABRIL	367.787	189.058	278.423	31,26%	16,07%	23,66%
MAYO	558.787	350.820	454.804	47,49%	29,81%	38,65%
JUNIO	682.711	555.556	619.134	58,02%	47,21%	52,62%
JULIO	855.457	684.680	770.069	72,70%	58,19%	65,45%
AGOSTO	885.769	685.127	785.448	75,28%	58,23%	66,75%
SEPTIEMBRE	684.814	519.752	602.283	58,20%	44,17%	51,19%
OCTUBRE	521.717	197.257	359.487	44,34%	16,76%	30,55%
NOVIEMBRE	189.394	68.743	129.069	16,10%	5,84%	10,97%
DICIEMBRE	65.202	30.321	47.762	5,54%	2,58%	4,06%

Tabla IV: Estimaciones consumo de antibióticos sector comunitario, sector hospitalario y total por CCAA y SNS. Año 2022. Escenarios 1 y 2.

2022	Receta Oficial	Mutuas	Receta Privada	Σ Consumo sector comunitario	Consumo sector hospitalario	Σ Consumo TOTAL
DHD CAIB oficial	11,21	0,44	7,93	19,58	1,6	21,18
DHD recalculadas_e1	8,60	0,34	6,09	15,02	1,23	16,25
DHD recalculadas_e2	8,77	0,34	6,20	15,32	1,25	16,57

Discusión

Los datos sobre consumo de antibióticos son fundamentales a la hora de establecer estrategias para reducirlo o mejorar la calidad de prescripción de los mismos. Disponer de un indicador consensuado internacionalmente es indispensable para la comparación entre países y para la fijación de objetivos, en este caso, de reducción de consumos.

No obstante, es también necesario disponer de datos fiables y comparables entre diferentes territorios. En el caso de las DHD, la estimación del numerador (DDD) se apoya en estándares internacionales que pueden no ajustar especialmente bien en el caso de algún tipo de asociaciones de fármacos o en el caso de las prescripciones para pediatría, pero que, en términos generales, aplicarían los errores a todo el universo de casos.

Sin embargo, en nuestro trabajo, ponemos el foco en el denominador del indicador. La hipótesis de partida es que el denominador basado en el padrón poblacional podría ser corregido por el impacto de la población flotante, de modo que se aproxime mejor al valor real de la población que realiza ese consumo.

En nuestro caso, el tema es especialmente relevante por varios motivos. En primer lugar, porque las Illes Balears recibe al año una población flotante (extranjeros y nacionales) que multiplica prácticamente por catorce la población oficial de residentes anual.

En segundo lugar, la distribución de esta población flotante a lo largo del año traspasa la tradicional estacionalidad. Las estancias que hasta hace unos años se limitaban a los meses de verano, ahora tienen lugar durante todo el año, tal y como puede observarse en los datos del indicador de población humana. En todos los meses del año, la población máxima y mínima estimada está por encima del valor de población oficial del padrón publicado por el INE. Además, prácticamente durante seis meses al año las cifras de población estimadas se sitúan por encima del 50%, llegando a valores superiores al 70% en los meses de mayor presión humana de la población residente del INE, y en ningún mes del año el balance entradas/salidas es negativo.

Otro factor a tener en cuenta son las características de esa población flotante. Si bien es verdad que durante los meses de verano se trata de un grupo bastante heterogéneo, se sabe que, en el caso de los meses de invierno, esta población tiene un perfil de personas de edad avanzada que pasan la época invernal en nuestras islas. Si tenemos en cuenta que el consumo de antibióticos se dispara en las edades avanzadas, se trata pues de una población susceptible de consumir estos medicamentos.

Cuando analizados los consumos desglosados por su origen, vemos que, según los datos publicados por el Ministerio, el consumo de Baleares en receta oficial y mutuas está por debajo de la media del SNS y, en cambio, el consumo de receta privada y hospitalario es superior. Estos datos se podrían explicar porque la población flotante extranjera utiliza de forma preferente la medicina privada del ámbito comunitario, pero los ingresos se producen, además de en los hospitales privados, también en los públicos de nuestra comunidad autónoma.

Nos encontramos ante la dificultad para calcular denominadores poblaciones que se aproximen a la realidad y que son fundamentales para hacer una adecuada estimación de los consumos.

La cuestión que nos hemos planteado es si realmente existe un impacto de la población flotante en el volumen de consumos de antibióticos de la comunidad autónoma. Nuestra opinión es que disponemos de algunos indicadores indirectos que nos permiten pensar que existe dicho impacto. Uno de ellos se encuentra relacionado directamente con el volumen de prescripción y tiene que ver con que seamos la segunda CCAA del estado con el mayor número de DHD de recetas privadas (un 21% por encima de la media nacional para los datos del año de estudio), y recordamos aquí la obligatoriedad de dispensar los antibióticos con receta médica que tienen las oficinas de farmacia. El segundo indicador es que se han identificado cepas resistentes concretas introducidas en CAIB importadas del extranjero y no de la península^{31,32}. El tercero que manejamos es que existe un patrón de consumos que está asociado a consumos elevados de antibiótico para las enfermedades de transmisión sexual³³ relacionados con los meses de verano que, en nuestro caso, es cuando se recibe más población flotante.

Cualquiera de los dos escenarios que planteamos con nuestro trabajo mejoran considerablemente el indicador de DHD y permite situar a las Illes Balears prácticamente en los niveles de consumo que propone la Unión Europea para el año 2030.

Este trabajo presenta una serie de limitaciones. La primera es que las estimaciones que hacemos de los denominadores para los dos escenarios que planteamos son poco sofisticadas, si bien se basan en los modelos utilizados por el IBESTAT para calcular el índice de presión humana que presentan cierta complejidad metodológica³⁴. Pese a su simplicidad, entendemos que se puede aproximar mejor al número real de residentes en las islas que el dato del padrón.

La segunda es que asumimos que la población flotante seguirá los mismos patrones de consumo que la población residente y eso puede no ser cierto.

Igualmente asumimos que los estilos de práctica de los médicos prescriptores serán los mismos frente a una persona residente que frente a una persona que esté de paso por nuestro territorio, sin tener en cuenta que podría haber diferencias que agrandarían aún más la variabilidad en la práctica clínica que contrastamos en los análisis de variaciones³⁵.

Sin embargo, pese a todas estas limitaciones, entendemos que es necesario mejorar la aproximación a la población real que soporta un territorio y que influirá en la utilización de recursos. Pensamos que nuestra propuesta mejora la utilización de un dato estático como es el del padrón y abre la puerta a nuevas investigaciones basadas, por ejemplo, en el análisis de series temporales de consumo mes a mes sobre población susceptible y real u otros modelos estadísticos aplicables.

A partir de los resultados obtenidos, proponemos las siguientes conclusiones:

- En comunidades autónomas que reciben mucha población flotante durante el año, está justificado ajustar el denominador poblacional en los cálculos

de consumo de antibióticos para corregir una sobreestimación del indicador que tiene un alto impacto tanto en la comparación entre territorios como cuando se proponen objetivos de reducción a corto y medio plazo.

- Hay que valorar cuidadosamente, teniendo en cuenta lo anterior, los indicadores para reducir consumos basados en denominadores poblacionales estáticos, así como las medidas que se implementen basándose en esos indicadores
- Conocer la población real que estamos tratando es fundamental para estimar consumos, parametrizar las intervenciones ligadas a esos consumos e identificar espacios de reducción y mejora.

Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses relacionado con el artículo.

También declaran que las opiniones expresadas son de exclusiva responsabilidad de los autores y no representan el pensamiento u opinión formal de la institución para la que trabajan.

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Estigmatización de las personas con enfermedades crónicas. Revisión bibliográfica

Stigmatization of People with Chronic Illnesses: Review

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Resumen

Introducción: El Estigma es un concepto que implica discriminación y autopercepción. Cuando se asocia a enfermedades crónicas y limitantes puede tener un impacto en la vida de los afectados en el ámbito personal, social y laboral, entre otros.

Metodología: Se revisa la bibliografía médica (PUB MED) referida a los últimos 10 años (2014-2025) relativa a estigmatización por enfermedad crónica, destacando: enfermedades mentales, dolor crónico HIV, COVID-19, Obesidad, enfermedades reumáticas/autoinmunes y epilepsia; se revisan las publicaciones relacionando el impacto del estigma por enfermedad en el ámbito social y laboral: salud laboral, prevención de riesgos, medicina del trabajo, lugar de trabajo y cuidado de la salud. Se comentan finalmente algunas de las publicaciones más representativas.

Resultados: El mayor número de publicaciones corresponden al concepto estigma asociado a enfermedades mentales y salud mental, destacando algunas de ellas como depresión y esquizofrenia; las relacionadas con HIV y con Covid-19. En el ámbito preventivo destacan las publicaciones relativas al impacto social, laboral y a su prevención global.

Conclusiones: El estigma por enfermedad forma parte de la investigación científica como variable de utilidad en patologías crónicas, limitantes y que tienden a ocultarse para evitar discriminación. Como estrategias preventivas se propone: educación, formación e información en el ámbito laboral y social, apoyar emocionalmente a los afectados, abrir vías de comunicación eficaces en la relación médico-paciente y hacerlas visibles para que se pueda avanzar en investigación, prevención y en cuidado de la salud atendiendo a la legislación preventiva y social vigente en España y países de nuestro entorno.

Palabras clave: Estigma, enfermedad crónica, enfermedad mental, obesidad.

Abstract

Introduction. Stigma is a concept that involves discrimination and self-perception. When associated with chronic and limiting illnesses, it can significantly impact the personal, social, and professional lives of affected individuals.

Method: A review of medical literature (PUBMED) from the last 10 years (2014–2025) was conducted, focusing on stigma related to chronic diseases. Key areas of emphasis included mental illnesses, chronic pain, HIV, COVID-19, obesity, rheumatic/autoimmune diseases, and epilepsy. Publications exploring the social and occupational impacts of disease-related stigma were analyzed, covering topics such as occupational health, risk prevention, workplace health, and care. Finally, some of the most representative studies were discussed.

Results: The majority of publications addressed the concept of stigma associated with mental health and mental illnesses, with particular attention to conditions like depression and schizophrenia, as well as HIV and COVID-19. In the preventive context, studies highlighted the social and occupational impact of stigma and the importance of global prevention strategies.

Conclusion: Disease-related stigma is a recognized area of scientific research and a valuable variable in the study of chronic and limiting conditions, which are often concealed to avoid discrimination. Preventive strategies include education, training, and dissemination of information in social and occupational settings, providing emotional support to affected individuals, fostering effective doctor-patient communication, and increasing visibility to advance research, prevention, and health care. These measures should align with existing preventive and social legislation in Spain and comparable countries.

Key words: Stigma, Chronical illness, Mental illness, obesity.

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Introducción

El estigma, según lo define la Organización Mundial de la Salud, es la marca que excluye a una persona de las demás y que disminuye su valor en el grupo social al que pertenece¹. La Real Academia de la Lengua Española incluye el término estigmatizar para hacer referencia a afrentar, mancillar, deshonrar o injuriar². En todos los casos, implica una correlación entre discriminación, estigma y autopercepción³.

Cuando el estigma se asocia a enfermedades crónicas puede tener un impacto significativo en la vida de las personas que las padecen y en distintos ámbitos: personal, social y laboral, entre otros.

Es objetivo de este trabajo revisar la bibliografía médica relativa a la estigmatización por enfermedad crónica, destacando algunas de las patologías más prevalentes y su impacto en el ámbito social y laboral

Metodología

Se realizó una revisión en enero de 2025 de la literatura científica recogida en Pub Med para analizar publicaciones relacionadas con estigma y enfermedades crónicas y su repercusión, sin límite de tiempo en su concepto global (stigma) y referida a los últimos 10 años (2014-2024) asociado a enfermedades: stigma and mental health, mental diseases, depression, schizophrenia, psychosis, bipolar disorders, HIV, obesity, diabetes, migraine, epilepsy, fibromyalgia, lupus, COPD, covid-19, cancer, chronic pain; Finalmente, se consideró la inclusión de las revisiones que hacían referencia al estigma y su componente social, preventivo u ocupacional: stigma and occupational health, occupational medicine, workplace, risk prevention, occupational risk prevention, occupational risk, occupational health care; social stigma and disease, occupational stigma.

Resultados

La búsqueda inicial del estigma como concepto genérico y sin acotar el tiempo de búsqueda identificó 47.845 documentos, que luego se delimitaron al periodo 2000-2025, obteniendo 46.671 documentos (**Gráfico 1**), asumiendo el sesgo de la probable no inclusión de publicaciones de los dos últimos años, que se incorporan a la base de datos de forma paulatina y más tardía.

Cuando el concepto de estigma se asocia a enfermedades crónicas de alta prevalencia, los resultados muestran que el mayor número de publicaciones corresponden al concepto estigma asociado a enfermedades mentales y salud mental, destacando algunas de ellas como depresión y esquizofrenia; también son abundantes las relacionadas con HIV y con Covid-19 (**Tabla I**). (**Gráfico 2**). (**Gráfico 3**).

Cuando el concepto de estigma se asocia al ámbito preventivo-laboral y social, destacan las publicaciones relativas al impacto social o laboral y a su prevención global, siendo más reducidas las relacionadas con aspectos concretos, como factores de riesgo laboral lugar de trabajo, medicina del trabajo o salud laboral (**Gráfico 4**).

Gráfico 1: Estigma. Publicaciones Pub Med.

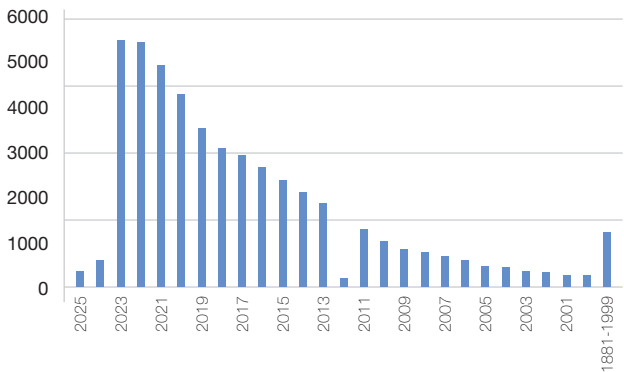
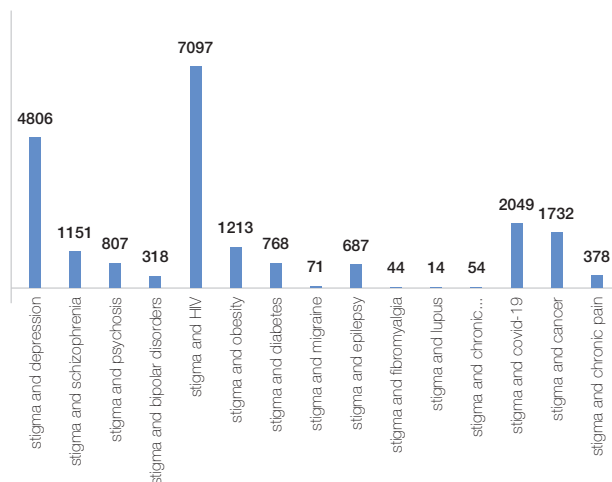
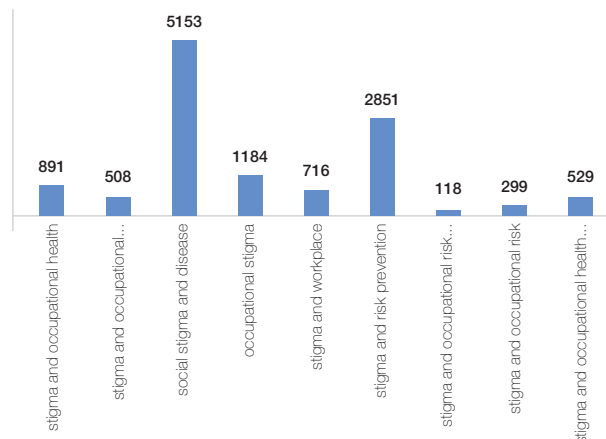
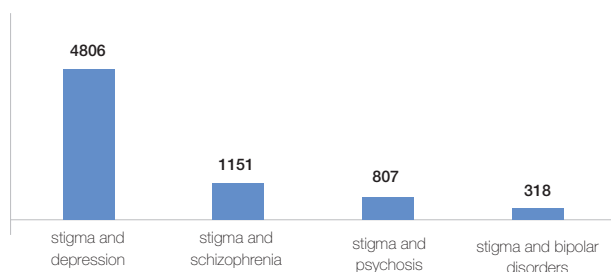


Tabla I: Estigma según el tipo de enfermedad.

Estigma y enfermedad asociada	Número de publicaciones	
stigma and mental health	11278	7082
stigma and mental diseases	1868	
stigma and depression	4806	
stigma and schizophrenia	1151	
stigma and psychosis	807	
stigma and bipolar disorders	318	
stigma and HIV	7097	7082
stigma and obesity	1213	
stigma and diabetes	768	
stigma and migraine	71	
stigma and epilepsy	687	
stigma and fibromyalgia	44	
stigma and lupus	14	
stigma and chronic obstructive pulmonary disease	54	
stigma and covid-19		
stigma and cancer	1732	
stigma and chronic pain	378	

Gráfico 2: Estigma según el tipo de enfermedad (2000-2024).

Gráfico 4: Estigma social y laboral (2000-2024).

Gráfico 3: Estigma y enfermedades mentales (2000-2024).


Discusión

La estigmatización por enfermedad ha adquirido gran relevancia en los últimos años, especialmente en el campo de la psiquiatría y en otros ámbitos médicos. Se asocia a diversas causas, entre las que destacan la falta de conocimiento sobre la enfermedad, la dificultad en algunas de ellas de objetivar la causa que las produce, especialmente en las que cursan con dolor crónico, los prejuicios socioeconómicos y culturales y, de forma general, un conjunto de todos ellos. Así lo especifica la Asociación Americana de Psiquiatría, resaltando este grupo de patologías como enfermedades destacadas en estigmatización⁴.

La legislación en nuestro país y la legislación internacional establecen unos derechos de igualdad y no discriminación que forman parte de la Declaración Universal de Derechos Humanos⁵, incluyendo el derecho a la salud y al trabajo, refrendado este último por el Convenio 111 de la OIT desde 1958 y recogido también en nuestra legislación española⁶.

Del mismo modo, la Convención sobre los Derechos de las Personas con Discapacidad (CDPD) de 2006 fue ratificada en nuestra legislación en 2008⁷ y protege los derechos de personas con enfermedades crónicas o discapacidades.

En nuestro país, se han producido importantes avances para facilitar el acceso al empleo público de personas con enfermedades crónicas que previamente eran causa de exclusión. El Acuerdo del Consejo de Ministros de 30 de noviembre de 2018 aprueba instrucciones para eliminar determinadas causas médicas de exclusión en el acceso al empleo público, como: VIH, diabetes, celiacía y psoriasis. Atendiendo a esto, se han revisado y modificado las tablas de exclusiones médicas para: la Policía Nacional, Guardia Civil, Cuerpo de Vigilancia Aduanera, Cuerpo de Auxiliares de Instituciones Penitenciarias, Centros de Formación Militar, Centros de Formación, para la incorporación a la báscula de Tropa e Infantería de Marina y la Escuela Nacional de Policía y se han derogado normativas previas para que estas enfermedades no sean un impedimento para el acceso de la Policía Nacional y la Guardia Civil en las convocatorias de los próximos ejercicios. De modo que el mero diagnóstico no impide el acceso al empleo público, sino que se tendrán en cuenta los avances médicos y la evidencia científica existente, así como la situación sanitaria de cada persona en particular⁸.

Así lo recogen ya algunas sentencias, como las del Tribunal de Justicia de Madrid, Sala de lo Contencioso Sección 7, Fecha: 17/10/2024, Nº de Recurso: 1314/2022, Nº de Resolución: 1367/2024⁹ y la de fecha 26/09/2024, Nº de Recurso: 68/2023, Nº de Resolución: 1118/2024¹⁰.

La bibliografía médica indica que existe una relación positiva entre el estigma experimentado, anticipado e internalizado y el autoconcepto de enfermedad y que el estigma se asocia con una mayor preocupación por la propia enfermedad y sobre uno mismo. El estigma internalizado se relaciona con los efectos de las variables de control, como el control personal en los grupos de personas con enfermedades crónicas, con un enfoque específico en aquellos con enfermedades crónicas ocultas. Es por ello que se recomienda promover

enfoques variados para afrontar la enfermedad, incluidos aspectos enriquecedores que potencialmente actúen como amortiguadores entre los efectos del estigma y el autoconcepto de enfermedad¹¹.

Desde un punto de vista preventivo, una variable clave para reducir las consecuencias negativas de la discriminación y la estigmatización es el autoestigma, es decir, el hecho de concebir el autoconcepto a través del filtro de los estereotipos negativos asociados a la característica percibida como discriminada. El autoconcepto alterado debería ser una diana diagnóstica y terapéutica básica en prevención de emociones negativas, como sentir vergüenza, y que se correlaciona con el autoestigma¹².

La pandemia Covid-19 supuso una mayor visibilización del concepto de estigma y esto explica la gran cantidad de publicaciones recogidas en un corto periodo de tiempo. Se consideró que estigmatizar a cualquier persona durante una pandemia supondría una amenaza para la salud pública y un obstáculo para el tratamiento de la enfermedad. El estigma en torno a la COVID-19 se correlacionó con el hecho de ser potencialmente mortal y al desconocimiento de muchos aspectos de ella. Se consideraron consecuencias del estigma de la COVID-19 el aislamiento social y la carga psicológica, la violencia y el acoso físico y mental, el ocultamiento de la enfermedad y la reducción de la búsqueda de atención médica. La experiencia vivida permitirá actuar en prevención del estigma en situaciones similares tanto a los administradores de casos/equipos de atención médica, a los formuladores de políticas sanitarias y a otros profesionales de planificación de recursos humanos que desarrollen planes para prevenir, combatir y detener el estigma relacionado con este tipo de situaciones y enfermedades de amplia expansión poblacional, como ha sido la COVID-19¹³.

En otras enfermedades infecto-contagiosas, como la hepatitis C, el conocimiento del estigma es fundamental para ayudar a las personas afectadas a autogestionar su enfermedad y reducir la carga de la enfermedad. Una característica central y distintiva del estigma de la hepatitis C en el mundo occidental es su asociación con el consumo de drogas ilícitas y el estigma se fundamenta en el miedo a la transmisión de una infección contagiosa y potencialmente mortal. Entre los sanitarios se asume el nivel aceptable de riesgo y el poder de imponer restricciones por parte de los profesionales de la salud, con el apoyo de las redes familiares y de amistad y la sociedad¹⁴.

En algunas enfermedades crónicas, como la epilepsia, el estigma percibido es bastante común entre las personas afectadas y puede resultar difícil que los pacientes lo expresen en situaciones clínicas¹⁵. El estigma percibido y la ansiedad social son dos problemas comunes en pacientes con epilepsia y comparten una relación importante. Las herramientas de prevención clínica y la

intervención del estigma percibido y la ansiedad social pueden ser de utilidad para evitar estas situaciones, aunque se necesita profundizar en investigación para poder avanzar¹⁶.

En situaciones de dolor crónico, las personas afectadas se ven frecuentemente expuestas al estigma, que suele ser angustiante y puede dar lugar a pensamientos estigmatizantes internos. El contenido de pensamiento asociado al estigma tiene similitudes con la catastrofización del dolor, aunque estos conceptos difieren en que el estigma es posiblemente de origen más social y se puede medir mediante escalas como la Escala de estigma para enfermedades crónicas¹⁷. Esta escala proporciona una medida adecuada para captar las experiencias de estigma y destaca la importancia de una perspectiva social sobre los resultados relacionados con el dolor y su impacto en su bienestar. Se destacan los posibles impactos negativos de las respuestas estigmatizadoras hacia las personas con dolor crónico¹⁸.

En enfermedades que cursan con dolor crónico, como la migraña, su alta prevalencia implica un impacto socioeconómico sustancial y una estigmatización que afecta la actitud social hacia esta enfermedad, impacta en la atención médica, en la relación médico-paciente, repercute en su calidad de vida y en su desempeño laboral y genera una carga adicional para las personas que la padecen, aislándolas del ámbito social en el que viven. Se proponen como estrategias de apoyo uso de un lenguaje unificado, nuevos medios de educación y defensa¹⁹.

La evaluación de estigma en personas con migraña mediante el cuestionario MiRS (Migraine-Related Stigma)²⁰ en un estudio realizado en Japón (OVERCOME) indica que la carga de la enfermedad y el estigma existen, pero pueden estar ocultos y poco reconocidos. Por ello, la concienciación y la educación sobre la enfermedad pueden ser importantes para prevenir y reducir su aparición e impacto²¹.

En otras enfermedades que cursan con dolor crónico, como la fibromialgia (FM) y la artritis reumatoide (AR), se destaca también el concepto de estigma en las personas afectadas. La presencia o ausencia de síntomas claramente definidos y de una fisiopatología subyacente puede ser una variable crucial relacionada con la variabilidad del bienestar y la estigmatización en las personas con dolor crónico. Comparando las personas con AR, las personas con FM y las personas con ambos diagnósticos, los peores resultados y mayor estigmatización se encuentra en las personas con FM, más que en las personas con AR. Las personas con ambos diagnósticos tienen estigmatización igual que las personas con FM, pero más estigmatización que las personas con AR. Los mayores niveles de estigma percibido se asociaron con un menor bienestar²².

En los últimos años se ha prestado especial atención al estigma relacionado con la obesidad y, fruto de ello es la *Declaración de consenso de la Asociación Estadounidense de Endocrinología Clínica: cómo abordar el estigma y el sesgo en el diagnóstico y el tratamiento de pacientes con enfermedades crónicas asociadas a la obesidad y la adiposidad y evaluar el sesgo y la estigmatización como determinantes de la gravedad de la enfermedad*, centrándose en la intersección de la percepción, el diagnóstico, el estigma y el sesgo de peso en el tratamiento de la obesidad y para obtener un consenso sobre medidas viables para mejorar la atención brindada a las personas con obesidad.

Este panel de consenso ha propuesto un enfoque para integrar el sesgo y la estigmatización, la salud psicológica y los determinantes sociales de la salud en un sistema de estadificación de la gravedad de la obesidad, como ayuda para el manejo del paciente. Se llega a la conclusión de que, para abordar eficazmente el estigma y la obesidad dentro de un modelo de atención crónica para estos pacientes, es necesario contar con sistemas de atención de la salud que estén preparados para proporcionar tratamientos basados en la evidencia y centrados en la persona; pacientes que comprendan que la obesidad es una enfermedad crónica y estén capacitados para buscar atención y participar en terapia conductual; y sociedades que promuevan políticas e infraestructura para una atención compasiva sin sesgos, acceso a intervenciones basadas en la evidencia y prevención de enfermedades²³.

En pacientes con diabetes el estigma surge de la idea errónea de que las personas con diabetes tomaron decisiones no saludables sobre su alimentación y estilo de vida, que dieron lugar a su diagnóstico. Estas creencias falsas no consideran factores clave que pueden causar diabetes, como los antecedentes médicos familiares o determinantes sociales de salud, como las condiciones en las que las personas crecen, trabajan, viven y envejecen. El estigma por la diabetes puede afectar especialmente a las personas con sobrepeso u obesidad.

Más de la mitad de las personas con diabetes refieren haber sufrido estigma, bien de forma interna, con sentimientos de culpabilidad y vergüenza, o bien de forma externa, que puede incluir miradas incómodas u hostiles, rechazo, exclusión y dificultad para mantener relaciones y amistades. El estigma por la diabetes puede existir en cualquier parte: en la familia, el lugar de trabajo e incluso en los entornos de atención médica.

En la bibliografía médica revisada, el mayor número de publicaciones relativas a estigmatización se corresponde con las enfermedades psiquiátricas, donde además se asocia el riesgo de ideación suicida.

El hecho de que el estigma público asociado a las enfermedades mentales afecte negativamente a una persona depende en gran medida de si se la ha etiquetado como "enferma mental". Para las personas etiquetadas, ocultar su enfermedad es una estrategia habitual para hacer frente al estigma de la enfermedad mental, a pesar de las posibles consecuencias negativas del secreto.

Se estima que existe un vínculo entre el estigma y la conducta suicida, pero faltan datos cuantitativos de muestras comunitarias. Una explicación de esta asociación es la relación que el estigma percibido tiene con el secretismo, que introduce consecuencias emocionales negativas. Es por ello que se proponen programas que empoderan a las personas en tratamiento por enfermedad mental para que puedan hacer frente a la discriminación anticipada y experimentada, así como las intervenciones para reducir el estigma público dentro de la sociedad, que podrían mejorar la prevención del suicidio²⁴.

Las tasas de suicidio aumentan entre las personas desempleadas y el estigma de las enfermedades mentales puede contribuir tanto al desempleo como a la tendencia suicida. Las personas con enfermedades mentales perciben actitudes negativas entre el público en general y experimentan discriminación en su vida cotidiana, lo que puede conducir al autoestigma y a la discriminación anticipada. Los programas que abordan múltiples componentes del estigma parecen ser los más eficaces para mejorar la prevención del suicidio. Además de las intervenciones dirigidas a las actitudes negativas y los comportamientos discriminatorios del público en general, los programas de apoyo a las personas con enfermedades mentales para que puedan hacer frente al estigma percibido y experimentado podrían mejorar la prevención del suicidio y las consecuencias emocionales (por ejemplo, la desesperanza y la soledad) en la asociación entre los componentes del estigma y la conducta suicida²⁵.

Conclusiones

El estigma como concepto sociolaboral ha entrado a formar parte de la investigación médica, especialmente relacionado con enfermedades crónicas.

El trabajo en una forma de integración laboral y, por ello, en salud laboral las intervenciones aplicadas deben ser multidisciplinarias, con especial atención al papel de la psicología de la salud ocupacional actuando conjuntamente con los sanitarios y técnicos de los servicios de prevención de riesgos laborales para tratar problemas de salud y bienestar de los empleados o prevenir que estos problemas se produzcan.

Hay variedad de tipos de intervenciones preventivas, incluidas las intervenciones centradas en cambiar al

empleado o a otras personas de lugar de trabajo cuando sea necesario (supervisores o compañeros de trabajo), valorar las características laborales y de salud del empleado o el clima de la organización.

Habitualmente, se proponen actuaciones con variables mediadoras entre las intervenciones y la salud o el bienestar reales de los empleados: reducciones del conflicto y el estigma de las enfermedades crónicas, destacando algunas como las vistas previamente y especialmente en lo relacionado con la salud mental y las enfermedades mentales e incluyendo en dichas intervenciones preventivas a toda la organización: supervisores o compañeros de trabajo de los empleados.

Se admite la variabilidad de los resultados obtenidos en función de moderadores de la efectividad de las

intervenciones, de modo que un tratamiento puede funcionar mejor en algunas personas, en algunas situaciones y en algunos momentos más que en otros.

El desconocimiento de una enfermedad por la estigmatización asociada impide la acción preventiva en el ámbito laboral. Solo trabajando de forma conjunta y con una visión integradora se puede avanzar evitando el estigma asociado a enfermedades crónicas, de larga duración o limitantes y a su impacto socio-laboral en las personas afectadas, atendiendo a lo establecido en la normativa nacional e internacional.

Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses relacionado con el artículo.

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ORIGINAL

An Examination of the Correlation Between Urethral Hypermobility and Point Aa in Women with Stress Urinary Incontinence

Un examen de la correlación entre la hipermovilidad uretral y el punto Aa en mujeres con incontinencia urinaria de esfuerzo

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Abstract

Background: Urethral mobility is a key factor in planning and executing surgical interventions for women with stress urinary incontinence. It helps surgeons assess the anatomy and function of the lower urinary tract, guiding the selection and adjustment of procedures to restore continence effectively.

Objective: We aimed to determine if point Aa in the pelvic organ prolapse quantification system could replace visual urethral mobility examination in confirming urethral hypermobility in women with stress urinary incontinence.

Methods: In a retrospective cohort study, we compare visual urethral mobility and Aa measurements in 131 women with predominant stress urinary incontinence. The Aa point corresponds to the urethro-cervical crease and is located 3 cm deep to the urethral meatus in the anterior vagina's midline.

Results: Among 131 patients, 67.2% had hypermobility, 22.1% had positive cough tests, and 12.2% had stage 1 Aa points. Additionally, 64.1% had stage 2 Aa points, and 23.7% had stage 3 Aa points. The Aa stage had a significant relation with age ($P<0.001$), menopause ($P<0.001$), hypermobility ($P<0.001$), and leak with cough in the urodynamic test ($P=0.008$). Moreover, the Aa stage has been found to possess high sensitivity and specificity and can be used as an alternative to visual hypermobility, particularly in stages 2 and 3 of prolapse.

Conclusions: This study found a significant relationship between hypermobility in the visual hypermobility and Aa point. The Aa stage has been found to possess high sensitivity and specificity and can be used as an alternative to visual hypermobility, particularly in stages 2 and 3 of prolapse.

Key words: visual urethral mobility examination, Aa point, urodynamic Test, urethral hypermobility.

Resumen

Antecedentes: La movilidad uretral es un factor clave en la planificación y ejecución de intervenciones quirúrgicas para mujeres con incontinencia urinaria de esfuerzo. Ayuda a los cirujanos a evaluar la anatomía y la función del tracto urinario inferior, guiando la selección y ajuste de procedimientos para restaurar la continencia de manera efectiva.

Objetivo: Nuestro objetivo fue determinar si el punto Aa en el sistema de cuantificación del prolapso de órganos pélvicos podría reemplazar el examen visual de la movilidad uretral para confirmar la hipermovilidad uretral en mujeres con incontinencia urinaria de esfuerzo.

Métodos: En un estudio de cohorte retrospectivo, comparamos la movilidad uretral visual y las mediciones del punto Aa en 131 mujeres con predominancia de incontinencia urinaria de esfuerzo. El punto Aa corresponde al pliegue uretro-cervical y se encuentra a 3 cm del meato uretral en la línea media de la vagina anterior.

Resultados: Entre las 131 pacientes, el 67.2% presentaba hipermovilidad, el 22.1% tuvo pruebas de tos positivas y el 12.2% tenía puntos Aa en estadio 1. Además, el 64.1% presentaba puntos Aa en estadio 2 y el 23.7% en estadio 3. El estadio del punto Aa mostró una relación significativa con la edad ($P<0.001$), la menopausia ($P<0.001$), la hipermovilidad ($P<0.001$) y las pérdidas con tos en la prueba urodinámica ($P=0.008$). Además, se encontró que el estadio del punto Aa posee alta sensibilidad y especificidad, y puede ser utilizado como una alternativa al examen visual de hipermovilidad, particularmente en los estadios 2 y 3 del prolapso.

Conclusiones: Este estudio encontró una relación significativa entre la hipermovilidad visual y el punto Aa. Se determinó que el estadio del punto Aa posee alta sensibilidad y especificidad, y puede ser utilizado como una alternativa al examen visual de hipermovilidad, especialmente en los estadios 2 y 3 del prolapso.

Palabras clave: examen visual de movilidad uretral, punto Aa, prueba urodinámica, hipermovilidad uretral.

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Introduction

Urethral hypermobility is common among women with stress urinary incontinence. It is considered one of the most important factors determining the prognosis and criteria for determining the type of surgery among these patients¹⁻⁶. Although there are various methods to evaluate urethral mobility, visual hypermobility is a reliable, easy, and low-cost test and the most widely used method⁷⁻¹⁰. Another method was the Q-tip test, which can cause discomfort to the patient due to foreign bodies entering the urethra and bacteria entering the bladder^{3,4,11,12}. This led some researchers to find a suitable alternative for non-invasive assessment of urethral hypermobility^{1,2,12}.

The pelvic organ prolapse quantification (POP-Q) system has been the target of many of these efforts to investigate urethral hypermobility, especially point Aa because it is believed to be at the junction of the bladder and urethra^{9,13,14}. It has been suggested that the distal movement of point Aa indicates urethral hypermobility, but there are controversial results^{3,7,9,11}. While Kim et al.³ investigated Point Aa of the POP-Q system as a predictive value of urethral mobility in women, they did not consider urodynamic testing (UDS) parameters. Based on the importance of this issue, we aimed to investigate the relation between point Aa in the POP-Q system and hypermobility assessed by visual method in women experiencing stress urinary incontinence and compared it with urodynamic results.

Methods and materials

Setting and population

This analytical retrospective cohort study was conducted on women with stress urinary incontinence who were referred to the pelvic floor clinic of an academic center from January 2020 to January 2021. The study population included women who underwent the POP-Q examination to determine the size of the Aa point and urodynamic tests. They were also examined for visual urethral hypermobility. Three pelvic floor specialists performed all examinations. A urodynamic study was done by a technologist supervised by pelvic floor specialists. Women with stress urinary incontinence had the results of Presence or absence of urethral hypermobility and the size of the Aa point recorded in their files, while those without complete records were excluded from the study. Participants with addiction, underlying medical issues, previous surgeries on the urethra, or incomplete records were not included in the study.

Data gathering

After obtaining permission from the hospital's ethics committee, the medical records of the patients were reviewed and recorded. Furthermore, Valsalva leak point pressure and cough-induced leak point pressure are another way to test for stress incontinence and were

assessed¹⁵⁻¹⁷. Also, hypermobility was assessed through visual examination by an expert urogynecologist on sonography¹⁸.

The Aa point was measured while the patient was lying on the gynecology bed in the lithotomy position. It was located on the front wall of the vagina, 3 cm proximal to the external urethral meatus, and measured during the Valsalva maneuver compared to the hymen. The size was based on the distance of this point during the Valsalva maneuver, and it ranged from -3 to 3. Negative numbers indicated a proximity to the hymen, while positive numbers indicated a distance from it. Stage 1 Aa point is defined as -2 to -3, stage 2 Aa point as -1 to +1, and stage 3 Aa point as +2 to +3^{19,20}.

Ethical consideration

Written informed consent had been obtained from all participants. This study has been approved by the Ethics Committee of an academic center, and the study was conducted according to the Declaration of Helsinki²¹.

Statistical analysis

Data were analyzed by IBM statistical software SPSS version 19. The normality was evaluated by the Kolmogorov-Smirnov test. Data were reported by mean ($\pm$ standard deviation) for quantitative variables and number (percent) for qualitative variables. Qualitative variables were analyzed using the chi-square test, and continuous quantitative variables with normal distribution were analyzed using the independent t-test. The sensitivity, specificity, and positive and negative predictive value of point Aa with visual hypermobility were assessed. A significance level of less than 0.05 was considered.

Results

In a study involving 131 patients with chief complaints of stress urinary incontinence, the average age of those with stress urinary incontinence was 53.57 ± 11.39 years. Among the participants, 74 individuals (56.6%) were postmenopausal. The number of pregnancies varied from 0 to 15, with 29.8% of women experiencing two pregnancies and 24.4% experiencing three pregnancies. Using the Aa point (pop-q system), the distribution among the patients was as follows: point -2, 16 people (12.2%); point -1, 28 people (21.4%); point 0, 42 people (32.1%); point 1, 14 people (7.10%); point 2, 7 people (5.3%); point 3, 24 people (18.3%). Visual hypermobility was seen in 67.24% of the participants. The average Valsalva leak point pressure (VLPP) was 93.66 ± 28 , categorized as follows: less than 60, 9 people (14.8%); 60-90, 18 people (29.5%); more than 90, 34 people (55.7%). The cough leak point pressure (CLPP) was categorized as follows: less than 60, 4 people (4.7%); 60-90, 15 people (18.1%); more than 90, 64 people (77.2%). Additionally, 77.9% of patients did not experience urine leakage during coughing or Valsalva in urodynamic testing.

There was a statistically significant relationship between average age and point Aa (P -value <0.05). Additionally, a statistically significant relationship exists between point Aa and menopause status (P -value <0.05). Results showed that 80.2% of people with menopause were in the 2nd and 3rd stages of the abnormal condition of point Aa. 72.4% of cough positives were in Aa stage 2, and 13.8% of cough positives were in stage 3 Aa. No significant relation was found between the cough test and the Aa stage (P -value: 0.238). There was a statistically significant relationship between the number of births and the stage of point Aa (P -value <0.05). 72% of people with two children were in stage 2 point Aa, 65.2% of people with 3-5 children were in stage 2 Aa, and 40% of people with six children were in stage 3 point Aa. Lastly, a statistically significant relationship between hypermobility and point Aa has been observed (P -value <0.05), with positive hypermobility in point Aa of stage 2 being higher than in other stages. The analysis revealed statistically significant findings regarding point Aa and CLPP pressure (P -value = 0.05). Among those

with positive CLPP Aa, 71.1% were classified as stage 2, while 15.6% were classified as stage 3. However, no significant relationship was found between the Aa stage and mean CLPP (P -value = 0.5). Similarly, there was no statistically significant relation between the presence of VLPP and Aa point (P -value = 0.3). Among individuals with positive VLPP Aa, 64.8% were in stage 2. No statistically significant relation was observed between point Aa and mean VLPP (P -value = 0.1). Furthermore, 73.5% of individuals with pressure exceeding 90 were classified as stage 2 for point Aa, while only three individuals with pressure below 60 were in stage 2 for point Aa. There were a total of 61 individuals who experienced leakage with Valsalva. For a detailed frequency table of the variables, please refer to **table I**.

Furthermore, Aa from stage 2 shows a specificity of 90% and 80% sensitivity. Point Aa can diagnose more patients in stage 2 than visual hypermobility and has a higher positive predictive value than other stages. For detailed information, please refer to **tables II** and **III**.

Table I: The Baseline Characteristics Information of the Participants and Aa Point.

Variables		Total	Aa point			P-value
Age (years) ¹			Stage 1	Stage 2	Stage 3	
		54.3 (11.3)	52.7 (8.9)	56.3 (9.4)	59 (10.2)	<0.05
Menopausal status	Menopause	74 (56.5)	8 (10.8)	36 (48.6)	30 (40.5)	<0.05
	Non menopausal	57 (43.5)	8 (14.0)	48 (84.2)	1 (1.8)	
Number of births	<3	50 (38.1)	10 (20.0)	36 (72.0)	4 (8.0)	<0.05
	3-5	66 (50.4)	2 (3.0)	43 (65.2)	21 (31.8)	
	>5	15 (11.5)	4 (26.7)	5 (33.3)	6 (40.0)	
Hypermobility	Positive	88 (67.2)	2 (2.3)	61 (69.3)	25 (28.4)	<0.05
	Negative	43 (32.8)	14 (32.6)	23 (53.5)	6 (14.0)	
Cough test	Positive	29 (22.1)	4 (13.8)	21 (72.4)	4 (13.8)	0.23
	Negative	102 (77.9)	12 (11.8)	63 (61.8)	27 (26.5)	
VLPP leak ²	Yes	71 (54.2)	11 (15.5)	46 (64.8)	14 (19.7)	0.30
	No	60 (45.8)	5 (8.3)	38 (63.3)	17 (28.3)	
CLPP leak ³	Yes	90 (68.7)	12 (13.3)	64 (71.1)	14 (15.6)	0.05
	No	41 (31.3)	4 (9.8)	20 (48.8)	17 (41.5)	
Average pressure VLPP	<60	9 (14.8)	2 (22.2)	3 (33.3)	4 (44.4)	0.10
	60-90	18 (29.5)	3 (16.7)	10 (55.6)	5 (27.8)	
	>90	34 (55.7)	5 (14.7)	25 (73.5)	4 (11.8)	
Average pressure CLPP	<60	4 (4.7)	0 (0)	4 (100)	0 (0)	0.50
	60-90	15 (18.1)	1 (6.7)	12 (80.0)	2 (13.3)	
	>90	64 (77.2)	11 (17.2)	42 (65.6)	11 (17.2)	

1: This variable is shown in mean (standard deviation), others are shown in number (percents).
 2: The Valsalva leak point pressure.
 3: Cough Leak Point Pressure.

Table II: The Relation Between Hypermobility and VLPP and CLPP.

Variables ¹		Hypermobility		P-value
		Negative	Positive	
CLPP ²	<60	1 (1.2)	3 (3.6)	0.2
	60-90	4 (4.8)	12 (14.5)	
	>90	24 (28.9)	39 (47.0)	
VLPP ³	<60	1 (1.6)	8 (13.1)	0.1
	60-90	8 (13.1)	10 (16.4)	
	>90	9 (14.8)	25 (41)	

1: number (percents), 2: Cough Leak Point Pressure, 3: The Valsalva leak point pressure

Table III: ROC Analysis of the Point Aa with Visual Hypermobility as a Reference Test for Hypermobility.

Variables	Aa point		
	Stage 1	Stage 2	Stage 3
Sensitivity	96%	80%	60.9%
Specificity	16%	90%	70%
Positive predictive values of diagnostic tests	7.1%	95%	80%
Negative predictive values of diagnostic tests	86%	87.5%	27.3%
P-value <0.001			

Discussion

This study investigated the relationship between the Aa point in POP-Q and hypermobility among women with stress urinary incontinence and revealed hypermobility and point Aa are statistically significant, with positive hypermobility in point Aa of stage 2 being higher than in other stages. Also, Aa can diagnose more patients in stage 2 than the visual hypermobility test and has a higher positive predictive value than other stages. Matisson et al.⁷ reported that the association between the Aa point in the POP-Q system and the Q-tip angle was moderately strong considering all degrees of prolapse (P-value=0.001), and only in stage IV prolapse hypermobility of the urethra was seen in 100% of patients. In our study, the second stage of POP-Q has the most relationship with hypermobility. In addition, in the Matisson study⁷, although in women with -3Aa value, it is believed that the bladder neck has adequate support. 56% had urethral hypermobility, and they concluded that it is not possible to reliably predict urethral hypermobility by just measuring POP-Q, and the Q-tip test is a necessary evaluation in these patients. In our study, there was a relation between the Aa point in the POP-Q system and the visual urethral hypermobility in all stages, but the degrees we defined were slightly different from the above study, and we did not define stage 4. Also, unlike the above study, there was no patient in -3 Aa in our study. By examining 250 patients with urinary incontinence, Kim et al.³ found a significant association (P-value<0.0001) between the Aa point and visual urethral hypermobility, which indicates that the Aa point strongly predicts the mobility of the bladder neck. In addition, our study indicated that Aa point and visual hypermobility are better diagnostic tools compared to UDS paramant.

In addition, they found no relation between visual hypermobility, age, BMI, parity, history of hysterectomy, menopause, and hormonal treatment. The results of our study, similar to the above study, had a significant relationship between the Aa point and visual hypermobility. Also, in our study, similar to the above study, there was no relationship between visual urethral hypermobility and age, parity, and menopause, but we did not examine the relationship with hysterectomy, hormone therapy, and BMI. Larrieux et al.⁹ analyzed the results of 323 patients who were evaluated for urinary incontinence and found that the Aa point strongly (P-value<0.001) predicted hypermobility in women with the prolapse of the anterior

wall is stage I or higher and did not find any confounding effect of age, body mass index (BMI), parity, history of hysterectomy, menopause status, and hormone use. The results of our study were in line with the above study and agreed with these results, but in our study, there were a few patients with stage 1 prolapse, and the largest number was stage 2. Also, we examined the relationship of urodynamic factors such as VLPP and CLPP and their average with Aa point factors, visual urethral hypermobility, age, menopause, and cough test, which was not done in this study. By examining 274 patients with pelvic organ prolapse or urinary incontinence, Cogan et al.¹⁰ found a strong association (P<0.001) between point Aa and urethral hypermobility only in stages II to IV prolapse. The results of our study were also similar to the results of the above study, but we also observed a relation in stage 1, due to the small number of patients in this stage, this result is not very reliable, and stage 4 was not defined in our definitions. By examining 134 patients referred for urogynecology evaluation, Noblett et al.¹¹ found that the POP-Q system is a very good predictor of the Q-tip angle in all stages of prolapse and a strong association (P<0.001) between urethral hypermobility and stages II to IV prolapse, but they could not show this association in stages 0 and I, which indicates that urethral hypermobility is possible in patients with stress urinary incontinence even in the absence of prolapse and in these women with stress urinary incontinence and stage 0 or I prolapse, it is necessary to perform a Q-tip test. In our study, even in stage 1, there was a relationship between visual urethral hypermobility and the Aa point, but we did not have the -3 point, and the -2 point was also very low. However, due to the existence of a positive visual urethral hypermobility, even in small amounts in these patients, we also agree with the opinion of the above study to check the test even in these points. Montella et al.¹⁴, by examining 111 patients with prolapse and/or urinary incontinence, did not find a relationship between urethral hypermobility and the amount of anterior wall lowering with POP-Q and concluded that the observational assessment of anterior wall lowering has diagnostic accuracy, sensitivity, and specificity. It is not acceptable to determine the mobility of the bladder neck. The results of our study were contrary to the above study, and we obtained an acceptable sensitivity and specificity for stage 2. Also, in line with our study in 2020, De Alessandro et al.²², intending to investigate the prediction rate of Q-tip using Aa point

and urodynamic tests by examining 501 patients with stress urinary incontinence, found that age and Aa point predict independent of Q-tip. The results of our study also showed that the non-invasive test of Aa point measurement can be replaced for urethral hypermobility instead of visual urethral hypermobility. We did not use the Q-tip test because it is invasive and outdated.

One of the strengths of this study was using the data through data registration in a referral center in Iran, however, the single-center study, not following up with the patients, and the small population were the limitations of the study. Another strength was urodynamic assessment in all patients with stress urinary incontinence. Additionally, the Aa point relation with hypermobility in the visual test was significant. Due to the high sensitivity and specificity of the Aa stage, the Aa stage can be used instead of visual urethral hypermobility, especially in stages 2 and 3 of prolapse. It is suggested that a study with a larger sample size that has a large number of samples in different stages should be compared, and it is also suggested that the visual urethral hypermobility be compared with the results of urodynamics in a larger sample size so that in the future, more non-invasive tests can be replaced with current test specially Q-tip test. Also, the type of

delivery, cesarean section, and difficult delivery should be considered as a variable.

In conclusion, This empirical investigation established a significant correlation between visual hypermobility and the Aa point metric. The findings indicate that the Aa stage exhibits both elevated sensitivity and specificity, making it a viable alternative diagnostic tool to assess visual hypermobility. This is particularly relevant in clinical scenarios concerning stages 2 and 3 of pelvic organ prolapse, where accurate measurement and assessment can significantly influence management strategies and patient outcomes. The implications of these findings suggest that integrating the Aa point evaluation into clinical practice could enhance diagnostic accuracy and facilitate more targeted therapeutic approaches for patients experiencing hypermobility-related disorders in the context of pelvic floor dysfunction.

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Not applicant

Conflicts of Interest

The authors declare no conflicts of interest.

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ORIGINAL

Sustainability and Sustainable Leadership in Hospitals

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Abstract

Introduction: This study aimed to determine what hospital managers do within the scope of economic, social and environmental sustainability. In addition, it was tried to determine the factors affecting sustainability and sustainable leadership in hospitals.

Methods: In order to obtain more comprehensive information about sustainability, the phenomenology method, which is one of the qualitative research methods, was used in the study. In line with the purpose of the study, managers working at different administrative levels and in different hospitals were interviewed. The data obtained from 13 hospital managers in the study were examined by content analysis.

Results: As a result of the analyses, four themes, 13 subthemes, 62 codes and 31 subcodes were determined. It was determined that the variables that attracted the most attention regarding the sustainability of hospitals and sustainable leadership were related to the manager. It was also determined that the participants mostly mentioned variables related to economic benefit.

Conclusions: It was determined that the practices related to environmental benefit were shallower than the practices related to economic and social benefit. It was determined that the elements most taken into consideration by the managers were education, legal regulations and inspections. This study aimed to draw attention to the sustainability practices in hospitals and to have hospital managers make more sustainable decisions.

Key words: Health institution, hospital, leadership, sustainability, sustainable leadership.

Resumen

Introducción: Esta investigación tuvo como objetivo determinar qué hacen los gerentes de hospitales en el ámbito de la sostenibilidad económica, social y ambiental. Además, se intentó determinar los factores que inciden en la sostenibilidad y el liderazgo sostenible en los hospitales.

Métodos: Con el fin de obtener información más completa sobre la sostenibilidad, en la investigación se utilizó el método fenomenológico, que es un método de investigación cualitativo. De acuerdo con el propósito de la investigación, se entrevistó a directivos que trabajan en diferentes niveles administrativos y en diferentes hospitales. En el estudio se examinaron mediante análisis de contenido los datos obtenidos de 13 gerentes de hospitales.

Resultados: Como resultado del análisis se identificaron cuatro temas, 13 subtemas, 62 códigos y 31 subcódigos. Se determinó que las variables que más llamaron la atención respecto a la sostenibilidad de los hospitales y el liderazgo sostenible fueron las relacionadas con el gerente. También se encontró que los participantes mencionaron principalmente variables relacionadas con el beneficio económico.

Conclusiones: Se determinó que las prácticas relacionadas con los beneficios ambientales fueron menos superficiales que las prácticas relacionadas con los beneficios económicos y sociales. Se determinó que los elementos más tomados en cuenta por los directivos fueron la capacitación, la normativa legal y las inspecciones. Esta investigación tuvo como objetivo llamar la atención sobre las prácticas de sostenibilidad en los hospitales y alentar a los gerentes de hospitales a tomar decisiones más sostenibles.

Palabras clave: Institución de salud, hospital, liderazgo, sostenibilidad, liderazgo sostenible.

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Introduction

The world population is increasing day by day for various reasons (technological developments, increased treatability of diseases, longer life expectancy, high birth rates in some regions, etc.). Along with the continuous increase in the world population, the changes brought about by the industrial revolution (social, economic and environmental changes)¹, technological developments, globalization and other reasons such as unconscious human actions are accelerating the consumption of natural resources². It is thought that the rapid consumption of natural resources will not be the living conditions we have today in the future and will cause various problems. It is stated that environmental problems such as depletion of water resources, drought, famine, climate change in the future; economic problems such as poverty, income inequalities, crises, decrease in welfare level; and social problems such as exclusion and inequalities will become even more important problems for future generations³.

Businesses operate within interconnected, dynamic and complex social, economic and environmental systems⁴. Although it is quite difficult to make sustainable decisions on social, economic and environmental issues from today to the future, ensuring this should be the main priority of senior managers⁵. Because the attitudes and behaviors that businesses exhibit for sustainability and the strategies they follow depend on the decisions of senior management⁶. The concept of sustainable leadership is related to seeing businesses as a part of the natural world in decision-making processes. This view is supported by social, environmental, economic, legal and ethical reasons⁷. Protecting the environment and solving social and economic problems require innovative approaches. These approaches should be adopted for sustainability. In this way, sustainability can be achieved both at the organizational level and beyond the boundaries of the organization⁸.

The sustainability of health services is based on an ecological basis. Accordingly, a sustainable health service should be provided in terms of both social, economic and environmental systems and human health should not be harmed. Safe, high-quality health services should be provided efficiently and effectively⁹. Environmental problems that also negatively affect human health should not be caused¹⁰. Because health institutions are responsible for approximately 4-5% of global greenhouse gas emissions¹¹. Health services are energy intensive. Hospitals in particular operate 24/7 and there are many medical devices in hospitals. Intense energy is consumed in air conditioning operations such as heating, cooling and ventilation, diagnosis and treatment processes, food and laundry services and many other service delivery. In addition, energy is used intensively in the production of inputs such as materials, equipment, devices and medicines used in the provision of health services¹². On the other hand, hospitals need a significant amount

of water for different purposes in all service processes. The lack of quality and sufficient amount of water used in hospitals negatively affects both the health of patients and daily functioning¹³.

Many wastes are produced in health institutions that both affect the environment and can have negative effects on health. While 85% of this waste is non-hazardous household waste, 15% is hazardous (medical, chemical, radioactive, etc.) waste. While an average of 0.5 kg of hazardous waste is produced per patient bed per day in developed countries, 0.2 kg is produced in developing and underdeveloped countries. While better separation of waste in developed countries increases the amount of hazardous waste in these countries, poor separation in other countries brings many risks¹⁴. In some cases, it has been stated that the production of this waste is much higher (e.g., during the COVID-19 pandemic, the amount of medical waste in all health facilities around the world increased by approximately five to seven times)¹⁵.

Health services should be accessible to the entire society regardless of income level. However, health inequalities cause social health problems and increase in health expenditures¹⁶. Especially in low-income countries, health service costs can push families into poverty. On the other hand, more children, mothers and young people can be lost due to health inequalities. Life expectancy is shortened in these countries and all these cause economic losses and increase in social costs¹⁷. Health institutions should not cause more social, economic and environmental problems while struggling with the health problems of the society. However, for the sustainability of the services provided, while meeting the needs of today, the ability to meet the needs of future generations should not be jeopardized⁷. The responsibility in this regard belongs to the leaders of health institutions. Health institution leaders should determine the negative effects of the services provided and develop strategies to reduce these negativities¹². In this context, the attitudes and behaviors of institution leaders and the decisions they make are gaining importance for a more sustainable health service¹⁸. In this context, this research has attempted to evaluate the sustainable leadership approach and practices in hospitals. In this context, the following questions were sought:

- What is effective on sustainable leadership and sustainability in hospitals?
- What do hospital managers consider regarding social issues for sustainability?
- What do hospital managers consider regarding economic issues for sustainability?
- What do hospital managers consider regarding environmental issues for sustainability?
- How do hospital managers ensure sustainability?

Research methodology

In today's conditions, competition has increased in every field. Making a profit is essential for the sustainability of businesses. Businesses may ignore social and environmental factors while conducting activities aimed at making a profit in order to be sustainable. However, it is extremely important to consider social and environmental factors for economic sustainability. Because damage to social and environmental factors causes the resources used in carrying out economic activities to be negatively affected. Businesses providing health services, on the other hand, affect the health of the society with the services they provide and consume many resources. These consumed resources threaten the sustainability of the services. In order to ensure the sustainability of the services, health institutions, like all businesses, need to take social and environmental factors into consideration while achieving their economic goals and consider future generations in these decisions. In this context, this research aims to determine the strategies that hospital managers follow in order to ensure economic, social and environmental sustainability, to determine the factors that affect sustainability in hospitals and to guide health institution leaders to make more sustainable decisions.

In order to obtain detailed and holistic information in line with the purpose of the research, phenomenology, one of the qualitative research approaches, was used. The phenomenology approach is used to determine, define, understand and interpret the details of a phenomenon by benefiting from the experiences of individuals or groups about this phenomenon¹⁹. Different methods are used to include participants in the study group within the scope of the research. In this research, it is aimed to determine what hospital managers do within the scope of sustainable leadership. Since the operating structures, decision-making methods, policies, basic objectives and capital resources of private and public hospitals are different, both public and private hospital managers were included in the research. In addition,

the areas of responsibility of managers vary according to their positions. On the other hand, the areas of responsibility of mid-level managers in hospitals are different from each other. For this reason, managers responsible for different areas were selected. Some participants in the study group are senior managers who make decisions about all processes. For these reasons, managers responsible from different administrative levels and different areas of authority were included in the study group. In addition, managers working in different provinces were reached due to the different regional dynamics. In this context, purposeful sampling and maximum variation sampling methods were used. In this way, more information was tried to be obtained about the studies of hospital managers on sustainable leadership. Since it was thought that managers should have knowledge about the research topic, the research was conducted with hospital managers who had at least five years of experience. In addition, since decisions regarding the operation of the institution are made by upper and middle level managers or under their control, lower level managers were not included in the study group. In this context, criterion sampling type was used. While the basic phenomenon is revealed with the purposeful sampling type, more comprehensive data and different perspectives are revealed with the maximum variation sampling type. In the criterion sampling type, participants who meet certain criteria are included in the study in order to collect data appropriate to the purpose of the research²⁰. Information about the managers in the study group is presented in **table I**.

The study group consists of 13 managers. The saturation level of the research data was taken into account in determining the number of participants. The saturation level is the level at which no new data can be obtained from the participants and the data begins to repeat itself²¹. In this study, the data collection process was terminated due to the lack of differentiation in the data obtained from the 13 managers.

Table I: Information on Managers in the Working Group.

Participants	Age	Experience Period	Management Level	Management Position	Ownership of the Hospital
M1	46	21 years	Intermediate Level	Administrative and Financial Affairs Manager	Public Hospital
M2	47	24 years	Intermediate Level	Administrative and Financial Affairs Manager	Public Hospital
M3	41	21 years	Intermediate Level	Administrative and Financial Affairs Manager	Private Hospital
M4	36	18 years	Intermediate Level	Administrative and Financial Affairs Manager	Public Hospital
M5	40	14 years	Intermediate Level	Administrative and Financial Affairs Manager	Public Hospital
M6	44	18 years	Intermediate Level	Health Care Services Manager	Public Hospital
M7	29	5 years	High Level	Chief Physician	Public Hospital
M8	64	43 years	High Level	General Manager	Private Hospital
M9	44	22 years	High Level	General Manager	Private Hospital
M10	43	24 years	Intermediate Level	Health Care Services Manager	Private Hospital
M11	55	37 years	Intermediate Level	Health Care Services Manager	Public Hospital
M12	47	18 years	High Level	General Manager	Private Hospital
M13	72	44 years	High Level	Chief Physician (Responsible Manager)	Private Hospital

In order to determine the questions appropriate for the purpose of the research, a literature review was conducted first. As a result of the literature review, seven open-ended questions related to sustainability and sustainable leadership were determined. In addition, five questions were created to define the participants. Semi-structured interview technique was used in the interviews conducted with the participants. In this context, some additional questions were asked in order to obtain more detailed information about the purpose of the research. In the semi-structured interview technique, the interview questions are semi-structured and flexible. More specific data can be obtained from the participants with this technique²¹.

The research data were collected between 04/09-20/11/2025. Before the interview, the participants were informed about the research by sharing the interview questions. Face-to-face interviews were conducted with participants who were close to the site, and via telephone with participants who were far away. The interviews were recorded for later analysis.

The transcripts obtained from the interviews consist of 101 pages and the total interview duration is 460.93 (average 35) minutes. In order to avoid data loss in the research, the interview transcripts were read three times at two-week intervals and codes related to the purpose of the research were determined. In order to determine the codes, the interview transcripts were analyzed with the content analysis method. Content analysis varies according to the technique used. In this research, the thematic-structural content analysis technique was used due to the specificity of the superordinate themes related to sustainable leadership. According to this technique, the analysis process consists of the stages of determining important places in the text, determining superordinate themes, placing the determined codes under the superordinate themes, combining similar codes under the superordinate data, determining sub-themes for similar codes, and re-coding the entire text according to the superordinate and sub-themes²². In this direction, codes were first determined according to the superordinate themes. The determined codes were grouped according to their similarities. Sub-themes were determined in line with these groups. In order to increase the reliability of coding, themes and codes were recoded after they were determined. In addition, the codes and themes determined were checked with an expert. Codes that could not be reconciled were not included in the data²². As a result of the analysis of the research data, a total of 62 codes and 31 subcodes were determined. These codes were combined into four themes and 13 subthemes. Maxqda analysis program was used in the analysis of the interview transcripts. In order to increase the reliability of the research, the opinions of some of the participants were included in the findings section.

Results

The findings section of this research, which was conducted to determine what hospital managers do about sustainability, includes the themes, subthemes and codes obtained as a result of the analysis of the participants' statements. The number of managers expressing the determined codes is shown with the letter "n" and the frequency of expression is shown with the letter "f".

Theme 1. Factors Affecting Sustainability and Sustainable Leadership

Sub-Theme 1.1. Factors Related to the Service Provided

It was determined that the characteristics of the health services provided in hospitals affect sustainability and sustainable leadership. It was determined that the sub-theme of factors related to the service provided consisted of five codes (Figure I).

Some statements of managers regarding the determined codes are as follows:

M2: "Because it is an issue that directly affects patient health. Therefore, our priority is patient health."

M8: "Of course mistakes happen from time to time. As is the case everywhere where there are people, so are ours..."

M13: "Health services are a service sector with high operating costs, high employment volume and intensity."

Sub-Theme 1.2. Environmental Factors

The theme of environmental factors was created within the scope of six codes determined in line with the participants' statements (Figure II).

The statements of some managers regarding the determined codes are as follows:

M1: "Unfortunately, there are political and policy approaches at the end of the job."

M4: "I look at whether any job I do is in accordance with the constitution and instructions."

M5: "I experience the advantage of being an administrator in a small district."

M12: "We provide service to the people of Çorum and Amasya, whose economic power is clear. Therefore, we do not avoid being social and we should not. We are also aware of this administratively. We make our decisions accordingly and implement them."

Sub-Theme 1.3. Institution-Related Factors

In line with the purpose of the research, it was determined that some factors related to the institution affected sustainability and sustainable leadership. In this context, eight codes and two sub-codes were determined (Figure III).

Some statements of managers regarding the determined codes are as follows:

M6: "Our physical conditions are problematic. In other words, our physical structure is actually a bit inadequate."

For example, we have been wanting to expand our emergency department for a long time. We want to expand our intensive care units."

M10: "We definitely provide training for this as well. As I said, everything goes through training."

M13: "They encourage you to invest in something like they will work for ten years with permission, but then you see they leave after a year. The doctor who comes the following year says they do not accept these devices."

Sub-Theme 1.4. Factors Related to the Manager

Within the scope of the research, it was determined that some factors related to the manager have an impact on sustainable leadership. This sub-theme was created in line with ten codes and five sub-codes (**Figure IV**).

Some statements of managers regarding the determined codes are as follows:

M2: "We have a committee. If the request is not urgent, it is evaluated in that committee. We have many questions such as whether this material was requested, how many were requested, how much was used before, is this material being purchased for the first time, what is the reason for purchasing, what is the purchasing method, if it was purchased before, how was it purchased. We ask these questions. If a purchasing decision is made by the committee, it is signed by everyone."

M7: "I believe that when a staff teacher says I want to do this but there is no material, we should reject him as much as possible."

M13: "For example, when I came, I requested the following authority: so that I can handle the things I need up to a certain point without the permission of the management, but my friends said that you cannot spend even 1000 liras without our knowledge."

Sub-Theme 1.5. Factors Related to Personnel

It was determined that various personnel-related factors also have some effects on sustainability. **Figure V** shows the nine codes determined for these factors.

The statements of some of the managers regarding the determined codes are as follows:

M2: "The training of the staff is important; the approach of the staff is important. We have cheerful people in our hospital."

M5: "I can say that we benefit from the knowledge and skills of our staff."

M9: "The new generation thinks that resources will not run out, but they are actually running out. They are not aware of it."

Theme 2. Activities for Environmental Benefit

Within the scope of the research, it was attempted to determine what hospital managers pay attention to and what they do regarding environmental benefits within the scope of sustainable leadership and sustainability. In this context, two sub-themes, eight codes and four sub-codes were determined (**Figure VI**).

Some statements of managers regarding the determined codes are as follows:

M4: "The hospital has a dialysis unit. Approximately 6 tons of water is used to wash dialysis devices and 5 tons of water is wasted. Normally, this water goes to the sewer as waste. In fact, all of this water is pure water. In other words, clean water. We had this water analyzed and received a water report stating that there is no problem. We use this water to water our lawns."

M7: "It is monitored. We have a friend who is responsible for waste. I sometimes visit the hospital with him. When we visit the units, we especially warn all the units."

M10: "We buy devices and materials that we can sterilize so that they do not become disposable."

Theme 3. Activities for Economic Benefit

The purpose of the research was to determine what kind of work healthcare institution managers do to achieve economic benefit. Two sub-themes, seven codes and twelve sub-codes were created based on the participants' statements (**Figure VII**).

The statements of some managers regarding the determined codes are as follows:

M1: "We have provided our hospital with a health tourism authorization certificate."

M5: "We primarily fix the malfunctions in the devices we use and all kinds of devices ourselves. We provide the spare parts ourselves. In this way, we have significantly reduced our dependency on external companies. I can say that we benefit from the knowledge and skills of our staff."

M6: "A good field research, detailed research, paying attention to quality and finding the most economically suitable one."

M10: "If we can provide the same material with another, lower-cost material, of course our priority is the one with the lowest cost. But our priority is the effective use for the patient."

M12: "What can we do to bring more patients to the hospital, advertising activities, promotion activities, visits... we do these. We do them in nearby cities, districts, municipalities, villages. We constantly advertise."

Theme 4. Activities for Social Benefit

Within the scope of the research, participants were asked what they did for social benefit and what services they provided for disadvantaged groups. Based on the answers given by the hospital managers who participated in the research, four sub-themes, nine codes and eight sub-codes were determined. These themes and codes are visualized as in **figure VIII**.

Some statements of the managers regarding the determined codes are as follows:

M1: "There was one dental x-ray that we call panoramic. We bought a second panoramic x-ray device."

M2: "There is a system called medication management system. We have a wide variety of medical supplies and medications. You work with people and there can be

human errors. This is very natural. We live in the age of e-technology. We have to use technology. "

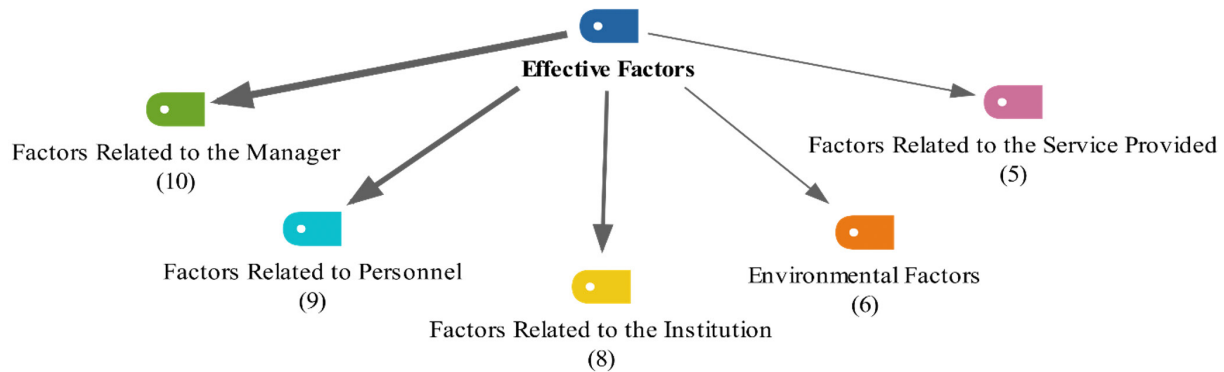
M4: "We built a playground. There is no such thing in any hospital or region. We built an outdoor playground. We designed our children's ward for children. "

M6: "When the disabled apply to our hospital, we give priority so that they can easily reach the doctor. This is already a legal obligation. "

M8: "This is a device that is limited in Turkey. We have it. "

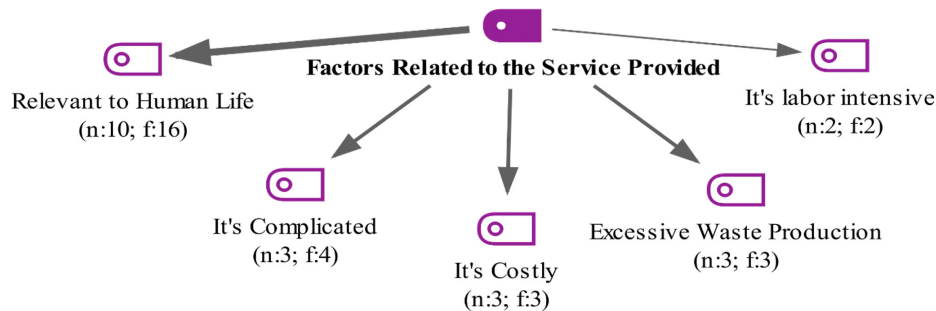
M12: "We go to the poor village schools here and do eye screenings and health screenings. We definitely do it once or twice a year. We donate books to them. We also organize walks and events for diabetic patients. Nature walks... like we organize plays with a theater group..."

Figure 1: Factors Affecting Sustainable Leadership.



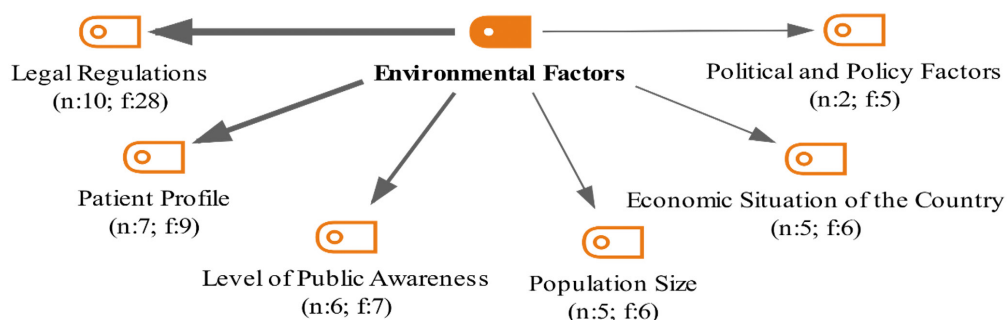
Within the scope of the research, the factors that affect sustainable leadership and sustainability were determined. Five sub-themes were identified regarding these factors. The codes that were effective in determining these themes are shown in the figures below (Figure 2, Figure 3, Figure 4, Figure 5 and Figure 6).

Figure 2: Factors Related to the Service Provided.



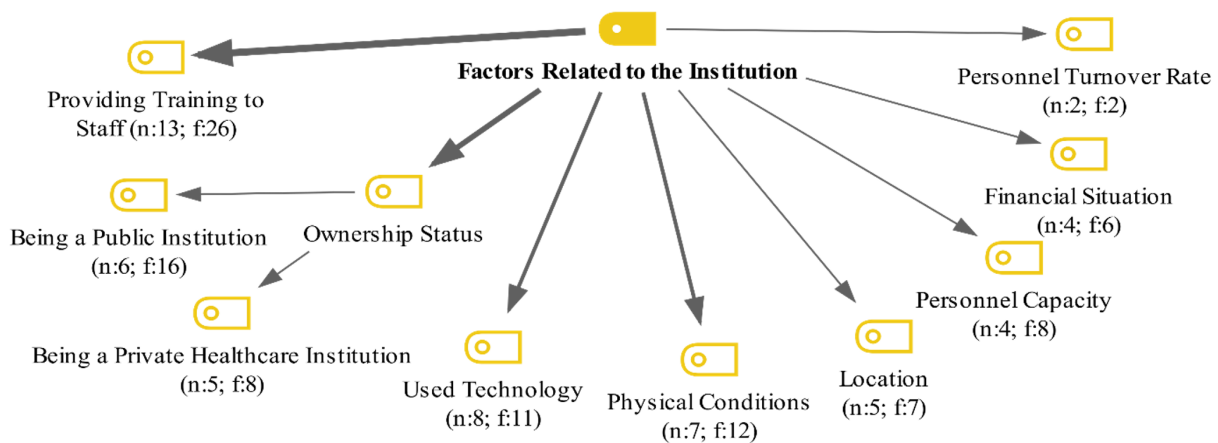
According to the codes in figure 2, it was determined that the service provided affects human life, is complex, costly, produces a lot of waste and is labor intensive, and this affects sustainability. Due to these factors, it was understood that hospital managers have some problems in making sustainable decisions due to the characteristics of health services.

Figure 3: Environment Related Factors.



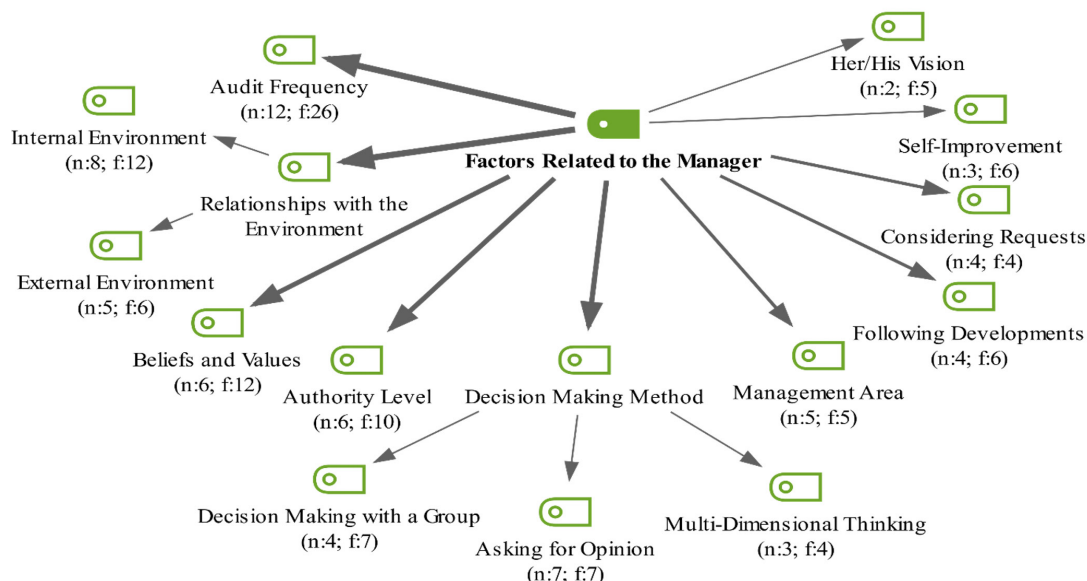
It was determined that legal regulations were the most mentioned factors among the environmental factors by the participants. According to the participants' statements, legal regulations were determined to be the most effective factor in purchasing decisions, waste management, regulations regarding the accessibility of disadvantaged groups, in-house training activities, assignment of personnel and service delivery processes. In addition, some hospital managers stated that the patient's living in a rural area, his/her age and cultural characteristics, the awareness level of the society regarding sustainability, and the population being high or low also affected their decisions. In addition, some managers stated that the economic situation of the country, political and policy factors affected their decisions and it was determined that the poor economic situation of the country affected the expenditures of public hospitals and political elements on the decisions taken.

Figure 4: Factors Related to the Institution.



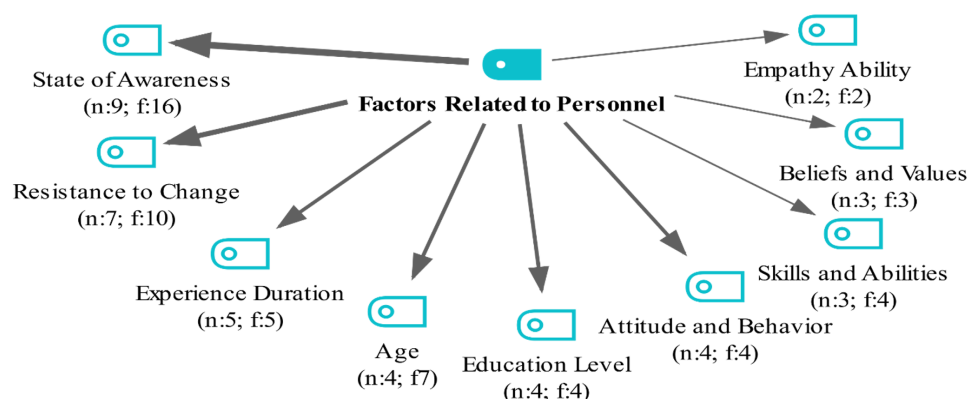
All managers participating in the research stated that they provided training to their staff in order to ensure sustainability. It was seen that the scope of these trainings was related to issues such as waste management, material/equipment/device usage, communication, savings, infection control, and approach to patient profiles. On the other hand, it was determined from the statements of almost all of the participants that the decisions taken were affected by whether the hospital belonged to the public or private sector. Some managers stated that they could not make some decisions because the physical conditions of the hospital were insufficient (building area, parking area). In addition, it was determined from the statements of some of the participants that the existence of technological elements such as digital systems, devices and equipment used in the hospital, having sufficient staff, being in a location that is easily accessible, central and close to production factors positively affected sustainability. Some of the managers mentioned that renewable energy sources are costly, that they consider financial issues when making some decisions and that they can make purchases if they have the financial means. On the other hand, some managers stated that the high staff turnover rate of the hospital caused some problems regarding the operation of the service and created additional costs.

Figure 5: Factors Related to the Manager.



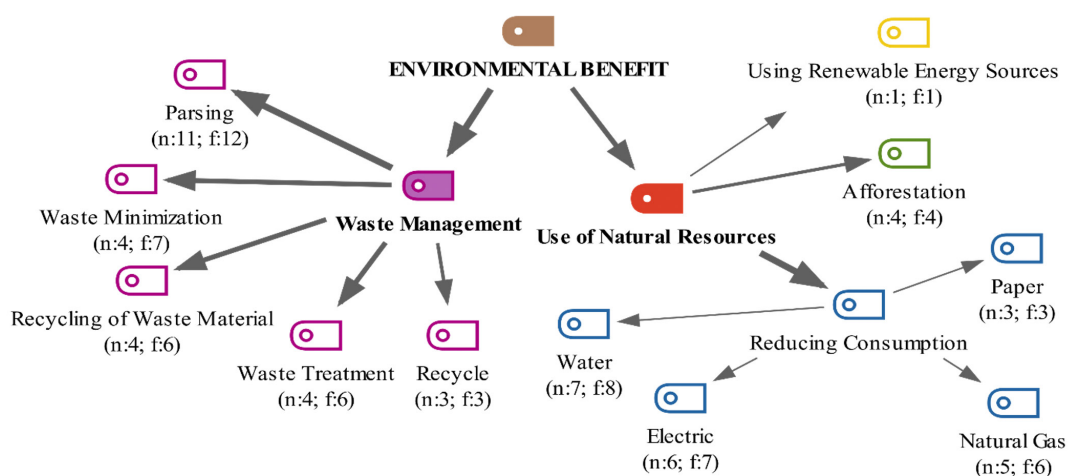
Among the factors related to managers, it was determined that the most mentioned factor was the supervision of managers. From the statements of the participants, it was determined that the beliefs and value judgments of the managers were effective on the decisions they made. Accordingly, it was determined that those working in public hospitals tried to make decisions regarding sustainability in order to protect state property, while managers working in the private sector tried to protect natural resources. On the other hand, some of the managers working in both public and private hospitals stated that they did not make some decisions alone (such as purchasing, spending, service delivery processes, identifying and solving problems), but made decisions as a committee, received opinions from the personnel on issues related to the operation, and had to think multi-dimensionally since health services affected every area. In addition, some of the managers said that they both followed the developments in the health field for sustainability and tried to improve themselves. Some managers stated that the vision of senior managers had an effect on sustainability. However, it was understood that managers followed the processes related to the issues within their authority and did not get involved in issues outside their authority. It was determined that some managers stated that they tried to meet the demands that had an impact on the health service provided.

Figure 6: Factors Related to Personnel.



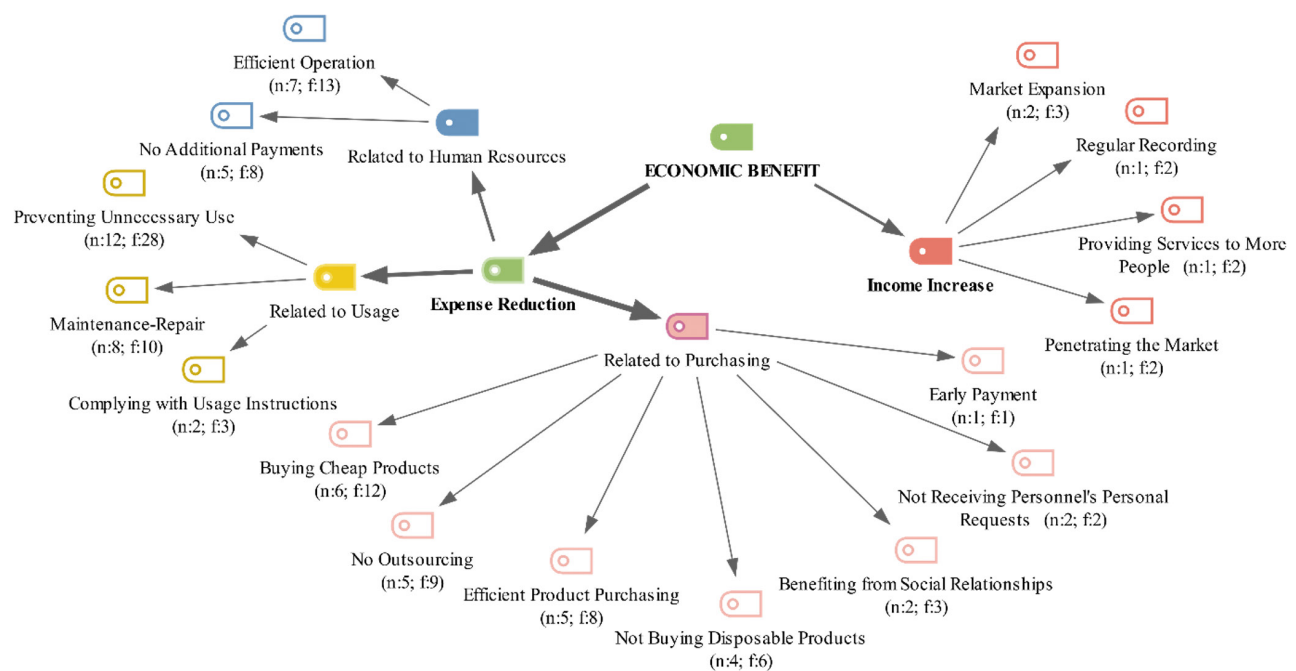
From the statements of the managers who participated in the research, it was determined that variables such as the awareness level of the staff on sustainability issues, the level of reaction to change, their age (generation Z), the length of experience, the level of education, and having different skills and abilities have an impact on sustainability. It was determined that some of the managers stated that the staff resisted some decisions made regarding sustainability, that they had problems with young staff on some issues, and that the experienced staff, who had a long education, and who had knowledge and skills in different areas had positive effects on sustainability.

Figure 7: Activities Conducted Within the Scope of Environmental Benefit.



Almost all of the managers stated that waste is separated as medical waste, household waste, hazardous waste, chemical waste. Some managers stated that they prefer products that can be used repeatedly instead of single-use products in order to reduce both costs and the damage to nature. It was determined that some managers use a product they use in another area for a different purpose in a way that does not harm human health. In addition, it was determined from the statements of some participants that liquid waste is purified and discharged into the sewage system and gases are filtered and released into nature. It was determined from the statements of the managers that the separated household waste is given to municipalities or contracted companies for recycling purposes. It was determined that the managers who participated in this research also have some practices regarding the protection of natural resources. In this context, some managers stated that they use economical tools to reduce water, electricity, natural gas and paper consumption, conduct inspections to reduce usage and use digital systems. In addition, some managers said that they carry out afforestation activities.

Figure 8: Activities Conducted Within the Scope of Economic Benefit.



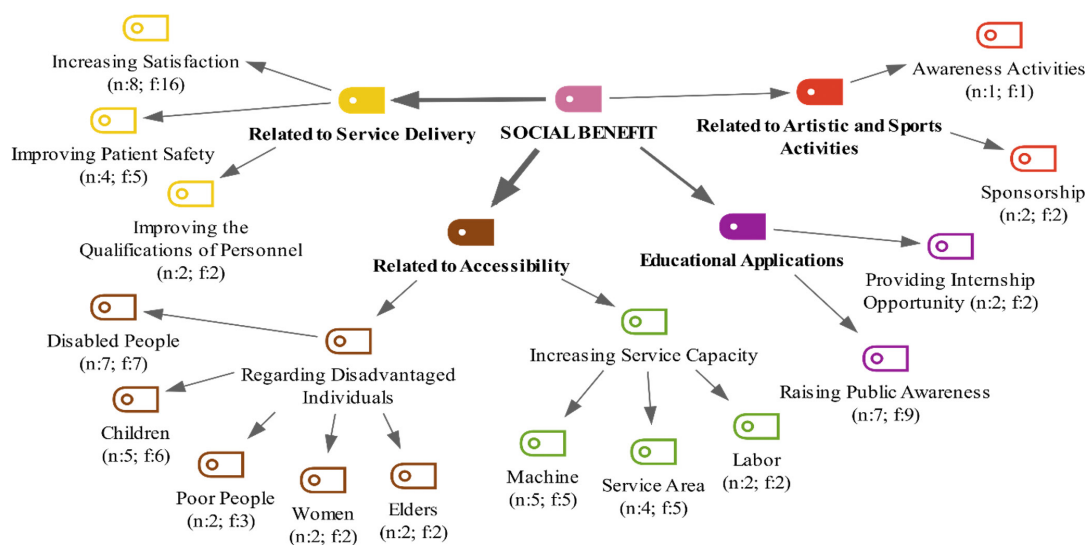
It was determined that the participants paid the most attention to issues related to product purchasing processes among the efforts to reduce expenses. Some of the hospital managers stated that they tried to prefer more affordable products that would not negatively affect human health and that they did a good market research for this. Some participants stated that instead of purchasing a product or service from outside, they primarily tended to use the resources within the institution (assigning personnel from within the institution to repair, maintenance, maintenance, construction, training, etc., and stopping purchasing food services from outside). It was determined that four managers paid attention to purchasing efficient products (long service life, non-faulty, quality and affordable, technical support provided, etc.). In addition, it was determined that some managers working in public hospitals took advantage of their social relations and obtained some products through donations.

It was determined that hospital managers carried out some studies in order to reduce personnel and product-related expenses. In this context, it was determined that some managers stated that they created a work plan by paying attention to the hours when the hospital is busy, the distribution of personnel in the areas, and the units with high shift numbers in order to make more efficient use of the personnel. In addition, it was determined that they made arrangements for the staff to work outside of working hours in units with high demand.

Almost all of the participants stated that they implemented practices to prevent unnecessary use in order to reduce usage-related expenses. Some managers touched on issues related to maintenance and repair of products and using them in accordance with the instructions for use. In this context, it was determined that managers turned off electricity, water and natural gas in unused areas, kept unused devices off, reduced energy consumption in areas that did not pose a risk, provided training to prevent consumables (gloves, syringes, napkins, other medical supplies,

etc.) from being used for purposes other than intended, and checked the staff in the processes after the training. It was determined that they carried out activities such as maintenance of radiators, renewal of installations, repair of windows, turning to alternative energy types (switching to electricity consumption instead of natural gas consumption) and creating two-stage entrance doors within the scope of maintenance and repair activities. It was determined that the activities carried out to increase income in hospitals were grouped under four codes. It was determined that some managers carried out activities aimed at health tourism (market expansion) within the scope of revenue increase efforts, while others resorted to practices such as advertising, promoting institutions and making agreements with institutions (market penetration), and providing services to more people by providing services outside of working hours. In addition, it was determined that one manager stated that they carried out efforts to reduce expenses that could not be converted into income (auditing, providing training and using digital systems) by ensuring that the services provided to patients were fully recorded.

Figure 9: Activities Conducted Within the Scope of Social Benefit.



It was determined that the hospital managers in the working group carried out activities to increase accessibility, provide higher quality service, engage in educational activities, and support artistic and sports activities within the scope of social benefit. Some of the participants stated that they opened new clinics, expanded the waiting area, opened a new service unit, expanded the parking area, and increased the number of personnel and medical devices in order to increase accessibility. In addition, some managers stated that they tried to prevent patients from going to other provinces by purchasing medical devices that were not available in the region, and that they provided service to more patients by operating medical devices at the upper limit they could operate (operating at maximum level).

More than half of the hospital managers who participated in the study were found to have made arrangements to increase the accessibility of the most disabled individuals from disadvantaged groups. It was understood that the main reason for this was legal regulations. The managers stated that they had a disabled ramp built in order to increase the accessibility of disabled individuals to health services, used the disabled alphabet in areas within the hospital, installed a voice system in the elevators, assigned a staff to accompany disabled individuals, and designed the WCs and bathrooms according to disabled individuals. Some managers said that they designed the hospital environment in a way that children would feel comfortable (painting the walls in colors, decorating them with cartoon characters, choosing furniture suitable for children, creating a playground, using toys, etc.). It was determined that two managers stated that services were provided for female patients only according to the standards determined for being a “mother-friendly hospital” for expectant mothers. In terms of services provided to the elderly, one hospital manager stated that they met the criteria of an “elderly-friendly hospital”, while another manager stated that they provided staff support during the service process of the elderly.

Another study on social benefit was determined to be aimed at increasing the quality of health service delivery. In this context, the majority of the managers participating in the study stated that they regularly measure patient satisfaction

and make arrangements in line with the feedback. Some of the managers stated that they ensured that the staff received certification in order to increase their knowledge and skills. Four managers said that they used systems to prevent human errors in order to increase patient safety.

It was determined that training was provided to the public, patients and relatives of patients in order to increase the health level of the society within the scope of social benefit. In addition, two managers mentioned that they provided internship opportunities to high school and university students studying in the field of health services. It was determined that some managers sponsored local theater teams and sports clubs and organized social activities for disadvantaged groups.

Discussion

This research has attempted to determine what is considered and what is done regarding sustainability in hospitals, which are the institutions that consume the most resources and produce waste among healthcare institutions. As a result of the research conducted for this purpose, it has been found that variables related to five factors have an effect on sustainability and sustainable leadership. One of these factors has been determined to be "characteristics of the service provided". Accordingly, it has been determined that sustainability is affected by reasons such as the service provided affecting human life, being a complex, costly, high waste production and labor-intensive service. It has been understood that some decisions of managers are limited due to these characteristics and that they have some problems in making sustainable decisions. It has been found that another factor affecting sustainable leadership and sustainability is related to environmental variables. It has been determined that legal regulations are the most mentioned among these variables. According to the statements of the participants, it has been determined that legal regulations are the most effective factor in purchasing decisions, waste management, regulations regarding the accessibility of disadvantaged groups, in-house training activities, assignment of personnel and service delivery processes. It has been determined that, together with legal regulations, the fact that the patient lives in a rural area, his/her age and cultural characteristics, the level of awareness of the society regarding sustainability, and the fact that the population is high or low also affect decisions regarding sustainability. In addition, it has been determined that the economic situation of the country, political and policy factors are decisive on the decisions to be taken in public hospitals. Similar results have been obtained in the studies in the literature. Accordingly, in the research of Şenol, Üstünkaya and Akkuş²³, it was stated that excessive waste is produced in health institutions and too many personnel are on duty, which has a negative effect. It was also stated that the awareness level of the society should be increased for the sustainability of hospitals. Research was conducted by Yılmaz, Gökmen and Erişen²⁴ in Konya province. According to the opinions of 11 health institution managers who participated in this research, it was determined that financial issues were

in the background since a service related to human health was provided. It was also determined that the participants stated that qualified human resources were important for sustainability. On the other hand, it was stated that the increase in the costs of health services and the inability to access financial resources in a short time in public hospitals negatively affected the sustainability of the service.

Within the scope of the research, it has been determined that various variables related to the institution and the manager also have an effect on sustainability and sustainable leadership. According to the statements of the participants, it has been determined that trainings are given to the personnel in order to ensure sustainability (waste management, material/equipment/device use, communication, savings, infection control, patient profile, etc.), that being a public or private hospital affects the decisions taken, and that inadequate physical conditions (building area, parking area) negatively affect sustainable decision-making. It has been determined that technological elements such as digital systems, devices and equipment used in the hospital; having sufficient staff, being easily accessible, central and close to production factors positively affect sustainability. It has also been determined that the poor financial situation of the hospital has a negative effect on the decisions to be taken. On the other hand, it has been determined that the high staff turnover rate of the hospital causes some problems related to the operation of the service and creates additional costs. Similar results have been obtained in the studies in the literature. In the research conducted by Şenol, Üstünkaya and Akkuş²³, it has been determined that the in-service trainings given, the awareness level of the personnel and the inspections carried out affect the sustainability of the hospitals. In the research conducted by Yılmaz, Gökmen and Erişen²⁴ with 11 public and private hospital managers in Konya province, it was determined that some managers had physical space problems.

In the study, 10 variables that have an impact on sustainability and sustainable leadership related to managers were determined. It was determined that managers working in public hospitals try to make

decisions about sustainability in order to protect state property, while managers working in the private sector try to protect natural resources. On the other hand, it was determined that managers in both public and private hospitals do not have sufficient authority to make some decisions. It was determined that managers make decisions as a team in order to ensure sustainability and make the right decisions, such as purchasing, spending, service delivery processes and identifying and solving problems, consult the opinions of the staff and think multi-dimensionally about what the decisions made may affect. It was also determined that managers both follow technological developments for sustainability and try to improve themselves. It was determined that some managers stated that the vision of senior managers has an impact on sustainability. However, it was understood that managers follow the processes related to the issues within their authority and do not get involved in issues outside their authority. It was determined that some managers stated that they try to meet the demands that affect the health service provided. In the study conducted by Šimanskienė and Župerkienė,⁸ it was stated that a sustainable leader is a person who has a vision, cooperates, adopts teamwork and shows regular development. As a result of the research conducted with academics by Zorlu and Korkmaz²⁵, sustainable leadership was associated with the manager's communication style, values, receiving employees' opinions, following vision and sectoral developments. Similar results were obtained in the research conducted with teachers by Çetin and Baş.²⁶ In the research, it was determined that cooperation, communication style, joint decision-making and values were effective on sustainable leadership in line with the statements of the teachers. In this context, it can be said that similar results were obtained with the studies in the literature.

It has been determined that the staff's awareness of sustainability, age, experience, participation in decisions, level of education, knowledge and skills in different areas affect sustainability. In addition, it has been understood that the communication of the staff with the patient, their attitudes and behaviors in service processes, and their beliefs and values regarding sustainability also have positive and negative effects on sustainability. In the research conducted by Boiral, Talbot and Paillé²⁷, it was stated that the staff should voluntarily carry out some practices and that voluntary practices ensure more success. It was determined that 30% of the participants in the research conducted by Yiğit and Yiğit²⁸ thought that the lack of education of the staff negatively affected economic sustainability.

Within the scope of the research, it was tried to determine what hospital managers pay attention to and what they do regarding environmental benefit within the scope of sustainable leadership. Activities related to environmental benefit are grouped under two sub-themes as waste management and use of natural resources. It was

determined that most attention is paid to separation regarding waste management. It was determined that they separate waste according to their types such as domestic waste, medical waste, hazardous waste, chemical waste and apply appropriate treatment or recycling to these wastes. In addition, it was determined that some managers reuse materials in different ways and prefer sterilizable, reusable products to reduce the amount of waste. It was determined that the managers participating in this research also have some practices regarding the protection of natural resources. In this context, it was determined that some managers use economical vehicles to reduce water, electricity and natural gas consumption, conduct inspections, and use some wastewater (water from dialysis units) for different purposes. It was determined that some managers turn to digital systems to reduce paper consumption. It was also determined that some managers carry out afforestation activities. Another manager stated that they use renewable energy sources (solar energy). In the study of Altın and Altın¹³, it was stated that the wastewater generated during the production of water by reverse osmosis from dialysis units can be used in lawn irrigation and flushing, and it was determined that 86% of the hospital managers who participated in the study supported the reuse of this water. In the study conducted by Çilhoroz and Işık²⁹, it was determined that both public and private hospitals examined met the standards regarding water management and sustainable facilities, but they were inadequate in energy management. In the study conducted by Turan Kurtaran and Yeşildağ³⁰ evaluating 7 hospitals in the province of Trabzon, it was determined that all hospitals paid attention to waste management, separated waste, tried to reduce it, and stored hazardous waste appropriately. It was also found that they carried out various activities to protect natural resources such as preventing water waste, providing heat insulation, and controlling plumbing leaks. In the study conducted by Baytaş and Aydın Çetin³¹ on green hospitals, it was stated that a clinical night guard was assigned and unused computers were turned off. In this way, it was stated that both energy savings were achieved and clinical costs were reduced. It was also mentioned that environmental benefits were achieved by cleaning and reusing the tools and equipment used in the hospital in appropriate ways. It was mentioned that in some hospitals that received a green hospital certificate, light sensor lighting was preferred, temperature balance was achieved, water use was reduced, and heat losses were prevented. In the study conducted by Yılmaz, Gökmen, and Erişen²⁴, attention was drawn to digital archive applications in order to reduce paper consumption. In this context, studies in the literature and the results of this study show that hospital managers take similar measures.

It has been determined that the managers participating in the research focus on studies aimed at reducing their expenses within the scope of economic benefit.

In this context, it has been understood that hospital managers tend to buy cheap products in order to provide economic benefit. It has been determined that managers who prefer cheap products are careful not to compromise on quality, conduct very detailed market research and prefer products with features that can meet their needs. It has also been determined that some managers prefer to assign personnel from within the institution for tasks such as repair, maintenance, construction and training rather than external sources. It has also been determined that they pay attention to purchasing products with a long service life, that do not malfunction, that are of high quality and at affordable prices. In addition, it has been determined that some managers working in public hospitals obtain some products through donations by taking advantage of their social relations and benefit from early payment discounts. It has also been determined that hospital managers carry out some studies regarding personnel and product use. In this context, it has been determined that some managers create work plans by paying attention to the hours when the hospital is busy, the distribution of personnel in the areas and the units where the number of shifts is high. In addition, it has been determined that some managers make arrangements regarding additional working hours in units where demand is high. It has been determined that the participants' cost reduction efforts regarding product use are aimed at preventing unnecessary use, using the products in accordance with their instructions, and having the products maintained and repaired. It has been determined that maintenance and repair activities are carried out within the scope of maintenance and repair activities such as maintenance of radiators, renewal of installations, repair of windows, switching to alternative energy type (switching to electricity consumption instead of natural gas consumption) and creating two-stage entrance doors. It has also been understood that some managers take precautions to prevent any malfunctions by ensuring that the products are used in accordance with the instructions for use. In this way, it has been determined that they aim to both prevent interruption of service and avoid additional costs. In the research conducted by Yiğit and Yiğit²⁸ on the economic sustainability of university hospitals, it has been stated that the number of services and capacity utilization are low, there are problems in the supply of medical supplies and human resources, some physicians prefer branded products and not all services produced are invoiced. In addition, 80% of the participants stated that purchasing costs are high due to the long payment period.

It has been determined that the efforts carried out to increase income in hospitals are grouped under four codes. It has been determined that some managers carry out activities aimed at health tourism (market expansion) within the scope of income increase efforts, while others resort to practices such as advertising, making

introductions to institutions and agreements (penetrating the market), and providing services to more people by providing services outside of working hours. In addition, it has been determined that one manager stated that they carry out efforts to reduce expenses that cannot be converted into income by ensuring that the services provided to patients are fully recorded in the records (auditing, providing training and using digital systems). As a result of the analysis of the data obtained from 70 private hospital managers by Çavmak³², cost management practices, logistics performance (various tasks such as demand management, purchasing, stock control, storage, waste management, transportation, invoicing etc.) and marketing efforts have been determined as variables potentially related to financial sustainability performance.

It has been determined that some activities are carried out to provide social benefits within the scope of sustainability and sustainable leadership. It has been determined that the hospital managers in the study group carry out activities to increase accessibility, provide higher quality service, engage in educational activities, and support artistic and sports activities. It has been determined that hospital managers carry out activities such as opening new clinics, expanding the waiting area, opening a new service unit, expanding the parking area, increasing the number of personnel, increasing the number of medical devices, purchasing medical devices that are not available in the region, and operating medical devices at the upper limit (maximum level) in order to increase accessibility. In addition, it has been determined that they carry out various activities in order to provide a more accessible service to disadvantaged groups. It has also been determined that internship opportunities are offered to their students. It has been understood that some managers sponsor local theater teams and sports clubs and organize social activities for disadvantaged groups. It has been determined that two managers mention that they provide free services in order to increase the accessibility of poor segments to health services. When the findings obtained in the research are evaluated in general, it has been determined that the participants mostly make statements about economic benefit, followed by social benefit. It was determined that variables related to environmental benefits were mentioned less by the managers participating in the study. A similar result was obtained in the study conducted by Toker and Çınar³³. In this study, it was determined that the level of implementation of sustainable environmental policies of hospitals was lower than the level of implementation of social policies. In the study conducted by Baytaş and Aydın Çetin³¹ in which they evaluated the criteria taken into account in the certification of green hospitals, it was noted that a hospital created playgrounds for children. In the study conducted by Yılmaz, Gökmen and Erişen²⁴ in Konya province, it was determined that midwives provided online education to pregnant women and their spouses.

Conclusion and recommendations

As a result of this research conducted on the sustainability of hospitals, five themes were determined for sustainable leadership and sustainability. Accordingly, it was determined that health services, managers, personnel, the environment and institutional characteristics were effective on the sustainability of hospitals. According to the views of the participants, it was determined that health services are costly, complex and labor-intensive services that affect human life, negatively affect sustainability and limit managers. It was understood that legal regulations are extremely effective on the decisions of managers. It was determined that the decisions of managers in private and public hospitals differ in some processes. It was determined that the decisions taken for sustainability in public hospitals are affected by the economic situation, political and policy structure of the country. In this context, legal regulations should be made for all processes in hospitals for a more sustainable health service. Decisions in public hospitals should be made independent of the political and policy structure. A simpler structure should be adopted in hospitals. As a result of the research, it was understood that increasing social awareness will positively affect sustainability. It was determined that the characteristics of the region where hospitals provide service also affect the decisions to be taken. It was determined that all managers constantly provide training to the staff for more sustainable activities and that inspections are carried out. It was determined that hospital managers try to benefit from technology in various areas within the scope of sustainability, constantly develop themselves and follow the changes in the environment. It was understood that the lack of authority of managers to make some decisions slows down the pace of action and this negatively affects sustainability.

It was determined that having good social relations with the environment positively affects making more sustainable decisions. In addition, it was determined that more benefits are obtained within the scope of sustainability as the quality and quantity of the personnel increase. In this context, importance should be given to raising the awareness of the society in every subject for a more sustainable health service. Public support should be provided to eliminate the disadvantages of hospitals related to their location. Trainings for personnel should be increased and educational opportunities that will improve the qualifications of the personnel should be provided together with these trainings. The authorities of hospital managers should be increased so that they can make faster decisions and evaluate opportunities in a timely manner. Hospitals' cooperation with other institutions should be increased and mutual solidarity should be ensured.

Within the scope of the research, it was determined what hospital managers pay attention to within the scope of sustainability and what kind of work they carry

out. In line with the opinions of the participants, it was determined that the most economic benefit was taken into consideration. It was determined that more limited work was carried out regarding environmental benefit. It was determined that the hospital managers' efforts to obtain economic benefit were aimed at reducing expenses, and more limited decisions were made regarding increasing income. It was determined that they tried to buy cheap products by conducting a good market research without compromising quality within the scope of reducing expenses. In addition, it was determined that the personnel tried to reduce the use of outsourcing by benefiting from their knowledge and skills in other areas in addition to their professional knowledge and skills, preferred products that could be used for a long time, took measures to prevent unnecessary use and were careful not to create additional costs as much as possible. It was determined that the activities carried out within this scope differed according to hospitals. In this context, good practice examples should be shared among managers for more sustainable activities. In addition, different skills can be provided to volunteer personnel and these personnel can continue to benefit in different areas. The personnel shortage, especially in public hospitals, should be eliminated, both the workload of the personnel should be reduced and additional payments given to the personnel should be reduced. The advantages and disadvantages of outsourcing in hospitals should be reviewed. In addition, it was determined as a result of the research that applications aimed at increasing income were extremely limited. Research should be conducted on how hospitals' incomes can be increased and action plans should be created. It was determined that various activities were carried out in hospitals regarding waste management and protection of natural resources within the scope of environmental benefits. It was determined that the participants paid more attention to waste management due to legal regulations, but only took some measures to reduce consumption within the scope of protection of natural resources. In this context, hospital managers should be given training on areas related to sustainability. Policies should be created regarding the protection of natural resources that will cover not only local hospitals but also the entire world. Hospitals should be encouraged to use sustainable resources. Both the protection of natural resources should be ensured and technology should be used more within the scope of economic benefits and the use of digital systems should be increased. Care should be taken to ensure that hospital managers are well-educated and visionary individuals.

It was determined that the participants made decisions to increase the accessibility of health services in order to provide social benefit. In this context, it was determined that they opened new service areas, purchased new medical devices, and increased the number of personnel. It was also determined that they organized the hospital environment for the disabled and children, and provided

personnel to accompany the elderly and the disabled. It was determined that the participants carried out various activities to raise public awareness, provided internship opportunities for students, regularly measured satisfaction, and took measures to increase satisfaction. Public hospitals provide free services to ensure access to health services for the poor. However, this situation should no longer be the responsibility of only public hospitals. Regulations should be made to increase the access of the poor to private hospitals within the scope of social benefit.

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Conflict of interest

There is no conflict of interest between the participants and the author.

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CASE REPORT

Neumonía necrotizante por *Staphylococo aureus* sensible a la meticilina ¿productor de leucocidina de Pantón-Valentine? A propósito de un caso

Necrotizing pneumonia due to methicillin-sensitive Staphylococcus aureus, producer of Pantón-Valentine leukocidin? A case report

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Resumen

Staphylococcus aureus (SA) es una bacteria grampositiva y anaerobia facultativa asociada con una amplia variedad de enfermedades, que van desde infecciones de piel y tejidos blandos hasta enfermedades invasivas como neumonía, infecciones osteoarticulares y bacteriemia, entre otras. La importancia de este patógeno radica en su fácil y rápida transmisión, junto con su significativa morbilidad y mortalidad. Es importante destacar que este patógeno puede ser sensible a la meticilina (SASM) o desarrollar diferentes mecanismos de resistencia (SAMR). Además, existen cepas que producen toxinas, como la leucocidina de Pantón-Valentine (LPV), que comúnmente se asocia con infecciones recurrentes de piel y tejidos blandos, y con menor frecuencia con neumonía necrotizante invasiva. La LPV es una toxina citopática compuesta por dos subunidades llamadas LukS-PV y LukF-PV, que son secretadas de manera independiente por el patógeno. Estas son capaces de generar poros en las membranas celulares, causando un daño letal inmediato y respuestas inflamatorias secundarias. La LPV suele afectar a los leucocitos, en particular a los neutrófilos, lo que provoca un deterioro significativo del sistema inmunitario innato y una intensa respuesta inflamatoria del huésped. En este artículo, se presenta el caso de un adulto con infección por MSSA (SASM) aislada en aspirado bronquial y hemocultivos. El paciente, que fue hospitalizado con neumonía necrotizante aguda, desarrolló posteriormente un choque séptico. Requirió ventilación mecánica invasiva y soporte inotrópico debido a disfunción miocárdica en el contexto de choque cardiogénico y sepsis. Adicionalmente, se inició terapia de reemplazo renal (TRR) como una de las principales complicaciones asociadas. Basándose en la evolución clínica, se sospechó la producción de LPV. El artículo revisa aspectos relacionados con la aparición de la enfermedad, diferentes procedimientos de reconocimiento y herramientas de manejo, con un enfoque en la terapia antibiótica y los agentes antitoxinas.

Palabras clave: Neumonía necrotizante, *Staphylococo aureus* sensible a la meticilina, toxina Pantón-Valentine.

Abstract

Staphylococcus aureus (SA) is a gram-positive and facultative anaerobic bacterium which is associated with a wide variety of diseases, ranging from skin and soft tissue infections to invasive diseases such as pneumonia, osteoarticular infections, and bacteremia, among others. The importance of this pathogen lies in its easy and fast transmission, along with its significant morbidity and mortality. It is important to note that that this pathogen can be methicillin-sensitive (SAMS) or develop different resistance mechanisms (SAMR). Moreover, there are strains that produce toxins, such as Pantón-Valentine leukocidin (PVL) which is commonly associated with recurrent skin and soft tissue infections, and less frequently with invasive necrotizing pneumonia. PVL is a cytopathic toxin composed of two sub-units named LukS-PV and LukF-PV, which are secreted separately by the pathogen. They are capable of generating pores within the cell membranes, which causes immediate lethal damage and secondary inflammatory responses. PVL usually affects leukocytes, particularly neutrophils, resulting in significant impairment of the innate immune system and an intense inflammatory response from the host. In this article, the case of an adult with MSSA infection isolated in bronchial aspirate and blood cultures is presented. The patient, who was hospitalized with acute necrotizing pneumonia, later developed septic shock. The patient required invasive mechanical ventilation and inotropic support owing to myocardial dysfunction in the context of cardiogenic shock and sepsis. Additionally, renal replacement therapy (RRT) was initiated as one of the main associated complications. Based on the clinical course, PVL production was suspected. The paper reviews aspects regarding the disease appearance, different recognition procedures, and management tools, focusing on antibiotic therapy and antitoxin agents.

Key words: Necrotizing pneumonia, methicillin-sensitive *Staphylococcus aureus*, Pantón-Valentine toxin.

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Descripción del caso clínico

Varón de 67 años, natural de Marruecos. Como antecedentes personales destaca ser ex-fumador, enolismo moderado, diabético tipo 2 y dislipémico, y presentó un ingreso en Agosto 2023 por sepsis respiratoria secundaria a neumonía viral (COVID-19) y sobreinfección bacteriana en lóbulo inferior izquierdo no filiada.

Acude a Urgencias por mal estado general, tos seca irritativa, odinofagia y dificultad respiratoria de tres días de evolución, sin datos a la exploración física destacables salvo febrícula. En las pruebas complementarias aparece una proteína C Reactiva (PCR) de 12 mg/dL sin leucocitosis y un aislamiento de virus Influenza A en una prueba de reacción en cadena de la polimerasa rápida. Se realiza una radiografía de tórax (RxTx) (**Figura 1**) anodina por lo que es dado de alta a domicilio bajo tratamiento sintomático.

A los dos días, es nuevamente atendido por deterioro respiratorio. En la evaluación inicial destacaba taquicardia de 138 latidos por minuto, sin inestabilidad hemodinámica, taquipnea de 35 respiraciones por minuto con una saturación de oxígeno del 97% sin aporte de oxigenoterapia y se encontraba afebril. El resto de la exploración general no fue destacable. La auscultación pulmonar reveló crepitantes gruesos en hemitórax derecho. La evaluación neurológica no mostró ningún déficit. Analíticamente, se objetivó hiperglucemia de 218 mg/dL, ascenso de PCR hasta 42,6 mg/dL y acidosis metabólica leve. En la radiografía de tórax (**Figura 2**) se observó un infiltrado difuso de tipo algodonoso en todo el hemitórax derecho.

Ante la sospecha de neumonía por gripe A se inició manejo con colocación de cánulas nasales a 5 litros para saturaciones de oxígeno del 95%, azitromicina 500 mg cada 24 horas y ceftriaxona 1 g cada 24 horas por sospecha de sobreinfección bacteriana, tras obtener los cultivos necesarios. Se añadió corticoterapia endovenosa y tratamiento broncodilatador con bromuro de ipatropio.

El paciente ingresó en planta convencional para continuar los cuidados. A las 7 horas, el paciente presentó bajo nivel de conciencia y arreactividad (CGS 3p: V1 M1 O1) por lo que se alertó al Servicio de Medicina Intensiva (SMI). En la exploración física destacaban pupilas midriáticas pero reactivas. Presentaba hipotensión 60/40 mmHg que se trató inicialmente con fluidoterapia.

Se decide ingreso en SMI donde se realiza intubación orotraqueal, conexión a ventilación mecánica invasiva e inicio de NorAdrenalina a dosis medias.

Los resultados de laboratorio mostraron una hemoglobina de 15,9 g/dL, leucopenia significativa con $2,6 \times 10^3/\mu\text{L}$ (con neutrofilia del 71%), plaquetopenia de $130 \times 10^3/\mu\text{L}$ e hiperglucemia de 450 mg/dL. Presentaba una lesión renal aguda con creatinina de 2,53 mg/dL y urea en sangre de 87 mg/dL, con un filtrado glomerular estimado de 25 mL/min/1,73 m². Los electrolitos se mantuvieron en rango. Los marcadores inflamatorios se mostraron elevados con una proteína C reactiva de 46,07 mg/L y una procalcitonina de 524 ng/mL. Además presentó elevación de la creatinina fosfoquinasa (CPK) a 553 mcg/L y el análisis de orina mostraba glucosuria de 2.000 mg/dL, proteinuria 300 mg/dL y cetonas positivas.

Figura 1: Radiografía de tórax inicial 31/12/2023.

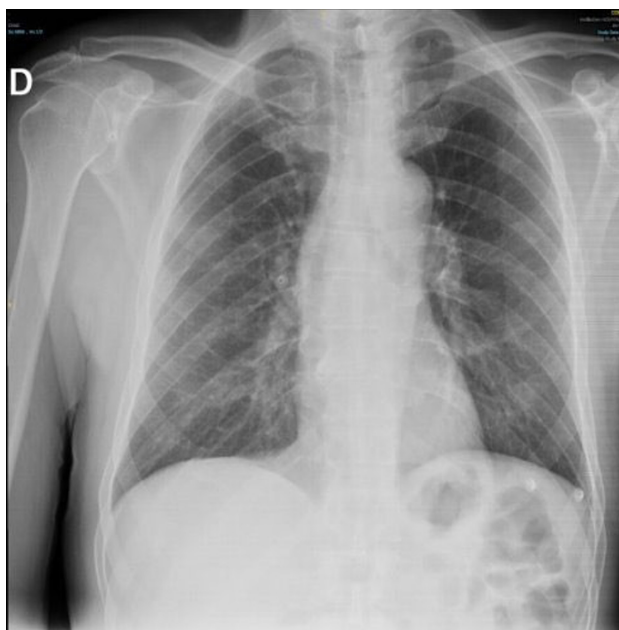
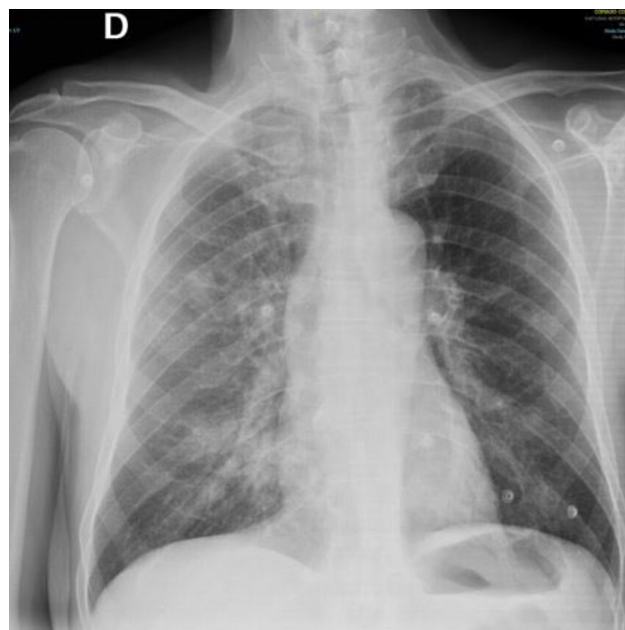


Figura 2: Radiografía de tórax 02/01/2024.



Las antigenurias fueron negativas y persistía positiva la PCR del virus de la gripe, mientras que la radiografía de tórax portátil tras intubación orotraqueal mostraba opacidades infiltrativas redondeadas difusas en hemitórax derecho sugestivas de neumonía condensante (**Figura 3**).

La sospecha clínica inicial fue de cetoacidosis diabética descompensada por proceso infeccioso respiratorio (neumonía grave adquirida en la comunidad) e insuficiencia respiratoria hipoxémica por lo que se inició cobertura con antibioterapia de amplio espectro empírica con Piperacilina – tazobactam 4,5 g cada 6 h y azitromicina 500 mg cada 24 h, corticoterapia a dosis de estrés y Oseltamivir 75 mg tras recogida de nuevos cultivos.

En vista a la inadecuada evolución clínica las primeras horas y evolución a shock séptico con fallo

multiorgánico, se rotó antibioterapia a Linezolid 600 mg/12h y Meropenem 1g/8h, mantenidos 7 y 5 días respectivamente.

La evolución clínica y complicaciones asociados sugirió el desarrollo de una neumonía necrotizante por SA productor de la toxina leucocidina de Pantón Valentine, por lo que se decidió mantener linezolid por el poder antitoxina hasta cumplir una tanda a pesar de aislarse SAMS resistente a clindamicina tanto en hemocultivos como en broncoaspirado (**Tabla I**).

El paciente se fue estabilizando. Los hemocultivos se negativizaron y en BAS se aisló nuevamente SAMS, por lo que a la semana del inicio de la antibioterapia se realizó desescalada antibiótica a cloxacilina 2 g cada 6 h, con una tanda de Clindamicina para favorecer el efecto antitoxina. (**Tabla II**).

Figura 3: Radiografía de tórax portátil 03/01/2024.

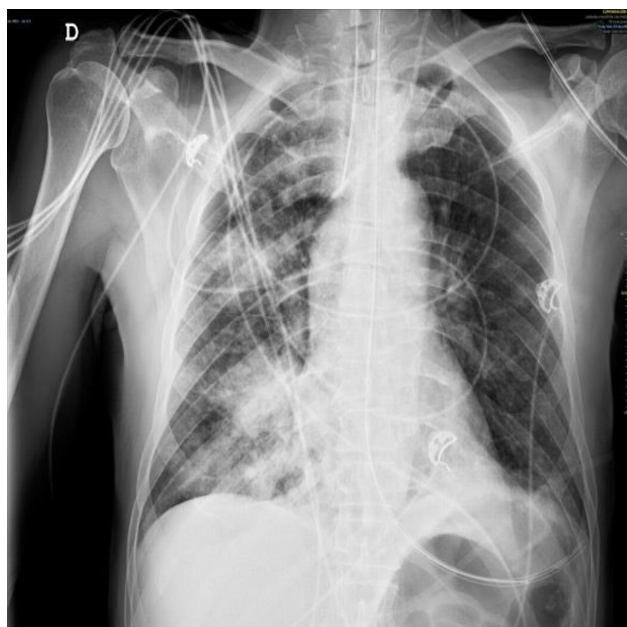


Figura 4: TC de tórax 20/01/2024.

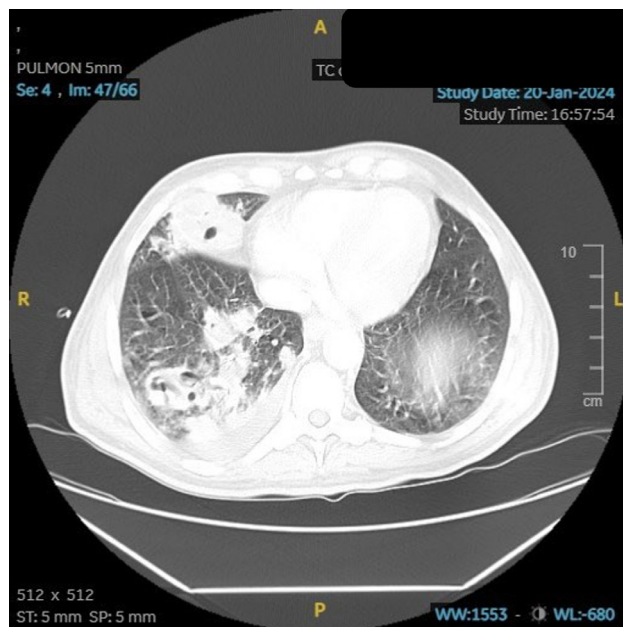
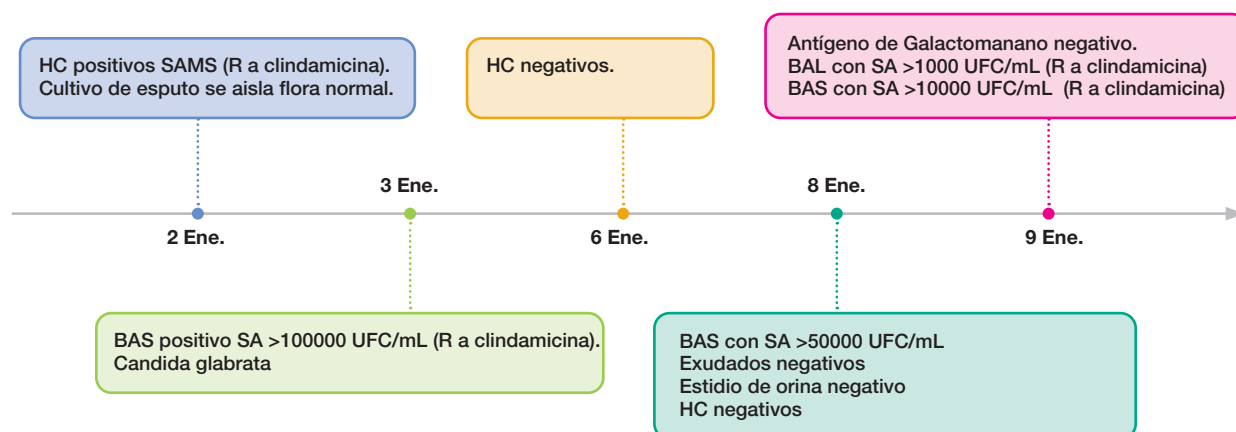


Tabla I: Registro resultados microbiología.



En todos los BAS/BAL se aísla virus de la gripe de forma concomitante.

Después de varios días, el paciente presentó fiebre y un discreto repunte de RFA y se realizó un TAC de tórax (**Figura 4**) donde se evidenciaron extensas consolidaciones parenquimatosas con cavitaciones centrales que comprometían particularmente el campo pulmonar derecho y segmento lingular del lóbulo superior izquierdo, hallazgos compatibles con proceso infeccioso en evolución además de un leve derrame pleural derecho, por lo que se decidió mantener cloxacilina y nuevo ciclo de Clindamicina durante dos días. (**Tabla II**).

Ante sospecha de neumonía necrotizante por SAMS productor de toxina de Pantón Valentine el manejo de la antibioterapia se realizó de forma empírica, ya que no se solicitó la determinación de la toxina durante el ingreso del paciente, debido a que las actuaciones clínicas deben ser inmediatas y los resultados de la toxina se demorarían varios días.

En cuanto al manejo de las complicaciones durante su ingreso, se realizaron varios ecocardiogramas transtorácicos que no lograron identificar una posible endocarditis infecciosa, pero sí mostró disfunción ventricular severa con necesidad de NorAdrelin a dosis altas, asociación de Vasopresina e inicio de Dobutamina para tratamiento del shock cardiogénico todo ello probablemente secundario a la disfunción miocárdica por la sepsis además de componente de shock de perfil distributivo también en probable relación a la sepsis pulmonar. Posteriormente, se consiguió estabilizar y normalizar los datos de hipoperfusión tisular con la consiguiente suspensión progresiva del soporte vasoactivo.

Otras complicaciones añadidas y descritas en este tipo de pacientes fue el fracaso renal anúrico con acidosis metabólica severa y consumo de bases que precisó de hemodiafiltración veno-venosa continua (HDFVC) mantenida durante 48 horas.

Con respecto a los trastornos hematológicos se fueron recuperando a la vez que la situación clínica del paciente se estabilizó, así como se observó mejoría del perfil de glucemias pudiendo controlarse con insulina subcutánea.

En total el paciente permaneció en UCI 29 días y pese a que en las radiografías de tórax posteriores mantienen los infiltrados alveolares alodonosos y fugaces de predominio derecho, pudo ser extubado y dado de alta a planta convencional para continuar con su recuperación.

Discusión

El *Staphylococcus Aureus* es una bacteria anaerobia facultativa, grampositiva, tratada desde hace años con penicilina (SAMS). Mediante la adquisición de distintos mecanismos de resistencia se ha desarrollado el *Staphylococcus Aureus* Meticilin Resistente (SARM). Ambos pueden ser adquiridos de forma comunitaria y hospitalaria.

Las cepas adquiridas en la comunidad se diferencian de las cepas adquiridas en el hospital por la presencia de los elementos genéticos móviles conocidos como cromosomas estafilocócicos del sette mec que codifican genes de resistencia a la meticilina.

Hay que destacar que existen cepas productoras de toxinas como la Leucocidina de Pantón- Valentine (PVL). Las cepas positivas para la toxina PVL se manifiestan en <5% de los aislamientos tanto de SAMS como del SARIM.

PLV fue descubierta en 1932. Es una exotoxina compuesta por dos subunidades, LukS-PV y LukF-PV que crean una unidad hetero-octamérica que se une principalmente a polimorfonucleares, monocitos y macrófagos, generando poros en las membranas celulares, con la consecuente lisis de la membrana y a la muerte celular.

El SAMS productor de PLV muestra un amplio espectro que incluye desde infecciones de piel y partes blandas que tienden a recurrir (furunculosis, folliculitis, abscesos y necrosis) hasta generar enfermedad invasiva del tipo neumonía necrotizante grave o fascitis necrotizante entre otras. En niños se presentan con enfermedad local agresiva, por ejemplo, con aparición de infecciones osteoarticulares.

Tabla II: Registro antibioterapia en unidad de cuidados intensivos.[illegible]

Por otro lado, puede presentar complicaciones ominosas como son la sepsis, la lesión renal aguda y la insuficiencia respiratoria.

La prevalencia de esta entidad no es bien conocida ya que se requiere de una alta sospecha clínica y solicitar el aislamiento de la toxina que no se realiza de forma rutinaria. Suele estar por tanto infraestimado.

Suele afectar a adultos jóvenes con muy poca exposición previa a los entornos sanitarios y en cuanto a los factores de riesgo asociados destacan: contacto estrecho, compartir elementos contaminados, condiciones de acinamiento, escasa higiene y daño con compromiso de la integridad de la piel.

Con respecto a la neumonía necrotizante, es una complicación rara y grave de la neumonía bacteriana adquirida en la comunidad (NAC). En los aislamientos prevalecen el *S. pneumoniae* y *S. aureus* ante *Klebsiella*, *Haemophilus*, y *Pseudomonas aeruginosa*.

En concreto, la neumonía necrotizante por SA productor de PLV cursa con una rápida progresión a insuficiencia respiratoria y shock y asociada con una alta tasa de mortalidad de hasta el 75%.

Esta neumonía suele ir precedida de una infección por gripe en muchas ocasiones y solo en el 25% de los casos presentan infección cutánea actual o como antecedente.

El pródromo de este síndrome es similar al de la gripe, cursando con fiebre, deterioro respiratorio y sepsis, con progresión a síndrome de dificultad respiratoria aguda que a menudo requiere soporte ventilatorio. Puede observarse consolidación multilobar progresiva, lesión pleural e infiltrados cavitarios. También se ha notificado la aparición de neutropenia en estos pacientes.

La neumonía necrotizante se ha definido radiográficamente como una inflamación parcheada con falta de perfusión y falta de captación de contraste en el parénquima junto a aparición de microabscesos en el TAC.

A medida que el tejido pulmonar sufre necrosis licuefactiva, los múltiples abscesos pueden fusionarse para formar cavidades. El proceso destructivo puede progresar a gangrena lobar, el extremo más grave del espectro. En ocasiones, se observa una masa móvil de tejido desvitalizado dentro de la cavidad, creando el llamado "signo de la media luna de aire".

En cuanto al manejo de la neumonía necrotizante por PVL no existen pautas firmes siendo el pilar de tratamiento una antibioterapia adecuada y realizar un abordaje quirúrgico sin conocerse con exactitud el momento de realizar el mismo.

Es importante identificar el patógeno solicitando tanto cultivo de esputo como hemocultivos y determinar la sensibilidad, solicitar pruebas de antígenos urinarios, incluso lavado broncoalveolar, y confirmar la producción de la toxina mediante PCR ante sospecha de esta entidad.

Tras esto, se debe iniciar de forma precoz la antibioterapia empírica con un régimen antiestafilocócico y un agente antitoxina capaz de bloquear la síntesis de proteínas. Entre estos agentes destaca tanto la clindamicina en dosis altas, el linezolid y el ácido fusídico que además presentan un buen perfil por adecuada penetración en los tejidos blandos.

Se deben tener en cuenta la epidemiología y las guías locales para la elección de la antibioterapia. La terapia antiestafilocócica estándar con dosis adecuadas es una opción valiosa mientras que estén por encima de la concentración inhibitoria mínima (CMI) ya que actúa tanto eliminando la bacteria como inhibiendo la producción de PVL. Si por el contrario se encuentra por debajo de la CMI, pueden aumentar la producción de PLV, un riesgo que puede remediarse añadiendo clindamicina.

Otro mecanismo para neutralizar las toxinas circulantes es emplear inmunoglobulinas adyuvantes tempranas en dosis únicas o dobles.

Se recomienda control con TC de tórax con contraste en neumonía progresiva o neumonía que no responde adecuadamente para evaluar el aporte vascular pulmonar y sobre todo de cara a realizar valoración por cirugía torácica para plantear el desbridamiento del parénquima pulmonar necrótico, ya que la gangrena pulmonar está ampliamente aceptada como indicación de cirugía. Sin embargo, en ausencia de gangrena pulmonar, se desconoce si la resección quirúrgica de la neumonía necrotizante es superior al tratamiento médico. Se necesitan más estudios para dilucidar las indicaciones y el momento óptimo de la intervención quirúrgica.

Por último, en cuanto a la prevención, ante sospecha se debe utilizar equipo de protección personal (EPI) y se requiere aislamiento del paciente.

Todos los pacientes y sus contactos cercanos deben someterse a un ciclo de descolonización tópica de 5 días con clorhexidina al 4% una vez al día y enjuague bucal combinados con ungüento nasal de mupirocina aplicado tres veces al día durante cinco días.

Juicio clínico

Se solicitó la determinación de diferentes toxinas varios meses después del ingreso del paciente, a destacar: toxina leucocidina de Panton-Valentine (PVL), toxinas exfoliativas (ETA, ETB), toxina Shock Tóxico (TSST-1) y otros genes de enterotoxinas que resultaron ser negativos.

En este contexto, la sospecha pasó a ser la de neumonía necrotizante por SAMS con especial virulencia al ser el mismo resistente a clindamicina.

Con este caso clínico hemos querido ilustrar la rápida progresión de la neumonía necrotizante y el daño pulmonar severo que puede causar, además de destacar algunas de las posibles complicaciones asociadas en el contexto del shock.

Se debe considerar la neumonía necrotizante en pacientes críticamente enfermos con una inadecuada evolución clínica a pesar de una antibioterapia correcta.

Por último, es esencial la sospecha clínica para solicitar las distintas pruebas complementarias, en este caso el estudio de toxinas pero sin perder de vista los datos clínicos y analíticos de los que disponemos en el día a día para poder tomar decisiones razonadas hasta la obtención de resultados.

Conflicto de intereses

La autora declara no tener ningún conflicto de intereses.

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CASE REPORT

Upper limb ischaemia in a patient with large-vessel vasculitis

*Isquemia de extremidad superior en una paciente con vasculitis de grandes vasos***Jorge Álvarez Gómez¹** , **Laura Pastor Alconchel¹** , **Leticia Ollero Domenche²** ,
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Received: 19 - XII - 2024**Accepted:** 16 - I - 2025**doi:** 10.3306/AJHS.2025.40.03.105**Abstract**

Large-vessel vasculitis is a multisystem disease, more common in women, with a higher incidence in Southeast Asia and Northern Europe. Its prognosis depends on early diagnosis and response to immunosuppressive treatment. It can cause claudication due to stenosis and inflammatory aneurysms. We present the case of a 76-year-old woman with type 2 diabetes and hypertension, who developed trophic lesions in her left-hand following trauma, severe pain, and a concomitant left carotid TIA. Angiography ruled out atherosclerosis but revealed signs of inflammatory arteriopathy in the left internal carotid and subclavian arteries. After medical treatment and analytical control, a subclavian-humeral bypass with an inverted saphenous vein was performed, achieving radial pulse recovery and complete lesion healing. Two months later, she developed critical limb ischemia due to a new inflammatory flare, with no surgical rescue option. Finally, ablative surgery was performed due to severe pain.

Key words: Vasculitis, ischemia, vascular surgery.**Resumen**

La vasculitis de grandes vasos es una enfermedad multisistémica, más frecuente en mujeres, con mayor incidencia en el sudeste asiático y el norte de Europa. Su pronóstico depende del diagnóstico temprano y la respuesta al tratamiento inmunosupresor. Puede causar claudicación por estenosis y aneurismas inflamatorios. Presentamos el caso de una mujer de 76 años con diabetes tipo 2 e hipertensión, quien sufrió lesiones tróficas en la mano izquierda tras un traumatismo, dolor intenso y un AIT carotídeo izquierdo concomitante. La angiografía descartó aterosclerosis, pero sí signos de arteriopatía inflamatoria en la carótida interna y subclavia izquierdas. Tras tratamiento médico y control analítico, se realizó bypass subclavio-humeral con vena safena invertida, logrando recuperación del pulso radial y cicatrización completa de lesiones. Dos meses después, presentó isquemia crítica por un nuevo brote inflamatorio, sin opción de rescate quirúrgico. Finalmente, se realizó cirugía ablativa debido al intenso dolor.

Palabras clave: Vasculitis, isquemia, cirugía vascular.

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Introduction

The most prevalent large vessel vasculitides are Giant Cell Arteritis (GCA) and Takayasu Arteritis (TAK). GCA primarily affects women of Northern European descent over the age of 50, while TAK is more common in women between the third and fourth decades of life¹. Although in clinical practice they may be difficult to distinguish, there are established clinical and histopathological criteria aid in the differential diagnosis, even though their etiologies remain unknown.

TAK has a global distribution with an estimated incidence of 1.2 to 2.6 cases per million inhabitants per year². It typically presents with nonspecific constitutional symptoms such as fatigue, anorexia, headache, myalgia, and arthralgia. Vascular involvement of the aorta and its branches, particularly the subclavian artery, can lead to limb claudication and, in advanced cases, pain and trophic lesions due to arterial ischemia in the affected limb³. Carotid and vertebral territory involvement has also been described, leading to symptoms compatible with cerebrovascular ischemia^{1,4}.

The initial treatment for TAK is medical and involves immunosuppression using high-dose oral corticosteroids along with immunosuppressive agents such as methotrexate, azathioprine, and in some cases tumour necrosis factor inhibitors (TNFi) during active disease phases. Surgical procedures may become necessary in cases where vascular involvement progresses, but their success is uncertain due to the natural course of the disease^{1,2}.

Case report

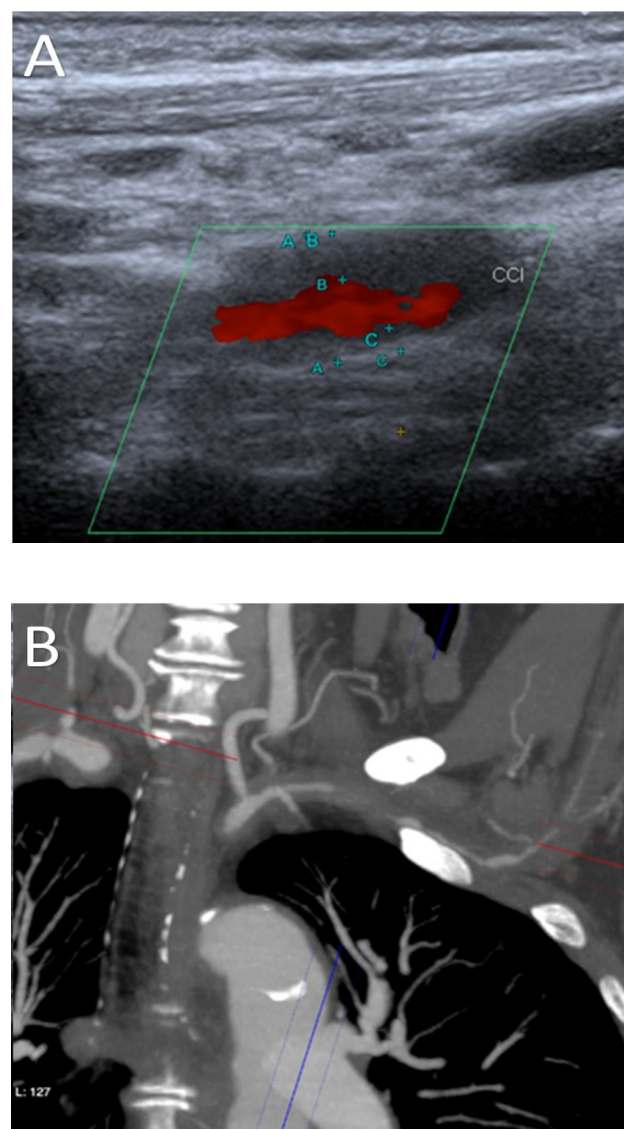
A 76-year-old woman with a history of non-insulin-dependent type 2 diabetes and hypertension presented to the emergency room with a two-month history of constitutional symptoms (hyporexia, weight loss, and pain). On arrival, she complained of intense pain in the left upper arm with trophic lesions on the fingers due to trauma from a fall on that limb. During her stay in the emergency room, she developed dysarthria. Physical examination revealed absent pulses at all levels in the left upper arm, with hand coldness, ischemic appearance, and dry necrosis on the fingers of the 1-3 fingers.

Neurology performed AngioCT and Transcranial Doppler Ultrasound due to dysarthria, which completely resolved within a few hours, diagnosed as a Transient Ischemic Attack (TIA) involving the territory of the left internal carotid artery with complete recovery. The AngioCT of the supra-aortic trunks showed signs of inflammatory arteriopathy with segmental obstruction of the left subclavian and proximal axillary arteries, with repermeabilization in the left humeral artery. Doppler ultrasound revealed marked thickening of the medial

layer of the left common carotid artery (**Figure 1**) and, especially, the left subclavian artery, with no detectable flow inside. Analytical studies showed elevated levels of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Interleukin 6 (IL-6) and ferritin, suggestive of active vasculitic disease, confirmed by PET-CT, reporting large vessel vasculitis with mild-to-moderate activity affecting the left carotid, brachiocephalic trunk, right and left subclavians, and aorta, primarily in its thoracic course.

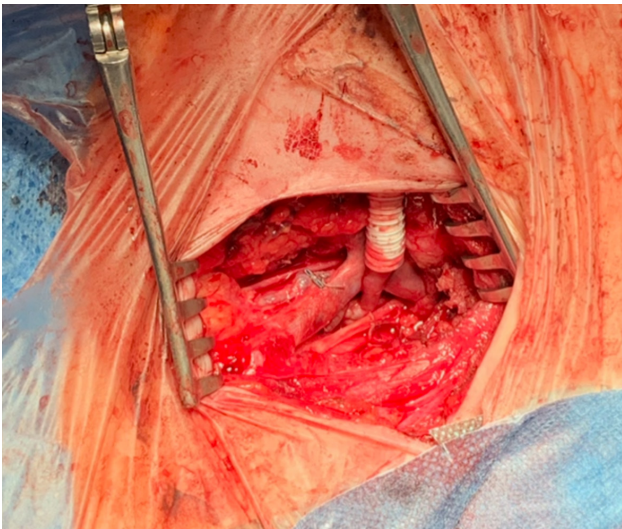
Despite the trophic lesions and pain, given the active phase of vasculitis, a joint decision was made with the Autoimmune Diseases department to prioritize high-dose immunosuppressive medical treatment with corticosteroids, methotrexate, tocilizumab, as well as alprostadil and analgesia until remission of the active phase.

Figure 1: A: Thickening of the medial layer of the left common carotid artery on ultrasound. B: Proximal obstruction of the left subclavian artery on AngioCT.



After two weeks, with a decrease in inflammatory parameters, the patient experienced increased pain and progression of necrosis in the third finger, extending from the fingertip to involve all three phalanges. Faced with this clinical worsening, revascularization was performed through subclavian-humeral bypass with tunneled inverted saphenous vein (subpectoral) on ringed ePTFE to prevent extrinsic compression by the pectoralis muscle (**Figure 2**). Due to the involvement of the middle segment of the subclavian artery, the proximal anastomosis was performed at the ascending portion of the subclavian,

Figure 2: Proximal anastomosis of tunneled subclavian-humeral bypass on ringed ePTFE prosthesis from the ascending portion of the left subclavian artery, proximal to the vertebral artery.



requiring partial clavicle resection in collaboration with the Thoracic Surgery department. Samples of the affected artery were sent for histopathological study, reporting nonspecific arteritis (**Figure 3**).

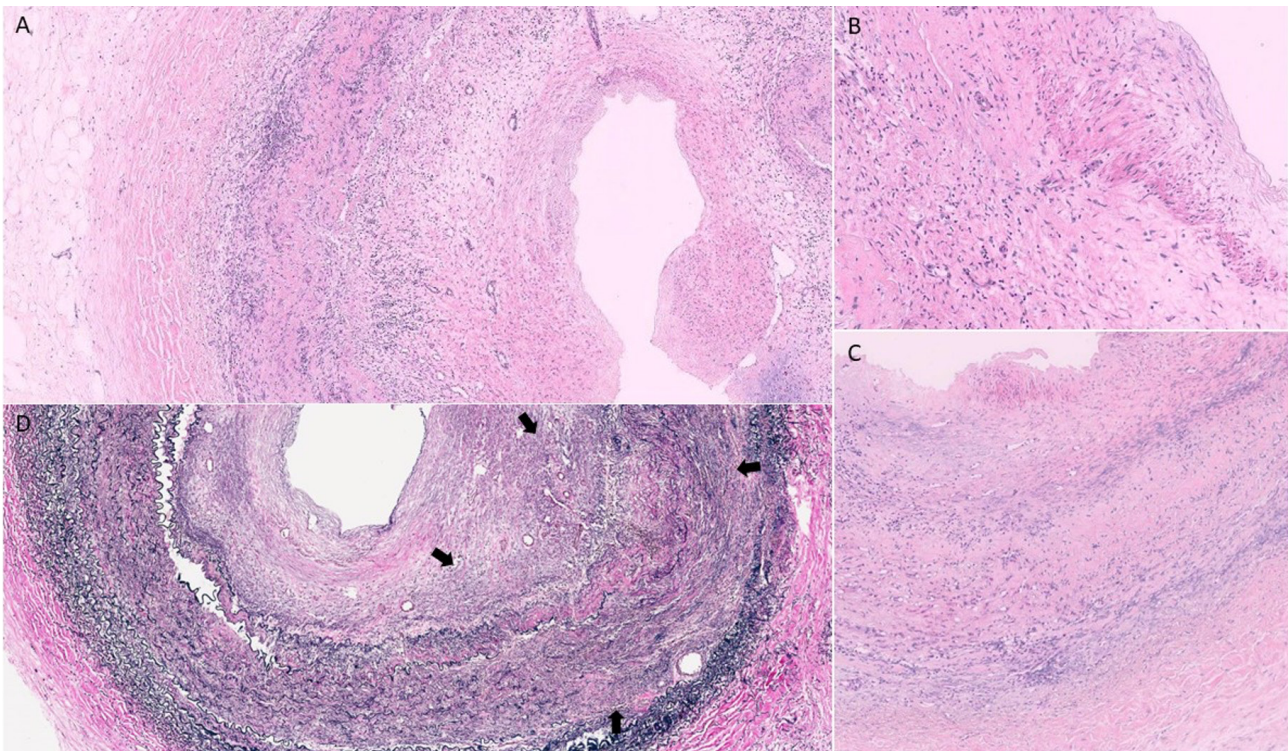
After surgery, the patient regained radial and ulnar pulses, as well as improvement in Doppler waveforms. Within 24 hours, necrosis progressed to wet gangrene in the third finger, leading to its amputation, along with debridement of the affected fingertips.

After a week, the patient was discharged pain-free, with distal pulses in the left upper arm and healing of the lesions. Additionally, pain management, antiplatelet therapy (daily aspirin 100 mg), and immunosuppression (tapering prednisone, weekly methotrexate, and weekly tocilizumab) were initiated.

During a follow-up two months post-surgery, the patient reported hand coldness with loss of distal pulses and two days of paresthesias. AngioCT revealed severe stenosis at the proximal anastomosis of the bypass. Repeat analytical studies indicated a new flare of inflammatory disease. Due to the low chances of success and high risk of complications, the option of new surgical intervention was dismissed, and intensive analgesic medical treatment was chosen.

Ultimately, worsening pain, lack of response to medical treatment, and the inability to perform further revascularization in that limb, the patient underwent supracondylar amputation of the left upper arm.

Figure 3: Elastic artery with increased intimal thickness and lymphoplasmacytic inflammatory infiltrate in the intima and medial layers, with focal necrosis and disruption of elastic laminae (arrows) (A: hematoxylin-eosin 40x; B: hematoxylin-eosin 100x; C: hematoxylin-eosin 40x; D: orcein 40x).



Discussion

Digital and upper limb ischemia is up to forty times less common than lower limb ischemia. Etiologies are diverse, with cardioembolism being the most common. A retrospective cohort study determined that up to 3.1% of patients with digital and upper limb ischemia had vasculitic causes⁵. While this etiology is uncommon, it associates stenotic lesions in up to 90% of patients and aneurysmal lesions in approximately 25%⁶.

In our case, the patient meets 5/6 criteria proposed by the American College of Rheumatology (**Table I**) for the diagnosis of Takayasu arteritis, except for age. Therefore, due to suspicion and being in an active phase, an initial expectant approach with immunosuppressive medical treatment was decided, with subsequent reevaluation for the need for revascularization.

When considering surgical rescue in Takayasu arteritis patients, it is advisable to perform it outside the active phase, as prognosis is mainly determined by the response to medical treatment⁷. During the active phase, the initial treatment involves high-dose glucocorticoids combined

with non-glucocorticoid immunosuppressive agents, with methotrexate being the most commonly used. In patients who do not achieve remission, adding another non-glucocorticoid immunosuppressant (azathioprine, tumor necrosis factor inhibitors, or tocilizumab) is indicated. Follow-up to establish remission should include history, laboratory tests, and/or imaging^{6,7}.

In cases where surgery is recommended, the need for reintervention due to restenosis is not uncommon, being more frequent in patients treated with endovascular techniques compared to open surgery^{6,7}.

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Conflict of Interest

The authors have no financial conflicts of interest.

Table I: American College of Rheumatology criteria for Takayasu arteritis classification. A patient has Takayasu arteritis if at least 3 of the 6 criteria are present. The presence of 3 or more criteria has a sensitivity of 90.5% and specificity of 97.8%. BP = blood pressure (systolic).

Criteria	Definition
Age at disease onset in years	Development of symptoms or findings related to Takayasu arteritis at <40 years of age.
Limb claudication	Development and worsening of fatigue and discomfort in muscles of one or more limbs during activity, especially the upper limbs.
Decreased pulse in the humeral artery	Decrease in the pulse of one or both humeral arteries.
BP difference >10 mmHg	Difference of >10mmHg in systolic blood pressure between arms.
Bruits over subclavian or aorta	Audible bruit on auscultation over one or both subclavian arteries or abdominal aorta.
Altered arteriography	Arteriographic stenosis or complete occlusion of the aorta, primary branches, or major proximal arteries in upper or lower extremities, not attributed to atherosclerosis, fibromuscular dysplasia, or similar causes: usually focal or segmental changes.

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