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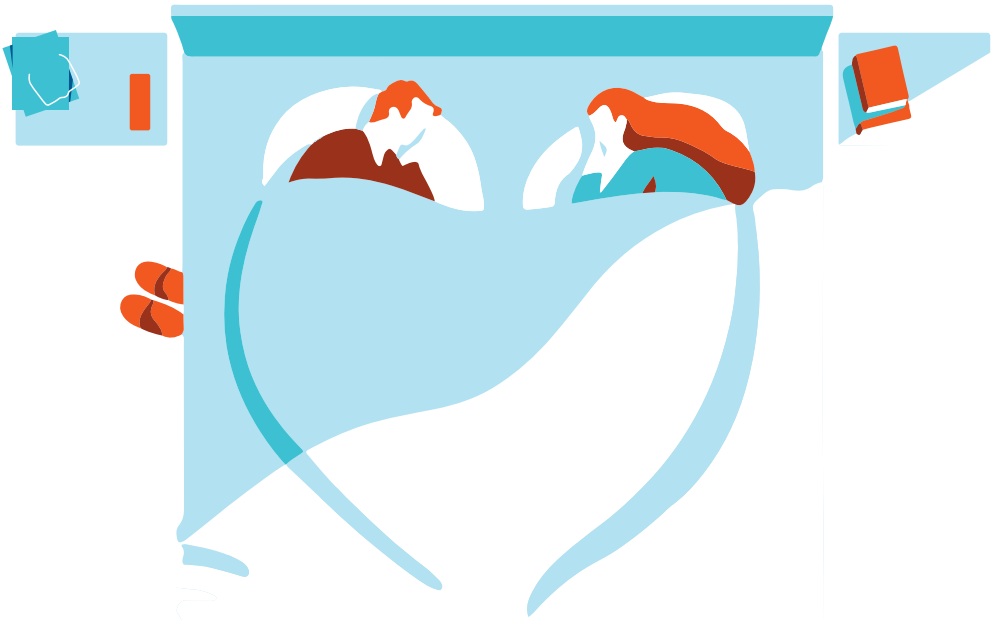

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EDITORIAL

Pasado, presente y futuro de Medicina Balear - Academic Journal of Health Sciences

Past, present and future of Medicina Balear - Academic Journal of Health Sciences

Ángel Arturo López González

Director

Una revista que cuenta ya con 37 años de historia tiene un amplio pasado, un presente en evolución y, esperemos, un espléndido futuro.

Las revistas de ámbito local, como era esta hasta hace unos años, sólo pueden sobrevivir en este complicado mundo actual de las revistas científicas sanitarias si realizan cambios sustanciales e inician el camino de la internacionalización. Hace unos años Medicina Balear logró el hito de ser incluida en el Journal Citation Reports en el apartado de Emerging Sources Citation Index. Para conseguirlo había sido necesario aumentar la periodicidad de la revista, cambiar su nombre e incluir mayor número de artículos en inglés.

Una vez lograda la deseada indexación la revista debe acometer ahora otros retos, el más importante de ellos ser incluida en la prestigiosa base de datos MEDLINE. Para alcanzar este objetivo debemos continuar el camino emprendido hace unos años de manera que cumplamos con los requerimientos solicitados por MEDLINE:

- Aumentar el alcance de la revista, publicando artículos que procedan de diferentes países.
- Publicar un alto número de artículos cada año.
- Cumplir con la periodicidad establecida.
- Estar indexados.
- Mayoría de artículos publicados en inglés y 100% de resúmenes en inglés.

Todos estos requerimientos son analizados por MEDLINE con intervalo bianual, periodo que se ha cumplido con este número, por lo que la revista solicitará de forma inmediata su inclusión, que esperemos sea aceptada, dado que creemos haber cumplido todos los requisitos en estos dos últimos años, tal como se detalla a continuación.

- El año 2021 se publicaron 4 números que incluían 65 originales, 9 casos clínicos y 6 artículos especiales: en total 80 artículos, de los cuales el 92,5% eran originales, un 79,7% en inglés.
- El año 2022 se publicaron 6 números con un total de 148 originales, 1 original breve, 15 casos clínicos, 2 revisiones y 6 artículos especiales: en total 172 artículos, de los que el 95,3% han sido originales, un 84,1% en inglés

En el año 2021 se recibieron 102 artículos y finalmente se publicaron 80 lo que indica una tasa de rechazo del 27,5%.
En el año 2022 se recibieron 241 artículos y se publicaron 172 lo que supuso una tasa de rechazo del 40,1%
En 2021 la revista recibió originales firmados por autores de 16 países diferentes, cifra que aumentó hasta los 63 en el año 2022, procedentes de los cinco continentes:

- 19 de América: Canadá, EEUU, México, Cuba, República Dominicana, Puerto Rico, Honduras, Surinam, Panamá, Trinidad y Tobago, Venezuela, Colombia, Ecuador, Perú, Chile, Argentina, Uruguay, Bolivia y Brasil.
- 10 de África: Marruecos, Argelia, Egipto, Nigeria, Camerún, Angola, Sudán, Tanzania, Somalia y Madagascar.
- 16 de Asia: Turquía, Azerbaiyán, Irán, Iraq, Arabia Saudí, Qatar, Pakistán, India, Nepal, Bangla Desh, Bután, China, Japón, Malaysia, Indonesia, Filipinas.
- 17 de Europa: España, Portugal, Italia, Reino Unido, Suiza, Alemania, Bélgica, Holanda, Suiza, Austria, Bulgaria, República Checa, Polonia, Ucrania, Noruega, Suecia, Rusia,
- 1 de Oceanía: Australia.

Desde la dirección de la revista y desde su Consejo Editorial y muy especialmente desde el conjunto académico de la Real Academia de Medicina de las Islas Baleares esperamos y deseamos, dado que la norma exigida la creemos cumplida, que 2023 sea el año de la entrada del Academic Journal of Health Sciences – Medicina Balear en MEDLINE.

A journal with 37 years of history has a long past, an evolving present and, hopefully, a splendid future.

Local journals, as this one was until a few years ago, can only survive in today's complicated world of scientific health journals if they make substantial changes and embark on the road to internationalization. A few years ago Medicina Balear achieved the milestone of being included in the Journal Citation Reports in the Emerging Sources Citation Index. To achieve this it had been necessary to increase the periodicity of the journal, change its name and include a greater number of articles in English.

Having achieved the desired indexing, the journal must now undertake other challenges, the most important of which is to be included in the prestigious MEDLINE database. To achieve this goal, we must continue on the path we took a few years ago in order to meet the requirements requested by MEDLINE:

- Increase the scope of the journal, publishing articles coming from different countries.
- To publish a high number of articles each year.
- Comply with the established periodicity.
- To be indexed.
- Majority of articles published in English and 100% of abstracts in English.

All these requirements are analyzed by MEDLINE with a biannual interval, a period that has been fulfilled with this issue, so the journal will immediately request its inclusion, which we hope will be accepted, given that we believe we have fulfilled all the requirements in the last two years, as detailed below.

- In 2021, 4 issues were published, including 65 original articles, 9 clinical cases and 6 special articles: a total of 80 articles, of which 92.5% were original, 79.7% in English.
- In 2022, 6 issues were published with a total of 148 originals, 1 short original, 15 clinical cases, 2 reviews and 6 special articles: a total of 172 articles, of which 95.3% were original, 84.1% in English.

In 2021 102 articles were received and 80 were finally published indicating a rejection rate of 27.5%. In 2022, 241 articles were received and 172 were published, indicating a rejection rate of 40.1%.
In 2021 the journal received originals signed by authors from 16 different countries, a figure that increased to 63 in 2022, coming from the five continents:

- 19 from the Americas: Canada, USA, Mexico, Cuba, Dominican Republic, Puerto Rico, Honduras, Suriname, Panama, Trinidad and Tobago, Venezuela, Colombia, Ecuador, Peru, Chile, Argentina, Uruguay, Bolivia and Brazil.
- 10 from Africa: Morocco, Algeria, Egypt, Nigeria, Cameroon, Angola, Sudan, Tanzania, Somalia and Madagascar.
- 16 from Asia: Turkey, Azerbaijan, Iran, Iraq, Saudi Arabia, Qatar, Pakistan, India, Nepal, Bangladesh, Bhutan, China, Japan, Malaysia, Indonesia, Philippines.
- 17 from Europe: Spain, Portugal, Italy, United Kingdom, Switzerland, Germany, Belgium, Netherlands, Switzerland, Austria, Bulgaria, Czech Republic, Poland, Ukraine, Norway, Sweden, Russia,
- 1 from Oceania: Australia.

From the direction of the journal and its Editorial Board and especially from the academic group of the Royal Academy of Medicine of the Balearic Islands we hope and wish, given that we believe that the required standard has been met, that 2023 will be the year of the entry of the Academic Journal of Health Sciences – Medicina Balear in MEDLINE.

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ORIGINAL

Staphylococcal cassette chromosome *mec* in the *Staphylococcus aureus* isolated from retail meat

Cromosoma de cassette estafilococo mec en el Staphylococcus aureus aislado de carne de venta al por menor

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Abstract

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) strains are among the most emerging causes of hospital- and community-acquired infections. Retail meat is considered as one of its sources. The present survey was performed to assess the distribution of Staphylococcal cassette chromosome *mec* (*SCCmec*) amongst MRSA isolates of retail meat.
Methods: A total of 28 MRSA isolates of retail meat samples were assessed to distribute the *SCCmec* type. MRSA. Isolates were confirmed using the biochemical tests and cefoxitin and oxacillin susceptibility tests. PCR was used to detect *SCCmec* types amongst the MRSA isolates.
Results: A total of 7 different *SCCmec* types were detected in the MRSA bacteria isolated from retail meat samples. *SCCmec* type V (46.4%) had the highest distribution amongst examined MRSA isolates, while SCCmec type I, IVb, and IVc (7.1%) had the lowest. There were no positive results for the *SCCmec* type II. Statistically, a significant difference was obtained between the source of MRSA isolation and *SCCmec* distribution (P <0.05).
Conclusion: As most isolates harboured *SCCmec* types IV and V, they originated from the community and called community-associated MRSA (CA-MRSA). Thus, the role of retail meat as a source of CA-MRSA was determined in this survey.

Keywords: *Staphylococcus aureus*, SCCmec, PCR, retail meat.

Resumen

Antecedentes: Las cepas de *Staphylococcus aureus* resistente a la meticilina (SARM) se encuentran entre las causas más emergentes de infecciones hospitalarias y comunitarias. La carne al por menor se considera una de sus fuentes. El presente estudio se realizó para evaluar la distribución del cromosoma de cassette estafilocócico mec (*SCCmec*) entre los aislados de SARM de la carne al por menor.
Métodos: Se evaluó un total de 28 aislados de SARM de muestras de carne al por menor para distribuir el tipo de *SCCmec*. MRSA. Los aislados se confirmaron mediante las pruebas bioquímicas y de susceptibilidad a la cefoxitina y la oxacilina. Se utilizó la PCR para detectar los tipos de *SCCmec* entre los aislados de SARM.
Resultados: Se detectaron un total de 7 tipos diferentes de *SCCmec* en las bacterias MRSA aisladas de las muestras de carne del comercio minorista. El tipo V de *SCCmec* (46,4%) fue el más distribuido entre los aislados de SARM examinados, mientras que los tipos I, IVb y IVc de *SCCmec* (7,1%) fueron los más bajos. No hubo resultados positivos para el *SCCmec* tipo II. Estadísticamente, se obtuvo una diferencia significativa entre la fuente de aislamiento de SARM y la distribución de *SCCmec* (P <0,05).
Conclusiones: Dado que la mayoría de los aislamientos albergaban *SCCmec* tipo IV y V, se originaron en la comunidad y se denominaron SARM asociados a la comunidad (CA-MRSA). Así pues, en este estudio se determinó el papel de la carne al por menor como fuente de SARM comunitario.

Palabras clave: *Staphylococcus aureus*, SCCmec, PCR, carne al por menor.

Introduction

Staphylococcus aureus (*S. aureus*), a Gram-positive and catalase-positive bacterium, is an important cause of foodborne diseases characterized by weakness, nausea, vomiting, abdominal cramps and toxic shock syndrome[1]. Foods with animal origins, particularly raw meat samples, are considered reservoirs of the bacterium[2]. Foodborne diseases caused by *S. aureus* are complicated owing to the high pathogenicity of bacterium and the emergence of antibiotic resistance[3]. Methicillin-resistant *Staphylococcus aureus* (MRSA) strains are among the most important causative agent of nosocomial infections and complicated foodborne diseases[4]. It is responsible for around 100,000 nosocomial infection cases with about 20-30% mortality rates in the USA[5]. Diseases caused by this bacterium are mostly resistant to antibiotic therapy and complicated owing to higher hospitalization procedure and loads of therapeutic charges[6].

MRSA strains have a small Staphylococcal cassette chromosome *mec* (*SCCmec*), preventing phagocytosis and indirect cellular immunity and producing an enzyme that inactivates most penicillin and methicillin-based therapies[7,8]. *SCCmec* elements are typically classified into types I, II, III, IV, and V concerning the pattern of the *ccr* and *mec* alleles. SCCmec IV is additionally classified into a, b, c and d subdivisions[9]. Assessment of the SCCmec profile of the MRSA bacteria may show their origins and severity of diseases they can occur.

Regarding the important role of meat as a reservoir of MRSAS strains, the present survey was performed to assess the distribution of SCCmec types amongst MRSA bacteria isolated from retail meat samples in Iran.

Materials and methods

Ethical consideration

The survey was confirmed by the Ethical Council of Research of the Department of Food Hygiene, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran.

Bacterial strains

From May to October 2018, a total of 28 MRSA bacteria were isolated from retail meat samples collected from Iran. Isolates were confirmed another time using some biochemical tests, including Gram staining, hemolytic activity on sheep blood agar (Merck, Germany), catalase activity, coagulated test (rabbit plasma), oxidase test, glucose O/F test, resistance to bacitracin (0.04 U), mannitol fermentation on Mannitol salt agar (Merck, Germany), urease activity, nitrate reduction, phosphatase, deoxyribonuclease (DNase, Merck, Germany) test, Voges-Proskauer (Merck, Germany) test and carbohydrate (xylose, trehalose, sucrose, and maltose, fructose, lactose, mannose) fermentation tests[10].

MRSA identification

Isolates were confirmed as MRSA bacteria using cefoxitin and oxacillin susceptibility testing[11-14].

DNA extraction and quality assessment

MRSA isolates were sub-cultured on TSB media (Merck, Germany) and incubated for 48 h at 37 oC. According to the manufacturer's instruction, genomic DNA was extracted from the bacterial colonies using the DNA extraction kit (Thermo Fisher Scientific, St. Leon-Rot, Germany)[15, 16]. Purity (A260/A280) and concentration of extracted DNA were then checked (NanoDrop, Thermo Scientific, Waltham, MA, USA)[17-22]. The quality of extracted DNA was assessed using electrophoresis of DNA on a 2% agarose gel stained with ethidium bromide (0.5 µg/mL) (Thermo Fisher Scientific, St. Leon-Rot, Germany)[23-25].

Polymerase Chain Reaction (PCR)-based detection of SCCmec types

Table I disclosed the PCR protocol used for SCCmec types detection[26, 27]. A programmable DNA thermo-cycler (Eppendorf Mastercycler 5330, Eppendorf-Nethel-Hinz GmbH, Hamburg, Germany) was used in

Table I: PCR protocol used for detection of SCCmec types [26, 27].

Target gene	Primer sequence (5'-3')	PCR product (bp)	PCR programs	PCR volume (50µL)
SCCmec I	F: GCTTTAAAGAGTGTCGTTACAGG R: GTTCTCTCATAGTATGACGTCC	613	**1 cycle:** 93°C ---------- 7 min **10 cycles:** 93°C ---------- 55 s 64°C ---------- 50 s 72°C ---------- 2 min **25 cycles:** 94°C ---------- 45 s 55°C ---------- 45 s 72°C ---------- 2 min **1 cycle:** 72°C ---------- 10 min	5 µL PCR buffer 10X 1.5 mM $MgCl_2$ 200 µM dNTP (Thermo Fisher Scientific, St. Leon-Rot, Germany) 0.5 µM of each primers F & R 1.25 U Taq DNA polymerase (Thermo Fisher Scientific, St. Leon-Rot, Germany) 2.5 µL DNA template
SCCmec II	F: CGTTGAAGATGATGAAGCG R: CGAAATCAATGGTTAATGGACC	398		
SCCmec III	F: CCATATTGTGTACGATGCG R: CCTTAGTTGTCGTAACAGATCG	280		
SCCmec IVa	R: GCCTTATTCGAAGAAACCG R: CTACTCTTCTGAAAAGCGTCG	776		
SCCmec IVb	F: TCTGGAATTACTTCAGCTGC R: AAACAATATTGCTCTCCCTC	493		
SCCmec IVc	R: ACAATATTTGTATTATCGGAGAGC R: TTGGTATGAGGTATTGCTGG	200		
SCCmec IVd	F: CTCAAAATACGGACCCCAATACA R: TGCTCCAGTAATTGCTAAAG	881		
SCCmec V	F: GAACATTGTTACTTAAATGAGCG R: TGAAAGTTGTACCCTTGACACC	325		

all PCR reactions[28,29]. Amplified samples were analyzed by electrophoresis (120 V/208 mA) in 2.5% agarose gel. The gel was stained with 0.1% ethidium bromide (0.4 µg/ml). The UVI doc gel documentation systems (Grade GB004, Jencons PLC, London, UK) were applied to analyze images[30-32].

Statistical analysis

Statistical analysis was done using the SPSS 21.0 statistical software (SPSS Inc., Chicago, IL, USA). Chi-square test and Fisher's exact two-tailed test were used to assess any significant relationship between collected data[33]. P-value <0.05 was considered as a significant statistical level[34].

Results

A total of 28 MRSA isolates of retail meat samples were assessed for the distribution of the *SCCmec* type. MRSA. **Table II** shows the *SCCmec* profile of the MRSA bacteria isolated from retail meat samples. Seven different *SCCmec* types were detected in the MRSA bacteria isolated from retail meat samples. *SCCmec* type V (46.4%) had the highest distribution amongst examined MRSA isolates, while SCCmec type I, IVb, and IVc (7.1%) had the lowest. There were no positive results for the *SCCmec* type II. Statistically, a significant difference was obtained between the source of MRSA isolation and *SCCmec* distribution (P <0.05).

Discussion

Several infectious diseases cause important mortality and morbidities in recent years[35-38]. Most of them are resistant to diverse classes of antimicrobial agents[39-42]. MRSA bacteria are emerging and antibiotic-resistant causes of diverse kinds of nosocomial and community-associated infections[43]. Methicillin resistance is one of the most important features of antibiotic resistance in the *S. aureus* strains. In the 1960s, as soon as methicillin was introduced, methicillin-resistant strains of *S. aureus* appeared. These bacteria were also resistant to all available penicillins and other beta-lactam antibiotics. Before 1990, MRSA strains were confined to healthcare centres and hospitals and were called Healthcare-Associated MRSA (HA-MRAS). Gradually, however, there were reports of MRSA disease in people who had no contact with healthcare centres and hospitals, and these new strains were called Community-Associated MRSA (CA-MRSA)[44,45]. The differences between the two groups are related to genotypic, epidemiological, clinical characteristics and the range of infections they cause. Reports have shown that HA-MRSA strains usually cause internal infections, pneumonia, bloodstream infections, and surgical site infections, but CA-MRSA strains usually cause soft tissue infections, skin, sores, boils, and severe cases of sepsis. HA-MRSA strains usually carry large *SCCmec* tapes, i.e. III, *SCCmec* I, *SCCmec* II and *SCCmec* III. These strains contain the *mecA* gene. Studies have shown that HA-MRSA strains are usually resistant to non-beta-lactam antibiotics (such as penicillins, cephalosporins, carbapenems, and macrolides) and rarely carry the Panton-Valentine Leukocidin (*PVL*) gene. In contrast, CA-MRSA strains have smaller *SCCmec* types, i.e. *SCCmec* IV and *SCCmec* V, are less resistant to non-beta-lactam antibiotics and often carry the *PVL* gene. In general, CA-MRSA antibiotic susceptibility is higher than HA-MRSA strains[46,47]. Studies have shown that all infections that are treated on an outpatient basis and those hospitalized for less than 48 hours are all caused by CA-MRSA. In contrast, if a person is hospitalized for more than 48 hours, the staph infection is caused by HA-MRSA. Studies have shown that the *SCCmec* IV cassette is strongly associated with infectious strains in patients with no risk factors for HA-MRSA[48]. Due to the higher frequency of *SCCmec* IV and V types in the present survey, it seems that most of the MRSA strains isolated in the present study belong to CA-MRSA strains. However, confirmation of this issue requires more information.

Some researches have been conducted in this field. Saadati et al. (2019)[49] reported that the MRSA strains isolated from fowl meat samples only harboured *SCCmec* IVa (50%), *SCCmec* IVd (8.33%) and *SCCmec* V (41.66%). However, there were no positive results for SCCmec types I, II, III, IVb, and IVc. Hanson et al. (2011)[50] stated that the *SCCmec* types IV and V were the most commonly detected amongst the MRSA isolates of meat samples. Wu et al. (2019)[51] reported that the *SCCmec* types III, IV and V were the most commonly detected amongst the *S. aureus* bacteria isolated from meat and meat products (bacon/

Table II: *SCCmec* profile of the MRSA bacteria isolated from retail meat samples.

Retail meat samples	N. MRSA isolates	N. isolates harboured each SCCmec (%)							
		I	II	III	IVa	IVb	IVc	IVd	V
Raw bovine	13	-	-	1 (7.6)	5 (38.4)	-	1 (7.6)	1 (7.6)	6 (46.1)
Raw ovine	9	1 (11.1)	-	1 (11.1)	4 ()	2 (22.2)	1 (11.1)	1 (11.1)	4 (44.4)
Raw caprine	6	1 (16.6)	-	2 (33.3)	3 (50.0)	-	-	1 (16.6)	3 (50.0)
Total	28	2 (7.14)	-	4 (14.2)	12 (42.8)	2 (7.1)	2 (7.1)	3 (10.7)	13 (46.4)

sausage, poultry, pork, mutton and beef) in China. A similar distribution of the *SCCmec* types amongst the MRSA isolates was also reported from Japan[52], Iran[53], and India[54].

The present survey was a preliminary survey on the distribution of *SCCmec* types in the MRSA bacteria isolated from retail meat samples. It is limited to the absence of *PVL* gene detection and antimicrobial resistance assessment of MRSA strains. Additionally,m absence of the sequencing analysis is another important limitation of the present research.

Conclusion

In conclusion, high distribution of *SCCmec* types, particularly types IV and V was reported in this survey. Because the frequency of *SCCmec* types in this sample was such that the isolated strains are related to CA-MRSA, meat samples can be used as sources of survival and transmission of CA-MRSA. Complete cooking of meat before consumption, observing scientific and ethical principles in prescribing antibiotics and using meat-based foods, especially from reputable brands, restaurants and factories, can prevent serious food poisoning and the survival and spread of MRSA at Prevent community level.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Evaluation of nitrofuran content in eggs and milk supplied in Tehran, Iran

Evaluación del contenido de nitrofuranos en los huevos y la leche suministrados en Teherán, Irán

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Abstract

Background: The frequent use of antibiotics causes antibiotic residues in various food of animal origin, including milk and egg. Nitrofurans are used as feed additives to prevent and treatment of intestinal infections. However, the use of nitrofurans is prohibited in livestock due to carcinogenicity. This survey was designed to measure the concentration of nitrofuran residues in milk and eggs.
Methods: The samples were selected from the Tehran market, Iran. The detection was done with the enzyme-linked immunosorbent assay (ELISA) method. The sample preparation was performed according to the kit protocol.
Results: The residue was detected in two samples of milk at 216.6 and 208.1ng/ kg. However, the residue of the drug was not detected in any of the egg samples. The estimated dietary intake based on the mean concentration of milk samples was calculated at 0.000000031 mg/kg BW/day.
Conclusion: The calculated EDI is not significant, but it is necessary to evaluate the residual nitrofuran based on the milk data regularly.

Keywords: Dietary exposure, nitrofuran metabolite, residues, milk, egg.

Resumen

Introducción: El uso frecuente de antibióticos provoca residuos de los mismos en diversos alimentos de origen animal, entre ellos la leche y el huevo. Los nitrofuranos se utilizan como aditivos en los piensos para prevenir y tratar las infecciones intestinales. Sin embargo, el uso de nitrofuranos está prohibido en el ganado debido a su carcinogenicidad. Este estudio se diseñó para medir la concentración de residuos de nitrofuranos en la leche y los huevos.
Metodología: Las muestras se seleccionaron en el mercado de Teherán (Irán). La detección se realizó con el método de ensayo inmunoenzimático (ELISA). La preparación de la muestra se realizó según el protocolo del kit.
Resultados: El residuo se detectó en dos muestras de leche a 216,6 y 208,1ng/kg. Sin embargo, no se detectó el residuo del fármaco en ninguna de las muestras de huevos. La ingesta dietética estimada basada en la concentración media de las muestras de leche se calculó en 0,000000031 mg/kg de peso corporal/día.
Conclusión: La IDE calculada no es significativa, pero es necesario evaluar regularmente el nitrofurano residual a partir de los datos de la leche.

Palabras clave: Exposición dietética, metabolito del nitrofurano, residuos, leche, huevo.

Introduction

Eggs are a well-known food that ranks second in quality after breast milk. Eggs are one of the highest quality protein sources and contain almost all of the vitamins (except vitamin C) and minerals needed by the human body. In other words, eggs are the best source of protein that contains essential vitamins and minerals. Milk is one of the most consumed foods in the world, according to the Food and Agriculture Organization of the United Nations[1].

Veterinary medicines for use in animals for specific purposes include the diagnosis, cure, mitigation, management, treatment, or prevention of disease in animals. They can also include modifying any structure or function of an animal's body, such as enhancing reproductive capabilities or other production uses, such as feed efficiency or growth promotion[2]. The presence of drugs or antibiotics residues in food above the maximum acceptable level has been recognized worldwide by various public authorities[3]. Furthermore, Antimicrobial Resistance (AMR) is an increasingly important global health problem, with the potential to render antibiotics unusable and negate medical treatments such as chemotherapy and organ transplant[4] for human concern, AMR in food of animal origin produces a potential threat to direct toxicity in human (cancers, allergic reactions, etc.), and low levels of antibiotic exposure results in alteration of microflora, and the possible development of resistance[5,6].

One of the drugs is nitrofuran, which is widely used as a veterinary drug or food additive in animal husbandry, especially for treating gastrointestinal infections in cattle, poultry, fish, and shrimp. It is an effective antibiotic for the treatment of bacteria and parasites[7]. Its low price and high efficiency are widely used[8].

Among the major compounds to be monitored, some zero-tolerance substances, like nitrofurans (NFs), are prohibited globally[9]. Nitrofurans and their metabolites are suspected of possessing carcinogenic and mutagenic potency[10]. This antibiotic has been used but has been banned in many countries due to its carcinogenicity[11]. Nitrofurans, including nitrofurazone (NFZ), nitrofurantoin (NFT), furaltadone (FTD), and furazolidone (FZD), are a class of synthetic broad-spectrum antibiotics that have been widely used in aquaculture and poultry farming to prevent and treat infections caused by Salmonella spp. and *Escherichia coli*. The presence of these residues in foods of animal origin may lead to adverse reactions in humans, including their carcinogenic, mutagenic and teratogenic effects[12]. In addition, the residues of this drug remain during various cooking processes such as frying, grilling, and microwave[13].

To confirm food safety, it is necessary to regularly check the residue of this drug in samples of animal origin. This article surveyed the number of nitrofurans in milk and eggs supplied in supermarkets in Tehran.

Materials and methods

Samples of eggs and milk were collected in Tehran's north, east, west, and south. According to the specified formula, 81 samples were collected.

Sample preparation for milk samples

Milk samples were transferred into a centrifugal glass vial and added Carrez I and Carrez II. Then, the samples were mixed and centrifuged. The supernatant was mixed with distilled water and HCl, and 2-Nitrobenzoic aldehyde (in DMSO) by shaking vigorously. The homogeneous sample was mixed with distilled water, HCL, and 2-nitrobenzaldehyde. Then, the samples were incubated 3 hours at 50°C and mixed 0.1 M K2HPO4, 0.4 ml of 1 M NaOH, and 5 ml of aniline acetate. The top layer was dried, and one milliliter of hexane and one milliliter of buffer were added to the vials and centrifuged for three minutes at 3000 rpm. The top layer for were used testing

Sample preparation for egg samples

1 g of a homogeneous sample was mixed with 3.9 ml of distilled water, HCl, and 200 ml of 10 mM 2-nitrobenzaldehyde in dimethyl sulfoxide. The samples were incubated for 3 hours at 50°C or 37°C overnight. Then, 5 ml of 0.1 M K2HPOA, 0.4 ml of 1 M NaOH, and 5 ml of ethyl acetate were added to the samples and centrifuged at room temperature for 3 minutes at 3000 rpm. The top layer was dried, and one milliliter of hexane and one milliliter of buffer were added to the vials and centrifuged for three minutes at 3000 rpm. The top layer for were used testing.

Nitrofuran Measurement

Fifty microliters of each standard and each sample are added to the houses with two repetitions. Then, 50 microliters of the conjugate solution were added, and 50 µl of antibody solution was added to each house, shaken gently, and placed at room temperature for one hour. The houses were washed three times with a wash buffer. Then add 100 microliters of dye substrate to each house and incubate for 15 minutes in the room. Finally, add 100 microliters of stopping solution and read to the spectrophotometer after 30 minutes at a wavelength of 450 nm.

Result and discussion

The concentration of nitrofuran in milk and egg samples

Figure 1 illustrates the calibration curve with six different standard concentrations (0, 25. 50,100,200ng/ml). The use of ELISA in the measurement of residual nitrofurans is a valid method and its validity has already been measured. A correlation has been obtained between the results obtained from ELISA and the LC-MS/MS method[14]. ELISA method is frequently used to

Figure 1: Standard curves of nitrofuran (0, 25. 50,100,200ng/ml).

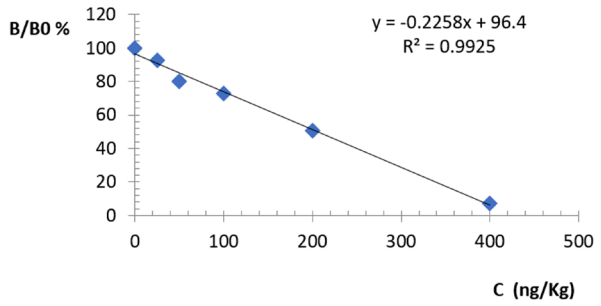

Table I: Nitrofuran metabolite detected (ng/kg) in milk and egg samples.

Product type	Mean ± SD(ng/kg)	EDI (mg/kg bw/day)
Milk	10.6±46.8	0.000000031
Egg	ND	-

evaluate nitrofuran antibiotic residues by government and research centers[15]. The remainder of this antibiotic was not isolated in egg samples but was detected in two milk samples with 216.6 and 208.1 ng/Kg (**Table I**). Cases of illegal or accidental use have been repeatedly recorded in veterinary medicine[16].

The drug is banned in the European Union, Switzerland, the USA, and China. An important global issue is the presence of drug residues in foods of animal origin[17]. Nitrofurans are frequently used in veterinary medicine due to their cheapness, availability, and efficiency[16]. Some foods are not allowed to enter the EU due to nitrofuran antibiotic residues[18]. The maximum residue limit was not set for it and its metabolites[15]. However, it is used in some Asian countries[19]. In previous studies, the residue of this antibiotic has been isolated in shrimp samples in Bangladesh and Irish samples[20]. In a study of animal products in Ireland, 1.8% of the samples had antibiotic residue[21]. Furthermore, it is allowed in animal food and water in Argentina[22].

One of the chemicals that cause problems in the trade of food of animal origin is the residual antibiotic nitrofuran, so these antibiotics should be evaluated regularly[23]. Between 2002 and 2003, the European nitrofuran crisis arose because chicken meat samples imported into Europe contained nitrofuran antibiotic residues[24].

Dietary survey of nitrofuran residue in milk and egg

The per capita consumption of milk in the country is about 80 kg. EDI was estimated using this formula:

$$EDI \text{ oral} = Ci \times Cc / \text{BW}$$

Ci: For the mean concentration of nitrofuran residue in milk (mg/kg) and Cc: The average daily consumption of milk (kg /person/day) and BW: (bodyweight).

Due to the ban on using this antibiotic, no ADI has been established for this antibiotic at the moment, but before 1992, the ADI of Furazolidine metabolite was set at 0004 mg/kg BW. The amount calculated in this study was 0.000000031 mg/Kg BW/day, much less than the ADI of furazolidone. The European Union has adopted a zero-tolerance for both antibiotics and metabolites[22]. Besides the chemical contamination of food samples[25] which was described nitrofurans in the present survey, microbial contaminations were also reported as dangerous issues in food samples[26-31]. Thus, proper food monitoring should perform to avoid their occurrence in food chain.

Conclusion

A total of 81 Samples of egg and milk from markets of Tehran with various commercial brands were collected and analyzed to detect the content of nitrofuran. This is the first report of the detection of nitrofuran metabolites in samples of eggs and milk. The residue of this antibiotic was not detected in all egg samples and most milk samples. In this study, EDI was also calculated for milk samples much lower than ADI previously approved for Furazolidine metabolite.

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Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Marcadores no invasivos de hígado graso no alcohólico y relación con parámetros de obesidad

Non invasive markers of non alcoholic fatty liver disease and relationship with obesity parameters

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Resumen

Introducción y objetivo: Analizar la utilidad de los índices predictivos FLI y FIB-4 en la detección de hígado graso asociado a disfunción metabólica (EHGM) como método no invasivo en salud laboral y su relación con parámetros de obesidad y riesgo metabólico.

Material y método: Estudio descriptivo y transversal en 815 trabajadores entre 18-65 años desde marzo de 2020- junio de 2021. Se utiliza FIB-4 Index for liver fibrosis y Fatty Liver Index (FLI) y se establece relación con el índice de masa corporal, y con índices de adiposidad: grasa corporal, grasa visceral, perímetro de cintura, índice cintura/cadera, índice cintura/altura y síndrome metabólico.

Resultados: Valores elevados de IMC con diferencias por sexo (sobrepeso 48,5% en hombres y 39,52% en mujeres) (obesidad 22,04% en hombres y 18,86% en mujeres), FLI muestra valores alterados en hombres y mujeres en todos los parámetros de obesidad y con el síndrome metabólico. FIB 4 muestra diferencias por sexo, en hombres con valores medios relacionados con grasa visceral y perímetro de cintura/altura elevado y en mujeres, en rangos sin relación con ninguno de los parámetros valorados.

Conclusión: FLI muestran relación con los valores elevados de IMC y parámetros de obesidad como la grasa visceral y el índice cintura cadera. FIB-4 solo muestra relación con grasa visceral y con el IMC. El síndrome metabólico solo se correlaciona con valores medios de FLI.

Palabras clave: Enfermedad hepática no alcohólica, obesidad, FLI, FIB-4, salud laboral.

Abstract

Introduction and objective: To analyze the usefulness of the FLI and FIB-4 predictive indexes in the detection of nonalcoholic fatty liver disease (NAFLD) as a noninvasive method in occupational health and its relationship with obesity and metabolic risk parameters.

Material and method: Descriptive and cross-sectional study in 815 workers aged 18-65 years from March 2020-June 2021. We used FIB-4 Index for liver fibrosis and Fatty Liver Index (FLI) and established relationships with body mass index, and with adiposity indices: body fat, visceral fat, waist circumference, waist/hip ratio, waist/height ratio and metabolic syndrome.

Results: High BMI values with differences by gender (overweight 48.5% in men and 39.52% in women) (obesity 22.04% in men and 18.86% in women), FLI shows altered values in men and women in all obesity parameters and with metabolic syndrome. FIB 4 shows differences by gender, in men with mean values related to visceral fat and high waist/height circumference and in women, in ranges unrelated to any of the parameters assessed.

Conclusion: FLI shows a relationship with elevated BMI values and obesity parameters such as visceral fat and waist/hip ratio. FIB-4 only shows a relationship with visceral fat and BMI. Metabolic syndrome only correlates with mean FLI values.

Keywords: nonalcoholic fatty liver disease, obesity, FIB-4, FLI, occupational health.

Introducción

La obesidad sigue siendo un problema de salud pública en todo el mundo y se relaciona con los comportamientos en estilo de vida y resultados en salud[1]. Es considerada una enfermedad multifactorial compleja. La prevalencia mundial, tanto de sobrepeso como de obesidad se ha duplicado desde 1980, hasta el punto de que casi un tercio de la población mundial se clasifica ahora como sobrepeso u obesidad[2].

La enfermedad del hígado graso asociado a disfunción metabólica (EHGM) está reconocida actualmente como la causa más común de enfermedad hepática crónica en todo el mundo y se considera manifestación hepática del síndrome metabólico[3]. Su incidencia mundial va en aumento y convierte a la EHGM en una epidemia y una amenaza para la salud pública[4] en todos los países.

Es objetivo de este trabajo analizar la relación entre los índices predictivos de EHGM: Fatty Liver Index (FLI) y Index for liver fibrosis (FIB-4) como métodos no invasivos, junto con los parámetros de obesidad.

Material y método

Estudio descriptivo transversal en una muestra de población laboral española de 815 trabajadores (481 hombres y 334 mujeres), de edades entre 18-66 años, que acudieron a los reconocimientos periódicos de vigilancia de la salud de las empresas participantes desde marzo de 2020 hasta junio de 2021, con participación voluntaria y consentimiento informado para el uso epidemiológico de los resultados obtenidos.

El IMC se calculó como el peso en kg dividido por el cuadrado de la altura en metros. Los rangos para IMC considerados por la OMS e incluidos en este trabajo son: normopeso <25; sobrepeso >25-<30; obesidad grado 1 (>30 - <35), obesidad grado 2 (>35 - <40) y grado 3 (>40)[5].

El síndrome metabólico se ha calculado con la aplicación disponible on line basado en la definición de la ATP-III y validada en pacientes españoles que incluye: sexo, perímetro abdominal, triglicéridos, tensión arterial máxima y mínima y glucemia basal[6].

La composición corporal se determinó con el analizador TANITABC-420MA, estimando el porcentaje de grasa corporal y grasa visceral. Como indicadores de adiposidad (IA) se han calculado los siguientes:

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

Para valorar riesgo de EHGM se utilizan las calculadoras fatty liver index-FLI validada para estimar riesgo de esteatosis que incluye: IMC, perímetro de cintura, GGT y triglicéridos[7] y la calculadora FIB 4 Index for liver fibrosis validada y que incluye: edad, TGO (o AST) y TGP (o ALT), recuento de plaquetas[8].

Análisis estadístico

Se realizó un análisis descriptivo de las variables categóricas, calculando la frecuencia y la distribución de las respuestas para cada una de ellas. Para las variables cuantitativas se calculó la media y la desviación estándar y, para las cualitativas, el porcentaje. Se realizó un análisis de asociación bivariante mediante el test de 2 (con una corrección con el test estadístico exacto de Fisher, cuando las condiciones lo requerían) y una prueba t de Student para muestras independientes. Para valorar la concordancia entre las diferentes escalas se aplica el test Kappa de Cohen. El análisis estadístico se realizó con el programa SPSS 27.0 y un valor p de <0,05 se consideró estadísticamente significativo.

Consideraciones éticas:

- se solicitó a los pacientes el consentimiento informado para participar en la investigación descrita.
- la investigación cumple con la normativa vigente en investigación bioética y obtuvo la autorización del comité de ética de la institución: fue aprobado por el Comité Ético de Investigación Clínica del Área de Salud de Baleares (IB 4383/20).
- este artículo no contiene información personal que permita identificar a los pacientes

Resultados

Población de 48 años de edad media, con mayor IMC en hombres, en valores de sobrepeso y límites superiores en todos los indicadores de adiposidad. Existen diferencias significativas en la presencia de síndrome metabólico con resultados peores en los hombres (**Tabla I**).

La comparativa de valores medios de FLI muestra valores alterados en hombres y en mujeres en todos los parámetros de obesidad y con la presencia de síndrome metabólico con significación estadística (p <0.001).

También se observa relación con significación estadística entre los valores medios de FIB 4, que son más elevados en los hombres relacionados con valores alterados de grasa visceral y corporal, perímetro de cintura/altura elevado y un IMC en sobrepeso/obesidad. En las mujeres los valores de FIB 4 no muestran significación estadística con ninguno de los parámetros valorados. (**Tabla II**).

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

Variables analizadas		Hombres n=481 Media	(dt)	Mujeres n=334 Media	(dt)	Valor_p
Variable Edad		48.25	8.35	48.89	8.16	0.277
Variables antropométricas	Peso	82.79	13.93	67.97	11.98	<0.0001
	Altura	173.42	6.81	160.72	5.98	<0.0001
	IMC	27.49	4.01	26.33	4.47	<0.0001
Indicadores de adiposidad	PCi	94.61	10.96	84.35	11.43	<0.0001
	ICA	0.55	0.06	0.53	0.07	<0.0001
	PCa	106.22	58.83	99.00	10.13	0.027
	ICC	0.92	0.07	0.85	(0.06	<0.0001
	GC	24.70	6.58	36.08	7.78	<0.0001
	GV	11.35	4.53	7.53	2.65	<0.0001
Clasificación IMC (porcentajes)	Normopeso	29.11		41.62		0.001
	Sobrepeso	48.86		39.52		
	Obesidad	22.04		18.86		
Presencia de Síndrome metabólico		28,88		16,82		<0.0001

IMC= Índice de masa corporal; Mets= síndrome metabólico; GV=grasa visceral ;GC=grasa corporal; PCi=perímetro de cintura; PCa= perímetro cadera; ICA= índice cintura/altura;ICC=índice cintura/cadera. Dt= desviación típica. Se consideran significativos valores de p<0,05.

Tabla II: Valores medios de FLI y FIB-4 según parámetros de obesidad y síndrome metabólico. Diferencias por sexo.

Parámetros	Hombres							Mujeres						
	n	FLI			FIB-4			n	FLI			FIB-4		
		media	Dt	p	media	Dt	p		media	Dt	p	media	Dt	p
GV valores normales	205	22,76	16,18	<0.001	1,09	0,37	<0.001	293	20,76	19,50	<0.001	1,11	0,40	0.637
GV valores alterados	274	60,90	22,67		1,20	0,44		40	60,14	22,22		1,12	0,42	
GC valores normales	114	18,37	14,74	<0.001	1,10	0,39	<0001	84	9,32	12,78	<0.001	1.19	0,38	0.289
GC valores alterados	363	52,92	25,45		1,17	0,42		249	31,26	24,34		1,18	0,40	
PC valores normales	232	24,13	16,21	<0.001	1,14	0,41	0.102	119	6,72	5,78	<0.001	1,15	0,35	0.138
PC valores alterados	247	64,24	21,65		1,17	0,42		214	36,30	23,71		1,13	0,42	
PCA valores normales	105	14,45	9,33	<0.001	1,07	0,40	<0.001	133	7,19	6,16	<0.001	1,16	0,38	0.457
PCA valores alterados	374	53,34	25,13		1,18	0,42		200	38,06	23,45		1,17	0,41	
PCC valores normales	308	34,70	24,85	<0.001	1,15	0,43	0,887	141	12,76	13,50	<0.001	1,12	0,40	0,664
PCC valores alterados	171	63,02	23,11		1,15	0,38		192	35,25	25,47		1,13	0,40	
IMC Normopeso	140	17,58	11,71	<0.001	1,11	0,40	<0.001	139	7,58	6,08	<0.001	1,18	0,38	0,094
IMC Sobrepeso	233	45,72	20,43		1,12	0,39		131	26,53	14,35		1,19	0,43	
IMC Obesidad	106	78,78	15,84		1,19	0,43		63	64,11	17,96		1,19	0,43	
No Mets	379	37,11	24,19	<0.001	1,15	0,41	0.776	277	19,56	18,87	<0.001	1,11	0,40	0,812
Si Mets	100	74,00	20,04		1,15	0,43		56	56,25	23,19		1,11	0,36	

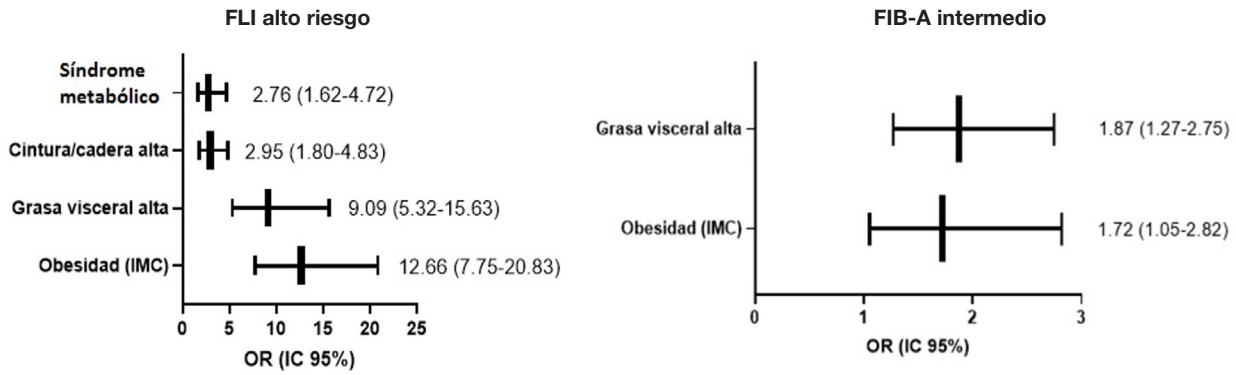
IMC= Índice de masa corporal; Mets= síndrome metabólico; GV=grasa visceral ;GC=grasa corporal; PCi=perímetro de cintura; PCa= perímetro cadera; ICA= índice cintura/altura;ICC=índice cintura/cadera. Dt= desviación típica. Se consideran significativos valores de p<0,05.

Tabla III: Prevalencia de valores elevados porcentualmente de FLI y FIB-4 según parámetros de obesidad y síndrome metabólico. Diferencias por sexo.

Parámetros	Hombres					Mujeres				
	n	FLI alto	p	FIB-4 medio	p	n	FLI alto	p	FIB-4 medio	p
		%		%			%		%	
GV valores normales	205	3,43	<0.001	16,18	<0.001	293	6,46	<0.001	17,01	0.088
GV valores alterados	274	53,13		25,45		40	57,50		18,13	
GC valores normales	114	2,61	<0.001	20,70	0.077	84	1,19	<0.001	21,43	0.721
GC valores alterados	363	40,93		22,53		249	16,40		21,80	
PC valores normales	232	3,88	<0.001	21,12	0.338	119	0,00	<0.001	19,33	0.661
PC valores alterados	247	58,23		21,69		214	19,53		20,08	
PCA valores normales	105	0,00	<0.001	16,19	<0.001	133	0,00	<0.001	19,55	0.410
PCA valores alterados	374	40,96		22,79		200	20,89		20,13	
PCC valores normales	308	17,74	<0.001	21,94	0.289	141	1,41	<0.001	19,01	0.772
PCC valores alterados	171	57,89		22,43		192	20,83		19,68	
IMC Normopeso	140	0,70	<0.001	19,29	0.224	139	0,00	<0.001	20,86	0.334
IMC Sobrepeso	233	25,96		19,81		131	2,27		21,12	
IMC Obesidad	106	86,79		20,13		63	61,90		22,08	
No Mets	379	20,84	<0.001	21,64	0.654	277	5,78	<0.001	16,25	0.889
Si Mets	100	75,00		21,88		56	46,43		16,27	

IMC= Índice de masa corporal; Mets= síndrome metabólico; GV=grasa visceral ;GC=grasa corporal; PCi=perímetro de cintura; PCa= perímetro cadera; ICA= índice cintura/altura;ICC=índice cintura/cadera. Dt= desviación típica. Se consideran significativos valores de p<0,05.

Figura 1: Análisis multivariante mediante regresión logística binaria.



Tanto en hombres como en mujeres, el porcentaje de FLI alto es mayor en relación con valores alterados de los distintos parámetros de obesidad y en presencia de síndrome metabólico, con resultados estadísticamente significativos (p <0.001).

En los porcentajes de FIB 4 en rango medio, se observan diferencias entre sexos. En los hombres existe relación con significación estadística entre porcentajes más altos de FIB 4 en rango medio y valores alterados de grasa visceral y perímetro de cintura/altura elevado En las mujeres, los porcentajes de FIB 4 en rangos por encima de la normalidad no muestran relación con significación estadística con ninguno de los parámetros valorados. (**Tabla III**).

El análisis multivariante muestra que, los parámetros que más incrementan el riesgo de presentar FLI de alto riesgo son la obesidad (IMC) con una OR de 12,66 (IC95% 7,75-20,83) seguido de grasa visceral alta, cintura cadera alta y presencia de síndrome metabólico. Sólo incrementan el riesgo de presentar FIB-4 intermedio la grasa visceral alta y la obesidad (IMC) (**Figura 1**)

Discusión

Los resultados de nuestro estudio reflejan cifras de prevalencia algo más elevadas, tanto en sobrepeso (48,5% en hombres y 39,52% en mujeres) como en obesidad (del 22,04% en hombres y 18,86% en mujeres), si bien el periodo de recogida de datos ha coincidido con el de aislamiento motivado por la pandemia COVID-19 con las modificaciones que ha supuesto en el estilo de vida (cambio de hábitos alimenticios y disminución de actividad física).

Estos resultados son algo más elevados que los que reflejan otros trabajos como el estudio IBERICAN, si bien en este trabajo de recogen datos de población general, entre 18 a 85 años y procedentes de consultas de Atención Primaria, mientras que nuestro trabajo se desarrolla en consultas de Medicina del Trabajo y con edades entre 18-66 años.

La prevalencia de obesidad del estudio IBERICAN fue del 35,7% de los cuales el 36,6% eran hombres y el 34,9% mujeres y muestra que aproximadamente un tercio de la población analizada cumple criterios de obesidad[9].

Los resultados de nuestro trabajo muestran valores por encima de lo normal en todos los indicadores de adiposidad (perímetro de cintura, índice cintura/altura, grasa corporal y visceral), y son más elevados en los hombres que en las mujeres, excepto el valor medio de grasa corporal que es más elevado en mujeres (p<0.0001).

Los trabajos más actuales en obesidad muestran la importancia de utilizar medidas antropométricas como herramientas sencillas, económicas no invasivas y útiles para diagnosticar la obesidad y evaluar el riesgo de morbilidad y mortalidad, algunas de ellas fáciles de obtener como el perímetro abdominal[10]. Los parámetros más utilizados, además del IMC son: la circunferencia de la cintura, las relaciones cintura-cadera y cintura-altura, la grasa visceral y la grasa corporal[11], todos ellos han sido utilizados también en nuestro trabajo. Entre ellos destacan la grasa corporal, la visceral y el índice cintura/altura parámetros que ha sido destacados en otros estudios como complementarios al IMC[12].

Si consideramos que el hígado graso es la enfermedad hepática más frecuente en los países occidentales podemos valorar la utilidad de métodos no invasivos para estimar el riesgo de su aparición o evolución. Tanto el FLI[13] como el FIB4[14] son fáciles de obtener y pueden ayudar a los médicos a seleccionar sujetos para ecografía hepática y asesoramiento intensificado sobre el estilo de vida, y a los investigadores a seleccionar pacientes para estudios epidemiológicos[15].

En nuestro trabajo el FLI en valores alterados ha mostrado relación significativa el índice cintura/cadera y estos resultados coinciden con lo reflejado por otros autores en sus estudios asociando los factores metabólicos con el daño hepático en pacientes con enfermedad de NAFLD y, de forma concreta con los indicadores de

adiposidad visceral como expresión de la disfunción del tejido adiposo tanto cualitativa como cuantitativa que se correlaciona de forma independiente con una fibrosis significativa[16]. También muestra una buena correlación como marcador de enfermedad de EHGM y los rangos de IMC, por lo que puede ser un marcador útil para caracterizar las primeras alteraciones metabólicas en personas con sobrepeso u obesidad coincidiendo con lo ya realizado por otros autores en sus trabajos con este indicador[17].

En nuestro trabajo se muestra una correlación significativa entre la presencia de síndrome metabólico y valores alterados del FLI en concordancia con lo reflejado en otros estudios que afirman, que el síndrome metabólico aumenta el riesgo de enfermedad cardiovascular y, que el FLI podría utilizarse para reconocer el síndrome, tanto en sujetos con, como sin enfermedad de hígado graso que requieren modificaciones en el estilo de vida y asesoramiento en salud[18].

Resultados menos concluyentes hemos obtenido con el FIB-4 que muestra relación en sus valores medios con la grasa visceral alta y el IMC en rango de obesidad.

En cuanto al IMC, la correlación entre obesidad y las puntuaciones no invasivas se utiliza cada vez más para detectar la fibrosis avanzada en la enfermedad del hígado graso asociada a EHGM, pero el efecto del IMC en su utilidad clínica sigue siendo incierto. Se admite que el FIB-4 y NAFLD fibrosis score pueden utilizarse con confianza para excluir la fibrosis avanzada en pacientes con sobrepeso, obesidad y obesidad severa. Sin embargo, no parecen ser clínicamente útiles en pacientes delgados y con obesidad mórbida[19]. Más clara parece ser la relación entre los valores altos de grasa visceral como factor de predicción de mayor riesgo de EHGM y de fibrosis avanzada con EHGM, especialmente en los sujetos obesos[20].

En nuestro trabajo no se ha observado una relación significativa entre los valores elevados de FIB-4 y la presencia de síndrome metabólico. Otros estudios, que también han analizado esta relación afirman que las puntuaciones elevadas de FIB-4 pueden proporcionar datos de interés para una evaluación clínica adicional de la enfermedad hepática en los entornos de atención primaria y también en medicina del trabajo, incluyendo entre los parámetros de estudio el síndrome metabólico[21].

Conclusión

Los índices predictivos FLI y FIB-4 de EHGM son métodos no invasivos, fáciles de utilizar y muestran relación con los valores elevados de IMC y parámetros de obesidad como la grasa visceral y el índice cintura cadera, especialmente FLI. FIB-4 solo muestra relación con grasa visceral y con el IMC. El síndrome metabólico solo se correlaciona con valores medios de FLI.

Conflicto de Intereses: en este estudio no existen conflictos de interés.

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ORIGINAL

Clinical Outcomes of COVID-19 Patients Following Treatment with Atorvastatin: A Non-Randomized Clinical Trial

Resultados clínicos de pacientes con COVID-19 después del tratamiento con atorvastatina: un ensayo clínico no aleatorizado

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Abstract

Objective: There are controversial data regarding the utility of statins in hospitalized COVID-19 patients. This study aimed to assess the efficacy of statins on clinical outcomes of patients hospitalized with COVID-19.
Methods: A non-randomized clinical trial was performed among confirmed COVID-19 patients who were admitted to the BooAli hospital in Tehran, Iran. The intervention group received atorvastatin 20 mg orally once daily plus standard of care, while the control group received standard of care alone. The primary endpoints were clinical improvement rate at day 7 as well as in-hospital mortality rate. The secondary endpoints were the duration of hospitalization, the number of intensive care unit (ICU) admissions, the number of patients who needed invasive mechanical ventilation, the incidence of acute respiratory distress syndrome (ARDS), and the reduction of inflammatory markers.
Result: In total 94 patients were enrolled (treatment group: 41 patients, control group: 53 patients). The results showed that nearly 59% of patients who received atorvastatin manifested clinical improvement within 7 days compared to 62% of patients in the control group ($P > 0.05$). There was no significant difference between treatment and control groups in terms of in-hospital mortality, duration of hospitalization, ICU admissions, need for invasive mechanical ventilation, and incidence of ARDS.
Conclusion: Atorvastatin 20 mg daily in hospitalized COVID-19 patients was not associated with significant changes in clinical improvement of patients within 7 days, in-hospital mortality rate, and other clinical outcomes.

Keywords: COVID-19, SARS-CoV-2, Statin, Atorvastatin.

Resumen

Objetivo: Existen datos controvertidos sobre la utilidad de las estatinas en los pacientes hospitalizados por COVID-19. Este estudio tiene como objetivo evaluar la eficacia de las estatinas en los resultados clínicos de los pacientes hospitalizados con COVID-19.
Métodos: Se realizó un ensayo clínico no aleatorizado entre pacientes con COVID-19 confirmados que fueron ingresados en el hospital BooAli de Teherán, Irán. El grupo de intervención recibió atorvastatina 20 mg por vía oral una vez al día más el tratamiento estándar, mientras que el grupo de control recibió únicamente el tratamiento estándar. Los criterios de valoración primarios fueron la tasa de mejora clínica en el día 7 y la tasa de mortalidad hospitalaria. Los criterios de valoración secundarios fueron la duración de la hospitalización, el número de ingresos en la unidad de cuidados intensivos (UCI), el número de pacientes que necesitaron ventilación mecánica invasiva, la incidencia del síndrome de dificultad respiratoria aguda (SDRA) y la reducción de los marcadores inflamatorios.
Resultado: En total se inscribieron 94 pacientes (grupo de tratamiento: 41 pacientes, grupo de control: 53 pacientes). Los resultados mostraron que casi el 59% de los pacientes que recibieron atorvastatina manifestaron una mejora clínica en un plazo de 7 días, en comparación con el 62% de los pacientes del grupo de control ($P > 0,05$). No hubo diferencias significativas entre los grupos de tratamiento y de control en cuanto a la mortalidad intrahospitalaria, la duración de la hospitalización, los ingresos en la UCI, la necesidad de ventilación mecánica invasiva y la incidencia de SDRA.
Conclusiones: La administración de 20 mg diarios de atorvastatina en pacientes hospitalizados por COVID-19 no se asoció a cambios significativos en la mejoría clínica de los pacientes en un plazo de 7 días, la tasa de mortalidad intrahospitalaria y otros resultados clínicos.

Palabras clave: COVID-19, SARS-CoV-2, Estatina, Atorvastatina.

Introduction

The coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has affected the lives of millions of people globally since its recognition in December 2019. The clinical spectrum of SARS-CoV-2 infection ranges from mild to critical. According to one of the earliest studies by the Chinese Center for Disease Control and Prevention, 81% of the patients exhibited mild illness, and about 14% had severe symptoms (dyspnea, hypoxia, or more than 50 percent lung involvement on imaging within 24 to 48 hours), and about 5% were critically ill (respiratory failure, shock or multiorgan dysfunction)[1,2]. In critically ill patients, viral pneumonia can progress to acute respiratory distress syndrome (ARDS)[1,2]. The in-hospital mortality rate among COVID-19 patients was reported to be between 9.3% and 19.7% in a study in 2020[3]. Among patients with COVID-19, there is a high prevalence of cardiovascular disease with a considerably higher mortality rate4. Because antiviral agents and vaccines are not easily available in some countries or not sufficiently effective against different SARS-CoV-2 variants[5], repurposing existing medicines with various mechanisms, that are widely available, safe, and inexpensive is of great importance for identifying effective therapies against COVID-19.

Statins are conventionally used as the first-line treatment of dyslipidemia. The clinical benefits of statins for patients with cardiovascular disease are firmly established, they are vastly used in patients with or at risk of cardiovascular disease to decrease the rate of myocardial infarction, stroke, and cardiovascular death[6]. Statins have antithrombotic and antifibrotic as well as anti-inflammatory effects[7-10]. In a previous study, statin use was associated with a decrease in inflammatory markers such as C-reactive Protein (CRP)[11]. An increase in several biomarkers including the level of CRP has been shown to be associated with an increased risk of mortality in COVID-19 patients[12-14]. Interestingly, in seasonal influenza outbreaks, statin use was associated with reduced mortality in patients hospitalized with influenza virus infection[15,16]. Thus, adding statins as adjuvant therapy seems to be beneficial for COVID-19 patients. To date, several studies have investigated the use of statins in the treatment of COVID-19[17-21]. However, the results have been discordant. Therefore, this prospective study was designed to evaluate the efficacy of statins on clinical outcomes of patients hospitalized with COVID-19.

Methods

Study Design and Sample Size

This prospective non-randomized study was conducted between April and May 2020 at the BooAli Hospital in Tehran, Iran. The sample size of the study was calculated based on our previous data which showed about 50% of patients admitted to the hospital found the criteria for clinical improvement on day 7. We set an α-error of 0.05 and a power of 0.8 and the sample size calculated was 38 patients for each group to show a 30% difference in recovery. This study was approved by the Ethics Committee and the Research Council of Islamic Azad University, Tehran Medical Branch (ID: IR.IAU.PS.REC.1399.002) and was approved by the Iranian Registry of Clinical Trials (ID: IRCT20200413047062N1).

Eligibility Criteria and Intervention

Eligible patients were men and non-pregnant women with COVID-19 who were aged at least 18 years with positive reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2 or confirmed computed tomography (CT) scan findings. Exclusion criteria included pregnancy or breastfeeding; hepatic cirrhosis; alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than five times the upper limit of normal; known severe renal impairment; estimated glomerular filtration rate (eGFR) <30 mL/min, history of allergy to atorvastatin and history of severe adverse effect with statins.

The study intervention was atorvastatin 20 mg orally once daily until discharge from the hospital. Patients in both treatment and control groups received hydroxychloroquine 200mg twice daily for 5 to 7 days or lopinavir/ritonavir 400/100 mg tablets twice daily for 5 to 7 days as the treatment protocol of the hospital.

Laboratory tests for hematological and renal functions were evaluated by white blood cells, hemoglobin, platelet counts, eGFR, and blood urea nitrogen (BUN); liver function was assessed with AST, ALT, alkaline phosphatase (ALP). The serum level of CRP was evaluated as a marker of inflammation.

Outcomes

The primary endpoint of the study was clinical improvement within 7 days from the first day of hospitalization. Clinical improvement was defined as the time from the first day of hospitalization to an improvement of two points on a seven-category ordinal scale or live discharge from the hospital, whichever came first[22]. The seven-category ordinal scale consisted of the following categories: 1, not hospitalized with resumption of normal activities; 2, not hospitalized, but unable to resume normal activities; 3, hospitalized, not requiring supplemental oxygen; 4, hospitalized, requiring supplemental oxygen; 5, hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both; 6, hospitalized, requiring invasive mechanical ventilation; and 7, death. Another primary endpoint was the in-hospital mortality rate of the patients in the treatment and control groups. The secondary outcomes evaluated were the duration of hospitalization, the number of patients who needed invasive mechanical ventilation, the number

of ICU admissions, the incidence of ARDS, and the comparison of baseline CRP and CRP level at the end of treatment between atorvastatin and control groups.

Statistical Analysis

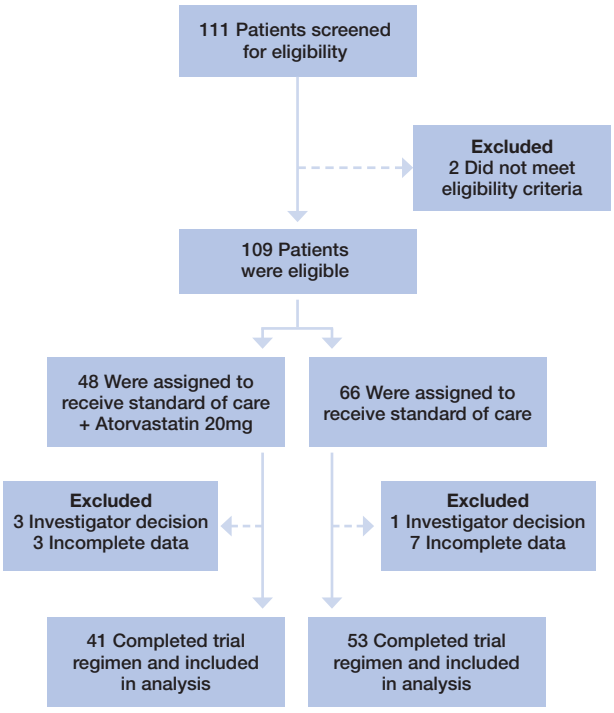
The results were analyzed using IBM SPSS ver. 26.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation and an Independent-Samples T-Test was used for group comparison. Categorical variables were presented as numbers and percentages. The Chi-square test was used for the comparison between the two groups. Paired-Samples T-Test was used for the comparison of baseline CRP level with CRP level at the end of treatment in the atorvastatin and control groups. Time to death was evaluated using survival analysis. The Kaplan-Meier method was used to estimate the time to death between the treatment and control groups, and the survival functions between the groups were compared using the Log-Rank (Mantel-Cox) test. $P < 0.05$ was considered statistically significant.

Results

General characteristics of the enrolled patients

Figure 1 shows the flow chart of all the patients evaluated and included in the study. Of 111 patients assessed for eligibility, 109 patients were enrolled in this study: 48 assigned to the atorvastatin group and 66 assigned to the control group. After the exclusion of 14 patients, 41 patients in the atorvastatin group and 53 patients in the control group were included in the analysis of the study.

Figure 1: Flow chart of patients enrolled in the study.



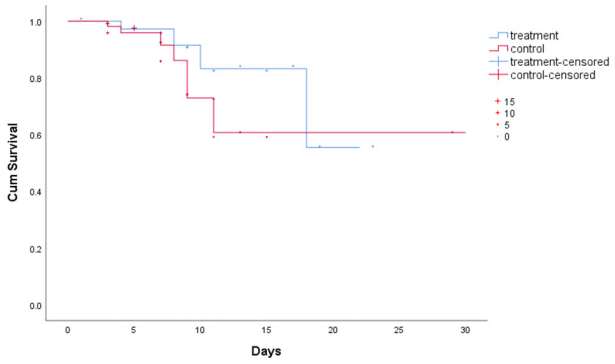
Analysis of baseline characteristics of both groups is summarized in **table I**. Overall, the mean age of study participants was 60 years and 42 (50.5%) were male. The mean BMI in the atorvastatin group and control group was 26.7 and 26.5 kg/m^2, respectively. The mean body temperature was 37.9°C in the atorvastatin group and 37.8°C in the control group and the mean respiratory rate at the time of enrolment was 19.5 and 18.6 breaths/min in the atorvastatin and control groups, respectively. The mean duration of symptoms before hospital admission was 5 days in both groups. In the atorvastatin group, 43.9% of the patients were previously diagnosed with hypertension while in the control group it was 32.0%. All the patients received hydroxychloroquine and 43.9% in the atorvastatin group and 41.5% in the control group received lopinavir-ritonavir as an antiviral medication. The data demonstrated that the demographic, clinical, and laboratory characteristics of the two groups were not significantly different.

Primary and secondary outcomes

The endpoint powered in this study was the clinical improvement rate at day 7 based on the seven-category ordinal scale. As shown in **table II** in the atorvastatin group, 24 (58.5%) patients were clinically improved by day 7, while in the control group 33 (62.3%) patients were improved. The difference was not statistically significant. The other primary endpoint was the assessment of the in-hospital mortality rate. The percentage of participants who died was 9.8% among those who received atorvastatin and 13.2% among the patients who did not. However, the difference in mortality rate between the two groups was not statistically significant. **Figure 2** shows the Kaplan-Meier survival curve of the two groups, and the log-rank test demonstrates no significant difference between atorvastatin and control groups.

The secondary endpoint of the study was the comparison of the duration of hospitalization between the two groups. In patients who received atorvastatin, the mean duration of hospitalization was not significantly different from the

Figure 2: Kaplan-Meier curves estimated the mortality of patients in the 2 groups of treatment and control. Log-rank test: $P = 0.26$.



control group (7.9 ± 5.0 days vs 6.8 ± 4.4 days). Also, the mean duration of hospitalization was assessed for survived patients (excluding deaths) which were 7.7 ± 5.0 days and 6.7 ± 4.6 days in the atorvastatin and control groups respectively with no significant difference (**Table II**).

Other secondary endpoints were to compare the number of patients who needed ICU admission during hospitalization, the number of patients who needed invasive mechanical ventilation, and the incidence of ARDS between the two groups. **Table II** shows the percentage of ICU admissions in patients who received atorvastatin compared to those in the control group (19.5% vs 24.5%). The percentage of invasive mechanical ventilated patients was 14.6% and 22.6% in the atorvastatin and control groups, respectively. In the atorvastatin group, 14.6% of patients experienced ARDS, whereas in the control group 26.4% of patients experienced it. The differences in all these secondary outcomes were not statistically meaningful.

Table I: Patient Characteristics and Baseline Values.

Characteristics	Atorvastatin N= (41)	Control N= (53)	P value
Male, N (%)	24 (58.5%)	24 (45.3%)	0.20
Age (year), Mean (SD)	62 (12)	60 (14)	0.36
BMI (kg/m^2), Mean (SD)	26.7 (3.6)	26.5 (4.8)	0.81
Clinical features at the time of enrollment, Mean (SD)			
Body temperature (°C)	37.9 (0.6)	37.8 (1.0)	0.57
Respiratory rate (breaths/min)	19.5 (3.8)	18.6 (2.8)	0.15
Duration of symptoms before hospital admission (days)	5.0 (2.7)	5.0 (2.4)	0.77
Underlying medical condition, N (%)			
Hypertension	18 (43.9%)	17 (32.0%)	0.23
History of Immunocompromised condition	3 (7.3%)	3 (5.7%)	0.74
Concomitant medications, N (%)			
Hydroxychloroquine	41 (100%)	53 (100%)	
Lopinavir-ritonavir	18 (43.9%%)	22 (41.5%)	0.81
Laboratory values at baseline, Mean (SD)			
White blood cells count (×109/L)	7.8 (4.5)	6.9 (3.5)	0.29
Absolute neutrophil count (×109/L)	6 (4.4)	5.3 (3.0)	0.36
Hemoglobin level (g/dL)	12.6 (2.3)	12.1 (1.5)	0.26
Platelet count (×109/L)	215.1 (88.5)	240.7 (98.7)	0.19
Estimated glomerular filtration rate (mL/min)	84.4 (32.0)	81.1 (33)	0.62
Creatinine (mg/dL)	1.01 (0.4)	1.10 (0.6)	0.39
Blood urea nitrogen (mg/dL)	21.6 (12.7)	19.0 (10.7)	0.28
Aspartate transaminase (U/L)	29.5 (11.3)	31.4 (15.4)	0.51
Alanine transaminase (U/L)	28.1 (13.1)	32.3 (17.0)	0.19
Alkaline Phosphatase (U/L)	204.5 (82.5)	191.6 (134.1)	0.59
C-reactive protein (mg/L)	37.4 (20.8)	37.0 (16.7)	0.93

N: Number; SD: Standard deviation; BMI: Body mass index; Independent-Samples T-Test was used for continuous variables; Chi-Square test was used for the categorical variables; P < 0.05 was considered significant.

Table II: Clinical outcomes.

Outcomes	Atorvastatin N= (41)	Control N= (53)	P value
Clinical improvement rate at day 7, N. (%)	24 (58.5%)	33 (62.3%)	0.71
Mortality during hospitalization, N. (%)	4 (9.8%)	7 (13.2%)	0.60
Duration of hospitalization (days), Mean (SD)	7.9 (5.0)	6.8 (4.4)	0.26
Duration of hospitalization among patients who survived, Mean (SD)	7.7 (5.0)	6.7(4.6)	0.73
Admission to ICU during hospitalization, N. (%)	8 (19.5%)	13 (24.5%)	0.56
Invasive Mechanical ventilation during hospitalization, N. (%)	6 (14.6%)	12 (22.6%)	0.32
Incidence of ARDS, N. (%)	6 (14.6%)	14 (26.4%)	0.16

N: Number; SD: Standard deviation; ICU: Intensive care unit; ARDS: Acute respiratory distress syndrome; Independent-Samples T-Test was used for continuous variables; Chi-Square test was used for the categorical variables; P < 0.05 was considered significant.

Table III: The behavior of CRP during the two different treatments.

	Atorvastatin N = (41)			Control N = (53)		
	Baseline	End of treatment	P Value	Baseline	End of treatment	P value
CRP (mg/L), Mean (SD)	37.3 (20.8)	27.2 (18.1)	0.006	37 (16.7)	35.2 (19.9)	0.418

CRP: C-reactive protein; SD: Standard deviation; Paired-Samples T-Test was used for the comparison of baseline CRP level vs. CRP level at the end of treatment; P < 0.05 was considered significant.

The comparison of CRP level, which was assessed as an inflammatory marker, on the first day of hospitalization and the end of treatment between the 2 groups is shown in **table III**. A significant decrease in CRP level was observed at the end of treatment in patients receiving atorvastatin (P=0.006), while it was not seen in the control group.

Discussion

In this study of patients with COVID-19 admitted to the BooAli hospital in Tehran, Iran, the use of atorvastatin 20 mg once daily compared with the control group was not associated with a significant difference in the primary outcome, clinical improvement within 7 days from the first day of hospitalization which was defined as the time from the first day of hospitalization to an improvement of two points on a seven-category ordinal scale or live discharge from the hospital, whichever came first. To our knowledge, this is the first study evaluating the effect of statins on clinical improvement based on a seven-category ordinal scale in COVID-19 patients. Results of our study were not associated with diminutions in in-hospital mortality and duration of hospital stay. This is in agreement with the results of a systematic review and meta-analysis of 3449 COVID-19 patients that evaluated the association between statin use and in-hospital outcomes of COVID-19 infection, suggesting that statin use did not improve mortality from COVID-19 infection[23]. Also, a randomized clinical trial of COVID-19 patients reported that adding atorvastatin to the standard of care in this study increased hospitalization days and the frequency of ICU admission[24]. In addition, a retrospective study evaluated the effect of statins on patients with COVID-19. The findings of this study could not demonstrate a significant association between statin use and a reduction in mortality rate in patients with COVID-19[25]. The INSPIRATION-S, a multicenter, randomized controlled trial also failed to show that atorvastatin was beneficial in critically ill COVID-19 patients[21].

However, there are studies reporting that statin use was associated with improved clinical outcomes in COVID-19 patients[26]. A meta-analysis of retrospective observational studies showed that statin therapy was associated with a 35% decrease in the adjusted risk of mortality in hospitalized COVID-19 patients[27]. In another study, 40 patients were randomized into a treatment group receiving atorvastatin + lopinavir/ritonavir or a control group receiving lopinavir/ritonavir alone. The primary endpoint of this study was the duration of hospitalization. The results showed that the duration of hospitalization in the lopinavir/ritonavir + atorvastatin group was significantly reduced compared to the control group, but there was no significant difference in the invasive mechanical ventilation reception[28]. In our study, the percentage of patients admitted to the ICU and invasive mechanical ventilated patients was lower in the treatment group, but the difference was not statistically significant. In another study that analyzed a retrospective cohort of patients admitted to a tertiary center in Singapore for COVID-19 infection in a nested case-control design, through logistic treatment models with 1:3 propensity matching for age, gender, and ethnicity, statin use was independently associated with lower ICU admission[29].

In the current study, due to anti-inflammatory effects reported for statins, the level of CRP, as a marker of inflammation, was measured at baseline and at the end of treatment in both groups to observe whether there was any difference in the behaviour of this marker between the two groups. The results showed a significant decrease in the amount of CRP at the end of treatment in patients who received atorvastatin, whereas no significant decrease was seen in the control group. Although the reduction of CRP level was significant for the treatment group, still it was not in the normal range at the end of treatment. This was in concordance with the result of another study investigating the effect of statins on the behaviour of CRP during hospitalization in COVID-19 patients[28]. One of the key features of COVID-19 is the overwhelming inflammation observed in some patients, especially those who develop severe illness; thus, it is important to determine the optimum method to reduce inflammation and statins could be a candidate[30]. However, some of the studies claimed that due to the lower anti-inflammatory effects of statins compared to corticosteroids, statins cannot make a significant change in the inflammation or occurrence of cytokine storm in COVID-19, thus statin administration is not associated with alterations in the in-hospital outcomes of COVID-19 patients[31,32]. Overall, the current trial could not support a large benefit from statin treatment in COVID-19 patients. Yet, the absence of clinical benefit of atorvastatin in this study might be due to the small sample size. Therefore, we suggest conducting further studies with larger sample size. A potential limitation of our study was that the patients were not randomized for the treatment assignment. The absence of long-term follow-up was another limitation of this study.

Conclusion

The results obtained in the present study showed that in patients with COVID-19 admitted to the BooAli Hospital in Tehran, Iran, treatment with atorvastatin 20 mg daily was not associated with a significant difference in clinical improvement rate at day 7, in-hospital mortality rate, length of hospitalization, ICU admissions, need for invasive mechanical ventilation or incidence of ARDS. The effect of atorvastatin was only significant in reducing CRP levels from the first day of hospitalization until the end of treatment. The effect of more potent doses of statins needs to be investigated using larger sample sizes in future studies.

Conflict of Interest

The authors declare no conflict of interest.

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ORIGINAL

Relationship between physical activity and adherence to the mediterranean diet with metabolic syndrome, hypertriglyceridemic waist phenotype and hypertensive waist

Relación entre la actividad física y la adherencia a la dieta mediterránea con el síndrome metabólico, el fenotipo de cintura hipertrigliceridémica y la cintura hipertensiva

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Abstract

Introduction: Metabolic syndrome is a very common clinical condition that includes a series of anthropometric, analytical and clinical alterations that result in an increased risk of cardiovascular disease and diabetes type 2.
Methods: Cross-sectional study carried out in 1457 persons assessing the effect of physical activity determined with the IPAQ questionnaire and the Mediterranean diet assessed with the PREDIMED questionnaire on the values and prevalence of metabolic syndrome calculated with the NCEP ATPIII, IDF and JIS scales and the hypertriglyceridemic waist penotype and hypertensive waist determined with the NCEP ATPIII and IDF criteria.
Results: The prevalence of metabolic syndrome with the three scales, hypertriglyceridemic waist phenotype and hypertensive waist decreases as the level of physical activity determined with the IPAQ questionnaire increases. A decrease is also observed in people with high adherence to the Mediterranean diet compared to those with low adherence in both metabolic syndrome (also with the three scales) and in both waistlines. In the multivariate analysis, physical activity decreases the risk of metabolic syndrome, hypertriglyceridemic waist phenotype and hypertensive waist while high adherence to the Mediterranean diet only decreases the risk of metabolic syndrome.
Conclusion: Both physical activity and the Mediterranean diet decrease the risk of metabolic syndrome, hypertriglyceridemic waist phenotype and hypertensive waist in the Spanish Mediterranean population.

Keywords: Metabolic syndrome, physical exercise, healthy food, Hypertriglyceridemic waist phenotype, hypertensive waist. Mediterranean diet, PREDIMED.

Resumen

Introducción: El síndrome metabólico es una condición clínica muy común que incluye una serie de alteraciones antropométricas, analíticas y clínicas que resultan en un mayor riesgo de enfermedad cardiovascular y diabetes tipo 2.
Métodos: Estudio transversal realizado en 1457 personas valorando el efecto de la actividad física, determinada con el cuestionario IPAQ, y la dieta mediterránea, evaluada con el cuestionario PREDIMED, sobre los valores y la prevalencia del síndrome metabólico calculado con las escalas NCEP ATPIII, IDF y JIS y el fenotipo de cintura hipertrigliceridémica y cintura hipertensiva determinados con los criterios NCEP ATPIII e IDF.
Resultados: La prevalencia del síndrome metabólico con las tres escalas, el fenotipo de cintura hipertrigliceridémica y la cintura hipertensiva disminuye a medida que aumenta el nivel de actividad física determinado con el cuestionario IPAQ. También se observa una disminución en las personas con alta adherencia a la dieta mediterránea en comparación con las de baja adherencia tanto en el síndrome metabólico (también con las tres escalas) como en ambas cinturas. En el análisis multivariante, la actividad física disminuye el riesgo de síndrome metabólico, fenotipo de cintura hipertrigliceridémica y cintura hipertensa, mientras que la alta adherencia a la dieta mediterránea sólo disminuye el riesgo de síndrome metabólico.
Conclusiones: Tanto la actividad física como la dieta mediterránea disminuyen el riesgo de síndrome metabólico, fenotipo de cintura hipertrigliceridémica y cintura hipertensiva en la población mediterránea española.

Palabras clave: Síndrome metabólico, ejercicio físico, alimentación saludable, fenotipo de cintura hipertrigliceridémica, cintura hipertensa. Dieta mediterránea, PREDIMED.

Introduction

Metabolic syndrome (MS), also called Reaven's syndrome, insulin resistance syndrome, plurimetabolic syndrome, or syndrome X, is a group of disorders that occur simultaneously and lead to an increased risk of heart disease, stroke, and type 2 diabetes. This syndrome includes insulin resistance, excess abdominal fat, atherogenic dyslipidemia, endothelial dysfunction, arterial hypertension, hypercoagulability and chronic stress.

The pathophysiology of MS is very complex and only part of it is known[1,2]. In general, patients are older, obese, have little physical exercise, and have a certain degree of insulin resistance. Insulin resistance is known to play an essential role in the development of this syndrome. Currently, the majority of calories consumed come from carbohydrates, especially so-called "simple carbohydrates", i.e. sugar, sweets and processed foods with added sugar (cakes, sodas, cookies, etc.). These foods are absorbed faster, which causes the pancreas to release more of them to keep blood glucose in normal values. If this food intake is maintained and no physical exercise is performed, the cells lose the ability to respond to insulin, becoming insulin resistant or glucose intolerant so that blood glucose will increase, when this occurs the pancreas releases more insulin to normalize blood glucose. The end result is an elevation of insulin in the blood.

Different factors are involved in the etiology of this syndrome, namely an excess consumption of calories, sugars, fats and salt, together with a decrease in the level of physical activity due to a great technological development that reduces the level of effort required to perform most tasks, to which we must add the increase in passive entertainment based on the use of electronic devices[3-6].

The prevalence of the metabolic syndrome will depend on the criteria used to define it, age, sex, race, and lifestyle. In the general population, the prevalence ranges from 15% to 40%[7], increasing to almost 50% in patients with ischemic heart disease or some other vascular condition[8]. The prevalence is higher in persons of Hispanic origin[9].

The aim of this study was to assess the influence of physical activity as determined by the IPAQ questionnaire and adherence to the Mediterranean diet on the appearance of metabolic syndrome as determined by the NCEP ATPIII, IDF and JIS criteria.

Methods

Retrospective and cross-sectional study of 1584 workers in the Balearic Islands and the Valencian Community (Spain) carried out between January 2017 and December 2017. A total of 127 were excluded (69 did not accept to participate and 58 due to ages not included in the study) leaving 1457 workers who are the ones finally included in the study, of whom 718 were women (mean age 43.30 years) and 739 were men (mean age 46.02 years). The workers were selected from among those who attended periodic occupational medical check-ups.

Inclusion criteria

- Age between 18 and 67 years old.
- Belong to one of the companies collaborating in the study.
- Agree to participate in the study.

The anthropometric, clinical and analytical determinations are performed by the health personnel of the different occupational health units participating in the study, after homogenizing the measurement techniques.

For the measurement of weight, which is expressed in kilograms, and height, which is expressed in cm, a scale with measuring rod is used: SECA model 700. The abdominal waist circumference (in cm) is measured with a measuring tape: SECA model 20 with the person in a standing position, feet together and trunk straight, abdomen relaxed and upper limbs hanging on both sides of the body. The tape measure is placed parallel to the floor at the level of the last floating rib. Hip circumference is measured with the same tape measure and adopting the same position as for the waist circumference and passing the tape horizontally at hip level. The waist/height and waist/hip indices are obtained by dividing the waist circumference by the height and hip circumference respectively. The cut-off point for the former is 0.50 and for the latter 0.85 for women and 0.95 for men[10].

Blood pressure was obtained in the supine position with a calibrated OMRON M3 automatic sphygmomanometer and after 10 minutes of rest. Three measurements are taken at one-minute intervals and the mean of the three is obtained. Blood tests are obtained by peripheral venipuncture after a 12-hour fast. Samples are sent to reference laboratories and processed within 48-72 hours. Automated enzymatic methods are used for blood glucose, total cholesterol and triglycerides. Values are expressed in mg/dl. HDL is determined by precipitation with dextran sulfate Cl2Mg, and values are expressed in mg/dl. LDL is calculated using the Friedewald formula (provided that triglycerides are less than 400 mg/dl). Values are expressed in mg/dl.

Friedewald's formula: LDL= total cholesterol -HDL-triglycerides/5

Glycemia figures were classified according to the recommendations of the American Diabetes Association[11]; hyperglycemia was considered to be 125 mg/dl or higher or if receiving hypoglycemic treatment.

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

For social class, we used the 2011 National Classification of Occupations (CNO-11) and the proposal made by the social determinants group of the Spanish Society of Epidemiology[12]. We opted for classification in 3 categories: Class I. Directors/managers, university professionals, athletes and artists. Class II. Intermediate occupations and self-employed workers without employees. Class III. Unskilled workers.

Diet is assessed by means of the Mediterranean diet adherence questionnaire[13] which is based on the Predimed test and consists of 14 questions scored with 0 or 1 point each. Scores below 9 are considered low adherence and above 9 good adherence.

Physical activity is determined by means of the International Physical Activity Questionnaire (IPAQ)[14]. This is a 7-question self-administered questionnaire that assesses the type of physical activity performed in daily life during the last 7 days.

The metabolic syndrome is determined with three models:

(a) NCEP ATP III (National Cholesterol Educational Program Adult Treatment Panel III). Metabolic syndrome is considered to be present when three or more of the following factors are present: waist circumference greater than 88 cm in women and 102 in men, triglycerides greater than 150 mg/dl or specific treatment of this lipid alteration, blood pressure greater than 130/85 mm Hg, HDL less than 50 mg/dl in women or less than 40 in men or specific treatment, and fasting blood glucose greater than 100 mg/dl or specific treatment of blood glucose.

b) International Diabetes Federation (IDF)[15] It requires the presence of central obesity (waist circumference above 80 cm in women and 94 cm in men), in addition to two of the other factors mentioned above for ATP III (triglycerides, HDL, blood pressure and glycemia).

c) JIS[16] model uses the same criteria as NCEP ATPIII but with waist circumference cut-off points from 80 cm in women and 94 cm in men.

Hypertriglyceridemic waist (ATPIII and IDF criteria)[17] The ATPIII model requires: waist circumference >102 cm (men) and >88 cm (women) and triglycerides greater than 150 mg/dL or treatment of hypertriglyceridemia. The IDF model requires: waist circumference >94 cm (men) and >80 cm (women) and triglycerides >150 mg/dl or treatment of hypertriglyceridemia.

Hypertensive waist circumference (ATPIII and IDF criteria)[18]. The ATPIII criteria include: waist circumference from 102 cm (men) and 88 cm (women) or more, plus Systolic blood pressure (SBP) from 130 mmHg or Diastolic blood pressure (DBP) from 85 mmHg or a history of hypertension under treatment. The IDF criteria require: waist circumference of 94 cm or more (men) and 80 cm or more (women), and na SBP of 130 mm Hg or a DBP of 85 mm Hg or more, or a history of hypertension in treatment.

Statistical analysis

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

Ethical aspects

The study was approved by the Clinical Research Ethics Committee of the Illes Balears health area no. IB 4383/20. All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 2013 Declaration of Helsinki. All patients signed written informed consent documents before participating in the study.

Results

The values of the anthropometric, clinical, analytical, sociodemographic and healthy habits variables of our population are more unfavorable, except for total cholesterol, among men. Most of the persons included in the study belong to social class III. Slightly more than 27% are smokers, more than 36% engage in intense physical activity and slightly less than 58% have a high adherence to the Mediterranean diet. In all cases except for total cholesterol and LDL cholesterol values, the differences observed were statistically significant. The complete data are presented in **table I**.

The prevalence of altered values of the metabolic scales (metabolic syndrome, Hypertriglyceridemic waist and hypertensive waist) decreases as the level of physical activity increases, and this can be observed in both sexes, the differences being statistically significant in all cases. The prevalence of all the variables are, in general, higher in men. (see **Table II**).

Table I: Characteristics of the population.

	Women (n=718) mean (SD)	Men (n=739) mean (SD)	Total (n=1457) mean (SD)	p-value
Age (years)	43.30 (8.44)	46.02 (8.50)	44.68 (8.57)	<0.0001
Height (kg)	66.29 (12.29)	82.24 (13.81)	74.38 (15.32)	<0.0001
Weight (m)	1.62 (0.06)	1.73 (0.07)	1.68 (0.09)	<0.0001
BMI (kg/m²)	25.36 (4.61)	27.40 (4.13)	26.39 (4.49)	<0.0001
Waist (cm)	89.44 (16.36)	97.00 (10.65)	93.27 (14.27)	<0.0001
Hip (cm)	105.78 (13.22)	108.77 (10.27)	107.29 (11.91)	<0.0001
Systolic Blood Pressure (mm Hg)	121.31 (17.05)	133.76 (18.11)	127.62 (18.66)	<0.0001
Diastolic Blood Pressure (mm Hg)	75.03 (10.58)	80.63 (11.43)	77.87 (11.36)	<0.0001
Cholesterol (mg/dl)	186.02 (31.14)	183.37 (31.72)	184.67 (31.46)	0.108
HDL (mg/dl)	60.18 (13.55)	49.83 (12.16)	54.93 (13.86)	<0.0001
LDL (mg/dl)	107.88 (28.16)	108.94 (29.15)	108.42 (28.66)	0.483
Triglycerides (mg/dl)	86.57 (43.59)	119.55 (87.42)	103.30 (71.28)	<0.0001
Glycemia (mg/dl)	92.16 (16.31)	98.68 (19.54)	95.47 (18.30)	<0.0001
	Percentage	Percentage	Percentage	p-value
<35 years	16.71	10.42	13.52	<0.0001
35-49 years	57.80	51.01	54.36	
≥ 50 years	25.49	38.57	32.12	
Social class I	18.94	8.80	13.80	<0.0001
Social class II	63.65	82.67	73.30	
Social class III	17.41	8.53	12.90	
No tobacco	71.87	72.94	72.41	<0.0001
Yes tobacco	28.13	27.06	27.59	
MET low	23.68	19.08	21.35	<0.0001
MET moderate	48.05	36.4	42.14	
MET high	28.27	44.52	36.51	
Predimed low	36.49	48.17	42.42	<0.0001
Predimed high	63.51	51.83	57.58	

Table II: Prevalence of altered values of the different metabolic and diabetes risk scales according to physical activity by gender.

	Women				Men			
	MET low n=170 %	MET moderate n=345 %	MET high n=203 %	p-value	MET low n=141 %	MET moderate n=269 %	MET high n=329 %	p-value
Metabolic syndrome NCEP ATPIII	22.94	18.84	7.88	<0.0001	34.04	27.88	12.46	<0.0001
Metabolic syndrome IDF	27.06	19.71	9.85	<0.0001	42.55	35.69	18.24	<0.0001
Metabolic syndrome JIS	27.65	20.29	9.85	<0.0001	46.10	39.03	20.36	<0.0001
Hypertriglyceridemic waist NCEP ATP III	10.59	4.64	2.96	0.003	13.48	8.55	4.56	0.002
Hypertriglyceridemic waist IDF	10.59	5.51	3.45	0.013	24.82	18.59	10.33	<0.0001
Hypertensive waist NCEP ATP III	31.18	23.19	14.78	0.001	29.79	21.93	17.33	0.010
Hypertensive waist IDF	36.45	26.38	16.75	<0.0001	50.35	46.84	32.22	<0.0001

Table III: Prevalence of altered values of the different metabolic and diabetes risk scales according to healthy food by gender.

	Women			Men		
	Predimed low n=262 mean (SD)	Predimed high n=456 mean (SD)	p-value	Predimed low n=356 mean (SD)	Predimed high n=383 mean (SD)	p-value
Metabolic syndrome NCEP ATPIII	19.85	14.91	0.097	26.40	18.29	0.010
Metabolic syndrome IDF	22.90	16.23	0.027	33.43	25.33	0.016
Metabolic syndrome JIS	23.28	16.67	0.030	36.52	27.94	0.013
Hypertriglyceridemic waist NCEP ATP III	6.49	5.04	0.038	8.71	6.79	0.042
Hypertriglyceridemic waist IDF	7.63	5.26	0.031	18.82	13.58	0.043
Hypertensive waist NCEP ATP III	24.43	21.71	0.041	23.60	19.32	0.015
Hypertensive waist IDF	28.24	24.78	0.033	42.98	39.16	0.021

Table IV: Logistic regression analysis.

	Men OR (CI 95%)	Age ≥50 years OR (CI 95%)	Tobacco consumption OR (CI 95%)	MET low-moderate OR (CI 95%)	Predimed low OR (CI 95%)	Social class II-III OR (CI 95%)
Metabolic syndrome NCEP ATPIII	1.38 (1.05-1.83)	2.13 (1.61-2.81)	ns	2.84 (2.05-3.94)	1.42 (1.08-1.87)	2.35 (1.42-3.91)
Metabolic syndrome IDF	1.73 (1.32-2.25)	2.51 (1.93-3.26)	ns	2.61 (1.95-3.51)	1.42 (1.10-1.84)	3.47 (2.04-5.90)
Metabolic syndrome JIS	1.98 (1.52-2.57)	2.39 (1.85-3.09)	ns	2.61 (1.96-3.47)	1.43 (1.11-1.85)	2.22 (1.41-3.50)
Hypertriglyceridemic waist NCEP ATP III	ns	1.68 (1.10-2.56)	ns	2.26 (1.37-3.72)	ns	5.42 (1.69-17.41)
Hypertriglyceridemic waist IDF	1.85 (1.45-2.36)	3.22 (2.53-4.10)	ns	1.99 (1.54-2.57)	ns	4.06 (2.54-6.49)
Hypertensive waist NCEP ATP III	ns	2.62 (2.02-3.40)	0.74 (0.55-0.99)	1.87 (1.40-2.49)	ns	5.01 (2.73-9.21)
Hypertensive waist IDF	1.85 (1.45-2.36)	3.22 (2.53-4.10)	ns	1.99 (1.54-2.57)	ns	4.06 (2.54-6.49)

Something similar to that obtained with physical activity can be found with the prevalence of high values of these scales in people with a high adherence to the Mediterranean diet as shown in **table III**.

In the multivariate analysis using binary logistic regression, male, age 50 years, and older, tobacco consumption, MET low-moderate, low adherence to mediterranean diet and social class II-III were established as covariates. Age, physical activity assessed with the IPAQ questionnaire and social class are the only variables that show an influence on all the scales analyzed. Of these, the one showing the greatest degree of influence is social class, with odds ratios ranging from 2.22 (95% CI 1.41-3.50) for metabolic syndrome with JIS criteria and 5.42 (95% CI 1.69-17.41-14.24) for Hypertriglyceridemic waist with NCEP ATP III criteria. All results are presented in **table IV**.

Discussion

In our investigation, persons who do intense physical activity have better values on the scales of metabolic syndrome, hypertriglyceridemic waist and hypertensive waist than those who do moderate physical exercise and these better than those who do sporadic physical exercise or do not exercise at all. Something similar occurs between people with high adherence to the Mediterranean diet and those with low adherence.

In the multivariate analysis, intense physical activity reduces the risk of suffering from metabolic syndrome (with the three scales), hypertriglyceridemic waist and hypertensive waist, while high adherence to the Mediterranean diet only protects from suffering from metabolic syndrome.

Most of the studies analyzed show a clear association between the level of physical activity and the presence of metabolic syndrome, with the higher the level of exercise, the lower the prevalence of metabolic syndrome, i.e. most studies coincide with the results obtained by us.

Several studies have used a methodology similar to ours and obtained similar results. For example, a study of 5040 people analyzed data from the 2009-10 Chilean national health survey, relating the level of physical activity measured with the GPAQ (Global Physical Activity Questionnaire) to the presence of metabolic syndrome using the ATP III criteria. The study associated a new and integrative classification of physical activity and sedentary lifestyle, as it not only considered the time spent exercising but also the time spent sitting down. The study concluded that there was a lower probability of presenting metabolic syndrome when the international physical activity recommendations were met, i.e., the person was physically active (>150 minutes/week) regardless of the time spent sitting down[19]. In this case, the association between leisure-time physical activity, cardio-respiratory fitness and metabolic syndrome was assessed and it was concluded that those with a low level of fitness (<29.1 ml x kg/min) were at least 7 times more likely to present metabolic syndrome than those above 35.5 ml x kg/min[20]. Lastly, an Australian study in 1563 adults showed that men who were inactive in their leisure time were twice as likely to be diagnosed with metabolic syndrome using the ATP-III model, while in women the risk was three times higher compared to those with a high level of physical activity[21].

Data similar to the above were obtained in studies that used methodologies different from ours. In a longitudinal study with a 4-year follow-up, Laaksonen et al. examined the relationship between the change in physical activity and the diagnosis of metabolic syndrome, in which men who performed more than 3 hours of moderate or vigorous physical exercise per week had half the risk of developing metabolic syndrome compared to those who were sedentary[22]. The KORA study evaluated physical activity by interview in 1653 adults aged 55-74 years and found that those who regularly engaged in sports activities, even at a frequency of 1 day/week, reduced the risk of metabolic syndrome according to the IDF criteria by 42%, while those with 2 hours or more per week reduced it by 61%[23].

Other studies have assessed the relationship between metabolic syndrome and physical exercise measured with accelerometers and have found results similar to those obtained in our work and in the studies cited above. Sisson et al found that the risk of metabolic syndrome decreased by 10% for every 1000 steps walked and that the probability of developing metabolic syndrome was 3, 5 times lower in very active adults, i.e., those who walked more than 10,000 steps/day, and 1.6 times lower in moderately active adults, between 5-10,000 steps/day, compared to those who were not very active and walked less than 5,000 steps/day[24]. Another study, in this case in 483 Japanese adults showed similar results, such that those who took less than 24 MET-h per week or 3-6 MET-h per day had a 2.2 times higher risk than those who took more than 24 MET-h/week[25].

However, we have also found research in which this beneficial effect of exercise is not found. Chimbo-Yunga et al. analyzed physical activity using the IPAQ questionnaire and the prevalence of metabolic syndrome with the ATPIII criteria in 387 older Colombian adults and observed that there were no differences between the different groups according to the level of exercise they performed[26]. Three other studies carried out in similar populations and also using the IPAQ questionnaire also found no differences in the prevalence of metabolic syndrome according to the level of physical activity[27-29].

We have found little literature evaluating the effect of the Mediterranean diet on the prevalence of metabolic syndrome, specifically only one study, in which high

adherence to this diet reduced the risk of presenting metabolic syndrome, as we observed in our study. Gouveri et al performed a cross-sectional study in 2074 adults and found that high adherence to the Mediterranean diet resulted in a 20% reduction in the risk of developing metabolic syndrome after adjusting for the main confounding factors[30].

Other studies have found an increase in the prevalence of metabolic syndrome in adults with a low consumption of vegetables and a high consumption of sugar-sweetened beverages[31,32].

Among the strengths of this study are the large sample size, the number of metabolic syndrome scales analyzed (specifically 3), the inclusion of two variables that assess cardiometabolic risk, such as the hypertriglyceridemic waist and hypertensive waist, and the fact that the assessment of physical activity and adherence to the Mediterranean diet was carried out with validated questionnaires (IPAQ and Predimed).

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

Conflict of Interest

The authors declare no conflict of interest.

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ORIGINAL

Análisis de los factores de riesgos psicosociales y el estrés laboral en médicos durante la pandemia COVID-19

Analysis of psychosocial risk factors and work stress in doctors during the COVID-19 pandemic

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Resumen

Objetivo: Determinar la magnitud en que los factores de riesgo predicen el estrés laboral en médicos que laboraron en cuatro hospitales de las ciudades de Quito, Ambato, Tulcán y Riobamba durante la pandemia COVID-19.
Métodos: Estudio no experimental, transversal, descriptivo y correlacional. A una muestra estratificada de 203 galenos, se les aplicó el cuestionario de factores de riesgo psicosociales del Ministerio de Trabajo de Ecuador (2018) y el Cuestionario de Estrés de Villalobos (2010). A través del coeficiente de correlación múltiple se identificaron las dimensiones de los factores psicosociales que explican de mejor forma la sintomatología fisiológica, social, intelectual y emocional del estrés.
Resultados: La capacidad de participar en las decisiones, las exigencias mentales derivadas de la carga laboral, y la falta de recuperación, fueron los factores de mayor exposición con el 63%, 58% y el 54% respectivamente. En referencia a las dimensiones del estrés laboral que más afectaron a los participantes, los síntomas fisiológicos y de comportamiento social registraron presencia en el 86% y al 74% correspondientemente. Tres de las 8 dimensiones de factores psicosociales pudieron explicar la presencia de estrés laboral: violencia laboral predice el 37%, la carga de trabajo pronostica el 41% y el liderazgo describe el 43%.
Conclusiones: La tensión emocional vivida durante los últimos 3 meses de emergencia sanitaria se debió a la falta de liderazgo y gestión laboral por parte de los jefes, al aumento de carga de trabajo y a la violencia psicológica y moobbing percibida por la población de estudio.

Palabras clave: Factores de riesgo psicosociales, estrés laboral, Pandemia COVID-19, carga laboral, moobbing, violencia psicológica, liderazgo.

Abstract

Objective: To determine the magnitude to which risk factors predict work stress in physicians who worked in four hospitals in the cities of Quito, Ambato, Tulcán and Riobamba during the COVID-19 pandemic.
Methods: Non-experimental, cross-sectional, descriptive and correlational study. To a stratified sample of 203 doctors, the questionnaire of psychosocial risk factors of the Ministry of Labor of Ecuador (2018) and the Villalobos Stress Questionnaire (2010) were applied. Through the multiple correlation coefficient, the dimensions of the psychosocial factors that best explain the physiological, social, intellectual and emotional symptoms of stress were identified.
Results: The ability to participate in decisions, the mental demands derived from the workload, and the lack of recovery were the factors of greatest exposure with 63%, 58% and 54% respectively. In reference to the dimensions of work stress that most affected the participants, physiological and social behavioral symptoms were present in 86% and 74%, respectively. Three of the 8 dimensions of psychosocial factors were able to explain the presence of work stress: work-related violence predicted 37%, workload predicted 41% and leadership described 43%.
Conclusions: the emotional tension experienced during the last 3 months of the health emergency was due to the lack of leadership and labor management by the bosses, the increased workload and the psychological violence and moobbing perceived by the study population.

Keywords: Psychosocial risk factors, work stress, COVID-19 pandemic, workload, moobbing, psychological violence, leadership.

Introducción

Los factores psicosociales y el estrés laboral son fenómenos que comienzan a estudiarse en las ciencias administrativas a partir de la mitad del siglo XX. El interés inicial en su descripción es hallar explicaciones de cómo el trabajo influye en el comportamiento individual para instaurar un mecanismo que posibilite obtener trabajadores más comprometidos y eficientes en el marco de un sistema capitalista de producción ilimitada.

Autores como Mayo, Fayol y Taylor, desarrollan conceptos innovadores como la división de tareas, sistemas de producción y técnicas de motivación, que logran los resultados esperados en cuanto a la mejora de ventas, bienes y servicios. Como es de esperar, el interés por generar más ganancias ocasiona enfermedades devenidas de la tensión, la preocupación y la ansiedad de los trabajadores[1].

Por ejemplo, las exigencias laborales; la carga de trabajo; el tipo de liderazgo; la burocratización; el control excesivo; y los métodos de supervisión, complican el medio ambiente de trabajo y la vida laboral. El aumento de estas exigencias laborales ocasiona ausentismo por pequeñas molestias fisiológicas, como los dolores de espalda y los trastornos músculo esqueléticos. Las múltiples demandas laborales como los requerimientos de estudios – capacitación y la competitividad son solo unos cuantos aspectos dentro de una gran lista de exigencias a las cuales los trabajadores se exponen[2].

Como resultado de ello, se hace habitual la segregación de cortisol en el eje hipotálamo – hipófisis, y la liberación de las catecolaminas de las glándulas suprarrenales. Hoy en día, la ciencia conoce a profundidad los efectos que el desbalance de estas hormonas (producidas por estos contaminantes en el lugar de trabajo) ocasionan en el metabolismo de los carbohidratos, en la presión sanguínea, en el sueño y las horas de descanso. Uno de los sistemas más perjudicados es el sistema inmunitario que pierde la función protectora de defender el organismo ante enfermedades respiratorias y problemas autoinmunes, al igual que el sistema gastrointestinal con inconvenientes como colon irritado, úlceras e inflamación de la mucosa[3].

En el sistema circulatorio, al incrementar la presión sanguínea se compromete la estructura de los vasos, lo cual hace más probables los infartos y patologías vasculares. El sistema metabólico ante la presencia en exceso de cortisol obliga a retener grasa en las células del cuerpo, lo que facilita la obesidad; además, crea desequilibrio en el metabolismo de los azúcares que puede ocasionar diabetes tipo II. Finalmente, el cortisol y la noradrenalina se relacionan con disfunción eréctil; interrupción del ciclo reproductivo en la mujer; envejecimiento prematuro; dermatitis; acné; y fatiga crónica[4].

La ciencia médica actual explica los riesgos físicos de esta exposición laboral en virtud de más de 50 años de estudios laborales, correlacionales y causales. Estos son datos relevantes que no se conocen en la década de los años 70, cuando se comienzan a estudiar los factores psicosociales de riesgo y el estrés laboral. La historia del desarrollo de estos conceptos se da cuando entra en crisis el sistema de producción con la salud del trabajador.

En primer lugar, el prolífico avance de las ciencias administrativas se critica cuando la psicología organizacional saca a la luz los primeros efectos negativos del contexto laboral en la salud y en el equilibrio psicológico. Y es que el progreso económico no puede estar a expensas de la integridad física y mental de los colaboradores, además que, se comprueba que la tensión emocional que causa el modelo productivo origina pérdidas millonarias en las industrias. Bajo este escenario las ciencias de salud ocupacional incluyen, en el estudio de los contaminantes ambientales, a los riesgos ergonómicos y psicosociales como parte del modelo de gestión para disminuir la probabilidad de siniestros (enfermedades y accidentes)[1].

Aunque se conocen muchas de las condiciones de trabajo y su influencia en la salud mental, tal vez la primera referencia en la que se utiliza el nombre de factores psicosociales se origina en 1984, en un estudio que realiza la Organización Internacional del Trabajo (OIT), en el cual se identifica el fenómeno y se establecen criterios de control. No obstante, desd e este inicio se concluye que, a diferencia del resto de contaminantes, al intervenir en estos factores la percepción subjetiva del individuo, es difícil coincidir en una única definición conceptual y operacional. La mente humana conceptualiza al trabajo (en su todo) como el conjunto de vivencias que comprenden un cúmulo de elementos distintos en cada persona[1].

Esta es la razón por la que los primeros intentos de clasificación terminan en la formulación de largas listas con aspectos referentes a la organización, a las actividades y al ambiente laboral (situación que no difiere en mucho con los actuales esquemas interpretativos). Con el aporte de la psicología organizacional, las dimensiones de clima laboral se suman a las listas de factores de riesgo psicosocial, y aparecen juntas en la tercera edición de la Enciclopedia de Seguridad y Salud en el Trabajo de la OIT (1998). Es en este mismo año, que la OIT se alarma por la influencia del estrés laboral, y las define como todas las condiciones que predisponen al individuo al surgimiento de la tensión, angustia y ansiedad; y a otras probabilidades de siniestralidad como los accidentes laborales. Este último modelo, propende a fusionar los factores psicosociales con las teorías del estrés laboral admitiéndolos como estresores desencadenantes de desequilibrio fisiológico, cognitivo, conductual y social[1].

Es de interés mencionar el segundo modelo interpretativo de los factores psicosociales desarrollado por aportes de Mintzberg (1993)5 y Moncada (2000)6; que se conciben como el resultado de las interacciones que el trabajador tiene con la empresa. Esto comprende:

- El tipo de relación que tiene el colaborador con sus tareas (¿cuenta con las competencias para desarrollar sus actividades y sabe cómo hacerlas?);
- La interrelación con el resto de los colaboradores (¿cómo son sus relaciones interpersonales?);
- La intercomunicación (¿le platican de su trabajo o puede expresar ideas y ser tomado en cuenta?);
- El intercambio de conocimiento (¿puede desarrollarse desde lo formativo e innovar su trabajo?);
- El ambiente físico (¿el empleado se desempeña en un lugar libre de contaminantes higiénicos y riesgos mecánicos?);
- La planificación (¿el trabajo está organizado de manera eficiente?); y
- Factores extralaborales (¿cómo se definen las experiencias que el individuo presenta en su esfera familiar – social?, ¿cómo está su salud y de su familia?, ¿tiene problemas económicos?).

El instrumento de medición de la presente investigación, para los factores psicosociales que desarrolla el Ministerio de Trabajo de Ecuador (2018), se basa en el modelo interaccionista (individuo – trabajo) y comprende una clasificación de 8 dimensiones:

- La carga de trabajo: percepción acerca de que las actividades obedezcan a una planificación y sean factibles de cumplirse.
- Desarrollo de competencias: satisfacción laboral ante los programas de capacitación y formación.
- Liderazgo: complacencia con la gestión de jefes y autoridades.
- Margen de acción y control: posibilidad de utilizar la creatividad e innovación.
- Organización del trabajo: agrado del colaborador ante la programación y planificación del trabajo.
- Recuperación: percepción positiva ante los esfuerzos del empleador por el descanso y la vida familiar.
- Soporte: regocijo por el trabajo en equipo y el interés por las personas.
- Otros puntos importantes: indaga la presencia de violencia psicológica y acoso laboral.

Algo más que añadir a la clasificación de los factores psicosociales es su dimensión de riesgo. Son muchas las investigaciones que se realizan desde el último tercio del siglo XX hasta la actualidad, que posibilitan la identificación de factores que están muy relacionados con las enfermedades y accidentes laborales. Cuando la evidencia empírica constata esta cualidad en el factor, se denomina factor de riesgo, e indica una probabilidad de daño si el individuo se expone y si no hubiera medidas de mitigación. Aunque el ojo humano tiende a enfocarse en lo nocivo y dañino, existen también, factores que se denominan eugenésicos que incrementan la probabilidad de bienestar y salud en el trabajo como, por ejemplo: la creatividad, la autoestima, la grupalidad, y el proyecto de vida, entre otros. Como se puede entender, las condiciones laborales determinan la salud o la enfermedad[7].

Respecto al modelo que explica los factores de riesgo a través de los esquemas interpretativos del estrés laboral, las investigaciones acerca del tema ubican al estrés como factor y como consecuencia o daño. Entiéndase al estrés en su rol de variable independiente, cuando el investigador asume que el factor psicosocial es un agente estresor, que puede generar aprendizaje (euestrés) o enfermedades (diestrés). Es decir, cuando se escoge el modelo del paradigma del estrés como mecanismo explicativo.

No obstante, si se admite que el conjunto de manifestaciones psicológicas, cognitivas, sociales y comportamentales son producto de la interacción del sujeto con la lista de factores psicosociales, se acepta que el estrés es la consecuencia de la acción de causas laborales explicadas en el modelo interaccionista individuo – trabajo. En este sentido, los resultados que se presentan en este estudio conciben al estrés como la consecuencia de la acción de los factores psicosociales[1].

El estrés laboral se nombra de esta manera por primera vez, por Hans Selye en 1950, para detallar una sintomatología que ocurre en sus pacientes que se abaten por jornadas extenuantes de trabajo de más de 12 horas, en los siete días de la semana. En su publicación detalla que el trabajador pasa por un síndrome general de adaptación que se constituye por tres fases. En la primera, llamada alarma, el individuo conciencia el problema y se agita, el sistema adrenérgico se activa y lleva grandes cantidades de sangre a músculos y cerebro. Se experimenta la sensación de miedo con tensión generalizada. En el segundo estado, que se conoce como resistencia, la persona trata de resolver el obstáculo mediante el uso de recursos (conocimientos, habilidades, destrezas), y activa el movimiento con un empeño de encontrar una conclusión definitiva al problema que presenta8. Selye indica que, de persistir el conflicto, el colaborador entra en la fase de agotamiento que se caracteriza por cansancio emocional y abatimiento, que conduce a la enfermedad.

Años más tarde, Lazarus y Folkman (1989) describen al fenómeno como la pérdida de recursos para hacer frente a las demandas. Ya sea porque el trabajador carezca de las aptitudes o porque la situación es tan intensa que consume los medios de afrontamiento, y apare en el individuo agotamiento, debilidad y fatiga, que lo lleva a la enfermedad. Para Siegrist (1993), el estrés laboral es un estado de tensión que se provoca por la percepción de injusticia. El colaborador hace comparaciones entre su esfuerzo laboral y la paga recibida por dicho ahínco y sacrificio. Si la ecuación está desbalanceada, habrá estrés laboral; si hay armonía entre las variables, existe aprendizaje y satisfacción. Karasek en (1995) desarrolla su teoría del estrés al ubicar tres factores que son: el control, la carga laboral y el apoyo social. Si una persona está impedida de hacer su trabajo a su propio ritmo y se ve sometida al dominio total de la supervisión; se frustrará, se enajenará y se alienará. Bajo esta premisa, el estrés se muestra cuando hay mucho control, gran volumen de trabajo y falta de apoyo de los compañeros[8].

A la luz de estos razonamientos y con base a la teoría de Siegrist, Villalobos (2010) se crea un instrumento para la medición de la sintomatología fisiológica, comportamental, intelectual y psicoemocional a causa del estrés laboral. En la sintomatología fisiológica, se indagan dolores y afectaciones en los sistemas gastrointestinal, digestivo, respiratorio, cardíaco y en la disfunción sexual. Respecto al comportamiento social, se inspecciona en los inconvenientes que se suscitan en las relaciones con la familia, amigos y compañeros.

Por su parte, para lo intelectual – laboral, se consulta acerca de las consecuencias que el trabajador tiene ante las malas condiciones de trabajo. Y, para terminar, en lo correspondiente a lo psicoemocional, se explora el miedo, la soledad, la tristeza, la baja autoestima, las adicciones y el desequilibrio de la vida en general. Estos criterios se utilizan para conocer la afectación de médicos que trabajan durante la emergencia sanitaria por la COVID-19, en el mes de diciembre de 2021.

A propósito de la pandemia COVID-19, no hay profesión con más afectaciones que los médicos que atienden a los pacientes con contaminación de esta enfermedad, que, de acuerdo con las investigaciones, registran un porcentaje de contagio del 34,5% en el ámbito mundial, producto de esta exposición. El desconocimiento en la atención y tratamiento, la carga de trabajo y la falta de insumos médicos, incrementan los índices de depresión en una salida ocupacional que ya cuenta con prevalencias alarmantes.

Uno de cada cuatro médicos posee altas probabilidades de sufrir trastornos mentales como la ansiedad mayor, trastorno depresivo persistente y bipolaridad, todos relacionados con el contenido de trabajo. A eso hay que sumar la enorme responsabilidad que representa el cuidado de la vida y que agrega tensión emocional adicional[9].

La emergencia de la pandemia dispara los factores de riesgo psicosociales que impactan en la sintomatología del estrés laboral en todo el sistema de salud del Ecuador. Sin embargo, en las fuentes de consulta no existen aún estudios que indiquen cuáles son los factores que golpean con mayor fuerza en la sintomatología fisiológica, comportamental social, intelectual laboral y psicoemocional. Esta información es vital para gestionar los planes de prevención psicosocial y para dotar a los organismos de control de una línea base sobre la cual se pueda determinar la efectividad de dichos planes.

Es por eso por lo que la presente investigación tiene el objetivo de determinar la magnitud en que los factores de riesgo predicen el estrés laboral en médicos que laboraron en cuatro hospitales de las ciudades de Quito, Ambato, Tulcán y Riobamba durante la pandemia COVID-19. Para tal cometido, se evalúan los factores psicosociales y se caracteriza el estrés laboral de la población. Finalmente, se elabora un marco metodológico sobre el cual se pueden interpretar los resultados.

Métodos

La investigación fue de tipo no experimental, transversal, prospectivo y analítico, correspondiente al nivel predictivo.

El universo del estudio comprendió a 431 médicos de cuatro hospitales del Ecuador. Se utilizó la prueba para muestreo estratificado proporcional con población finita, cuyos cálculos se muestran a continuación:

$$n_o = \frac{(Z^2\, pq)}{e^2}$$

$$n = \frac{n_o}{1 + \frac{n_o - 1}{N}}$$

En dónde:

N: Es el tamaño del universo (431).
Z: Es la prueba de nivel de confianza (α-1) =95%.
p: Es la proporción (0,5).
q: Es la varianza (0,5).
e: Es el error (0,05 para estudios sociales).
n: Es la muestra.

Una vez realizados los cálculos se determinó una muestra de 203 sujetos. Para conocer el número de participantes

a seleccionar para cada hospital, se extrajo el índice de estratificación (Ie) al dividirse la muestra para el universo:

$$I_e = \frac{n}{N} = 0{,}47$$

Este valor se multiplicó por el personal médico total de cada hospital investigado, lo cual arrojó los resultados que se muestran en la **tabla I**.

Tabla I: Obtención de la muestra estratificada.

Ciudad a la que pertenece el hospital	Número total (n) de médicos por hospital	Índice de estratificación (Ie)	Muestra (n*Ie)
Quito	116	0,47	55
Ambato	104	0,47	49
Riobamba	64	0,47	30
Tulcán	147	0,47	69
Total	203		

De esta forma, se seleccionaron a 55 médicos del hospital de Quito, 49 de Ambato, 30 de Riobamba, y 69 de la casa de salud de Tulcán. Las encuestas fueron administradas por *Google Forms* a todo el universo, y una vez completada la cuota de la muestra estratificada, se empleó la fórmula aleatoria del paquete estadístico Microsoft Excel 2019, para asegurar que cada uno de los informantes tuviera la oportunidad de ser parte de la muestra final. Al mismo tiempo, como criterios de selección, se incluyó al personal de relación de dependencia con más de tres meses de permanencia y con su consentimiento informado para participar en el estudio. Se excluyeron a los médicos en proceso de desvinculación y se eliminaron a los participantes cuyas encuestas fueron remitidas de manera incompleta.

En referencia a los instrumentos empleados, el cuestionario de factores psicosociales fue desarrollado en el 2018 por el Ministerio de Trabajo del Ecuador y consta de 58 ítems dispuestos en 8 dimensiones que son: 1- La carga de trabajo; 2-El desarrollo de competencias; 3-El liderazgo; 4-El margen de acción y control; 5-La organización de trabajo; 6-La recuperación; 7-El soporte y apoyo; y 8-La violencia – discriminación.

El alpha de Crombach demostró alta fiabilidad con un valor de 0,96. Las afirmaciones presentaron cuatro opciones de respuesta en escala Likert (completamente, parcialmente, poco de acuerdo, y en desacuerdo), mientras más alto fue el puntaje, mejor fue la percepción de las condiciones indagadas. Los autores crearon una escala de calificación en la cual la sumatoria de cada dimensión pudo obtener tres criterios de riesgo: alto, medio y bajo.

El segundo instrumento empleado fue la encuesta de estrés laboral de Villalobos (2010) tercera versión, que indagó la sintomatología del estrés laboral en función de cuatro dimensiones: síntomas fisiológicos; síntomas de comportamiento social; síntomas intelectuales y laborales; y síntomas psico emocionales. Estuvo compuesto de 31 preguntas y ha sido validado con una población de 4.521 individuos con un alpha de Crombach de 0,889. La escala de respuesta fue de tipo Likert que reflejó la frecuencia con la que ocurrieron los malestares propuestos (siempre, casi siempre, a veces y nunca).

La interpretación del cuestionario presentó cinco niveles de estrés: muy bajo (ausencia de síntomas); bajo (frecuencia baja); medio (respuesta moderada); alto (presencia importante de estrés); y muy alto (presencia severa y perjudicial de estrés).

Por lo que se refiere a las pruebas estadísticas, en primer lugar, se realizó un análisis descriptivo de las variables socio demográficas (género, ciudad y edad), y de los datos categóricos ordinales de los test (grado de exposición de los factores psicosociales y de la afectación del estrés laboral) para cada una de las dimensiones.

La hipótesis de investigación indicó que existía correlación lineal múltiple entre los factores psicosociales con la afectación del estrés laboral, por lo que se optó por utilizar la regresión lineal, la correlación de Pearson y el coeficiente de determinación. En este sentido, existió la posibilidad de una hipótesis alterna en la que las dimensiones correlacionadas disminuían la sintomatología de estrés.

La regresión lineal siguió el método de por pasos, para advertir los factores que explican el daño provocado por estrés. Es necesario indicar que, para este conjunto de análisis, se utilizaron únicamente los registros numéricos o los datos continuos de ambos cuestionarios.

Además, se efectuaron dos tipos de análisis estadísticos. En primer término, se calcularon las frecuencias y porcentajes de las variables categóricas nominales (género, edad, puesto, estado civil y escolaridad). También se calcularon los resultados de la encuesta de factores de riesgo con los porcentajes y frecuencias de las categorías alto, medio y bajo. Adicionalmente, en este análisis se halló la sumatoria de las personas expuestas sumando los valores de alto y medio, y los registros de bajo representaron a los no expuestos.

El estudio fue aprobado por los cuatro comités de ética de las cuatro casas de salud, mismas que condicionaron la divulgación de los nombres de los hospitales. Al personal encuestado se le hizo firmar el consentimiento informado donde se expresó que los resultados serían socializados y entregados a los departamentos de seguridad y salud para la adopción de medidas de

mitigación. En todo momento se aseguró el carácter confidencial de la información recolectada. Por ello, se tuvo en cuenta, en todo momento, la Declaración de Helsinki de la Asociación Médica Mundial, incluyendo sus posteriores actualizaciones.

Resultados

La **tabla II** refleja los resultados sociodemográficos obtenidos.

En la **tabla III** se exponen los resultados de la encuesta del cuestionario de evaluación de riesgo psicosocial (MDT).

En la **tabla IV** se evidencian los resultados de la encuesta del estrés laboral.

Análisis inferencial, comprobación de hipótesis

La regresión lineal múltiple estuvo basada en los modelos de intro y por pasos, cuyos resultados se observan en la **tabla V**.

Los resultados de la regresión lineal múltiple por pasos, se observa en la **tabla VI**.

Tabla II: Datos sociodemográficos.

Género	Frecuencia	Porcentaje
Mujer	75	36,9
Hombre	128	63,1
Hospital - Provincia	Frecuencia	Porcentaje
Quito	55	27,1
Ambato	49	24,1
Riobamba	30	14,8
Tulcán	69	34,0
Edad	Frecuencia	Porcentaje
21,00 - 30,00	90	44,3
31,00 - 40,00	51	25,1
41,00 - 50,00	37	18,2
51,00 - 60,00	25	12,3

X=203

Tabla III: Resultados, frecuencias y porcentajes del cuestionario de factores psicosociales.

Factores psicosociales	Alto	Medio	Bajo
	Expuestos		No expuestos
Carga de trabajo	10 (4,9%)	48 (23,6%)	145 (71,4%)
Desarrollo de competencias	5 (2,5%)	31 (15,3%)	167 (82,3%)
Liderazgo	4 (2%)	29 (14,3%)	170 (83,7%)
Margen de acción	8 (3,9%)	55 (27,1%)	140 (69%)
Organización	10 (4,9%)	17 (8,4%)	176 (86,7%)
Recuperación	6 (3%)	48 (23,6%)	149 (73,4%)
Soporte	3 (1,5%)	34 (16,7%)	166 (81,8%)
Otros puntos	12 (5,9%)	22 (10,8%)	169 (83,3%)

X=203

Tabla IV: Resultados, frecuencias y porcentajes del cuestionario de Estrés laboral.

DIMENSIONES ESTRÉS	Muy alto	Alto	Medio	Bajo	Muy bajo
	Presentan daño			No presentan daño	
Estrés fisiológico	119 (58,6%)	34 (16,7%)	21 (10,3%)	17 (8,4%)	12 (5,9%)
Estrés comportamental social	4 (2%)	11 (5,4%)	14 (6,9%)	58 (28,6%)	116 (57,1%)
Estrés intelectual laboral	24 (11,8%)	46 (22,7%)	81 (39,9%)	52 (25,6%)	0 (0%)
Estrés psicoemocional	0 (0%)	36 (17,7%)	3 (1,5%)	19 (9,4%)	145 (71,4%)

X=203

Tabla V: Regresión lineal múltiple intro.

Resumen del modelo[b]									
Modelo	R	R cuadrado	R ajustado cuadrado	Error estándar de la estimación	Estadísticos de cambio				
					Cambio en R cuadrado	Cambio en F	gl1	gl2	Sig. Cambio en F
1	,666[a]	,443	,420	24,74405	,443	19,312	8	194	,000

a. Predictores: (Constante), violencia, carga de trabajo, liderazgo, recuperación, desarrollo de competencias, margen de acción, soporte, organización (datos continuos).
b. Variable dependiente: estrés (datos contínuos).

Tabla VI: Regresión lineal múltiple por pasos.

Resumen del modelo[c]									
Modelo	R	R cuadrado	R ajustado cuadrado	Error estándar de la estimación	Estadísticos de cambio				
					Cambio en R cuadrado	Cambio en F	gl1	gl2	Sig. Cambio en F
Violencia	,609[a]	,371	,368	25,83914	,371	118,582	1	201	,000
Carga de T	,643[b]	,414	,408	25,00488	,043	14,636	1	200	,000
Liderazgo	,655[c]	,429	,420	24,75379	,015	5,078	1	199	,025

a. Variable dependiente: estrés.

Discusión

En la **tabla II** se observa ventaja en la participación del grupo masculino con el 63,1%, la mayor parte de la población de estudio proviene de Tulcán, seguida de Quito, Ambato y Riobamba. En su mayoría, la población se ubica en una edad promedio de 35,7 años, y el rango (21-30 años) registra el 44,3%.

De acuerdo con los resultados de la **tabla III**, si se suman los valores altos y medios de las dimensiones, el resultado responde al número de médicos que se encuentran expuestos a los riesgos. En tanto que, las valoraciones de bajo corresponden al grupo de los no expuestos. Con este criterio, el margen de acción (31%) revela que, en 63 personas, no hay espacios de discusión ni trabajo colaborativo y que la opinión e ideas de los participantes no son tomadas en cuenta. En segundo lugar, la carga de trabajo obtiene una percepción negativa del 29%, por lo que se constata que los requerimientos de carga y ritmo durante la pandemia son intolerables.

En la dimensión de recuperación, 54 personas (27%) admiten que no se garantiza su derecho al descanso y a la vida familiar. El resto de las dimensiones presentan porcentajes menores al 19%, siendo la organización del trabajo, el sub-factor que mejor se califica con el 87% de aprobación.

Según lo expuesto en la **tabla IV**, se procede a conformar dos grupos de análisis, aquellos informantes que se encuentran con daño por estrés (sumatoria de las categorías muy alto, alto y medio) y el grupo con ausencia o frecuencia baja de síntomas (sumatoria de los bajo y muy bajo que no presentan daño).

El estrés fisiológico es el de mayor frecuencia con el 86% (174 personas) que manifiestan molestias en cuello, espalda, padecimiento en sistemas gastrointestinal, circulatorio y cardíaco, además de trastornos de sueño. Le sigue la sintomatología intelectual con el 74% (151 médicos) quienes se quejan por sobrecarga de trabajo, olvidos, mayor probabilidad de siniestros, fatiga, cansancio, problemas para la toma de decisiones, baja motivación y el deseo de no asistir a laborar.

Las dos dimensiones restantes tienen 19% (comportamiento social) y 14% (estrés psicoemocional), lo que podría indicar que, en la gran mayoría de la población, no hay incomodidad con el trabajo en equipo, la familia, el autocuidado, la autoestima y el equilibrio de vida.

En concordancia con los resultados de la **tabla V**, el resumen del modelo arroja un valor correlacional de Pearson de 0,66, lo que indica la existencia de una correlación positiva media entre factores y estrés laboral. El coeficiente de determinación que se representa en R cuadrado revela que los factores psicosociales pueden explicar hasta el 42% de la existencia de estrés laboral, y que únicamente un 24,7% de los indicadores de su sintomatología obedecen a otros criterios distintos a los que se evalúan en la encuesta de factores de riesgo.

El grado de significación en el estadístico f confirma la existencia de relación inferencial entre las variables independiente y dependiente. Este hecho rechaza la hipótesis nula y confirma que varias dimensiones de los factores psicosociales incrementan la sintomatología del estrés laboral.

Al realizar la regresión múltiple bajo el método de pasos y eliminar las dimensiones que no explican la presencia de estrés laboral, se obtiene que, la violencia, la carga de trabajo y el liderazgo, son los únicos factores correlacionales con la variable dependiente. Vale la pena indicar que las otras dimensiones obtienen valores por encima del 0,05: desarrollo de competencias (0,07); margen de acción (0,10); organización del trabajo (0,52); recuperación (0,81); y soporte (0,11).

En la **tabla VI**, aparecen las tres dimensiones que originan la sintomatología de estrés en los médicos que se encuestan. Los problemas en el liderazgo pronostican hasta el 42,9% de los dolores y molestias por estrés, y presenta una correlación positiva media de 0,65 y un valor de significación de 0,02. La carga de trabajo explica el 41,4% de la incomodidad que se halla en la variable dependiente, con un índice de correlación de 0,64 y valor inferencial de 0,00.

Por último, la violencia psicológica y el mobbing predicen hasta el 37,1% de la sintomatología de la tabla IV, con un nivel de correlación media de 0,60 y un valor de p= 0,00. El signo positivo de la correlación ratifica la hipótesis de investigación: existen factores que se correlacionan con el daño causado por estrés laboral en los médicos.

Los resultados de los factores psicosociales no se muestran más allá del 31% de exposición. El margen de acción, la carga de trabajo y la recuperación, son las dimensiones con mayor desfavorabilidad, y en un razonamiento puramente descriptivo, se podría esperar que estas tres subvariables influyan en la sintomatología de estrés. Pero cuando se hace el diseño de regresión se descubre que solo la carga de trabajo coincide en el método predictivo, y que aún más, la *violencia laboral* y el *liderazgo*, que presentan exposición inferior al 18% (ubicándose entre los de mayor valoración) son los que explican de mejor manera las dolencias sintomatológicas.

Para responder a estas interrogantes, los estudios de[10, 11 y 12], que proponen una metodología predictiva similar, coinciden en indicar que el resultado de percepción de un factor únicamente describe la opinión de los sujetos en un momento dado, pero no llegan a explicar relaciones con otras variables. Solamente cuando se

analiza la relación estadística causal a través de métodos correlacionales, se puede entender el comportamiento real de una variable que aparentemente es inofensiva.

El liderazgo, concebido en el instrumento del Ministerio de Trabajo de Ecuador, como el factor que evidencia la incapacidad de los directivos en gestionar eficazmente el talento humano, pronostica el mayor porcentaje de dolencias laborales. Al respecto, tres investigaciones que se realizan en el contexto de la pandemia COVID-19 sobre estrés laboral y burnout, que desarrollan[9,13,14]; ubican a la incapacidad administrativa de los gerentes y directores de los hospitales, como la causa más frecuente de tensión emocional, agotamiento y despersonalización; además de resaltar la necesidad de implementar políticas de trabajo en tiempos de pandemia con mucho dinamismo.

En este contexto, la emergencia sanitaria evidencia profundas grietas en los sistemas administrativos de los hospitales públicos y la falta de reacción ante emergencias. Se devela la falta de preparación de las autoridades de libre nombramiento y remoción que carecen de las competencias necesarias para enfrentar la crisis a través de los planes de contingencia.

En este mismo sentido, la carga de trabajo es más intensa en el personal médico, no solo por las causas evidentes ocasionadas por el aumento de contagios y miedo generalizado de la población, sino por la improvisación administrativa. Hongn (2020), por ejemplo, Hongn (2020), en su estudio sobre residencias médicas[15], acota que las jornadas dobles se hicen más frecuentes y hay colapsos por la infinidad de tareas que se deben cumplir, especialmente durante los tres primeros meses de la emergencia sanitaria.

Por otra parte, Navinés (2021) al igual que Pérez (2021)[16y17], determinan un aumento de más de 35 puntos porcentuales de las tareas laborales durante la época de crisis, y concluyen que, este factor es el responsable de la fatiga emocional por parte de galenos de los centros de cuidado intensivo. Estas evidencias empíricas explican que esta dimensión sea la segunda constante del sistema predictivo del estrés.

La violencia laboral es el último factor que se correlaciona como modelo predictivo en el padecimiento sintomatológico de los participantes. Con base a los aportes hechos por Vargas (2020)[18] y Ruiz (2022)[19]; se conoce que la inestabilidad y precariedad económica-laboral, activan impulsos de supervivencia para la conservación de los puestos de trabajo. De las relaciones inequitativas de poder se desprenden ataques sistemáticos de violencia psicológica con aumento de carga laboral y aislamiento, a las personas más vulnerables con el objetivo de cumplir con cuotas de reducción de personal.

De por sí, la rama médica ya es una profesión de alto riesgo a sufrir violencia, en especial las mujeres y personas con interculturalidad minoritaria. La pandemia incrementa la probabilidad de estos ataques hasta en un 42% más[20]. Con base a estas consideraciones, es evidente que el modelo predictivo incluya los factores que se relacionan con el mobbing y la violencia psicológica.

Es importante indicar que en esta investigación se utiliza una prueba estadística de regresión múltiple que evalúa la causalidad entre tres o más variables independientes y una dependiente con datos continuos. En este sentido se puede considerar como una limitación del estudio el hecho que la sintomatología del estrés laboral no cumpla cabalmente con esta condición, dado que, se utilizan las sumatorias de la escala de Likert del instrumento de medición.

Frente a este detalle Céspedes (2010)[21], en su análisis de regresión para datos categóricos, afirma que, si bien este procedimiento no es lo que se recomienda en estos casos, ya que es infructuoso la obtención de las ecuaciones constantes del modelo final, si es posible utilizar el criterio del coeficiente de determinación cuando se trate de cuestionarios con amplitud en la escala de Likert y que poseen más de 20 preguntas. Por lo tanto, el valor predictivo del modelo es válido y establece con precisión el grado en que la variable independiente afecta la presencia de la dependencia. Es preciso acotar que, en las fuentes de consulta primaria de los últimos cinco años, no se encuentran estudios psicosociales bajo este modelo inferencial.

Con referencia a los resultados descriptivos de daño por estrés laboral, dos dimensiones registran indicios de afectación severa que son los fisiológicos y los intelectuales-laborales. En investigaciones hechas durante la crisis sanitaria como, por ejemplo, la de Mera (2020)[22], Pinargote (2021)[23], y Curiel (2022)[24]; indican el incremento de dolencias en articulaciones, en cuello, espalda, malestares digestivos, alteraciones respiratorias y circulatorias en un 31%, 85% y 74%, respectivamente.

Estas dos últimas lecturas son similares a las que se encuentran en la sintomatología de los médicos que se encuestan (86%), lo que comprueba una vez más el impacto de la COVID-19 en el funcionamiento general del cuerpo, tratándose de una pandemia ya considerada como un cisne negro, por tratarse de una rareza de alto impacto, fuera de las expectativas, cuyos acontecimientos vencidos no apuntan hacia su aparecimiento, con una predictibilidad retrospectiva[25], y una generación de riesgos y afectaciones psicológicas en el contexto laboral[26].

Los síntomas intelectuales-laborales exploran el efecto emocional de los factores de riesgo que se analizan, que devienen en frustración; desánimo; tedio; bajo

compromiso; baja autoestima; poca auto eficiencia; y tentativas de cambio de trabajo. Restrepo (2021)[27], al analizar el impacto del estrés en médicos, determina un conjunto de síntomas en una muestra de 521 trabajadores de la salud, que se caracterizan por la desesperanza, desánimo y tristeza. Esta situación impide que se puedan concentrar y origina errores que los predisponen a accidentes laborales. Al medir esta dimensión, encuentra una exposición de 71%. Este valor es compatible al expuesto en la tabla IV y permite asumir que esta situación se presenta en todas las casas de salud, debido al aumento de tensión y sobre todo el temor de contagio.

Finalmente, será necesario realizar en el futuro, estudios complementarios que analicen cada una de las dimensiones de la sintomatología del estrés laboral. Ya que, en este estudio se puede pronosticar en porcentajes como los factores generan el estrés en su conjunto, pero no así la participación que ellos tienen en las cuatro sintomatologías: fisiológicas, comportamentales, intelectuales-laborales y psicoemocionales. Así mismo, se debe contrastar estos datos con registros numéricos continuos de la fisiología de los participantes, como la presión arterial, glucosa, e índice de masa corporal, entre otros.

Conclusiones

Se ha confirmado que tres de los ocho factores psicosociales (liderazgo, carga de trabajo y violencia), explican la sintomatología del estrés laboral en los médicos pertenecientes a hospitales de cuatro ciudades de Ecuador. La mala gestión de los líderes, el aumento de trabajo al personal médico y la violencia suscitada durante la pandemia COVID-19, incrementaron los dolores, las molestias y los padecimientos en la fisiología, en el comportamiento social-familiar, en el aspecto intelectual-laboral, y en la esfera psicoemocional.

Todos los datos descriptivos de los instrumentos empleados fueron similares a los estudios de los dos últimos años, con lo que se infiere que la emergencia económica y social de la pandemia, disparó la exposición de los contaminantes higiénicos, en especial en las profesiones de contacto directo con pacientes infectados.

Es urgente el diseño y elaboración de planes integrales de mitigación psicosocial para fortalecer los estilos de liderazgo, mejorar las competencias de los jefes, redistribuir técnicamente el trabajo, y eliminar toda forma de menoscabo a la integridad y la honra de los colaboradores. Así también, se deben incluir en los modelos predictivos, datos de morbilidad laboral con lo que se podrá evitar el surgimiento de enfermedades derivadas de la sintomatología por estrés en el trabajo.

Conflicto de intereses

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

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ORIGINAL

Exercise barriers contributing to reduced physical activity in chronic stroke survivors in a multi-ethnic population: a cross-sectional study in Suriname.

Barreras del ejercicio que contribuyen a la reducción de la actividad física en los supervivientes de accidentes cerebrovasculares crónicos en una población multiétnica: un estudio transversal en Surinam

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Abstract

Objectives: Despite all the recommendations physical activity (PA) and participation in structured PA programs remains low among the stroke survivors. Compared to high-income societies, these patients face unequal socio-economic challenges in countries with low- and middle-income and in multi-ethnic populations. We therefore aimed to explore factors associated with reduced PA levels in chronic stroke patients living in a middle-income country with a multi-ethnic population, Suriname. Furthermore, we explored possible barriers that may prevent participation in exercise programs.
Methods: We recruited participants from the general population and the Academic Hospital, and used energy expenditure (EE) and step count, measured with the GARMIN Forerunner 225 for seven consecutive days to evaluate PA. With the Barriers to Physical Activity and Disability (BPAD) questionnaire we identified exercise barriers and obtained demographic and socio-economic characteristics. We used regression analyses to assess associations with reduced PA levels, and descriptive analyses to assess exercise barriers based on socio-economic diversity.
Results: The mean age of the 44 participants was 58.2 ± 10.0 years and 21 were men. The median EE and steps were 24.2 (min-max: 16.1-53.7) Cal/kg/day and 3165.5 (min-max: 1093.0-9727.00) steps/day, respectively. Reduced PA levels were not related to demographic or socio-economic variables. Overall, patient-reported environmental exercise barriers were (1) "cost of the program" (45%) followed by (2) "lack of transportation" (34%). Personal barriers were (1) "feeling that an exercise instructor is incapable to set up an exercise program to meet their needs" (88%) and (2) "not willing to spend money" (40%). Different personal exercise barriers between ethnic groups were reported, but environmental barriers were the same.
Conclusions: Reduced PA levels in chronic stroke survivors were not explained by demographic or socio-economic variables. The participants reported several exercise barriers. In addition to the most common occurring barriers, future research should also evaluate feasibility and (cost-) effectiveness of tailored PA programs.

Keywords: Physical activity, ethnicity, stroke, exercise barriers.

Resumen

Objetivos: A pesar de todas las recomendaciones, la actividad física (AF) y la participación en programas estructurados de AF sigue siendo baja entre los supervivientes de un accidente cerebrovascular. En comparación con las sociedades de altos ingresos, estos pacientes enfrentan desafíos socioeconómicos desiguales en países con ingresos bajos y medios y en poblaciones multiétnicas. Por lo tanto, nuestro objetivo fue explorar los factores asociados con niveles reducidos de AF en pacientes con accidente cerebrovascular crónico que viven en un país de ingresos medios con una población multiétnica, Surinam. Además, exploramos las posibles barreras que pueden impedir la participación en programas de ejercicio.
Métodos: Reclutamos participantes de la población general y del Hospital Académico, y utilizamos el gasto energético (EE) y el conteo de pasos, medidos con el GARMIN Forerunner 225 durante siete días consecutivos para evaluar la AF. Con el cuestionario Barriers to Physical Activity and Disability (BPAD) identificamos barreras para el ejercicio y obtuvimos características demográficas y socioeconómicas. Utilizamos análisis de regresión para evaluar las asociaciones con niveles reducidos de actividad física y análisis descriptivos para evaluar las barreras al ejercicio en función de la diversidad socioeconómica.
Resultados: La edad media de los 44 participantes fue de 58,2 ± 10,0 años y 21 eran hombres. La mediana de EE y los pasos fueron 24,2 (mín.-máx.: 16,1-53,7) Cal/kg/día y 3165,5 (mín.-máx.: 1093,0-9727,00) pasos/día, respectivamente. Los niveles reducidos de AF no se relacionaron con variables demográficas o socioeconómicas. En general, las barreras ambientales para el ejercicio informadas por los pacientes fueron (1) "costo del programa" (45%) seguido de (2) "falta de transporte" (34%). Las barreras personales fueron (1) "sentir que un instructor de ejercicios es incapaz de establecer un programa de ejercicios para satisfacer sus necesidades" (88%) y (2) "no estar dispuesto a gastar dinero" (40%). Se reportaron diferentes barreras de ejercicio personal entre grupos étnicos, pero las barreras ambientales fueron las mismas.
Conclusiones: Los niveles reducidos de AF en sobrevivientes de accidentes cerebrovasculares crónicos no fueron explicados por variables demográficas o socioeconómicas. Los participantes informaron varias barreras al ejercicio. Además de las barreras que ocurren con mayor frecuencia, la investigación futura también debe evaluar la viabilidad y la (costo) efectividad de los programas de AF personalizados.

Palabras clave: Actividad física, etnicidad, accidente cerebrovascular, barreras para el ejercicio.

Introduction

Suriname is a middle-income country (LMIC) with a prevalence of stroke ranging from 1.8 to 4.1% among different ethnic groups[1]. Like most LMIC's, chronic patient care is less developed, and resources are not readily available compared to high-income countries (HIC)[2]. One of the factors that may contribute to an additional poor patient care is low Physical Activity (PA). Lack of sufficient PA increases the possibility of recurrent stroke, even in highly active subjects suffering from an initial stroke[3,4]. In addition, PA is a simple and modifiable tool to improve post-stroke mobility[5] and adherence to health enhancing structured PA programs is therefore strongly encouraged by leading current management guidelines for stroke patients[6]. Notwithstanding this, healthy Surinamese show insufficient PA which varies along ethnic lines[7]. In addition to stroke related impairments, low PA can be related to income and education level, marital status and perceived exercise barriers and motivators[8,9]. The latter two may vary among countries and populations and may depend on distinct sociocultural factors.

To date, most of the studies on factors associated with lower PA levels show data from HICs. These studies[3,10,11] include diverse determinants of decreased exercise participation after stroke when compared to middle-income countries[8,12]. However, environmental and facility barriers including costly exercise programs, transportation unavailability, bad local infrastructure and weather conditions are reported in both HIC and LMIC as barriers for exercise[13]. On the other hand, a Nigerian study[14] reports personal exercise barriers such as the notion that people in exercise outfit look funny and are embarrassed to exercise. This shows that cultural aspects may also influence PA behavior. Furthermore, a USA study reports personal exercise barriers like lack of interest in PA programs and concerns that exercise might worsen the health condition[13].

From the abovementioned reports, it can be concluded that generalization of study findings requires caution and that it is relevant to explore factors associated with low PA levels as well as exercise barriers further in stroke survivors from diverse ethnic populations, to be able to advise effective interventions to increase post-stroke PA in the future. As exercise is, by definition, planned structured, repetitive, and intentional movement to improve or maintain physical fitness (PF), low PA levels might result in decreased physical fitness levels. This study is aimed to identify the role of demographic and socio-economic factors in reduced PA levels and to identify barriers in a multi-ethnic stroke population from a LMIC setting.

Methods

Participants

From April 2016 to April 2017, we recruited participants from the database of the Rehabilitation Center Paramaribo and from the local community. Inclusion criteria included: being able to understand simple instructions (Mini Mental Scale Examination >24); living at home; being in the chronic stage after stroke (last stroke >6 months ago); walk independent or with supervision (Functional Ambulation Category score ≥3); not presenting any serious cardiac condition 15 or other neurological deficits or uncontrolled blood pressure (systolic pressure >140 mmHg, diastolic pressure >90 mmHg) 15 and willingness to provide written informed consent.

Baseline Characteristics and Cardiovascular Risk Factors

A questionnaire was administered to obtain demographic and socio-economic characteristics including sex, age, self-reported ethnicity (Asian, African or other), education level (less than high school or high school and higher), monthly income level (≤1000SRD or >1000SRD), and marital status (married or single). Weight and height were measured using an electronic scale (Seca 750) and a stadiometer (Seca 213). Type of stroke (ischemic or hemorrhagic) and the time post stroke were noted from medical records.

We used the daily steps and energy expenditure (EE) measured by the Garmin forerunner 225 to obtain data on PA level. The watch was worn on the non-paretic wrist for 7 consecutive days. It collected daily step counts and energy expenditure per day. PA measurement was considered valid when the watch was worn for at least 22 hours on at least five days, including the weekend, of the measurement week. For invalid measurements, missing data was completed using missing value analysis by SPSS. No registration of PA data resulted in exclusion from further data analysis.

To collect information on exercise barriers, a Dutch translation of the Barriers to Physical Activity and Disability (B-PAD) questionnaire was used[13]. Forward and backward translation was performed by a professional translator and reviewed by two researchers. To assess clarity and readability, the usefulness of the translated questionnaire was piloted in five healthy Surinamese Dutch speaking individuals before being used in the study.

The SCI Exercise Self-Efficacy Scale (ESES Dutch version) was used to obtain information on the participants' level of confidence with regard to carrying out regular physical activities[16]. The ESES consists of 10 items to be scored on a 4-point Likert scale; the total score can range from 10 to 40. The higher the total score the higher the exercise self-efficacy[17].

Statistical analysis

Data were assessed for normality using the Shapiro-Wilk statistic. Data and survey responses were summarized descriptively (for continuous variables, mean and standard deviation were provided; median and range when not normally distributed, categorical variables were described by frequency and percentages). To study significant differences of the PA outcome measures compared to the global PA recommendations, a one-sample T-test was performed for parametric data. Independent students' T-test were used to compare outcomes between sex and ethnic groups. Pearson's correlation was used to study correlation within continuous data. Univariate regression analysis was used to study the factors associated with low PA, quantified as average calories/kg/day (energy expenditure, EE) and average steps/day (the dependent variables). Independent variables were sex, age, education level, income level, marital status, ethnicity, self-efficacy. Multivariate regression analysis was used to study which variables were independent predictors of PA. Hereby, the stepwise method was used in order to prevent multicollinearity. The difference between perceived exercise barriers according to education level, income level, marital status and ethnic background were completed using descriptive analyses. Statistical analyses were undertaken using IBM SPSS Statistics version 21.1. Statistical significance was set at $p < 0.05$.

Ethics

All participants provided written consent to participate in the study. At all times a Medical Doctor was available in case of emergency and the emergency department of the Hospital was within close proximity. All procedures were completely in line with the declaration of Helsinki. The Institutional Review Board of The Ministry of Health of Suriname formally approved the study including all procedures and interventions (reference number: VG-023-15).

Results

Baseline characteristics and PA

Fifty participants (48% males, mean age 58.2 ± 9.5 years) in the chronic phase after stroke (93.2% ischemic stroke and 46% left hemisphere affected) were included. Collection of the data regarding daily EE and steps/day of three participants was incomplete and were supplied for by using missing value analysis. The data of 6 participants was not registered and therefore excluded from further analysis, ultimately resulting in a total study group of 44 (**Table I**). Most of the 44 participants were Asian (N=25, 56.8%) followed by African (N=13, 29.5%) and other ethnic backgrounds (N=6, 13.6%). The latter two were regrouped together as Non-Asians (N=19, 43.2%) to prevent defragmentation in ethnic groups. Twenty-one participants (47.7%) had a monthly income lower than 1000 SRD (at that time roughly 100 Euro), and most of the participants (68.2%) had an educational degree lower than high school and thirteen were single (29.5%). Median time post-stroke was 2.5 (range 0.5-16.6) years. Hypertension (N=37, 84.1%) and diabetes (N=23, 52.3%) were the most common comorbidities.

Factors associated with low physical activity

A priori correction was done for weight in the data of EE/day and this data did not show a normal distribution (p=0.000). Data from steps/day showed a normal distribution after transformation with the Ln function (p=0.006). Moreover, education level was associated to income level (r=0.457, p=0.002).

A univariate regression analysis was run to predict physical activity (steps/day) from age, sex, education level, income level, marital status, exercise self-efficacy and ethnicity (**Table II**). Furthermore, PA was not explained by these variables (**Table III**), therefore no multivariate regression analysis was conducted with these variables. No association was found between energy expenditure and steps/day (r =0.027, p =0.863).

Table I: Characteristics of all participants included in data analysis (N=44).

Age (years, mean ± SD)	58.2 ± 9.5
Sex (N, female)	23.0
Weight (kg, mean ± SD)	72.1 ± 13.4
PA level	
EE (calories / kg / day, median (min-max))	24.2 (16.1-53.7)
Steps / day (median, min-max)	3165.5 (1093.0-9727.0)

EE: Energy Expenditure; PA: Physical Activity; SD: Standard Deviation.

Table II: Univariate regression analysis between PA measures and independent variables.

Independent variables	Total, N=44	PA level and PA intensity			
		Average steps /day		Average EE	
		p-value	r-square	p-value	r-square
Sex (N, females)	23	0.93	0.00	0.24	0.03
Age (years, mean ± SD)	58.2 ± 10.0	0.97	0.00	0.34	0.02
Marital status (N, single)	13	0.47	0.12	0.19	0.03
Education level (N, lower than high school)	30	0.32	0.02	0.84	0.00
Income level (N, lower than 1000SRD)	21	0.77	0.00	0.99	0.00
Ethnicity (N, Asian/ Non-Asian)	25/19	0.25	0.03	0.18	0.41
Exercise Self-Efficacy score (median (min-max))	35 (10-40)	0.56	0.32	0.98	0.15

*EE: Energy Expenditure; Max: Maximum; Min: Minimum; PA: Physical Activity; R-square: percentage of variance explained by independent variable; SRD: Surinamese Dollar

BPAD questionnaire

Barriers to exercise can be found in **table II**. One participant (2.3%) was enrolled in a structured exercise program. About 9% of the participants stopped exercise due to health problems. Another 11.4% had an injury after participating in an exercise program. Most participants were interested in (re)starting an exercise program (81.8%) and felt that exercise would help their condition (93%). The most common patient-reported environmental exercise barriers were (1) "cost of the program" (45%) followed by (2) "lack of transportation" (34%). The most reported personal barriers were (1) "feeling that an exercise instructor is incapable to set up an exercise program to meet their needs" (88%), (2) "not willing to spend money" (40%), (3) "don't know a fitness center"(38%), (4) "never exercised regularly (25%), (5) "lack of personal care attendant who help for exercise" (20%) (**Table II**). On average, each participant reported seven exercise barriers.

Table III: Exercise Barriers (N=44).

BARRIERS to exercise	N, yes
Lack of transport facilities	15
Lack of time	7
Lack of energy	3
Lack of motivation	5
Lack of family and friends support*	2
Ever afraid to leave your home*	6
Costly exercise program	20
Lack of interest in exercise	1
Lack of personal care attendant who will help with exercise	9
Lack of accessible fitness center	4
Exercise is monotonic and dull	0
Exercise will not improve my condition	1
Exercise will worsen my health	1
Exercise is too difficult	3
Not knowing how to exercise	8
Not knowing where to exercise	5
Health concerns prevent from exercise	4
Pain prevents exercise	4
Too old for exercise	0
Feeling uncomfortable and self-conscious in a fitness center	3
Injury due to exercise	5
Any concerns about exercising in a fitness center	5
Had a bad experience in a fitness center	4
Satisfied with physical appearance and does not need to exercise	7
Family responsibilities prevent to exercise	2
Work prevents to exercise	5
Feeling that exercise instructor is incapable to set up an exercise program to meet your needs	39
Know a fitness center where you could exercise	27
Willing to pay for exercise program	26
Would like to start exercise program	36
Feel that an exercise program could help	41
Doctor advised exercise	27

EE: Energy Expenditure; BPAD: Barriers to Physical Activity and Disability.

Within group analysis of the BPAD results

There were no significant differences found in the number of exercise barriers between participants with low and high education level (p=0.765). This was also the case for groups with low- and high-income level (p=0.644), marital status (p=0.290) and people from different ethnic backgrounds (p=0.388).

Figures 1 to **3** show the most common reported exercise barriers for every ethnic group, marital status group, education- and income level group. Three of the top five barriers are common between low education, low income and single marital status group and included "not exercised regularly" and "don't know how to exercise". Furthermore, environmental PA barriers were a commonality across all groups. Both, the high and low education group, reported that they did not know a fitness center where they could go to and that they thought that the cost of the program was an issue. This was also the case for people from the low- and high-income groups. Moreover, both income level groups identified "not willing to spend money for a PA program", as a barrier for PA. All the top five barriers between the single and married marital status group were identical and included "feeling that the exercise instructor is incapable of to help", "doesn't know a fitness center" and "lack of transportation". The least common reported exercise barriers were: 1) exercise will worsen my health; 2) exercise will not improve my condition; 3) lack of interest; 4) exercise is too difficult and 5) lack of support from family and friends.

Discussion

In this study, factors associated with low PA levels were explored and barriers to exercise were described in chronic stroke survivors from a LMIC country with a multi-ethnic background. Results show that reduced PA levels were not explained by demographic or socio-economic variables. Between ethnic groups, personal exercise barriers were distinct, but environmental/facility exercise barriers were common. The most common reported environmental exercise barriers were (1) "cost of the program" followed by "lack of transportation". The most common reported personal barrier was "feeling that an exercise instructor is incapable to set up an exercise program to meet their needs".

Overall, PA levels were low compared to other stroke studies[3,18]. Lower median steps/day and lower median values for EE were seen in our cohort, which might be explained by the difference in age (21 to 96 years) and PA monitoring tools (accelerometers and pedometers) in reviews of heterogeneously designed studies[3,18]. Moreover, demographic and socio-economic variables did not explain these low levels of PA in our study population. Previous studies[19,20] showed conflicting results and suggest research in other potential factors limiting post-stroke PA. Perhaps, stroke-related impairments play a role here. Previous studies have highlighted influential factors on post-stroke PA level such as poor walking ability, sensorimotor dysfunction and low mood[3,21]. On the other hand, balance and degree of physical fitness (PF) were positively associated with higher PA levels[21]. A minimum level of PF is a prerequisite for maintenance of a physically active lifestyle, while at the

Figure 1: The most common reported PA-barriers across ethnic groups.

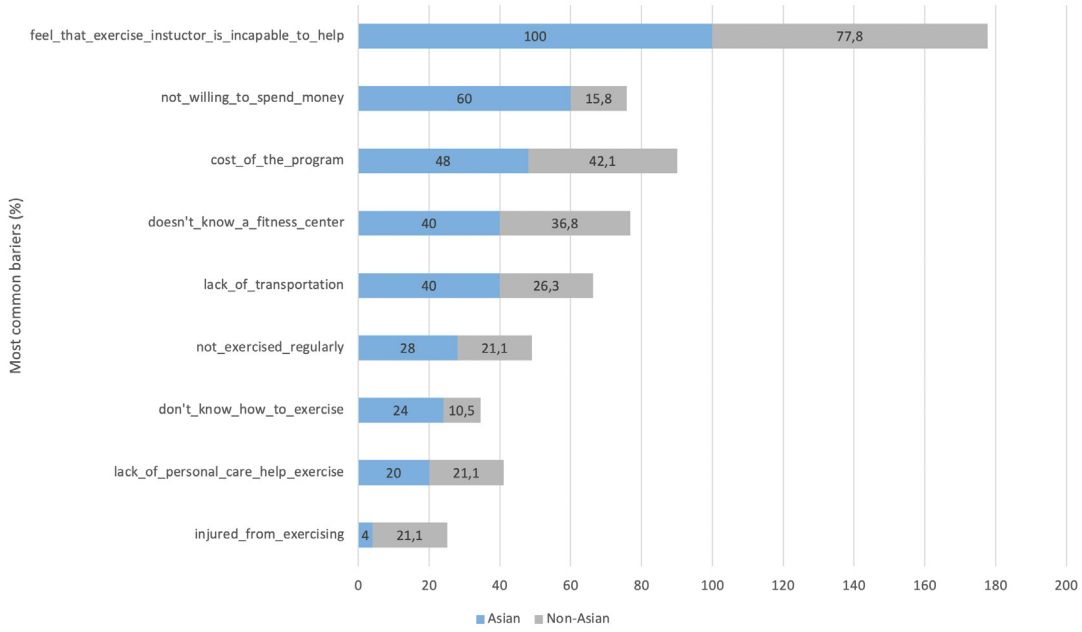


Figure 2: The most common PA barriers in the group with low education, low income and single marital status.

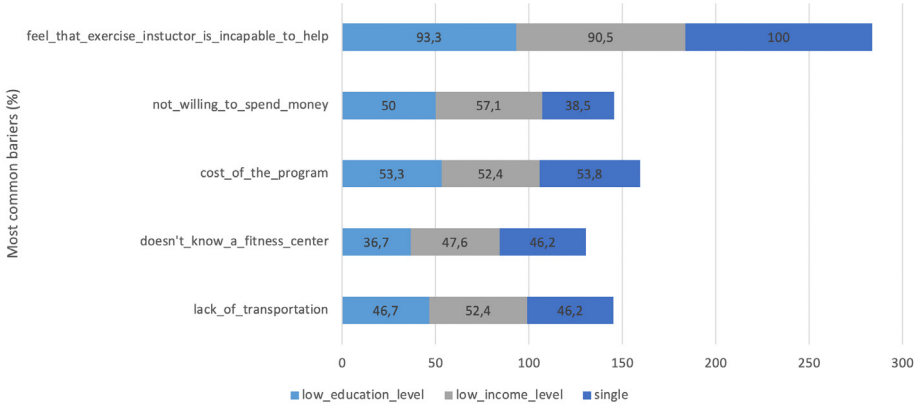
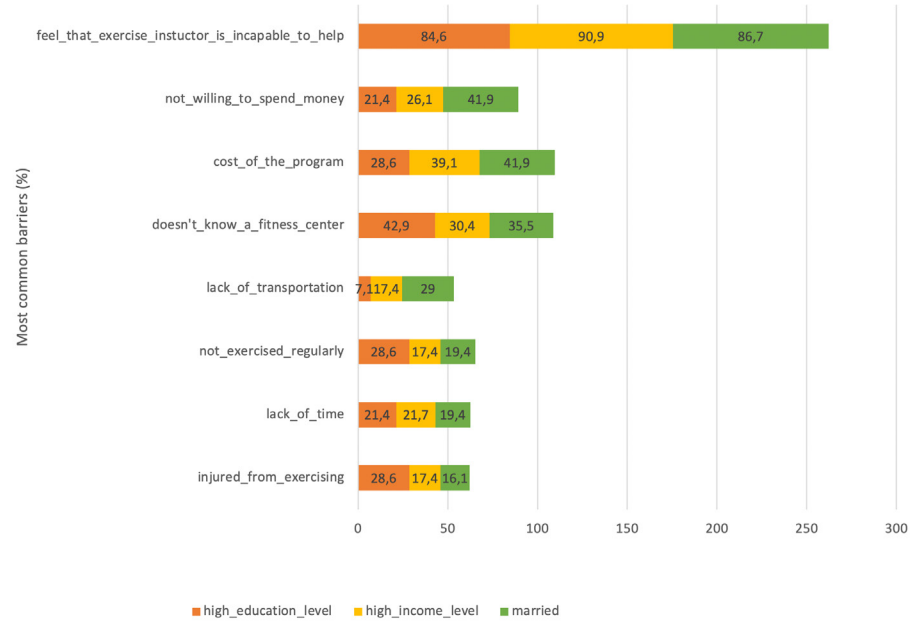


Figure 3: The most common PA barriers in the group with high education, high income and married marital status .



same time PA is important for improving and maintaining adequate levels of PF[5,22], so both PA and PF need attention. PF is stimulated by participation in structured PA programs[3,5,22]. Stroke survivors might not participate enough due to high-perceived exercise barriers.

Our results indicate that all the top five barriers for exercise were common for people from the low education (N=30) and low-income group (N=21) (**Figure 2**). Education levels have previously been shown to be associated with both work-related and leisure-time physical activity and somewhat to total PA[23]. Healthy persons with lower educational levels show more work-related physical activity, but less leisure-time physical activity. Lower education levels can be accompanied by lower income, which is depicted by the commonality of exercise barriers found across these groups in this study (**Figure 2**) and in line with findings of other stroke survivors[8,24]. Lower incomes could result from difficulties of stroke survivors to find work which in turn could induce low self-esteem, and low confidence which may further lower participation in exercise, as such introducing a negative vicious circle[25,26]. Similar to findings from HIC[13], LMIC[8], general population[27] as well as specific neurological populations[13,28], we found that participants in our study reported costly programs and lack of transport facilities as a barrier for participation in exercise programs. As many reported the incapability of the fitness instructor for setting up an individualized exercise program that meets their specific needs, this warrants further attention in stroke management policies. Therefore, targeting education, income, and environmental factors, might eventually help in successful improvement of participation in structured PA programs. Furthermore, ethnic differences were seen in the reported frequencies of the barriers. Therefore, research should be promoted on the change in physical fitness levels after barrier removal, as exercise barriers might change over time and people might still not feel comfortable or see the need to exercise. For instance, if there is a cultural difference in acceptance of a larger body size across ethnic groups or a need to uphold sociocultural identity, a person might still not be motivated to maintain the recommended PA level[29]. Perhaps, an intervention to alter this complex behavior, such as awareness campaigns or exercise programs must have behavior, or a measurable consequence of behavior, as its outcome measure[30]. Conclusively, exercise barriers are not similar enough across ethnic groups in this cohort to be targeted by one generalized intervention. Additionally, a HIC study[13] reported lack of energy as a common barrier to exercise and lack of time as a least reported exercise-barrier, whilst our study participants from a high-income and high education level reported lack of time, being injured during an exercise session and the fact that they haven't exercised regularly as exercise barriers. The exercise-barrier "lack of time" was least reported and might reflect the employed status of a part of this group, as this is largely reported as an exercise-barrier by healthy employed adults[31]. This in contrast to the HIC study amongst stroke survivors where "lack of time" reflected their unemployed stroke population[13]. However, people from India also reported lack of time as an exercise-barrier whilst they were unemployed[32]. Hence, careful individualized assessment is necessary in order to understand why people have low participation in structured PA programs.

Moreover, despite a low PA level, scores on exercise self-efficacy were good. And most of our participants were interested in starting an exercise program and felt that it would improve their condition. Literature shows that self-efficacy explains exercise adherence in chronic stroke survivors[33]. The high level of self-efficacy in our cohort might indicate that they believe to have the capability to reach and maintain a healthy level of exercise. That it still does not result in a higher PA level in our study might be due to the presence of several environmental/facility exercise barriers and the lack of specific exercise programs and specialized coaching during exercise after stroke.

Strengths and limitations

It should be kept in mind that the imbalance of the ethnic groups, the high-ambulating group of participants as well as the sample size within this study might prevent generalization of results. Nevertheless, an important strength of this study is the first in its kind for Suriname and that it provided information on patient-reported exercise barriers after stroke for a setting with scarce resources in a multi-ethnic population with a high level of confidence to perform exercise. Furthermore, we were not able to explore PA facilitators[34]. The importance of facilitators is emphasized in the study by Simpson et al. (2011)[34]. Information of facilitators might have facilitated the development of successful structured PA programs. The study by Simpson et al. (2011)[34] suggested support to exercise (external encouragement/qualified personnel) as a facilitator and at the same time lack of support to exercise was identified through our survey as a barrier. Findings of this study might serve as a strategy for physiotherapists to tailor exercise interventions in order to improve exercise participation of the participants.

Data on PA in our study was obtained from a Garmin device of which the algorithm for calculation of energy expenditure and steps/day was not known. This algorithm is likely to be based on healthy individuals whilst stroke survivors might show an increased energy expenditure for the same activity compared to healthy age-matched controls[4]. We tried to minimize bias as much as possible by putting the Garmin device on the non-paretic side of the body for 7 consecutive days.

Furthermore, self-reported data such as the exercise barriers in this study are subject to response bias ('socially desirable

responding')[35] which we need to take into account when designing and conducting PA programs. Moreover, there is no known evaluation of reliability and validity of the BPAD in stroke survivors, but the study by Rimmer et al. (2001)[24] suggests adequate reliability and validity for the use of the BPAD in people with chronic disabilities (N=149). Eventually, we advise that it would be best to design feasibility studies before conducting large PA programs in order to develop the best possible intervention.

Conclusions

Demographic and socio-economic variables did not explain the low PA level in our study population. These stroke survivors reported several barriers. Physiotherapists can therefore tailor stroke exercise programs according to personal barriers, include policy-making bodies to tackle environmental barriers and educate movement instructors for customized post-stroke exercise. Future research should evaluate feasibility and (cost) effectiveness of tailored exercise programs.

Geolocation information

This study was performed in the urban area of Suriname.

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ORIGINAL

Oligomenorrhoea – is it more frequent in women wtih type 1 diabetes mellitus?

Oligomenorrea: ¿es más frecuente en mujeres con diabetes mellitus tipo 1?

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Abstract

Introduction: Recent studies have shown an association of diabetes mellitus type 1 (DMt1) with reproductive disturbancies-delayed puberty and menarche, menstrual cycle abnormalities (oligomenorrhoea/amenorrhea /polymenorrhoea), polycystic ovary syndrome (PCOS) like phenotype, and potentially early menopause.
Objective: To assess menstrual cycle abnormalities in DMt1 women at reproductive age in comparison with age and BMI matched clinically healthy women.
Materials and methods: The study comprised of 37 women with DMt1 and 83 clinically healthy women serving as a control group. A detailed disease history was obtained regarding the duration of DMt1, type of insulin administered, total daily insulin dose (TDD); age at menarche, menstrual cycle (MC) interval, menstruation duration, dysmenorrhea and MC irregilarities, number of pregnancies, births, miscarriages. Oligomenorrhoea was defined as MC longer than 35 days or less than 9 MC throughout at least the past year. Polymenorrhea was defined as menstrual periods occuring at intervals of less than 21 days. Primary dysmenorrhea was interpreted as painfull menstruation unrelated to a secondary pelvic disease. Anthropometric measurements and basal levels of testosterone (T), thyroid-stimulating hormone (TSH) and prolactin (Prl) were studied in all participants. Fasting blood glucose (FG) and glycated hemoglobin (HbA1C) were also evaluated. Body mass index (BMI) and total daily insulin dose per kg body weight (TDD / kg) were calculated. Descriptive statistics, parametric and non-parametric methods were applied. Statistical significance was set at $p<0.05$.
Results: There was no statistically significant difference in terms of age (U=1789, p=0.149) and BMI (U=1686, p=0.392) between patients and controls. Euthyroid function and normoprolactinaemia were reported in all 120 subjects. Women with DMt1 had significantly higher T levels, FG and HbA1C compared to controls (U=2364, t=8.78, t=13.61, p=0.000, resp.). No significant differences were proven in the age at menarche (U=1601, p=0.623) and MC length (U=1574, p=0.564) between the women with DMt1 and the healthy controls. The mean duration of MC interval was significantly longer in DMt1 group as compared to the control group (32;10 days vs. 30;3 days, p=0.018). There was an association between oligomenorrhoea and the groups under consideration (chi-square=27.01, p=0.000). We demonstrated a statistically significant difference between the relative proportion of diabetic women with oligomenorrhoea (40.5%) compared to healthy controls with oligomenorrhoea (3.6%) (z=5.2, p=0.000). There was also an association between dysmenorrhea and the groups under consideration (chi-square=12.16, p=0.000). The relative part of women with dysmenorrhea was higher for DMt1 group compared (51.4%) to the control group (19.8%) (z=3.5, p=0.001). In the group of DMt1 there was a higher number of pregnancies (U=1925, p=0.007) and miscarriages (U=1837p=0.005) compared to healthy controls. In the DMt1 group a significant correlation was found between MC interval and both T levels (rho=0.634, p=0.000) and dysmenorrhea (rho=0.542, p=0.001). Moreover, a positive significant relationship between dysmenorrhea and T concentrations was observed (rho=0.507, p=0.001). When dividing the group of DMt1 into two subgroups – women with MC interval ≥35/<35 days, women with oligomennorhea had signigicantly higher serum T compared to those with normal MC interval (p=0.000). In the oligomennorhea subgroup a positive correlation of MC duration with TDD (rho=0.750, p=0.001) as well as with TDD / kg (rho=0.693, p=0.04) was observed.
Conclusion: Women with DMt1 have higher frequency of menstrual cycle abnormalities compared to age and BMI matched healthy women. Early and precise assessment of DMt1 MC characteristics is essential for the appropriate and complex treatment approach in these women.

Keywords: type 1 diabetes mellitus, oligomennorhea, dysmenorrhea, menstrual cycle, testosterone.

Resumen

Introducción. Estudios recientes han demostrado una asociación de la diabetes mellitus tipo 1 (DMt1) con las alteraciones reproductivas: retraso de la pubertad y la menarquia, anomalías del ciclo menstrual (oligomenorrea/amenorrea/polimenorrea), fenotipo similar al del síndrome de ovario poliquístico (SOP) y, potencialmente, menopausia precoz.
Objetivo: Evaluar las anomalías del ciclo menstrual en mujeres con DMt1 en edad reproductiva en comparación con mujeres clínicamente sanas emparejadas por edad e IMC.
Materiales y métodos: El estudio comprendió 37 mujeres con DMt1 y 83 mujeres clínicamente sanas que sirvieron como grupo de control. Se obtuvo una historia clínica detallada sobre la duración de la DMt1, el tipo de insulina administrada, la dosis diaria total de insulina (TDD); la edad de la menarquia, el intervalo del ciclo menstrual (CM), la duración de la menstruación, la dismenorrea y las irregularidades del CM, el número de embarazos, los partos y los abortos. La oligomenorrea se definió como un ciclo menstrual de más de 35 días o de menos de 9 durante al menos el último año. La polimenorrea se definió como periodos menstruales que ocurren a intervalos de menos de 21 días. La dismenorrea primaria se interpretó como una menstruación dolorosa no relacionada con una enfermedad pélvica secundaria. Se estudiaron las medidas antropométricas y los niveles basales de testosterona (T), hormona estimulante de la tiroides (TSH) y prolactina (Prl) en todas las participantes. También se evaluaron la glucosa en sangre en ayunas (FG) y la hemoglobina glicosilada (HbA1C). Se calcularon el índice de masa corporal (IMC) y la dosis diaria total de insulina por kg de peso corporal (TDD / kg). Se aplicaron métodos estadísticos descriptivos, paramétricos y no paramétricos. La significación estadística se fijó en p<0,05.
Resultados: No hubo diferencias estadísticamente significativas en cuanto a la edad (U=1789, p=0,149) y el IMC (U=1686, p=0,392) entre pacientes y controles. La función eutiroidea y la normoprolactinemia se registraron en los 120 sujetos. Las mujeres con DMt1 tenían niveles de T, FG y HbA1C significativamente más altos en comparación con los controles (U=2364, t=8,78, t=13,61, p=0,000, respectivamente). No se demostraron diferencias significativas en la edad de la menarquia (U=1601, p=0,623) y la duración del MC (U=1574, p=0,564) entre las mujeres con DMt1 y los controles sanos. La duración media del intervalo del CM fue significativamente mayor en el grupo de DMt1 en comparación con el grupo de control (32;10 días frente a 30;3 días, p=0,018). Hubo una asociación entre la oligomenorrea y los grupos considerados (chi-cuadrado=27,01, p=0,000). Se demostró una diferencia estadísticamente significativa entre la proporción relativa de mujeres diabéticas con oligomenorrea (40,5%) en comparación con los controles sanos con oligomenorrea (3,6%) (z=5,2, p=0,000). También hubo una asociación entre la dismenorrea y los grupos considerados (chi-cuadrado=12,16, p=0,000). La parte relativa de mujeres con dismenorrea fue mayor para el grupo de DMt1 en comparación (51,4%) con el grupo de control (19,8%) (z=3,5, p=0,001). En el grupo de DMt1 hubo un mayor número de embarazos (U=1925, p=0,007) y de abortos (U=1837p=0,005) en comparación con los controles sanos. En el grupo DMt1 se encontró una correlación significativa entre el intervalo MC y tanto los niveles de T (rho=0,634, p=0,000) como la dismenorrea (rho=0,542, p=0,001). Además, se observó una relación positiva y significativa entre la dismenorrea y las concentraciones de T (rho=0,507, p=0,001). Al dividir el grupo de DMt1 en dos subgrupos -mujeres con intervalo de MC ≥35/<35 días-, las mujeres con oligomenorrea presentaban una T sérica significativamente mayor en comparación con las que tenían un intervalo de MC normal (p=0,000). En el subgrupo de oligomenorrea se observó una correlación positiva de la duración de la CM con la TDD (rho=0,750, p=0,001) así como con la TDD / kg (rho=0,693, p=0,04).
Conclusiones: Las mujeres con DMt1 tienen una mayor frecuencia de anomalías del ciclo menstrual en comparación con las mujeres sanas emparejadas por edad e IMC. La evaluación precoz y precisa de las características del CM de la DMt1 es esencial para el enfoque terapéutico adecuado y complejo en estas mujeres.

Palabras clave: diabetes mellitus tipo 1, oligomenorrea, dismenorrea, ciclo menstrual, testosterona..

Introduction

The regularity of a menstrual cycle is an indicator of women's reproductive health. An irregular menstrual cycle (MC) is considered to be menstrual bleeding occurring more frequently than a 21-day cycle, less frequently than 35-day cycles, or an irregular bleeding pattern (such as bleeding between periods or abnormally heavy cycles)[1]. Menstrual cycle irregularities in women without diabetes are associated with increased cardiovascular risk, insulin resistance and hyperinsulinemia, as well as a risk of developing type 2 diabetes mellitus[2]. The most frequently observed cause of MC irregularity is functional hypothalamic amenorrhea, being associated with decreased gonadotropin-releasing hormone (GnRH) secretion and hypothalamic–pituitary–adrenal (HPA) axis dysregulation[1]

Insulin plays a key role in regulating female reproductive function through its effects on both GnRH neurons in the central nervous system and the granulosa, thecal, and stromal components in the ovaries[3]. The importance of insulin action on reproductive function in humans is highlighted by insulin receptor expression in most tissues, including the hypothalamus, pituitary, uterus and the ovaries[4].

Type 1 diabetes mellitus (DMt1) is a chronic autoimmune metabolic disease, characterised by a lack of insulin secretion from the pancreas as a result of beta-cell destruction. Insulinopenia causes a number of systemic effects on the every aspect of human health, in terms of its protein, fat and carbohydrate metabolism and not least on

the reproductive system. Is it the hypoinsulinemia or the hyperglycemia, insulin treatment itself or the combination of all affecting and disrupting the hypothalamic-pituitary-ovarian (HPO) axis in women with DMt1 is still a matter of scientific research.

Numerous studies have shown a higher freqency of reproductive disorders in DMt1 women such as late menarche and early menopause, hypothalamic anovulation, MC disorders-oligo-/amenorrhea, polymenorrhea, autoimmune disorders (greater frequency of ovarian antibodies and premature ovarian failure), PCOS-like phenotype (hyperandrogenism and anovulation)5. Women with DMt1 have an increased frequency of MC disorders compared to the healthy population, and this has been shown to increase the risk of coronary artery disease[6]. Given the increasing incidence of diabetes mellitus worldwide and reported gonadal dysfunction, assessment of MC characteristics in women with DMt1 has a wide clinical implication.

The *aim* of the study was to assess menstrual cycle abnormalities in DMt1 women at reproductive age in comparison with age and BMI matched clinically healthy women.

Materials and methods

We performed a transversal, observational, case-control study comprising 37 women with DMt1 and 83 age and BMI matched clinically healthy women. The study was conducted in the Clinic of Endocrinology and Metabolic Diseases at the University Hospital "Sveti Georgy", Faculty of Medicine, Medical University of Plovdiv, Bulgaria. All participants have given their written consent in accordance with the Declaration of Helsinki, as the study was approved by the Scientific Ethics Board of the Research Council at the Medical University of Plovdiv.

Inclusion criteria: women with type 1 diabetes mellitus on insulin treatment;
Exclusion criteria: pregnant and lactating women, presence of heart, respiratory, renal or hepatic failure, proliferative retinopathy, diabetic macroangiopathy, presence of acute decompensation of metabolic disease at the time of the study, contraceptive therapy or less than 3 months prior to study enrollment, treatment of chronic concomitant pathology that could affect hormonal and metabolic parameters.

The participants' data included diabetes mellitus duration, type of insulin administration, total daily insulin dose. A detailed gynecological history was obtained including age at menarche, MC interval, menstruation lenght, MC irregularities, dysmenorrhea, pregnancies, births, miscarriages. Oligomenorrhoea was defined as having a menstrual cycle longer than 35 days or less than 9 periods throughout at least the past year. Polymenorrhea was defined as menstrual periods occuring at intervals of less than 21 days. Primary dysmenorrhea wad defined as painfull menstruation unrelated to a secondary pelvic disease. The following anthropometric measurements were performed: weight, height, and body mass index (BMI) was calculated according to the standard formula[7]. Glycated haemoglobin (HbA1c) and fasting glucose (FG) were assessed. Basal levels of testosterone (T), thyroid-stimulating hormone (TSH), prolactin (Prl), and 17-hydroxyprogesterone - 17(OH)PG were studied in all participants.

Blood samples for laboratory tests were collected under standard conditions - early in the morning, after a 12-hour period of night fasting, during the early follicular phase of MC (3rd-5th day after spontaneous MC). The venous samples were studied in the Central Clinical Laboratory at the University Hospital "Sveti Georgy "- Plovdiv. Serum concentrations of T and PRL were determined by enzyme-linked immunosorbent assay with chemiluminescent detection, analyzer system: Access 2 Immunoassay System, Beckman Coulter, Inc., US. Serum TSH concentration was tested by competitive chemiluminescent immunochemical analysis (CLIA), analyzer system: Access 2 Immunoassay System, Beckman Coulter, Inc., USA. Venous blood sample with EDTA anticoagulant was obtained for HbA1C. Immunoinhiting test of turbodimetric analysis was applied with analyzer system AU 480, Beckman Coulter, Inc., USA. 17(OH)PG was tested by Enzyme-Linked Immunosorbent Assay (ELISA), analyzer system Sirio SEAC – Microplate reader.

Descriptive and inferential statistics were performed. Continuous variables were first tested for normality of statistical distribution by Shapiro–Wilk test. All normal distribution measurement data are expressed as the mean ± standard deviation (SD). Comparisons between two groups were analysed with Student's t-tests for independent samples, with Bonferroni correction for pairwise comparisons. The non-normally distributed data were expressed as median and interquartile range. Comparisons between groups were carried out with use of the nonparametric Mann-Whitney test for two independent groups. Categorical variables were presented as absolute/relative frequencies (counts / %). The Chi-square test was employed to analyse the association between two categorical variables and if proven z-test was applied to test for difference of relative parts between the groups. Significant correlations were presented by Spearman's rho coefficient. Statistical analysis of the data was performed using SPSS v.26 for Windows (IBM Corp. Released 2019. Armonk, NY: IBM Corp). For all tests p-value <0.05 indicated the statistical significance.

Results

Basic demographic, anthropometric, clinical, biochemical and hormonal characteristics of the studied women are summarized in **table I**. The mean age of the subjects in the present study was 30; 9 years with no significant difference between the participants with DMt1 and the control group (31; 8 ys) *versus* (30; 9 ys), (U=1789, p=0.149). In addition, no significant difference in terms of BMI between the DMt1 women and the controls (23.3; 4.9 kg/m^2) *versus* (22.3; 4.9 kg/m^2), (U=1686, p=0.392). Euthyroid function and normoprolactinaemia were reported in all 120 subjects. The participants presented with normal levels of 17(OH)PG, without significant difference between the two groups (U=1187, p=0.551). Thus, non-classic congenital adrenal hyperplasia (CAH) was excluded.

Table I: Basic demographic, anthropometric, clinical, biochemical and hormonal characteristics of the women studied.

	DMt1 (n=37)	Controls (n=83)	p-value
Age (years), *median; IQR*	31;9	30;9	0.149[1]
BMI (kg/m2), *median; IQR*	23.3;4.9	22.3;4.9	0.392[2]
Fasting glucose (mmol/l), *mean±SD*	7.5±2.5	5.0±0.3	**0.000[1]**
HbA1C (%), *mean±SD*	7.8±1.5	4.8±0.3	**0.000[1]**
Testosterone (ng/ml), *median; IQR*	0.6;0.4	0.4;0.2	**0.000[2]**
TSH (mU/l), *median; IQR*	2.2;1.8	1.7;1.2	0.104[2]
Prolactin (mU/l), *median; IQR*	210.6;126	232.6;145.5	0.548[2]
17(OH)PG (ng/ml), *median; IQR*	1;1.6	1.2;2	0.551[2]
Age at menarche (years), *median; IQR*	13;2	13;2	0.623[2]
MC interval (days), *median; IQR*	32;10	30;3	**0.018[2]**
MC duration (days), *median; IQR*	6;2	6;1	0.564[2]
Pregnancies (number), *median; IQR*	1;2	0.0;1	**0.007[2]**
Births (number), *median; IQR*	1;1	0.0;1	0.089[2]
Miscarriages (number), *median; IQR*	0.0;1	0.0;0.0	**0.005[2]**
DMt1 duration (years), *mean±SD*	13.8±8.3	-	-
TDD insulin (units), *mean±SD*	54.3±17.3	-	-
Insulin dose/kg, *mean±SD*	0.9±0.2	-	-

[1] - T-test; [2] - Mann-Withey U test

Women with DMt1 did not differ in terms of age at menarche and MC duration with the control group (U=1601, p=0.623; U=1574, p=0.564, resp.). However, we observed significantly longer MC interval in the diabetic women compared to healthy controls (U=1926, p=0.018). It turned out that in the DMt1 group there was a higher number of pregnancies (U=1925, p=0.007) and miscarriages (U=1837, p=0.005) compared to the healthy group. The two groups did not differ in terms of number of births (U=1758, p=0.089). An association between the number of pregnancies and the examined groups in our study (chi-square=16.43, p=0.002) was observed. The relative proportion of women with no pregnancies was higher in the control women (59.3%) compared to diabetic women (32.4%) (z=2.8, p=0.006). On the contrary, the relative proportion of diabetic women with 3 pregnancies was higher (13.5%) compared to controls (1.2%) (z=2.9, p<0.004).

In our study 40.5% (n=15) with DMt1 and only 3.6% (n=3) in the control group fulfilled the oligomenorrhoea criteria. 51.4% (n=19) with DMt1 and 19.3% (n=16) of the controls reported dysmenorrhea. Only one woman with DMt1 had polymenorrhea. No one reported amenorrhea. There was an association between oligomenorrhoea and the groups under consideration (chi-square=27.01, p=0.000). We demonstrated a statistically significant difference between the relative proportion of diabetic women with oligomenorrhoea (40.5%) compared to healthy controls with oligomenorrhoea (3.6%) (z=5.2, p=0.000). There was also an association between dysmenorrhea and the groups under consideration (chi-square=12.16, p=0.000). The relative part of women with dysmenorrhea was higher for DMt1 group compared (51.4%) to the control group (19.8%) (z=3.5, p=0.001).

As expected, HbA1C and FG were higher in DMt1 women (t=13.61, p=0.000; t=8.78, p=0.000, resp.) compared to healthy individuals. The average duration of the DMt1 was 13.8±8.3 years, the average TDD of insulin was 54.3±17.3 E, and the average calculated insulin dose per kg was 0.9±0.2 E/kg. Women in the DMt1 group had significantly higher serum T levels than healthy controls (U=2364, p=0.000).

In the DMt1 group a significant correlation was found between MC interval and both T levels (rho=0.634, p=0.000) and dysmenorrhea (rho=0.542, p=0.001). Moreover, a positive significant relationship between dysmenorrhea and T concentrations was observed (rho=0.507, p=0.001). As expected, HbA1C demonstrated a strong postive correlation with TDD (rho=0.359, p=0.003) and TDD/kg (rho=0.432, p=0.008).

For more precise assessment of women with DMt1 and oligomenorrhoea, we further divided the DMt1 group into two subgroups – women with MC interval ≥35 and with MC interval <35 days (**Figure 1** and **table II**). The only stastistically significant deference between the subgroups concerned serum T levels. They were significantly higher in the oligomenorrhoea subgroup compared to the subgroup with normal MC interval (U=309, p=0.000). There was also a tendency for prolonged MC duration in women with DMt1 and oligomennorhea compared to those normal MC (U= 224, p=0.070), without reaching statistical significance. No other significant differencies were observed among the examined parameters. In the oligomennorhea subgroup a positive correlation of HbA1C with DM duration was observed (rho=0.603, p=0.020). There was also a positive correlation of MC duration with TDD (rho=0.750, p=0.001) and with TDD/kg (rho=0.693, p=0.040). Diabetic women with MC interval < 35 days were found to have positive correlation of MC duration with FG levels (rho=0.499, p=0.020). The same subgroup presented with negative correleation between dysmenorrhea and number of pregnancies, but without reaching significant level (rho=0.395, p=0.060).

Figure 1: Distrubution of women in DMt1 group and control group by MC interval.

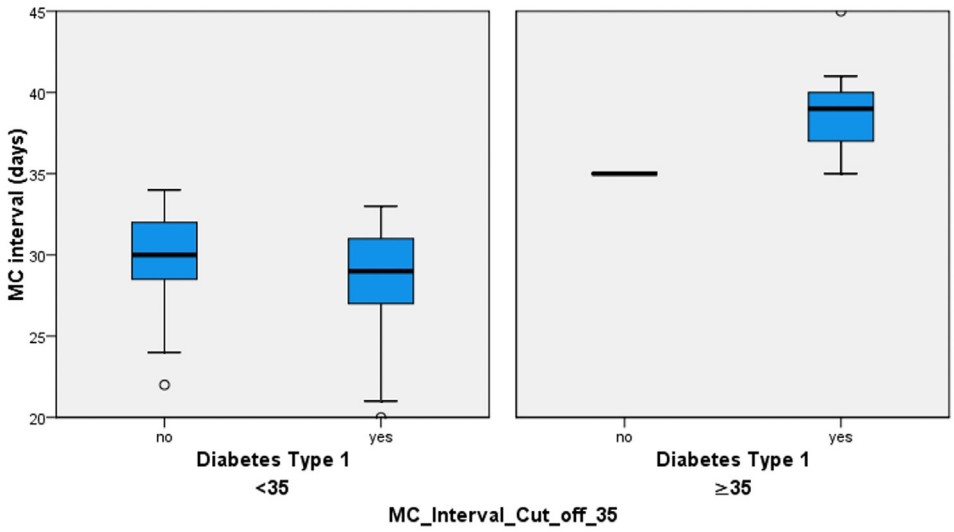

Table II: Anthropometric, anamnestic and hormonal parameters in women with DMt1 according to the MC interval.

DMt1	MC interval≥35 (n=15)	MC interval<35 (n=22)	p-value
Age (years), *mean±SD*	29.3±4.8	31.8±6.5	0.383[1]
BMI (kg/m2), *mean±SD*	23.3±3.7	23.5±3.5	0.680[1]
Fasting glucose (mmol/l), *mean±SD*	7.5±2.9	7.5±2.3	0.725[1]
HbA1C (%), *mean±SD*	7.9±1.6	7.7±1.4	0.531[1]
Testosterone (ng/ml), *median; IQR*	0.9;0.4	0.6;1.2	**0.000[2]**
TSH (mU/l), *mean±SD*	2.5±1.2	2.3±1.2	0.614[1]
Prolactin (mU/l), *median; IQR*	180.6;89.9	224.8;153.3	0.092[2]
17(OH)PG (ng/ml), *median; IQR*	0.6;1.7	1.1;1.6	0.290[2]
Age at menarche (years), *median; IQR*	13;4	13;2	0.614[2]
MC duration (days), *median; IQR*	6;1	5;1	0.070[2]
Pregnancies (number), *median; IQR*	1;2	1;2	0.891[2]
Births (number), *median; IQR*	1;1	1;1	0.636[2]
Abortions (number), *median; IQR*	0.0;1	0.0;1	0.531[2]
DMt1 duration (years), *mean±SD*	11.6±7.0	15.3±8.9	0.680[1]
TDD insulin (units), *mean±SD*	54.4±18.58	54.18±16.76	0.867[1]
Insulin dose/kg, *mean±SD*	0.9±0.3	0.8±0.2	0.703[1]

[1] - T-test; [2] - Mann-Withey U test

Discussion

The DMt1 women in our study presented with oligomenorrhoea and dysmenorrhea more frequently, with higher number of pregnancies and abortions, but with similar age of menarche as compared to healthy controls.

The regularity of the menstrual cycle requires an intact hypothalamus-pituitary-gonadal axis. Back in 1994 Griffin et al. reported that the menstrual cycle disorders in DMt1 might be of hypothalamic origin and represent GnRH pulse generator failure[8]. Central nervous system mediators - dopaminergic, opioidergic activity, catecholamine levels might also have a role in the pathophysiology of hypogonadism in patients with DMt1[9]. Hyperglycemia itself may affect the ovary both directly and through the induction of insulin resistance. Last but not least exogenous insulin administration may cause overstimulation of the IGF-1 receptors in the ovary, increasing steroid secretion stimulating the development of PCOS[10].

A number of studies presented a delay in the age of thelarche, pubarche, and most importantly menarche in girls with DMt1[11,12]. This delay was estimated to be about one year if the onset of disease occurred before puberty[13,14,15]. Even after improvement of insulin therapy and intensification of insulin injections, girls still experienced a delay in the age of menarche compared to the nondiabetic girls of the same age[16]. A research from the year 2010 demonstrated that although there was a decline in age of menarche for the past 4 decades among girls with DMt1, the ones diagnosed prior to menarche still experince a delay compared to those diagnosed after menarche[17]. Codner et al. summarized that the factors associated with the delay in menarcheal age have been poor metabolic control, lower BMI, prepubertal onset of the diasease with a longer duration[18]. In our study we did not find a significant difference in age of menarche in diabetic women compared to healthy population (U=1601, p=0.623), taking into account that the number of participants diagnosed with DMt1 before the age of menarche was only 5. We can conclude that menarcheal age of diabetic women in the study is comparable to the one in healthy individuals if DMt1 occurs after puberty. Further investigation including more women with prepubertal onset of DMt1 is under consideration.

A lot of studies demonstrated the presence of menstrual cycle disorders in women with DMt1[12,14,15]. Strotmeyer et al. reported that type 1 diabetic women have an increased

risk of menstrual disturbancies only at a younger age. Besides, statistical analysis revealed that DMt1 causes an approximate twofold increased risk of menstrual problems before the age of 30 years[19]. The mean age of women with DMt1 in our study was 30; 9 years and still we demonstrated prolonged MC interval compared to healthy individuals (p=0.018). In the DMt1 group there were 15 women (40.5%) with oligomennorhea. Gaete et al. demonstraed oligomenorrhea (58.9% vs. 19.6%) and amenorrhea (10.7% vs. 1.8%) in adolescent girls with type 1 diabetes mellitus compared to controls. When performing regression analysis the authors concluded that for each point of increase in HbA1c, the menstrual cycle duration increased by 5.1 days[20]. The relationship between menstrual cycle disturbances and metabolic control remains not entirely studied. Deltsidou et al. concluded that adolescent girls with DMt1 experience delayded menarche and oligomenorrhoea more frequently. What is more, the relative risk of presenting with oligomenorrhoea is greater when there is an increased value of HbA1c[21].

The mean level of HbA1C in DMt1 group was 7.8±1.45% and FG 7.5±2.5 mmol/l. Only 6 women presented with strict metabolic control (HbA1C <6.5%) and 31 were with HbA1C>6.5%. In addition oligomennorhea and dysmenorrhea did not show any correlation with HbA1C, FG and disease duration. Hypogonadotropic hypogonadism was demonstrated in women with type 1 diabetes mellitus with poorly controled diabetes. Djursing et al. reported that the hypogonadotropic hypogonadism presented in amenorrheic DMt1 women might be similar to the one in anorexia nervosa and heavy exercise with impared LH secretion[22].

But is the metabolic control that only matters in terms of menstrual cycle abnormalities in DMt1? By performing the further subdivision, we tried to look for other markers related with menstrual cycle disorders in DMt1. Still, diabetic women with oligomennorhea did not differ in terms of metabolic control with the normal cycle DMt1 women. Escobar-Morreale proposed that exogenous insulin administered in nonphysiological way results in ovarian huperinsulinemia, PCOS like phenotype and menstrual cycle irregularities[23]. Indeed, only women with oligomennorhea demonstrated positive correletaion of MC duration with TDD and TDD/kg (rho=0.750, p=0.001; rho=0.693, p=0.04 resp.) It was already mentioned that insulin and insulin-like growth factor 1 (IGF-1) receptors are present in the ovary, including theca, granulosa, and stromal cells[3,4]. Since insulin stimulates steroidogenesis and folliculogenesis in theca cells, irregular menstrual cycles may depend on the direct effect of exogenous insulin on the ovaries.

Women with DMt1 are reported to have reduced fertility[24,25]. Wiebe et al. found that women with type 1 diabetes have fewer children than their unaffected siblings but later age of onset of diabetes was associated with a higher number of the offspring[25]. In our study women with DTt1 had a greater number of pregnancies (U=1925, p=0.007) and miscarriages (U=1837, p=0.005) compared to the healthy controls. We also observed an association between the number of pregnancies and the examined groups in our study (chi-square – 16.43, p=0.002). The relative proportion of women with no pregnancies was higher in the control women (59.3%) compared to diabetic women (32.4%) (z=2.8, p=0.006). On the contrary, the relative proportion of diabetic women with 3 pregnancies was higher (13.5%) compared to controls (1.2%) (z=2.9, p<0.004). A study from Finland reported that later age at onset of diabetes was associated with a higher rate of having a second live birth among women (p=0.002)[26].

Developed countries are witnessing a marked change in the pattern of childbearing as increasing numbers of women postpone childbearing until their 30s and 40s[27]. As numerous studies showed that maternal and fetal complications are substantially higher, especially in advanced age in women with type 1 diabetes than in women from the general population, we can assume that this might be the answer to the higher rate of pregnancies in the DMt1 group[28]. Early assessment of reproductive status in women with DMt1 is found to be important for adequate planning of future normal pregnancy, selection of appropriate contraception, improvement of glycemic control and thus reducing the number of miscarriages. Probably this was the main reason for the better reproductive results in the women with DMt1 in our study.

Conclusion

Women with DMt1 have higher frequency of menstrual cycle abnormalities compared to age and BMI matched healthy women. Early and precise examination of menstrual cycle characteristics of women with DMt1 is essential for developing a better approach towards their treatment. Further purposeful studies with higher number of participants are needed to elucidate these observations.

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Conflict of Interest

The authors report no conflicts of interest.

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ORIGINAL

Efectos del ejercicio y condición física sobre la atención en población infantil de 5 años: una prueba piloto

Effects of exercise and physical condition on attention in 5-years old population: a pilot study

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Resumen

Introducción: Los trastornos sobre la atención pueden relacionarse con el rendimiento físico y la actividad física.
Material y métodos. Se presenta una evaluación antropométrica y de condición física básica y comparándola con la prueba del Trail Marking Test para evaluar la capacidad atencional, y evaluar si el ejercicio físico contribuye a la mejora de las capacidades atencionales en sujetos de 5 años.
Resultados: Existen diferencias significativas y más acentuadas en la mejora de variables atencionales en aquellos sujetos con sobrepeso y baja actividad física.
Conclusiones: El ejercicio físico, incluso a baja intensidad produce una mayor mejora atencional en aquellos sujetos con sobrepeso o baja actividad física.

Palabras clave: Actividad física, Atención, condición física, sobrepeso.

Abstract

Introduction: Attention disorder that can be related to physical performance and physical activity.
Material and methods. An anthropometric and basic physical condition assessment is presented, comparing it with the Trail Marking Test to assess attentional capacity, and to assess whether physical exercise contributes to the improvement of attentional capacities in 5-years old childs.
Results: There are significant and more accentuated differences in the improvement of attentional variables in those subjects with overweight and low physical activity.
Conclusions: Physical exercise, even at low intensity, produces an attentional improvement in those who have low physical activity or overweight.

Keywords: Attention, overweight, physical condition, physical activity.

Introducción

El Trastorno por Déficit de Atención e Hiperactividad (TDAH) se define como un trastorno neurobiológico o trastorno del neurodesarrollo en el que se ven implicados diversos genes responsables de la transmisión de serotonina y del control o regulación de la norepinefrina y de la dopamina[1]. Suele presentarse en la infancia y no solamente afecta a la persona que lo padece, sino también a su entorno[2] que se presenta por falta de capacidad atencional, o trastornos de la conducta, insomnio[3], agresividad, impulsividad o falta de autocontrol, ansiedad o depresión, escasa coordinación motriz, dificultad de aprendizaje y dificultad seguir las normas[4,5].

Diversos estudios[6] afirman que los problemas atencionales están relacionados con una escasa práctica de ejercicio físico. Además, Pontifex et al[7], McKune, Pautz y Lombard[8] afirman que el ejercicio físico puede aportarles beneficios muy positivos a las personas con problemas de concentración y atención, en su comportamiento, en su función neurocognitiva.

El objetivo del estudio es comparar el desempeño en pruebas atencionales según diversas medidas antropométricas, condición y actividad física.

Materiales y métodos

El estudio piloto se llevó a cabo con 58 alumnos (50.4% de mujeres y 49.6% varones). Los criterios de inclusión fueron:

- Pertenecer a población escolar infantil con 5 años.
- Aceptar participar en el estudio por parte de los representantes legales.

Las pruebas que se llevaron a cabo fueron de tipo antropométrico, de capacidad y actividad física (ver **tabla I**) así como la prueba del Trail Marking Test (TMT) para valorar la capacidad atencional de los sujetos.

La prueba del TMT consta de dos partes: en la primera, el sujeto debe conectar en orden secuencial los números del 1 al 25; en la segunda parte, los puntos van del 1 al 5 e incluyen letras de la A a la E (una versión reducida, ya que el TMT original tiene 23 números y letras a relacionar). Al igual que en la primera parte, el sujeto debe conectar los puntos en orden alternando letras y números, como en 1-A-2-B- 3-C..., en el menor tiempo posible y sin levantar el bolígrafo del papel. La primera parte se utiliza principalmente para examinar la velocidad de procesamiento cognitivo mientras que la segunda parte de la prueba, en la que el sujeto alterna entre números y letras, se utiliza para examinar el funcionamiento ejecutivo[9].

Tabla I: Índices antropométricos.

Masa corporal y Altura	Balanza: modelo SECA 700 con divisiones de 50 gramos, con una vara de medir telescópica SECA 220 con división milimétrica y un intervalo de 60-200 cm.
Circunferencia abdominal	Cinta métrica modelo SECA 20, con un intervalo de 1-200 cm y división milimétrica
Fuerza de prensión Manual	Se midió la prensión manual con un dinamómetro manual
Salto de longitud	Se midió saltando con los pies juntos con una cinta métrica con división centimétrica
Equilibrio	Se calculó el tiempo en el que podían mantenerse sobre un pie, y luego el otro y se promedió
Actividad física	Se midió con el cuestionario IPAQ-C
Índice de Masa Corporal (IMC)	IMC= peso/altura^2
Clínica Universidad de Navarra *Body Adiposity Estimator*[10]	-44.988 + (0.503 x edad) + (10.689 x sexo) + (3.172 x IMC) - (0.026 x IMC^2) + (0.181 x IMC x sexo) - (0.02 x IMC x edad) - (0.005 x IMC^2 x sexo) + (0.00021 x IMC^2 x edad)
Equation Córdoba for Estimation of Body Fat[11]	-97.102 + 0.123 (edad) + 11.9 (sexo) + 35.959 (LnIMC)
Deurenberg *(Fat mass index)*[12]	Fat mass %= 1.2 x (IMC) + 0.23 x (edad) - 10.8 x (sexo) - 5.4
Normalized weight-ajusted index (NWAI)[13]	NWAI= (masa/10) - (10 x altura) + 10
Body Adiposity Index (BAI)[14]	BAI = ((diámetro cintura)/((altura)1.5)-18)
Body roudness index (BRI)[15]	BRI = 364.2-365.5x√1-[(diámetro cintura/(2π)2)/(0.5 x masa)2]
Body Surface Index (BSI)[16] y Body Surface Area (BSA)	BSA = masa^{0,425} x altura^{0,725} x 0,007184; BSI = masa/√ BSA

Tabla II: Valores de índices antropométricos.

	Peso	Altura	IMC	Cintura	CUN -BAE	ECORE -BF	Deuremberg (Fat Mass index)	NWAI	BAI	BSA	BSI	BRI
Masculino	22,75±3,93	1,18±0,05	16,41±2,1	59,25±5,94	13,44±4,63	15,79±4,37	15,46±2,53	12,16±0,39	28,59±4,36	0,86±0,08	24,48±3,02	6,76±0,83
Sobrepeso	26,08±0,79	1,16±0,02	19,37±0,94	66,25±1,53	19,98±2,13	21,91±2,06	19,05±1,12	12,49±0,08	35,18±2,37	0,9±0,02	27,42±0,74	7,98±0,5
Normopeso	21,56±4,11	1,17±0,05	15,62±2,27	57,16±6,1	11,7±5,01	14,16±4,72	14,5±2,73	12,04±0,41	27,07±4,69	0,84±0,08	23,51±3,19	6,5±0,88
Femenino	21,14±3,83	1,16±0,06	15,75±1,86	58,77±6,39	11,95±4,13	14,34±3,91	14,67±2,26	12±0,38	29,32±4,67	0,82±0,08	23,23±2,88	6,95±0,91
Global	21,86±3,85	1,17±0,05	16,04±1,97	58,98±6,12	12,61±4,35	14,99±4,11	15,02±2,38	12,07±0,38	28,99±4,48	0,84±0,08	23,79±2,93	6,87±0,86

La metodología se basó en una fase de evaluación inicial de la atención (pre-test) y una fase posterior (una semana más tarde) con la misma prueba atencional (post-test). Dicha intervención buscó aumentar la frecuencia cardiaca de los alumnos con juegos aeróbicos y anaeróbicos realizados durante una sesión de educación física con una duración de 20 minutos y evaluar si mejoraba la capacidad atencional de los sujetos, así como comparar si las variables medidas podían presentar variación según la capacidad y actividad física medida mediante el test iPAQ-C (adaptado a menores).

Análisis estadístico

Se ha llevado a cabo un análisis descriptivo de las frecuencias y distribución de las diferentes variables, midiendo la media y la desviación típica, así como un análisis de componentes principales entre las variables BAI, tiempos en la prueba de atención (pre-test y post-test) y las pruebas sobre condición física.

El análisis estadístico se realizó con el software XLSTAT.

Resultados y discusión

A continuación se muestran los resultados de los diferentes índices y variables antropométricas (**Tabla II**), las variables sobre la condición física (**Tabla III**), así como la prueba sobre capacidad atencional (**Tabla IV**).

Los resultados muestran que existe una homogeneidad entre ambos sexos, tanto en la condición de normopeso como mientras que los sujetos con sobrepeso masculino y/o baja actividad física mostraron una variabilidad mayor en cuanto a las pruebas analizadas como se refleja en el análisis de componentes principales de la **figura 1**, en el que se aprecian dos grupos diferenciados, uno homogéneo con los sujetos con normopeso y actividad física moderada, mientras que los sujetos con sobrepeso o baja actividad física presentan una distribución heterogénea.

Tras la realización de la revisión bibliográfica, se puede observar que estudios como el de Gapin y Etnier[17], Chang, Liu, Yu y Lee[18] , Pontifex et al.[7] , Hillman et al.[19] y Ma[20] coinciden en que la actividad física puede mejorar la función cognitiva y ejecutiva de los alumnos. Lo demuestran evaluando aspectos como el control inhibitorio, la velocidad de procesamiento, la memoria y la capacidad atencional de los alumnos tras realizar una o varias sesiones de ejercicio físico. Aunque otros estudios como el de Verret, Guay, Berthiaume, Gardiner y Béliveau[21], el de Smith et al.[22] y el de Ziereis y Jansen[23] demuestran que el ejercicio físico también puede aportar beneficios a nivel cognitivo y ejecutivo aplicando un programa de intervención más prolongado en el tiempo. Como se ve en este estudio piloto, aunque los sujetos no tengan un diagnóstico de TDAH, los que presentan sobrepeso y/o baja actividad física són los que más se ven beneficiados en la mejora de la capacidad atencional. Varios autores defienden la influencia del ejercicio físico sobre su estado de ánimo, y previniendo aspectos relacionados con la ansiedad y la depresión[24] y a su vez el ejercicio físico favorece las relaciones sociales entre iguales sociales[25,26].

Figura 1: Análisis de componentes principales sobre las variables y distribución de los grupos de estudio. Las variable usadas fueron: Var1(Pre-Test Prueba A), Var2 (Post-Test Prueba A), Var3 (Pre-Test Prueba B), Var4 (Post-Test, Prueba B) y Var5 (IPAQ-MET).

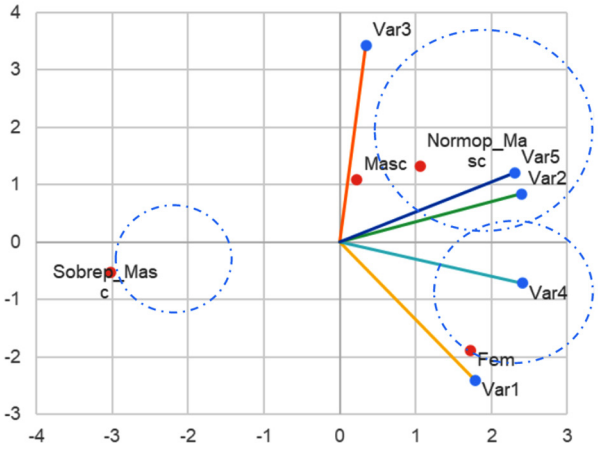

Tabla III: Pruebas de valoración de condición y actividad física.

	salto	ED	EI	PD	PI	Velocidad	IPAQ-MET
Masculino	103,46±21,49	15,81±10,3	16,39±10,72	9,12±1,68	8,28±1,74	14,76±1,76	760,85±208,98
Sobrepeso	103±7,09	14,02±8,11	15,25±13,97	7,43±0,85	7,13±1,43	16,17±0,55	450,75±170,41
Normopeso	101,47±23,4	16,09±10,66	16,74±10,26	9,45±1,79	8,54±1,83	14,55±1,92	858,53±220,29
Femenino	106,67±20,27	28,29±14,61	21,46±16,37	7,9±1,62	7,79±1,6	16,26±2,61	767,77±282,46
Global	105,24±20,56	22,74±13,93	19,21±14,11	8,44±1,66	8,01±1,66	15,58±2,29	764,48±254,71

Tabla IV: Valores de la prueba atencional TMT.

	Prueba A (pre-test)	Prueba A (post-test)	Prueba B (pre-test)	Prueba B (post-test)
Masculino	33,13±8,16	25,38±6,21	31,9±7,36	21,25±5,19
Sobrepeso	32,3±7,68	20,01±8,52	31,13±8,31	17,62±3,96
Normopeso	33,48±8,47	26,83±5,94	31,96±6,96	21,86±4,64
Femenino	37,22±12,05	26,1±8,81	30,81±14,61	24,01±10,66
Global	35,4±10,47	25,78±7,68	31,29±11,86	22,78±8,92

Khalife et al.[27] proponen que el ejercicio físico requiere poseer o adquirir determinadas capacidades que pueden resultar de mayor dificultad para el alumnado con TDAH (concentración, percepción y autocontrol), Kim, Mutyala, Agiovlasitis y Fernhall[28] demostraron con su estudio que el resto de la sociedad realiza más ejercicio que este tipo de alumnos, factor que, según Khalife et al.[27], puede ser una de las causas del factor de riesgo de obesidad que sufren estos alumnos, concluyendo que esta inactividad física podría relacionarse con los síntomas del trastorno.

Conclusiones

Existen diferencias entre ambos sexos en cómo el ejercicio y la actividad física afecta a las capacidades cognitivas tanto de velocidad como de procesamiento, al mismo tiempo la condición física también influye en las capacidades cognitivas, siendo los sujetos con sobrepeso aquellos que presentan unas mejoras respecto al grupo control.

Conflicto de Intereses: en este estudio no existen conflictos de interés.

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ORIGINAL

Comparación entre el manejo tradicional frente a leche materna exclusiva en recién nacidos con enterocolitis necrosante: estudio de cohortes retrospectiva

Comparison between the traditional management and human milk in newborn babies with necrotizing enterocolitis: retrospective cohort study

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Resumen

Antecedentes: La enterocolitis necrosante es una patología que afecta al tracto gastrointestinal.
Objetivo: Comparar el uso de leche materna exclusiva y el manejo tradicional en recién nacidos con enterocolitis necrosante.
Material y métodos: Se diseñó un estudio observacional, transversal y retrospectivo de expedientes de recién nacidos con enterocolitis necrosante que ingresaron en el servicio de neonatología. Los casos de enterocolitis necrosante se definieron y clasificaron siguiendo los criterios de Bell.
Resultados: Se analizaron 42 pacientes que fueron divididos en dos grupos: grupo 1 con leche materna exclusiva (23 pacientes) y grupo 2 con manejo tradicional (19 pacientes). La media de la edad en días hasta la presentación de enterocolitis necrosante en el grupo con leche materna exclusiva fue de 13,4 días con desviación estándar 8,2, y en el grupo con manejo tradicional 8,6 días con desviación estándar 7,39 (p 0.03). La estancia intrahospitalaria en promedio fue de 21,6 días con desviación estándar 15,6 y 33,8 días con desviación estándar 20,3 (p 0.03). El requerimiento de cirugía en el grupo 1 fue del 22% y en el grupo 2 del 63% (p 0.01). El grupo 2 tuvo mayor necesidad de ventilación mecánica, en un 58% (p 0.06). Y la complicación más frecuente fue sepsis en los dos grupos, con 39% en el grupo 1 y 84% en el grupo 2.
Conclusiones: La leche materna exclusiva presenta menor frecuencia de complicaciones, de intervención quirúrgica, días de estancia hospitalaria y de necesidad de ventilación mecánica.

Palabras clave: Leche materna, enterocolitis necrotizante, nutrición parenteral, ayuno.

Abstract

Background: Necrotizing enterocolitis is a pathology that affects the gastrointestinal tract.
Objective: Compare the use of breast milk, and traditional management in newborn babies with necrotizing enterocolitis.
Methods: An observational, transversal and retrospective study of newborn medical records with necrotizing enterocolitis who have entered to the neonatology service, was designed. The necrotizing enterocolitis was defined and classified based on Bell's staging criteria.
Results: We analyzed 42 patients, which were divided into two groups: group 1 with exclusive maternal feeding (23 patients) and group 2 with traditional management (19 patients). With a mean age in days at the necrotizing enterocolitis presentation of 13.4 days with standard deviation 8.2 in the exclusive maternal feeding, and 8.6 days with standard deviation 7.4 in the group with traditional management (p 0.03). The hospital stay mean was 21.6 days with standard deviation 15.6, and 33.8 days with standard deviation 20.3 respectively (p 0.03). The surgical requirement in group 1 was 22% in group 1 and 63% in group 2 (p 0.01). Group 2 has the major requirement of mechanical ventilation with 84% (p 0.06). And the most frequent complication was sepsis in both groups, with 39% in group 1 and 84% in group 2.
Conclusions: The human milk presented a lower frequency of complications, surgical interventions, days of hospital stay, and use of mechanical ventilation.

Keywords: Breast milk, necrotizing enterocolitis, parenteral nutrition, fasting.

Introducción

La enterocolitis necrosante (ECN) es una patología que afecta al tracto gastrointestinal. Se caracteriza por una necrosis intestinal inflamatoria. Existe una disbiosis intestinal, un aumento de la respuesta inflamatoria e inmadurez de la barrera de la mucosa intestinal[1,2].

Para su clasificación y diagnóstico se utilizan los criterios de Bell modificados, que incluyen signos sistémicos, signos abdominales y signos radiológicos. Estos criterios tienen tres etapas; estadio I sospecha, estadio II certeza y el III complicación[3].

Esta patología afecta al 5-7% de los recién nacidos pretérmino y con peso muy bajo al nacimiento, menor de 1,500 gramos. Si el peso es menor de 1,000 gramos la incidencia aumenta a 14%. Cerca del 90% de los pacientes afectados son menores de 34 semanas de gestación. Por lo que representa una de las principales causas de mortalidad en este grupo de edad, con una tasa de 30-40%[4,5]. Actualmente se ha avanzado mucho en el conocimiento de la enfermedad, su diagnóstico y tratamiento, sin embargo, continua como una de las patologías más graves en recién nacidos y de gran mortalidad, con áreas controvertidas respecto al manejo.

Los principales factores de riesgo son prematuridad, bajo peso al nacimiento, alimentación con fórmula y presencia de bacterias[4,6]. Los oligosacáridos promueven la proliferación de microbiota intestinal y actúan como antiadhesivos para evitar la unión de patógenos virales y bacterianos a la pared intestinal. Por lo que provee al recién nacido de inmunidad pasiva al tracto gastrointestinal, siendo un factor protector ante esta patología[7,8].

El objetivo de este estudio es comparar el uso de leche materna exclusiva (LME) y el manejo tradicional en recién nacidos con ECN

Material y métodos

Se realizó un estudio de observacional, descriptivo, retrospectivo y transversal, en el que se recabaron los casos de ECN de un hospital general del Estado de Puebla, durante el periodo de 1 de enero del 2016 al 15 de junio del 2021. Se realizó de acuerdo con las recomendaciones STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) para el reporte de estudios de cohorte. El estudio fue aprobado por el Comité de Ética e Investigación Biomédica del hospital.

Los pacientes fueron seleccionados por medio de revisión de base de datos. Para la descripción de la cohorte de pacientes, se incluyeron las siguientes variables: edad gestacional, sexo, peso al nacimiento, edad del recién nacido al presentar ECN, manejo, infecciones, ventilación mecánica, manejo quirúrgico y estancia intrahospitalaria.

Los casos de ECN se definieron y clasificaron por parte del servicios de neonatología, siguiendo los criterios de Bell. Los pacientes seleccionados para el estudio fueron neonatos con enterocolitis grado 1, los cuales al momento del ingreso se encontraban estables, sin requerimiento de ventilación mecánica ni apoyo hemodinámico, y que fueron manejados con leche materna exclusiva o de manera tradicional, para posteriormente separarlos en los dos grupos de interés: grupo 1 (manejo tradicional) y grupo 2 (leche materna exclusiva). Los neonatos asignados al grupo 1, fueron manejados con alimentación parenteral (NPT), ayuno y descompresión gástrica. En cuanto al grupo manejado con leche materna exclusiva (grupo 2), inició con 20mL/kg/día de leche materna por tres días, avanzando 20mL/kg/días según la tolerancia, hasta llegar a 140-160mL/kg/día. Dándose en ambos casos antibiótico de amplio espectro (cefotaxima más amikacina).

Se excluyeron expedientes incompletos o ilegibles y se eliminaron a pacientes con otra patología gastrointestinal (íleo meconial, tapón meconial, fibrosis quística), pacientes con tratamiento quirúrgico de patología neurológica, cardiopulmonar y pacientes que fueron trasladados a otra unidad.

A fin de encontrar la asociación entre los pacientes con LME y manejo convencional se utilizó la ji cuadrada o la prueba Exacta de Fisher cuando la primera no se pudiera ocupar, con una $p \leq 0,05$. Para los cálculos estadísticos se utilizaron medidas de tendencia central y de dispersión. Y se buscó saber la normalidad de la muestra con la prueba de Kolgomorov-Smirnof. Al tener normalidad, se empleó estadística paramétrica mediante la prueba T de student, de lo contrario la prueba de U de Mann-Whitney. Se recolectaron y analizaron los datos utilizando el programa IBM SPSS en su versión 25 para Windows.

Resultados

Se revisaron 65 expedientes de 1 de enero del 2016 a 15 de junio del 2021, de los cuales se excluyeron 12 por no contar con archivo clínico completo, se eliminaron a 5 que fueron operados en otra unidad y a 6 por presentar patología asociada. Se obtuvo una muestra de 42 pacientes los cuales fueron divididos en dos grupos: grupo 1 con LME (23 pacientes) y grupo 2 con manejo tradicional (19 pacientes). En el grupo 1, 43% fueron del sexo masculino y 57% del femenino. Y en el grupo 2, 58% correspondieron al sexo masculino y 42% al sexo femenino. La edad en días, semanas de

gestación, peso en kilogramos y estancia intrahospitalaria se encuentran en la **tabla I.** 78%[18] de los pacientes con LME se resolvió sin intervención quirúrgica y solo el 22% (5 pacientes) necesitaron intervención quirúrgica. El grupo manejado con tratamiento tradicional, en cambio tuvo necesidad de intervención quirúrgica en un 63% (12 pacientes) p 0.01. **Tabla II**.

Requirieron ventilación mecánica 17% (4 pacientes) de los pacientes con LME y 58% (11 pacientes) de los pacientes con tratamiento convencional. **Tabla II**. Los días de ventilación fueron de 1 a 3 días en un 26% (5 pacientes) de los pacientes con tratamiento convencional, de 4 a 6 días de un 16% (3 pacientes) de los recién nacidos con manejo convencional y 9% (2 pacientes) de los pacientes con LME, de 7 a 10 días en 9% (2 pacientes) de los pacientes con leche materna exclusiva, y mayor a 10 días en un 16% (3 pacientes) de los de manejo convencional y, requiriendo únicamente en los pacientes con manejo tradicional ventilación mecánica por un tiempo mayor de 10 días ($p \leq 0,05$). **Tabla III**.

Los pacientes con LME que presentaron clínica de sepsis durante el padecimiento fueron el 39% (9 pacientes) y de los manejados con tratamiento convencional fueron 84% (16 pacientes).

Discusión

La leche materna disminuye el pH gástrico, aumenta la motilidad intestinal, cambia la flora bacteriana a especies no patógenas y disminuye la permeabilidad epitelial. También tiene componentes inmunes que fomentan la maduración del sistema inmunológico de la mucosa intestinal[9]. Tal como se comprueba en el actual estudio la leche materna exclusiva genera un factor protector ante la ECN.

En el actual estudio las semanas de gestación y el peso al nacimiento no fueron significativos, en cambio en el estudio de Huston, et al[10]. sí tuvieron relevancia significativa. En otro estudio Zamrik et al[11] demostraron que existe un cambio relacionado con la edad gestacional, el peso al nacer y la edad materna con respecto al grupo con manejo tradicional y al grupo alimentado con LME, mientras que en el actual estudio encontramos que existe un cambio relacionado con la edad del paciente en días y la estancia intrahospitalaria (EIH).

Sullivan et al[12] mencionan que los grupos que recibieron una dieta con LME tuvieron tasas significativamente más bajas de enterocolitis necrotizante que requirieron intervención quirúrgica. Por su parte Hair et al[13] encontraron que el uso de LME disminuyó la incidencia tanto médica como quirúrgica y la aparición de infecciones tardías, lo que respalda aún más los resultados del actual estudio.

En cuanto a la EIH, encontramos que fue significativamente mayor en el grupo con manejo tradicional en comparación con el grupo de LME. Así mismo, Assad et al[14] demostraron que la EHI disminuyó estadísticamente en los pacientes con ECN alimentados con LME.

En el estudio de Assad et al[14] no se encontraron cambios significativos en el manejo respiratorio o cambios en el protocolo de selección de oxígeno durante el período de estudio. En cambio, en el actual estudio se demostró que no solamente disminuyó la necesidad de ventilación mecánica (VM) en el grupo alimentado con LME, sino que también mejoró el pronóstico en relación los días de necesidad de VM.

Se concluye que la leche materna tiene un efecto positivo en los pacientes con ECN, declaración demostrable en los resultados del proyecto, siendo destacable la diferencia

Tabla I: Medidas de tendencia central y de dispersión de la edad, peso, SDG y EIH.

	Manejo tradicional				Leche materna exclusiva				p
	Media	Mediana	DE	Rango	Media	Mediana	DE	Rango	
Edad (días)	8,6	8	7,4	1:31	13,4	12	8,2	3; 30	0.03
Peso en Kg	1,8	1,8	0,8	0,7; 3,8	1,9	1,91	0,8	0,9; 3,3	0.46
SDG	33,1	33	3,8	27,4; 39	34,9	35,4	3,5	28; 41	0.13
EIH	33,8	30	20	8; 68	21,6	18	15,6	4; 62	0.03

Tabla II: Requerimiento de ventilación mecánica y cirugía en los dos grupos de enterocolitis necrosante.

	Manejo tradicional	Leche materna exclusiva	p
Ventilación	11 (58%)	4 (17%)	0.006
Cirugía	12 (63%)	5 (22%)	0.01

Tabla III: Ventilación mecánica.

	MANEJO TRADICIONAL					LECHE MATERNA EXCLUSIVA					p
	No tuvo	1-3 días	4-6 días	7-10 días	>10 día	No tuvo	1-3 días	4-6 días	7-10 días	>10 días	
Tiempo en días de uso de VM	8(42%)	5 (26%)	3(16%)	0	3 (16%)	19 (84%)	0	2 (9%)	2 (9%)	0	0.001
TOTAL					19					23	42

VM: Ventilación mecánica.

en cuanto al requerimiento de intervención quirúrgica entre los pacientes del grupo con manejo tradicional y los pacientes manejados con LME. Resultados esperados ya que esta brinda protección inmunológica por sus características mismas. Por lo que es de importancia incentivar la leche materna, ya sea de la misma madre o donada, siendo necesario el uso de lactarios y la promoción de la donación de leche materna.

Conflicto de Intereses: en este estudio no existen conflictos de interés.

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ORIGINAL

Age and gender-associated radiological findings in COVID-19 infection

Hallazgos radiológicos asociados a la edad y al sexo en la infección por COVID-19

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Abstract

Objectives: At present, the novel coronavirus disease 2019 (COVID-19) pandemic is the most important infectious disease worldwide. Due to false positives and false negatives of PCR results in the diagnosis of coronavirus infection, Computed Tomography (CT) is especially important in the initial diagnosis and assessment of the intensity of COVID-19 infection. According to the stage and intensity of COVID-19 infection chest CT scan findings display different features. Although men, women, and different age groups may be equally affected, different epidemiological studies have shown differences in gender and age in intensity and mortality. Although there are many studies on radiological findings in COVID-19 infection, however limited literature reviews have been stated on the relationship between age and gender with radiological finding. Methods: This reviews summarized studies that evaluated the association age and gender with radiologic CT fndings.
Results: In general, the findings of these studies show that different age and gender groups have different characteristics which can role in primary diagnosis, facilitate the classification of the initial prognosis in COVID-19 pneumonia.
Conclusions: As an indicator for outcome, treatment, determining the intensity of the disease as well as the prognosis, nevertheless studies with higher sample sizes and multicenter are required.

Keywords: COVID-19, Ct scan findings, age, gender.

Resumen

Objetivos: En la actualidad, la pandemia de la nueva enfermedad por coronavirus 2019 (COVID-19) es la enfermedad infecciosa más importante a nivel mundial. Debido a los falsos positivos y falsos negativos de los resultados de la PCR en el diagnóstico de la infección por coronavirus, la Tomografía Computarizada (TC) es especialmente importante en el diagnóstico inicial y la evaluación de la intensidad de la infección por COVID-19. Según el estadio y la intensidad de la infección por COVID-19, los hallazgos de la TC torácica presentan características diferentes. Aunque los hombres, las mujeres y los diferentes grupos de edad pueden estar igualmente afectados, diferentes estudios epidemiológicos han mostrado diferencias de género y edad en la intensidad y la mortalidad. Aunque hay muchos estudios sobre los hallazgos radiológicos en la infección por COVID-19, sin embargo se han establecido revisiones bibliográficas limitadas sobre la relación entre la edad y el género con el hallazgo radiológico. Métodos: Esta revisión resume los estudios que evaluaron la asociación entre la edad y el género con los hallazgos radiológicos de la TC.
Resultados: En general, los hallazgos de estos estudios muestran que los diferentes grupos de edad y género tienen características diferentes que pueden jugar un papel en el diagnóstico primario, facilitando la clasificación del pronóstico inicial en la neumonía por COVID-19.
Conclusiones: Como indicador del resultado, del tratamiento, determinando la intensidad de la enfermedad así como el pronóstico, no obstante se requieren estudios con mayor tamaño de muestra y multicéntricos.

Palabras clave: COVID-19, hallazgos de la tomografía computarizada, edad, género.

Introduction

At present, the novel coronavirus disease 2019 (COVID-19) p pandemic is the most important infectious disease worldwide and causing the death of 5,484,439 people until January 06, 2022[1].The virus is transmitted through airborne droplets, air, and physical contact from person to person. The incubation period of this disease differs between 2 to 7 days (average 4 days) and can even last up to 24 days[2]. The range clinical finding of COVID-19 are wide, from no symptoms to fever, acute respiratory distress syndrome, multiple organ failure, and death[3]. The most important common symptom of COVID-19 is fever, dry cough and tiredness. Symptoms of this condition might comprise of shortness of breath or difficulty breathing, muscle aches, chills, sore throat, runny nose, headache, or chest pain[4]. Although the clinical signs are mild in more than 80% of patients, however risk factors advanced age and comorbidity (eg. diabetes mellitus, high blood pressure, heart disease, chronic kidney failure and tumor linked with increase admission to intensive care unit (ICU), need mechanical ventilation, and death or critical states of the disease especially acute respiratory distress syndrome[5,6]. Therefore, early isolation and diagnosis and timely treatment can be effective in reducing mortality[7].

Diagnosis of COVID-19

çFast and precise diagnosis of COVID-19 is essential to detect and manage infected individuals, track contact, epidemiological identification, and make general health decisions[8]. COVID-19 can be diagnosed by clinical diagnostics and molecular tests[9]. Clinical diagnostics such as symptoms, laboratory indicators are not limited to SARS-CoV-2 infection, and totally of them might be suspected of having COVID-19, nevertheless it does not show conclusive confirmation[10]. Molecular reverse-transcription polymerase chain reaction (RT-PCR) is the definite and golden standard diagnostic test for recognition of RNA virus in nasal or throat swab SARS-CoV-2 infected patients, but have low sensitivity[11]. Nevertheless, this method may have false-negative results because of improper sampling time relative to infection, inappropriate sampling method, insufficient preservation of specimens, and technical limitations[12]. On the other hand, false-positives might happen lead to technical errors, specially contamination during the manual RT-PCR method. Subsequently, RT-PCR alone cannot be a reliable, independent, and exclusive test for screening people suspected of having COVID-19[13]. Therefore, negative results do not indicate that a person does not have COVID-19 infection and CT scans should be used in addition to PCR testing to screen and diagnose COVID-19 infection[14].

COVID-19 infection according to age and gender

Currently, epidemiological statistics show that age, gender and type of underlying disease are high risk factors for COVID-19 disease. Related risk factors, underlying diseases, and biological differences that differ with gender and age may lead to in outcomes COVID-19 infection specially mortality[15,16]. Also susceptibility COVID-19 varies due to biological differences at different ages and between gender. Mortality from COVID-19 increases dramatically in older ages, with very few deaths demonstrated under the age of 50. Therefore, the age and gender pattern of infections in combination with the age and gender composition of the population is essential to describe the difference between COVID-19 transmission and mortality worldwide[17]. Elderly is known as a risk factor compared to young and middle-aged people, which is mostly due to reduced immunity due to weakness and higher prevalence of chronic diseases in the elderly population[18]. Another important factor in the difference in COVID-19 mortality is gender, in which there are many gender differences and men are at higher risk than women, which may be related to gender hormones such as testosterone and estrogen, so that the immune response and the presence of other risk factors, for example diabetes, hypertension and cardiovascular disease that affects men more than women[19,42]. In general, the detected COVID-19 positive cases are high, especially in people between 35 and 65 years old. This group, which comprises mainly of the elderly population, accounts for 50% of the confirmed positive cases, indicating that the infection does not only affect the elderly. COVID-19 is more common in men aged 55 to 80 than in women, but more positive cases have been seen in women aged 15 to 55 and over 80[19]. In general, the mortality rate is higher among men for all age groups. Male and older patients with more comorbidities have an unfavorable survival outcome[20]. The immune system plays an important role in preventing various viruses, including COVID-19. The human's natural immune system adapts from the embryonic to the neonatal stage, matures from adolescence to adulthood, changes during pregnancy, and decreases in old age[21]. These changes in the immune system have a higher risk of complications in infants, pregnant women and the elderly. Numerous factors role in discriminating the immune system based on gender and age[22]. Changes in the level / number of immunoglobulins, CD4 and CD8 cells, B cells, T cells in men and women may cause changes in COVID-19 cases and death. Overall age and gender differences in COVID-19 infection can be effective as a prognostic factor in determining survival outcome, prevention and treatment[23].

CT findings and COVID-19

Chest CT scanning is convenient, fast with higher sensitivity than RT-PCR which used for early diagnosis and evaluation intensity COVID-19 infection[24]. Numerous studies have shown specific features of lung CT images in patients with COVID-19, which is a reliable source for diagnosis[25]. The CT intensity score index was calculated according the amount of lobar involvement (0:0%; 1, <5%; 2:5-25%; 3:26-50%; 4:51-75%; 5, >75%; range 0-5; total score 0-25)[26]. Based on the stage and intensity of COVID-19 infection chest CT scan findings display different features and could contain several bilateral ground-glass opacities in the peripheral lower lung zones[27]. The ground glass opacities (GGO), consolidation, septal thickening mostly with the subpleural lungs or bronchovascular bundles or diffusely in the whole lungs reported as CT characteristic features of COVID-19[28]. Although men, women, and different age groups may be equally affected, different epidemiological studies have shown differences in gender and age in intensity and mortality. Many studies on radiological findings in infection have been done[29,43-45]. Although there are many studies on radiological findings in COVID-19 infection, however limited literatures have been shown the relationship between age and sex with radiological finding and most of the available studies have compared the COVID-19 disease between children and adults without age group[30]. This reviews summarized studies that evaluated the association age and sex with radiologic CT fndings.

Classification of chest CT results in COVID-19 patients by gender and age

In the Alper Karacan et al study in Turkey the ground-glass opacity and consolidation, the tree-in-bud pattern, the halo signs, the thin reticular pattern and crazy-paving pattern were the most common CT scan fndings in age groups under 20 years of age, 20-29 age group, 30-39 years, 60-79 years and over 80 years respectively. Also in men centrilobular nodules, airway changes, and tree-in-bud pattern were considerably greater compared with women. They concluded that due to the high prevalence of radiological findings in the elderly and men, therefore, the prognosis of the disease plays an important role in these groups[31]. Another study by Behnaz Moradi et al. in Iran reported that peripheral distribution was more frequently in men >60 years than, while women >60 years demonstrated peribronchovascular distribution pattern. Also in men <60 years' anterior distribution of opacities more frequently than with women. In term of CT-scores women <60 years have been shown significantly lower intensity scores which is associated with predicting poor prognosis[32].

The study by Selçuk Parlak et al. examined the effect of age on CT scan features and the intensity of COVID-19 disease. Their results showed that ground-glass opacity was the most common CT scan features in all age groups. CT scan findings including consolidations, crazy-paving patterns, air bronchograms and the number of lesions were higher frequency in older patients than other age groups. Also the upper lobe and right middle lobe were more involved in older patients. Overall, they concluded that these CT scan findings observed in older patients are associated with as an indicator for worse outcomes[33].

Huanhuan Liu et al study in China evaluated that GGO and consolidation were the typical CT scan finding in non-pregnant adults and the pregnant women respectively, while children shown mild pulmonary involvement with a focal GGO or consolidation[34].

Dangis et al showed that CT intensity scores were significantly higher in men with a tendency to bilateral lung involvement. The difference in the score of lung involvement was more noticeable in the advanced and peak stages of the disease[35].

In a study by Wang et al. in China surveyed the relationship different CT findings in three age groups. The results of this study presented that in the elderly, more lobes as well as more subpleural lesions were affected and also on the other hand in term of crazy paving sign, bronchodilatation and pleural thickening a significant difference was observed between Group 1&2, Group 2&3 with more frequently in the elderly group. They concluded that determining the radiological characteristics of patients based on age will be useful in the primary definitive diagnosis COVID-19[36]. Ammar Mosa et al in Iraq showed that there is a noteworthy relationship between male gender and enhancing age between CT intensity scores[37].

A study by Abdelwahab et al indicated that in terms of gender distribution, consolidation of CT scan findings was significantly more common in women than men, while other radiological patterns, distribution of radiological abnormalities, and CT intensity score in both there was no statistically significant difference between the gender groups[38].

The study of Qianbiao Gu et al. in China demonstrated that although there is no statistically significant relationship between gender distribution in radiological characteristics of patients, but thickened interlobular, honeycomb pattern and nodular infiltration there were significant differences between younger and elderly group patients. Also there was also a statistically noteworthy relationship between patient CT score and age[39].

A study by Chao Jin and colleagues showed that there are significant differences between pattern-categories CT

scan with age. As the age increases, the scoring pattern of CT scan findings increases and the older patients show diffuse alveolar damage pattern. Also in this study most men indicated multifocal lesions with a peripheral distribution predominantly in the middle to lower lung zones and GGO or consolidation, or interlobular septal thickening pattern. They concluded that classification of the CT pattern along with clinical features such as age could facilitate the classification of the initial prognosis in COVID-19 pneumonia[40].

The study by Russell et al. exhibited that there was no statistically significant difference in age and gender distribution in different categories of radiological abnormalities from mild to severe, however, the frequency of multifocal and bilateral findings was higher in women than men, but this was not statistically significant. They concluded that neither age nor gender had a statistically significant effect on the intensity or type of CT scan findings[41]. **Table I** presented studies which compare CT findings of COVID-19 infection in different gender and age.

Table I: Summary of studies conducted from compare CT findings of COVID-19 infection in different gender and age.

Study (year)	Country	Common or compare CT scan finding according gender or age group	Conclusion
Alper Karacan	Turkey	· Under 20 years: GGO and consolidation · 20-29 years: tree-in-bud pattern · 30-39 years: halo signs · 60-79 years: thin reticular pattern and crazy-paving pattern · over 80 years: crazy-paving pattern · Also in men centrilobular nodules, airway changes, and tree-in-bud pattern were considerably greater compared with women	They concluded that due to the high prevalence of radiological findings in the elderly and men, therefore, the prognosis of the disease plays an important role in these groups
Selçuk Parl	Turkey	· CT scan findings including consolidations, crazy-paving patterns, air bronchograms and the number of lesions were higher frequency in older patients compared with other age groups · the upper lobe and right middle lobe were more involved in older patients	CT scan findings observed in older patients are associated with as an indicator for worse outcomes.
Moradi	Turkey	· Peripheral distribution was more frequently in men > 60 years than, while women > 60 years demonstrated peribronchovascular distribution pattern · In men <60 years' anterior distribution of opacities more frequently than women · In term of CT-scores women < 60 years have been shown significantly lower intensity scores	Chest CT stratified by age can used for evaluation prognosis infection
Huanhuan Liu et	China	· Pregnant women: GGO · Non-pregnant adults: consolidation · Children: mild pulmonary involvement with a focal GGO or consolidation	CT can be a reliable method for primary diagnosis, evaluate the intensity and timely impact of therapeutic effects
Dangis	Belgium	· Dangis et al showed that CT intensity scores were significantly higher in men with a tendency to bilateral lung involvement.	The difference in the score of lung involvement between men and women was more noticeable in the advanced and peak stages of the disease.
Wang et al	China	· In the elderly, more lobes as well as more subpleural lesions were affected · -crazy paving sign, bronchodilatation and pleural thickening were more frequently in the elderly group.	Determining the radiological characteristics of patients based on age will be useful for the early definitive diagnosis of COVID-19.
Abdelwahab	Egypt	· Consolidation of CT scan findings was significantly more common in women than men · Other radiological patterns, distribution of radiological abnormalities, and CT intensity score in both there was no statistically significant difference between the gender groups.	---
Ammar Mosa	Iraq	· CT intensity score is higher with male and older patients.	---
Qianbiao Gu	China	· There is no statistically significant relationship in terms of gender distribution in radiological characteristics of patients · Thickened interlobular, honeycomb pattern and nodular infiltration there were noteworthy differences between younger and elderly group · A statistically significant relationship among patient CT score and age.	CT classification, especially by age, can play an important role in early diagnosis and intervention
Chao Jin	China	· There are significant differences between pattern-categories CT scan with age. · As the age increases, the scoring pattern of CT scan findings increases and the older patients show diffuse alveolar damage pattern. · Most men indicated multifocal lesions with a peripheral distribution predominantly in the middle to lower lung zones and GGO or consolidation, or interlobular septal thickening pattern	Classification of the CT pattern along with clinical features such as age could facilitate the classification of the initial prognosis in COVID-19 pneumonia
Russell	USA	· That there was no statistically significant difference in age and gender distribution in different categories of radiological abnormalities from mild to severe · The frequency of multifocal and bilateral findings was higher in women than men, but this was not statistically significant	Neither age nor gender had a statistically significant effect on the intensity or type of CT scan findings.

Conclusion

Given that CT scan have an essential impress in the diagnosis, treatment and intensity of COVID-19 disease, therefore the relationship between demographic information and other clinical findings of patients with CT scan findings is important. As mentioned, few studies have been conducted to evaluate radiological findings in terms of age and gender distribution. Overall, the findings of these studies show that the characteristics and scores of CT scans vary in different age and gender groups, however, in a number of studies, this relationship was not statistically significant. In general, the intensity and type of radiological findings were higher in the elderly compared to other groups, but these findings varied by gender in different studies. Differences in the characteristics and scores of CT scans in diverse age and gender groups can role in primary diagnosis, facilitate the classification of the initial prognosis in COVID-19 pneumonia, as an indicator for outcome, treatment, determining the intensity of the disease as well as the prognosis, nevertheless studies with higher sample sizes and multicenters are required.

Conflicto de Intereses: en este estudio no existen conflictos de interés.

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ORIGINAL

Impact of pharmacist intervention on prescribing pattern of anticoagulation in patients admitted to intensive care unit in a Tertiary Care Hospital, India

Impacto de la intervención del farmacéutico en el patrón de prescripción de anticoagulación en pacientes ingresados en la unidad de cuidados intensivos en un Hospital de Atención Terciaria, India

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Abstract

Objectives: To assess and compare the International Normalized Ratio (INR) results between a physician (Retrospective) and clinical pharmacist dosing (Prospective) of Oral Anticoagulation drugs and to analyze the control of INR and incidence of complications during clinical pharmacist managed therapy.
Methodology: A prospective hospital-based observational study was carried out for 6 months at Tertiary Care Hospital, Bangalore. The research student attended ward rounds on daily basis and collected the cases which were mentioned under inclusion criteria. The pattern of prescribing was checked from the medication chart and the case sheet was analyzed for any drug-related problems.
Results: During our study period, 86 patients were forwarded by the physicians to the clinical pharmacist managing the oral anticoagulation clinic. Only 70 patients could complete the study, where 4 patients did not visit the clinic, other 12 patients did not meet the inclusion criteria and hence they are excluded. The data were collected using the data collection form for the study sample. After the interventional study, there was a significant improvement in patients maintaining % of INRs which were in target therapeutic range, % of transthyretin (TTR) along with decreased adverse effects. It was also found that patient's awareness of the target INR values is correlated with the improved accuracy of anticoagulation control.
Conclusion: Hence, our study results reflect the need for a clinical pharmacist in oral anticoagulation management and the necessity of implementing anticoagulation services in various hospital settings. The clinical pharmacist managing anticoagulation service was able to achieve the INRs of the patient in to target therapeutic range by proper and timely dose adjustments based on the INR value, to identify adverse drug reactions/ adverse events, drug-drug interactions, and drug-food interactions and bring about proper interventions by working in association with physicians.

Key words: Anticoagulant, clinical pharmacist intervention, INR results, physician intervention.

Resumen

Objetivos: Evaluar y comparar los resultados del índice internacional normalizado (INR) entre un médico (Retrospectivo) y la dosificación del farmacéutico clínico (Prospectivo) de los fármacos de Anticoagulación Oral y analizar el control del INR y la incidencia de complicaciones durante la terapia gestionada por el farmacéutico clínico.
Metodología: Se llevó a cabo un estudio observacional prospectivo basado en el hospital durante 6 meses en el Tertiary Care Hospital, Bangalore. El estudiante de investigación asistió a las rondas diarias y recogió los casos mencionados en los criterios de inclusión. Se comprobó el patrón de prescripción a partir del cuadro de medicación y se analizó la hoja de casos para detectar cualquier problema relacionado con los medicamentos.
Resultados: Durante el período de estudio, los médicos remitieron 86 pacientes al farmacéutico clínico que gestionaba la clínica de anticoagulación oral. Sólo 70 pacientes pudieron completar el estudio, donde 4 pacientes no acudieron a la consulta, otros 12 pacientes no cumplían los criterios de inclusión y por tanto están excluidos. Los datos se recogieron mediante el formulario de recogida de datos de la muestra del estudio. Tras el estudio de intervención, hubo una mejora significativa en los pacientes que mantuvieron el % de INRs que estaban en el rango terapéutico objetivo, el % de transtiretina (TTR) junto con la disminución de los efectos adversos. También se descubrió que el conocimiento de los pacientes de los valores INR objetivo se correlaciona con la mejora de la precisión del control de la anticoagulación.
Conclusión: Por lo tanto, los resultados de nuestro estudio reflejan la necesidad de un farmacéutico clínico en la gestión de la anticoagulación oral y la necesidad de implementar servicios de anticoagulación en varios entornos hospitalarios. El farmacéutico clínico que gestiona el servicio de anticoagulación fue capaz de conseguir que los INR de los pacientes estuvieran dentro del rango terapéutico objetivo mediante ajustes de dosis adecuados y oportunos basados en el valor del INR, para identificar reacciones adversas a los fármacos/eventos adversos, interacciones entre fármacos y alimentos y llevar a cabo intervenciones adecuadas trabajando en asociación con los médicos..

Palabras clave: Anticoagulante, intervención del farmacéutico clínico, resultados del INR, intervención del médico.

Introduction

The primary intent of the drug utilization pattern is to smooth the process & rational use of drugs in the population. Drug Utilization Evaluation (DUE) is a study to identify variability in drug use & to support interventions that will improve patient's therapeutic outcomes. Drug use indicators are intended to measure specific aspects of health providers & drug use in a hospital or health center. Indicators will provide information to health care managers concerning drug use, prescribing habits & important views of patient care[1].

Anticoagulants are the drugs which are usually referred to as blood thinners[2] and these are prescribed in clinical settings to treat hospitalized patients like acute and deep venous thromboembolism (VTE), unstable angina, atrial fibrillation[3] and to prevent coronary arteries from blockage and in cardiac invasive procedures. Anticoagulants are highly prescribed in cardiology and neurology departments. For more than 40years the only anticoagulants available to clinicians are Coumarins and unfractionated Heparin (UFH)[4]. With the simplicity of subcutaneous administration treatment and prevention of thromboembolism by Unfractionated Heparins and Coumarins are potentially now replaced during the past decade by Enoxaparin and Dalteparin which are low molecular weight heparins[2]. Anticoagulation management is a challenging task for health care professionals especially for clinical pharmacists, because of the individual variability in response to the anticoagulants, alterations in a patient's consumption of vitamin K- rich foods and alcohol, change in medications, or change in health status all of which can alter the INR values. It is important to manage anticoagulation therapy of patients in a department like cardiology as many drug-related problems and patient non-compliance are common and hence there is a need for better pharmaceutical care and effective care that can be provided by a clinical pharmacist[5]. Pharmacists can also bring expertise in managing oral and parenteral anticoagulation therapy of both inpatients and outpatients by providing important information regarding therapy through effective counseling and about potential interactions[6]. Therefore, we aimed to study the drug utilization pattern of anticoagulants among inpatients of Tertiary Care Hospital. Bangalore, India.

Materials and methods

The study was conducted in the cardiology ward at Tertiary Care Hospital. Tertiary Care Hospital is a 1200 bedded hospital providing secondary health care to people. A Bidirectional (prospective and retrospective) observational and interventional study will be conducted to include patients receiving oral anticoagulation drugs (Warfarin, Acitrom) among adult patients.

Data was collected using a well-structured data collection form which includes patient's demographics, clinical information which includes (indication for anticoagulation therapy, desired INR range, expected duration of therapy, anticoagulation therapy received), social habits, past medical history, current medications and the prescribed oral anticoagulant (Warfarin/Acitrom).

The International Normalized Ratio (INR) values of the study sample were collected from the hospital medical record database for 3 consecutive reviews for the physician dosing retrospectively, the PT (prothrombin time) and INR values were recorded prospectively in the clinical pharmacist managed oral anticoagulation clinic during the study period for the same selected patients on 3 regular follow-ups with the relevant source of information. INR values were monitored for the patients included in the study and dosage adjustment was done according to the standard protocol based on the INR value. The patients were also provided with effective counseling regarding the therapy and dietary modifications. All the patients were monitored for any adverse drug events/effects or any possible drug and food interactions during the study period. In case of any reported adverse events/drug interactions in the anticoagulation clinic, the proper intervention was done by the clinical pharmacist in association with a physician to achieve rational drug therapy.

Result

A total number of 70 patients who met inclusion criteria from the Inpatient ward of Tertiary Care Hospital were recruited. Out of which 34 (48%) were male and 36 (52%) were female. My result was found to be similar to the study carried by RC Anakwul et al[7] and differs from the study conducted by Hossien khalili et al[8] and Singh V *et al*.[9]

Among 70 patients included, 34 (48.19%) patients were found to be in the age group of 51-60 years which covered the majority of patients in the study, followed by 20 patients (28.91%) between the age group of 41-50 years, 46 (25%) patients between the age group of 31-40, 10 (15.66%) patients were lesser than 30 years and only one patient (7.23%) and the results are found to be similar with the study carried out by Singh V et al[9]. **Table I**.

Table I: Age distribution in the study sample.

Age Group	No. of Patients	% of Patients
18 - 30	6	7.23
31- 40	10	15.66
41-50	20	28.91
51-60	34	48.19
Total	70	100

Out of 216, INRs checked for 70 patients (total of 3 follow-ups), the target therapeutic range was found to be 100 (45.78%) and 140 (64.25%) respectively for physician and clinical pharmacist dosing. **Figure 1**, Our study results showed a significant increase in target INR values during the period of clinical pharmacist managing oral anticoagulation therapy. **Table II**, Similar results were found in the study carried out by Nadia a Amruso[10].

Figure 1: Physician Vs Clinical Pharmacist Dosing in the study sample.

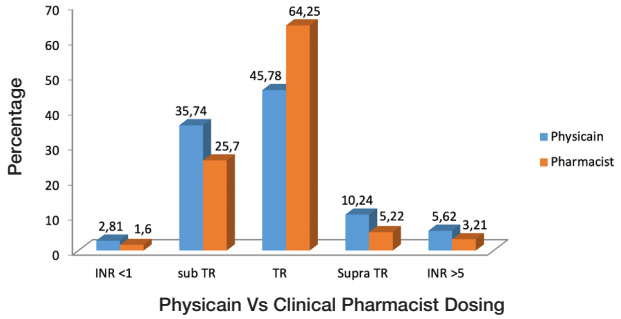

Table II: Indications for Oral Anticoagulation in the study sample.

Indications	No. of patients	% of patients
Mitral Valve Replacement (MVR)	32	38.55
Atrial Fibrillation (AF)	12	16.86
Deep Vein Thrombosis (DVT)	10	13.25
Aortic Valve Replacement (AVR)	8	12.04
Pulmonary Embolism (PE)	6	9.63
Mitral Valve Replacement MVR + Atrial Fibrillation AF	2	6.02
Total	70	100%

Table III: Management of patients with Oral Anticoagulation drugs.

Management	No. of Patients	% of Patients
Warfarin	30	45.12
Acitrom	40	54.87
Total	70	100

Table IV: Paired sample t-test for comparison of INR results in Physician and Clinical Pharmacist intervention:

INR results	Differences of the Mean	Paired t-value	Degree of Freedom	P-value
INRs in target value	-0.6642	4.803	82	< 0.0001
INRs > target value	0.1646	2.541	82	0.0088
INRs < target range	0.3002	2.608	82	0.0044
INRs > 5	0.07229	1.228	82	0.1114
INRs < 1	0.03814	1.398	82	0.1813

p value < 0.01 is significant

Tables V and **VI** show the evaluation of the frequency and cause of oral anticoagulant-related adverse effects/ events are mainly due to lack of knowledge regarding anticoagulation therapy, irregular follow-up, and unavailability of 0.5mg of Acitrom and concurrent administration of other drugs. Some of the occurred events were taken to the knowledge of the physician for further management whereas in remaining patients dose adjustment was done according to the standard protocol of oral anticoagulation therapy along with effective counseling. Our study results are also supported by the Gregory Piazza *et al.*, who conducted a similar study in anticoagulation–associated adverse events[11]. Apart from the above, drug and food interactions were also observed in few patients receiving oral anticoagulation therapy which was depicted in **table VII**.

Most of the patients received useful information from an anticoagulation service and the convenience, accessibility, and services provided by the clinical pharmacist were better. This was assessed by questioning patients/caretakers answering a set of satisfaction assessment questionnaires and about satisfaction was reported in the present study. Similar studies Lakshmi R *et al.*[12], also support the fact of patient satisfaction by the anticoagulation service offered by the clinical pharmacist.

Table V: Fraction of INRs in the therapeutic range for the study sample.

INR results	Physician	Clinical Pharmacist
Total INR's checked	216	216
INR's within TR	86	130
Fraction of INR within TR	0.457	0.642

After the interventional study, there was a significant improvement in patients maintaining % of INRs which were in target therapeutic range, % of transthyretin (TTR) along with decreased adverse effects. It was also found that patient's awareness of the target INR values is correlated with the improved accuracy of anticoagulation control. Hence, our study results reflect the need for a clinical pharmacist in oral anticoagulation management and the necessity of implementing anticoagulation services in various hospital settings.

My study suggests that there is a strong relationship between the safety of anticoagulants and BMI. According to my study, adverse drug reactions were observed mostly in patients with normal BMI compared to overweight and obese patients with a P-value of 0.058, which is statistically significant. The result was found to be similar to the study carried out by Avgil *et al*[13].

The fate of the ADR is decided based upon the severity of the reactions and also by the need for the drug. Out of 15 ADRs, 11 (73.33%) drugs withdrawn, 3 (20%) dose was tapered and one drug was continued.

In all drug interactions identified, it was observed that Enoxaparin was involved in interactions with other drugs like Aspirin, Acenocoumarin, and Fondaparinux, and the results were found to be similar to the study carried out by Sing V *et al*[9]. **Table IX**.

The safety and effectiveness of any medical therapy depend on taking their medication as prescribed and the extent of this is defined as medication adherence.

Table VI: Adverse Drug Event Occurred in Anticoagulation Clinic:

Enrolling anti-coagulation clinic	Drug	Adverse event	Hospitalalized	Cause	Clinical Pharmacist Intervention	Outcome
Subtherapeutic INR (< 2)						
Yes	Acitrom	Chest tightness, Upper body discomfort	No	Missed follow-up	Dose adjustment done	Recovered
Yes	Acitrom	Tenderness in shoulder Joints	No	Took Hopace (Ramipril) Thinking as Acitrom	Counseled the patient about the drug	Recovered
Yes	Acitrom	Chest tightness	No	Took 2MG Instead of 2.5Mg (due to unavailability of (0.5mg) at Hospital Pharmacy	Dose adjusted	Recovered
Yes	Acitrom	Chest tightness	No	Patient Stopped Drug By Tappering the Dose And Tried to Manage by yoga (not took drug)	Counseled the patient about the Disease And Therapy	Recovered
Supra therapeutic INR (> 5)						
Yes	Acitrom	Haematuria	Yes	Took 8mg instead of 4mg	Informed to Physician	Recovered
Yes	Warfarin	Tongue Bleeding	Yes	Took NSAID's	Informed to Physician	Recovered
Yes	Warfarin	Bleeding Stools	Yes	Missed Follow up with anticoagulation clinic	Informed to Physician Hb-6gm/dl	Transfused, Recovered
Yes	Warfarin	Black color stool	Yes	Irregular follow-up	Informed to physician	Recovered
Yes	Acitrom	Haematuria	Yes	Unknown cause	Informed to physician	Recovered

Table VII: Drug and Food Interactions observed in the study sample.

	Interacting agents	Drug	Interactions	Nº of occurrence	Clinical Pharmacist intervention
Drug Interaction	Tegritol (Carbamazepine)	Warfarin	Increased anticoagulation effect	1	Informed to physician and regimen was changed to Epilive (Levetiracetam)
	Trapic-MF (Tranexamic Acid)	Warfarin	Increased anticoagulation effect	1	Patient Counseled not to take OTC medications and to consult physician on any disability and inform the physician about the anticoagulant drug
Food Interactions	Green Tea	Warfarin (3) /Acitrom (2)	Decreased INR	3	Patient Information given on interaction of green tea with the drug

Table VIII: Distribution of ADRs Based on BMI.

BMI	SAFETY		TOTAL	P-Value*
	ADR	NO ADR		
UNDERWEIGHT	1(8.3%)	5(4.1%)	6(4.4%)	0.058
NORMAL	9(75%)	50(40.7%)	59(43.7%)	
OVERWEIGHT	2(16.7%)	44(35.8%)	46(34.1%)	
OBESE	0(0%)	24(19.5%)	24(17.8%)	
TOTAL	12(100%)	123(100%)	135(100%)	

Table IX: Details on Individual Drug-Drug Interactions.

DRUG-DRUG COMBINATION	INTERACTING DRUG	PHARMACOLOGICAL RESPONSE	FREQUENCY
Enoxaparin	Aspirin	Hemoptysis	1
Enoxaparin	Aspirin	Epistaxis	1
Enoxaparin	Acenocoumarin	Increase INR	2
Enoxaparin	Fondaparinux	Hypokalemia	1
	TOTAL		5

Poor adherence is an important factor to consider when explaining the instability of anticoagulation control and the impact of under-dosing on the outcomes of patients receiving anticoagulants. In my study, poor adherence was observed in conditions such as cancer, deep venous thrombosis, and embolic encephalopathy. Fever, forgetfulness, and cost were the most common reasons for non-adherence. Our results were found to be similar to a study carried by RA Rodriguez *et al*[3]. **Table X**.

Table X: Medication Adherence Level of Patients.

DRUG	FREQUENCY	PATIENT CONDITION	MMAS- 8 SCORE	LEVEL OF ADHERENCE	REASON FOR NON-ADHERENCE
Inj.Enoxaparin 40mg	OD	Cancer	4	Poor	Fever
Tab.Dabigatran (110mg)	BD	DVT	3	Poor	Costly
Tab.Acenocoumarol (2/3mg)	OD	Embolic Encephalopathy	4	Poor	Forgetness
Inj.Enoxaparin 60mg	BD	Sub Clavian Thrombosis	8	High	_
Tab.Acenocoumarol (10mg)	OD	Respiratory Disorders	6	Moderate	_
Inj.Enoxaparin 40mg	OD	Pulmonary Embolism	8	High	_
Inj.Enoxaparin 40mg	BD	Cortical venous Thrombosis	6	Moderate	_
Tab.Acenocoumarol (1mg)	OD	LRTI	7	Moderate	_
Tab.Acenocoumarol (3mg)	OD	Shock	7	Moderate	_

Conclusion

Anticoagulants are medicines that help prevent blood clots. They're given to people at a high risk of getting clots, to reduce their chances of developing serious conditions such as strokes and heart attacks. A blood clot is a seal created by the blood to stop bleeding from wounds. While they're useful in stopping bleeding, they can block blood vessels and stop blood from flowing to organs such as the brain, heart, or lungs if they form in the wrong place. Anticoagulants work by interrupting the process involved in the formation of blood clots. They're sometimes called "blood-thinning" medicines, although they don't make the blood thinner. Although they're used for similar purposes, anticoagulants are different from antiplatelet medicines, such as low-dose aspirin and clopidogrel.

Due to the increased number of patients receiving OAT it is quite difficult for the physician to educate all the patients due to lack of time. From our study, we concluded that the clinical pharmacist managing anticoagulation service was able to achieve the INRs of the patient in to target therapeutic range by proper and timely dose adjustments based on the INR value, to identify adverse drug reactions/ adverse events, drug-drug interactions and drug-food interactions and bring about proper interventions by working in association with physicians. Poor doctor-patient communication can also be overcome by the involvement of clinical pharmacists in anticoagulation management through effective counseling regarding the medication, the importance of monitoring INR values, lifestyle, and dietary modifications. Moreover, clinical pharmacists can also act as good communicators between physicians and patients.

In my study, 15 adverse drug reactions were observed in 13 patients and out of 15 ADRs, statistical analyzing, gender and BMI and the result was found to be statistically insignificant for age and gender with P-value of 0.462 and 0.217 respectively, whereas the result was found to be statistically significant for BMI with P-value of 0.058is was done concerning. Thus, there is a strong association between BMI and ADRs related to anticoagulants. Drug interactions related to anticoagulants were observed in only 5 patients and the most common anticoagulant prone to interact with other drugs was found to be enoxaparin. Adherence to therapy is the most important factor in the success of the treatment. In my study, poor medication adherence was observed in cases of DVT, cancer, and embolic encephalopathy.

Conflict of Interest

The authors report no conflicts of interest.

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ORIGINAL

The impact of heart failure on renal functions in patients admitted to Wad-Madani Heart Center in Gezira State, Sudan 2018

El impacto de la insuficiencia cardíaca en las funciones renales en los pacientes ingresados en el centro cardíaco de Wad-Madani en el estado de Gezira, Sudán 2018

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Abstract

Background: Renal dysfunction is one of the most common co-morbidities in heart failure, and it raises mortality, morbidity, complexity, and cost of care dramatically. Renal impairment is linked to poor outcomes in heart failure patients.
Objectives: The goal of this study was to assess the prevalence of renal function impairment, as well as clinical predictors and hospital outcomes of renal impairment, among hospitalized heart failure (HF) patients.
Methods: The study was conducted at Wad-Madani Heart Center, a tertiary hospital that serves Gezira and the surrounding state. All adults admitted to Wad-Madani Heart Center and diagnosed with heart failure between June and August 2018 are included in the study. Patients with a known instance of kidney illness, those on dialysis, and those who had had a kidney transplant were excluded. Patients file, echography report, and Renal function test reported personal and clinical data were collected in a questionnaire. There may be multiple reasons for hospitalization or etiological diagnoses for each patient.
Results: Males made up 54.5 % of the 55 patients in the study, while females made up 45.5%. Below forty years, 3.6%, between forty and sixty years, 32.7%, and above sixty years, 63.6%. Mild HF affects 29.1% of the population, whereas moderate HF affects 52.7%and severe HF affects 18.2%. Hypertension, diabetes, and smoking were the most common cofactors for HF, accounting for 81.8%, 70.9%, and 43.6%of cases, respectively. Impaired renal function developed in 87.3%of cases, whereas 16.4%had mild impairment. Renal failure developed in 32.7%of the intermediate cases, 36.4% of the severe cases, and 1.8%of the cases. Hyperkalemia affects 3.6%of people. More than 5.5 mmol/l and 52.7 hyponatremia in 1.8%of people. Heart failure is caused by isquemic heart disease (IHD) in 78.2% of cases, valve disease in 10.9% of cases, and cardiomyopathy in 20% of cases.
Conclusion: Heart failure is common in Sudan, and it is one of the leading causes of hospitalization. It is more common in men, and it increases in proportionality with age, with most cases occurring beyond sixty years. IHD is responsible for more than three-quarters of HF cases. Renal dysfunction is predicted by increased baseline serum creatinine, urea, and eGFR90 ml/min, as well as a patient's history of diabetes, high blood pressure, and smoking.

Key words: Renal dysfunction, heart failure, Heart Center.

Resumen

Antecedentes: La disfunción renal es una de las comorbilidades más frecuentes en la insuficiencia cardíaca, y aumenta la mortalidad, la morbilidad, la complejidad y el coste de la atención de forma espectacular. La disfunción renal está vinculada a malos resultados en los pacientes con insuficiencia cardíaca (IC).
Objetivos: El objetivo de este estudio fue evaluar la prevalencia del deterioro de la función renal, así como los predictores clínicos y los resultados hospitalarios del deterioro renal, entre los pacientes con insuficiencia cardíaca hospitalizados.
Métodos: El estudio se llevó a cabo en el Centro Cardíaco de Wad-Madani, un hospital terciario que atiende a Gezira y el estado circundante. Se incluyen en el estudio todos los adultos ingresados en el Centro Cardíaco Wad-Madani y diagnosticados con insuficiencia cardíaca entre junio y agosto de 2018. Se excluyeron los pacientes con un caso conocido de enfermedad renal, los que estaban en diálisis y los que habían recibido un trasplante de riñón. Se recogió en un cuestionario el expediente de los pacientes, el informe de la ecografía y los datos personales y clínicos comunicados por la prueba de función renal. Puede haber múltiples motivos de hospitalización o diagnósticos etiológicos para cada paciente.
Resultados: el 54,5% de los 55 pacientes del estudio eran varones, mientras que el 45,5% eran mujeres. Menores de cuarenta años, 3,6%, entre cuarenta y sesenta años, 32,7%, y mayores de sesenta años, 63,6%. La IC leve afecta al 29,1% de la población, mientras que la moderada afecta al 52,7% y la grave al 18,2%. La hipertensión, la diabetes y el tabaquismo fueron los cofactores más frecuentes de la IC, representando el 81,8%, el 70,9% y el 43,6% de los casos, respectivamente. El 87,3% de los casos presentaba deterioro de la función renal, mientras que el 16,4% tenía un deterioro leve. La insuficiencia renal se desarrolló en el 32,7% de los casos intermedios, en el 36,4% de los casos graves y en el 1,8% de los casos. La hiperpotasemia afecta al 3,6% de las personas. Más de 5,5 mmol/l y 52,7 de hiponatremia en el 1,8% de las personas. La insuficiencia cardíaca está causada por la Cardiopatía isquémica (CI) en el 78,2% de los casos, la valvulopatía en el 10,9% de los casos y la miocardiopatía en el 20% de los casos.
Conclusión: La insuficiencia cardíaca es frecuente en Sudán y es una de las principales causas de hospitalización. Es más frecuente en los hombres y aumenta proporcionalmente con la edad, presentándose la mayoría de los casos después de los sesenta años. La CI es responsable de más de tres cuartas partes de los casos de IC. La disfunción renal se predice por el aumento de la creatinina sérica, la urea y el FGe90 ml/min, así como por los antecedentes de diabetes, hipertensión arterial y tabaquismo del paciente.

Palabras clave: Disfunción renal, insuficiencia cardíaca, centro cardíaco.

Introduction

Heart failure is a medical disorder in which the heart is unable to provide enough oxygen to the tissues. The most frequent cause of HF is coronary heart disease, which affects the majority of patients. Valvular disease, cardiomyopathy, and hypertension are all key causes.

The clinical sickness is known as "heart failure," although with therapy, a patient can become asymptomatic. Patients with chronic heart failure have had heart failure for an extended period of time[1]. Congestive heart failure is defined as acute or chronic heart failure with signs of congestion, such as salt and water retention. The management of the body's salt and water levels by the kidneys is directly dependent on the heart, and the kidneys are directly dependent on the heart's blood flow and pressure. This is especially true in cases like heart failure (HF), where the interdependence of both organs can lead to a vicious circle in which the degeneration of one organ leads to a severe, possibly self-perpetuating, high-mortality condition. The cardiac renal syndrome is a term that stresses the fact that it comprises a variety of frequently overlapping sickness symptoms that are all part of the same disease[2]. It is now well understood that renal disease can cause heart disease, and that heart disease can wreak havoc on the kidneys. One of the most powerful predictors of a poor clinical outcome in heart failure (HF) is renal impairment[3]. Heart failure affects at least 26 million individuals globally and is becoming more common[4].

A link between reduced renal function and poor outcomes has been found in several investigations of heart failure patients. Health-care costs for the elderly are high and will continue to rise as the population ages. Patients with renal impairment have a death rate that is more than double that of those without. Furthermore, a decrease in eGFR is linked to a 60-80% increase in mortality[5]. Worsened renal function (WRF) was defined as a rise in serum creatinine of _0.3 mg/dl (26.5 mol/l) in a study of Medicare seniors with HF[6].Patients with WRF also had longer hospital stays, greater in-hospital expenses, higher in-hospital mortality, and a higher risk of readmission.

Despite major breakthroughs in treatments and prevention, mortality and morbidity remain high, and quality of life remains low[4]. Congestive Heart Failure accounts for 15% of all heart illness, and the incidence of heart disease in Khartoum, Aljazeera, the White Nile, the Red Sea, and the West of Sudan was 40%, 25%, 20%, 10%, and 5%, respectively[7].

Subject and methods

Study design: A hospital-based prospective, quantitative, descriptive analytical study.

Study area: This research is being carried out at the Wad-Madani Heart Centre, a tertiary hospital that serves Gezira and the surrounding states in the center.

Study population: Between June and August 2018, a total of 55 adult patients were admitted to Wad-Madani Heart Center with heart failure. With an age range of 35 to 90 years, 45.5 percent (n=25) were female and 55.5 percent (n=30) were male.

Exclusion criteria: Patient had a history of kidney disease, was on dialysis, and had a kidney transplant.

Sample size: Except for those listed above, all adult patients diagnosed with heart failure

Sampling method and Data collection tools: Renal function test, questionnaire, patient data, patient ECHO report.

GFR calculation: Cockcroft, Gault calculator was employed in this investigation with four variables: age, weight, gender, and serum creatinine. (140-age) (weight by kg)/(72*serum Cr) in ml/min is the creatinine clearance value. multiply by 0.85 in females (Cockcroft DW, Gault MH prediction of creatinine clearance from serum creatinine Nephron 1976).

Data analysis: SPSS was used to analyze the data from this investigation (Statistical Package for Social Sciences 25). The numerical value data will be reported as (mean+/- standard division SD). The Chi-square test was done to determine whether the variables were significantly different. P=0.05 is regarded as statistically significant.

Ethical consideration: The research was carried out in conformity with the ethics committee of the faculty of medicine at Gezira University. Wad-Madani cardiac centre granted administration authority. The patient's informed consent is protected by a high level of secrecy.

Result

54.5% of the study population were male and 45.5% were female with mean age 65 years, EF 41.8%, Mild HF 29.1%, moderate 52.7%and sever in18.2%.All patient presented with SOB, 85.5% with LL swelling,63.6% with abdominal distention. No one presented shock. On examination 16.4% had tachycardia 80% had normal pulse rate and 3.6% had bradycardia. 89% were tachypneic and 11% had normal respiratory rate. Systolic blood pressure was normal in 70.9%, high in 27.3% and low in1.8%.Diastolic BP was normal in 89.1%, high in 9.8% and low in 1.8%.HTN was measured in 81.8%, DM in 70.9% and smoking in 43.6%. IHD was diagnosed in78.2%, valvular in 10.9%,cardiomyopathy in20% and

mixed cause in 3.6%.Regarding Base line renal function, impaired renal function (Urea > 50 mg/dl) was detected in 61.8 % and (Creatinine > 1.4 mg/dl) in 49.1 %. Basal crepitation demonstrated in all subject, LL edema in 91%, JVP raised in 56.4 % of subject. 1.8% had renal failure (GFR<15 ml/ min) and 36.4% with severely decreased GFR (15- 29) ml/min, 32.7% moderate decrease in GFR (30-59) ml/min, 16.4% mild decrease GFR (60-89) ml/min, and 12.7 had normal GFR.3.6% with hyperkalemia (more than 5.5 mmol/l)and 52.7% with hypernatremia. Proteinuria was detected in 1.8%. All patient given loop diuretic. 92,7% anti-ischemic. After admission and medication urea impaired in 7.3%, Creatinine in 7.3% and 29.1% with hypernatremia. 5.5% with severely decreased GFR, 54.5% moderate, 27.3% mild, and12.7% had normal GFR (**Table I**, **Figure 1-5**).

Table I: The frequency of participants in the study population.

Variable	Age group	Frequency	Percent%
Age	<40 40-60 >60	2 18 35	3.6 32.7 63.6
Presentation	SOB LL swelling Abd distension cardiogenic shock	55 47 35 0	100 85.5 63.6 0
Risk Factor	HTN DM Smoking	45 39 24	81.8 79.9 43.6
Causes	IHD Cardiomyopathy valvular lesion Mixed	43 11 6 2	78.2 20 10.9 3.6
RR	Normal Tachypnea	6 49	10.9 89.1
SBP	Normal High Low	39 15 1	70.9 27.3 1.8
DBP	Normal High Low	49 1 5	89.1 1.8 9.1
Serum urea (Admission)	Normal<50 > 50 Impaired	21 34	38.2 61.8
Serum urea (Discharge)	Normal<50 > 50 Impaired	51 4	92.7 7.3
Serum Creatinine (Discharge)	<1.4 >1.4	51 4	92.7 7.3
Serum Na+(Admission)	<135 hypernatremia 135-145 normal	29 26	52.7 47.3
K+ (Discharge)	<3.5 3.5-5.5	18 37	32.7 67.3
Proteinuria	Yes No <90 normal	1 54 7	1.8 98.2 12.7
GFR (Admission)	60-90 mildly decreased 30-60modarate to sever decreased 15-29 severely decreased <15 kidney failure	9 18 20 1	16.4 32.7 36.4 1.8
GFR categories at (Discharge)	<90 normal 60-90 mildly decreased 30-60modarate to sever decreased 15-29 severely decreased	7 15 30 3	12.7 27.3 54.5 5.5
Echo ejection fraction	45-55 Mild 35-45 moderate <35 sever	16 29 10	29.1 52.7 18.2
ACEI	Yes No	38 17	69.1 30.9
ARP	Yes No	11 44	20.0 80.0
Anti-ischemic	Yes No	51 4	92.7 7.3

Figure 1: The incidence percent of heart failure based on gender.

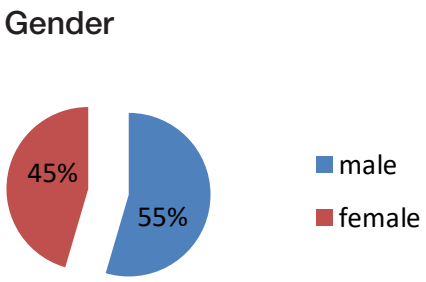


Figure 2: Heart rate at admisson.

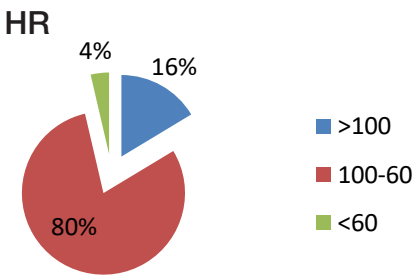


Figure 3: Basal crepitation at admission.

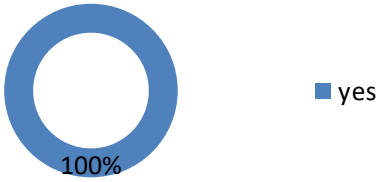


Figure 4: Lower limb edema at admission.

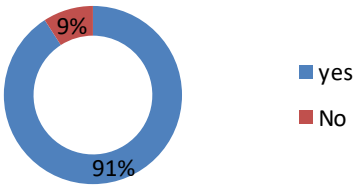
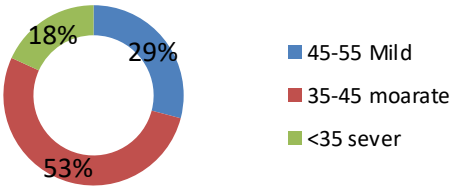


Figure 5: Classification of heart failure according to EF.



Discussion

Heart failure can arise as a result of almost any abnormality of the structure, mechanical function, or electrical activity of the heart, each of which may require quite different treatments, emphasizing the importance of appropriate investigation of patients with suspected heart failure. Many of the typical clinical symptoms and signs of heart failure do not arise directly as a result of the cardiac abnormality but rather from secondary dysfunction of other organs and tissues, such as the kidneys.

Analysis reveals that heart failure is predominant among male with a percent of 54.5% relative to 45.5% among female. In comparison with the study carried out by Omer et al.[7] in Sudan showed that HD were predominant among male by 56% than female 44%, ascribed to different factors such as social stress, poor economic and heavy responsibility. Moreover, 63.6% of patient with heart failure were more than sixty years. This finding was in agreement with Omer, M. A et al 2016 and Go, et al 2013[7,8] which showed that HD were pre dominant among 65-77 years old and the incidence of condition increase with age.

Watson, RD9 showed that Presentation, most of the study population complained of dyspnea 95.6%, and two-thirds had lower limb swelling with no specific symptom of heart failure despite that the symptom mention above considered with major presentation, this in agreement with our study who patient presented with SOB 85.5% Odema and 63.6% with abdominal distention no one presented shock, reflecting that most complain of patient result from fluid retention.

HTN, DM, IHD and smoking may induced or accelerate heart failure increases the events of cardiovascular diseases by two to three folds relative to normal people[10,11] in different areas such as Europe, North America and Australasia. In Sudan indications for admissions by heart disease were ADHF (acute decompensate heart failure) 73%, ACS (acute coronary syndromes) 47%, Arrhythmia 20%, IE (infective endocarditis) 3%, and others 3%. Etiological diagnoses given to patients were IHD (ischemic heart disease) 65%, HHD (hypertensive heart disease) 28%, NIDCM (non-ischemic dilated cardiomyopathy) 11%, RHD (rheumatic heart disease) 7%, pericardial disease 4(%), Others (2%)., HHD and IHD common in 51-60 years old[11].

Data which obtained from this study reveal that more than three quadrant of patient of heart failure attending Wad-Madani heart center from June to august had significant reduction on renal function, estimated GFR less than 90 ml/min in 87.3%.This agree with other studies done worldwide[9]. Among 1,004 HF patients studied, WRF developed in 27%. this approve that renal dysfunction is highly prevalent in the HF population. GFR as predictor

of renal affection show 1.8% had renal failure 36.4% sever 32.7% moderate and 16.4 % mild decrease in GFR compared to12.7% with normal function. Urea increased in 61.8% and creatinine in 49.1% 3.6% with hyperkalemia more than 5.5 mmol/l and 52.7% hyponatremia less than 135 mmol/L, proteinuria in 1.8%. Landmark papers established the relationship between renal hemodynamics, GFR and the severity of HF were published by Cody colleagues[12]. They demonstrated the reduction in RBF was out of proportion to the reduction in cardiac index, while GFR was relatively maintained; a phenomenon now easily explained by renal autoregulation. Then, when RBF drops further, GFR declines as autoregulatory capacity is exhausted. These findings have been reproduced in patients on ACEi, with the difference that RBF and GFR declined in parallel since compensatory efferent arteriolar vasoconstriction is reduced by ACEi[13] then, focused has shifted to venous congestion as another important determinant of reduced GFR It has now been convincingly shown in modern HF patients that, independent of a reduction in RBF, there is an epidemiologic association between increased CVP or venous congestion and reduced GFR[14].

Conclusion

Heart failure is prevalent in Sudan, and it is one of the major causes of hospital admission with higher incidence among male and has increasing proportionality with aging and mostly occur after sixty year. More than three quadrant of HF cases caused by IHD. Significant predictors of renal dysfunction include elevated baseline serum creatinine, and urea and eGFR<90 ml/min, patients history of diabetes, elevated BP and smoking increase the risk.

Recommendations

Heart failure not a disease it is syndrome need systemic approach, which include good control of blood pressure and diabetes beside stop alcohol and smoking to maintain health.

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Abbreviations

ACEi = Angiotensin converting enzyme inhibitor, eGFR = Estimated glomerular filtration rate, GFR = Glomerular filtration rate, HF= Heart failure, HHD=Hypertensive heart disease, HTN= Hypertension, IHD= ischemic heart disease, K= Potassium, Na= Sodium, BP= Blood pressure, WRF =Worsening renal function

Conflict of Interest

The authors report no conflicts of interest.

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ORIGINAL

Evaluate efficacy and safety of stem cells on bone regeneration: a systematic review and meta-analysis

Evaluar la eficacia y seguridad de las células madre en la regeneración ósea: una revisión sistemática y un meta-análisis

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Abstract

Objectives: The present study tries to reach a consensus on the results of studies on the efficacy and safety of stem cells-based scaffolds in disorders related to the jaw bone and Provides sufficient and strong evidence. Therefore, the present study aims to evaluate the efficacy and safety of Stem Cells on bone regeneration.

Methods: Present study is based on PRISMA guidelines; all articles published in international databases such as PubMed, Scopus, Science Direct, ISI Web of knowledge, and Embase between March 2010 and May 2022 are included. 95% confidence interval for effect size with fixed effect modal and in-variance method were calculated. Meta-analysis of data collected from selected studies was performed using STATA.V16 software.

Results: In the initial review, the abstracts of 336 studies were reviewed, two authors reviewed the full text of 136 studies, and finally, ten studies were selected. The prevalence of bone formation due to using stem cell-based scaffolds was 32% (95% CI, 1 % to 63%; p=0.04).

Conclusions: Based on the findings of the present meta-analysis, stem cell-based scaffolds can significantly cause bone formation and regeneration, and as a result, they can significantly improve maxillofacial bone disorders.

Key words: Stem cells, bone regeneration, meta-analysis.

Resumen

Objetivos: El presente estudio trata de consensuar los resultados de los estudios sobre la eficacia y la seguridad de los andamiajes basados en células madre en los trastornos relacionados con el hueso de la mandíbula y trata de proporcionar pruebas suficientes y sólidas. El presente estudio tiene como objetivo evaluar la eficacia y la seguridad de las células madre en la regeneración ósea.

Métodos: El presente estudio se basa en las directrices PRISMA; se incluyen todos los artículos publicados en bases de datos internacionales como PubMed, Scopus, Science Direct, ISI Web of knowledge y Embase entre marzo de 2010 y mayo de 2022. Se calculó el intervalo de confianza del 95% para el tamaño del efecto con el método de efecto fijo y de in-varianza. El meta-análisis de los datos recogidos de los estudios seleccionados se realizó con el software STATA.V16.

Resultados: En la revisión inicial se revisaron los resúmenes de 336 estudios, dos autores revisaron el texto completo de 136 estudios y, finalmente, se seleccionaron diez estudios. La prevalencia de la formación de hueso debido al uso de andamiajes basados en células madre fue del 32% (IC del 95%, 1 % a 63%; p=0,04).

Conclusiones: En base a los resultados del presente meta-análisis, los andamiajes basados en células madre pueden mejorar significativamente la formación y regeneración ósea, y como resultado, pueden mejorar significativamente los trastornos óseos maxilofaciales.

Palabras clave: Células madre, regeneración ósea, meta-análisis.

Introduction

According to the statistics available worldwide, the prevalence of bone disorders of the jaw and face is high and different, and the reason for this difference can be due to economic, cultural, environmental, and social factors[1]. The result of treatment of maxillofacial bone disorders is often unfavorable due to the complexity of the injuries; also, jaw and facial bone disorders may be associated with other injuries such as injuries to the abdomen, spine, head, pelvis, and organs[2]. These disorders may occur due to trauma, congenital abnormalities, or periodontal diseases and cause the loss of alveolar bone[3]. These injuries must be treated because they do not heal alone, and bone grafting must be done[4]. A treatment considered the gold standard for these disorders is an Autogenous bone graft[5]. However, despite the advantages of this method, disadvantages have also been reported, including loss of function, risk of infection, bleeding after surgery, and painful surgery; Therefore, it is very important to use an alternative treatment that minimizes these disadvantages[6]. Recently, tissue engineering has been introduced, a multidisciplinary field of the principles and applications of engineering methods and biological sciences, and is used in connection with the basic understanding of the structure and function of natural and diseased tissues[7]. The purpose of this type of method is to maintain the stable condition of the tissue and better the performance of the target tissue. The use of stem cells is a logical method due to its advantages, such as repair and self-renewal, as well as the ability to differentiate into different cells, and it can affect the host's tissues[8]. Therefore, the use of this method in bone tissue engineering has received much attention[9]. According to the available literature, three components (bone progenitor cells, bone growth factor, and scaffolding) are required for bone tissue engineering[10-12]. Of these three, the most key role is scaffolding, which transfers cells to the lesion site[13]. Scaffolds use an appropriate extracellular matrix to allow cell growth and differentiation to restore tissue function[14]. The use of this new method is very important, and many studies must be done to be able to hope for the treatment results; therefore, the present study tries to reach a consensus on the results of studies on the efficacy and safety of stem cells-based scaffolds in disorders related to the jaw bone and Provide sufficient and strong evidence. Therefore, the present study aims to evaluate the efficacy and safety of Stem Cells on bone regeneration.

Methods

Search strategy

Based on PRISMA guidelines[15], the present study is a systematic review and meta-analysis that includes all articles published between March 2010 and May 2022 in international databases such PubMed, Scopus, Science Direct, ISI Web of Knowledge, and Embase. It used the Google Scholar search engine.

The following keywords were used to search: (((((“Maxillofacial Prosthesis”[Mesh] OR “Oral and Maxillofacial Surgeons”[Mesh] OR “Maxillofacial Abnormalities”[Mesh] OR “Maxillofacial Injuries”[Mesh] OR “Maxillofacial Development”[Mesh] OR “Surgery, Oral”[Mesh] OR “Oral Surgical Procedures”[Mesh]) AND “Bone Diseases”[Mesh]) AND “Stem Cells”[Mesh]) OR (“Stem Cells/surgery”[Mesh] OR “Stem Cells/therapy”[Mesh])) AND “Tissue Scaffolds”[Mesh]) AND “Bone Regeneration”[Mesh].

Inclusion and exclusion criteria

In the current study, human and animal studies were included, and studies using stem cells for jaw and facial bone disorders are considered.

Study selection, Data Extraction, and method of analysis

Studies data were reported by first author name, years, number of Participants, mean of age, cell type, scaffold, location of the lesion, and duration.

STATA.V16 software was used to analyze the data. The level of heterogeneity was evaluated using the I^2 index test (I^2< 50% = low levels, 50<I^2< 75% = moderate and I2>75% = high levels). Calculated was the effect size's 95% confidence interval with a fixed effect mode and invariance.

Results

Four hundred thirty-nine studies were found when the existing literature was reviewed using the studied keywords. Duplicate studies were removed from the original review, and 336 study abstracts were reviewed. Two hundred studies were first excluded because they did not fit the criteria for inclusion, and in the subsequent step, two authors reviewed the full texts of 136 studies. One hundred twenty-six studies had already been removed from the study at this stage for various reasons, including incomplete data, inconsistent research results, poor studies, a lack of full-text access, and data that did not match with the study's objectives. Ultimately, ten studies were selected (**Figure1**).

Characteristics

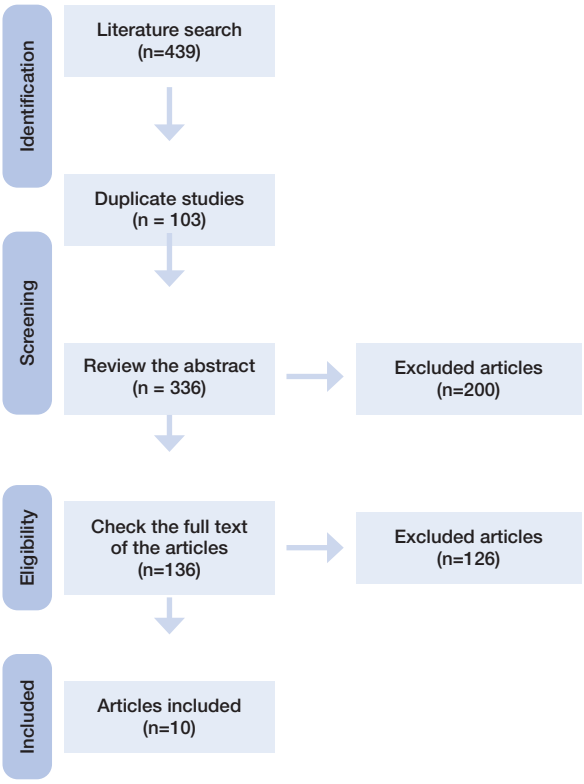
In the present study, nine studies were conducted on animal models, and only one was found in the considered human study period. In animal studies, 16 dogs, 88 rats, 5 rabbits, and 12 pigs were used. A total of 23 patients with a range of 43-74 years were examined in one study. Two studies used ADSCs, and eight studies used BMSCs. The range of study duration was 8-26 weeks. (**Table I**).

Table I: Data extracted from studies.

No.	Study. Years	Sample size		Type of Cell	Scaffold	Location of the lesion		Duration of study
		Animals	Human			Maxilla	Mandible	(weeks)
1	Lee et al., 2021 (16)	10/dog	-	ADSCs	βTCP	-	√	8
2	Prahasanti et al., 2020 (17)	14/rats	-	BMSCs	CAS	-	√	8
3	Zhang et al., 2020 (18)	17/rats	-	BMSCs	βTCP	-	√	8
4	Lopez et al., 2018 (19)	5/rabbits	-	BMSCs	βTCP	-	√	8
5	Moser et al., 2017 (20)	24/rats	-	BMSCs	βTCP	-	√	26
6	Tee et al., 2016 (21)	12/pigs	-	BMSCs	βTCP	-	√	12
7	Lee et al., 2015 (22)	28/rat	-	ADSCs	PLGA	-	√	12
8	Yun et al., 2014 (23)	6/dogs	-	BMSCs	βTCP	-	√	8
9	Yamada et al., 2013 (24)	-	23	BMSCs	PRP	√	-	24
10	Zou et al., 2011 (25)	5/rats	-	BMSCs	βTCP	-	√	8

ADSCs: Adipose-derived mesenchymal stem cells; BMSCs: Bone marrow-derived mesenchymal stem cells; CAS: Carbonate apatite scaffold; PRP: Platelet-rich plasma.

Figure 1: PRISMA flowcharts.



Stem cells-based scaffolds

Meta-analysis showed that stem cell-based scaffolds could significantly cause bone formation and regeneration, and as a result, they can significantly improve maxillofacial bone disorders. Prevalence of bone formation due to using stem cells–based scaffolds was 32% (95% CI, 1 % to 63%; p=0.04) (I^2=0%; P=1.00; low heterogeneity). (**Figures 2, 3**).

Discussion

The present study aimed to evaluate the efficacy and safety of stem cells on bone regeneration. Based on the findings of the meta-analysis, it can be seen that this method is a key factor in the success of tissue engineering, but more studies should be conducted in this field, and more research is needed to introduce this treatment method as an ideal treatment method. BMSCs have been used in most of the selected studies, and these cells are considered a gold standard in bone tissue engineering. Also, BMP2 and PRP have been used as scaffolds. Based on the studies, organic scaffolds, PRP, and natural scaffolds are more popular, and more satisfactory findings are observed using collagen. The present analysis shows that stem cell-based scaffolds can improve bone regeneration, and positive results are observed.

Figure 2: The Forest plot showed the effectiveness of using scaffolds based in stem cells on bone formation.

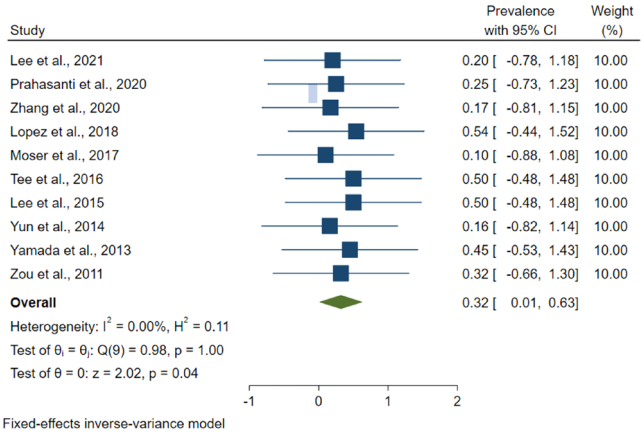
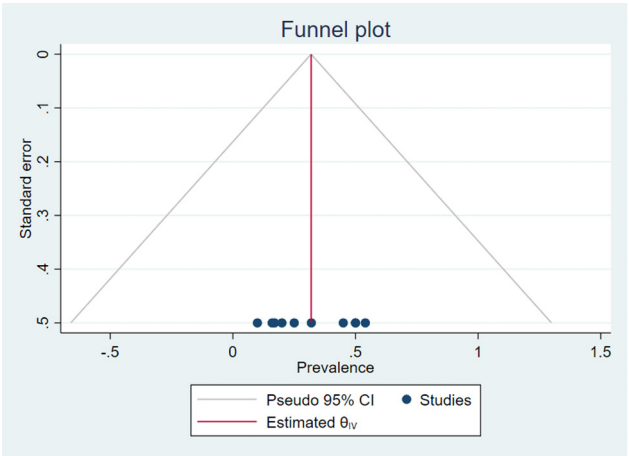


Figure 3: Funnel plot for graphical diagnostics of small-study effect.



Recent studies show that stem cells can be a promising technique for reconstructing bone defects[26]. Also, the results of another study conducted by Dong et al., 2020 showed that MSC-based tissue engineering scaffolds could increase osteogenesis[27]. As mentioned earlier, self-renewal and differentiation are the prominent features of stem cells, making them important in tissue engineering, and mesenchymal stem cells have become important because of their unique properties(28). Based on the available evidence, recent advances have shown that stem cells based on scaffold properties can be considered a very suitable therapeutic option in treating bone defects, although more research is needed[26].

The cell is considered one of the most important and main components of cell tissue engineering, and target tissue cells and stem cells are the two main sources of cells. The findings of the present meta-analysis show that poly (lactic-co-glycolic acid) is most commonly used in treating bone defects. In line with these findings, the results of the study by Zhao et al., 2021 showed that poly (lactic-co-glycolic acid) could be used in bone treatment and regeneration due to its mechanical properties, biocompatibility, and degradability[29]. Also, the present meta-analysis showed that combined scaffolding (PCL/hydroxyapatite) has positive results in bone regeneration. Studies have reported that coral scaffolds have the best therapeutic results[30,31].

Human studies are of great importance to confirm the results of the present study and previous studies and provide stronger evidence for conducting studies with large sample size. Most animal studies have been done on the reconstruction of small lesions, and their findings cannot be generalized to humans; also, the immune system issue should be considered. Using a control group to compare the findings can show the effectiveness of the treatment. Also, the duration of the experiments and research in the studies was very short, so to achieve better results, it is necessary to spend more time and consider all the possible side effects. Also, as discussed in relation to the three components of tissue engineering, all three components were used together in quantitative studies. In the end, it is emphasized that important factors in bone regeneration, such as immunological reactions and angiogenesis, should be considered for this treatment.

Conclusions

So far, an ideal scaffold has not been designed and reported, and important factors in bone regeneration, such as angiogenesis and bone physiology, have not been studied. Therefore, many studies are needed in this field so that an important step in the treatment and regeneration of bone can be taken to confirm the evidence. The rapid prototyping method can be used to construct composite scaffolds with the help of CT and MRI images and genetically modified stem cells.

Conflict of Interest

The authors report no conflicts of interest.

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ORIGINAL

Possible etiological role of Ezrin and Moesin in progression of breast cancer in Iraqi woman

Posible papel etiológico de Ezrin y Moesin en la progresión del cáncer de mama en la mujer iraquí

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Abstract

Background: Breast cancer (BC) is the most common malignancy in women and the second greatest cause of cancer death in Iraq (BC) reported the first type of cancer.
Methods: A case-control study was conducted to assess the role of Moesin and Ezrin in pathogenicity of breast cancer in Iraqi women. The study included 50 patients with BC age matched with 50 healthy individuals served as a control group. The Moesin and Ezrin concentrations were determined by enzyme-linked immunosorbent assay (ELISA) technique.
Results: The result showed that there was a significant increasing in Ezrin and Moesin serum level in Patients Versus control and there was significant difference in both adherent molecule serum as related with age group of the two under studied groups. But there is no significant difference between serum level of (EZ andMO) with grade and stage of disease.
Conclusion: According to the current result, Ezrin and Moesin may has a role in the aggressiveness of diseases, so it may consider a good therapeutic target to reduce the aggressiveness of disease.

Key words: Breast cancer, Moesin, Ezrin, metastasis.

Resumen

Antecedentes: El cáncer de mama (CB) es la neoplasia maligna más frecuente en las mujeres y la segunda causa de muerte por cáncer en Irak.
Métodos: Se realizó un estudio de casos y controles para evaluar el papel de Moesin y Ezrin en la patogenicidad del cáncer de mama en mujeres iraquíes. El estudio incluyó a 50 pacientes con CB emparejados por edad con 50 individuos sanos que sirvieron de grupo de control. Las concentraciones de Moesin y Ezrin se determinaron mediante la técnica de ensayo inmunoenzimático (ELISA).
Resultados: Los resultados mostraron que hubo un aumento significativo del nivel sérico de Ezrin y Moesin en los pacientes frente al grupo de control y hubo una diferencia significativa en el suero de ambas moléculas adheridas en relación con el grupo de edad de los dos grupos estudiados. Sin embargo, no hay diferencias significativas entre el nivel sérico de (EZ andMO) con el grado y el estadio de la enfermedad.
Conclusión: De acuerdo con los resultados actuales, la Ezrina y la Moesina pueden desempeñar un papel en la agresividad de las enfermedades, por lo que pueden considerarse una buena diana terapéutica para reducir la agresividad de la enfermedad.

Palabras clave: Cáncer de mama, Moesin, Ezrin, metástasis.

Introduction

Cancer is widely known as a silent killer and continues to list as one of the leading causes of death worldwide, claiming millions of lives every year .It is quite common around the world, in both developing and developed countries Despite the dangers associated with cancer, awareness is yet poor in our society. Prevention and mitigation of risk factors are the best way of combating cancer, and poor awareness could delay the process[1]. Breast cancer (BC) is defined as a malignant tumor that arises from the breast's ducts or lobules[2]. It is the most often diagnosed cancer in women, accounting for 11.6% of newly diagnosed cancer cases and 6.6% of estimated cancer mortality worldwide between 2006 and 2012, the incidence of breast cancer in Iraq increased significantly, rising from 30 per 100000 to 40 per 1000003. In 2011, there were 3763 cases of breast cancer in Iraq, with an incidence rate of around 23.01 per 100000 females, compared to 16.65 per 100000 females in 2008[4]. In Iraq, breast cancer was the most frequent malignancy, with 4529 cases reported in 2013, with 4422 females and 107 males, a proportion of the total of 18.84% and a rate of 12.9 per 100.000 people. As a result, breast cancer is the first of the top ten malignant neoplasms affecting the community[5-6]. In 2016, 897 women died as a result of this disease, which is the leading cause of cancer-related mortality among Iraqi females 23.6% and the second overall 12.1% among males and females after bronchogenic carcinoma[1-3]. The main characteristic of tumor cells is their disrupted adhesion to the ECM, which results in the loss of control over normal cell function. This attachment is important for signal transduction from the outside to the inside of the cell, which stimulates many activities such as cell cycle progression, and cells that separate from the ECM die via apoptosis[4-5].

Metastasis of malignant tumors are the cause of over 90% of cancer related deaths. The primary tumor cells attack the local environment and infiltrate blood or lymphatic vessels walls in order to produce a metastatic lesion, to survive in the circulatory system, and invade to the distant organ[7].

Cell adhesion molecules are glycoproteins expressed on the cell surface and play an important role in inflammatory as well as neoplastic diseases. There are four main groups: the integrin family, the immunoglobulin superfamily selectins, and cadherins[8-9]. Moesin is an Ezrin-radixin-Moesin (ERM) family protein and connects the actin cytoskeleton to transmembrane receptors. It belongs to the band 4.1 superfamily, which share a 300-amino-acid domain termed the 4.1 ERM domain. ERM members serve an important role in regulating cell adhesion, migration and morphogenesis, by regulating actin cytoskeleton remodeling. Ezrin, which is known as a cytoskeleton linker protein, is closely linked with the metastatic progression of cancer and is frequently abnormally expressed in aggressive cancer types. However, the possible involvement of Ezrin in metastasis and angiogenesis in breast cancer remains unclear. Ezrin, an important member of the Ezrin-radixin-Moesin (ERM) family of cytoskeleton-associated proteins, is a transit protein between membrane proteins and actin filaments.

Materials and methods

Subject: Baghdad, Iraq's capital, receives thousands of visitors each day. The medical city's oncology teaching hospital in Baghdad is one of Iraq's largest centers, employing thousands of Iraqis from all around the country. As a result, the participants in the study may be representative of the Iraqi population .From November 2021 to January 2022, a case-control study was done in the biology department ,college of education, university of Baghdad. This study involved 100 women who were separated into two groups: breast cancer woman (n=50) as patients group and apparently healthy women (n=50) who served as controls. Woman diagnosed with breast cancer by specialist physicians. Mammography or histological findings confirmed the diagnosis of breast cancer. The study excluded cases that had other forms of cancer or were treated with mastectomy, chemotherapy, or radio therapy. A healthy control group was enrolled that did not have breast cancer, other types of cancer, or any history of acute or chronic disease (T2DM, liver disease, or autoimmune disease). Questionnaires were used to ask all participants in the current study about their age, family history, medical history, and other diseases. The ethical committee at Baghdad University accepted the study procedure, and all participants completed a written informed consent document. Blood samples: In a plain tube, all individuals' peripheral blood samples were collected. By using an enzyme linked immunosorbent assay (ELISA), adhesion molecules markers such as Human Moesin (MSN) and Human cytovillin /Ezrin ELISA were measured. The concentrations of circulating Moesin and Ezrin in plasma were determined using a commercial ELISA kit (My Bio source) according to the manufacturer's instructions (Cat .No: MBS076337 and Cat.No:MBS162342 respectively).

Statistical analysis

Statistically, all data were analysis SPSS program (IBM V .28); Independent T test and one way ANOVA test were used to measure P value using least significant differences (LSD). All data were presented as mean ±S.E., and p value <0.05 was considered as significant differences.

Results

Ezrin serum level

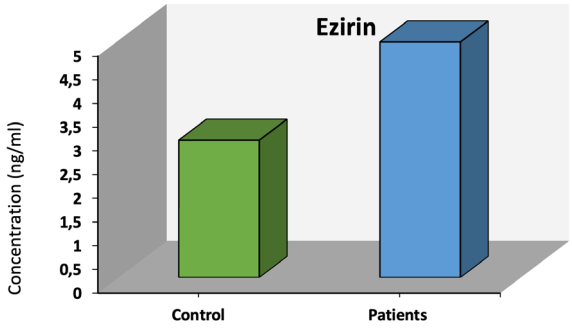
As show in **table I** and **figure 1** which demonstrate the serum level of Ezrin in patients and control, the

result represented by (mean± SE), the result for Ezrin serum level in patient and control was (2.895±0.178, 4.967±0.128) Pg/ml respectively P value was (<0.001) the result showed a high significant increase in patient compared to control.

Table I: Serum level of Ezrin in patients and control.

Group	Ezrin (Mean±S.E.)	P value
Control (N=40)	2.895±0.178	<0.001**
Patients (N=50)	4.967±0.128	

Figure 1: Serum level of Ezrin in patients and control.



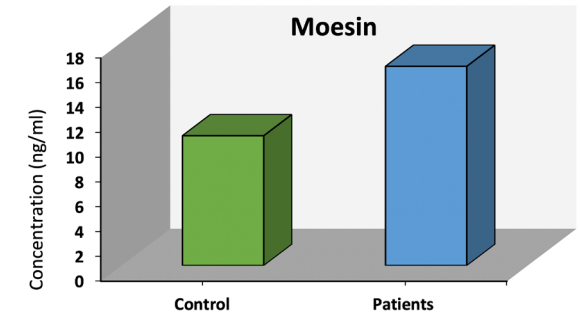
Moesin serum level

In **table II** and **figure 2** we observed a high significant increase in serum level of Moesin in patient as compared to control P<0.001.the result for Moesin serum level in patient and control was (10.463±0.554, 16.061±0.281) PG/ml respectively .

Table II: Serum level of Moesin in patient and control.

Group	Moesin (Mean±S.E.)	P value
Control (N=40)	10.463±0.554	<0.001**
Patients (N=50)	16.061±0.281	

Figure 2: Serum level of Moesin in patient and control.



Ezrin serum level distribution according to age groups

As shown in **table III** which demonstrated the distribution of Ezrin serum level according to the age group. Ezrin serum level for age groups (30-40/41-50/51-65) Years was (3.097±0.254, 4.724±0.369/2.824±0.464, 5.11±0.171/2.734±0.25, 4.968±0.194) pg/ml respectively. There was a non-significant difference among the age group patient p (0.537). Also there was no significant difference among control age groups p (0.678) while there was a significant difference between patients and control in each age group.

Table III: Ezrin serum level distribution according to age groups in patients and control.

Age Group (yrs.)	Control	Patients	P value
	(Mean±S.E.)		
30-40	3.097±0.254	4.724±0.369	<0.001
41-50	2.824±0.464	5.11±0.171	<0.001
51-65	2.734±0.25	4.968±0.194	<0.001
P value	0.678	0.537	-

Moesin serum level distribution according to age group

As shown in **table IV** which demonstrated the distribution of Moesin serum level according to the age group. Moesin serum level for age groups (30-40/41-50/51-65) Years was (10.833±0.946, 10.027±0.989, 10.408±0.992, 15.847±0.615, 16.098±0.468, 16.125±0.442) pg/ml respectively. There was a non-significant difference among the age group patient p (0.932). Also there was no significant difference among control age groups p(0.85) while there was a significant difference between patients and control in each age group.

Table IV: Moesin serum level distribution according to age groups in patients and control.

Age Group (yrs.)	Control	Patients	P value
	(Mean±S.E.)		30-40
30-40	10.833±0.946	15.847±0.615	<0.001
41-50	10.027±0.989	16.098±0.468	<0.001
51-65	10.408±0.992	16.125±0.442	<0.001
P value	0.85	0.932	-

Ezrin serum level according to grade in patients

The result as shown in **table V** Ezrin serum level in patients according to grade of disease which were (grade I, II, III) was (4.868±0.266, 4.876±0.136, 5.387±0.385) PG/ml respectively ,There was no significant differences among the grade of disease p value (0.991, 0.465, 0.991, 0.132, 0.132, 0.132) for each grade respectively.

Table V: Ezrin serum level according to grade in patients.

Grade	Ezrin	P value		
	(Mean±S.E.)	Grade I	Grade II	Grade III
Grade I (n=2)	4.868±0.266	-	0.991	0.132
Grade II (n=39)	4.876±0.136	0.991	-	0.132
Grade III (n=9)	5.387±0.385	0.465	0.132	-

Moesin serum level according to grade in patients

In **table VI** which clarify Moesin serum level in patients according to grade of disease which were (grade I, II, III) the result was (17.246±4.175, 15.811±0.29, 16.879±0.562) PG/ml respectively ,There was no significant differences among the stages of disease p

value (0.319, 0.812, 0.319, 0.15, 0812, 0.15) for each grade respectively .

Table VI: Moesin serum level according to grade in patients.

Grade	Ezrin (Mean±S.E.)	P value		
		Grade I	Grade II	Grade III
Grade I (n=2)	17.246±4.175	-	0.319	0812
Grade II (n=39)	15.811±0.29	0.319	-	0.15
Grade III (n=9)	16.879±0.562	0.812	0.15	-

Ezrin serum level in related to stage in patients

As shown in **table VII** which explain Ezrin serum level in patients according to stage of disease which were (stage IA, IIA, IIB, IIIA, IIIC, 4) The result was (5.015±0.432, 4.82±0.203, 5.363±0.317, 5.078±0.297, 4.351±0.372, 5.124±0.369) PG/ml respectively ,There was no significant differences among the stages of disease except in stage IIB and IIC there was a significant decrease Ezrin serum level p (0.035, 0.035).

Table VII: Ezrin serum level in related to stage in patients.

Stage	Ezrin (Mean±S.E.)	P value					
		Stage IA	Stage IIA	Stage IIB	Stage IIIA	Stage IIIC	Stage 4
Stage IA (n=4)	5.015±0.432	-	0.701	0.515	0.914	0.259	0.843
Stage IIA (n=16)	4.82±0.203	0.701	-	0.141	0.552	0.281	0.439
Stage IIB (n=10)	5.363±0.317	0.515	0.141	-	0.541	0.035	0.577
Stage IIIA (n=6)	5.078±0.297	0.914	0.552	0.541	-	0.168	0.925
Stage IIIC (n=8)	4.351±0.372	0.259	0.281	0.035	0.168	-	0.118
Stage 4 (n=2)	5.124±0.369	0.843	0.439	0.577	0.925	0.118	-

Moesin serum level according to stage in patients

As shown in **table VIII** which illustrated Moesin serum level in patients according to stages of disease (stage IA, IIA, IIB, IIIA, IIIC,4) the result was(15.822±1.639, 15.745±0.558, 16.252±0.558, 16.127±0.390, 16.031±0.946, 16.545±0.632) PG/ml respectively. There was no significant differences among the stages of disease.

Table VIII: Moesin serum level according to stage in patients.

Stage	Moesin (Mean±S.E.)	P value					
		Stage IA	Stage IIA	Stage IIB	Stage IIIA	Stage IIIC	Stage 4
Stage IA (n=4)	15.822±1.639	-	0.947	0.727	0.82	0.876	0.572
Stage IIA (n=16)	15.745±0.558	0.947	-	0.547	0.702	0.774	0.377
Stage IIB (n=10)	16.252±0.558	0.727	0.547	-	0.908	0.838	0.767
Stage IIIA (n=6)	16.127±0.390	0.82	0.702	0.908	-	0.937	0.711
Stage IIIC (n=8)	16.031±0.946	0.876	0.774	0.838	0.937	-	0.649
Stage 4 (n=2)	16.545±0.632	0.572	0.377	0.767	0.711	0.649	-

Correlation between Ezrin and Moesin related to age

According to the correlation result, we observed that There was a moderate significant correlation between age and Ezrin, and no correlation between age and Moesin, however according to the findings there was a high significant correlation between Ezrin and Moesin.

Table IX: Correlation between Ezrin and Moesin related to age.

	Parameter	Ezrin	Moesin
Age	Pearson Correlation Sig. (2-tailed)	0.203* 0.05	0.201 0.057
Ezrin	Pearson Correlation Sig. (2-tailed)	- -	0.776** <0.001
Moesin	Pearson Correlation Sig. (2-tailed)	0.776** <0.001	- -

Correlation between Ezrin and Moesin related to grade and stage

According to the findings There was no correlation with stage and the two adherent molecules Ezrin and Moesin, The result for stage was (-0.135, 0.352, -0.063, 0.662) and no correlation between grade and the two adherent molecules Ezrin and Moesin. The result for grade was (0.198, 0.167, 0.113, 0.433).

Table X: Correlation between Ezrin and Moesin related to grade and stage.

	Parameter	Grade	Stage
Ezrin	Pearson Correlation Sig. (2-tailed)	0.198 0.167	-0.135 0.352
Moesin	Pearson Correlation Sig. (2-tailed)	0.113 0.433	-0.063 0.662

Discusion

Previous studies have confirmed that metastasis is a complex process involving. A series of changes, such as mesenchymal transition of local cancer cell, reorganization of actin cytoskeleton, remolding of the micro-environment and colonization of metastatic cell, plasminogen, fibronectin, Moesin, Ezrin, an important member.

Ezrin. radixin-Moesin (ERM) Family Cytoskeleton associated protein, is a transit protein between membrane Protein and actin filament, never the less emerging evidence has demonstrated that Ezrin may serve as metastasis-related oncogene through modulating multiple cellular process, including the formation of Microvilli maintenance of cellular morphology and intracellular connection and promotion of cellular motility and invasion.

To determine the potential function of Ezrin adherent molecule in the pathogenesis of BC, we first assessed the Ezrin serum level by ELISA techniques. and the result found that there was a significant elevation in Ezrin serum level in patients versus control as shown in **table I**.

This result was Correspond with study performed by[10] which recorded an up regulation in Ezrin expression in BC and correlated with poor outcome and they suggest that Ezrin may function as oncogene while[11] observed a down regulation in intra hepatic cholangiocarcinoma and its loss was shown to result a more aggressive phenotype, so this data indicated that Ezrin may also serve as a tumor Suppressor.

The investigation done by[12] who studied Ezrin expression in breast carcinoma using tissue micro array, in most breast cancer (70.3%) the Ezrin staining in normal breast epithelium localized in the cytoplasm and there was a significant positive association between cytoplasmic and adverse tumor properties such a high grade, hormonal receptor negativity and Lymph node metastasis, so they suggest that the Change of Ezrin localization from apical membrane to the cytoplasm is correlated with adverse feature in invasive breast tumor. In spite of the difference between our study and David's study, but we share the same result which indicated this indicate to the increasing expression of Ezrin rather than their switch Localization.

In related to age group which demonstrated in **table III** the result showed that there was a significant difference between each age group for patient versus control p<0.001, while there is no significant difference among each group p(0.678, 0.537) respectively this indicate that age has an impact on disease but with no association with the disease duration time.

In regard to grade, our result indicated that there is no association between Ezrin serum level as described in **table V** and grade (1, 11 and III). this result did not consistent with result recorded by[13-14].

Also 15 which indicated that the over expression of Ezrin affect the process of hepatocellular Carcinoma cell proliferation and migration and invasion found that Ezrin was upregulated in BC disease which was linked with aggressive tumor characteristic and poor prognosis more over they showed that Ezrin promote BC proliferation, migration, invasion and angiogenesis in vitro and in vivo and this can be mediated by interact Ezrin with AKT, and promoted its kinase activity ,there by regulation the AKT pathway in BC and there was a decreased Ezrin serum Level was found in these two progressed Stage about the stage of BC (IA, IIA, I1B,IIIA, IIIC, Stage 4) as Shown in **table VII**.

The statistical result showed a nonsignificant association between Ezrin serum level and each stage, except the Ezrin serum Level in stage IIB and stage IIIC, we observed a significant decrease in Ezrin serum level.

Also This finding is disagree with previous studies16 it's Kinase activity, there by regulating the AKT Pathway in BC and there was a decreased Ezrin serum Level was found in these two progressed Stage About the stage of BC (IA, IA, 1B, IIIA, stage 4).

The statistical result showed a nonsignificant association between Ezrin serum level and each stage, except the Ezrin serum Level in stage IB significant difference. stage IIIC, observed is disagree with previous studies.

Also This finding[17] which indicated that Expression of Ezrin correlate with malignant Phenotype and Ezrin knockdown reverses the aggressive biological behavior of lung cancer cell.

The discrepancy between the present result and Previous studies may return to the small sample size and to the type of Samples.

Moesin is a member of Ezrin radxin Moesin family as mentioned above ,It has been demonstrated to be a prognostic significance in tumor progression, due to its role in the metastatic process, however its role in breast cancer is not well under stood.

The current result clarified that Moesin has a significant increase in patients versus to control .as mention in **table II** this result was correspond with previous study's[18], which recorded a significant increasing in BC (tissue) by using IHC technique and more high than fibroadenoma notably over expression of Moesin was significantly associate with poor prognosis in patient with ER-positive breast cancer but in this point our result didn'tagree with this study because the current result demonstrated that therewas no association between Moesin serum level andthe pathological characteristic (grade andstage) as shown in **table VI** and **VIII** and the explain for this difference may related to the sample type and sample size.

Also the result showed a nonsignificant correlation between disease and age as mentioned in **table IV** which illustrated that there was a significant difference between age group of patient versus control p<0.001 while there was no significantly among age group for each one (patient andcontrol) p=0.678, 0.537 respectively. The significance difference between age group of patients versus control may indicated that age has an impact on disease. There is no previous studies that correlate age with Moesin serum level.

Conclusion

According to the current result, Ezrin and Moesin may has a role in the aggressiveness of diseases, so it may consider a good therapeutic target to reduce the aggressiveness of disease.

Abbreviation list

BC: Breast cancer
ELISA :Enzyme linked immunosorbent assay
ERM: Ezrin –radixin- Moesin
ANOVA: Analysis of variance
ECM: Intracellular matrix
AKT: protein kinase B
SPSS : Statistical package for social sciences

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: Fieldwork was done by Mariam Qassim Al-Dulemey And Haizma Mossa Alabassi. Mariam Qassim Al-dulemey performed statistical analysis. Hazima Mossa Alabassi supervised the study and Mariam Qassim Al-dulemey drafted the manuscript under his supervision. The final manuscript was read and accepted by all authors.

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ORIGINAL

Knowledge attitude and practice of occupational safety among health workers in Tertiary Hospital Mogadishu-Somalia

Conocimiento, actitud y práctica de la seguridad laboral entre los trabajadores sanitarios del hospital terciario de Mogadiscio-Somalia

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Abstract

Introduction: Occupational health and safety (OHS) is concerned with workers' health, safety, and well-being. Over 59 million people worldwide work in health care facilities (HCFs), which are hazardous and high-risk workplaces. Like other high-risk workplaces, healthcare institutions expose workers to harmful agents, endangering their health and lives.
Method: This study was conducted in Mogadishu, Somalia's capital. It's the country's only teaching hospital. This study was descriptive cross-sectional. All consenting healthcare personnel participated. Due to the study's purpose, administrative healthcare staffs were excluded.
Results: 124 (59.0%) of the respondents were male, aged 25-35 (73.3%), with a mean age (SD) of 28.31 4.11 years. Most participants (48.6%) were nurses, followed by doctors (43.3%) and medical technicians (17%). (8.1 percent). Most respondents were unmarried, with 51.9% working in the medical service and 35.7% having fewer than five years of professional experience (80.5%). 96% of respondents knew that all patients, healthcare personnel, and communities are at risk of healthcare-related infection. 95% of respondents recognized Universal Precautions and Standard Precautions protect health staff and patients from infection. Similarly, 94.3% recognized there must be an occupational safety and health policy authorized by management with regular talks between management and workers in the hospital, and 93.8% said it's common to train and educate personnel about occupational safety and health.
Conclusion: All employees should have sufficient safety kits, timely replacement of worn-out ones, and current job aids based on their assigned jobs. Pre-employment, continuous, and preventive safety training for health care workers should be institutionalized. Government, employers, company management, and employees work together to handle OHS. National policy must govern occupational health and safety to keep unwanted aspects from the workplace. Management and employers must be committed to workplace health and safety to provide a decent place to work. Employees must obey safety rules.
Key words: Occupational hazards, healthcare workers, healthcare facilities, public health.

Resumen

Introducción: La salud y la seguridad en el trabajo (SST) se ocupan de la salud, la seguridad y el bienestar de los trabajadores. Más de 59 millones de personas en todo el mundo trabajan en centros sanitarios, que son lugares de trabajo peligrosos y de alto riesgo. Al igual que otros lugares de trabajo de alto riesgo, los centros sanitarios exponen a los trabajadores a agentes nocivos, poniendo en peligro su salud y su vida.
Método: Este estudio se realizó en Mogadiscio, la capital de Somalia. Es el único hospital universitario del país. Este estudio fue descriptivo transversal. Participó todo el personal sanitario que dio su consentimiento. Debido a la finalidad del estudio, se excluyó al personal sanitario administrativo.
Resultados: 124 (59,0%) de los encuestados eran hombres, con edades comprendidas entre los 25 y los 35 años (73,3%), con una edad media (DE) de 28,31 4,11 años. La mayoría de los participantes (48,6%) eran enfermeros, seguidos de médicos (43,3%) y técnicos médicos (17%). (8,1%). La mayoría de los encuestados eran solteros, el 51,9% trabajaba en el servicio médico y el 35,7% tenía menos de cinco años de experiencia profesional (80,5%). El 96% de los encuestados sabía que todos los pacientes, el personal sanitario y las comunidades corren el riesgo de contraer una infección relacionada con la atención sanitaria. El 95% de los encuestados reconoció que las Precauciones Universales y las Precauciones Estándar protegen al personal sanitario y a los pacientes de las infecciones. Asimismo, el 94,3% reconoció que debe existir una política de seguridad y salud en el trabajo autorizada por la dirección con charlas periódicas entre ésta y los trabajadores del hospital, y el 93,8% dijo que es habitual formar y educar al personal en materia de seguridad y salud en el trabajo.
Conclusión: Todos los empleados deben disponer de kits de seguridad suficientes, sustituir a tiempo los que estén desgastados y disponer de ayudas de trabajo actualizadas en función de los trabajos asignados. Debe institucionalizarse la formación en seguridad previa al empleo, continua y preventiva para los trabajadores sanitarios. El gobierno, los empleadores, la dirección de la empresa y los empleados trabajan juntos para gestionar la salud y la seguridad en el trabajo. La política nacional debe regir la seguridad y la salud en el trabajo para alejar los aspectos no deseados del lugar de trabajo. La dirección y los empresarios deben comprometerse con la salud y la seguridad en el trabajo para ofrecer un lugar de trabajo decente. Los empleados deben obedecer las normas de seguridad.
Palabras clave: Riesgos laborales, personal sanitario, instalaciones sanitarias, salud pública.

Introduction

Occupational health and safety (OHS) is concerned with employees' health, safety, and well-being at work[1]. Health care facilities (HCFs) employ over 59 million people worldwide and provide a wide range of services to clients and patients, making them hazardous and high-risk workplaces. Like other high-risk workplaces, healthcare facilities are characterized by a high level of dangerous agent exposure, which significantly endangers the health and life of workers Health Care Workers (HCWs)[2].

Physicians, dentists, nursing and midwifery experts, pharmacists, and other allied health professionals were among the HCWs listed by the WHO[3].

Work-related injuries and diseases kill an estimated 2 million people worldwide, which is more than the yearly number of malaria deaths. Work-related ailments, such as respiratory and cardiovascular diseases, cancer, hearing loss, musculoskeletal, reproductive disorders, mental and neurological illnesses, affect an estimated 160 million people globally yearly[4]. The International Labor Organization (ILO) estimates that compensation, production disruption, and medical expenses connected with occupational health and safety (OHS) cost USD1.25 trillion every year[5].

Protecting HCWs' health improves public health because they make up 10 to 18 percent of every country's workforce[3]. The inadequacy of facilities and equipment that might promote best practices in developing countries like Somalia exacerbates the vulnerability of personnel in HCFs. The occupational exposure of HCWs, particularly among doctors, nurses, and nursing assistants, poses a danger to the quality of health care delivery in developing nations[2]. While the majority of occupational injury cases are documented in underdeveloped countries such as Somalia, assessing the degree of awareness, mindset and practice is one way to prevent them.

In this study, we aimed to determine occupational safety knowledge, attitude, and practice level among health workers in Mogadishu, Somalia's tertiary hospital.

Methods

This study was conducted at Mogadishu Somali Turkey Training and Research Hospital in Mogadishu, the capital of Somalia. It is the largest and only teaching and referral hospital in the country. The study design of this study was a descriptive cross-sectional design. All healthcare workers who consented to participate in the study were included. Administrative healthcare personnel, regardless of their profession, were excluded from the study due to the nature of the study.

The sample size for the study was calculated using the Lemeshow formula for sample size determination (Lemeshow, 1991) in health studies. Allowing a 30% non-response rate, the adjusted sample size needed was 220. A stratified random sampling technique, a proportion-to-size method, was used.

Data were collected using a modified pretested self-administered questionnaire adapted from a previous study[2]. The questionnaire addressed the following socio-demographic characteristics (6 items), knowledge (6 items), attitude (6 items Likert scale ranging from strongly agree to strongly disagree), and practices (6 items) toward occupational hazards. Correct responses of knowledge and practice were given a score of "1", while wrong responses were given a score of "0". Furthermore, the median (inter-quartile range) for the knowledge score achieved was 6^{4-8}. So a score below six was considered low, and a score equal to or greater than 6 was high. Similarly, a score of 19^{13-24} and 2^{2-4} were used for attitude and practice, respectively.

The study protocol gained ethical approval from the institutional review board (IRB) of Mogadishu Somali Turkey Training and Research Hospital before the initiation of the study. Only members of the study team had access to electronic data, which were encrypted and kept on the external hard drive of the lead investigator.

The data collected was checked and cleaned. The questionnaires were coded, entered, and analyzed using IBM- SPSS version 27. We used descriptive statistics, including mean, median, and standard deviation for continuous variables and frequency/percentages for categorical categories, as well as chi-square.

Results

Socio-demographic Factors

Table I shows the socio-demographic characteristics of participants. This study showed that the majority of the respondents were male, 124 (59.0%), aged 25-35years, 154 (73.3 %), with a mean age (SD) of the respondents being 28.31± 4.11 years. The study revealed that most participants were nurses 102 (48.6%), followed by doctors 91 (43.3%), and medical technicians 17 (8.1%). Most of the respondents were unmarried, with 108 (51.9%) working in the medical service, 75 (35.7%), and less than five years of work experience 169 (80.5%).

Knowledge of participants on occupational hazards in health care facilities

Table II shows the knowledge of respondents on occupational hazards and safety. Around ninety-six percent of the respondents had good knowledge that all patients, healthcare workers, and communities in

healthcare facilities are at risk of healthcare-related infection. Similarly, 95% of the respondents knew Universal Precautions and Standard Precautions (infection control and management methods) protect both health workers and patients from infection. Similarly, among all respondents, 94.3% knew there must be occupational safety

and health policy endorsed by management with regular consultations between management and workers in the hospital, while most of the respondents 93.8% it's usual to conduct training and education on workers about occupational safety and health.

Additionally, the majority of the respondents, 88%, knew that standard precautions should be applied to all patients regardless of their infectious status, while most of the respondents, 92%, knew that there is a demand for routine assessment of workplace health and safety risks and controls carried out by a trained person.

Table I: Socio-demographic factors of the participants.

Risk Factors	Total N %
Age	
<25	48 (22.9%)
25-35	154 (73.3%)
35-45	8 (3.9%)
χ^2 (P-value)	
Gender	
Male	124 (59.0%)
Female	86 (41.0%)
Department	
Medical service	75 (35.7%)
ICU	45 (21.4%)
OPD	9 (4.3%)
Emergency service	14 (6.7%)
Delivery room	9 (4.3%)
Operation Theatre	13 (6.2%)
Surgical Service	40 (19.0%)
Laboratory service	5 (2.4%)
Profession	
Doctors	91 (43.3%)
Nursing	102 (48.6%)
Medical Technicians	17 (8.1%)
Years of Experience	
<5 years	169(80.5)
>5years	41(19.5%)
Marital status	
Married	101(48.1%)
Unmarried	108(51.9%)

Attitude of respondents to occupational hazards in health care facilities

In this study, 205 (72.2%) respondents believed that exposure and infection control policies (standard operating procedures) should be regularly reviewed and updated by the hospital management, and 102(48.6%) thought that precautions are meant only for theatre workers and when to attend to high-risk patients. In addition, 287 (99%) agreed that adequate staffing of HCFs and avoiding prolonged standing of HCWs would reduce occupational hazards, while 105 (50.0%) consider that Occupational hazards should be taken seriously and given prompt attention in the hospital. Also, 108 (51.4%) respondents believed that training staff and providing personal protective equipment are necessary to reduce the risk of exposure to occupational hazards and that occupational hazards are preventable.

Furthermore, 98(46.7%) of the respondents believe that all occupational exposures should be reported and documented by appropriate authorities. This study showed that 108 respondents, constituting 51.4%, had negative attitudes in contrast to 49.4 %, that had positive attitudes towards occupational hazards and preventive safety practices.

Table II: Distribution of knowledge among respondents.

No	Knowledge Questionnaire	Poor knowledge		High knowledge	
		Frequency	Percentage %	Frequency	Percentage %
1.	All patients, healthcare workers and communitiesin healthcare facilities are at risk of health care related infection	9	4.3%	201	95.7%
2.	Universal and standard precautions (infection control and management methods) Protect both health workers and patients from infection.	11	5.2%	199	94.8%
3.	There must be a management-endorsed occupational safety and health policy with regular consultations between management and hospital workers.	12	5.7%	198	94.3%
4.	It's usual to conduct training and education of workers about occupational safety and health	13	6.2%	197	93.8%
5.	Standard precautions should be applied to all patients regardless of their infectious status	26	12.4%	184	87.6%
6.	There is a demand for routine assessment of workplace health and safety risks and controls carried out by a trained person.	17	8.1%	193	91.9%
A total score of knowledge [Mean SD]		5.58 ±.702			
Good		143 (68.1%)			
Poor		67 (31.9%)			

Table III: Distribution of knowledge among respondents.

No	Attitude questionnaire	Strongly disagree	Disagree	Agree	Strongly agree
1.	Exposure and infection control policies (standard operating procedures) should be regularly reviewed and updated by the hospital management	4 (1.9%)	12 (5.7%)	205 (72.2%)	2 (0.7%)
2.	Percussions are meant only for theatre workers and when attending to high risk patients	55 (26.2%)	23 (11.0%)	30 (14.3%)	102 (48.6%)
3.	Adequate staffing of HCFs and avoiding prolonged standing of HCWs will reduce occupational hazards.	1 (0.5%)	35 (16.7%)	126 (60.0%)	48 (22.9%)
4.	Occupational hazards must be taken seriously and should be given prompt attention in the hospital	2 (1.0%)	6 (2.9%)	97 (46.2%)	105 (50.0%)
5.	Training of staff and provision of personal protective equipment is necessary to reduce the risk of exposure to the occupational hazard	1 (0.5%)	9 (4.3%)	92 (43.8%)	108 (51.4%)
6.	All exposures to occupational hazards should be reported and documented by appropriate authorities	5 (2.4%)	12 (5.7%)	95 (45.2%)	98 (46.7%)
A total score of attitudes [Mean SD] Good Poor		19.41±2.35 108 (51.4%) 102 (48.6%)			

Table IV: Disturbution of practive among respondents.

Risk Factors	Total N %	Knowledge		Attitude		Practice	
		Poor	Good	Negative	Positive	Poor	Good
Age							
	48 (22.9%)	14 (29.2%)	34 (70.8%)	30 (62.5%)	18 (37.5%)	30 (62.5%)	18 (37.5%)
25-35	154 (73.3%)	50 (32.5%)	104 (67.5%)	74 (48.1%)	80 (51.9%)	71 (46.1%)	83 (53.9%)
35-45	8 (3.9%)	3 (37.5%)	5 (62.5%)	4 (50.0%)	4 (50.0%)	3 (37.5%)	5 (62.5%)
X^2 (P-value)		0.303 (0.859)	3.065 (0.216)	4.416 (0.11)			
Gender							
Male	124 (59.0%)	36 (29.0%)	88 (71.0%)	65 (52.4%)	59 (47.6%)	50 (40.3%)	74 (59.7%)
Female	86 (41.0%)	31 (36.0%)	55 (64.0%)	43 (50.0%)	43 (50.0%)	54 (62.8%)	32 (37.2%)
X^2 (P-value)		1.150 (0.178)	0.119 (0.419)	10.255 (0.001)*			
Years of Experience							
<5 years	169 (80.5)	52 (30.8%)	117 (69.2%)	85 (50.3%)	84 (49.7%)	78 (46.2%)	91(53.8%)
>5years	41 (19.5%)	15 (36.6%)	26 (63.4%)	23 (56.1%)	18 (43.9%)	26 (63.4%)	15 (36.6%)
X^2 (P-value)		0.514 (0.295)	0.445 (0.312)	3.933 (0.035)*			
Profession							
Doctors		24 (26.4%)	67 (73.6%)	47 (51.6%)	44 (48.4%)	32 (35.2%)	59 (64.8%)
Nurses		36 (35.3%)	66 (64.7%)	50 (49.0%)	52 (51.0%)	60 (58.8%)	42 (41.2%)
Medical technicians		7 (41.2%)	10 (58.8%)	11 (64.7%)	6 (35.3%)	12 (70.6%)	5 (29.4%)
X^2 (P-value)		2.493 (0.287)	1.438 (0.487)	14.052 (0.001)*			
Marital status							
Married	101 (48.1%)	31 (30.7%)	70 (69.3%)	52 (51.5%)	49 (48.5%)	48 (47.5%)	53 (52.5%)
Unmarried	108 (51.9%)	36 (33.0%)	73 (67.0%)	56 (51.4%)	53 (48.6%)	56 (51.4%)	53 (48.6%)
X^2 (P-value)		0.132 (0.415)	0.00 (0.549)	0.311 (0.337)			

Practice of respondents on occupational hazards in health care facilities

As shown in **table IV**, our study showed that most respondents, 159 (75.7%), were not using PPE always regardless of the patient diagnosis, even in inpatient departments, and changed gloves for different patients. At the same time, 171 (81.4%) reported that there is poor appropriate monitoring of the health of individual health workers concerning their jobs, such as regular preventive medical examinations. Most of the respondents, 149 (71.0), state there are available procedures for post-exposure prophylaxis, such as HIV and Hepatitis B, in the hospital. Almost half of the respondents reported that they had been exposed to occupational hazards.

In addition, most of the respondents, 142 (67.6), had never been trained in infection control and management before, while 178 (84.8%) had never been vaccinated against HBV and tetanus (vaccine-preventable diseases).

Our study revealed statistically significant associations between gender and practice (χ^2 = 10.26, P = 0.001), years of experience and practice (χ^2= 3.933, P = 0.035), and profession and practice (χ^2 = 14.052, P = 0.001) while there were no significant differences between age (χ^2 = 4.416, P = 0.11) and marital status (χ^2 = 3.933, P = 0.035) in their practice. Similarly, this study had no statistically significant association between all variables and knowledge and attitude.

Table V: Association between socio-demographic factors and occupational hazard.

No	Practice Questionnaire	Poor practice		Good practice	
		Frequency	Percentage %	Frequency	Percentage %
1.	I always use PPE regardless of the diagnosis of the patient, even in hospital departments, and change gloves for different patients.	159	75.7%	51	24.3%
2.	There is appropriate monitoring of the health of individual health workers in relation to their jobs, such as regular preventive medical examinations	171	81.4%	39	18.6%
3.	There is available procedures for post-exposure 149 prophylaxis, such as, for HIV, Hepatitis B in the hospital	71.0%	61	29.0%	
4.	Ever exposed to occupational hazards	106	50.5%	104	49.5%
5.	I have been trained in infection control and management before	142	67.6%	68	32.4%
6.	I am vaccinated against HBV, tetanus (vaccine-preventable diseases)	178	84.8%	32	15.2%
A total score of practice Poor Good Poor		1.69±1.34 104(49.5%) 106(50.5%) 102 (48.6%)			

Discussion

Healthcare facilities are places of work where healthcare-associated diseases are common. Lack of suitable protective measures, excessive workload, and poor training of workers on safety standards, among other factors, could exacerbate the situation, particularly in developing nations. Occupational dangers, injuries, and infections are common among healthcare workers.

The situation in a tertiary HCF, which should be recognized and copied as an example of good practices in the health care industry, was investigated to determine the scale of occupational hazards and problems.

Nurses made up about half of the respondents in our study. This is comparable to a study done previously[6]. The mean age of respondents was 28 years, lower than 33 years reported by Aluko et al.[2].

According to the Oxford Concise Dictionary, knowledge is information and skills gained through experience and/or education. In HCFs, understanding potential occupational health and safety is critical to developing a positive attitude that will guide behavior. In this aspect, most responders were aware of potentially dangerous circumstances regarding occupational safety and health. Unlike Anisha[6] and Viragi et al.[7], over half of the respondents in our study received a good knowledge rating in the questionnaire.

In our study, most of the respondents knew that healthcare workers and communities in healthcare facilities are at risk of healthcare-related infection. Similarly, most of them knew Universal Precautions, and Standard Precautions (infection control and management methods) protect health workers and patients from infection. Despite having a good knowledge of that, there must be a management-endorsed occupational safety and health policy with regular consultations between management and hospital workers; only 34% of our respondents had formal infection control and management training. Most respondents in comparable studies in the Indian city of Belgaum and the Nigerian city of Ile Ife learned about occupational hazards and safety procedures via post-employment seminars, which was at variance with the results of this study[7,8].

Due to the particular nature of their profession, healthcare workers are exposed to a variety of occupational hazards[9]. Consequently, this study looked at preventive coping mechanisms. Most of our respondents didn't wear personal protective equipment regardless of the patient's status of the disease. This may be because most of our participants didn't have formal training in infection control precautions.

Since the majority of respondents (50.5%) were at risk of occupational hazards, the exposure risk was considerably high in our study. But this percentage is far less than the previous studies by Orji et al. (10), Manyele et al.[11] Amosun et al.[12] and Enwere and Diwe[13].

According to the respondents' profession and sex findings, categories were strongly correlated with practice, while the experience was also related to practice, comparable to Tziaferi et al.[14]. According to the reasonable model, people with a high level of expertise have more than five years of experience[15]. To implement safety measures that will reduce the prevalence of occupational hazards in the HCF, Respondents' actions, on the other hand, were unaffected by age or marital status, and respondents' knowledge and attitude toward workplace dangers and safety practices were unaffected by any factor.

Conclusion

All staff members should have access to sufficient safety kits, timely replacement of worn-out ones, and modern job aids based on their assigned tasks.

Health care personnel should get institutionalized pre-employment, ongoing, and safety preventive training on job hazards and safety measures.

Government, employers, management of companies, and employees all work together to effectively manage occupational health and safety. The management of occupational health and safety must be governed by national policy in order to keep undesired aspects as far away from the workplace as feasible. To ensure that everyone has a decent place to work, management and employers must also be committed to workplace health and safety. Additionally, it is the obligation of the employee to follow safety regulations.

Conflict of Interest

The authors report no conflicts of interest.

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ORIGINAL

Computed tomographic assessment of relationship between renal volume and second vertebral body volume in healthy adult dogs

Evaluación por tomografía computarizada de la relación entre el volumen renal y el volumen del segundo cuerpo vertebral en perros adultos sanos

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Abstract

Kidney has an important role in controlling hemostasis, therefore pathological changes that affect the size and function of kidneys can alter the normal status of the body. Various diseases alter function and normal anatomical structure of the kidney and increase the total volume of the organ. The object of this study was evaluation of the renal volume relationship to the vertebral body volume of second lumbar vertebra in normal adult dog by means of helical computed tomography and presenting a standard index for evaluating mongrel canine renal volume. In this study, 11 adult mongrel dogs with no sign of renal involvements were entered into the study and the volumes of vertebral body of the second lumbar vertebra were calculated from obtained and reconstructed scans. There was a strong linear association between renal volume and the volume of vertebral body of the second lumbar vertebral ($r^2 \approx 100$) Canine renal volume will change during pathological disease so evaluation of volume can be a good prediction of disease progression. Statistical correlation between renal volume and second vertebral body volume in this study shows the benefit of presenting a standard index for canine renal evaluation by the mean of computed tomography. Findings from this study supported the use of CT renal volumetry in future clinical and research studies.

Key words: Computed tomography, renal volume to vertebral body of the second lumbar vertebral ratio, adult dogs.

Resumen

El riñón tiene un papel importante en el control de la hemostasia, por lo tanto, los cambios patológicos que afectan el tamaño y la función de los riñones pueden alterar el estado normal del cuerpo. Varias enfermedades alteran la función y la estructura anatómica normal del riñón y aumentan el volumen total del órgano. El objetivo de este estudio es evaluar la relación del volumen renal con el volumen del cuerpo vertebral de la segunda vértebra lumbar en un perro adulto normal mediante tomografía computarizada helicoidal y presentar un índice estándar para evaluar el volumen renal de un perro mestizo. En este estudio, se incluyeron 11 perros mestizos adultos sin signos de afectación renal y se calcularon los volúmenes del cuerpo vertebral de la segunda vértebra lumbar mediante los escaneos obtenidos y reconstruidos. Utilizando las pruebas Kolmogorov-Smirnov y Shapiro-Wilk, se evaluó la distribución normal de los datos y hubo una fuerte asociación lineal entre el volumen renal y el volumen del cuerpo vertebral de la segunda vértebra lumbar ($r^2 \approx 100$). El volumen renal del perro cambiará durante la enfermedad patológica, por lo que la evaluación del volumen puede ser una buena predicción del avance de la enfermedad. Correlación estadística entre el volumen renal y el volumen del segundo cuerpo vertebral en este estudio, que son el volumen del riñón derecho y el volumen de L_2 (RKV)=2.336+10.05 L_2V, El volumen del riñón izquierdo y el volumen de L_2 (LKV) = 1.923 + 10.459L_2V , La altura del riñón derecho y la altura de L_2 (RKH) = - 0.544 + 2.592L2H, La altura del riñón izquierdo y la altura de L_2 (LKH) = 0.324 + 2.302L2H, muestra el beneficio de presentar un índice estándar para la evaluación del riñón del perro mediante tomografía computarizada. Los resultados de este estudio apoyaron el uso de la volumetría renal por TC en futuros estudios clínicos y de investigación.

Palabras clave: Tomografía computarizada, la relación del volumen renal con el volumen del cuerpo vertebral de la segunda vértebra lumbar, perros adultos.

Introduction

Kidney has an important role in controlling hemostasis, therefore pathological changes that affect the size and function of kidneys can alter the normal status of the body. Various diseases such as tumors, polycystic kidney disease, hydronephrosis alter function and normal anatomical structure of the kidney and increase the total volume of the organ. There are also other common diseases, including pyelonephritis, interstitial nephritis and glomerulonephritis which increase the total volume of the kidney due to acute inflammatory reactions in early stage of the disease[1]. According to Jeon et al. (2012) and Zachary's (2017) studies, the total volume of kidney has a strong correlation with the number of functional nephrons, so if necrosis of the nephrons occurs followed by obstinacy, kidney volume will be decreased[1,2]. In the study done by Herts et al. (2009), glomerular filtration rate was expressed as the best indicator of renal function. In current study by the creation of a model, estimation of GFR was performed by measuring renal volume and it was shown that kidney volume has significant correlation with GFR. Therefore, kidney volume can be considered as an indicator for determining the normal status of the kidney[3]. Nephrectomy surgery due to tumor removal is the other factor that can change the kidney volume. Studies about nephrectomy showed correlation between loss of renal function and loss of renal volume after partial nephrectomy for tumors. The existence of this correlation helps surgeons to estimate the volume of the kidney before surgery and to predict the postoperative renal parenchymal volume[4]. Helical computed tomography (sometimes referred to as a spiral) was introduced to diagnostic imaging science in 1990. Multi slice CT is able to scan the entire body due to improved image quality as a result of increasing the spatial resolution, reduced motion artifacts, thin slice and increased color resolution. In this model, while the patient is simultaneously transported into the gantry with the spiral rotation of the tube and detectors, volumetric data is continuously collected at different locations and then reconstruction of images can be provided[5-7].

Material and methods

Eleven mixed adult dogs were randomly selected and kept in separate cages for five days in the experimental animals department of the Small Animal Hospital of Tehran University. All of them were fed with commercial foods. After the end of the fifth day, each dog underwent a complete physical examination and full examination of urinary tract including the hydration rate and the presence of ascites and subcutaneous edema, which are symptoms of nephrotic syndrome. Palpation of left kidney (in dog, right kidney is not touchable) was done for evaluation of possible pain, size and position of the kidney. Blood samples were taken in order to evaluate the cell blood count and differential blood count and biochemical panel. The measurement of serum creatinine and blood urea nitrogen which are known as the most common renal functional tests, were also done. Urine test was performed to examine the appearance, chemical characteristics and presence of possible urine sediment. Finally 11 intact healthy dogs of both sexes were selected. Dogs were placed under anesthesia by intravenous injection of ketamine 10% (5 mg/kg) and diazepam (0.25 mg / kg) after the installation of catheter on the cephalic vein. Dogs were positioned in sternal recumbency, the legs were thoroughly drawn. Plain CT examinations of the kidneys were acquired for each dog (80 mAs, 130 kV, pitch factor of 1mm, and rotation time of 0.8 s). Images were reconstructed at 1-mm for volume estimation using the defined algorithm for the abdomen with Syngo MMWP VE40A software. For contrast, CT examination, Iohexol (Omniopaque® 300 mgI/ml) was injected to each dog with dosage of 2 cc/kg body weight and the images were taken after 4 second delay. The kidney volume after the increase of the cortical contrast was measured by the hand tracing option with 1 mm 3D reconstruction, and the volume of the body of the second lumbar spine was also calculated by the same method.

Statistical Analysis

After data gathering, statistical analysis was performed using SPSS 16 software. For the normal index of volume and height of the kidney and second lumbar vertebra, the mean, standard deviation, maximum and minimum of measurements were calculated. By using Kolmogorov-Smirnov and Shapiro-Wilk test, the normal distribution of data was evaluated. Correlation between the volume of the kidney and second lumbar vertebra volume and height were investigated by Pearson method. The linear regression equation was used for evaluation of the relationship between volume of the kidney and the volume and height of second lumbar vertebra.

Results

In this study, the height and volume of 22 healthy kidneys and 11 second lumbar vertebrae were evaluated. Mean, maximum, minimum and standard deviation of each parameter are shown in **table I**.

Table I: Mean, maximum, minimum and standard deviation of each parameter.

Parameters	N	Min	Max	Mean	SD
Right kidney volume	11	1.77	103.18	37.0618	36.82428
Left kidney volume	11	1.92	110.61	38.0627	38.21223
L_2 volume	11	0.16	9.99	3.4555	3.62002
Right kidney height	11	3.20	8.76	5.4191	1.83132
Left kidney height	11	3.53	8.53	5.6200	1.63459
L_2 height	11	1.80	3.40	2.3009	0.57185

All data were analyzed by Kolmogorov-Smirnov test and Shapiro Wilk test. According to the results of these two tests, which are indicated in **table II**, data were distributed normally.

Table II: Data analysis by Kolmogorov-Smirnov test and Shapiro Wilk test.

Parameter	Kolmogorov–Smirnov			Shapiro–Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Right kidney volume	0.250	11	0.053	0.828	11	0.022
Left kidney volume	0.244	11	0.065	0.827	11	0.021
L_2 volume	0.298	11	0.007	0.792	11	0.007
Right kidney height	0.184	11	0.200	0.922	11	0.335
Left kidney height	0.190	11	0.200	0.928	11	0.390
L_2 height	0.274	11	0.021	0.830	11	0.023

There is significant correlation between the volume of the kidney and the volume and height of second lumbar vertebra, which are shown by Pearson correlation coefficient in **table III**.

Table III: Pearson correlation coefficient of data.

Data	Pearson correlation coefficient
Volume right kidney and L_2	98.8
Volume of left kidney and L_2	99.1
Height of right kidney and L_2	80.9
Height of left kidney and L_2	80.5

According to the **table III**, data have a high correlation coefficient. Regression analysis showed the linear relationship between volume of kidney and the volume and heights of L_2 vertebral body (**Table IV**). These data are demonstrated in **figures 1** to **4** respectively.

Table IV: Linear regression has been used to obtain a correlation between the data.

Parameter	Equation
The right kidney volume and volume of L_2	**RKV=2.336+10.05 L_2 V**
The left kidney volume and volume of L_2	**LKV=1.923+10.459L_2 V**
The height of right kidney and height of L_2	**RKH=-0.544+2.592L_2 H**
The height of left kidney and height of L_2	**LKH= 0.324+2.302L_2 H**

RKV: Right kidney volume	RKH: Right kidney height	L_2V: Volume of L_2
LKV: Left kidney volume	LKH: Left kidney height	L_2H: Height of L_2

Figure 1: Scatter plot showing the linear relationship between the volume of left kidney and the volume of the second lumbar vertebra.

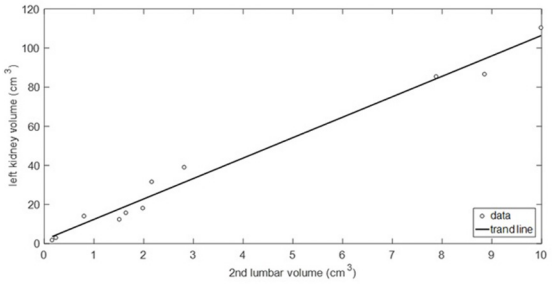


Figure 2: Scatter plot showing the linear relationship between the volume of right kidney and the volume of the second lumbar vertebra.

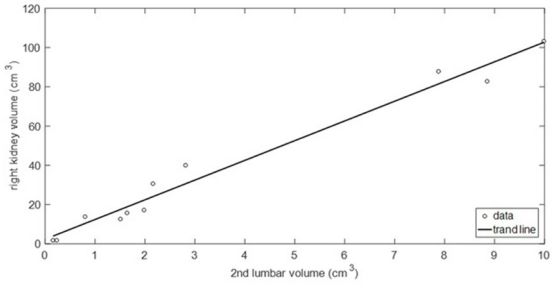


Figure 3: Scatter plot showing the linear relationship between the left kidney height and the height of the second lumbar vertebra.

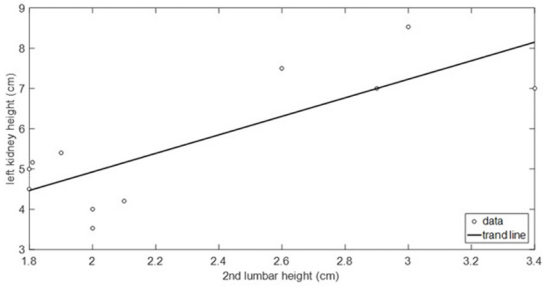
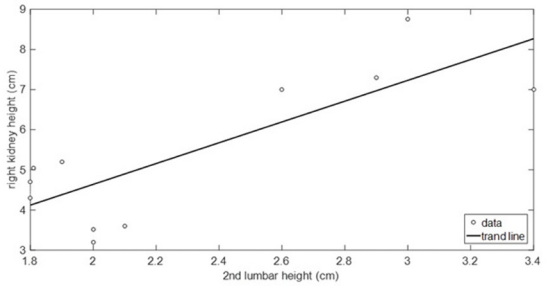


Figure 4: Scatter plot showing the linear relationship between the right kidney height and the height of the second lumbar vertebra.



Discussion

The results of this study showed the relationship between volume and height of second lumbar vertebra with volume of the kidney in computed tomography due to the high breed variation and consequently the difficulty in providing standard indices and, on the other hand, the difference in chest structure and the weight of the animals can provide an important role in assessing the volume of the organs. Vali and Molazem in 2016 announced the relationship between the volume of the kidneys and the volume of the body of the second lumbar spine in a cat, and considered this relationship as an advantage in predicting renal disease[8]. Hoey et al. (2016), measured the height of the kidneys to the height of the second lumbar spine using CT scan, and a significant correlation was reported between them[9]. Due to the variety of diagnostic imaging techniques, in this study, CT scan as a non-invasive diagnostic tool with high precision is proposed as the most accurate volumetric method. Tyson et al., in 2013,

examined two methods of ultrasonography and CT scan with a real measurement method through an autopsy in feline renal volumetric measurement and it was determined that the obtained volume by CT is similar to the actual volume[10]. Also, studies on human and animal liver volume have shown that CT scan is the most accurate method of volumetric analysis[11-15]. In current study, after selecting the best imaging method, manual method of volumetric measurement and 1 millimeter thickness were considered in order to increase the accuracy of measuring the volume of the kidneys and vertebrae in this study. According to the experience of current study and study of Lim et al in 2014 and Sharma et al. in 2015, the freehand scripting approach is a precise method and is useful for measuring kidney volume and excluding vascular structure, urinary collection system and hyper dense cyst, whereas the semi-automated approach yielded somewhat higher parenchymal volume estimates on average. In each instance, the semi-automated approach may occasionally capture other structures such as hilar vessels, or Para pelvic cysts, or a collecting system that may not be segmented out because of similar levels of attenuation. Automatic segmentation is a difficult task because images are often complex and rarely have simple linear features[11,16]. Lim et al. (2014) believed that there is an inverse relationship between the section thickness and the calculated organs volumes. For this reason, in this study the thickness section was considered as thin as possible[11]. Based on the study of Lobacz et al. (2012), in the present study, the dogs were adult and one year old. In that study, there was a relationship between age factor and ratio of kidney height to height of second lumbar spine, so that in dogs below one year, this ratio was larger and no significant changes were observed in dogs over one year[17]. According to the study of Vali and Molazem (2016) and our assumption, the weight range was not considered because the second lumbar vertebra can act as an indicator with any weight[8].

Conclusion

Since the kidneys are considered as vital organs for the body and their volume can be changed due to pathological conditions, and on the other hand, due to the lack of comprehensive studies of volumetric measurement of canine kidney, the assessment of the normal volume of kidneys and presenting standard index aids the technician in determining early treatment. According to the results, a significant correlation was found between the volume of the kidneys and the volume of the second lumbar spine in dogs, suggesting a strong correlation between these two parameters (the volume of right kidney and L_2, r= 98.8), (the volume of left kidney and L_2, r= 99.1).

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The study was conducted at the Veterinary Teaching Hospital, Department of Surgery and Radiology, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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ORIGINAL

The effect of clinical hypnosis and self-hypnosis on pain intensity in moroccan cancer patients: a pilot study

El efecto de la hipnosis clínica y la autohipnosis sobre la intensidad del dolor en pacientes marroquíes con cáncer: Un estudio piloto

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Abstract

Background: Pain is a common symptoms in cancer patients.
Objectives: This pilot study evaluated the feasibility, acceptability, and potential efficacy of a 4-week hypnosis intervention in cancer patients with pain.
Methods: The study was conducted at the Regional Oncology Centre in Agadir, Morocco. The favourable opinion of the Ethics Committee was registered under No.06/19. The study population consisted of 20 patients. Each patient received four hypnosis sessions. Assessments with the Visual Analogue Scale (VAS) for pain and evaluation of opiate and analgesic use were carried out at the beginning and after 2-4 weeks of hypnosis treatment.
Results: The mean age of the subjects was 43.25 years (±14.05). For the VAS score at baseline: (35%) had severe pain, (30%) very severe pain and (35%) intolerable pain with an average VAS of 6, 8 and 9 respectively. The mean VAS value decreased from baseline to 3.71 (±0.48), 6.00 (±0.5) and 6.86 (±0.69) respectively at two weeks of follow-up, and 2.43 (±0.5 3), 4.67 (±0.51), 5.14 (±1.07) respectively at four weeks of follow-up (P<0.001). The results showed a significant decrease in the doses of analgesic drugs consumed by the patients in the study after 2 to 4 weeks of hypnosis treatment compared to baseline (P<0.001).
Conclusion: Our results suggest that Clinical hypnosis is feasible and beneficial for pain control in cancer diseases.

Key words: Clinical hypnosis, self-hypnosis, cancer, pain, visual analogue scale.

Resumen

Antecedentes: El dolor es un síntoma común en los pacientes con cáncer.
Objetivos: Este estudio piloto evaluó la viabilidad, la aceptabilidad y la eficacia potencial de una intervención de hipnosis de 4 semanas en pacientes de cáncer con dolor.
Métodos: El estudio se realizó en el Centro Regional de Oncología de Agadir, Marruecos. Se registró el dictamen favorable del Comité de Ética con el número 06/19. La población del estudio consistió en 20 pacientes. Cada paciente recibió cuatro sesiones de hipnosis. Las evaluaciones con la Escala Visual Analógica (EVA) para el dolor y la evaluación del uso de opiáceos y analgésicos se llevaron a cabo al principio y después de 2-4 semanas de tratamiento con hipnosis.
Resultados: La edad media de los sujetos fue de 43,25 años (±14,05). En cuanto a la puntuación de la EVA al inicio del tratamiento: (35%) tenían dolor intenso, (30%) dolor muy intenso y (35%) dolor intolerable con una EVA media de 6, 8 y 9 respectivamente. El valor medio de la EVA disminuyó desde el inicio hasta 3,71 (±0,48), 6,00 (±0,5) y 6,86 (±0,69) respectivamente a las dos semanas de seguimiento, y 2,43 (±0,5 3), 4,67 (±0,51), 5,14 (±1,07) respectivamente a las cuatro semanas de seguimiento (P<0,001). Los resultados mostraron una disminución significativa de las dosis de fármacos analgésicos consumidos por los pacientes del estudio después de 2 a 4 semanas de tratamiento con hipnosis en comparación con la línea de base (P<0,001).
Conclusión: Nuestros resultados sugieren que la hipnosis clínica es factible y beneficiosa para el control del dolor en las enfermedades oncológicas.

Palabras clave: Hipnosis clínica, autohipnosis, cáncer, dolor, escala visual analógica.

Introduction

Pain is a common symptom in cancer patients[1]. The prevalence and severity of pain progresses with the spread of the disease: almost half of cancer patients report some degree of pain, but this percentage increases to 74% in the advanced and terminal stages[2]. In advanced cancer patients, pain is moderate to severe in 40-50% of cases and very severe or unbearable in 25-30% of cases[3]. Cancer pain is a multidimensional and complex phenomenon made up of sensory, emotional, cognitive and behavior factors. It is the product of a complex combination of physiological, cognitive, social and other parameters. Cancer-related pain is either caused by the tumor itself or is related to treatment, because treatments such as chemotherapy, radiotherapy and surgery can cause pain[4]. This pain leads to disturbances in several aspects of daily life, such as restriction in range of motion, problems with self-image, and psychological difficulties[5]. Indeed In severe chronic diseases such as cancer, chronic pain, which continually stimulate the fight or flight response, lead to the production and secretion of catecholamines. This has various physiological consequences, including anxiety. Because some catecholamines, such as norepinephrine, act as neurotransmitters in the brain, these substances can alter cognition and other mental processes[6].

The conventional approach uses often very high doses of opioids, which increases the risk of immediate side effects such as respiratory depression and/or constipation associated with opioids[7]. This pharmacology-only approach has a high failure rate. Indeed, several studies have shown that the use of opioids for chronic pain may actually worsen the pain[8]. This was confirmed by a 3-year observational study conducted in 2016 by CDC (Centers for Disease Control and Prevention) involving more than 69,000 women with recurrent pain, which showed that patients who received opioid treatment were less likely to experience improvement in pain[9]. However, an approach to cancer pain that combines non-pharmacological therapies shows their impact on chronic pain while significantly reducing the risk to patients[8]. Hypnosis certainly modulates the phenomenological aspects of the cognitive experience, such as the sensation of pain. It is likely that hypnotic analgesia is due to a variety of factors, including changes in expectations about the imminence of painful events, as well as attentional, cognitive, and emotional problems[10].

Several previous research studies conducted in the field psycho-oncology, have shown that hypnotherapy is an effective non-conventional method to alleviate cancer pain, reduce anxiety, and alleviating disorders in cancer patients. However, all research has been conducted outside of Morocco so far. In Morocco, not a single empirical research has been conducted on hypnosis and cancer, indicating a need for more productive studies in this area. The present study was therefore designed to examine the effect of clinical hypnosis and self-hypnosis on pain intensity in cancer patients.

Methods

Participants

This study was conducted with a total of 20 participants using the convenience sampling method; a non-probability sampling technique. Patients who were diagnosed with cancer and met the inclusion and exclusion criteria were included in the study. They were selected at the Regional Oncology Center of Agadir, Morocco.

This study is approved by the Ethics Committee for Biomedical Research (ECBR) of Mohamed V University - Faculty of Medicine and Pharmacy of Rabat. The favourable opinion of this committee was registered under No.06/19. All participants also signed a written informed consent to voluntarily participate in this study.

The group, composed of 20 participants, received an intervention in the form of hypnotherapy at the same time as the medical treatments. Socio-demographic and clinical data are presented in **table II**.

Eligibility criteria for participants

Inclusion criteria

The criteria for inclusion are: i) People with cancer ii) Patients with Stage II or IV cancer whose pain score on the Visual Analog Scale (VAS) should be between 4 and 7; iii)Individuals must be 18 years of age or older, regardless of gender iv) Individuals must be able to understand and speak French and/or Arabic, v) Individuals should be interested in a complementary approach to their pharmacological and interventional treatment, vi) Patients could only be enrolled in the groups if they were using only pharmacological therapy with opioids and/or analgesics vii) Participants classified as highly susceptible to hypnosis (SHCS score of 6 or higher) will be selected for enrollment in the hypnosis group in order to maximize the potential of hypnosis to reduce pain;

Exclusion criteria

The exclusion criteria are: i) Age <18; ii) Patients must not have had severe cognitive impairment; iii) Patients must not have suffered from major psychiatric disorders, such as schizophrenia; iv) The patient could not be enrolled if he or she was using additional therapies and not only drugs, for example, psychotherapies or blocks of anesthesia (these therapies could compromise the pain study); v) Inability to give informed consent; vi) Terminally ill patients (One of the objectives of the study was a 4-week follow-up).

The recruitment procedure

It was a clinical trial. Since all the patients were suffering

from cancer. The effect of the intervention was evaluated by comparing the group before and after an interventional treatment with hypnosis as an adjunctive therapy in addition to the standard pharmacological intervention. This study began in May 2020 at the Regional Oncology Centre in Agadir, Morocco, and was approved by the Board of Directors. All patients gave their informed consent in writing. In the first six months, we examined 44 cancer patients. Only 26 people were included and 6 refused to participate in the study.

Design of the study

This study was systematically planned by a pilot group, with comparison of results before and after; a quasi-experimental research design. People who volunteered to participate and who were sensitive to hypnosis (SHCS score of 6 or higher) were assigned to the experiment. Scores on the dependent variables were obtained for the group before an a posteriori analysis was carried out.

Hypnosis treatment

The subjects participating in this investigation received a total of 4 individual sessions of hypnosis (one session per week). The hypnotic intervention followed scenario designed by the principal investigator (HS) using procedures similar to those used by Dorfman and colleagues (2008)[11]. The scenarios focused on relaxation and reduction of pain sensation. The scenario began with an induction focusing on progressive muscle relaxation and suggestion designed to generate feelings of calmness and ease, followed by a visualization of a beach scene or exercise refuge to reinforce feelings of relaxation and bring the patients into a deeper trance state. Patients were encouraged to "let go of tension as they were ready to do it; allowing themselves to go further and into a deeper state of relaxation; abandoning all preoccupation and worry", for pain management, participants were encouraged to distract themselves, which is, "in a movie, you can be absorbed and distracted so that you don't even notice a headache". It was also suggested that patients could control sensation by "easing the pain" and "placing their breath in the area that needed it most". The script also provided suggestions for a "cool and comfortable numbing", «Magic Gloves», and suggestions for images associated with these feelings were provided. Towards the end of each session posthypnotic suggestions were provided assured patients that they "have within them the ability to return to that special place in the future whenever they need it".

(i) The general objective of the complementary hypnosis treatment was to teach patients clinical hypnosis and self-hypnosis as a complementary treatment to their pharmacological therapy for pain relief. (ii) The clinical hypnosis and self-hypnosis techniques used in this study are explained in the **table I**; (iii) Hypnosis treatment lasted 4 weeks; (iv) For 4 weeks, a series of weekly one-hour individual workshops were held. Pain assessment and doses of analgesic medication consumed were carried out. (v) The group had to attend 100% of the sessions for 4 weeks; (vi) Hypnosis treatment sessions were held in each patient's hospital room at the Regional Oncology Centre in Agadir, Morocco, where the participant was encouraged to use hypnosis while sitting in their chair or bed.

Figure 1 shows a timeline of study participants receiving hypnotherapy for 4 weeks.

After the demographic data and pre-tests, the VAS Scale were explained and administered to the group to assess the baseline study. After the last hypnosis session (after 4 weeks), all participants in the group were asked to complete the follow-up with the VAS post-test questionnaires. The principal investigator assessed (mg/day) opioid use and pharmacological analgesic therapies for each patient on medical records at baseline and 4 weeks. Assessments of pain a were conducted using validated tests: VAS for pain assessment.

The Visual Analogue Scale (VAS) for pain evaluation

VAS has been used to measure the intensity of pain in cancer patients. It is a one-dimensional measure of pain intensity. introduced by Hayes and Patterson in 1921[12], (VAS) is a visual analog scale, in which the person chooses a number (0-10). The interpretation of the notes is as follows: 0 = "no pain". 1-3 = "mild pain", 4-6 = "moderate pain", 7-9 = "severe pain", and 10 = "worst possible pain"[13].

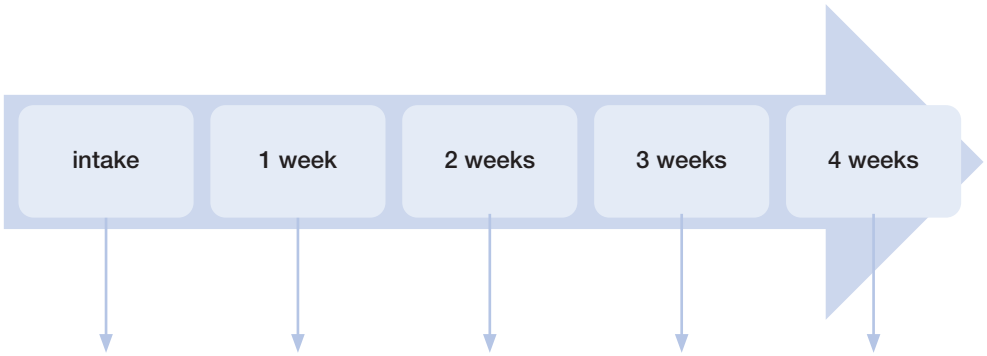
The Stanford Hypnotic Susceptibility Scale, Form C (SHSS: C)

Hypnotizability scores predict the effectiveness of analgesia suggestions in both ordinary states of consciousness[14,15]. The Stanford Clinical Hypnotic Scale (SCHS; Morgan & Hilgard, 1975) was utilized to measure degree of hypnotic responsiveness of the subjects[16]. Created a few years after Forms A and B, Form C contains some of the elements of Form B, but has more difficult elements so that when subjects are selected for advanced testing in which knowledge of their ability to experience more varied articles is required[17]. After a standardized hypnotic induction, the hypnotized person receives suggestions relating to the list below (see **Table II**).

The Montreal Cognitive Assessment (MoCA)

The MoCA it was created in 1996 by Ziad Nasreddine in Montreal, is a short 30 point test which evaluates 8 cognitive domains; including visuospatial abilities, executive functions, naming, attention, language, abstraction, short term memory and orientation[18]. Also, according to previous studies, MoCA is more sensitive than Mini-Mental State Examination (MMSE) in diagnosis of Mild Cognitive Impairment (MCI)[18,19].

Figure 1: Schematic time-line of patient's participants of study receiving hypnotherapy during 4 weeks. Measuring instruments.



	Information session	Session 1	Session 2	Session 3	Session 4
Hypnosis	+	+	+	+	+
MOCA	+				
SHSS:C	+				
VAS	+	+	+	+	+
Use of analgesics	+	+	+	+	+
Evaluation			+		+

Table I: Themes covered in each individual session.

Participants (N=20)	
General information session on hypnosis treatment	**Explanation: What is hypnosis?** - Common beliefs about hypnosis. - Answers to participants' questions. - Hypnotic induction exercises to determine SHSS: C. - Identification of a safe place.
Session 1	**Definition of three realistic objectives to be achieved** - List of things in life that are pleasant and comforting. - Discussion on pain: What does it mean? When does it happen, and what does it do to your body? - Discussion on balancing personal resources and environmental demands. - Optical illusions: Everyone looks at the same thing but does not see the same thing. The same situation can be differently perceived by different people - Hypnosis exercise: floating on a cloud. - At the end of the session: suggestion of self-hypnosis
Session 2	**Reflection on personal qualities and the importance of knowing them** - Find an object that will be associated with a "Stop! To use when we feel stressed. - Breathing exercise with imagery (coloured air flow). - Hypnosis exercise: Adaptation of the "refuge" exercise. (Finding and imagining a peaceful and pleasant place). - At the end of the session: suggestion of self-hypnosis
Session 3	- Discussion on how we talk to each other at ourselves and our self-esteem. - Creation of a timeline with moments of happiness, self-confidence and pride with an emphasis on body sensations. - Breathing exercise (abdominal breathing) with imagery (flow of coloured air). - Hypnosis exercise: Pain and colours. - At the end of the session: suggestion of self-hypnosis
Session 4	- Discussion on self-respect and care for bring to yourself. - Use of imagination to turn pain into more positive thoughts: drawing something scary, then changing the drawing to make it less scary. - Hypnosis exercise: magic gloves At the end of the session - Revision of the objectives determined at the beginning of the exercise of the sessions: Have they been carried out? The importance of being proud of us, to congratulate us.

N: number of patients, SHSS: C: Stanford Hypnotic Susceptibility Scale, Form C.

Table II: Stanford Clinical Hypnotic Scale (form c).

0	**Eye closure**
1	Hand Lowering (right hand)
2	Moving Hands Apart
3	Mosquito Hallucination
4	Taste Hallucination
5	Arm Rigidity (right arm)
6	Dream
7	Age Regression (school)
8	Arm Immobilization
9	Anosmia to Ammonia
10	Hallucinated Voice
11	Negative Visual Hallucination (Three Boxes)
12	Post-Hypnotic Amnesia

Statistical analyses

Data analyses were performed using IBM SPSS Statistics version[23] (Chicago, IL, USA). Participants' characteristics are expressed as absolute and relative frequencies (n, %) for categorical data or mean and standard deviation (SD) for continuous variables. To adjust for between-group baseline differences, changes from pre to post-test assessment were analyzed by calculating the difference between the two moments (Δ=T1 %-T2 %).

Statistical significance was set at $p<0.05$. Since null hypothesis significance testing and, consequently, p values, depend on sample size, the meaningfulness of differences was determined through the associated effect sizes (ES). These were expressed as Kruskal-Wallis test for continuous variables and Pearson's coefficient (r) for nominal variables. The interpretation of Pearson's coefficient (r) is analogous to the correlation coefficient, expressing the strength of association between two variables.

Results

Demographic data and characteristics of the participants at baseline

Twenty subjects - 7 men and 13 women - participated in the study. The mean age of the subjects was 43.25 years {±14.05} ranging from a minimum of 21 years old to a maximum of 67 years old (average age = 43,25±14,05). The patients suffered from 3 main types of cancer: (i) Digestive cancer (n=35%); (ii) Hematological cancer (n=30%); (iii) Breast cancer (n=25%).

Ten patients (50%) in this study are at stage III (**T1N1M0**); (**T3N0M0**) of cancer and undergoing chemotherapy (80%). Most subjects reported pain ranging from severe (35%) to intolerable (35%) on the VAS score with the use of Tramadol Hydrochloride (35%) and Morphine Sulphate (35%) as analgesic pain relievers. The hypnotizability score for most participants in this study was between medium (10%) and high (10%). The demographic and medical data of the sample are presented in **table III**.

Table III: Demographic data and characteristics of participants.

Characteristics	N (%)
Gender	
Male	7 (35%)
Female	13 (65%)
Tumor location	
Breast	5 (25%)
Hematological	6 (30%)
Digestive	7 (35%)
Lung	1 (5%)
Gynecological	1 (5%)
Stage of cancer (TNM)	
Stage II(T2N0M0)	6 (30%)
Stage III(T1N1M0); (T3N0M0)	10 (50%)
Stage IV (T2N1M1); (T4N0M0)	4 (20%)
Type of treatments	
Chemotherapy	16 (80%)
Radiotherapy	3 (15%)
No treatment	1 (5%)
MOCA score	
Normal > or = to 26/30	20 (100%)
Low < to 26/30	--------
SHSS:C	
Medium (5-7pt)	10 (50%)
High (8-12pt)	10 (50%)
VAS score	
Severe pain	7 (35%)
Very severe pain	6 (30%)
Intolerable pain	7 (35%)
Use of Analgesics	
Tramadol Hydrochloride	7 (35%)
Morphine Sulphate	7 (35%)
Nephopam Hydrochloride	6 (30%)

Data expressed in n [%], VAS: Visual Analogue Scale, SHSS: C: Stanford Hypnotic Susceptibility Scale: Form C (SHSS: C), MOCA Score: Montreal Cognitive Assessment, TNM: an international cancer classification system

Two-week follow-up

Looking at the two-week follow-up (n=20), the methods used at the first follow-up included VAS and the use of opioids. After 2 weeks of follow-up, there were no dropouts. The average VAS score at baseline was 6, 8 and 9 respectively.

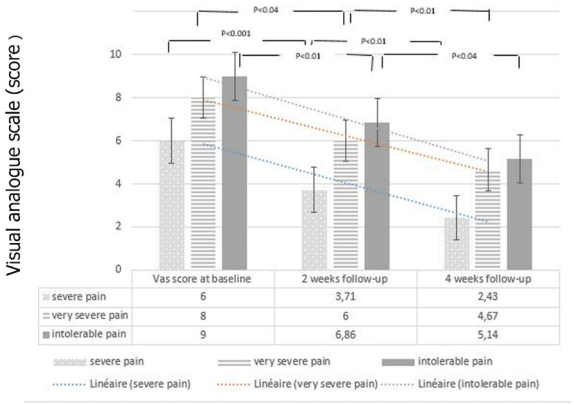
After 2 weeks, the score decreased from the baseline score and was significantly lower at 3.71 (±0.48), 6.00 (±0) and 6.86 (±0.69) respectively (**Figure 2**).

The mean reduction in the VAS score was significantly greater after 2 weeks of treatment with hypnotic therapy compared to baseline (before hypnosis) ($P<0.001$).

Four-week follow-up

The average VAS score after two weeks of hypnosis was 3.71 (±0.48), 6.00 (±0) and 6.86 (±0.69) respectively. After four weeks, the score decreased from the two-week score and was significantly lower, at 2.43 (±0.5 3), 4.67 (±0.51) and 5.14 (±1.07) respectively (**Figure 2**). The mean reduction in the VAS score was significantly greater after 4 weeks of hypnosis treatment compared to the baseline (pre-hypnosis) score ($P<0.001$).

Figure 2: Assessment of subjects according to VAS score at baseline, 2- and 4-weeks of hypnosis treatment.



¥ test de Kruskal-Wallis , SD: standard deviation

The administration of hypnotic therapy and the VAS score have been significantly associated with the change in VAS score after 4 weeks in univariate analysis. The sex, age of the patients and Tumor location were not associated with a significant decrease in the VAS score. In multivariate analysis, hypnosis treatment was associated with a greater decrease in VAS score (P<0.01) compared to baseline. Moreover, the decrease in the VAS score was statistically significantly different according to cancer stage (p = <0.01). The associations of the variables with reduction of the VAS score after one month of hypnotic intervention follow-up are presented in **table IV**.

In a 2- and 4-week follow-up of hypnosis treatment, we compared the doses of analgesic drugs consumed by the participants in this study to the doses used at baseline (mg/day). According to **table V**, the group of participants in this study had to significantly reduce the doses of analgesic drugs consumed after 2 to 4 weeks of hypnosis treatment compared to baseline (before hypnosis) (p< 0.05). On the other hand, this present study noted that 10% of the subjects who were on analgesics at the beginning had to stop the pharmacological treatment of pain after 4 sessions of individual hypnotic intervention.

Table IV: Variables associated with changes in VAS pain score after 4 weeks of hypnosis treatment.

Variables	r	P value
Baseline VAS score	0.81	<0.001
Sex (male vs. female)	-0.02	0.919
Age	0.44	0.051
Tumor location	0.13	0.569
Stage of cancer (TNM)	0.81	<0.001

r: The Pearson Correlation Coefficient, VAS: Visual Analogue Scale, TNM: an international cancer classification system.

Table V: Opioid consumption at baseline, 2- and 4-weeks of hypnosis treatment.

Use of opioids (mg/day)at baseline	Opioid consumption follow-up N (%)	2 weeks N (%)	P value ¥	4 weeks follow-up	P value ¥
Chlorhydrate de tramadol					
300	1 (5%)	-------		-------	
200	2 (10%)	1 (5%)		-------	
180	-------	1 (5%)		-------	
150	3 (15%)	1 (5%)	<0.001	1 (5%)	<0.001
120	-------	-------		1 (5%)	
100	1 (5%)	3 (15%)		2(10%)	
50	-------	-------		1 (5%)	
Stop of treatment				1 (5%)	
Sulfate de Morohine					
120	1 (5%)	-------		------	
90	4 (20%)	1 (5%)		------	
60	1 (5%)	4 (20%)		2 (10%)	
30	-------	1 (5%)		4 (20%)	
20	1 (5%)	--------		--------	
10	--------	1 (5%)		1 (5%)	
Nephopam Hydrochloride					
60	2 (10%)	-------		-------	
40	4 (20%)	2 (10%)	0.026	-------	0.178
20	-------	2 (10%)		1 (5%)	
stop of treatment	-------	-------		5(25%)	

Discussion

Cancer pain can have a serious impact on patients' quality of life, which is the reason why best management practices are of paramount importance.

Barriers to optimizing cancer pain management frequently cited by professionals and patients included knowledge deficits, inadequate pain assessments

and misconceptions about pain[9]. It is well known that opioids have been the main therapeutic method for the management of moderate to severe cancer pain[20]. Nevertheless when opioid drugs were involved, effects regarding addiction, tolerance and side events were mentioned by both doctors and patients[2,8]. Other factors include high costs (non-reimbursable expenses) and unavailability of treatment[5]. The results of this study corroborate with research that has reported the beneficial effects of clinical hypnosis on pain in cancer patients[4,21-27].

Individual differences in responses to hypnosis are referred to as "hypnotizability" or "hypnotic susceptibility". These terms essentially refer to a person's ability to experience hypnosis and demonstrate the behaviors associated with it. Hypnotisability was most often associated with hypnotic analgesia[28-29]. In our investigations we decided, as other authors have done in the field of clinical hypnosis research[30-32], to use hypnotic induction to determine hypnotizability. It is interesting to note that all patients participating in this study had a medium to high SHSS: C, regardless of gender. in fact no relationship between the degree of hypnotizability and time and gender variables could be detected from the results of other trials[31-33]. There are a number of important clinical implications in the results of this research concerning the effects and mechanisms of hypnosis on pain. Firstly, there is ample evidence that hypnosis is an effective treatment for chronic pain, is cost-effective and has minimal side effects. In fact, none of our patients participating in hypnosis treatment have reported side effects. Secondly, we have found a statistically significant reduction in pain in cancer patients receiving clinical hypnosis as adjunctive therapy to analgesic drugs (Opioids, Nephopam Hydrochloride) compared to baseline (before hypnosis).

Statistics showed that clinically significant reductions in pain (VAS) experienced by each study participant were independent of gender, age or cancer type, however hypnosis treatment was associated with a greater reduction in VAS score ($P<0.01$) compared to baseline. Subjects were at a lower risk of taking increased doses of pharmacological analgesics for pain control. This study showed a significant reduction in the use of analgesic drugs (opioids and Nephopam Hydrochloride) in the participant group after 2 and 4 weeks of hypnosis treatment.

The present study has enriched the data on hypnosis treatment in oncology from several points of view: in particular, with hypnosis and self-hypnosis techniques, we have observed the positive impact of treatment on the participants' ability to control pain. Thus, hypnosis treatment has proven to be effective, even without a therapist, by practicing self-hypnosis at home. This is obviously essential for its implementation in clinical practice, particularly in the care of cancer patients. The results of our investigations assume that in the future clinical psychologists, psychotherapists and hypnosis practitioners will be able to successfully integrate hypnosis treatment into oncology services. This suggests that hypnosis treatment is a promising option for cancer patients and a well-accepted intervention in chronic and acute populations.

Another clinical consequence is that when hypnosis is used or patients are taught self-hypnosis for pain management, practitioners can use different suggestions to alleviate the many components of pain (e.g. sensory, affective, cognitive, motivational). Patients in this study appreciated that a pharmacological solution, such as the use of analgesics, was not the only therapy for their symptoms and were therefore willing to undergo physical testing and pain management through hypnosis and self-hypnosis.

Self-hypnosis was practiced directly and easily with the patients and the latter were not only able to experience pain relief, but some of them also talked about achieving psychological and psychosocial well-being. Indeed, the patients participating in this study said that through self-hypnosis they had found a sense of inner peace, acceptance and spiritual healing This sense of spiritual well-being and healing helped the patients and their direct family in the cancer treatment process.

Even though hypnotic suggestibility and self-hypnosis training was different in all our subjects, scientific data revealed that hypnosis could not only decrease pain and the average daily dose of analgesics, but also that all patients felt more comfortable. Hypnosis has had benefits in other aspects of suffering for many people, more and more patients reported that hypnosis gave them increased energy, better sleep and improved resilience. Finally, follow-up at two and four weeks demonstrated the stability of the effects of hypnosis treatment.

A limitation of this study was the small sample size ($n = 20$), which limits the generalizability of the conclusions, the lack of a control group and lack of patient blindness.

However, the effectiveness of hypnosis in pain control, and the reduction in analgesic drug doses observed in this study are encouraging. The results of this pilot study strongly suggest that an additional study is warranted to establish the potential benefits of hypnosis for pain management in cancerology in particular by measuring serum cortisol levels, which is a new approach to pain monitoring. It is a direct and objective indicator of pain stimulation by the brain. Also other aspects should be examined such as the suggestion sets and hypnosis models used to determine their effectiveness in treatment.

Conclusion

This is the first study done in Morocco on the use of clinical hypnosis and self-hypnosis in the oncology department

with clinically relevant results. This feasibility study of clinical hypnosis and self-hypnosis for pain showed promise as a possible treatment for cancer. Therefore, policy on the care and treatment of patients with chronic and serious diseases, such as cancer, should focus on: (i) Ways of optimizing multidisciplinary care by adopting clinical hypnosis as adjunctive therapy; (ii) The use of hypnosis and self-hypnosis as adjunctive therapy for patients with advanced serious diseases; (iii) The development of trials to study results of clinical hypnosis in palliative care with appropriate comparison groups are necessary and (iv) More research on the effects and effectiveness of Hypnosis is necessary in oncology care.

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Conflict of interest statement

Authors have no conflicts of interest to declare.

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ORIGINAL

Exploring biomedical waste management and disposal practices among hospitals in Port Harcourt, Rivers State

Exploración de las prácticas de gestión y eliminación de residuos biomédicos en los hospitales de Port Harcourt, Estado de Rivers

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Abstract

Background: Globally, disposal of biomedical waste is an environmental concern, as most medical wastes are infectious and could potentially lead to the spread of infectious diseases. The aim of this study was to assess the biomedical waste management and disposal practices among hospitals in Port Harcourt, Rivers state.
Method: A hospital based cross sectional design was adopted for this study on the biomedical waste management and disposal practices among hospitals in Port Harcourt, Rivers state. Statistical package for Social Sciences (SPSS) version 22.0 was used for the analysis of the study and chi square to determine association between variables (P=0.05). A structured questionnaire was used for data collection and a stratified and simple random sampling technique was used to draw out a total of 202 respondents who participated for the study.
Results: The study revealed that 35% (70) of the respondents were between 35-44 years of age. Overall knowledge of biomedical waste management among the health workers was 80.2%. From the study, Age (p=0.00923), Level of Education (p= 0.0025) and Length of experience (p= 0.0457) were all associated with the level of knowledge of biomedical waste management.
Conclusion: A significant number of hospital workers are aware of biomedical waste generation, management and disposal practices. Although, attitude to biomedical waste management and disposal practices among health workers is average therefore a challenge. Sensitization of hospital staff by the public health personnel to improve biological waste disposal among the inexperienced is recommended. Also the government and policy makers should design laws that would facilitate the reduction and susceptibility of improper hospital waste disposal.

Key words: Waste Management, Biomedical waste, Knowledge, Attitude, Waste Disposal, Hospitals .

Resumen

Antecedentes: En todo el mundo, la eliminación de los desechos biomédicos es una preocupación ambiental, ya que la mayoría de los desechos médicos son infecciosos y podrían conducir a la propagación de enfermedades infecciosas. El objetivo de este estudio era evaluar las prácticas de gestión y eliminación de residuos biomédicos en los hospitales de Port Harcourt, estado de Rivers.
Método: Se realizó un diseño transversal sobre las prácticas de gestión y eliminación de residuos biomédicos en los hospitales de Port Harcourt, estado de Rivers. Se utilizó el paquete estadístico para las ciencias sociales (SPSS) versión 22.0 para el análisis del estudio y el chi cuadrado para determinar la asociación entre las variables (P=0.05). Se utilizó un cuestionario estructurado para la recogida de datos y una técnica de muestreo aleatorio estratificado y simple para extraer un total de 202 encuestados que participaron en el estudio.
Resultados: El estudio reveló que el 35% (70) de los encuestados tenía entre 35 y 44 años de edad. El conocimiento general de la gestión de residuos biomédicos entre los trabajadores sanitarios era del 80,2%. Del estudio se desprende que la edad (p=0,00923), el nivel de estudios (p= 0,0025) y la antigüedad (p= 0,0457) están asociados al nivel de conocimientos sobre la gestión de residuos biomédicos.
Conclusiones: Un número significativo de trabajadores hospitalarios conoce las prácticas de generación, gestión y eliminación de residuos biomédicos. Sin embargo, la actitud hacia las prácticas de gestión y eliminación de residuos biomédicos entre los trabajadores sanitarios es media, por lo que constituye un reto. Se recomienda la sensibilización del personal hospitalario por parte del personal de salud pública para mejorar la eliminación de residuos biológicos entre los inexpertos. Asimismo, el gobierno y los responsables políticos deberían diseñar leyes que faciliten la reducción y la susceptibilidad de la eliminación inadecuada de residuos hospitalarios.

Palabras clave: Gestión de residuos, residuos biomédicos, conocimientos, actitud, eliminación de residuos, hospitales.

Introduction

Biomedical waste or hospital waste is any kind of waste containing infectious (or potentially infectious) materials[1]. It may also include waste associated with the generation of biomedical waste that visually appears to be of laboratory or medical origin (example unused bandages, packaging, infusion kits), also research laboratory waste containing organisms or biomolecules that are mainly restricted from environmental release[1]. Biomedical waste is a type of biowaste and they may also be called medical or clinical waste. Biomedical waste is spawned from medical and biological sources and activities such as the diagnosis, prevention or treatment of diseases. Common producers of biomedical waste include hospitals, health clinics, nursing homes, and medical research laboratories, dentists, and emergency medical services, offices of physicians, veterinarians, morgues or funeral homes. Biomedical waste can be solid or liquid[2].

Biomedical waste management involves activities from generation of waste to final disposal. It includes those measures taken in the generation, characterization, quantification, storage, handling, collection, transportation, and disposal of wastes[1]. Biomedical waste is separate from normal trash or general waste and differs from other type of hazardous waste such as chemical, industrial and radioactive waste. It has become a major public health concern globally due to the potential of poorly managed hospital waste to cause disease and injury. The sustainable management of hospital waste has continued to generate increasing public health interest due to the health problems associated with exposure of human beings to potentially hazardous wastes arising from healthcare[3].

In Nigeria, hospital waste is divided into two different groups which include infectious and non-infectious wastes. Infectious wastes include unwanted microbiological cultures and stock of infectious agents, pathological waste, waste from surgery or autopsy that were in contact with infectious agents, sharps (which includes potentially contaminated used and unused discarded needles, syringes, scalpels, lancets and other devices that can penetrate the skin), waste from human blood and products of blood, laboratory waste and other medical supplies that may have come in contact with blood or body fluids[4]. The non- infectious wastes includes general hospital wastes generated in the course of administrative and housekeeping functions of hospital establishments; and hence are comparable to the usual domestic waste.

Presently, considerable gap exist with regard to the assessment of hospital waste disposal practices in line with the hospital waste management and disposal plan particularly in Nigeria and in other countries in Sub-Saharan Africa. The need to absorb the processes prescribed in the hospital waste management and disposal plan becomes a necessity in view of the promiscuous dumping of hospital waste in the metropolitan city of Port Harcourt, Rivers State, Nigeria. The nature and quantity of hospital waste generated as well as institutional practices with regards to sustainable methods of hospital waste management and disposal, including waste segregation and waste recycling are often poorly examined and documented. This is seen in several countries of the world including Nigeria, despite the health risks posed by the improper handling of hospital waste[5]. However, about 10-25% of hospital wastes is hazardous, and can create variety of health risks if not properly managed and disposed.

WHO estimates that over 20 million infections of hepatitis B, hepatitis C and HIV occur yearly due to unsafe sharp disposal following the re-use of syringes and needles without sterilization[6], while the indiscriminate dumping of other hospital wastes can lead to ground and surface water contamination, and even cancer[7]. Other health problems associated with improper collection, treatment and disposal of hospital wastes include cholera, skin diseases, typhoid fever, malaria and gastroenteritis[8]. Indiscriminate burning and incineration of hospital waste have been linked to serious public health threat and pollution resulting in the release of toxic dioxin, mercury and many other toxic substances. These substances produce remarkable variety of adverse effects in humans even at extremely low doses[9]. Putrefaction occurs in portions of open refuse dumps, which have not been fully burnt and add to air pollution through foul smells and release of greenhouse gases. Sanitary landfill of hospital waste can lead to pollution of ground water if not properly managed. These make the safe waste disposal of biomedical wastes a necessity, a fact that has been emphasized in various international conventions including Agenda 21, adopted in 1992 at United Nations Conference on the Environment and Development (UNCED) which recommends the prevention and minimization of waste production, the reuse or recycling of waste to the extent possible, and the treatment of waste by safe and environmentally sound methods[10]. It is also of serious concern that the level of awareness and practice, particularly of health workers regarding biomedical or hospital waste management and disposal plan has not been adequately documented. WHO Program activities include developing technical guidance materials for assessing the quantities and types of waste produced in different facilities, creating national action plans, developing national healthcare waste management and disposal guidelines and building capacity at national level to enhance the way biomedical waste is dealt with in low-income countries[11]. Classification of hospital wastes shows that of the total amount of waste generated by hospital activities, about 80% is general waste. The remaining 20% is considered hazardous material that may be infectious, toxic or radioactive. Every year an

estimated 16,000 million injections are administered worldwide[6], but not all of the needles and syringes are properly disposed of afterwards.

Biomedical waste contains potentially harmful micro-organisms which can infect hospital patients, hospital workers and the general public. Hospital activities protect and restore health and save lives and reverse should not be the case in the various hospitals across the country. Disposal of biomedical waste is an environmental concern, as most medical wastes are infectious and could potentially lead to the spread of infectious diseases. Daily exposure to biomedical wastes leads to accumulation of harmful microorganisms in the body of exposed persons[8]. Improper disposal of hospital waste can have both direct and indirect health consequences on humans and the environment. Indirect consequences in form of toxic emissions from inadequate burning of biomedical waste[12]. In developing countries like Nigeria, where many hospitals are competing for limited resources, the management and disposal of hospital wastes has received less attention and the precedence it deserves. Some hospitals dispose their biomedical wastes to municipal dumpsites without pre-treatment, leading to an unhealthy and hazardous environment. When dumped into the sea, it discharges poisons into the waters and it would be consumed by the marine creatures, the toxins would inject into the food chain and finally reach humans who consume the sea foods. Human exposure to such toxins can stunt human growth development and also cause birth defects. This trend is currently being experienced in Port Harcourt, Nigeria even when every disposal site is required by law to have environmental pollution prevention and control measures. Hundreds of tons of biomedical wastes are deposited in open dumpsites at the hospitals and on the roadsides of Port Harcourt metropolis, untreated and nonhazardous solid wastes, which now pose health risks to health workers, cleaning staff, patients, visitors, waste collectors, disposal site staff, waste pickers, drug addicts that use the contaminated syringes and needles. The overall objective of this study was to assess the biomedical waste management and disposal practices among hospitals in Port Harcourt, Rivers state.

Methods

Study Design and Setting

A hospital based cross sectional survey research design was adopted for the study to assess the biomedical waste management and disposal practices among hospitals in Portharcourt, Rivers State Nigeria, from May, 2021 to October, 2021.

The study was carried out within the capital of Rivers state known as Portharcourt city. Portharcourt is located in the southern Nigeria (Niger Delta).

Study Population

The study population includes health workers of the hospitals in the group of doctors, nurses, pharmacists, staff of laboratory departments and waste handlers. The study population also included the public and private hospitals.

The hospitals in Port Harcourt is 253 in number and it comprises of one (1) Federal Government owned, one (1) State Government owned and 251 individually owned hospitals.

Sample Size and Sampling Methods

Sample size for comparison of two proportions was used to determine minimum number of staff to be interviewed from each hospital and a total sample size of 218 was obtained.

A stratified and simple random sampling technique was used to draw out the number of respondents from each hospital using a table of random numbers for the study. The health workers were stratified according to their professional groups: doctors, nurses, pharmacists and laboratory staff, which amounted to four categories of health workers and the waste handlers. Then selection of respondents was done using simple random sampling via a computer generated table of random numbers. There was a list of staff in each stratum in all of the selected hospitals. Then serial numbers was assigned to each staff in keeping with the order of the list. Using the computer generated table of random numbers, participants was selected daily from each stratum in proportion to sample size until the total sample size was reached for both public and private hospitals.

Note: The selected hospitals in Portharcourt for the study included: University of Portharcourt Teaching Hospital (Owned and managed by the Federal Government of Nigeria), Braithwaite Memorial Specialist Hospital (BMH) Portharcourt (Owned and managed by the Rivers State Government), Queens Clinic and Pamo Clinic Portharcourt (owned by Individuals and managed privately).

Instruments for Data Collection

A well-structured questionnaire for information gathering was used in this study. the questionnaire contained information on the socio-demographic characteristics of the respondents, information about the respondents knowledge on biomedical waste management and information on the attitude of the respondents towards biomedical waste management and disposal practices.

Validity and Reliability

The questionnaire for this study was subjected to face validity. The questionnaire was designed in a simple language to avoid ambiguity, misinterpretation or misunderstanding of the questions or statements.

The test-retest method was used to test the reliability of the questionnaire using 10% of the sample size. This exercise was necessary because it enhanced the collection of relevant data, which also reduced bias. The analyzed data was reliable and the significant association set at p<0.001 with Fisher's Exact Test. A Cronbach coefficient of 0.88 was obtained for the study.

Method of Data Collection

The questionnaire was administered to the health workers of the hospitals in the category of doctors, nurses, pharmacists and staff of laboratory departments, and waste handlers. Field observation of biomedical waste generation rate and quantification in both public and private hospitals was also carried out. The data collection tool was adapted from the rapid assessment tool developed for sub- Saharan African countries by the World Health Organization and the secretariat of the Basel Convention of the United Nations Environmental Program (UNEP). This tool was a biomedical waste management inventory questionnaire that was used in assessment of biomedical waste disposal practices in hospital.

Method of Data Analysis

Data collected in this study were edited, coded and entered into the Statistical Product and Service Solutions (SPSS) version 22.0 and Microsoft Excel 2010. Table of frequencies and percentages were constructed. Chi-squared test and p-value less than 0.001 was used to show that there is a significant association between the hospital workers and the assessment of biomedical waste disposal practice in the selected hospitals.

Ethics

An approval was obtained from the research ethical committee of Public Health Department, School of Health Technology, Federal University of Technology Owerri alongside a letter of introduction issued from the administrative office before carrying out this research. The questionnaire was completed privately and anonymously (none of the respondents was identified by name at any point during data collection). Verbal informed consent was obtained from all the participants before being allowed to participate in this study.

Results

Socio demographic Factors of the respondents

From the **table I** below, 35% (70) of the respondents were between 35-44 years of age, 23% (46) had respondents between 15-24 years, 19% (60) were aged 25-34 and just 13% (27) included respondents between ages 45-50. Majority of the respondents were of Igbo origin (58%), 17% (34) were Yoruba, 15% (13), Hausa, 5% (10) Fulani and 6% (11) of the respondents chose options not listed but label 'Others'. Considering education level, 44% (89) had attained the tertiary level of education, 38% (77) secondary, 13% (25) primary level of education and under 6%(10) had Informal education levels. When asked about their length of experience, 29% (58) replied "1-5 years", 28% (57) 6-10 years, 22% (45) said "11-15 years", 19% (38) had experience of 16-20 years and only 2% (4) had an experience of 21 years and above. Majority (71%) of the respondents accepted they were hospital staff, while 29% (59) replied "No". 61.5% 988) (n = 143) affirmed they were public staff, while about 38.4% (55) chose 'Private'. Contractors accounted for 74.1% (106) of the hospital staff while 25.8% (37) replied "No". On the positions of the respondents, 27% were Laboratory technicians, 28% (40) were Nurses, 26% (37) Pharmacists, and 11% (15) were Medical Doctors. (n = 143). 8% (12) of the respondents were waste handlers.

Table I: Socio demographic Factors of the respondents.

Characteristics	Frequency (n=202)	Percentage (%)
Age		
15-24	46	23%
25-34	60	19%
35-44	70	35%
45-50	27	13%
Total	**202**	**100**
Ethnicity		
Igbo	118	58%
Hausa	13	15%
Yoruba	34	17%
Fulani	10	5%
Others	11	6%
Total	**202**	**100**
Educational level		
Informal education	10	5%
Primary	25	13%
Secondary	77	38%
Tertiary	89	44%
Total	**202**	**100**
Length of experience in years		
1-5 years	58	29%
6-10 years	57	28%
11-15 years	45	22%
16-20 years	38	19%
21 years and Above	4	2%
Total	**202**	**100**
Are you a Hospital Staff		
Yes	143	71%
No	59	29%
Total	**202**	**100**
Hospital category		
Public	88	61.5%
Private	55	38.4%
Total	**143**	**100**
Are you a contractor?		
Yes	106	74.1%
No	37	25.8%
Total	**143**	**100**
What is your position?		
Doctor	15	11%
Nurse	40	28%
Pharmacist	37	26%
Laboratory Technician	39	27%
Waste Handlers	12	8%
Total	**143**	**100**

Respondents Knowledge on Biomedical Waste Management and Disposal Practices

Revealed in **table II** below is the knowledge of respondents on biomedical waste management and disposal practices. 83% (168) of the respondents accepted it was important to know about biomedical medical waste generation, its hazards and safe management, while 17% (34) did not accept. When they were asked if they thought it was good to put all types of hospital waste into one container, 55% (110) replied "No", 41% (82) said "Yes", 5% (10) replied "Maybe". On question concerning knowledge of color-coding segregation of biomedical wastes, 61% (124) replied "Yes", 33% (68) said "No", and about 5% (10) replied "Maybe". 77% (155) of the respondents demonstrated that they followed color-coding for biomedical waste, while 23% (47) denied. 65% (122) of the respondents also took precautionary measures in handling hospital wastes according to the colors of their containers, while 35% (70) did not. Additionally, 65% (131) believed Personal protective equipment (PPES) can be useful in handling hospital waste, while 35% (71) denied. 32% (65), (n = 202), used PPEs such as Cover-alls, 22% (45) used Safety boots, 17% (33) used personal protective gear not listed but label 'Others', 15% (31) used Hand gloves while 14% (28) used safety goggles. 49% (65) (n = 131) of the respondents always wore PPEs, 29% (38) rarely, and 22% (28) only wore PPEs occasionally. When asked concerning disposing needles in general waste containers, 67% (135), replied "No", while 33% (67) said "Yes". 46% (94), reported they re-capped the used needles before disposal, 44% (89) said "Not always", and 10% (19) replied "No". 61% (124) also discarded the used needles immediately, while 39% (78) did not. Concerning needle stick injuries, 83% (167) obliged it was a problem, while 17% (35) did not accept. 24% (49) reported to be victims of Needle stick injuries while 76% (153) had not experienced such accidents. Majority (72%), (n = 49), of the Needle stick injury victims had experienced it about 1-5 times and 74% (36) of them filed a report. 62% (126) of the respondents demonstrated awareness of the consequences of needle-stick injuries, while 38% (78) denied. On disposal of hospital wastes in open places, 86% (174) denied, while a small 14% (28) accepted, the former said to have buried them (30%), Incinerate the waste (27%), Burn them (6%), land fill them (7%) and 29% (51) of the respondents opted for disposal methods not listed but label 'Others'. 65% (131) of the respondents demonstrated use of covered trucks for hospital waste disposal, while 35% (71) used open trucks. Majority of the respondents (92%, 185), also dumped hospital wastes in Municipal dumpsites, while under 8% (17) reported 'Rivers'. From figure 1, the respondent's good knowledge of biomedical waste was 80.2% and poor knowledge was 19.2%

Respondents Attitude on Biomedical Waste Management and Disposal Practices

Illustrated in **table III** below, 83% (168) replied "Yes" when asked if biomedical wastes are hazardous, while 17% (34) replied "No". The respondents (n = 168) reported they handles such wastes carefully, 28% (48) replied "Like common waste", 32% (53) did not specify but opted to choose 'Others'. 52% (104) scored safe management of biomedical waste as Good, 35% (71) Poor, and 13% (27) Fair. When the respondents were asked if proper management of biomedical waste can be seen as a financial burden on the hospital management, 64% (129) replied "Yes" and 36% did not oblige. 26% (52) of the respondents confirmed proper management of biomedical waste be achieved in the hospital through Team work, 25% (50) opined "Public Health Awareness", 18% (38) chose individual efforts, 11% (22) accepted all options were necessary and 19% (39) rejected all available options. 76% (150) of the respondents reported that safe management of biomedical waste disposal was an extra burden on the workers duties, and 58% (117) obliged containers should be labeled before filling with waste. Also 65% (130) of the respondents agreed that infectious waste should be sterilized from infections before disposal. The respondents were asked if they would voluntarily attend program that will enhance and upgrade their knowledge about biomedical waste, 87% (175) agreed, while 13% (27) did not accept.

Association between Socio demographic characteristics and Level of Knowledge of biomedical waste among health workers

Revealed in **table IV** below are the results for the test of a statistically significant relationship between Socio-demographic characteristics and Level of knowledge of biomedical waste among health workers. There was a statistically significant relationship between Age and Level of knowledge of biomedical waste among health workers in the study population, $\chi 2 = 1.342$, df=3, p= 0.00923. We therefore reject the null hypothesis of no significant relationship between Age and Level of knowledge of biomedical waste among health workers in the study population. Considering the hypothesis between Level of Education of health workers and knowledge of biomedical waste among health workers among relevant population, there was a statistically significant relationship between them, $\chi 2 = 1.2348$, df=3, p= 0.0025, therefore we reject the null hypothesis of no significant relationship between Level of Education of health workers and knowledge of biomedical waste among health workers in the study population. Given the relationship between Length of experience in years and knowledge of biomedical waste in the study population, there was a statistically significant association; $\chi 2 = 3.432$, df=3, p= 0.0457, therefore we reject the null hypothesis of no significant association between Length of experience in years and knowledge of biomedical waste in the study population. On the hypothesis between Being a Hospital Staff and knowledge of biomedical waste among primal population, There was a statistically significant relationship between Being a Hospital Staff and knowledge of biomedical waste in the study population, $\chi 2 = 2.653$, df=1, p= 0.00789. We therefore reject the

Table II: Respondents Knowledge on Biomedical Waste Management and Disposal Practices.

Variables	Frequency (n=202)	Percentage (%)
Do you think it is important to know about biomedical medical waste generation, its hazards and safe management?		
Yes	168	83%
No	34	17%
Total	**202**	**100**
Do you think it is good to put all types of hospital waste into one container?		
Yes	82	41%
No	110	55%
Maybe	10	5%
Total	**202**	**100**
Do you know about colour-coding segregation of biomedical wastes?		
Yes	124	61%
No	68	33%
Maybe	10	5%
Total	**202**	**100**
Do you follow colour-coding for biomedical waste?		
Yes	155	77%
No	47	23%
Total	**202**	**100**
Do you take precaution in handling hospital wastes according to the colours of their containers?		
Yes	132	65%
No	70	35%
Total	**202**	**100**
Do you believe that personal protective equipments (PPES) like gloves can be useful in handling hospital wastes?		
Yes	131	65%
No	71	35%
Total	**202**	**100**
Do you wear Personal Protective Equipments?		
Hand Gloves	31	15%
Cover-alls	65	32%
Safety booth	45	22%
Safety goggle	28	14%
Others	33	17%
Total	**202**	**100**
If Yes, how often do you wear PPEs?		
Rarely	38	29%
Always	65	49%
Occasionally	28	22%
Total	**131**	**100**
Are needles supposed to be put into general waste containers?		
Yes	67	33%
No	135	67%
Total	**202**	**100**
Do you re-cap the used needle?		
Yes	94	46%
No	19	10%
Not always	89	44%
Total	**202**	**100**
Do you discard the needle Immediately?		
Yes	124	61%
No	78	39%
Total	**202**	**100**
Is needle-stick injury a concern?		
Yes	167	83%
No	35	17%
Total	**202**	**100**
Have you had needle stick injury in the past one year?		
Yes	49	24%
No	153	76%
Total	**202**	**100**
If Yes, how many times?		
1-5	39	72%
6-10	9	17%
Above 10	6	11%
Total	**49**	**100**
Did you fill an incident report?		
Yes	36	74%
No	13	26%
Total	**49**	**100**

Table II: Respondents Knowledge on Biomedical Waste Management and Disposal Practices.

Variables	Frequency (n=202)	Percentage (%)
Are you aware of the consequences of needle-stick injury?		
Yes	126	62%
No	76	38%
Total	**202**	**100**
Do you dispose hospital waste in open Places?		
Yes	28	14%
No	174	86%
Total	**202**	**100**
If No, What do you do with them?		
Burn Them	11	6%
Bury Them	52	30%
Incinerate Them	47	27%
Land fill Them	13	7%
Others	51	29%
Total	**174**	**100**
What kind of trucks do you use in disposal of hospital wastes?		
Covered Trucks	131	65%
Open Trucks	71	35%
Total	**202**	**100**
Where do you dump the hospital wastes?		
Municipal dumpsites	185	92%
Rivers	17	8%
Total	**202**	**100**

Table III: Respondents Attitude on Biomedical Waste Management and Disposal Practices.

Variable	Frequency (n=202)	Percentage (%)
Is biomedical waste a hazardous waste?		
Yes	168	83%
No	34	17%
Total	**202**	**100**
If Yes, how do you handle such waste?		
Carefully	67	40%
Like common waste	48	28%
Others specify	53	32%
Total	**168**	**100**
How can you score safe management of biomedical waste?		
Good	104	52%
Poor	71	35%
Fair	27	13%
Total	**202**	**100**
Can proper management of biomedical waste be seen as a financial burden on the hospital management?		
Yes	129	64%
No	73	36%
Total	**202**	**100**
How can proper management of biomedical waste be achieved in the hospital?		
Individual Effort	38	19%
Team Work	52	26%
Public Health Awareness	50	25%
All of the Above	22	11%
None of the Above	39	19%
Total	**202**	**100**
Is safe management of biomedical waste an extra burden on the workers duties?		
Yes	150	76%
No	52	24%
Total	**202**	**100**
Do you think that labeling the container before filling it with waste is of any clinical concern?		
Yes	117	58%
No	85	42%
Total	**202**	**100**
Do you think that infectious waste should be sterilized from infections before its disposal?		
Yes	130	65%
No	72	35%
Total	**202**	**100**
Will you like to attend voluntarily programmes that will enhance and upgrade your knowledge about biomedical waste?		
Yes	175	87%
No	27	13%
Total	**202**	**100**

null hypothesis of no significant relationship between Being a Hospital Staff and knowledge of biomedical waste in the study population. There was no statistically significant relationship considering the hypothesis between being a contracted worker and knowledge of biomedical waste among relevant population. $\chi 2$ = 5.235, df=1, p= 0.01934, therefore we fail to reject the null hypothesis of no significant relationship between being a contracted worker and knowledge of biomedical wastes. Considering the association between position in the hospital and knowledge of biomedical wastes, there was a statistically significant relationship. $\chi 2$ =1.324, df=1, p= 0.00765, Therefore we reject the null hypothesis of no significant association between position in the hospital and knowledge of biomedical wastes among relevant population.

Table IV: Association between Socio demographic characteristics and Level of Knowledge of biomedical waste among health workers.

Socio Demographics	Knowledge of Biomedical Wastes		X2	P-value	Decision
	High (%)	Low (%)			
Age			1.342	0.00923	**Sig.**
15-24	16(40.0)	34(60.0)			
25-34	36 (60.0)	24(40.0)			
35-44	40(57.1)	30(42.9)			
45-50	25(92.5)	2(7.4)			
Educational level			1.2348	0.0025	**Sig.**
Informal education	3(30.0)	7(70.0)			
Primary	14(56.0)	11(44.0)			
Secondary	47(61.0)	30(39.0)			
Tertiary	59(66.2)	30(33.8)			
Length of experience in years			3.432	0.0457	**Sig.**
1-5 years	27(46.5)	31(53.4)			
6-10 years	37(64.9)	20(35.1)			
11-15 years	33(73.3)	12(26.7)			
16-20 years	36(94.7)	2(52.6)			
21 years and Above	4(100)	0(0)			
Are you a Hospital Staff			2.653	0.00789	**Sig.**
Yes	73(51.0)	70(48.9)			
No	39(66.1)	20(33.8)			
Are you a contractor?			5.235	0.1934	**Insig.**
Yes	80(75.4)	26(24.5)			
No	30(81.0)	7(18.9)			
What is your position?			1.324	0.00765	**Sig.**
Doctor	10(66.6)	5(33.3)			
Nurse	29(72.5)	11(27.5)			
Pharmacist	30(81.0)	7(18.9)			
Laboratory Technician	20(51.2)	19(48.7)			
Waste Handlers	8(66.6)	4(33.3)			

Discussion

The objective of this study was to evaluate biomedical waste management and disposal practices in hospitals in Port Harcourt, Rivers State, Nigeria. Considering the socio-demographic characteristics, with regards to age, findings from the study showed that 35% of the respondents were within the age group 35-44 years, the age seen in this study, is in consistence with the statement by John *et al*,[14] that 34.5% of hospital workers fall within this age category. Further findings from this study showed that 58% of the respondents were of Igbo origin and Christians. This could be because the study was conducted in the Southern part of Nigeria and the hospitals surveyed were located in Port Harcourt, Rivers State which is a neighboring eastern state of the federation predominated by Igbo people. This is also in consistence with the study conducted by Brisbe and Ordinoha[10], this study revealed that majority of the respondents (71%) are hospital staff and 74.1% are contractors. This signifies that majority of the hospital staff is not permanent staff and probably have other clinics or hospitals they earn a living out of and hence attention to work might be divided. This connotes a consistence with a similar study conducted by Cheeseman & Townend[12] and in contrast with a statement made in a publication by Grioult[15].

The findings of the study considering the knowledge of the forms of biomedical waste management and disposal practices revealed that 83% of the respondents accepted it was important to know about biomedical medical waste generation, its hazards and safe management. This implies that health workers have significant knowledge of the importance of controlled generation and disposal of biomedical wastes. This corroborates a publication by Da Silva *et al*[3], that 85.2% of health workers in hospitals have an awareness of biomedical disposal practices. Concerning knowledge of color-coding segregation of

biomedical wastes, 61% affirmed. This could be due to the fact that color-coding segregation of waste is a standard practice and has been adopted by most health facilities. A study byKevin & Oguamanam[16] is in consistence with this finding. Further investigation into the finding of this study shows that majority (77%) of the respondents demonstrated that they followed color-coding for biomedical waste, as corroborated by a previous finding by Ferreira[2] that medical facilities are required to ensure biomedical wastes are color-coded for disposal. Several studies also support this finding[17,3,18,19,2,15,20]. This study revealed that 35% of the respondents did not take precautionary measures in handling hospital wastes according to the colors of their containers. This could be due to lack of provision of relevant colors of containers for biomedical waste disposal by the health facilities. This goes in contrast to a statement made in a publication by Adogu & Ubajaka[21] that under 10% of hospital workers in a survey did not take precautions in handling hospital wastes according to the colors of their containers. Some studies by Buregyega *et al*[22], Caviar *et al*[9], Chauhan *et al*[7], disagree with this finding. Additionally, 65% of hospital workers believed Personal protective equipment (PPES) can be useful in handling hospital waste, and the most adopted PPES are the cover-alls (35%). This could be because the cover-all ensures limbs and trunk are fully protected from biomedical wastes. This is in consistence to a similar study conducted by Abitebul and Loft[23] on the adoption of cover-all by hospital workers (39%). 83% of the respondents obliged Needle stick injuries are common, while 76% had not experienced such accidents. This finding falls in line with a previous study by[12] that 81% of hospital workers demonstrated knowledge of needle stick injuries and that 74% in a survey conducted did not experience needle stick injuries. This is in contrast to a publication by[22].On disposal of hospital wastes in open places, 86% denied. This implies stringent adherence to laws put in place to check the disposal of biomedical wastes. Numerous publications support this finding[24,25,23,26]. 65% of the respondents illustrated use of covered trucks for hospital waste disposal which is in line with required standard procedure, also Majority of the respondents (92%) also dumped hospital wastes in Municipal dumpsites, advance findings from this study show that under 8% reported 'Rivers'. This could be due to nonavailability of designated dumpsites in proximity or no dumpsites at all provided by relevant bodies.

Considering the information attitude on biomedical waste management and disposal Practices among respondents, the study revealed that based on overall response from the participants that 83% affirmed biomedical wastes are hazardous. This falls in line with previous studies[27,17,3]. 52% of the respondents scored safe management of biomedical waste as 'Good', while 64% think that proper management of biomedical waste can be seen as a financial burden on the hospital management. This could mean the hospitals lack adequate resources for proper management of biomedical wastes and is corroborated by a publication by Alagoz & Kocasoy[28]. 76% of the respondents reported that safe management of biomedical waste disposal was an extra burden on the workers duties. The implication here could be that most hospitals are understaffed and hence workers have to engage in more tasks than they should perform. A previous study by Adetunji *et al*[29], explicitly explained the problems of under-staffing. Also 65% of the respondents agreed that infectious waste should be sterilized from infections before disposal. 87% of the respondents accepted to voluntarily attend programs that will enhance and upgrade their knowledge about biomedical waste, further check into this study revealed that 13% did not accept. This could be due to lack of motivation and poor attitude to work created as a result of untimely and underpaid monthly earnings. This is in consistence to several studies[14,16,30,31].

Findings from this study regarding the association between Socio demographic Characteristics and Level of knowledge of biomedical wastes revealed that Age is significantly associated with level of knowledge of biomedical wastes among health workers (P = 0.00923). This implies that there was a significant increase in the level of knowledge of biomedical wastes as the age of the respondents under consideration increased. This could be due to the exposure that come with increased age, which could imply increase length in practice and is in line with studies by Da Silva *et al*[3], which found age to be associated with knowledge of biomedical wastes. (P=0.00861). Moving further, the study also demonstrated that the level of education of health workers is significantly associated with the knowledge of biomedical waste (P = 0.0025). This could be due to the fact that the higher the education level of the respondents the more likely they must have come across biomedical waste management and disposal practices. This goes in contrast with a report published by Abitebul & Loft[23], that the education level of health workers may not affect the level of knowledge of biomedical wastes among primal population. Also, from the study among health workers in selected hospitals in Portharcout, Rivers State, it was posited that length of experience in years shows significant association with level of knowledge of biomedical wastes (P = 0.0457). Study shows that the level of knowledge of biomedical wastes was minimal among respondents who have practiced for 1-5 years, compared to health workers with 21 years and above practice experience. This is in consistence to studies conducted by Buregyega *et al*[22], Caviar et al[9], and Chauhan et al[7], but goes against a publication by Grioult[15]. The study revealed that level of knowledge of biomedical wastes was high among the waste handlers 66.6% compared to any other position among health workers in the Portharcourt hospitals and hence a significant relationship (P = 0.00765). Studies according to Cheeseman & Townend[12] stated that health workers who are responsible for waste handling

in hospitals had the highest knowledge of biomedical wastes and disposal practices. This level of knowledge could be due to the position of employment in these hospitals respectively.

Conclusion

Based on the outcomes of the study, it could be seen that a significant number of hospital workers are aware of biomedical waste generation, management and disposal practices. This includes the use of PPES and color-coding hospital wastes before disposal. However, the attitude to biomedical waste management and disposal practices is average and therefore a challenge. The study also reveals that medical facilities lack adequate resources needed to properly dispose of biomedical wastes. Strict laws to guide disposal of hospital waste which have been put in place need to be reinforced. Also Ease of biomedical wastes disposal by creating dumpsites at strategic points should be considered. Hospital staff/ workers should also be sensitized, encouraged on the hazards of biomedical wastes and Importance of good waste management. Understaffed hospitals are required to hire workers with relevant qualifications to promote biomedical waste management and disposal.

Recommendations

Based on the finding of this study, it is recommended government and policy makers should design laws that would facilitate the reduction and susceptibility of improper hospital waste disposal. Also Provision of disposal facilities such as landfills sites and incinerators at strategic points to increase ease in disposition of biomedical wastes is imperative.

Ethics Approval and consent to Participate

Not Applicable

Consent to Publish

Not applicable

Availability of Data and Materials

The Data set from the study are available to the corresponding author upon request.

Competing Interests

Authors have declared that they have no competing interests

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ORIGINAL

A study of evaluation and proper diagnosis of stroke in CT scan and MRI

Un estudio sobre la evaluación y el diagnóstico adecuado del ictus en la TC y la RM

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Abstract

Objective: This project has taken to know why CT remains the primary imaging modality in stroke evaluation while is associated with high ionizing radiation, and to know when CT can be replaced by MRI as primary imaging.
Methodology: The study was carried out in different hospitals in Dhaka city using data collection from 120 patients suspected of stroke.
Results: the study showed that CT is the most common imaging modality used in stroke imaging mainly due to its practicality, speed, and availability in most clinical centers. An CT is more accessible in the emergency setting of stroke evaluation than MRI, thus is preferred in most centers as the primary imaging modality. CT has been proved to be very sensitive, especially in the detection of acute hemorrhage. However, its accuracy is decreasing with time from the symptom onset and this is a disadvantage, MRI has been proved much more accurate modality in both types of strokes, thus it can be used as a sole imaging modality for the evaluation of patients with suspected stroke. Theoretical and practical implications are discussed.
Conclusion: This study tried to find out if MRI becomes the primary imaging modality and can replace CT scan as primary imaging for stroke evaluation also this study presented compression between them, whether it is good to use MRI or CT furthermore, we presented the future study.

Key words: Ischemic stroke, intracerebral hemorrhage, transient ischemic attack, computed tomography, non-contrast computed tomography, magnetic resonance imaging, diffusion-weighted imaging, perfusion-weighted imaging.

Resumen

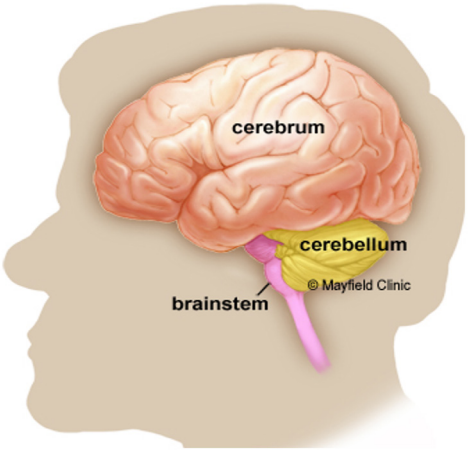
Objetivo: Este proyecto ha tenido como objetivo conocer por qué la Tomografía computarizada (TC) sigue siendo la modalidad de imagen primaria en la evaluación del ictus mientras se asocia a una alta radiación ionizante, y saber cuándo la TC puede ser sustituida por la (Resonancia Magnética (RM) como imagen primaria.
Metodología: El estudio se llevó a cabo en diferentes hospitales de la ciudad de Dhaka mediante la recogida de datos de 120 pacientes con sospecha de ictus.
Resultados: el estudio demostró que la TC es la modalidad de imagen más utilizada en el diagnóstico por imagen de los accidentes cerebrovasculares debido principalmente a su practicidad, rapidez y disponibilidad en la mayoría de los centros clínicos. La TC es más accesible en el entorno de emergencia de la evaluación del ictus que la RM, por lo que se prefiere en la mayoría de los centros como modalidad de imagen primaria. La TC ha demostrado ser muy sensible, especialmente en la detección de hemorragias agudas. Sin embargo, su precisión disminuye con el tiempo desde el inicio de los síntomas y esto es una desventaja, la RM ha demostrado ser una modalidad mucho más precisa en ambos tipos de accidentes cerebrovasculares, por lo que puede utilizarse como única modalidad de imagen para la evaluación de pacientes con sospecha de accidente cerebrovascular. Se discuten las implicaciones teóricas y prácticas.
Conclusiones: Este estudio intentó averiguar si la RM se convierte en la modalidad de imagen primaria y puede sustituir a la TC como imagen primaria para la evaluación del ictus también este estudio presentó la compresión entre ellos, si es bueno utilizar la RM o la TC además, presentamos el estudio futuro.

Palabras clave: accidente cerebrovascular isquémico, hemorragia intracerebral, ataque isquémico transitorio, tomografía computarizada, tomografía computarizada sin contraste, resonancia magnética, imágenes ponderadas por difusión, imágenes ponderadas por perfusión.

1. Introduction

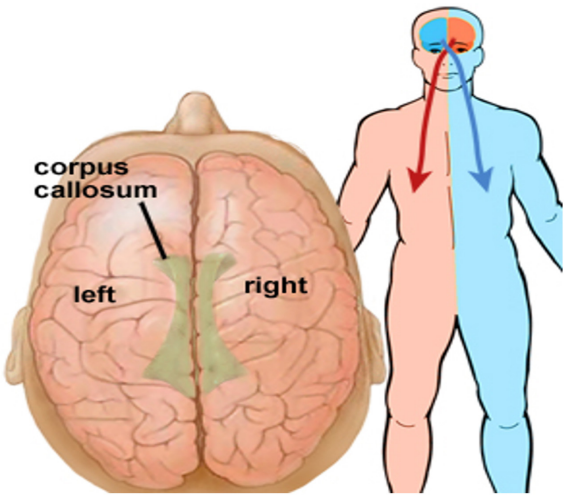
Stroke is the immediate or unexpected loss of brain function where there is decreased or cut off of the blood supply to the brain. It is one of the major healthcare problems as it is the third leading of death[1]. With the aging of population of the earth, the number of deaths caused by stroke is expected to increase in the near future[2]. the disturbance of blood supply to the brain which causes to a stroke event can be due to ischemia (thrombosis or embolism) or hemorrhage[3]. The term 'stroke' was coined and introduced to medicine by William Cole in the late 17th century[4] and has remained a generic definition since. The WHO describes stroke as a clinical syndrome typified by "rapidly developing clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause apart that of vascular origin[5]. Normally we classified two main types, one is Ischemic stroke, is the most common type of stroke and it refers to the 80% of all cases[6]. Ischemic stroke occurs when an artery which provides blood to the brain is occluded due to thromboembolic events and the blood supply to the brain is greatly decreased or even cut off. The normal cerebral blood flow (CBF) is 50-80 ml/100g/min and when CBF is reduced into less than 8 ml/100g/min brain cells start to die and that causes an irreversible injured core within minutes. If the CBF is reduced to 20 ml/100g of tissue per minute to an area of the brain, this area represents an ischemic penumbra which is still viable and can be fully recovered if perfusion of the blood is restored in time[7]. The second is Hemorrhagic stroke is less frequent compared to ischemic (20% of all strokes) but much more fatal[8]. When the wall of a blood vessel becomes weak, it ruptures and bleeds into the surrounding brain, which causes buildup of pressure into the brain parenchyma, which distorts and injures brain tissue and this can cause death to the 40% to 50% of the patients[9]. There is another sub type of stroke which called Transient ischemic attack (TIA), is a subtype of the main types (Ischemic and Hemorrhage). TIA refers to a ''mini stroke" or to a ''warning stroke"[10]. TIA has similar symptoms to stroke, but with the difference that they last for few seconds to minutes without causing any infarction or severe problems to the brain[11]. The basic anatomy of the brain has three main parts first is the Cerebrum, which is the largest part of the brain and is composed of the right and left hemispheres. it performs higher functions like interpreting touch, vision, and hearing as well as speech, reasoning emotions, learning, and fine control of movement. The second Cerebellum- is located under the cerebrum. Its function is to coordinate muscle movements and maintain posture and balance. Thirdly Brainstem- acts as rarely center connecting the cerebrum and cerebellum to the spinal cord. It performs many autonomic functions such as breathing, heart rate, body temperature wake, sleep cycles, digestion, sneezing, coughing, vomiting, and swallowing.

Figure 1.1: three main brain components.



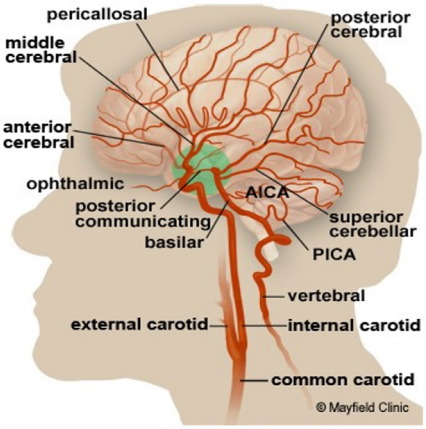
Moreover, the cerebrum is divided into two halves: the right and left hemispheres (**Figure 1.2**) they are joined by bundle of fibers called the corpus callosum that transmits messages from one side to the other. Each hemispheres controls the opposite side of the body. If the stroke occurs on the right side of the brain, your left arm or leg may be weak or paralyzed. Not all functions of the hemispheres are shared. In general, the left hemisphere controls speech, comprehension, arithmetic, and writing. The right hemisphere controls creativity, spatial ability, artistic, and musical skills. The left hemisphere is dominant in hand use and language in about 92% of people.

Figure 1.2: The cerebrum is divided into left and right hemispheres. The two sides are connected by the nerve fibers corpus callosum.



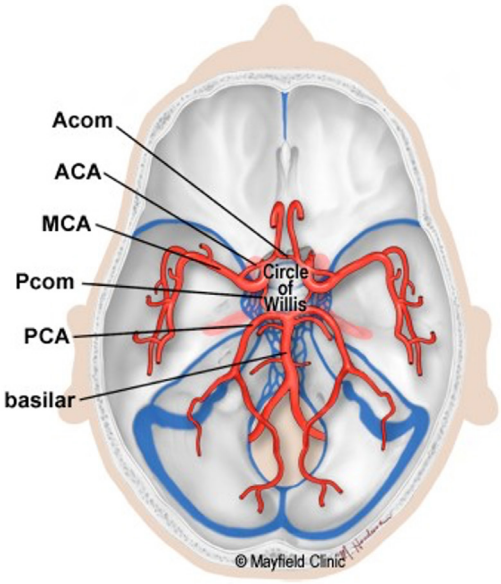
The also main important things we need to mention here is blood supply of the brain, Blood is carried to the brain by two paired arteries, the internal carotid arteries and the vertebral arteries (**Figure 1.3**). The internal carotid arteries supply most of the cerebrum.

Figure 1.3: The common carotid artery courses up the neck and divides into the internal and external carotid arteries. The brain's anterior circulation is fed by the internal carotid arteries (ICA) and the posterior circulation is fed by the vertebral arteries (VA). The two systems connect at the Circle of Willis (green circle).



The vertebral arteries supply the cerebellum, brainstem, and the underside of the cerebrum. After passing through the skull, the right and left vertebral arteries join together to form the basilar artery. The basilar artery and the internal carotid arteries "communicate" with each other at the base of the brain called the Circle of Willis (**Figure 1.4**). The communication between the internal carotid and vertebral-basilar systems is an important safety feature of the brain. If one of the major vessels becomes blocked, it is possible for collateral blood flow to come across the Circle of Willis and prevent brain damage.

Figure 1.4: Top view of the Circle of Willis. The internal carotid and vertebral-basilar systems are joined by the anterior communicating (Acom) and posterior communicating (Pcom) arteries.



The venous circulation of the brain is very different from that of the rest of the body. Usually, arteries and veins run together as they supply and drain specific areas of the body. So, one would think there would be a pair of vertebral veins and internal carotid veins. However, this is not the case in the brain. The major vein collectors are integrated into the dura to form venous sinuses — not to be confused with the air sinuses in the face and nasal region. The venous sinuses collect the blood from the brain and pass it to the internal jugular veins. The superior and inferior sagittal sinuses drain the cerebrum, the cavernous sinuses drain the anterior skull base. All sinuses eventually drain to the sigmoid sinuses, which exit the skull and form the jugular veins. These two jugular veins are essentially the only drainage of the brain[12].

1.1 Justification of the study

- Clinical evidence might suggest stroke, only imaging modalities can provide enough information to identify acute stroke symptoms, either ischemic or hemorrhagic.
- On the hand CT ca detect accurately any intracranial hemorrhage.
- On the other hand, DWI is a sensitive technique for the detection of early ischemic changes and can visualize them within minutes after the symptom onset.
- Obviously, this is an advantage in stroke evaluation as 80% of all strokes are ischemic and treatment should be administered in the first 3 hours from the symptom onset.
- Furthermore, MRI has been proved to be as accurate as CT for the detection of acute intracerebral hemorrhage.
- New imaging techniques like Angiography and Perfusion with Diffusion imaging can provide all the vital information to the clinician to choose the correct treatment path
- With MRI and CT, enough information can be provided for the selection of patients eligible for thrombolysis, based not on clinical evidence and time from the stroke onset, but on pathophysiology of the brain.

1.2 Research question

Can MRI be a better imaging modality that can replace CT scan as primary imaging for diagnosis and evaluation of stroke?

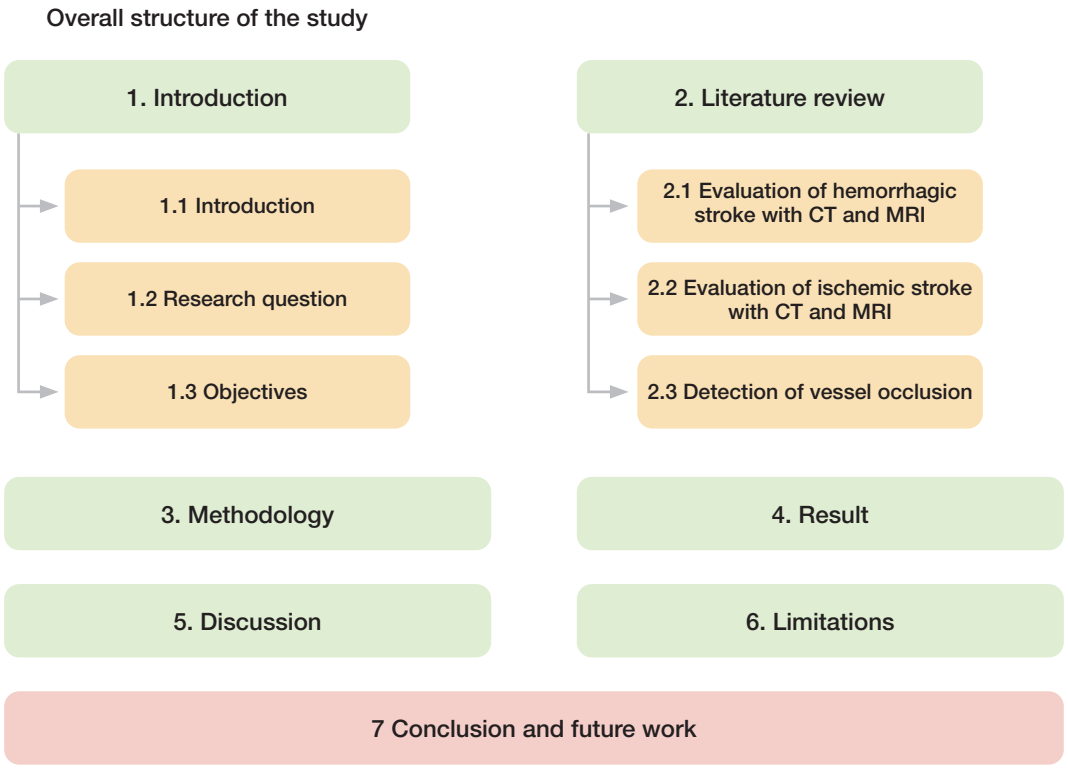
1.3 Objectives

The General objectives is to compare the diagnostic accuracy of diffusion-weighted MRI (DWI) and CT for acute ischemic stroke, and to estimate the diagnostic accuracy of MRI for acute hemorrhagic stroke. and the Specific objectives is to know why CT remains the primary imaging modality in stroke evaluation while is associated with high ionizing radiation? To know which gender is highly affected by the stroke, to compare CT and MRI for their detection and diagnosis of stroke.

1.4 Ethical consideration

Ethical clearance to conduct the study was obtained from the Bangladesh University of Health Sciences (BUHS).

Figure 1.5: Overall organized of the paper process.



2. Literature review

2.1. Evaluation of hemorrhagic stroke with CT and MRI

The detection of intracerebral hemorrhage is the first step in stroke diagnosis, as its detection differentiates the ischemic from hemorrhagic stroke, and defines the treatment path. Computed tomography due to its high sensitivity in hemorrhage remains the primary modality for its detection, however according to published literature MRI using special sequences might prove to be an even more accurate method in the detection of any hemorrhage. This chapter will provide answers regarding the detection of intracranial hemorrhage with both methods in acute, and subacute and chronic hemorrhage, micro bleeds, plus hemorrhage after thrombolysis.

2.1.1. Detection of acute intracerebral hemorrhage

Non-enhance CT remains first step in stroke imaging because of its high accuracy in the detection of intracranial hemorrhage. Intracranial blood in CT appears as a hyper attenuated area 1.due to the different attenuation of the x rays, but when blood intermixes with Cerebral Blood Flow (CBF) or brain tissue might cause a hypo attenuation thus, the density of the hemorrhagic area will appear as the adjacent normal brain and this is more often in subarachnoid hemorrhage.

2.1.2. Detection of Subarachnoid Hemorrhage

Subarachnoid hemorrhage is most severe case of hemorrhagic stroke and refers to 1-7% of all strokes14. The most common imaging modality which is used for the detection of SAH is NCCT in which illustrates hyper intensity area filling the Cisterns and Sulci.

MRI uses a different philosophy in the detection of SAH, as it relies on the blood degradation, which produces DE oxyhemoglobin which can be detected by MR. Specifically, the sensitivity of MRI in the detection of hemorrhage increases with time[13].

Compared MRI sequences and NCCT to measure their sensitivity to SAH. His study included 41 patients and it was proved that T2* GRE and Fluid Attenuation Inversion Recovery (FLAIR) sequences had an overall sensitivity of 94% and 87% respectively and 95% for CT in the acute phase. Basic T1 and T2 sequences were less sensitive in the detection of acute SAH with percentages between 50-56%. In the subacute phase the sensitivity for T2*GRE and FLAIR sequences increased, reaching 100% for T2* GRE and 87% for FLAIR sequence and 90% for CT. However, the percentage for T1, T2 sequences was reduced to 33%, 47% and 33% respectively. Only one patient with SAH was not detected by MRI but with CT.

2.1.3. Detection of Chronic Hemorrhage

Computed Tomography might have an accuracy of almost 100% in the detection of acute intracranial hemorrhage however, its sensitivity on subacute and chronic hemorrhage cannot be compared with the sensitivity of MRI. Blood appears differently in diagnostic imaging at each phase (acute, subacute and chronic) and MRI has been found to be more accurate than CT in detection in the subacute and chronic setting[14].

Overall Result in the detection of any hemorrhage: MRI has been shown in this enquiry to be as accurate as CT in the detection of both intracranial and subarachnoid hemorrhage but more reliable and accurate in subacute and chronic hemorrhage.

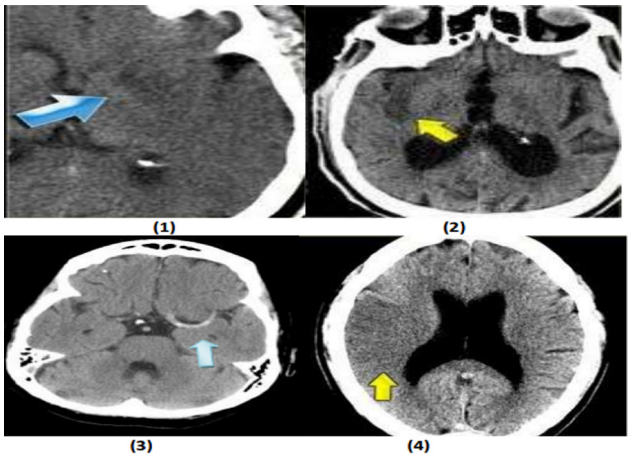
2.2. Evaluation of ischemic stroke with CT and MRI

Ischemic stroke is the most common type of stroke as it refers to the 80% of all cases. An ischemic stroke occurs when the blood supply to the brain is reduced significantly, most of the times due to clot. Ischemic penumbra is the area of the brain which is still viable and can be fully recovered if perfusion of the blood is fully restored in time. In the case where intracerebral hemorrhage is not detected, the next step in stroke evaluation is to check for early ischemic signs which can be found very frequently in a percentage of 92% and according to. Their detection is associated with a poor overall outcome.

2.2.1. Detection of Early Ischemic Changes

The major disadvantage of CT in ischemic stroke is that it cannot detect any ischemic changes with accuracy in the acute setting. early ischemic changes might be detected and clarified correctly approximately 6 hours after the onset symptom if a CT scanner is used[15] but usually this cannot be fully justified and especially in the hyper acute setting (3 hours) where EIS (early ischemic) appear to be subtle and don't provide enough evidence which can lead to thrombolytic treatment (**Figure 2.1**).

Figure 2.1: Early Ischemic Changes and CT 1. Obscuration of the lentiform nucleus. 2. Insular ribbon sign. 3. Hyper attenuating media sign. 4. Hypo attenuation areas appear over time after the symptom onset.



Aside from specialized MR imaging techniques like DWI, conventional sequences are used as well in ischemic stroke evaluation. T2-Weighted imaging is well correlated with tissue prognosis as it can illustrate infracted tissue but, as on CT, definitive early ischemic changes can only be seen 6 hours from the symptom onset. With a T1-weighted sequence, an early infarction might be diagnosed by focal swelling and parenchymal hypo intensity because of the Cytoxan edema

Over all Result for the detection of Ischemic Changes: MRI is superior to CT in the detection of Early Ischemic Changes.

2.3. Detection of vessel occlusion

If an intracranial hemorrhage is not detected, and early ischemic changes might confirm an ischemic stroke then the next step to be performed in stroke imaging is to evaluate if a large vessel is occluded. Both CTA and MRA are noninvasive imaging techniques which can be used for the evaluation intracranial and cervical vessels for the detection of an arterial occlusion or stenosis in the circle of Wills and confirm the ischemic changes.

Overall Result for the detection of an occlusion: MRI might not be able to provide as accurate results and high-resolution images as CT, however it can lead to the same treatment decisions.

3. Methodology

The study design was a descriptive multidimensional and multiple sequence taken for the study.

And the study population was the patients of both outdoor and indoor patients, admitted different hospitals in Dhaka, who came in the Department of Radiology and Imaging for MRI or CT scan for diagnosis evaluation of stroke. The place of the study was carried out six different hospitals in Dhaka and the study period was carried out from 01/December/ 2020 to 31/march/ 2021. The sample size was determined purposively, 120 cases of suspected cases who developed sign and symptoms of stroke, has been diagnosed by MRI or CT scan, and uncooperative cases were excluded from the study. Moreover, we used sampling technique that was taken purposively, and the data collection tools was a semi structure questionnaire was prepared according to clinical symptoms, Risk factors, and the objectives of the study. The data collection procedure was taken from the Head of the Department of Radiology and Imaging in each hospital and verbal consent from Radiology & imaging Department In-charge. Prior to interview the purpose of the study was clearly elaborated to the patient and guidance of the patient and their verbal consent was taken before filling the questionnaire. I collected data by face-to-face interview. At first find the lists/prescription of stroke and collected

data by face-to-face interview, one by one, separately. Furthermore, Imaging and image analysis all patients referred to the Department of Radiology for MRI and CT of Brain underwent examinations as per protocols. MRI The routine protocol included was sagittal and axial T1- and T2-weighted images, diffuse weighted image (DWI), FLAIR and short tau inversion recovery (STIR) coronal images. All MRI examinations were performed on a 1.5 Tesla Siemens and Philips MRI scanner. CT- the routine protocol included was sagittal, axial and coronal images. All CT examinations were performed on a 128 slice and 64 slice Siemens and Philips respectively. All images were reviewed by radiologists, and a consensus diagnosis was given by different radiologists in controversial cases. Finally, data was analyzed after collection, also data was checked, verified, and processed to reduce error. Then it was analyzed by computer using SPSS software version 16.0.

4. Results

Table and Figure 4.1: Shows the age of the participants.

Age	Frequency	Percent
20-40	40	33.3%
41-60	44	36.7%
61-80	32	26.7%
above 80	4	3.3%
Total	**120**	**100.0%**

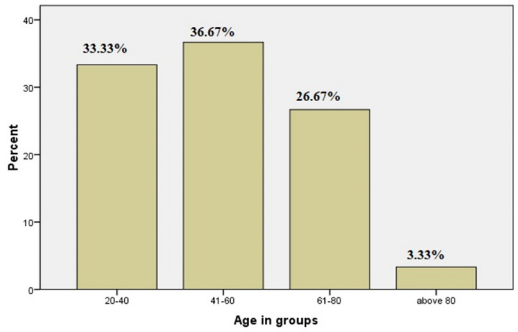


Table and Figure 4.2: Demonstrates the gender information.

Gender	Frequency	Percent
Male	62	51.7%
Female	58	48.3%
Total	**120**	**100.0%**

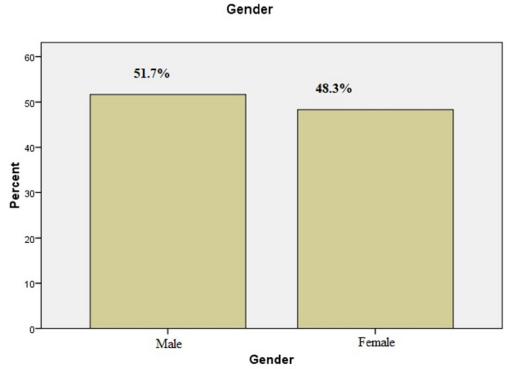


Table 4.3: Demonstrates the Educational status.

Level of education	Frequency	Percent
Below school level	27	22.5%
School level	47	39.2%
College level	34	28.3%
University level	12	10.0%
Total	**120**	**100.0%**

Table 4.4: Shows that occupational status off the study.

Services	Frequency	Percent
No service	26	21.7%
Service	94	78.3%
Total	**120**	**100.0%**

Table and Figure 4.5: Shows the clinical history of the participants.

Clinical history	Frequency	Percent
Right sided weakness	12	10.0%
Left sided weakness	20	16.7%
General weakness	32	26.7%
Headache	35	29.2%
memory loss	11	9.2%
Unconsciousness.	5	4.2%
Slow movement	5	4.2%
Total	**120**	**100.0%**

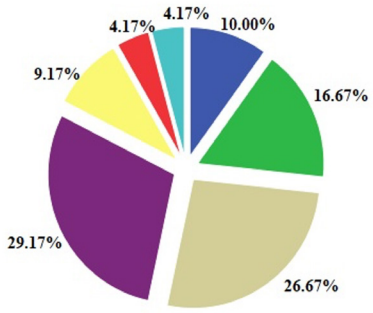


Table and Figure 4.6: Shows the risk factors of stroke.

Risk factors	Frequency	Percent
Diabetes and hypertension	35	29.2%
Hypertension and smoking	16	13.3%
Smoking	11	9.2%
Diabetes only	9	7.5%
Family history of stroke	7	5.8%
All of the above except family history	18	15.0%
All	7	5.8%
Hypertension only	17	14.2%
Total	**120**	**100.0%**

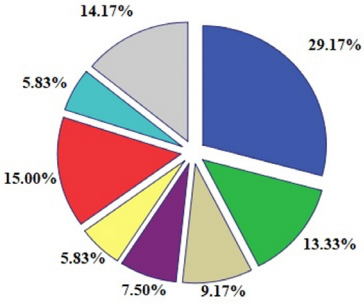


Table and Figure 4.7: Show the trauma history of the study participants.

Trauma	Frequency	Percent
No	109	90.8%
Yes	11	9.2%
Total	**120**	**100.0%**

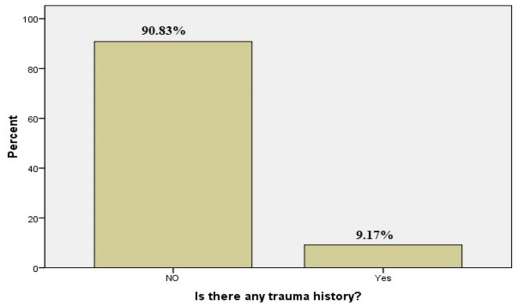


Table and Figure 4.8: Demonstrated which modalities is used?

Modality	Frequency	Percent
MRI	45	37.5%
CT scan	75	62.5%
Total	**120**	**100.0%**

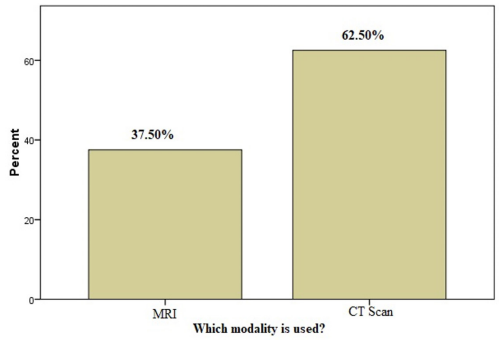


Table and Figure 4.9: Show the factors of influence the decision to use a CT scan or MRI as the primary imaging modality.

Factors	Frequency	percent
MRI takes longer than CT scan.	27	22.5%
Most centers offer CT scans, but MRIs are not	25	20.8%
MRIs are more expensive than CT scans.	11	9.2%
CT scans do not cause claustrophobia but MRIs do	12	10.0%
CT scans are less accurate than MRIs.	21	17.5%
No idea	24	20.0%
Total	**120**	**100.0%**

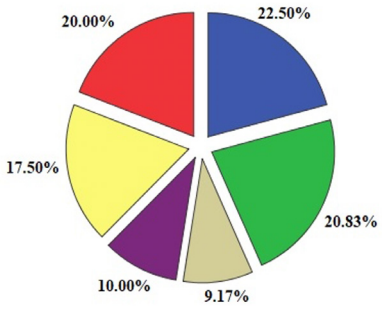
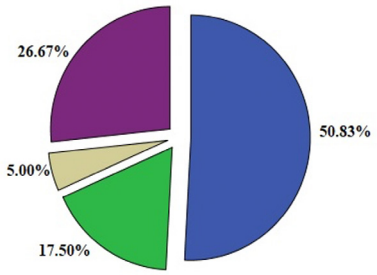


Table and Figure 4.10: Show the radiological findings of the study participants.

Radiological findings	Frequency	Percent
Ischemic stroke	61	50.8%
Hemorrhagic stroke	21	17.5%
Transient ischemic stroke (TIS)	6	5.0%
Normal	32	26.7%
Total	**120**	**100.0%**



5. Discussion

5.1. Sex participant of the study

Among 120 participant 51.67% (N=62) were male, were 48.33 %(N=58) were female. Stroke is more common among men, but women are more severely ill. According to[16]. 98 articles that contained relevant sex-specific information, including 59 incidence studies from 19 countries and 5 continents. The mean age at first-ever stroke was 68.6 years among men, and 72.9 years among women. Male stroke incidence rate was 33% higher and stroke prevalence was 41% higher than the female, with large variations between age bands and between populations. The incidence rates of brain infarction and intracerebral hemorrhage were higher among men, whereas the rate of subarachnoid hemorrhage was higher among women, although this difference was not statistically significant. Stroke tended to be more severe in women, with a 1-month case fatality of 24.7% compared with 19.7% for men.

5.2. Different age groups

Aging is the most robust non-modifiable risk factor for incident stroke, which doubles every 10 years after age 55 years. Approximately three-quarters of all strokes occur in persons aged ≥60 years. As the number of people aged ≥ 60 years is projected to grow, the number of incident strokes in older adults is expected to rise, presenting major challenges for clinicians and policy makers in the foreseeable future 44. According to national stroke association (NAS) The word “hemi” means “one side” and “paresis” means “weakness.” About 80% of people who have had a stroke have some degree of trouble moving one side, or suffer from weakness on one side of their bodies. This condition, called hemiparesis, is most often caused by stroke and cerebral palsy. But hemiparesis can also be caused by brain tumors, multiple sclerosis, and other diseases of the brain or nervous system. People with hemiparesis

may have trouble moving their arms and legs, difficulty walking and may also experience a loss of balance. As a result, doing simple everyday activities can be difficult. This includes grabbing objects, dressing, eating and problems using the bathroom. The loss of abilities that follow a stroke depend on the area of the brain that has been damaged from stroke. Right-sided hemiparesis involves injury to the left side of the brain, which controls language and speaking. People who have this type of hemiparesis may also have problems talking and/or understanding what people say. They also may have trouble determining left from right. Left-sided hemiparesis involves injury to the right side of the brain, which controls the process of how we learn, non-verbal communication, hear, touch, be aware of your own body and certain types of behavior. Damage to this area of the brain can also cause people to talk excessively, have memory problems and short attention spans. Damage to the lower part of the brain can affect the body's ability to coordinate movement. This is called ataxia and can lead to problems with posture, walking and balance.

5.3. Modifiable risk factors for stroke

Diabetes and hypertension are the most common modifiable risk factors for stroke. Major modifiable risk factors for stroke include hypertension, diabetes, and smoking. Diabetes is a well-established risk factor for stroke. It can cause pathologic changes in blood vessels at various locations and can lead to stroke if cerebral vessels are directly affected. Risk for stroke is actually higher in the young population with diabetes. According to data from the Greater Cincinnati/Northern Kentucky stroke study, diabetes increases ischemic stroke incidence in all age groups, but this risk is most striking before the age of 55 years in African Americans and before the age of 65 years in Whites[17]. Individuals with diabetes are more likely to suffer from hypertension, myocardial infarction (MI) and high cholesterol than individuals without diabetes. Even prediabetes (defined as impaired glucose tolerance or a combination of impaired fasting glucose plus impaired glucose tolerance) has been linked to a greater risk of stroke[18]. Uncontrolled diabetes puts subjects at risk for both ischemic and hemorrhagic strokes. There are specific clinical patterns of ischemic stroke in individuals with diabetes. For example, individuals with diabetes are more likely to have limb weakness and dysarthria as signs of lacunar cerebral infarction when compared with those without diabetes. In the Lausanne Stroke Registry between 1983 and 2002, patients with diabetes had higher relative prevalence of subcortical infarction and lower relative prevalence of intracerebral hemorrhage (ICH)[19]. In another study, significant differences were observed in patients with ischemic stroke along with diabetes in comparison with nondiabetics with higher frequency of lacunar infarct and hypertension[20].

5.4. Comparison between CT and MRI in stroke.

CT is the most common imaging modality used in stroke imaging mainly due to its practicality, speed and availability in most clinical centers. A NCCT is more accessible in the emergency setting of stroke evaluation than MRI, thus is preferred in most of the centers as the primary imaging modality. However, is it able to provide the same information like MRI? NCCT has been proved to be very sensitive especially in the detection of acute hemorrhage. However, its accuracy is decreasing with time from the symptom onset and this is a disadvantage. Furthermore, subacute and especially chronic hemorrhage cannot be detected accurately with CT due to its physical principles in the attenuation of x rays. The advantage of MRI in the detection of hemorrhage compared to CT is that its sensitivity is increasing with time and it can be very accurate apart from the acute setting, in subacute and chronic stage as well whereas CT cannot. Furthermore, MRI is more accurate in the detection of micro bleeds which can be missed by CT in most of the cases. The detection of micro bleeds is very important because is a contraindication for the administration of any thrombolytic treatment. MRI and CT use Perfusion imaging technique to evaluate the ischemic penumbra. CT perfusion appears to be more practical generally and offers advantages over MR. Scanning time takes less than two minutes, and the technique provides good quality images even if the patient cannot remain perfectly still. The only disadvantage of Perfusion CT at the moment is that it cannot cover the whole brain, even with modern multi slice scanners. Thus, this technique is performed in specific areas (most likely affected by ischemia) of just few centimeters. On the other hand, MRI can perform Perfusion imaging and cover all the brain area, and this is the major advantage of MRI in Perfusion technique. How large is the irreversible injured core? The identification of the irreversibly injured core is a predominant advantage of MRI. It is well established that MRI using Diffusion Weighted Imaging can identify infarct core in the very acute setting. This technique can detect early ischemic changes and irreversibly injured core within minutes from the symptom onset whereas CT can detect them accurately within 6 hours as findings of NCCT in ischemic stroke appear to be normal in the acute setting. Apparently, this is an important disadvantage for CT because in the case of ischemic stroke, as soon the treatment is administered the better the results are.

5.5. Findings

Study of 120 participants, out of 120, 32 participants are seen normal, whereas others find out different types of strokes as illustrated in the (**Figure 4.10**) most common frequent of the study findings was the ischemic stroke, Ischemic stroke is the most common type of stroke and it refers to the 80% of all cases[6]. Ischemic stroke occurs when an artery which provides blood to the brain is occluded due to thromboembolic events and the blood supply to the brain is greatly decreased or even cut off. The normal cerebral blood flow (CBF) is 50-80 ml/100g/min and when CBF is reduced into less than 8 ml/100g/min brain cells start to die and that causes an irreversible

injured core within minutes. If the CBF is reduced to 20 ml/100g of tissue per minute to an area of the brain, this area represents an ischemic penumbra which is still viable and can be fully recovered if perfusion of the blood is restored in time[7].

Hemorrhagic stroke is less frequent compared to ischemic (20% of all strokes) but much more fatal When the wall of a blood vessel becomes weak, it ruptures and bleeds into the surrounding brain, which causes buildup of pressure into the brain parenchyma, which distorts and injures brain tissue and this can cause death to the 40% to 50% of the patients[9].

Intracranial hemorrhage is divided into two main categories: Intracerebral Hemorrhage (ICH): An artery within the brain ruptures and releases blood within the brain tissue because of brain trauma or a hemorrhagic stroke[21]. ICH comprises the 20% of all cerebrovascular diseases in the US, behind cerebral thrombosis (40%) and cerebral embolism (30%)[22]. Subarachnoid Hemorrhage (SAH): An artery on the surface of the brain ruptures and causes a release of blood into the subarachnoid space outside of the brain due to a ruptured cerebral aneurysm or head trauma. Subarachnoid hemorrhage is a dangerous and refers to 1-7% of all strokes[23].

6. Limitations

With a successive completion of this project, there are some limitations.

Related to the study. Some of them are pointed out below:

- This study will not be representative one, because it is hospital-based study.
- The sample was purposively, so it may reflect the actual situation.
- The cost is high; therefore, some patients cannot afford.
- For Both imaging modalities there are contraindications which will prevent patient to undergo examination. Generally, MRI appears to have more contraindication than CT and this one of the major disadvantages in diagnostic imaging. MRI uses magnetic field to produce images, metallic objects or electric device within the patients which might interact with these magnetic fields cannot be entered into the room., On the other hand CT uses high doses of radiation, but since the patients with acute stroke, in whom life may depend on time-rigid therapeutic window benefits definitely outweigh risk of radiation exposure.
- Claustrophobia and disorientated patients are difficult to have MRI.
- During my data collection, Due to this pandemic it was a very difficult to stay a long time in a hospital, for my safety and others as well.
- Due to MRI time consumption, unconsciousness patients cannot be done.

7. Conclusion and future work

This study tried to find out if MRI become primary imaging modality and can replace in CT scan as primary imaging for stroke evaluation. MRI has been finding to be accurate in the detection of both types of strokes, hemorrhagic and ischemic and it can be used as a primary imaging technique for the evaluation of a stroke patient. Acute, subacute and chronic stroke can be identified accurately with the special techniques of MRI whereas the information provided by CT remains subtle. MRI (DWI) is superior rather than CT for the detection of early ischemic changes within the hyper acute setting, whereas CT can identify EIS with accuracy 6 hours from symptom onset. Subacute, chronic hemorrhage and bleeding can be detected more accurate by MRI, whereas CT cannot even illustrate this type of hemorrhage. CT might have the advantage of speed, accessibility and widespread availability but it cannot provide all necessary information for the accurate evaluation of stroke and more specifically in the case of ischemic stroke. Stroke. MRI has been proved much more accurate modality in both types of strokes, thus it can be used as a solo imaging modality for the evaluation of patients with suspected Although CT is granted as ideal choice for imaging stroke, many studies has shown that MRI has many advantages compared to CT, even though the contraindications of MRI is more than CT.it could be the primary imaging modality. In the future studies we would provide further insight into CT scan determination of stroke. It needs further study to identify any relationship between educational status and incident stroke. and also, the penumbra may be seen with both CT and MRI; however, this concept may be over is not clear.

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Conflict of interest

There is no conflicts of interest to publish the present work.

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ORIGINAL

Efectos inmediatos de la fisioterapia respiratoria en lactantes con infección respiratoria aguda

Immediate effects of respiratory physiotherapy in infants with acute respiratory infection

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Resumen

Fundamento: La fisioterapia respiratoria ha demostrado efectos positivos en la bronquiolitis aguda, pero se necesitan estudios en lactantes con infecciones respiratorias agudas (IRA) similares en entorno ambulatorio. El objetivo fue evaluar los cambios en pacientes ambulatorios con IRA tras la primera sesión de fisioterapia.
Material y métodos: Estudio cuasi-experimental realizado entre febrero de 2019 y febrero de 2020 en pacientes menores de 24 meses con diagnóstico de IRA atendidos por un servicio de Fisioterapia domiciliaria. Se recogieron las variables de la Escala de Severidad de Bronquiolitis Aguda (ESBA) antes y después de la intervención. Se analizaron las diferencias entre ambas mediciones con la prueba t Student, el tamaño del efecto con d Cohen, y la asociación entre variables iniciales y cambios de ESBA mediante regresión lineal y análisis de varianza (ANOVA).
Resultados: 74 pacientes recibieron intervención (50,7% varones y 7,92 meses de edad media). En la valoración inicial, la ESBA media fue de 3,24 puntos, 77,3% pacientes con afectación leve (ESBA<4). En la valoración final, más del 95% no presentaron sibilancias, esfuerzo respiratorio ni relación inspiración/espiración alterada; la ESBA media fue de 1,09 puntos, 95,9% pacientes con afectación leve. Se detectaron cambios significativos (p<0,05) moderados (d>0,05) en sibilancias y grandes (d>0,8) en crepitantes y ESBA total. Se obtuvo una asociación significativa (p<0,05) entre los cambios de ESBA total y frecuencia cardiaca, ESBA total, crepitantes y relación inspiración/espiración iniciales.
Conclusiones: La fisioterapia respiratoria favorece cambios moderados, inmediatos y relevantes en la severidad de la infección respiratoria aguda en lactantes.

Palabras clave: Enfermedades respiratorias, pediatría, terapia respiratoria, atención ambulatoria.

Abstract

Background: Respiratory physiotherapy has shown positive effects in acute bronchiolitis, but studies in infants with similar acute respiratory infections (ARI) in outpatient setting are needed. The aim of the study was to evaluate the changes in outpatients with ARI after the first physiotherapy session.
Methods: Quasi-experimental, interventional study conducted between February 2019 and February 2020 in patients under 24 months diagnosed with ARI treated by a home-based physiotherapy service. The variables of the Acute Bronchiolitis Severity Scale (ABSS) were collected before and after the intervention. The differences between both measurements were analyzed with the Student's t-test, the effect size with Cohen's d and the association between initial variables and ABSS changes with linear regression and analysis of variance (ANOVA).
Results: 74 patients received intervention (50.7% males and mean age 7.92 months). In the initial assessment, ABSS mean was 3.24 points, 77.3% patients with mild involvement (ABSS<4). In the final assessment, more than 95% didn't present wheezing, respiratory effort or altered inspiration/expiration ratio; ABSS mean was 1.09 points, 95.9% patients with mild involvement. Significant (p<0.05) and moderate (d>0.05) changes in wheezing and large (d>0.8) in crackles and total ABSS were detected. A significant association (p<0.05) was obtained between ABSS changes and baseline heart rate, ABSS score, crackles, and inspiration/expiration ratio.
Conclusion: Respiratory physiotherapy favors moderate, immediate, and relevant changes in the severity of acute respiratory infection in infants.

Key words: Respiratory tract diseases, pediatrics, respiratory therapy, ambulatory care.

Introducción

Las Infecciones Respiratorias Agudas (IRA), principalmente por neumonía y bronquiolitis agudas (BA), son una de las principales causas de morbimortalidad infantil en el mundo[1]. Sus manifestaciones comprenden desde formas clínicas leves atendidas de forma ambulatoria hasta cuadros clínicos más graves que precisan de ingreso hospitalario[2]. En España, la incidencia de ingresos por BA es de alrededor un 2%, similar a la de otros países del entorno, y que aumenta considerablemente si se presentan otras patologías de riesgo asociadas[3]. Los costes directos e indirectos asociados a estas IRA son importantes, no solo sanitarios, si no familiares y sociales[4,5].

En la mayoría de las IRA, y en especial en BA, no hay evidencia de que los fármacos modifiquen la evolución de la enfermedad, por lo que el tratamiento suele consistir en medidas de soporte y confort6. Además, existe controversia científica en cuanto al diagnóstico[7] de la BA, lo que provoca una gran variabilidad en su abordaje[8].

Aunque existen múltiples escalas para valorar la gravedad en las IRA[9], únicamente la Escala de Severidad de la Bronquiolitis Aguda (ESBA) está validada en España para medir la gravedad de la BA[10]. Esatá compuesta por 6 parámetros graduales acumulativos: frecuencia respiratoria (FR), frecuencia cardíaca (FC), esfuerzo respiratorio, auscultación de sibilancias, auscultación de crepitantes y la relación inspiración/espiración (**Tabla I**). Tanto la FR como la FC se estratifican por edad. Ramos et al.10 establecen 3 estratos en la puntuación en función de la gravedad: leve (0 a 4 puntos), moderada (5 a 9 puntos) y grave (10 a 13 puntos).

La fisioterapia respiratoria basada en el drenaje de secreciones aparece con frecuencia en las guías clínicas del manejo de la BA en pediatría[8], a pesar de que algunas técnicas pueden implicar riesgos y efectos secundarios[11]. Las técnicas de espiración lenta han demostrado efectos positivos en pacientes con IRA leve[12], incluyendo la disminución de severidad y el tiempo de ingreso[13], aumento de la calidad de vida[14], además de una mejora en la auscultación y el esfuerzo respiratorio[15], en ausencia de riesgo[16]. Sin embargo, es necesario un mayor número de estudios científicos que respalden estos hallazgos[8] así como su estudio en lactantes con infecciones respiratorias similares, tanto en entorno ambulatorio como hospitalario.

Por todo ello, el objetivo de este estudio fue evaluar los cambios en lactantes con infección respiratoria aguda tras la primera sesión de Fisioterapia respiratoria ambulatoria.

Material y Método

Se llevó a cabo un estudio cuasi-experimental con evaluación antes-después de los lactantes atendidos en un servicio de fisioterapia respiratoria domiciliaria entre febrero de 2019 y febrero de 2020, a través de un muestreo de conveniencia. El estudio fue aprobado previamente por el Comité de Ética de Investigación Clínica (CEIC) del Hospital Universitario Clínico San Carlos de Madrid (Código de aprobación del proyecto: 19/058-E_TFM) y se cumplieron las normas de la Declaración de Helsinki de 1975 con la revisión de octubre del 2000.

Para la selección de los participantes se aplicaron los siguientes criterios de inclusión: lactantes (menores

Tabla I: Escala de Severidad de Bronquiolitis Aguda (ESBA).

	Puntuación				
Variables	**0**	**1**	**2**	**3**	**4**
Sibilancias	No	Al final de la espiración	En toda la espiración	Inspiratorias y espiratorias	Hipoflujo
Crepitantes	No	En 1 campo	En 2 campos	En 3 campos	En 4 campos
Esfuerzo respiratorio	Ningún esfuerzo o aleteo	Tiraje subcostal o intercostal inferior	+ Tiraje supraesternal	+ Aleteo nasal y supraesternal (universal)	
Relación inspiración/espiración	Normal	Simétrica	Invertida		
Frecuencia respiratoria (rpm)					
Edad (meses) < 2 2 – 6 6 – 12	 < 57 < 53 < 47	 57 – 66 53 – 62 47 – 55	 > 66 > 62 > 55		
Frecuencia cardiaca (lpm)					
Edad (meses) < 2 2 – 12	 125 – 152 120 –140	 153 – 180 140 – 160	 > 180 > 160		

Rpm: respiraciones por minuto; Lpm: latidos por minuto.

Fuente: Adaptado de Ramos Fernández JMM, Cordón Martínez A, Galindo Zavala R, Urda Cardona A. Validación de una escala clínica de severidad de la bronquiolitis aguda. An Pediatr. 2014 Jul 1;81(1):3-8.

de 24 meses) con diagnóstico de IRA y que recibieran el tratamiento por primera vez en el proceso de IRA. Se consideraron criterios de exclusión el diagnóstico de enfermedades crónicas (neurológicas, cardiacas, respiratorias, endocrinas, etc.) y presentar en la valoración inicial una puntuación en ESBA ≥ 710, temperatura ≥ 38ºC, estridor[17], quejido espiratorio[18], hundimiento esternal[19], o cualquier signo o síntoma indicativo de necesidad de evaluación médica[20]. Todos los padres o tutores legales firmaron el consentimiento informado para la participación de los lactantes y la confidencialidad de los datos fue garantizada de acuerdo con la legislación vigente.

En la evaluación inicial, antes de comenzar la intervención de fisioterapia respiratoria, se recogieron variables sociodemográficas de edad y sexo, y variables clínicas de calidad de ingesta y calidad de sueño, existencia de vómitos por tos, ronquidos nocturnos, reflujo gastroesofágico (activo, solucionado o sospechado), tipo de respiración (nasal o bucal), tos (ausencia, seca, productiva o espástica) y medicación administrada. Además, se recogieron mediante observación y auscultación con fonendoscopio 3M™ Littmann® Classic II, antes y después del tratamiento de fisioterapia respiratoria, las variables que componen la ESBA[10].

La intervención con fisioterapia respiratoria comprendió las técnicas habituales en el tratamiento de lactantes. Se comenzó con la limpieza de la vía respiratoria superior con Desobstrucción Rinofaríngea Retrógrada (DRR)[21] y, posteriormente, se llevó a cabo el drenaje de secreciones de la vía respiratoria inferior con Espiración Lenta Prolongada (ELPr) y Tos Provocada (TP)[15]. Se realizaron tantas maniobras como el fisioterapeuta consideró oportunas guiado por la auscultación pulmonar.

Las variables cuantitativas se describieron mediante la media, desviación estándar (DE) y el rango intercuartil (P25 – P75); sus diferencias antes y después del tratamiento se analizaron mediante la prueba t de Student para muestras pareadas y el efecto clínico se calculó con la d de Cohen, clasificada en pequeña (0,2 – 0,49), moderada (0,5 – 0,79) o grande (> 0,8)22. Las variables categóricas se describieron con frecuencias y porcentajes, las asociaciones entre estas variables se analizaron con la prueba de Chi cuadrado y las diferencias de frecuencias antes y después del tratamiento con la prueba pareada de McNemar. Para analizar las variables resultado se emplearon la prueba de análisis de la varianza (ANOVA) o regresión lineal múltiple, según si eran variables cualitativas o cuantitativas. El estudio estadístico se realizó con el programa SPSS v.22.0, considerando resultados estadísticamente significativos en base a un nivel de significancia del 5% ($p < 0.05$) para un intervalo de confianza del 95%.

Resultados

Se incluyeron en el estudio 96 pacientes que cumplieron los criterios de selección y recibieron tratamiento; se recogió la evaluación inicial y final de 74 pacientes, pues no se realizó la evaluación final de 22 lactantes por dificultades asociadas al llanto.

Respecto a las características de los pacientes, 38 eran varones (50,7%), la edad media fue de 7,92 (± 4,99) meses, con el 86,7% de los lactantes de edad igual o inferior a 12 meses, y el tiempo medio entre diagnóstico y tratamiento fue de 1,43 (± 2,47) días. Las características clínicas y el tratamiento farmacológico se detallan en la **tabla II**. En el análisis entre la variable sexo y el resto de las variables iniciales se encontraron diferencias estadísticamente significativas entre sexos, siendo 3,4 veces más probable los vómitos en mujeres (p = 0,013), 5,58 veces más probable el diagnóstico activo de RGE en mujeres (p = 0,009) y 4,76 veces más frecuente la tos productiva en varones (p = 0,047).

Tabla II: Variables recogidas en la valoración inicial.

Variables clínicas	Frecuencia
Ingesta disminuida	28 (37,3%)
Vómitos	28 (37,3%)
Ronquidos nocturnos	24 (32%)
Sueño alterado	45 (60%)
Reflujo gastroesofágico	
Ausencia	53 (70,7%)
Diagnóstico activo	14 (18,7%)
Diagnóstico solucionado	3 (4%)
Sospecha	5 (6,7%)
Tos	
Ausencia	9 (12,0%)
Seca	6 (8,0%)
Productiva	59 (78,7%)
Espástica	1 (1,3%)
Rinorrea	22 (29,3%)
Medicación	
Broncodilatadora	23 (30,7%)
Corticoides orales	2 (2,7%)
Corticoides inhalados	4 (5,3%)
Antibióticos	6 (8%)
Mucolíticos	0 (0%)
Nebulización	8 (10,7%)

En la valoración inicial mediante la ESBA (**Tabla III**), predominaron los lactantes sin sibilancias (68,9%), seguidos de los que las presentaron al final de la espiración (25,7%); dos tercios presentaron crepitantes en algún campo, siendo los presentes en cuatro campos el grupo más numeroso (37,3%); el 18,9% presentaron esfuerzo respiratorio adicional y la gran mayoría (94,6%) demostraron una relación inspiración/espiración normal. La media de ESBA fue 3,24 (± 2,20) puntos, con un 77,3% de los lactantes con afectación leve. Además, el tipo de respiración fue bucal en el 36% de los lactantes.

En la valoración final, destaca que más del 95% de los lactantes ya no presentaron sibilancias, esfuerzo respiratorio, relación inspiración/espiración alterada ni

Tabla III: Variables clínicas recogidas en la valoración inicial y final mediante la Escala de Severidad de Bronquiolitis Aguda (ESBA)[10].

Variables	Valoración inicial		Valoración final		Diferencia de medias (DE)	d de Cohen
	Frecuencia	Media (DE)	Frecuencia	Media (DE)		
Frecuencia respiratoria (rpm)		45,15 (11,49)		41,66 (9,33)	3,55 (11,21) *	0,32
Frecuencia cardiaca (lpm)		128,65 (14,31)		129,55 (13,75)	- 0,70 (10,72)	0,07
Sibilancias		0,39 (0,68)		0,04 (0,20)	0,34 (0,65) *	0,53
Ausencia	51 (68,9%)		71 (95,9%)			
Final espiración	19 (25,7%)		3 (4,1%)			
Toda la espiración	2 (2,7%)		0 (0%)			
Inspiración y espiración	2 (2,7%)		0 (0%)			
Crepitantes		2,05 (1,74)		0,43 (0,95)	1,65 (1,85) *	0,89
Ausencia	25 (33,3%)		57 (77,0%)			
En un campo	7 (9,3%)		8 (10,8%)			
En dos campos	10 (13,3%)		6 (8,1%)			
En tres campos	5 (6,7%)		0 (0%)			
En cuatro campos	28 (37,3%)		3 (4,1%)			
Esfuerzo respiratorio		0,22 (0,48)		0,01 (0,12)	0,21 (0,44) *	0,47
Ninguno	60 (81,1%)		73 (98,6%)			
Tiraje subcostal o intercostal inferior	12 (16,2%)		1 (1,4%)			
Tiraje subcostal o intercostal inferior y tiraje supraesternal	2 (2,7%)		0 (0%)			
Relación inspiración/espiración		0,07 (0,30)		0 (0)	0,07 (0,3)	0,22
Normal	70 (94,6%)		74 (100%)			
Simétrica	3 (4,1%)		0 (0%)			
Invertida	1 (1,4%)		0 (0%)			
Puntuación ESBA		3,24 (2,20)		1,09 (1,45)	2,15 (2,10) *	1,02

DE: desviación estándar; rpm: respiraciones por minuto; lpm: latidos por minuto.
(*) p valor < 0,05

Tabla IV: Asociación entre variables iniciales y cambios en las puntuaciones clínicas principales (*)

	Variables cuantitativas			Variables categóricas		
		Coeficiente (IC 95%)	R cuadrado		F de Fisher	R cuadrado
Cambios en ESBA	FC inicial ESBA inicial	0,041 (0,02, 0,06) - 0,851 (-1, - 0,71)	0,661	Relación inspiración/espiración inicial Crepitantes inicial	7,65 25,39	0,599

(*) Cambios interpretados como comparación entre evaluación final y evaluación inicial
IC: intervalo de confianza al 95%; FC: frecuencia cardiaca; ESBA: Escala de Severidad de Bronquiolitis Aguda.

respiración bucal. La media de ESBA fue 1,09 (± 1,45) puntos, con un 95,9% de los lactantes con afectación leve. Se detectaron cambios estadísticamente significativos tras el tratamiento en las variables frecuencia respiratoria, sibilancias, crepitantes, esfuerzo respiratorio y puntuación total de ESBA. Los cambios tuvieron una relevancia clínica pequeña (d > 0,2) para frecuencia respiratoria, esfuerzo respiratorio y relación inspiración/espiración, moderada (d > 0,5) para sibilancias y grande (d > 0,8) para crepitantes y puntuación total de ESBA (**Tabla III**). Respecto al tipo de respiración, únicamente un niño tuvo respiración bucal, por lo que se detectaron diferencias estadísticamente significativas respecto a la valoración inicial (p < 0,05).

En el estudio de la relación estadísticamente significativa entre los cambios en la puntuación de ESBA y las variables clínicas iniciales (**Tabla IV**), ninguna de las variables clínicas recogidas en la **tabla II** mostró asociación. Respecto a la asociación con las variables cuantitativas, se encontró que a menor frecuencia cardiaca inicial y a mayor puntuación ESBA inicial hubo mayor cambio en la puntuación ESBA. Los valores de R cuadrado muestran el porcentaje de varianza de la variable que se podría explicar con la asociación. El R cuadrado de la relación de ambas variables cuantitativas indica que estas podrían explicar el 66% de los casos que obtienen mejoría en la puntuación ESBA. Respecto a la asociación con las variables categóricas, se encontró que los lactantes con relación inspiración/espiración simétrica al inicio obtuvieron mayores cambios en la puntuación ESBA respecto a la relación inspiración/espiración normal; y que los lactantes con crepitantes en 4 o 3 campos pulmonares al inicio obtuvieron mayores cambios en la puntuación ESBA respecto a los crepitantes en 1 o 2 campos y la ausencia de crepitantes. El R cuadrado de la relación de ambas variables cualitativas indica que estas podrían explicar el 59,9% de los casos que mejoran en la puntuación ESBA.

No se detectaron efectos adversos o signos de alarma en ninguno de los sujetos que recibieron la intervención.

Discusión

El presente trabajo aporta resultados muy positivos respecto a los cambios asociados a la fisioterapia respiratoria en pacientes pediátricos con infección respiratoria aguda en ámbito domiciliario, similares a los de otros estudios que emplean las mismas intervenciones en pacientes ambulatorios con bronquiolitis semejantes[23,24]. En un estudio cuasi-experimental en pacientes ambulatorios con BA leve o moderada evaluada con la escala Wang (que valora FR, FC, sibilancias, esfuerzo respiratorio y estado general del niño), tras la primera intervención se observaron mejorías significativas de la severidad de la afectación, además de la FC y la saturación de oxígeno[23]. Mientras que en un ensayo clínico aleatorizado en el mismo tipo de pacientes evaluados con Kristjansson Respiratory Score y las mismas intervenciones, obtuvieron que, a pesar de que ambos grupos mejoraron, únicamente el grupo de intervención demostró diferencias significativas a los 15 días de tratamiento[24]. A pesar de la reducida evidencia existente de las intervenciones en pacientes ambulatorios, los resultados disponibles podrían indicar que la fisioterapia basada en técnicas de ELPr y tos provocada muestra mejoría inmediata de síntomas respiratorios, pero es posible que estos efectos sean temporales y no mejores que la ausencia de intervención si no se realiza durante varios días. Sin embargo, en contraste con la población ambulatoria, existe en la actualidad evidencia en pacientes hospitalizados de que las técnicas como espiración lenta, tos provocada o DRR mejoran la severidad en pacientes con BA moderada, pero no se reportan mejorías en pacientes graves, evolución de la afección o días de estancia hospitalaria[16,25].

En cuanto a las características de la muestra estudiada, destaca que 32 lactantes habían recibido al menos un medicamento (42,6%), lo que se contrapone a la evidencia actual que no reconoce eficacia farmacológica en la mayoría de las infecciones respiratorias infantiles por ser de etiología vírica[8,26,27]. La severidad de infección valorada con ESBA al inicio fue leve en la mayoría de los pacientes, como se describe en la mayoría de los casos las IRAs atendidos por fisioterapia ambulatoria, a diferencia de los lactantes atendidos en ámbito hospitalario[15]. Por ello, al igual que en el estudio de Ramos et al.[10], se escogió como criterio de exclusión una puntuación igual o mayor que 7 en ESBA.

Los cambios tras la intervención con fisioterapia respiratoria fueron muy positivos y clínicamente muy relevantes, no solo en la valoración global con ESBA sino en sus componentes por separado: frecuencia respiratoria, sibilancias, crepitantes y esfuerzo respiratorio. En el caso de la variable relación inspiración/espiración no se detectaron diferencias entre la evaluación inicial y final, sin embargo, todos los pacientes con posibilidad de mejorar lo hicieron. En el caso de la frecuencia cardiaca, que no varíe significativamente o incluso aumente podría deberse al estado emocional de los pacientes tras la sesión. Aunque las técnicas de fisioterapia respiratoria no son dolorosas ni agresivas y carecen de efectos secundarios importantes[12], es frecuente el llanto en esta población. Los hallazgos de cambios en ESBA se asemejan a los de Conesa y cols. con lactantes similares, con ESBA moderada o alta, ingresados en hospital15, donde se obtuvo mejoría significativa 10 minutos y 2 horas después del tratamiento, que se mantuvo hasta el alta hospitalaria.

En el caso de las sibilancias, es probable que la mejoría en su auscultación se deba a que la causa de estas fuera el acúmulo de secreciones y no tanto la inflamación o broncoespasmo. De haber sido así no hubieran mejorado si no que posiblemente se hubieran mantenido o incluso agravado. Es de esperar que esto fuera lo que sucedió en los tres lactantes que mantuvieron sibilancias espiratorias en la evaluación final. La reducción de sibilancias tras fisioterapia coincide con estudios similares en población adulta[28]. En cambio, los cambios en la captación de los crujidos fue el esperado teniendo en cuenta que el principal objetivo de la fisioterapia respiratoria en pediatría es el drenaje de secreciones[29]. En el 23% de los lactantes se encontraron crepitantes en uno, dos o cuatro campos. Esto se puede deber a que, con las técnicas aplicadas, el moco que antes estuviese adherido a las vías respiratorias se despegase y vibrase con el paso del aire, lo que supondría una mejoría para su drenaje. Por este motivo, se podría proponer que la escala ESBA incluyese ruidos adventicios, principalmente crepitantes, para valorar los resultados de la intervención de una manera más completa. Sin embargo, hay poca evidencia sobre los cambios en la auscultación tras una sesión de fisioterapia respiratoria para drenaje de secreciones, aunque tal y como concluye Marques en su estudio, puede ser una manera prometedora de medir los resultados del drenaje de secreciones[30].

Con la excepción de uno, todos los lactantes finalizaron la sesión con respiración nasal, pudiendo estar asociado este beneficio a la intervención de DRR. Este resultado concuerda con investigaciones publicadas al respecto, como la de Gomes y cols. de 2016[21], donde se demostró tanto la seguridad como la efectividad del DRR en comparación con la aspiración nasal. Son necesarios más estudios para poder evaluar su efectividad a largo plazo, así como en diferentes IRAs y diferentes edades.

Respecto a los factores asociados con los cambios en la puntuación ESBA (**Tabla IV**), al obtener únicamente variables incluidas en la misma escala de severidad, los hallazgos indican de manera lógica que tienen mayor capacidad de mejoría aquellos sujetos con mayor afectación (mayor puntuación en ESBA). Se demuestra en la **tabla III** que, por un lado, la relación inspiración/

espiración se consigue mejorar por completo en los 4 sujetos que demostraron afectación inicial, y, por otro lado, que al final de la evaluación la gran parte de los pacientes no demostraron crepitantes o lo hicieron únicamente en 1 o 2 campos.

Las limitaciones de nuestro estudio son el diseño cuasi-experimental, en el que cada paciente es su propio control, ya que éticamente no se podía negar tratamiento de fisioterapia a ningún niño que acudiera al servicio; así como la falta de cegamiento, por ser el mismo fisioterapeuta el que evaluó y realizó el tratamiento. Asimismo, la auscultación tiene un alto grado de subjetividad, se empleó la escala ESBA que ha sido validada únicamente en lactantes menores de 12 meses ingresados y no se realizó un seguimiento de los pacientes. Por último, la muestra estudiada puede no resultar representativa de toda la población pediátrica susceptible de recibir fisioterapia respiratoria.

Debido a la escasa evidencia sobre FRA en lactantes menores de 24 meses y su valoración con escalas que midan parámetros ajustados por la edad, se abre un amplio y novedoso campo de investigación. En un futuro se podrían proponer modelos predictivos que estimen con precisión el posible resultado de las puntuaciones finales para entender mejor la interacción de las variables entre sí y conocer posibles resultados de la intervención para optimizar su ejecución. Por todo ello, futuros estudios deberían realizarse también en diferentes tipos de IRAs y por grupos de edad, facilitando la validación de ESBA en esta población diana. Adicionalmente, podría ser de utilidad incluir información acerca del tipo de ruidos respiratorios adventicios (crujidos y sibilancias), además de su localización, dentro de la ESBA con el objetivo de mejorar la evaluación del paciente, así como el control de la evolución de los síntomas y la intervención terapéutica.

En conclusión, la fisioterapia respiratoria ambulatoria basada en técnicas de espiración lenta prolongada y tos provocada favorece cambios moderados, inmediatos y relevantes en la severidad de la infección respiratoria aguda en pacientes pediátricos. La frecuencia cardiaca baja, la relación inspiración/espiración simétrica y los crepitantes en 3 o 4 campos son factores relacionados con mayores cambios en la puntuación de la ESBA.

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SHORT ORIGINAL

Cervical cytology: Abnormal results

Citología cervical: resultados anormales

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Abstract

Data regarding current rates of abnormal cytology results reported in the first half of 2022 are presented and compared with those referenced in the Spanish cooperative study published seventeen years ago. It is concluded that the screening model in application is ineffective and inefficient and that it must be modified, adapting it to the requirements of the Spanish Ministry of Health and the World Health Organization.

Key words: Cytology, cervical cancer, screening.

Resumen

Se presentan los datos relativos a las tasas actuales de resultados citológicos anormales comunicados en el primer semestre de 2022 y se comparan con los referidos en el estudio cooperativo español publicado hace diecisiete años. Se concluye que el modelo de cribado en aplicación es ineficaz e ineficiente y que debe ser modificado, adaptándolo a las exigencias del Ministerio de Sanidad español y de la Organización Mundial de la Salud.

Palabras clave: Citología, cáncer de cuello uterino, tamizaje.

In 2005, in an experience of collecting and analyzing cytological results that has not been reproduced or modified, we published[1] the data provided by fourteen Spanish cytology laboratories – ours among them – on the rates of cervical cytology results issued as atypia or high/low grade lesion. Out of almost half a million results, 3.56% reported some degree of undetermined atypia (2.08%) or a low-grade (1.10%) or high-grade lesion (0.28%). Since then, these data have been considered a quality reference in the evaluation or discussion of the diagnostic activity of the laboratories that deal with cervical-vaginal cytology.

During the first semester of 2022, from January 1 to June 30, our laboratory has processed 8,833 cervical-vaginal smears. Of these, 67 cases (0.75%) have been reported with a result of undetermined atypia (34 cases, 0.38%), low-grade lesion (29 cases, 0.32%) or high-grade lesion (4 cases, 0.04%). These figures are clearly below those published in the reference Spanish survey. Are we undervaluing samples? We do not think so: the follow-up provided by our clinical colleagues confirms that false negatives are absolutely exceptional in our diagnostic experience[2]. But 0.75% of cytological results of undetermined atypia or intraepithelial lesion is far from the 3.56% that we published sixteen years ago. Reflecting on this fact leads us to think that the fundamental cause is the revision care model practiced. The opportunistic model –I check who consults me– is the one that continues to be practiced in our Community, and also in the majority of the Spanish Communities[3], both in Public and Private Health. In the referenced publication, published by a group led by the University of Castilla-La Mancha, it is detailed that 3 or 4 out of 10 Spanish women are not routinely checked in either the Public or Private Health Services and that there is, moreover, a clear preventive neglect of women over 50 years of age, of low socio-economic status and who live in rural areas, resulting in a very evident inequity in the procedure. Continually checking the same women represents an over control of this group, which is reflected in the poor numbers of abnormal cytological results that we present here, once again highlighting that the opportunistic structure of any screening program is

ineffective and inefficient. In addition, a very important detail, the group of unscreened women accounts for 8 or 9 out of every 10 incident cancers of the cervix[4]. These data from the Catalan Institute of Oncology, published by Raquel Ibañez, are very similar to those published in 2009 in the AFRODITA study[5]. In other words, the methodological circumstances of cervical cancer prevention remain the same. In the prevention of cervical cancer we are repeatedly ineffective and inefficient, but the most important thing is that we know what we have to do and what we do not do: an order from the Ministry of Health of April 2019 details it[6]: In Public Health policy, screening of cervical cancer must be population-based and will be applied in general to women between the ages of 25 and 65. Primary screening test and interval between examinations:

1. Women between the ages of 25 and 34: Cytology every three years.
2. Women between the ages of 35 and 65: Determination of high-risk human papillomavirus.

In Private Health, in times like the current one of databases and computerized records, it is very easy to find out which women have not accessed the consultation for more than three to five years, locate them and write them a letter recommending their review.

As we have already denounced in previous publication[7], the Spanish situation is far from being the desired one and ordered by the Ministry, but without a doubt we have the technical and assistance capacity to correct it. We know what we have to do. Let's do it. Only in this way will we comply with the recommendation of the World Health Organization[8], which asks exactly to follow the preventive policy detailed above to achieve something extremely important, that cervical cancer in a 20-year horizon can be the first cancer eradicated in the world.

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REVIEW

Evidencia científica y recomendaciones sobre la dieta vegetariana durante el embarazo y la lactancia materna. Revisión bibliográfica

Evidence and recommendations on the vegetarian diet during pregnancy and breastfeeding. A bibliographic review

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Resumen

Introducción: Durante los últimos años se ha producido un crecimiento exponencial de personas que siguen una dieta vegetariana. Durante el embarazo y la lactancia este tipo de dietas podrían causar deficiencias nutricionales y efectos adversos a corto y largo plazo. El objetivo de esta revisión fue analizar la evidencia científica sobre la adecuación de la dieta vegetariana durante el embarazo y la lactancia.
Metodología: Revisión bibliográfica a través de los metabuscadores Biblioteca Virtual de Salud (BVS) y EBSCOhost y de las bases de datos PubMed, Cochrane y CINAHL. Se han seleccionado los artículos cuya publicación se encuentra entre los últimos 10 años, los cuales estuvieran redactados en castellano, inglés y francés.
Resultados: Tras realizar un cribado y una lectura crítica de los estudios recopilados se seleccionaron un total de 22 artículos (3 estudios experimentales, 13 estudios transversales y 6 estudios de cohortes).
Conclusiones: Las dietas vegetarianas durante el embarazo y la lactancia son métodos alternativos cada vez utilizados y son aptas si su planificación es nutricionalmente adecuada. La diversidad en la alimentación materna es una preocupación añadida entre embarazadas y madres lactantes, hecho que plantea la necesidad de mejorar los programas educacionales para garantizar un correcto asesoramiento y detectar posibles desequilibrios nutricionales en ambos periodos.

Palabras clave: dieta vegetariana, embarazo, lactancia materna, nutrición.

Abstract

Background: In recent years there has been an exponential growth of those people who follow a vegetarian diet. Due to this increase, a new food trend emerges during two vital stages, pregnancy and lactation, which can cause nutritional deficiencies and adverse effects in the short and long term. For this reason, a compilation of studies based on the effects of said diet in these periods is carried out. The objective of this review was to analyze the compatibility of the vegetarian diet and the correct development of pregnancy and lactation.
Methodology: A search of the existing bibliography is carried out, through the Biblioteca Virtual de la Salud (BVS) and EBSCOhost metasearch engines, as well as in the PubMed, Cochrane and CINAHL databases, using the DeCS and MeSH descriptors. Articles whose publication is within the last 10 years, which were written in Spanish, English and French, have been selected.
Results: After screening and critical reading of the collected studies, a total of 22 articles were selected (3 clinical trials, 13 cross-sectional studies and 6 longitudinal studies).
Conclusions: Vegetarian diets during pregnancy, lactation and weaning are alternative methods that are being applied more and more frequently and that are suitable for these stages if their planning is nutritionally adequate. It is observed that the diversity of maternal nutrition is an added concern among pregnant and lactating mothers, a fact that raises the need to improve educational programs to guarantee correct advice and detect possible nutritional imbalances in both periods.

Key words: vegetarian diet, pregnancy, breastfeeding, nutrition.

Introducción

Una alimentación saludable debe ser apropiada, satisfactoria, suficiente, equilibrada, segura y adaptada a las necesidades de cada individuo y de cada situación[1,2]. Existen diversos modelos alimenticios, entre ellos la dieta vegetariana, que incluye distintos patrones que van desde el más restrictivo, el veganismo (carente de productos cárnicos, lácteos, pescado, miel y huevos), hasta los más permisivos, como la lacto-vegetariana (contiene productos lácteos), ovo-vegetariana (incluye el huevo) y ovo-lacto-vegetariana (abarca alimentos lácteos, huevos y miel). Estos modelos dispares muestran variaciones en lo que se refiere a la ingesta nutricional y sus posibles deficiencias. En cualquier caso, la base de cualquier dieta vegetariana está compuesta por cereales, legumbres, frutos secos, semillas, verduras, frutas, hortalizas y aceites[1-3].

Recientemente las dietas vegetarianas, sobre todo veganas, se han popularizado a nivel mundial por diversos motivos: éticos, ecológicos, filosóficos, creencias religiosas o problemas de salud; aumentando hasta en un 350% en la última década4. Actualmente, en Europa se estima que el incremento de las dietas vegetarianas oscila entre el 1,2% y el 1,5% de la población en Portugal y España, ascendiendo hasta el 7% en el Reino Unido y al 10% en Alemania[2]. En España se observa un crecimiento de las familias vegetarianas y, por tanto, el número de niños que siguen este tipo de alimentación aumenta, incluyendo las etapas de lactancia y destete, surgiendo así la necesidad de aumentar los conocimientos nutricionales por parte de los profesionales sanitarios, con el fin de garantizar un correcto asesoramiento nutricional[2,5,6].

Una de las consecuencias más comunes que pueden presentar las personas vegetarianas es la deficiencia de vitamina B12, debido a que esta no se encuentra disponible en los productos vegetales6. En relación a su consumo, las personas ovo-lacto-vegetarianas la adquieren a través de productos lácteos y huevos, por el contrario, las personas veganas, al no ingerir estos alimentos, pueden llegar a requerir el uso de suplementación para garantizar niveles adecuados[1-4,7].

Existen dos etapas vitales, la gestación y la lactancia, en las que el riesgo de padecer deficiencias nutricionales aumenta al seguir una alimentación vegetariana. Además, los requerimientos nutricionales en el segundo y tercer trimestre de embarazo aumentan, siendo necesario el uso de suplementación para cubrir las necesidades nutritivas[8]. Por tanto, se requiere de una atención materno-fetal durante el embarazo con el fin de prevenir, controlar, minimizar o revertir los efectos derivados de las deficiencias nutricionales[2,6,8].

El déficit materno de vitamina B12 durante el embarazo puede producir defectos en el tubo neural (DTN) y concentraciones neonatales en plasma deficientes asociadas con bajo peso al nacer[9]. En consecuencia, es imprescindible su suplementación, incluyendo las mujeres ovo-lacto-vegetarianas[8-13]. Respecto a la lactancia materna, uno de los elementos imprescindibles para una correcta salud intestinal y una idónea maduración del sistema nervioso del recién nacido son los esfingolípidos presentes en la leche[2]. Y, aunque la composición de la leche es relativamente independiente de la dieta los esfingolípidos podrían experimentar variaciones en función de la ingesta.

El objetivo general de esta revisión es analizar la adecuación de la dieta vegetariana durante el embarazo y la lactancia. Además de identificar el posible efecto de la suplementación materna con vitamina B12 durante el embarazo y la lactancia en el desarrollo fetal y del lactante, determinar la influencia de la dieta materna en los esfingolípidos de la leche y en el desarrollo cognitivo del bebé. Y, por último, examinar los conocimientos de los profesionales sanitarios, madres vegetarianas y madres no vegetarianas sobre el destete vegetariano y el impacto en el lactante.

Metodología

Se llevó a cabo una revisión bibliográfica sobre los efectos del consumo de una dieta vegetariana durante el periodo de embarazo y de lactancia.

Estrategia de búsqueda

Dicha búsqueda incluyó artículos comprendidos entre enero de 2011 y diciembre de 2021, y se realizó a través de los metabuscadores Biblioteca Virtual de la Salud (BVS) y EBSCOhost y en las bases de datos internacionales CINAHL, PubMed y Cochrane.

Tanto en los metabuscadores como en las bases de datos se aplican 2 niveles de búsqueda. El primero, aplicado en los metabuscadores y en las bases de datos es: (Diet vegetarian AND (Pregnancy OR infant nutrition)). En el segundo nivel de búsqueda, se utiliza la siguiente combinación: (*Diet, Vegetarian* AND (*Pregnancy OR Infant nutrition*) AND (*Breast feeding* OR *Infant food* OR *Bottle feeding*) AND (*Deficiency* OR *Dietary Supplements*)).

Utilizando los resultados de la búsqueda se analizaron las referencias bibliográficas de los artículos incluidos a fin de identificar otros posibles estudios potencialmente incluibles para la revisión.

Criterios de selección de estudios

Criterios de inclusión: estudios realizados exclusivamente en humanos, población adulta embarazada o madres adultas lactantes que siguen una dieta vegetariana en alguna de sus formas, personas sin enfermedades

de base, aquellos artículos redactados en inglés, castellano y francés.

Criterios de exclusión: duplicados en varias bases de datos, no centrados en objetivo general del estudio o presentan resultados nulos; tras la lectura de título y resumen pueden considerarse válidos para su inclusión, pero que tras la lectura completa no aportan información relacionada con el tema a tratar; casos de gestantes con posibles complicaciones gestacionales debidas a otras causas no relacionadas con la alimentación, cartas al editor y literatura gris.

Para llevar a cabo la síntesis de los estudios seleccionados y exponer las características principales, se extrajo de cada artículo la siguiente información: año de publicación, autor principal, lugar de realización, fecha de recolección de datos, casos incluidos, sujetos a estudio, diseño del estudio, tamaño muestral, rango de edad de los participantes, nivel de evidencia y grado de recomendación. Para determinar el nivel de evidencia y el grado de recomendación se utilizó la escala SIGN[16].

Resultados

Se detectaron un total de 1.738 artículos para su posterior análisis (**Tabla I**). Tras llevar a cabo la lectura del título y del resumen, se descartaron 1.708 artículos, quedando 30 artículos que cumplían con los criterios de inclusión y exclusión (**Figura 1**). Por último, se lleva a cabo la lectura completa de dichos 30 artículos, de los que finalmente 22 conformaran la muestra final para esta revisión.

En relación con el diseño de estudio, 19 fueron estudios observacionales (13 estudios transversales, 5 cohortes prospectivas y 1 cohorte retrospectiva) y 3 estudios experimentales (Tabla 2). Dichos estudios se realizaron en diferentes áreas geográficas, 6 se llevaron a cabo en EE.UU., 5 en la India, 4 en Italia, 1 en Indonesia, 1 en Francia, 1 en España, 1 en China, 1 en Alemania, 1 en Polonia y 1 en Países Bajos.

Discusión

La evidencia científica muestra en los últimos años un incremento a nivel mundial del número de personas que optan por una alimentación vegetariana, incluyendo este patrón dietético en etapas infantiles. Por esta razón, se precisa evaluar si este modelo alimenticio es adecuado para satisfacer los requerimientos nutricionales en cualquier etapa vital[7,13,15].

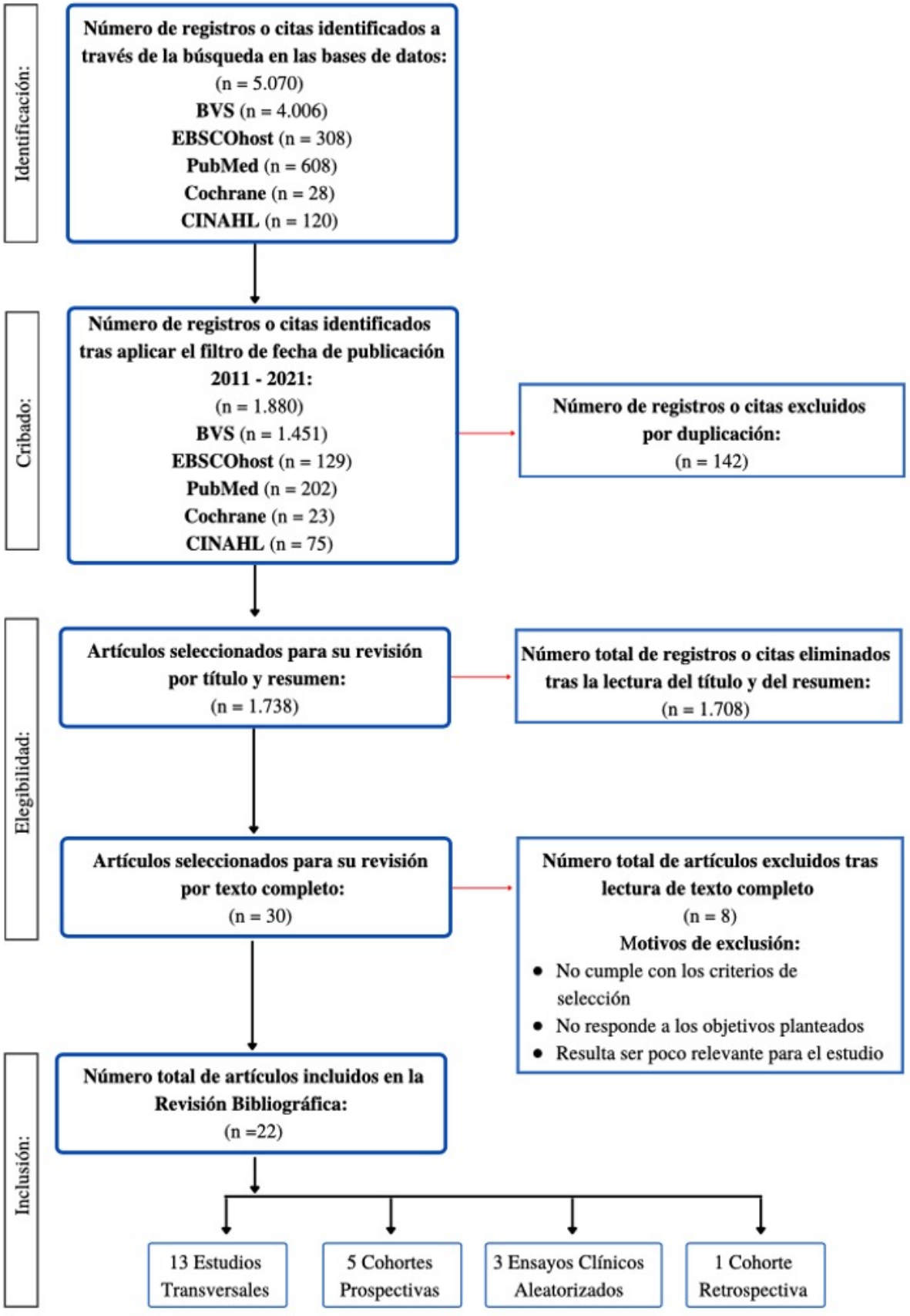
Tras llevar a cabo el análisis de los artículos, se observa una relación entre la dieta vegetariana y el aumento del riesgo de padecer ciertas deficiencias nutricionales en comparación con aquellas personas que siguen una alimentación omnívora[6,8,9,13,17,22,28].

Las necesidades nutricionales de las mujeres se incrementarían durante dos etapas vitales importantes[6,13,15,17]: la primera es el embarazo, donde estos requerimientos se ven aumentados y una alteración en la ingesta materna puede afectar a la salud materno-fetal. El siguiente periodo es la lactancia materna, donde si se mantiene una alimentación inadecuada,

Tabla I: Resumen estrategia de búsqueda y resultados.

Bases de datos	Nivel de búsqueda	Estrategia de búsqueda	Nº resultados	Tras aplicar filtros	Tras lectura de título-resumen	Tras lectura completa	Incluidos
BVS	1r nivel	"Diet, vegetarian" AND" "Pregnancy OR infant nutrition	3.991	1.444	11	11	3
	2º nivel	"Diet,vegetarian" AND "Pregnancy OR infant nutrition" AND (Breast feeding OR infant food OR bottle feeding) AND (deficiency OR Dietary Supplements)	15	7	4	4	4
EBSCOhost	1r nivel	"Diet, vegetarian" AND "Pregnancy OR infant nutrition"	305	126	13	1	1
	2º nivel	"Diet,vegetarian" AND "Pregnancy OR infant nutrition" AND (Breast feeding OR infant food OR bottle feeding) AND (deficiency OR Dietary Supplements)	3	3	1	0	0
PubMed	1r nivel	"Diet, vegetarian" AND "Pregnancy OR infant nutrition"	502	172	12	5	5
	2º nivel	"Diet,vegetarian" AND "Pregnancy OR infant nutrition" AND (Breast feeding OR infant food OR bottle feeding) AND (deficiency OR Dietary Supplements)	196	30	14	8	8
Cochrane	1r nivel	"Diet, vegetarian" AND "Pregnancy OR infant nutrition"	28	23	1	0	0
CINAHL	1r nivel	"Diet, vegetarian" AND "Pregnancy OR infant nutrition"	118	73	7	1	1
	2º nivel	"Diet,vegetarian" AND "Pregnancy OR infant nutrition" AND (Breast feeding OR infant food OR bottle feeding) AND (deficiency OR Dietary Supplements)	2	2	2	1	0

Figura 1: Diagrama de flujo de la información a través de las diferentes fases. Fuente de elaboración propia.



pueden desarrollarse problemas en el desarrollo físico y neurológico del lactante.

Debido a posibles dificultades en el mantenimiento de una dieta vegetariana equilibrada y adecuada durante el embarazo y la lactancia y con el fin de preservar una buena salud materno-infantil, diversos autores coinciden en la importancia de que el personal sanitario conozca sus características principales y su composición nutricional[1,13,18].

Efecto de la suplementación materna con vitamina B12 durante el embarazo y la lactancia en el desarrollo fetal y del lactante.

Al analizar el efecto de la suplementación oral en mujeres vegetarianas durante el embarazo y su impacto en las concentraciones séricas, en la leche materna y en el plasma infantil, se identifica una asociación positiva al observarse concentraciones de vitamina B12 superiores entre la población que recibían suplementos vitamínicos[19]. Además, se ha observado que mayores concentraciones de vitamina B12 se distribuyen hacia el complejo holotranscobalamina (vitamina B12 activa) durante el proceso de embarazo con el propósito de garantizar la totalidad de los requisitos vitamínicos en el tejido maternal, dado que el aumento de estos requerimientos aparece como consecuencia a la alta demanda fetal (227 pmol/L en participantes que recibían suplementación vitamínica frente a 172 pmol/L en aquellas que no ingerían dicho suplemento)[12].

En esta misma línea de estudio, Avnon et al.[20] pretenden determinar la influencia del modelo dietético en los niveles de vitamina B12 en hemoglobina materna y en el cordón umbilical. En su investigación se observan diferencias estadísticamente significativas (**Tabla III**). Otros estudios afirman que, al recibir la suplementación vitamínica adecuada durante la gestación en embarazadas veganas, los niveles de vitamina B12 en sangre y en cordón umbilical no se ven afectados, disminuyendo así el riesgo de presentar deficiencias, dado que los valores nutricionales maternos están asociados al cordón umbilical y por consiguiente al feto[6,8].

Además, cabe destacar que varios estudios muestran una correlación positiva entre concentraciones elevadas de vitamina B12 en el periodo de embarazo y un bajo peso para la edad gestacional, un peso al nacer inferior y una disminución del incremento de peso durante el embarazo en madres cuya alimentación es vegetariana y que presenten concentraciones deficientes de esta vitamina[21]. Dado que no se aprecia relación entre el consumo de dieta vegetariana y la morbilidad neonatal, se sugiere que la limitación del crecimiento posiblemente se deba a un motivo constitucional y no a un patrón de alimentación materno específico. Por otra parte, en este mismo estudio, se analiza la eficacia de la suplementación materna con vitamina B12 y no se observan diferencias estadísticamente significativas en la concentración de dicha vitamina en la leche materna, ya que los valores medianos son 558 pmol/L (331, 759 pmol/L) en veganas, 509 pmol/L (368, 765 pmol/L) en vegetarianas y 444 pmol/L (355, 777 pmol/L) en omnívoras. Por tanto, se observa que aquellas madres que siguen una dieta vegana hacen uso de tal suplementación con la intención de obtener concentraciones en leche comparables a una alimentación omnívora[22]. Cabe tener en cuenta que, al aplicar el umbral de deficiencia de vitamina B12 en leche materna en 310 pmol/L, el 20% de las participantes mostraba concentraciones inferiores, independientemente del modelo alimenticio materno, coincidiendo así con las conclusiones del posterior estudio de Kadiyala et al.[23] en el que se especifica que incluso aquellas embarazadas no vegetarianas, que mantienen una calidad o cantidad nutritiva inadecuada, pueden no cumplir con los requerimientos nutricionales diarios recomendados.

Asimismo, debemos tener en cuenta que las concentraciones de vitamina B12 disminuidas se encuentran asociadas a concentraciones séricas de homocisteína (Hcy) y de ácido metilmalónico (MMA) urinario aumentadas. En el caso de los lactantes menores de 6 meses con concentraciones elevadas de Hcy y por tanto, niveles deficientes de vitamina B12, pueden presentar consecuencias negativas para su salud, entre ellas: retraso en el desarrollo y crecimiento, problemas neurológicos, hiperpigmentación de la piel, hipotonía y anomalías hematológicas[22-24].

En esta línea, varios autores analizan las concentraciones de vitamina B12 en lactantes donde se observan tasas alarmantemente bajas de dicha vitamina en madres y bebes alimentados exclusivamente con lactancia materna, siendo estos valores medianos de 168 pg/mL en lactantes de 1-3 meses y 192 pg/mL en infantes de 3 a 6 meses; en el caso de las madres el promedio de concentración está en 216 pmol/mL. En este análisis se establecieron como concentraciones adecuadas de vitamina B12 aquellos valores ubicados entre 200-700 pg/mL[14,19]. Por tanto, el estado deficiente de vitamina B12 materno lleva a bajas reservas fetales y a bajas concentraciones de esta vitamina en la leche materna, empobreciendo así nutricionalmente a los embriones y a los lactantes. Se concluye que el patrón dietético materno es el único factor diferenciador, con una prevalencia de deficiencia de esta vitamina del 68,9% en bebés de madres vegetarianas y del 52,1% en bebés de madres no vegetarianas. Observando, además, una relación significativa entre niveles socioeconómicos bajos y concentraciones inferiores de esta vitamina durante el embarazo y la lactancia[24].

Debido al aumento del interés por la alimentación vegetariana entre las mujeres, surgen varios aspectos a considerar para futuras áreas de investigación, como:

la importancia funcional de la vitamina B12, establecer valores normativos de esta vitamina en leche materna para un desarrollo infantil favorable y la evaluación de la eficacia del uso de alimentos fortificados para alcanzar niveles adecuados de esta vitamina sin requerimiento de suplementación en una dieta vegetariana[12,19,30,32].

Influencia de la dieta materna en los esfingolípidos de la leche y en el desarrollo cognitivo del bebé.

Los esfingolípidos son un conjunto de moléculas bioactivas interconectadas esenciales para llevar a cabo una amplia sucesión de procesos orgánicos, entre ellos la maduración cerebral. Dado que la lactancia materna es la recomendación inicial para la alimentación de un bebe, diferentes estudios han analizado la composición de esfingolípidos en la leche materna[26].

En los últimos años, el consumo de bebidas vegetales, cuya intención es reemplazar las fórmulas infantiles, ha aumentado, aunque podría tener consecuencias negativas en lactantes menores de 1 año. Un estudio sobre composición y efectos de este tipo de bebidas concluye que la sustitución de las fórmulas infantiles por bebidas vegetales, expone al lactante a deficiencias nutricionales, además no cumplirían con la normativa de la legislación europea, presentando concentraciones inferiores a las recomendadas de proteínas, vitamina A, sodio, potasio, fósforo y calcio entre otros[25]. Diferentes estudios indican que las fórmulas infantiles no solo presentan diferencias en los niveles de esfingolípidos en comparación con la leche materna, sino que entre ellas también se observan grandes variaciones[27,28]. De igual modo, se han evaluado las concentraciones de esfingomielina en aquellos productos nutricionales infantiles introducidos en los 3 primeros meses de vida, estudiando el desarrollo cognitivo y la mielinización en los lactantes, demostrando que mayores niveles de esfingomielina se asocian a un mayor desarrollo verbal durante los 2 primeros años de vida, al igual que tasas más extendidas de mielinización en diversas áreas cerebrales, resaltando así la importancia de los niveles de los esfingolípidos en la leche materna, y por consiguiente, de la dieta materna[28]. Los esfingolípidos se encuentran en cantidades más elevadas en los productos de origen animal, razón por la cual se observa que las madres que siguen una dieta vegetariana presentan concentraciones inferiores a aquellas que optan por dieta omnívora.

En general, las madres vegetarianas presentan un IMC previo al embarazo significativamente inferior a las omnívoras (19,2 versus 21,8), junto con menores reservas de grasa en el postparto debido a un consumo energético significativamente más bajo en comparación con las madres omnívoras (1855,4 kcal/día versus 2360,7 kcal/día), aumentando el riesgo de padecer resultados adversos y dificultando la realización de una lactancia materna exclusiva eficaz[27]. Por ello, se debería controlar el IMC de las embarazadas y madres lactantes vegetarianas.

Por otra parte, Barrera et al.[17] han evaluado el consumo de ácidos grasos omega-3 durante la lactancia, concretamente el ácido docosahexaenoico (DHA), un ácido graso esencial para el correcto desarrollo cerebral y visual del lactante. Se observa una reducción del consumo energético y de carbohidratos entre el 1º y 6º mes de lactancia, además de una ingesta inferior a la recomendada de ácidos grasos omega-3. Se concluye que existe la necesidad de fomentar el consumo de alimentos naturales con alto contenido en DHA o en modo de alimentos fortificados durante el periodo de lactancia, con el fin de obtener concentraciones adecuadas[8]. Posteriormente, y en la misma línea de estudio, se evalúan posibles diferencias en los niveles de DHA en la leche materna según 3 patrones alimenticios distintos (vegana, vegetariana y omnívora), y no se observan diferencias significativas entre los diferentes grupos y en el 82% de las participantes, independientemente del patrón dietético materno presentan niveles inferiores a los recomendados. Se establece una dosis diaria recomendada de 200 mg/día de DHA durante el periodo de embarazo y lactancia. Además, se vincula el uso de la suplementación con el aumento de las concentraciones de DHA en leche materna, siendo así, una estrategia para alcanzar un suministro adecuado en aquellas mujeres que llevan una dieta pobre en DHA[29].

Se requiere mayor investigación para tratar de comprender el vínculo entre el estado de DHA materno durante la gestación, las concentraciones de DHA en la leche materna y el impacto de su suplementación en mujeres lactantes y sus bebés.

Conocimientos de los profesionales sanitarios, madres vegetarianas y madres no vegetarianas sobre el destete vegetariano y su impacto en el lactante.

Más de la mitad de los profesionales sanitarios considera que la dieta omnívora es más beneficiosa para la salud que la dieta vegetariana y un porcentaje inferior al 25% de dichos profesionales afirma tener conocimientos adecuados para asesorar sobre la alimentación vegetariana en estas etapas vitales[13,18].

En una reciente revisión, se pretendió estimar la prevalencia del destete vegetariano entre las familias italianas, concluyendo que este método se aplica frecuentemente entre aquellas familias que siguen una alimentación vegetariana, siendo más prevalente en los casos donde son las madres quienes optan por este modelo alimenticio (51,5%) que en las situaciones donde solo son los padres (27,3%). En más del 50% de las ocasiones, el equipo médico no cuenta con los conocimientos apropiados para poder guiar adecuadamente a los padres, pudiendo propiciar así la aparición de deficiencias nutricionales graves a corto y largo plazo[1].

En este mismo estudio se analizan las motivaciones familiares que conllevan a seguir este tipo de alimentación

durante el proceso de destete, además de evaluar la adherencia de los adultos a las recomendaciones dietéticas actuales en este tipo de alimentación. En este estudio se observa un alto porcentaje de padres (36,2%) que deciden no informar a su equipo médico sobre la realización del destete vegetariano. Además, el 51,5% de los casos comunican haber recibido información insuficiente por parte de su equipo asistencial, respaldando así las conclusiones de otros estudios sobre la falta de conocimiento sobre el destete vegetariano por parte del personal sanitario[18,30].

En relación con los conocimientos existentes entre madres vegetarianas y no vegetarianas en la introducción de la alimentación complementaria, se halla un número elevado de padres vegetarianos que declaran haber consultado información sobre la adecuación nutricional de la dieta vegetariana antes de tomar la decisión de criar a sus hijos con este tipo de alimentación. Además, las madres vegetarianas tienden más frecuentemente a introducir las verduras y frutas a través del método *Baby Led Weaning* que aquellas madres que siguen una dieta tradicional y parecen contar con conocimientos superiores sobre alimentación complementaria entre los 6-12 meses[15].

Las principales limitaciones de esta revisión incluyen: 1) Que la mayoría de artículos se realizan en ciertas áreas geográficas delimitadas (EEUU, India e Italia) cuya etnia y cultura son muy diferentes a la nuestra. Estas diferencias podrían interferir en los resultados si dichos estudios se llevaran a cabo en España. Actualmente, la información existente del estado nutricional de las personas vegetarianas en España es muy limitada; 2) Debido al bajo nivel socioeconómico de ciertos países, los resultados podrían ser no extrapolables a otras poblaciones con recursos superiores, ya que la elección de alimentos vegetarianos puede no ser una opción sino una necesidad; 3) Además, los resultados obtenidos podrían variar según los alimentos permitidos y excluidos en cada subtipo de dieta vegetariana; 4) Finalmente, se debe tener en cuenta que aproximadamente el 40% de los artículos incluidos en esta revisión se basan en la cumplimentación de cuestionarios y encuestas, pudiéndose producir así sesgos de participación.

Tabla II: Síntesis artículos seleccionados.

Año	Autor principal	Lugar	Fecha recolección de datos	Inclusión de casos	Sujetos de estudio	Fuentes de datos	Tamaño muestral	Rango de edad	Nivel de evidencia	Grado recomendación
Comparison of Lactational Performance of Vegetarian and Non-Vegetarian Mothers in Indonesia										
2014	S. Fikawati	Yakarta, Surabaya, Pontianak, Palembang Pekanbaru (Indonesia)	2012	Mujeres postparto en áreas urbanas	Madres vegetarianas y no vegetarianas postparto	Mediciones del recién nacido. Medición estado nutricional materno. FFQ.	33 parejas madre-bebe	Adulta Edad fértil	2+	C
Severe nutritional deficiencies in young infants with inappropriate plant milk consumption										
2014	B. Le Louer	Francia	2008 - 2011	Hospitales de París	Lactantes que han consumido pre año de vida y durante más de 1 mes, una bebida vegetal que no cumple con la normativa europea.	Expediente médico: demografía, edad inicio tipo y duración de consumo de bebida, evaluación del crecimiento talla y peso, evaluación parámetros biológicos	9	4 -14 meses	2+	C
Pregnancy Outcome and Breastfeeding Pattern among Vegans, Vegetarians and Non-Vegetarians										
2014	P. Roman	Carolina del Este (EE.UU)	Otoño 2011 – Verano 2012	Escuelas e Iglesia Adventista del Séptimo Día.	Madres y lactantes vegetarianos	Cuestionarios socioeconómico y antropométrico	613	Lactantes hasta 12 meses Madres adultas	3	D

Tabla II: Síntesis artículos seleccionados.

Año	Autor principal	Lugar	Fecha recolección de datos	Inclusión de casos	Sujetos de estudio	Fuentes de datos	Tamaño muestral	Rango de edad	Nivel de evidencia	Grado recomendación
Vitamin B-12 supplementation during pregnancy and early lactation increases maternal, breast milk, and infant measures of vitamin B-12 status										
2014	C. Duggan	Bangalore (India)	Diciembre 2008 - Diciembre 2010	Hosahalli Referral Hospital, centro guberna mental de atención a la salud materna	Embarazadas con atención prenatal previa a las 14 SG.	Entrevista sobre información sociodemográfica, régimen diario, FFQ, analítica sanguínea, muestra de leche materna y heces maternas	366	>18 años	++1	A
Low serum vitamin B-12 concentrations are prevalent in a cohort of pregnant Canadian women										
2016	C. Visentin	Toronto, Canadá EE. UU	Noviembre 2010 – Enero 2012	Hospital St. Michael. Estudio PRE-FORM.	Mujeres embarazadas y recién nacidos	Evaluación ingesta dietética y suplementaria mediante Block FFQ + Muestra sanguínea	368	18 – 45 años	2+	C
Perturbing Status of Vitamin B12 in Indian Infants and Their Mothers										
2017	M. Mittal	India	Noviembre 2010 – Enero 2012	Hospital pediátrico de atención terciaria	Lactantes y sus madres	Muestras venosas de 3ml	100	1 - 6 meses	2+	C
The Impact of Maternal Diet during Pregnancy and Lactation on the Fatty Acid Composition of Erythrocytes and Breast Milk of Chilean Women										
2018	C. Barrera	Chile (EE.UU.)	6º mes de embarazo - 6º mes de lactancia	Servicio de Salud obstétrica y Ginecológica del Hospital Clínico	Mujeres embarazadas sanas entre 22 y 25 sg e historia de lactancia exitosa.	Cuestionario de frecuencia alimentos. Muestras sanguíneas y de leche materna.	50	20 - 33 años	2+	C
Vitamin B-12 content in breast milk of vegan, vegetarian, and nonvegetarian lactating women in the United States										
2018	R. Pawlak	Carolina del Norte y Carolina del Este (EE.UU)	Noviembre 2016 – Abril 2017	Organizaciones vegetarianas y veganas, instituciones religiosas	Madres lactantes	Elegibilidad a través de BSQ (cuestionario básico de selección en línea). Muestras de leche materna.	74	18 - 46 años	3	D
The Effects of Vegetarian and Vegan Diet during Pregnancy on the Health of Mothers and Offspring										
2019	G. Sebastiani	Barcelona (España)	Enero 2000 – Diciembre 2018	Estudios existentes sobre efectos de la dieta vegetariana y vegana en embarazo	Embarazadas y lactantes vegetarianos	MEDLINE, PubMed, Cochrane. Pautas de la Asociación Dietética Estadounidense en embarazo y Pautas internacionales para dietas vegetarianas y veganas.	165	Adultas	1 ++	A
A cross-sectional study of fatty acids and brain-derived neurotrophic factor (BDNF) in human milk from lactating women following vegan, vegetarian, and omnivore diets										
2019	M. Perrin	EE.UU	Noviembre 2016 – Abril 2017	Comunidades en línea centradas en la lactancia materna o el vegetarianismo y comunidades religiosas.	Mujeres lactantes	BSQ (cuestionario básico de detección en línea) + Cuestionario digital + muestras de leche materna	74	Adultas (media de 32 años)	3	D

Tabla II: Síntesis artículos seleccionados.

Año	Autor principal	Lugar	Fecha recolección de datos	Inclusión de casos	Sujetos de estudio	Fuentes de datos	Tamaño muestral	Rango de edad	Nivel de evidencia	Grado recomendación
Knowledge of health professionals regarding vegetarian diets from pregnancy to adolescence: An observational study										
2019	M. Bettinelli	Milán (Italia)		Profesionales del área materno-infantil de los hospitales terciarios	Enfermería enfermeras pediátricas, matronas, personal de enfermería, trabajadores en salud.	Cuestionario (sociodemográfico, conductas alimenticias de los profesionales y sus conocimientos sobre alimentación)	418	Adultos (<30 y >55)	3	D
Effects of dietary intervention on vitamin B 12 status and cognitive level of 18-month-old toddlers in high-poverty areas: a cluster-randomized controlled trial										
2019	X. Sheng	Xichou, Yunnan (China)	Marzo 2009 – Diciembre 2011	Sub-estudio dentro de ensayo de eficacia controlado aleatorizado	Lactantes y niños pequeños	Muestreo sanguíneo y mediciones antropométricas. Prueba de detección de *Bayley Scales of infant development*	1465	3 – 18 meses	2-	D
Does vegan diet influence umbilical cord vitamin B12, folate, and ferritin levels?										
2020	T. Avnon	Alemania	Mayo 2018 – Junio 2019	Centro médico terciario	Mujeres con un embarazo único	Archives of gynecology and obstetrics	273	Adultas > 18 años	2++	C
Dietary Patterns and Determinants of Pregnant and Lactating Women from Marginalized Communities in India: A Community-Based Cross-Sectional Study										
2020	S. Sharma	Delhi, Karnataka, Bihar, Rajasthan (India)	Octubre 2016- Diciembre 2016	Atención comunitaria	Embarazadas (entre 4º y 9º mes) y madres lactantes (hijo entre 0-2 años)	Cuestionario cualitativo estructurado sobre datos demográficos y nutrición.	922	20 – 28 años	3	D
Human breast milk as source of sphingolipids for newborns: comparison with infant formulas and commercial cow's milk										
2020	M.Dei	Italia	Abril - Octubre 2019	Banca de Latte Umano Donato	Mujeres donantes de leche	Análisis lipidómico de muestra de leche madura + Cuestionario	23	27-37 años	1+	B
Vegetarian and Vegan Weaning of the Infant: How Common and How Evidence-Based? A Population-Based Survey and Narrative Review										
2020	M. Baldassarre	Bari (Italia)	Enero 2019 – Diciembre 2019	Atención primaria	Lactantes en proceso de destete vegetariano	PubMed, Embase, Medline, Cochrane Library y Web of Sciencie	360	Adultos	1++	A
Raising Children on a Vegan Diet: Parents' Opinion on Problems in Everyday Life										
2021	D. Bivi	Italia	Julio – Septiembre 2020	Grupos online de nutrición / destete vegetariano	Padres/ madres de hijos vegetarianos	Cuestionario frecuencia y diversidad alimenticia	176	Adultos > 20	1+	B
Knowledge on the complementary feeding of infants older than six months among mothers following vegetarian and traditional diets										
2021	M. Kostecha	Lublin (Polonia)	Enero - Agosto 2021	Clínicas pediátricas	Padres de niños de 10-12 meses	Evaluación dietética del lactante y niño pequeño y cuestionario de frecuencia de alimentos complementarios	251	Adultas > 18 años	3	D
Prevalence of Vitamin B12 Deficiency among Exclusively Breast Fed Term Infants in South India										
2021	A. Kadiyala	India	Agosto 2018 - Enero 2020	Clínica bienestar del bebé	Bebes alimentados con lactancia materna exclusiva	Diversidad consumo alimenticio materno, medición antropométrica del lactante, muestras sanguíneas.	149	1 – 6 meses	2+	C

Tabla II: Síntesis artículos seleccionados.

Año	Autor principal	Lugar	Fecha recolección de datos	Inclusión de casos	Sujetos de estudio	Fuentes de datos	Tamaño muestral	Rango de edad	Nivel de evidencia	Grado recomendación
Care by Midwives, Obstetricians, and Dietitians for Pregnant Women Following a Strict Plant-Based Diet: A Cross-Sectional Study										
2021	D. Meulenbroeks	Países Bajos	2019	Sociedad Holandesa Obstetricia Ginecología	Parteras, obstetras y nutricionistas	Cuestionarios sobre el conocimiento de la dieta basada en plantas y el embarazo	411	Adultas > 18 años	3	D
Maternal dietary diversity during lactation and associated factors in Palghar district, Maharashtra, India										
2021	S. Rajpal	Maharashtra (India)	Mayo – Junio 2020	Centros Anganwadi (AWC). Sistema atención médica de la India	Madres lactantes con anemia	Cuestionario diversidad y frecuencia alimenticia.	400	15-48 años	3	D
Vegetarian diets during pregnancy, and maternal and neonatal outcomes										
2021	S. Yisahak	EE. UU	2009 - 2013	Eunice Kennedy Shrivertal Grow Studies -Sigletons Instituto Nacional de Salud Infantil y Desarrollo Humano	Mujeres embarazadas	Cuestionario + Mediciones antropométricas neonatales y maternas	1948	27 – 30 años	2+	C

Tabla III: Niveles de vitamina B12 en función de la dieta.

		Niveles vitamina B12 materna (pg/ml)	Niveles vitamina B12 umbilical (pg/ml)
Vegana	Ingesta de suplementación No ingesta de suplementación	388,29 ± 209,54 219,63 ± 95,26	1002,63 ± 608,56 442.57 ± 151.30
Omnívora	Ingesta de suplementación No ingesta de suplementación	330.47 ± 163.16 292,45 ± 82,22	794.55 ± 423.69 558.57 ± 282.96
Vegetariana		378.94 ± 282.85	778.89 ± 481.94
Pescetariana		375.78 ± 301.33	778.89 ± 481.94

Conclusiones

Según la presente revisión y tal y como indican diferentes asociaciones y organismos, entre ellos la Academia Americana de Nutrición y Dietética, las dietas vegetarianas reúnen los requisitos para el aporte energético y nutritivo necesario para un correcto desarrollo y crecimiento. Por tanto, se consideran adecuadas para cualquier etapa del ciclo vital, incluyendo los periodos de embarazo, lactancia e infancia. No obstante, durante estas dos primeras etapas es fundamental asegurar la suplementación regular de vitamina B12 materna, sobre todo en aquellas poblaciones con bajo nivel socioeconómico.

La leche materna, es considerada la mejor fuente de esfingolípidos para un lactante y es además la alimentación más adecuada durante esta etapa también en madres vegetarianas. En cambio, la composición inadecuada de las bebidas vegetales hace que puedan producir deficiencias nutricionales graves, por lo que los lactantes menores de 1 año tienen totalmente contraindicado su consumo como substituto de la leche de fórmula.

Es necesario aumentar los conocimientos de los profesionales de la salud en relación a los diferentes patrones alimenticios, para aportar recomendaciones nutricionales adecuadas para cualquier etapa vital, incluyendo el embarazo y la lactancia materna.

Se requiere realizar un número mayor de investigaciones y estudios a gran escala, considerando los diferentes patrones dietéticos y posibles déficits nutricionales, tanto maternos como fetales y del lactante. Además, también son necesarios estudios experimentales que aporten

mayor calidad de evidencia científica para respaldar con firmeza la seguridad y la viabilidad de la dieta vegetariana durante el proceso de embarazo, lactancia y destete.

Conflicto de inetereses

Los autores declaran que no existe ningún conflicto de interés.

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SPECIAL ARTICLE

La metodología de cortes histo-topográficos de Salvador Gil Vernet, aplicada al estudio de los divertículos de uretra, permitió la primera descripción de la etiopatogenia y anatomía patológica. Análisis y valoración histórica de su investigación

The methodology of histotopographic cuts of Salvador Gil Vernet, in the study of urethral diverticula, allowed the first descripcion of the etiopathogenesis and pathological anatomy. Analysis and historical assessment of his research

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Resumen

El diagnóstico de los Divertículos Uretrales suele hacerse tardíamente al investigar la etiología de infecciones urinarias reiteradas a pesar de un tratamiento antibiótico correcto, sólo después de descartar las más frecuentes, se piensa en Divertículos Uretrales, ahí radica su principal dificultad diagnóstica. Actualmente se diagnostican mediante análisis de imágenes, bien sean por Ecografía, o más comúnmente por TAC. Al efectuar la seriación de imágenes de la uretra peneana, se identifica el foco infeccioso, cartografiando la zona diverticular en todo su recorrido hasta la desembocadura en la uretra. Cuando no se disponía de esta tecnología, bastantes décadas atrás, el diagnóstico era muchísimo más difícil y la etiología era poco menos que especulativa. No era fácil entender, la fisiopatología y la anatomía patológica de esta patología infecciosa. Ello queda claramente expuesto al analizar las aportaciones de Salvador Gil Vernet, hace décadas, sobre esta patología donde él ya expone con clara evidencia el proceso fisiopatológico y describiendo el substrato anatómico. Sólo una mentalidad de investigador perspicaz, con una metodología propia ampliamente divulgada, conocida y aceptada, y sin disponer entonces de la alta tecnología de imágenes, permitió, hace décadas, describir la fisiopatología de los Divertículos Uretrales. Esta capacidad de observación queda claramente demostrada, más si cabe, por el hecho de que no estaba investigando concreta y selectivamente esta patología en el paciente estudiado, sino que colateralmente observó las imágenes analizando cortes histo-topográficos seriados al investigar la anatomía del nervio pudendo y expuso su concepción fisiopatológica que exponemos en el presente trabajo de investigación histórica.

Palabras clave: Divertículos de uretra, infección urinaria crónica, glándula de Cooper, Salvador Gil Vernet.

Abstract

The diagnosis of urethral diverticula is usually made late when investigating the cause of repeated urinary tract infections that are difficult to explain and locate. Only in these situations, therein lies its main diagnostic difficulty, and only after ruling out the most frequent etiologies, is Urethral Diverticula considered, which is when it is currently easily diagnosed. Currently the diagnosis is made by image analysis, either by ultrasound, or more commonly by ACT. And if a serialization of the area to be investigated is carried out in the urinary tract of the penile urethra, not only is the infectious focus identified, but we can follow it all the way through the union channel to the urethra, to which it empties. But before this technology was available, many decades ago, diagnosis was much more difficult. Analyzing the contributions of Salvador Gil Vernet of the studied work, this previous premise is well demonstrated. And it was not easy to understand either, the pathophysiology and the pathological anatomy of this infectious and anatomical pathology, and he explains the pathophysiological process and the anatomical substrate. Decades ago, without high imaging technology, only a perceptive researcher's mentality and a proprietary methodology allowed us to demonstrate its pathophysiology. This perceptive observation mentality is clearly demonstrated by the fact that he did not study this pathology in the referred patient, but collaterally observed the serial histo-topographic images and presented his pathophysiological conclusion that we studied.

Key words: Urethral diverticula, chronic urinary tract infection, Cooper's gland, Salvador Gil Vernet.

Introducción

Los divertículos de uretra tanto masculina como femenina son muy poco frecuentes. Generalmente se diagnostican en pacientes con infecciones urinarias repetidas en espacios de tiempo corto a pesar de una antibióticoterapia correcta y toda vez que se han descartado las causas más frecuentes. Solamente entonces es cuando extremando minuciosamente las exploraciones de la vía urinaria inferior, revisando la seriación de imágenes de manera milimétrica de todo el trayecto, se diagnostican estas anomalías. Muy pocas veces el diagnóstico se evidencia en el inicio asistencial muy a pesar de una meticulosa historia clínica que debe guiarnos hacia la sospecha diagnóstica, puesto que no ocupan un lugar preferente en la lista de posibles diagnósticos. La imagen que proporciona una placa miccional muestra la zona diverticular directamente unida y dependiente de la imagen uretral.

Estado del arte: el origen y la cronobiología de los Divertículos de la Uretra esponjosa actualmente se conocen con detalle. Una placa postmiccional los pone de manifiestos. (**Figura 1**). Se puede seguir la fisiopatología mediante múltiples cortes seriados de TAC, cartografiando la dilatación diverticular hasta identificar la zona canalicular obstruida de la glándula de Cooper, origen topográfico y causal de la patología. Es decir, la tecnología actual nos permite tener una visión anatómica de la evolución en el tiempo y espacio de la patología gracias a la seriación tomográfica, que está al alcance de cualquier servicio de Urología de cualquier hospital mediano del país. Pero situémonos en el segundo tercio y mitad del siglo pasado cuando esta disponibilidad tecnológica no tan solo no existía, sino que ni siquiera se podría imaginar su descubrimiento y menos su aplicación a la medicina. Sin embargo, la mente clara de un investigador perspicaz y dedicado al estudio sistemático de la anatomía y patología urológica, mediante una metodología de estudio novedoso para su tiempo, "cortes Histotopográficos del sistema excretor urinario", supuso avances científicos reconocidos en internacionalmente, en el campo de la Urología. El resultado es que fue ya capaz en el año 1959, de demostrar y explicar la fisiopatología de los Divertículos de la Uretra esponjosa. (**Figuras 2** y **3**).

Figura 1: Divertículo uretral lleno de contraste en un paciente prostático con retención urinaria postmiccional.

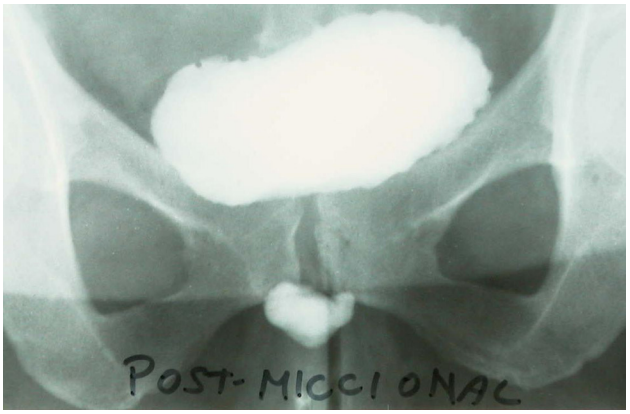


Figura 2: Fotografía de la separata de la comunicación al Congreso de la *Società Italina di Urologia*; septiembre de 1959.

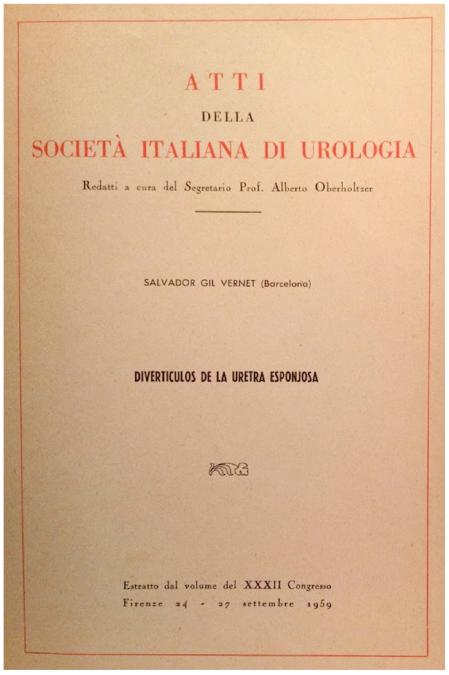
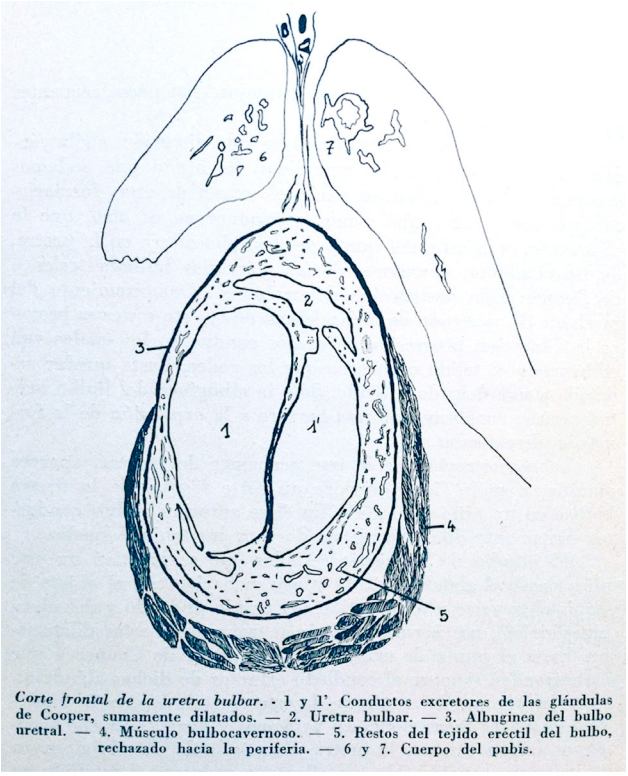

ATTI
DELLA
SOCIETÀ ITALIANA DI UROLOGIA
Redatti a cura del Segretario Prof. Alberto Oberholtzer
SALVADOR GIL VERNET (Barcelona)
DIVERTICULOS DE LA URETRA ESPONJOSA
Estratto dal volume del XXXII Congresso
Firenze 24 - 27 settembre 1959

Figura 3: Dibujo de la imagen microscópica del divertículo uretral estudiado, hecha por el mismo autor, S. Gil Vernet.



Corte frontal de la uretra bulbar. - 1 y 1'. Conductos excretores de las glándulas de Cooper, sumamente dilatados. — 2. Uretra bulbar. — 3. Albuginea del bulbo uretral. — 4. Músculo bulbocavernoso. — 5. Restos del tejido eréctil del bulbo, rechazado hacia la periferia. — 6 y 7. Cuerpo del pubis.

"(sic)…La casualidad ha hecho que podamos encontrar la explicación, es decir, el origen de estas formaciones, que en el caso que vamos a exponer no es otro, que la obstrucción congénita del punto de desembocadura en la uretra, de los conductos excretores de las glándulas bulbouretrales o de Cooper. Esta obstrucción determina el almacenamiento del producto de secreción de dichas glándulas y esto a su vez provoca la dilatación progresiva de dichos conductos, los cuales van rechazando el tejido cavernoso que los rodea, hasta quedar reducido a una delgada película. Sólo la albugínea del bulbo uretral resiste, constituyendo una barrera a la expansión de la formación diverticular.

La demostración de lo que acabamos de indicar, parece manifiesta en la* Figura 1*, que es un corte frontal de la uretra bulbar en un niño de 5 años. En él se aprecian ambos conductos sumamente dilatados, separados por un tabique medio.

El estudio de los cortes seriados que se practicó en este niño, desde el glande hasta la vejiga urinaria (con el objeto de seguir el trayecto y terminación del nervio pudendo y del plexo hipogástrico), nos permitió seguir el trayecto de estas dilataciones hasta el punto de origen en la glándula de Cooper y que corresponden siempre al conducto excretor de dichas glándulas."[1]

Las observaciones son exquisitamente analizadas, valoradas e interpretadas con una visión fisiopatológica del proceso morboso ya que en su persona coincidían el anatomista, el investigador y el clínico, tríada nada frecuente ni entonces ni ahora.

"(sic)… Del examen del conjunto de estos cortes, se saca la impresión que estas formaciones en principió y durante mucho tiempo, no comunican con la uretra. Es más tarde cuando alcanzan un volumen considerable, que llegan a provocar el estallido en el punto más débil, que como se ve en la* Figura 1*, corresponde a la pared inferior de la uretra esponjosa."

Con buen criterio, tras afirmar que por las observaciones efectuadas, estas eran sus propias propuestas fisiopatológicas y etiopatogénicas de los divertículos de la uretra esponjosa, pero como corresponde a alguien con mentalidad abierta a nuevos conocimientos, prosigue aceptando que los avances son la suma de aportaciones diversas; y prosigue:

"(sic) … Esta demostración no excluye la posibilidad de que los divertículos de la uretra esponjosa puedan ser originados o provocados por otros patologismos."

Comentario

El mismo Salvador Gil Vernet revela que este hallazgo no fue fruto de una investigación propiamente dicha dirigida a profundizar en el conocimiento de la fisiopatología de esta patología, sino que, al estudiar otros aspectos de la patología urológica, las relaciones del nervio pudendo, observó colateralmente esta patología y se puso a investigar logrando su esclarecimiento. Es decir, su mente perspicaz para detectar los más mínimos detalles en su investigación central, el esclarecimiento del trayecto del nervio pudendo, permitieron detectar otras anomalías las que, haciendo un aparte, siguió hasta su esclarecimiento. Esto es propio de una mente clara, incisiva, con una profundidad de conocimientos y dotes de observación nada comunes, como era su caso.

Conflicto de Intereses

No existe conflicto de interés alguno en la realización de este trabajo de investigación histórica, ni se ha recibido financiación alguna.

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CASE REPORT

Ozono y factores de crecimiento en el tratamiento de artralgias secundarias a la vacunación contra la Covid-19. Reporte de caso

Ozone and growth factors in the treatment of arthralgias secondary to vaccination against Covid-19. Case report

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Resumen

Introducción: El uso de vacunas como agentes preventivos de la infección por el SARS-CoV-2, ha generado la aparición de efectos colaterales entre los que se encuentran las artralgias. El presente reporte de caso tuvo como objetivo describir el tratamiento y evolución, de un paciente con artralgia secundaria a la vacunación con BNT162b2 (Pfizer - BioNTech), con ozono y factores de crecimiento ozonizados.
Métodos: Se trataba de un paciente de 53 años, masculino de raza blanca, sin antecedentes patológicos que había recibido 2 dosis de la vacuna BNT162b2. Después de la segunda dosis, el paciente refirió la permanencia de artralgia en el quinto dedo de la mano derecha, y tercer dedo de la mano izquierda con una intensidad de 9-10 en la escala EVA. El paciente fue infiltrado localmente con ozono 6 µg/mL, dos veces por semana por 2 semanas, y posteriormente se trató con factores de crecimiento derivados de plaquetas Silfradent® CGF (*Concentrated Grow Factors*), activados con ozono, en una única sesión.
Resultados: El paciente evolucionó de manera satisfactoria con una reducción final del EVA a un valor de 1-2 y la reducción de los síntomas clínicos.
Conclusiones: El ozono médico puede representar un complemento útil en el mitigar los efectos colaterales como las artralgias posteriores a la vacunación, se necesitan estudios clínicos más amplios para demostrar su eficacia clínica en esta indicación.

Palabras clave: BNT162b2, artralgias vacunación, ozono médico, factores de crecimiento activados con ozono, COVID-19, SARS-CoV-2.

Abstract

Background: The use of vaccines as preventive agents for SARS-CoV-2 infection has generated collateral effects, including arthralgias. The objective of this case report was to describe the treatment and evolution of a patient with arthralgia secondary to vaccination with BNT162b2 (Pfizer - BioNTech), with ozone and ozonized growth factors.
Methods: The patient was a 53-year-old, white male with no medical history who had received 2 doses of the BNT162b2 vaccine, with an interval of 6 weeks. After the second dose, the patient reported the permanence of arthralgia in the fifth finger of the right hand, and the third finger of the left hand with an intensity of 9-10 on the visual analog scale (VAS) scale. The patient was locally infiltrated with ozone 6 µg/mL (intra articular and with the glove technique), twice a week for 2 weeks, and was subsequently treated with platelet-derived growth factor, Silfradent® CGF (Concentrated Grow Factors) activated with ozone, in a single session.
Results: The patient evolved satisfactorily with a final VAS reduction to a value of 1-2 and reduction of clinical symptoms. Medical ozone and regenerative medicine using CGF, can represent a useful complement in mitigating collateral effects such as post-vaccination arthralgias.
Conclusions: Larger clinical studies are needed to demonstrate its clinical efficacy in this indication.

Key words: BNT162b2, arthralgia vaccination, medical ozone, ozone activated growth factors, COVID-19, SARS-CoV-2.

Introducción

El SARS-CoV-2 es un virus que causa una enfermedad grave potencialmente mortal conocida como COVID-19. Se observó por primera vez en Wuhan, China, en noviembre de 2019 y la OMS informó el primer caso el 31 de diciembre de 2019[1]. El brote se declaró una pandemia mundial el 11 de marzo de 2020 y en septiembre de 2021, se registró un total 219 millones de casos positivos y 4,5 millones de fallecidos en todo el mundo. El SARS-CoV-2 se dirige principalmente al pulmón y entra al cuerpo a través de los receptores ACE2[2]. Los síntomas típicos de COVID-19 incluyen fiebre, tos, dificultad para respirar y fatiga, aunque también se han descrito algunos síntomas atípicos como pérdida del olfato y el gusto. El 20% requiere ingreso hospitalario por enfermedad grave, un tercio de los cuales necesita cuidados intensivos. El tratamiento es principalmente de apoyo, sin embargo, el pronóstico es desalentador en aquellos que necesitan ventilación invasiva. Se están realizando ensayos para descubrir vacunas y medicamentos eficaces para combatir la enfermedad. Las estrategias preventivas tienen como objetivo reducir la transmisión de enfermedades mediante el rastreo de contactos, el lavado de manos, el uso de máscaras faciales y limitar actividades innecesarias para reducir el riesgo de transmisión[3].

En diciembre de 2020, la FDA aprobó las dos primeras vacunas mediante autorización de uso de emergencia en los Estados Unidos[4]. Estas vacunas se basan en la plataforma de vacunas de ARNm y fueron desarrolladas por Pfizer / BioNTech y Moderna. Los ensayos publicados de seguridad y eficacia informaron altas tasas de eficacia de 94-95% después de dos dosis, junto con efectos secundarios limitados y una baja tasa de reacciones adversas. El rápido ritmo de desarrollo de la vacuna y la incertidumbre de los posibles efectos adversos a largo plazo, generaron cierto nivel de vacilación contra las vacunas de ARNm en la comunidad mundial[5].

Hasta el momento no se han identificado efectos secundarios graves en los ensayos clínicos de fase 3 en curso, para las vacunas de ARNm de Moderna y Pfzier/BioNTech[6,7]. Los efectos secundarios locales leves, como calor, dolor, eritema e inflamación, son más frecuentes con las vacunas que con el placebo (solución salina normal)[6,7]. Otros efectos secundarios sistémicos, como fatiga, fiebre, dolor de cabeza, mialgias y artralgias, se producen con más frecuencia con la vacuna que con el placebo, y la mayoría se produce entre 1 y 2 días después de la vacunación[6,7]. Este trabajo tuvo como objetivo describir la evolución de un paciente vacunado con dos dosis de la vacuna ARNm Pfzier/BioNTech (BNT162b2), que presentó artralgia en las articulaciones de la mano y fue tratado con infiltraciones de ozono y concentrados de factores de crecimiento activados con ozono.

Presentación del caso

Se presentó a la consulta un paciente de 53 años, masculino de raza blanca, sin antecedentes patológicos que había recibido 2 dosis de la vacuna Pfizer – BioNTech COVID-19 (BNT162b2) formulado con nanopartículas lipídicas, con un intervalo de 6 semanas. El paciente refirió que 24h después de la primera dosis percibió síntomas neurológicos de baja intensidad (cansancio) que se revirtieron a las 48h. Pasados 15 días de la primera dosis, notó dolor en todas las articulaciones de ambas manos que fueron disminuyendo a lo largo del tiempo. Después de la segunda dosis, los dolores en las articulaciones de la mano se volvieron a presentar después de 24h y nuevamente fueron disminuyendo en el tiempo (30 d), sin tratamiento. En dos articulaciones: 1) quinto dedo de la mano derecha, entre la segunda y tercera falange y tercer dedo de la mano izquierda entre la primera y segunda falange; el dolor articular permaneció con una intensidad de EVA (Escala analógica visual)[8] = 9-10. La exploración física de las articulaciones implicadas evidenció síntomas de inflamación articular, disminución de la capacidad para mover la articulación, enrojecimiento, calor de la piel alrededor de una articulación y rigidez articular, especialmente en la mañana. El paciente no refirió padecer de síntomas de esta naturaleza con anterioridad, por lo cual estos síntomas se asociaron a efectos colaterales de la vacunación.

El tratamiento con ozono, como único tratamiento, se realizó 30 días después de la segunda dosis y consistió en la infiltración intra articular (0,5 mL) y con la técnica del guante (3 mL) de ozono a una concentración de 6 µg/mL dos veces por semana durante 2 semanas. La técnica del guante consiste en la inyección de ozono por vía subcutánea, y su posterior dispersión mediante masaje, a toda el área afectada. Una semana después se aplicó una infiltración articular de 0,5 mL de plasma autólogo rico en factores de crecimiento activados con ozono. Para la generación del ozono médico, se utilizó un equipo marca Ozonette (SEDECAL, España) certificado CE IIb, siguiendo los protocolos de infiltración referidos por el ISCO3[9]. Para la preparación de los factores de crecimiento, se utilizó una centrifuga Medifuge (Silfradent, Italia) y el protocolo de preparación estándar. Una vez obtenido el concentrado de factores de crecimiento se activaron con ozono 50 µg/mL en proporción 1:1[10,11] y cloruro de calcio. Para practicar la infiltración intraarticular de ozono o factores de crecimiento y la técnica del guante con ozono, se utilizó una aguja 37 G x ½" (0,4 mm x 12,7 mm). La evolución del paciente se siguió mediante la evaluación clínica de las zonas afectadas y la escala de valoración del dolor EVA.

Consideraciones éticas: el manejo del paciente se realizó siguiendo las consideraciones y recomendaciones nacionales e internacionales de las buenas

prácticas clínicas (Declaración de Helsinki (Fortaleza, Brasil, 2013)[12]: así como de las normas, reglamentos y leyes que favorecen una relación médico-paciente adecuada. Por lo tanto, el paciente firmó un documento para el consentimiento del uso y preservación de sus datos personales. Además, una vez que se le informó de manera oral y escrita el procedimiento a seguir, firmó el consentimiento al tratamiento médico.

Evolución: El paciente experimentó una reducción gradual del dolor articular que pasó de un estado ini-cial medido con la escala EVA de 9,5 / 10 a un valor de 5/6 después de 4 aplicaciones de ozono intra articular combinadas con la técnica del guante. Desde el punto de vista clínico se apreció una reducción de los signos de inflamación local. Los valores de EVA disminuyeron a valores entre 1 y 2 una semana después de la aplicación intra articular de factores de crecimiento (PRP) activados con ozono. Durante la aplicación de ozono o factores de crecimiento, no se apreciaron eventos colaterales relacionados con la terapia; el paciente no siguió otro régimen terapéutico que no fuera el descrito anteriormente. Después de la infiltración local con ozono, el paciente percibió un ligero dolor local que pasó en un tiempo breve (aproximadamente 15 min) seguido de una percepción de alivio del dolor de base previo a la infiltración.

Discusión

El ozono administrado de manera infiltrativa a nivel articular, a concentraciones adecuadas, tiene efectos analgésicos y antinflamatorios[13-15]. Los efectos relativos al mecanismo de control del dolor se han estudiado desde el punto de vista preclínico. Se ha demostrado que inhibe receptores purinérgicos P2X3 y P2X7, por lo que interrumpe la transmisión de la señal periferia al SNC[16]; adicionalmente disminuye la apoptosis y la autofagia de las raíces nerviosas[17]; incrementa la 5'-adenosina monofosfato (AMP) -proteína quinasa activada (AMPK), decisiva en los efectos analgésicos[18]. Desde el punto de vista molecular se conoce que el ozono, bloquea la síntesis de las caspasas 1, 8, 12 y TNF-α que son media-dores del dolor y la inflamación[19,20]. En cuanto a estudios clínicos existen numerosas evidencias de que estos efectos tienen lugar. Los tratamientos infiltrativos con ozono se han probado en la clínica en el con-trol del dolor lumbar[21], cervical[22], de la rodilla[23], entre otros.

La artralgia, es uno de los efectos colaterales de las vacunas anti SARS-CoV-2; por ejemplo, la incidencia de artralgia después de la primera dosis de la vacuna ChAdOx1nCoV-19 (Oxford-AstraZeneca) es de 56%, mientras que para la vacuna BNT162b2 (Pfizer BioNTech) es de un 6,7%[24]. El mecanismo por el cual se produce este efecto colateral a la vacunación es desconocido. Sin embargo, en los pacientes con la COVID-19 se pueden presentar características que imitan enfermedades reumáticas, como: artralgias, neumonía intersticial aguda, miocarditis, leucopenia, linfopenia, trombocitopenia y tormenta de citocinas con características similares a la linfohistiocitosis hemofagocítica secundaria[25].

Teniendo en cuenta los efectos reportados para el ozono en cuanto a control de la inflamación y el dolor, consideramos que su efectividad en el presente caso, se pueden deber al menos en parte, a la participación de los mecanismos descritos. Durante el curso clínico se observó una disminución del dolor que se caracterizó por dos fases, un alivio inmediato (después de aproximadamente 15 min) y un alivio progresivo del dolor. El alivio inmediato pudo deberse a la interacción directa del ozono con mediadores locales del dolor o sus receptores, como se describió con anterioridad[26]. El alivio progresivo después de 4 aplicaciones estabilizó al paciente en una reducción del EVA inicial del 50 %. En este momento se decidió aplicar PRP activados con ozono. Los factores de crecimiento autólogos derivados de plaquetas, además de sus efectos regenerativos, contienen compuestos como la lipoxina A4, con efectos analgésicos y antinflamatorios[27,28]. La terapia con PRP se basa en el hecho de que los factores de crecimiento plaquetario apoyan las tres fases de la cascada de curación y reparación de heridas (inflamación, proliferación, remodelación)[29]. El uso del ozono como activador de las plaquetas incrementa la liberación de factores de crecimiento[30] y han sido utilizados con eficacia en diferentes patologías articulares, para el control de la inflamación y el dolor[31,32]. En el caso que describimos, la infiltración con PRP activados con ozono y cloruro de calcio, disminuyó el EVA de 5-6 a 1-2, 7 días después de una sola administración.

En este caso, es posible que la administración concomitante de una vía sistémica de ozono, como la solución salina ozonizada, hubiera contribuido a acelerar el proceso de curación, mediante el control de la liberación de citocinas inflamatorias[33]. El uso del ozono médico como terapia complementaria en el Covid-19 puede ser de utilidad desde las fases de prevención, tratamiento y rehabilitación del paciente. También como describimos en este caso, puede contribuir a la rehabilitación de secuelas del proceso de vacunación y a reducir algunos efectos colaterales como las artralgias. Se recomienda realizar estudios clínicos más amplios para poder llegar a conclusiones más precisas sobre este potencial uso terapéutico del ozono.

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Conflicto de Intereses

Los autores manifiestan que no presentan conflictos de intereses.

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CASE REPORT

Impact of domestic violence on adolescent self-esteem: A case study

Impacto de la violencia doméstica en la autoestima adolescente: estudio de un caso

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Resumen

Domestic violence is a risk of suicide associated with low self-esteem and self-harm. This case illustrates how domestic violence affects mental health.
The client was often pinched, beaten and compared to other siblings by her mother. She never got recognition from her mother. This experience made her insecure, hurting herself when she could not control her emotions and using alcohol. Clients often have the mind to die and pray to die quickly to meet their father immediately. Mental health nursing management for clients is a positive affirmation. The evaluation results from the care management showed an increase in self-esteem, a positive mind and an adaptive coping mechanism. Mental health nursing management with positive affirmation is essential in helping adolescents who experience domestic violence. It can increase self-esteem and change negative thoughts and self-harm behaviour that arises due to domestic violence.

Palabras clave: Adolescente, autoestima, estudio de caso, violencia doméstica.

Abstract

La violencia doméstica es un riesgo de suicidio asociado con baja autoestima y autolesiones. Este caso ilustra cómo la violencia doméstica afecta la salud mental.
La cliente a menudo era pellizcada, golpeada y comparada con otros hermanos por su madre. Nunca obtuvo el reconocimiento de su madre. Esta experiencia la volvió insegura, lastimándose cuando no podía controlar sus emociones y consumiendo alcohol. Los pacientes a menudo tienen en mente la muerte y rezan para morir rápidamente para encontrarse con su padre de inmediato. La gestión de enfermería en salud mental para los pacientes es una afirmación positiva. Los resultados de la evaluación de la gestión del cuidado mostraron un aumento de la autoestima, una mente positiva y un mecanismo de afrontamiento adaptativo.
El manejo de enfermería en salud mental con afirmación positiva es esencial para ayudar a los adolescentes que experimentan violencia doméstica. Puede aumentar la autoestima y cambiar los pensamientos negativos y el comportamiento de autolesión que surge debido a la violencia doméstica.

Key words: Adolescent, case study, domestic violence, self esteem

Introduction

Domestic violence is a multifactorial phenomenon that requires intervention from a multidisciplinary team for comprehensive care for victims. It is excruciating when done on children. Domestic violence is a life event that can change children's behaviour over a long period. The impact on children can be seen directly or in the medium and long term. Feelings of pain caused by acts of violence are most often suppressed, forgotten, and rejected but never disappeared. Psychological trauma can develop and negatively affects the child's personality[1,2].

Youth victims of domestic violence have a greater tendency to be involved with substance abuse, show suicidal behaviour and injury to themselves, and have difficulty in building interpersonal[3]. Youth victims of domestic violence have lower self-esteem[4].

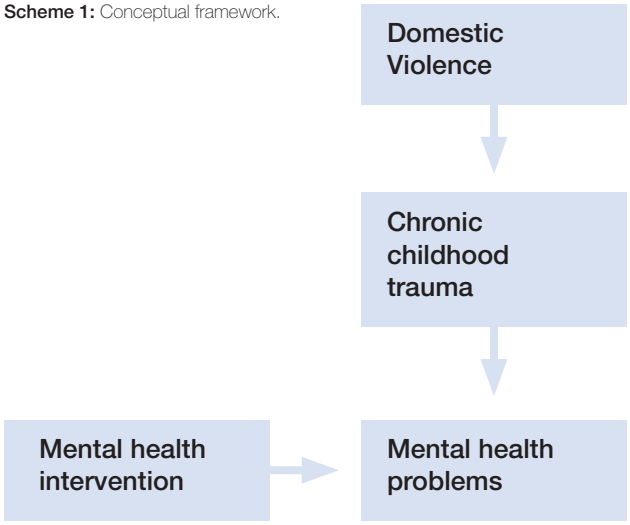
Good self-esteem is an essential component of mental health. It can help the achievement of individual life. Teenagers with low self-esteem have worse mental health conditions[5,6]. Low self esteem in adolescents can increase the risk of suicide[7].

This case describes a teenage girl who is traumatized by domestic violence. The trauma experienced affects the psychological aspects so that they have low self-esteem, self-harm and suicide. The purpose of the study is to describe case reports and mental health nursing management from the client.

Conceptual framework

Children and adolescents with a history of trauma are at risk of experiencing mental health problems[8,9]. Children and adolescents with a history of trauma need mental health intervention[8].

Scheme 1: Conceptual framework.



Case Introduction

A client is 18 year old, single, female sex with medium socioeconomic status. She came from a city in Bengkulu Province and was a second-year student at a university in West Java.

The stages of mental health nursing management are assessment, nursing diagnosis, goals and intervention, implementation and evaluation.

Mental health nursing management

Stage 1: Assessment

Main complaint

The client has felt increasingly insecure since college. She felt the most stupid in class and shunned by friends, revealed low academic achievement, and could not understand each topic. According to the client, since childhood, she has been said to be stupid by his mother. For one month, the client increasingly had difficulty concentrating, felt sad, had trouble sleeping, and had no appetite.

Treatment history

The Client is being counselling for the first time. Clients have never visited health services before.

Assessment

The assessment uses the Psychiatric-Mental Health Nursing practice standards. The Proforma Gives Guides for Assessment of Past and Current Health History, Mental Status Examination (Physical Behavior, Nonverbal Communication, Appearance, Speech Pattern, Mood and Affect, Thought Content, Perceptions, Cognitive Ability, Insight and Judgment Assessment, Cultural and Social Assessment[10].

Individual interview

In the current condition, the client is not confident and gets a rejection by friends. Screening results using SRQ -29 (Self Reporting Questionnaire) = 26 (0 - 29). The self-esteem identification results using the Rosenberg Self Esteem Scale = 20 (10 - 40).

History, since childhood, often accepts acts of violence from the mother, often compared to other siblings, not recognised and undesirable. As a result, she is not confident and often hurts herself by scratching her hand and banging her head when she cannot control her emotions. The client has a habit of drinking red wine to overcome the problems experienced. Clients often have the mind to die and pray to die to meet their father's

Mental Status Examination

The client tends to bow during the interview, and the tone of voice is slow. Affect appropriate, the mood looks sad. The client has the mind to commit suicide and hurt himself.

Psychosocial Assessment

The mother is distinguished and loves her brother more than her. She judges her daughter as stupid and never gives recognition and praise. This situation causes the client to lose confidence and want to harm herself. The client has a feeling of having no friends, away from friends because of stupid. If the client feels unable to control herself, feels comfortable when self-harm and drinks red wine. The client reveals the frequency of drinking red wine is uncertain but done when feeling stressed with the amount that drinks about 3-4 cups (1 glass = 100 ml).

Spiritual Assessment

The client runs worship according to his religion.

Cultural and Social Assessment

The client is the second child of three siblings from the Batak tribe. Since college, the client has lived alone.

Stage 2: Nursing Diagnosis

The nursing diagnosis refers to the Nanda International diagnosis[11] :

Domain 6. Class 2. Diagnosis Code 00119 Chronic Low Self Esteem
Domain 9. Class 2. Diagnosis Code 00069 Ineffective Coping

Stage 3: Purpose and Intervention

The interventions focus on building mutual trust relationships with clients, increasing self-esteem and strengthening practical coping skills—the interventions of positive affirmation in 4 sessions, each session for 90 minutes.

Stage 4: Implementation

The implementation aims to help clients recognize their potential, act according to their abilities and improve coping skills.

The implementation process includes:

Know self-potential

Therapists help clients to recognize their abilities or advantages. The knowledge possessed is written in the client's notebook. This potential or ability is important to increase the client's self-esteem.

Developing positive activities according to their abilities

Therapists help clients to do the capabilities in the client's notebook. The success of the ability exercise will cause valuable feelings and increase the client's self-esteem.

Practice effective coping

Therapists help clients to overcome the problems experienced in an effective way in solving the problems encountered. This exercise forms the client's ability to deal with problems in an adaptive way.

Self-affirmation

Self-affirmation allows the client to reflect on the core value that can give individuals a broader view of themselves. It helps clients reduce stress, overcome situations that are considered a threat to self-integrity or competence and make them more open to changing behaviour.

Stage 5: Evaluation

Evaluation of the implementation of increasing the client's self-esteem, the client can carry out activities that boost self-esteem and coping skills.

Discussion

Domestic violence is a traumatic experience for the Client. The traumatic experience experienced by the Client since childhood affects their mental health condition. These conditions are low self-esteem, self-harm, low academic achievements, consuming alcoholic drinks and having suicidal ideas. This case study is similar to the research; adolescents who have had chronic trauma experience since childhood tend to experience academic difficulties, emotional problems and behaviour and use of substances[9]. Traumatic experiences such as emotional abuse are low self-esteem contributors. Low self-esteem people risk self-harm to reduce negative emotions and overcome life difficulties[12,13]. Domestic violence is associated with a decrease in mental health conditions. Individuals who experience domestic violence are more at risk of experiencing anxiety and depression[14]. The results of the study state that the idea of suicide is related to the history of emotional violence. The use of alcohol in adolescents is associated with an account of physical violence[15].

The Client is often compared to her siblings because their academic achievements are not like her brothers. since childhood, she was often pinched and beaten by her mother, Which shows the form of domestic violence is physical and emotional violence. Physical and emotional violence committed by parents can occur because of inappropriate parenting. The results of previous studies state that physical and emotional hardness can affect self-esteem and that parenting that is hard or inconsistent negatively affects children[16,17].

The therapist gives positive affirmation. The exercise expands the individual perspective as a whole. Affirming positive practice done by clients with therapists or independently can reduce negative emotions and increase self-esteem. Self-esteem is one component of the self-concept. Positive affirmation helps maintain self-integrity when there is a threat to self-esteem. Self Affirmation is an intervention widely used in health, clinical and social psychology. Self-affirmation helps increase self-esteem, improve cognitive and academic performance and reduces cortisol and epinephrine levels[18].

The affirmation can increase focus on the source of positive individual values. Giving actions and exercises for self-affirmation helps clients know positive things about themselves and develop their abilities to increase self-esteem. Positive affirmation interventions depend on the ability to reflect on personal core values and valuable experiences. Biologically involves nerve mechanisms related to appreciation and optimistic assessment. A meta-analysis shows that the most prominent brain regions involve rewards and positive judgment, including Ventral Striatum (VS) and ventral medial prefrontal cortex[19]. Self Affirmation decreases stress using neural mechanisms Increasing the activity of the ventral striatum and ventromedial prefrontal cortex (VMPFC) and decreasing the anterior insula (AI) activity[20].

Implications of Mental Health Nursing Management

Teenagers with low self-esteem impacted by domestic violence risk experiencing anxiety and depression. The self-affirmation focuses on making clients aware of

themselves, receiving and cooperating in overcoming the problems encountered and strengthening coping skills.

Limitations and challenges of case management

The author is a client-therapist, so the potential bias is difficult to avoid, even though the author wrote the article after the mental health nursing management was complete. This case study is the result of an in-depth analysis of one case. This situation will be difficult to generalize to all teenagers with domestic violence. Differences in the family's characteristics and context can affect the study's results.

Case study management using Self Affirmation can cause discomfort in clients with chronic low prices. It is due to the presence of self-criticism in the client. So that at the beginning of the session, it is essential to foster a relationship of mutual trust and explore the cause of low self-esteem and the client's ability.

Recommendation

It is essential to conduct research and apply case study management by using self-affirmation to clients who experience self-esteem problems due to domestic violence at different stages of life (such as school-age children or young adults).

Conclusion

Teenagers with domestic violence experience cause low self-esteem. Increasing self-esteem by thinking and positive behaviour can overcome mental health problems in adolescents with a history of domestic violence. Mental health nursing management plays an essential role in treating mental health problems.

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Availability of data and materials

Not appicable

Authors' contributions

SN evaluated and examined the client, drafted and prepared the manucript. LNS did the nursing assesment the client. All authors read and appoved the final manuscript.

Conflict of interest

Authors have no conflicts of interest to declare.

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CASE REPORT

Pyoderma gangrenosum on an amputation stump treated with ustekinumab

Pioderma gangrenoso sobre un muñón de amputación tratado con ustekinumab

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Abstract

Wound care in the post-operative setting is of great importance in the Traumatology patient. Regular cleaning and evaluation are crucial. However, some cases, may evolve with wound dehiscence and ulceration of the skin borders. These patients might benefit from a multidisciplinary collaboration.
Herein, we describe a case of a pyoderma gangrenosum developed above the knee amputation.
This report described the difficulties in the management of this patient and the evolution of the wound once the correct diagnosis was made, as well as highlights the importance of collaboration between different medical fields in the clinical setting.

Key words: Pyoderma gangrenosum, ulceration

Resumen

El cuidado de las heridas durante el postoperatorio es de gran importancia en el paciente de traumatológico, siendo cruciales la limpieza y la evaluación periódica de las mismas.
Sin embargo, algunos casos pueden evolucionar a una herida dehiscente o a la ulceración. Estos pacientes pueden beneficiarse de una colaboración multidisciplinar.
Aquí describimos un caso de pioderma gangrenoso desarrollado sobre un muñón de amputación de la rodilla.
En este caso se describen las dificultades en el manejo de este paciente y la evolución de la herida una vez realizado el diagnóstico correcto, así como se destaca la importancia de la colaboración entre los diferentes especialistas en el ámbito clínico.

Palabras clave: Pioderma gangrenoso, ulceración.

Case report

A 58-year-old male was admitted to the Gastroenterology department in due to fever and abdominal pain secondary to a case of ileitis.

The patient had a history of hypertension, diabetes, chronic ischemic heart disease, chronic lower limb ischemia (treated via a femoral popliteal bypass in previous years), as well as Crohn disease (treated with a daily dose of 40 mg of hydrocortisone).

The patient developed severe knee pain associated with high fever, and presented erythematous plaques and fluctuating nodules, some of which showed spontaneous external fistulisation.

Then he was assessed by Traumatology and Dermatology department, which determined the infectious nature of the lesions as a first diagnostic possibility. Bacterial cultures were positive for *Staphylococcus aureus*. The diagnosis of erythema nodosum and pyoderma gangrenosum, were taken into consideration but ruled out as exclusion diagnosis due to low clinical suspicion after examination and the positivity of bacterial cultures.

Due to lack of improvement after antibiotic treatment, the skin lesions were surgically debrided as subcutaneous abscesses.

In early post-operative period, deep cutaneous ulcers formed (**Figure 1**). The ulcers progressed rapidly in the following weeks, leading to exposure of both the anterior muscular compartment of the thigh and bone at the previously debrided site.

The patient developed worsening of his general state, and showed signs of septic shock, requiring hospitalization in the Intensive Care Unit.

Figure 1: Appearance of the lession before amputation.

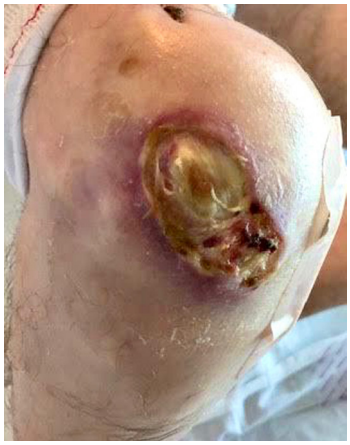


Figure 2: Clinical appearance of the lession after amputation.

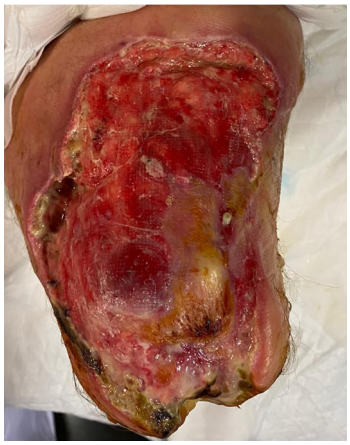
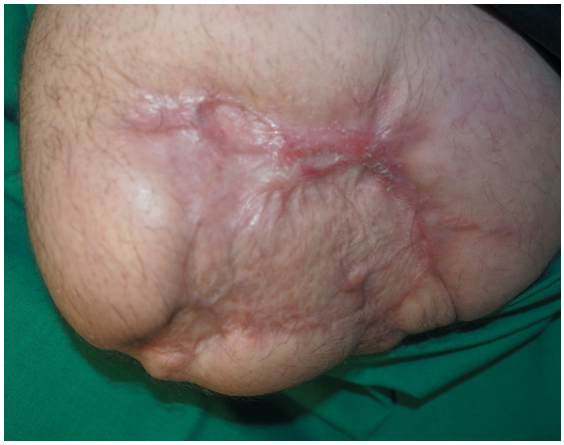


Figure 3: Amputation stump after ustekinumab treatment.



Positive blood cultures for *Klebsiella pneumoniae* were obtained as well as growth of multiresistent *Pseudomonas aeruginosa* and *Escherichia coli* in samples taken from the ulcer. Intravenous antibiotic treatment was started with linezolid and piperacillin-tazobactam.

He was then evaluated together with the Traumatology, Vascular Surgery and Plastic Surgery team. Given that the bypass in the affected leg was non-functioning, the inability to perform knee extension due to quadricipital tendon injury caused by and old injury, and that he was not a candidate for coverage due to a possible active infection, supracondylar amputation was proposed as the best option.

Postoperatively, the patient presented with dehiscence of the surgical wound on the amputation stump, sphacelus and necrotic tissue, and fever.

It was decided to extend the level of the supracondylar amputation. After the second operation, a new ulcerated lesion with violaceous borders appeared. The defect was covered with a meshed partial skin graft, which necrosed. The ulcer persisted and grew. A new medical interconsultation was made to the Dermatology department Under suspicion of pyoderma gangrenosum (PG), prednisone at 60mg/day and topical tacrolimus were started.

A new bacterial culture was positive once more for a multidrug-resistant *Pseudomona aeruginosa*, which was interpreted as a colonization after consultation with the Infectious Diseases unit. The biopsy showed a neutrophilic infiltrate without vasculitis, compatible with PG. Three days after starting prednisone, the ulcer bed began to epithelialize.

As the patient also had decompensation of his Crohn's disease, it was agreed with the gastroenterologists to start ustekinumab as a treatment for extensive PG and Crohn's disease, allowing the prednisone dose to be progressively reduced. Three months after the start of treatment, the patient completely re-epithelialized the ulcer.

He is currently being followed up by different specialists and maintains treatment with ustekinumab every 2 months.

Discussion

Pyoderma gangrenosum is a rare inflammatory disease of reactive origin that belongs to the group of neutrophilic dermatoses. Up to 85% of cases present as a painful ulcer with rapid growth and violaceous borders, although pustular, vegetating, periostomal, superficial granulomatous, malignant, and bullous variants have been described. It most often occurs in the lower extremities. In patients diagnosed with pyoderma gangrenosum, an underlying systemic disease should be ruled out since in about 50% there are other coexisting disorders, mainly inflammatory bowel disease (30%), rheumatoid arthritis (10%) or hematologic disorders (5%)[1,2]. The etiopathogenesis of PG is not well known, but the importance of neutrophils and increased proinflammatory and neutrophil chemotactic factors such as IL-1B, IL-17, TNF alpha, IL-8, IL-6, IL-17 and IL-23 has been widely described. Major and minor diagnostic criteria have been defined, but it should be kept in mind that the definitive diagnosis is always one of exclusion[1,3]. To make the diagnosis of PG, infection must be ruled out, preferably by biopsy. The presence of a neutrophilic infiltrate on histology, in the absence of infection, supports the diagnosis of PG, although a mixed inflammatory infiltrate or leukocytoclastic vasculitis may be seen[3].

Given the absence of complementary tests, the diagnosis of PG can be difficult, as was the case in our patient. Cases have been described in which PG lesions were diagnosed as soft tissue infections (mainly cellulitis or necrotizing fasciitis) or skin tumors, sometimes leading to amputation of the affected limb. It should be considered that surgical interventions can trigger PG lesions, this is since patergia phenomenon can be present in patients presenting this skin lession. The literature reports

cases in which post-surgical PG has even taken years to be diagnosed, which has harmed the patient with unnecessary treatments and prolonged admissions[4].

The assessment of the patient's comorbidities, negative cultures, the evolution of the lesions and poor response to antibiotic therapy can be useful in the diagnosis of PG. It should be considered that the presence of positive cultures does not exclude the possibility of PG and its relevance in the clinical context should always be assessed[4,5].

In our case the patient presented sepsis, whose only apparent origin was the skin ulcers, from which microorganisms had also been isolated in the cultures. We hypothesize that the lesions could be compatible with a case of pyoderma gangrenosum, which would have been overinfected and that acted as the entrance point for the infection.

Imaging tests do not aid in distinguishing with certainty between PG and cases of skin infection[5]. In addition, magnetic resonance imaging of PG lesions may show osteomyelitis (which can be sterile), skin thickening and an increase in the intensity of the subcutaneous soft tissue, among other alterations, which can easily be confused with abscesses, cellulitis, or tumors[6].

For this reason, given the clinical similarity between PG and necrotizing fasciitis, when a patient is suspected of having necrotizing fasciitis, prior to surgery, whenever feasible, the possibility of having PG should be assessed, since the treatments would be the opposite and the performance of debridement in PG would significantly worsen the evolution.

The treatment of choice in PG is corticosteroids, often systemic, and immunosuppressants, which can be complemented with local treatments such as corticosteroids or topical calcineurin inhibitors. Cyclosporine has been frequently used in patients with PG as a corticosteroid sparing agent. In addition, there have been published cases successfully treated with biologic treatments such as anti-TNF alpha, anti-IL1, anti-IL6 or with anti-IL23 drugs, as was the case in our patient, in which we initiated treatment with ustekinumab, an anti-IL-12/23 agent, which is also effective in the treatment of Crohn's disease[2,7,8].

We would like to highlight the importance of multidisciplinary treatment, especially in complex patients with multiple comorbidities, since management between different specialists was the key in our patient to reach the definitive diagnosis allowing subsequent cure.

Ethical approval

Patient´s consent has been obtained before writing this manuscript.

Declaration of interest

The authors declare no competing interest.

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