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Contenido

Editorial

Original research

Reflection paper

Review article

Case report

Editorial

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Publishing biomedical research articles in English, but in quality English

Latin American biomedical researchers are increasingly prone to publish their scientific production in indexed scientific journals published in English as this ensures greater visibility and impact, which in turn leads to a greater number of citations. (1,2)

This implies that researchers, in addition to writing articles with the utmost rigor and quality in their native language, should also seek a high-quality translation into English to make sure that the article submitted to the editorial process (editorial and peer review) is correctly written, and also that the contents of the source text are expressed in a clear, precise and natural way in the target language, which will undoubtedly increase their chances of acceptance and publication.

However, not all researchers are aware of the importance of submitting a high-quality translation that meets the requirements made by most of these journals or that improves the chances of publishing their work. Many times, they resort to automated translators that are freely accessible on the Internet, such as Google Translate (3), Traductor El Mundo (4), Cambridge Dictionary Translator (5), DeepL Translator (6), among others. In general, these tools yield a mediocre and literal translation, which may be accurate regarding some specialized terms, but does not ensure the quality of the whole text, particularly in the academic-scientific context of biomedical publications, because in most cases the authors only perform the automatic translation and do not review its logic or its consistency.

Another common phenomenon is that several researchers, either because they have completed studies abroad or have an acceptable level of English, perform the translation themselves relying on these services, without considering that this process requires prior preparation and having a certification of proficiency in the English language, and not only being a native speaker; if this logic were applied, no scientific journal publishing contents in Spanish would hire proofreading services. It is worth noting that people certified or with experience in academic and scientific writing in English should also rely on the authors as experts in the subject matter for the resolution of questions of terminology, among others.

Furthermore, different translation companies that offer their services at different costs can be found online, and in some cases, they also provide advice during the submission process. But these companies do not always provide clear information about the certifications, experience or quality standards applied by the people who will translate the documents, which may lead to an inaccurate translation without the possibility of making a complaint. In general, the costs of these services are high for most Latin American researchers (bearing in mind that they are usually charged in USD or EUR), who do not always include them in the budget of the final product. Others only translate the article but do not guarantee subsequent corrections, feedback or accompaniment in the publication process.

So, what do authors need to do to get an English translation that ensures that the article will be considered, reviewed and successfully published? Needless to say, the quality of the document submitted for editorial and peer review must be as high as possible to be approved, regardless of whether it was submitted in English or will be translated once accepted (both options are allowed by the Journal of the Faculty of Medicine). This requires advanced knowledge of English and biomedical English from the editorial team of the respective scientific publication, in addition to a group of peer reviewers with an advanced level of understanding in this language, as well as a support group made up of professional translators, recognized, certified and specialized in biomedical English, to ensure a high level of quality in the publication of the content in English.

Some universities provide financial support to their researchers to promote the publication of scientific articles in English in journals indexed in the main bibliographic databases. (7,8) For example, the Universidad Nacional de Colombia has opened calls for researchers to submit scientific articles to be translated by official translators, recognized and certified for their quality and command of the English language; however, the requirements are often demanding and the supply does not always meet the demand. (9)

But then, how should authors proceed? Some time ago, the Journal of the Faculty of Medicine decided to take the first step towards publishing its contents in English only. (10) This has been a progressive process that started with the inclusion of articles written in English (reviewed by the official translation team and the journal's editorial team) in recently published issues and the publication of at least one full English issue per volume, as is the case with this issue, which also includes two original articles that reinforce the Journal's final purpose of being a biomedical scientific publication with content in English only. (10-12)

This editorial policy has led some authors to submit their articles to our Journal in English, without meeting the minimum language requirements and thus leading to an initial rejection and recommendation to improve the quality of the text, either by contacting the certified and specialized professional staff with whom the Journal has been working or with an external and certified specialized professional. In this regard, the Journal's guidelines for submitting articles, available at Open Journal System website of the journal (13), offers two possibilities in the letter of commitment for publication in English, which must be signed by the authors: to submit the article in English together with a letter signed by a certified professional (translator, philologist, etc.) stating that the article was reviewed and complies with the required quality for academic and scientific articles in English, or to commit to cover the cost of the translation directly with one of the certified translators of our team in order to avoid processes such as a new proofreading; this option will be discussed in more detail below.

This means that the Journal is currently only accepting articles in English that are supported by a certification from a recognized and certified official translator; however, the articles will always be reviewed by the editorial team to determine if they meet the minimum standards or if they are not accepted. In Colombia, official translators, once they pass the official translation and interpretation exam (14-16), are certified by means of a resolution that is acknowledged by the Ministry of Foreign Affairs and allows them to sign and seal any official document.

The second option, for those interested in submitting their articles to our Journal, is to submit them in Spanish or Portuguese, together with the commitment letter to publish in English (13), duly signed, committing to translate the final version of the manuscript, once approved for publication, with one of the official translators who have been working with the Journal and who are duly certified and have studies and have experience in biomedical publications; this service is offered to authors at reasonable rates. (13)

It is important to mention that the Journal still has a large number of articles accepted in Spanish, which were submitted before this editorial policy was established (10); in consequence, they will be published in the upcoming issues, to make way for the complete publication of issues in English. (17)

In this manner, the editorial team of the Journal aims to achieve the publication of scientific articles of the highest quality, meeting the standards of academic and scientific writing in English, in order to allow for a better understanding and visibility of the work of researchers in our region.

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ORIGINAL RESEARCH

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Prevalence of surgical complications in gynecological surgery at the Hospital Universitario San José in Popayán, Colombia. 2015

Prevalencia de complicaciones quirúrgicas en cirugía ginecológica, Hospital Universitario San José de Popayán, Colombia. 2015

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| Abstract |

Introduction: Every surgery has risk of complications; prognosis depends on prompt diagnosis and timely management.

Objective: To determine the prevalence of surgical complications in gynecological surgery in a tertiary care hospital and to explore associated factors.

Materials and methods: Prevalence study with secondary analysis of medical records of patients who underwent scheduled gynecological surgery. The outcome variable was complications reported during a period of less than 30 days. The universe was established, and clinical, biological and sociodemographic variables were collected. To determine prevalence, the total number of complications was taken as the numerator and the total number of records was used as the denominator. To explore associated factors, odds ratio (OR) was used as a measure of association with a 95% CI.

Results: 591 records were reviewed, finding a surgical management of ectopic pregnancy prevalence of 3.8% (OR=3.73, CI95%: 2.41-92.52). Obesity (OR 12.47, CI95%: 4.48-33.19) and gynecological surgery for malignancy (OR 3.73, CI95%: 1.14- 10.48) were associated with complications.

Conclusion: The prevalence found in our institution was similar to what most studies have reported.

Keywords: Prevalence; Surgery; Gynecology (MeSH).

| Resumen |

Introducción. Toda cirugía implica riesgo de complicaciones; el pronóstico depende de su pronto diagnóstico y manejo oportuno.

Objetivo. Determinar la prevalencia de complicaciones quirúrgicas en cirugía ginecológica en un hospital de alta complejidad y explorar factores asociados.

Materiales y métodos. Estudio de prevalencia con análisis secundario en el que se incluyeron historias de pacientes sometidas a cirugía ginecológica programada. La variable resultado fue la complicación reportada durante un periodo <30 días. Se tomó el universo y se recolectaron variables clínicas, biológicas y sociodemográficas. Para determinar la prevalencia se tomó como numerador el total de complicaciones y como denominador el total de historias; para explorar los factores asociados se utilizó el Odds Ratio como medida de asociación con un índice de confianza al 95%.

Resultados. Se revisaron 591 historias clínicas y la prevalencia encontrada fue del 3.8% (IC95%: 2.3-5.4). La historia de manejo quirúrgico del ectópico (OR: 16.89; IC95%: 2.41-92.52), la obesidad (OR: 12.47; IC95%: 4.48-33.19) y la cirugía ginecología por malignidad (OR: 3.73; IC95%: 1.14-10.48) se asociaron con complicaciones.

Conclusión: La prevalencia encontrada fue similar a la de la mayor parte de los estudios consultados.

Palabras clave: Prevalencia; Cirugía; Ginecología (DeCS).

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Introduction

The gynecological surgery service is responsible for surgical procedures in the female genital tract. It also treats breasts and pelvis and carries out procedures related to the uterus, its appendages and correction of urinary incontinence. (1) The most common gynecological procedure is hysterectomy, with an incidence in the USA of 510 per 100 000 inhabitants reported in 2004, in Denmark of 173 per 100 000 inhabitants in 2011 (2), and in Brazil of about 300 000 per year. (3) Other gynecological procedures include tubal ligation, curettage, cystectomy and salpingectomy. (1,4)

All surgical procedures may have complications; indications of unsafe care derived from medical care include complications, adverse events and incidents. A complication is any undesirable and involuntary outcome derived from the surgery that affects the patient, which would not have occurred if the surgery had been performed following the corresponding procedures. (5-7) An adverse event is an injury or unintentional damage caused by the intervention and not by the pathology. (5-7) Finally, an incident is defined as an event or circumstance that could have caused or caused unnecessary harm and may originate from unintentional or involuntary acts. (5-7) Surgical complications are considered a relevant issue from a clinical, legal and public health point of view due to the cost they generate to the health system.

Expenses related to health care have been increasing around the world. In 2007, the total hospital care expenditure in the USA was estimated at 696.5 million dollars, which corresponds to 31% of total health cost. In 2013, these costs in Switzerland were 69 million dollars, of which 28% were allocated to surgical departments. This situation is similar in most European countries. (8,9)

Surgical complications are, in part, responsible for this increase. The average hospital cost for all patients without complications is USD 27 496, but when there is at least one surgical complication of any severity, the amount increases to USD 62 392. (10) The cost of complications depends on their classification. Volanthen *et al.* (10) report that, according to the Clavien-Dindo classification —the most widely accepted—, a grade I complication generates a cost of USD 2 793 and a grade IV, a cost of above USD 130 000. Complications classified as grade IIIb or higher lead to a significant increase in care costs compared to procedures without post-operative complications. (10)

The prevalence of surgical complications in gynecological surgery varies depending on the population. After reviewing 22 214 gynecological procedures, the American College of Surgeons found 3.7% complications (11); Brazil reports a higher percentage with 8.9% (1), while Colombia reports 12.5%. (4) Many studies focus on the rate of complications related to hysterectomy because it is the most frequent gynecological surgical procedure.

In 5 279 procedures, Brummer *et al.* (12) reported a higher complication rate related to laparoscopic, abdominal and vaginal hysterectomy of 4.3%, 4.0% and 2.3%, respectively, and an overall complication rate of 15.4%, 19.2% and 11.7%, respectively. In turn, McPherson *et al.* (13) reported a frequency of severe complications of 3% in 37 512 women. However, the results of research on surgical complications vary widely and depend on the type of route used; thus, regarding laparoscopic hysterectomy, other investigations report global complication rates ranging between 0.2% and 10.3%. (14) These non-homogeneous reports were corroborated in another study. (15)

In a series of 3 190 women undergoing hysterectomy through different routes, Donnez *et al.* (15) reported a prevalence of complications for laparoscopic subtotal hysterectomy of 1.36% (CI95%: 0-3.15) and for total hysterectomy of 1.59% (CI95%: 0.01-3.1), which was statistically similar to the values of vaginal and abdominal procedures found in this research with 1.10% (CI95%: 0.013-1.2) and 1.22% (CI95%: 0.16-2.3), respectively.

Sociodemographic conditions, comorbidities, medical history, indications of the procedure, equipment and experience of the surgeon are characteristics that also affect the outcome of the surgery. (11) The risk increases with the complexity of the surgical procedure and the experience of the surgeon, hence the accumulation of surgical experience with the help of preventive maneuvers is useful to significantly reduce the rate of complications. (16)

Martino *et al.* (17) reported that patients undergoing robotic-assisted laparoscopic hysterectomy have a significantly lower probability of re-admission when compared to laparoscopic, abdominal and vaginal hysterectomy; furthermore, the robotic technique has a lower rate of hospital stay and generates less bleeding, as well as cost savings due to re-admission.

Regarding the socioeconomic situation, women with scarce resources and unemployed have a much higher probability of complications after hysterectomy when compared with employed women (OR: 1.20, CI95%: 1.06-1.36), which is similar for women with low educational attainment (OR: 1.18, CI95%: 1.05-1.33). These differences may be explained, in part, by an unhealthy lifestyle and the presence of comorbidities in women of low socioeconomic status. (18,19)

Individual characteristics such as age, comorbidities, functional status and unintentional weight loss are also related to complications. (20) Barbosa & Garnica (4) found diabetes mellitus (OR: 75.5, CI95%: 4.84-117), chronic anticoagulation (OR: 24, CI95%: 2.73-214.59) and myomatosis (OR: 35.1, CI95%: 3.85-298.87) as associated factors. Likewise, Erekson *et al.* (11) reported an age of >80 years (OR: 1.91, CI95%: 1.22-3.00), malignant disease (OR: 2.98, CI95%: 1.77-5.01) and obesity (OR: 1.95, CI95%: 1.57- 2.41) as influential factors for complications.

Some of the complications associated with gynecological surgery are urinary tract injury (0.3-1%), bowel injury (0.4%), ureteral injury (0.25%), fever (0.47%), bleeding (0.06%) and rectal perforation with very low frequencies (0.09%). (4,15) The most common complication is surgical site infections, which occur between 2.2% and 10% (1,4,21,22), followed by transfusion (4%), pelvic abscesses (1.5%), reoperation (2 %) and wound dehiscence (1.5%). (4,22)

The topic of surgical complications is widely studied worldwide, but this is not the case locally; in Colombia, limited research hinders its efficient assessment. Consequently, in addition to its clinical relevance, the costs to the health system and the legal implications of surgical complications, this research was proposed to determine the prevalence of surgical complications of gynecological surgery at the Hospital Universitario San José of Popayán (HUSJ), Colombia, in 2015 and explore possible associated factors.

Materials and methods

This was a cross-sectional study in which the clinical records of patients who undwent gynecological surgery at the Hospital Universitario San José (HUSJ) between January and December 2015 were included.

The HUSJ is an institution that provides tertiary care services, and is a reference center of the department of Cauca, located in southwestern Colombia, which treats population enrolled in the contributory insurance scheme, as well as patients subsidized by the State through the social security system.

All clinical records of patients undergoing scheduled gynecological surgical procedures were included in the research, and patients who presented incomplete data in more than 10% of the variables analyzed, were pregnant or underwent emergency procedures were excluded. Outcome variables include a surgical complication reported within

30 days after the procedure, which was defined as any undesirable, involuntary outcome that results from surgery, affects the patient and would not have occurred if the surgery would have been performed following the established procedures. (5-7)

Complications were obtained from institutional records, both from the outpatient clinic and the emergency department. The presence of a complication was reported according to the program for improvement of institutional quality. The members of this program were in charge of analyzing the possible complications and defined whether the analyzed case was a complication or not. The different types of complications were also considered and were classified according to the literature as major (reoperation, bladder injury, nosocomial urinary infection, transfusion, bleeding, postoperative ileus) or minor (surgical site infections, hematoma, wound hemorrhage and wound dehiscence). (11,15)

It should be noted that the protocols for antibiotic prophylaxis and antithrombotic prophylaxis in all surgical procedures were the same and followed the institutional guidelines. On the other hand, and in compliance with the safe surgery institutional program, at the time of discharge, both the patient and the family were informed in writing about the post-surgical follow-up that must be performed in the institution by external consultation and on warning signs that, if necessary, should lead the patient to visit the emergency gynecology service of the HUSJ. The whole universe of patients was considered for the sample size in the period under study.

Process

Once the institutional ethical approval was obtained through Minutes 6 issued on May 13 2016 by the HUSJ ethics committee, a first filter was applied: searching for all surgical procedures performed in the institutional databases. Then, a second filter allowed identifying all the scheduled gynecological procedures; once this was done, the medical records that met the inclusion criteria were analyzed and the information was collected by means of a semi-structured instrument designed by the researchers, reviewed by experts and adjusted through a pilot test.

Variables

Clinical, biological and sociodemographic variables were collected including age, origin (urban, rural), marital status (stable, not stable), gynecological and obstetric history, presence and type of comorbidities (obesity, diabetes mellitus, smoking, hypothyroidism, adherence syndrome and the remaining were classified as other) (11,15), type of surgical procedure and indication thereof, surgical time (> or <3 hours), surgical route (laparoscopic, abdominal or vaginal) and type of pathology (malignant or benign).

Statistical analysis

To determine the prevalence of surgical complications, the total number of surgical complications found in women undergoing gynecological surgical procedures was taken as the numerator, and the total number of records reviewed as the denominator. The variables were analyzed individually and from an exploratory point of view to verify the normality of their distribution and identify extreme and lost values that could affect the result. Student's t-test was used for continuous variables with normal distribution, after analyzing the variance, and Mann-Whitney U for non-normal distribution variables, following the Shapiro–Wilk normality test and chi-square or Fisher's, as appropriate. To explore the factors possibly associated with surgical complications, a bivariate analysis was performed, where the OR with its respective CI95% was used as a measure of association between the different variables, thus generating a contingency table. Records with complications reports were taken as a case and those that do not have this report as controls. For this analysis, age was categorized in ≤39 years (reference category), from 40 to 49, and ≥50 years. The study was endorsed by the HUSJ Ethics Committee (approval act number 6) and the analysis was carried out using the Stata 10.0 program.

Results

During 2015, 593 scheduled gynecological surgical procedures were performed in the HUSJ, of which two were excluded due to incomplete data, so 591 were included in the final analysis. The average age of the population under study was 39.99 years with a standard deviation of 12.17 years; 72.25% came from urban areas, 81.05% had at least one birth, 43.49% had a cesarean section and 1.35% had a history of surgical management due to ectopic pregnancy.

Regarding comorbidities, 58% presented at least one of them, the most frequent being adherent syndrome (33.6%), obesity and high blood pressure (17.4%). The most frequent surgical procedure was Pomeroy tubal ligation (29.10%), followed by hysterectomy (22.34%) and curettage (15.74%). Regarding the indication of the procedure, having enough children was the most frequent (29.10%), followed by abnormal uterine bleeding (13.37%), complex adnexal mass (12.86%) and myomatosis (10.83%). 98.31% of the surgical procedures lasted less than 3 hours. The most used surgical route was the abdominal with 53.81%, followed by vaginal and laparoscopic with 28.60 and 17.60, respectively. Benign pathology was the most frequent (90.69%) (Tables 1, 2 and 3).

Table 1. General characteristics of the study population with gynecological surgery complications at the Hospital Universitario San José of Popayán, Colombia. 2015.

Variable		n=591 (%)
Age-years	Average (SD)	39.99 (12.17)
	≤39	294 (49.75)
	40-49	177 (29.95)
	>50	120 (20.30)
Marital status	Stable	234 (43.49)
	Unstable	257 (56.51)
Origin	Urban	427 (72.25)
	Rural	164 (27.75)
Gravidity	Nulliparous	112 (18.95)
	Not nulliparous	479 (81.05)
Births	No deliveries	250 (42.30)
	At least one birth	341 (57.70)
Abortions	No	488 (82.57)
	Yes	103 (17.43)
Caesarean sections	No	334 (56.51)
	Yes	257 (43.49)
Ectopic pregnancies	No	583 (98.65)
	Yes	8 (1.35)

SD: standard deviation.
Source: Own elaboration.

Table 2. Comorbidities, surgical time and type of pathology found in the Hospital Universitario San José of Popayán, Colombia. 2015.

Variable		n=591 (%)
Comorbidities	No	344 (58.21)
	Yes	247 (41.79)
Type of comorbidity	Adhesion	83 (33.60)
	Obesity	43 (17.41)
	Arterial hypertension	43 (17.41)
	Smoker	11 (4.45)
	Hypothyroidism	14 (5.67)
	Diabetes	9 (3.64)
	Other	44 (17.82)
Time	<3 hours	581 (98.31)
	>3 hours	10 (1.69)
Pathology	Benign	536 (90.69)
	Malignant	55 (9.31)

Source: Own elaboration.

Table 3. Type, indication and route of the procedure conducted at the Hospital Universitario San José of Popayán, Colombia. 2015.

Variable		n=591 (%)
Type of surgery	Pomeroy	172 (29.10)
	Hysterectomy	132 (22.34)
	Curettage	93 (15.74)
	Cystectomy	54 (9.14)
	Other	140 (23.68)
Indication for the procedure	Satisfied parity	172 (29.10)
	AUB	79 (13.37)
	Complex adnexal mass	76 (12.86)
	Myomatosis	64 (10.83)
	Endometrial thickening	48 (8.12)
	Other	152 (25.72)
Route of surgery	Abdominal	318 (53.81)
	Vaginal	169 (28.60)
	Laparoscopic	104 (17.60)

AUB: abnormal uterine bleeding.
Source: Own elaboration.

With respect to the main objective, it was found that the prevalence of complications was 3.8% (95% CI: 2.3-5.4); after classifying them, major complications pralence was 1.8% (CI95%: 0.76-2.9), while for minor complications it was 2% (CI95%: 0.8-3.1). Major complications included reoperation (0.51%), bladder injury (0.34%) and nosocomial urinary tract infection (0.34%), while minor complications were infection of the operative site (1.52%), hematoma (0.17%), wound hemorrhage (0.17) and wound dehiscence (0.17%) (Table 4). It should be noted that there were no deaths during the period studied.

Table 4. Type of gynecological surgery complications in the Hospital Universitario San José of Popayán, Colombia. 2015.

Variable	n=591 (%)
Overall complications	3.8 (2.3-5.4)
Major complications (CI95%)	1.8 (0.76-2.9)
Reoperation	3 (0.51)
Bladder injury	2 (0.34)
Nosocomial urinary infection	2 (0.34)
Blood transfusion	2 (0.34)
Hematoma	1 (0.17)
Post-operative ileus	1 (0.17)
Minor complications (CI95%)	2.0 (0.8-3.1)
Operative site infection	9 (1.52)
Hematoma	1 (0.17)
Wound bleeding	1 (0.17)
Wound dehiscence	1 (0.17)

Source: Own elaboration.

The bivariate analysis showed that having a history of surgical management of ectopic pregnancy was positively associated with complications (OR: 16.89, CI95%: 2.41-92.52); the same happened with having at least one comorbidity (OR: 3.33, CI95%: 1.27-9.72), of which only obesity had statistical significance (OR: 12.47, CI95%: 4.48-33.19). It was also found that malignant pathology was positively associated with complications (OR: 3.73, CI95%: 1.14-10.48), but with respect to surgery routes, no statistical significance was found for laparoscopic route (OR: 1.18, CI95%: 0.32-3.65) and vaginal route (OR: 0.71, CI95%: 0.19-2.18). The other variables analyzed did not show statistical significance (Table 5).

Tabla 5. Explanatory variables of gynecological surgery complications in the Hospital Universitario San José of Popayán, Colombia. 2015.

Variable		No complications n=568 (96.11%)	Complications n=23 (3.89%)	OR	CI95 %	P
Age-years	≤39	284 (50.00)	10 (43.48)	Ref.		
	40-49	169 (29.75)	8 (34.78)	1.34	0.41-3.86	0.38
	>50	115 (20.25)	5 (21.74)	1.23	0.32-4.07	0.14
Marital status	Stable	325 (57.22)	9 (39.13)	Ref.		
	Unstable	243 (42.78)	14 (60.87)	2.08	0.82-5.53	0.08
Origin	Urban	409 (72.01)	18 (78.26)	Ref.		
	Rural	159 (27.99)	5 (21.74)	0.71	0.20-2.04	0.51
Gravidity	Nulliparous	109 (19.19)	3 (13.04)	Ref.		
	Not nulliparous	459 (80.81)	20 (86.96)	1.58	0.45-8.46	0.54
Births	No deliveries	238 (41.90)	12 (52.12)	Ref.		0.32
	At least one birth	330 (58.10)	11 (47.83)	0.66	0.25-1.66	
Abortions	No	466 (82.04)	22 (95.65)	Ref.		
	Yes	102 (17.96)	1 (4.35)	0.2	0.00-1.31	0.09
Caesarean sections	No	322 (56.69)	12 (52.17)	Ref.		
	Yes	246 (43.31)	11 (47.83)	1.19	0.47-3.02	0.66
Ectopic pregnancies	No	563 (99.12)	20 (86.96)	Ref.		
	Yes	5 (0.88)	3 (13.04)	16.89	2.41-92.52	0.00
Comorbidities	No	337 (59.33)	7 (30.43)	Ref.		
	Yes	231 (40.67)	16 (69.57)	3.33	1.27-9.72	0.00
Adherence syndrome	No	486 (85.56)	22 (92.65)	Ref.		
	Yes	82 (14.44)	1(4.35)	0.26	0.00-1.71	0.17
Obesity	No	535 (94.19)	13 (56.52)	Ref.		
	Yes	33 (5.81)	10 (43.48)	12.47	4.48-33.19	0.00
Arterial hypertension	No	526 (92.61)	22 (95.65)	Ref.		
	Yes	42 (7.39)	1 (4.35)	0.56	0.01-3.70	0.58
Hypothyroidism	No	556 (97.89)	21 (91.30)	Ref.		
	Yes	12 (2.11)	2 (8.70)	4.41	0.44-21.74	0.05
Diabetes	No	559 (98.42)	23 (100)	Ref.		
	Yes	9 (1.58)	0 (0.00)	NA	NA	NA
Smoker	No	557 (98.06)	23 (100)	Ref.		
	Yes	11 (1.94)	0 (0.00)	NA	NA	NA
Time	<3 hours	560 (98.59)	21 (91.30)	Ref.		
	>3 hours	8 (1.41)	2 (8.70)	6.66	0.64-36-14	0.05
Surgical route	Abdominal	305 (53.70)	13 (56.52)	Ref.		
	Laparoscopic	99 (17.43)	5 (21.74)	1.18	0.32-3.65	0.75
	Vaginal	164 (28.87)	5 (21.74)	0.71	0.19-2.18	0.52
Type of pathology	Benign	519 (91.37)	17 (73.91)	Ref.		
	Malignant	49 (8.63)	6 (26.09)	3.73	1.14-10.48	0.00

OR: Odds ratio; 95% CI: 95% confidence interval; Ref.: reference; NA: not applicable; AUB: abnormal uterine bleeding.
Source: Own elaboration.

Discussion

The final analysis was carried out in 591 clinical records, finding a general complications prevalence of 3.8%, a figure that coincides with that described by Erekson *et al.* (11), who report 3.7%, but which contrasts with the figures of Coelho *et al.* (1) and Barbosa & Garnica (4), who report 12.5% and 8.9%, respectively. This figure also differs from Putz *et al.* (9), who report 2.8% for laparoscopy. These differences can be explained by the fact that only scheduled surgeries were considered in this study, and it was assumed that the patients would be in better shape, which does not happen with patients undergoing an emergency procedure, as they have greater probability of complications. Another explanation for this difference in prevalence could be that the most frequent type of procedure found in this study, which is Pomeroy tubal ligation (29.10%), is less complex and therefore less likely to lead to complications. (16)

Regarding the major and minor complication classification, a 1.8% and 2% prevalence, respectively, was found for each case, which differs from the figures reported by Barbosa & Garnica (4), where the values were 7.5% and 12%, respectively. Regarding the type of complications, bladder injury was one of the most studied due to its frequency, anatomical relationship and clinical relevance.

It is estimated that injuries in the genitourinary tract (bladder and ureter) occur between 1-2% of all major gynecological surgeries (23). The present study found a frequency of 0.34%, which agrees with Lee *et al.* (24), who report 0.28%; slightly higher figures are reported by Valle *et al.* (25) with 0.5%, and Teeluckdharry *et al.* (26) with 0.8-1%. Likewise, Vakili *et al.* (27) and Ibeanu *et al.* (28) report a frequency of 3.6% and 2.9%, respectively, for this same type of injury in patients undergoing hysterectomy, figures higher than those found here and that could be explained due to the fact that hysterectomy represented 22.34% of the total procedures included in this study and because this is a more complex procedure, and therefore it has a higher risk of complications.

The most frequent major complication was reoperation (0.51%), but this figure is still lower than that reported by Barbosa & Garnica (2%) (4) and by Valle *et al.* (1.3-1.6%). (25) With regard to minor complications, surgical site infection was the most frequent with 1.52%; Coelho *et al.* (1) and Barbosa & Garnica (4) also report this complication as the most frequent, but with figures higher than those described here: 4.5% and 2.2%, respectively. (1,4)

Regarding possible associated factors, no significance was found in the socioeconomic stratum, unlike Daugbjerg *et al.* (19), who reported that this factor was significant (OR: 1.20, CI95%: 1.06-1.36). With regard to obstetric history, a relationship was found between surgical complications and history of ectopic pregnancy with surgical management (OR: 16.89), but no studies were found for this specific variable; however, taking into account that this is an abdominal surgical procedure, the studies by Barbosa & Garnica (4) and Brummer *et al.* (12) did not find any difference with respect to a history of previous abdominal surgery.

Unlike Brummer's study, which reports that bladder injury was associated with cesarean section history (OR: 4.01, CI95%: 2.06-7.83) (12), this research did not find any association. In relation to individual characteristics, it was found that the presence of at least one comorbidity (OR: 3.33) was associated with complications. Specifically, in the present study, obesity had an OR: 12.47 for a body mass index (BMI) >30kg/m^2; for this same BMI, Erekson *et al.* (11) reported an OR: 1.77 (CI95%: 1.45-2.17), which is lower but significant. On the other hand, Olsen *et al.* (29) reported an OR: 3.0 (CI95%: 1.0-9.6) for BMI=30-35 kg/m^2 and an OR: 5.7 (CI95%: 2.1-15.6) for BMI >35 kg/m^2. (29) Unlike other studies, other comorbidities were not significant. (4,11)

In relation to malignant disease, a significant association was found, coinciding with Erekson *et al.* (11) for gynecological cancer (OR: 1.60, CI95%: 1.27-2.0) and for dissemination (OR 2.57; CI95%: 1.64-4.03). (11) Age and surgical time reported in this study were not significant, but Brummer *et al.* (12) found a negative association for women >55 years who underwent vaginal hysterectomies (OR: 0.45; CI95%: 0.30-0.68), while Erekson *et al.* (11) reported an OR: 1.8 (CI95%: 1.25-2.58) for women >80 years. In this study, surgical time was associated with complications, contrary to Erekson *et al.* (11) (OR: 2.91; CI95%: 2.18-3.89). No statistical difference was found regarding the route used for surgery, contrary to the study by McPherson *et al.* (13), where laparoscopic surgery presented an OR: 1.9 (CI95%: 1.5-2.5) when compared with abdominal surgery.

The strengths of this research include a good sample size, little loss of data and a definition of standardized complication provided by a multidisciplinary team of the program for improvement of institutional quality. In addition, the institutional guidelines for antibiotic prophylaxis and thrombosis prophylaxis were met. There is also a low probability of underreporting, since complications were extracted from institutional records of both external consultation and emergency services, a process that was facilitated by compliance with the patient follow-up program. One of the weaknesses of this study is that it did not consider the history of previous abdominal surgery —hence this variable could not be analyzed—, as well as time of discharge, days of re-admission and type of anesthesia. Another possible weakness is that surgeries such as tubal ligation or curettage have a lower risk of complications than surgeries such as abdominal or vaginal hysterectomy; this may generate a lower overall prevalence, although the objective of the present study was to determine the prevalence of surgical complications related to gynecological surgery.

Conclusions

A low prevalence of complications was found, which is similar to the results reported in most studies. Some of the possible associated factors include history of surgical management of ectopic pregnancy, obesity and gynecological surgery due to malignant pathology. New studies regarding this topic are suggested to find out the actual situation of these procedures and their associated factors and, in the same way, expose care costs according to the type of classification of the complication.

Conflicts of interest

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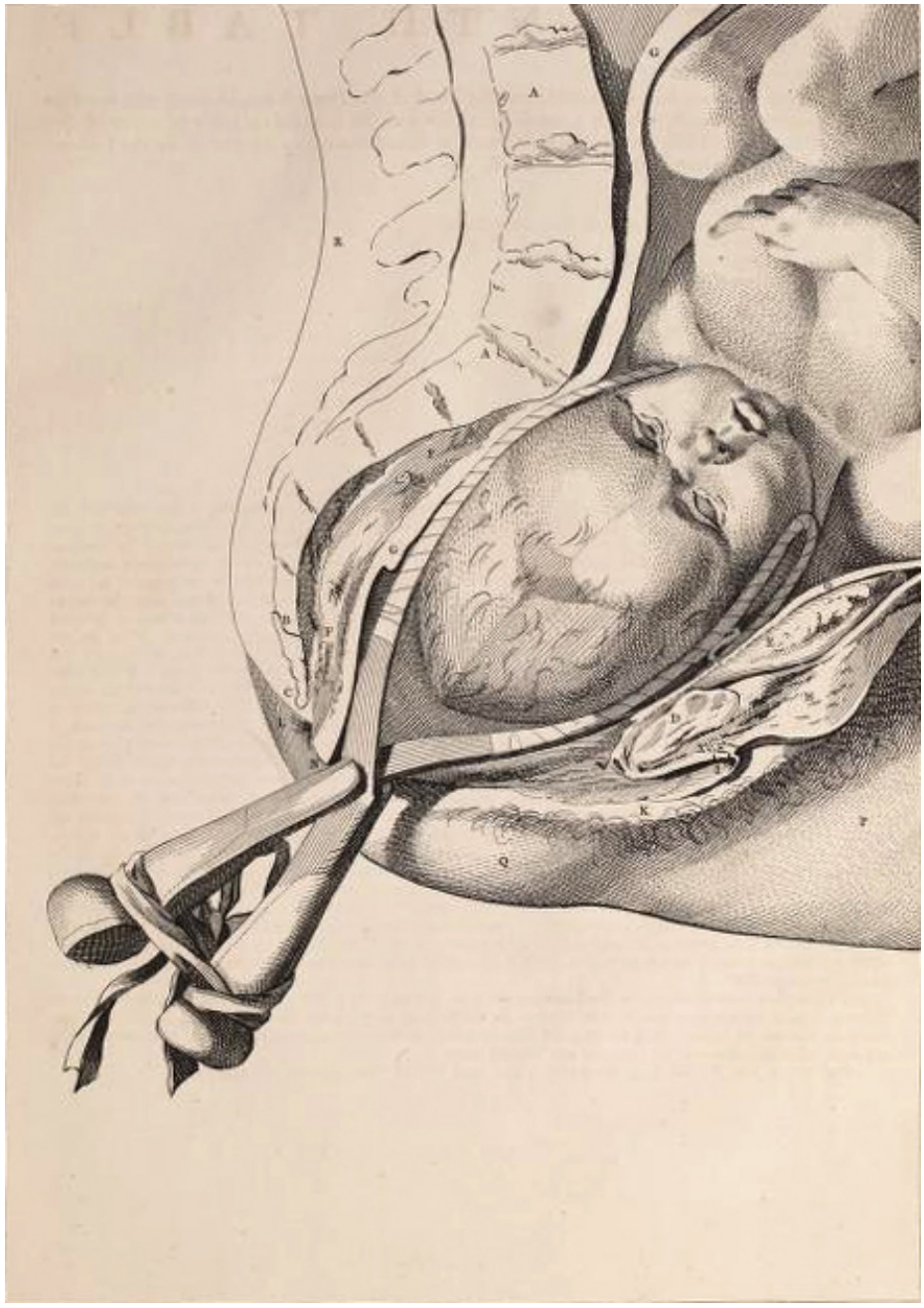

William Smellie, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

ORIGINAL RESEARCH

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Physical activity, eating habits and tobacco and alcohol use in students of a Catalan university

Actividad física, hábitos alimenticios y consumo de tabaco y alcohol en estudiantes de una universidad catalana

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| Abstract |

Introduction: University populations are considered as vulnerable groups when it comes to acquiring health habits.

Objective: The aim of this study is to know the levels of physical activity and health habits of the students of the University of Lleida.

Methods: Healthy habits and the practice of physical activity in university students were evaluated through the Global Physical Activity Questionnaire (GPAQ).

Results: 600 students from the University of Lleida participated during the period 2014-2015. 30.7% of them smoked, while 96.7% reported alcohol consupmtion, and 75.5% practiced physical activity. More than 62% of male students practiced physical activity between 3 and 7 days a week compared to 33.5% of women (p=0.000). More than 30% of the students ingested fruit every day and 65% did so at least 4 days a week. 19.4% of women and 7.9% of men consumed fruit daily, finding significant differences (p=0.001).

Conclusions: 30% of the participant did not meet the minimum recommendations of physical activity. A high percentage of participants have a low fruits and vegetables consumption and a high prevalence of risk of alcohol consumption. An educational intervention by universities is suggested to encourage the practice of healthy habits in students.

Keywords: Physical Activity; Tobacco; Feeding Behavior; Students; Alcoholism (MeSH).

| Resumen |

Introducción. La población universitaria se considera un colectivo vulnerable a la hora de adquirir hábitos de salud.

Objetivo. Conocer los niveles de actividad física y los hábitos de salud de los estudiantes de la Universidad de Lleida.

Materiales y métodos. Se valoraron los hábitos saludables y la práctica de actividad física en estudiantes universitarios mediante el cuestionario Global Physical Activity Questionnarie.

Resultados. Participaron 600 estudiantes de la Universidad de Lleida durante el periodo 2014-2015; 30.7% fumaba, 96.7% consumía alcohol y 75.5% practicaba actividad física. Más del 62% de los hombres practicaban actividad física entre 3 y 7 días a la semana frente al 33.5% de las mujeres (p=0.000). Más del 30% de estudiantes ingirió fruta cada día y 65% lo hizo al menos 4 días a la semana; en específico, 19.4% de las mujeres y 7.9% de hombres consumía fruta a diario, encontrándose diferencias significativas (p=0.001).

Conclusiones. El 30% de los estudiantes no cumple con las recomendaciones mínimas de actividad física. Un alto porcentaje de los participantes tiene escaso consumo de frutas y verduras y presenta elevada prevalencia de consumo de riesgo de alcohol. Se sugiere una intervención educativa en estudiantes y por parte de las universidades respecto a la práctica de hábitos saludables.

Palabras clave: Actividad física; Tabaquismo; Conducta alimentaria; Estudiantes; Alcoholismo (DeCS).

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Introducción

The promotion of healthy habits, particularly those related to physical activity (PA) and eating, is one of the primary work functions of health and education professionals. (1)

University students are a vulnerable group in terms of the influence of current lifestyles according to trends, usually characterized by health-risk behaviors. These behaviors include diets saturated in fat that lead to high cholesterol levels, low consumption of fruits and vegetables (2) and high levels of tobacco and (3) alcohol use (4) and sedentary lifestyle. (5) Therefore, universities are a strategic place to promote, on the one hand, patterns of behavior that favor health and, on the other, effective ways that lead to increased participation in healthy habits. (6)

It is of great interest for public health to know the evolution and trends of the university population, especially regarding sedentary lifestyles and healthy habits. (7) This allows establishing strategies to prevent and promote health, particularly among social groups that are consolidating their lifestyles and whose future behavior should be a model to imitate. (5) In Catalonia, Spain, the Secretaria General de l'Esport (General Secretary of Sports) promotes the University Sports of Catalonia Strategic Plan 2013-2020 (PEUC), which shows the need to analyze the current situation in the different Catalan universities to establish specific action plans in each institution to promote physical activity.

Several studies have attempted to determine proper levels of physical activity and health in university students to establish prevention and health promotion strategies. (8-11) With the aim of developing education and intervention actions aimed at introducing possible modifications in the behavior of university students, it is essential to determine which habits are predominant. To obtain this type of information, questionnaires are usually used (12), including the Global Physical Activity Questionnaire (GPAQ) — recommended by the World Health Organization —, which was elaborated to study PA and eating habits, and has acceptable levels of reliability and validity. (13,14)

The objectives of this study were to know the levels of physical activity and health habits — feeding and consumption of tobacco and alcohol— of the students of the University of Lleida (UDL) and to identify inappropriate behaviors related to healthy habits.

Materials and methods

This is a cross-sectional, observational and descriptive study on eating habits and behaviors related to physical activity in students of the UDL enrolled during the period 2014-2015.

Participants

A non-probabilistic sample was taken for convenience, stratified by sex and studies completed, and representative of the UDL students, which implies a confidence level of 95% and a maximum sampling error of ±5%. The population consisted of 290 men (48.3%) and 310 women (51.7%), with an average age of 21.69 years [standard deviation (SD): 4.61]. Trained surveyors applied 600 questionnaires using a face to face modality and convenience with respect to the places, days and times of greatest transit of students within the university.

Measurements

To estimate PA, the Spanish version of the GPAQ was used (15), which consists of a series of questions grouped into domains: work, transport, recreation, tobacco consumption, alcohol consumption and diet. The questions about work and recreation inquired about the frequency and duration of different types of PA according to their intensity. Regarding diet, questions sought to find about the intake of fruits and vegetables, frequency of consumption, etc.

Participants provided their informed consent in writing and the study was evaluated and approved by the Ethics and Good Practices Committee of the UDL on April 10, 2014.

Statistical analysis

The statistical program SPSS Statistics version 20.0 was used for analysis. The exact chi-square test was applied to evaluate the differences in PA according to sex and alcohol and tobacco use, while the Student's t-test was used to evaluate the differences in the time of practice of PA according to sex and free time.

Results

The research involved 600 subjects, 290 (48.3%) men and 310 (51.7%) women, with an average age of 21.6 years (SD: 4.61).

When examining the variables tobacco use, alcohol consumption and PA (Figure 1), it was found that 30.7% of students smoked and 96.7% reported alcohol consupmtion. When distributing the sample by sex, tobacco use was higher in women than in men (34.8% vs. 26.2%, p=0.027). Regarding alcohol consumption, a very similar percentage was found in men and women (96.9% vs. 96.5%, p=0.623). The question about whether students travel by foot or bicycle for at least consecutive 10 minutes showed that 73.8% of the sample did so, with a higher percentage observed in women (78% vs. 69.3%; p=0.019).

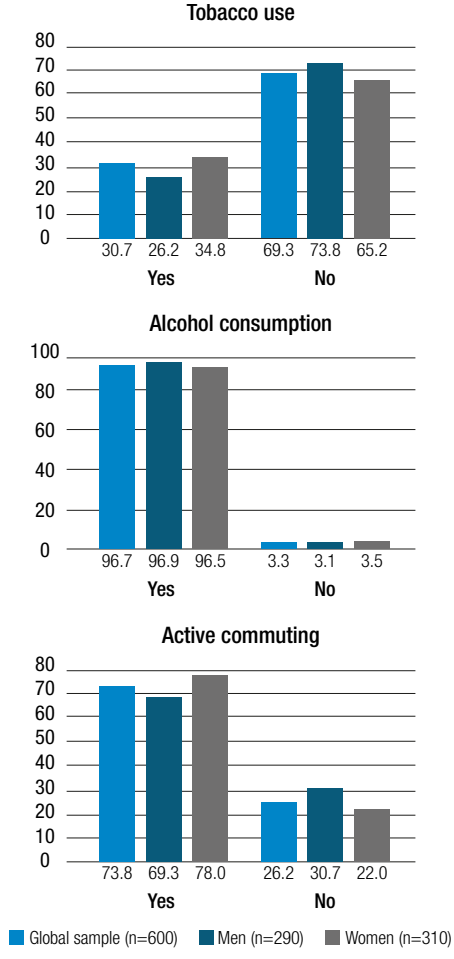

Figure 1. Descriptions of health habits.
Source: Own elaboration.

Table 1 shows that most university students practiced vigorous (66.2%) or moderate (63.5%) PA. With respect to the number of days they practiced vigorous PA, 62% of men and 33.5% of women did it between 3 and 7 days a week. For moderate PA, 54% of men and 33% of women practiced it between 3 and 7 days per week. In both cases, significant differences were found (p=0.000).

Table 2 shows the time, expressed in minutes, that students spent on PA; for the most part, the practices were over 60 minutes.

Table 3 shows that more than 30% of respondents ingested fruit every day and more than 65% did so at least 4 days a week. When analyzing daily vegetable consumption, it was found that women ingested more than men (19.4% vs. 7.9%; p=0.001).

Table 1. Descriptive index of physical activity practices.

Frequency	Vigorous						Moderate					
	Global sample		Men		Women		Global sample		Men		Women	
	f	%	*f*	%	*f*	%	*f*	%	*f*	%	*f*	%
Every day	22	3.7	11	3.8	11	3.5	36	6.0	16	5.5	20	6.5
5-6 days per week	78	13.0	54	18.6	24	7.7	81	13.5	55	19.0	26	8.4
3-4 days per week	184	30.7	115	39.7	69	22.3	143	23.8	87	30.0	56	18.1
1-2 days per week	113	18.8	41	14.1	72	23.2	121	20.2	45	15.5	76	24.5
No	203	33.8	69	23.8	134	43.2	219	36.5	87	30.0	132	42.6
Total	600	100	290	100	310	100	600	100	290	100	310	100

f: frequency.
Source: Own elaboration.

Table 2. Time spent doing physical activity.

Duration	Vigorous						Moderate					
	Global sample		Men		Women		Global sample		Men		Women	
	f	%	*f*	%	*f*	%	*f*	%	*f*	%	*f*	%
<60 min	148	24.7	74	25.5	74	23.8	160	26.6	73	25.2	87	28.1
61-100 min	108	18.0	66	22.8	42	13.5	55	9.2	38	13.1	17	5.5
>100 min	139	23.2	81	27.9	58	18.7	140	23.3	75	25.9	65	21.0
0 min	205	34.2	69	23.8	136	43.9	245	40.8	104	35.9	141	45.5
Total	600	100	290	100	310	100	600	100	290	100	310	100

f: frequency.
Source: Own elaboration.

Table 3. Description of eating habits.

Variable		Fruits						Vegetables					
		Global sample		Men		Women		Global sample		Men		Women	
		f	%	*f*	%	*f*	%	*f*	%	*f*	%	*f*	%
Daily consumption	0 days	24	4.0	11	3.8	13	4.2	17	2.8	10	3.4	7	2.3
	1 day	27	4.5	12	4.1	15	4.8	51	8.5	29	10.0	22	7.1
	2 days	52	8.7	22	7.6	30	9.7	125	20.8	72	24.8	53	17.1
	3 days	77	12.8	42	14.5	35	11.3	121	20.2	59	20.3	62	20.0
	4 days	76	12.7	33	11.4	43	13.9	94	15.7	50	17.2	44	14.2
	5 days	88	14.7	47	16.2	41	13.2	66	11.0	26	9.0	40	12.9
	6 days	50	8.3	23	7.9	27	8.7	34	5.7	15	5.2	19	6.1
	7 days	197	32.8	93	32.1	104	33.5	83	13.8	23	7.9	60	19.4
	DK/DA	9	1.5	7	2.4	2	0.6	9	1.5	6	2.1	3	1.0
	Total	600	100	290	100	310	100	600	100	290	100	310	100
Number of servings per day	0 servings	20	3.3	9	3.1	11	3.5	13	2.2	9	3.1	4	1.3
	1 serving	261	43.5	130	44.8	131	42.3	399	66.5	204	70.3	195	62.9
	2 servings	226	37.7	106	36.6	120	38.7	122	20.3	55	19.0	67	21.6
	3 servings	55	9.2	22	7.6	33	10.6	27	4.5	8	2.8	19	6.1
	4 servings	13	2.2	7	2.4	6	1.9	12	2.0	2	0.7	10	3.2
	> 4 servings	8	1.3	5	1.7	3	1.0	4	0.7	0	0.0	4	1.3
	DK/DA	17	2.8	11	3.8	6	1.9	23	3.8	12	4.1	11	3.5
	Total	600	100	290	100	310	100	600	100	290	100	310	100

f: frequency; DK/DA: do not know/do not answer.
Source: Own elaboration.

Discussion

Most students drink alcohol at least once a month, without significant differences between men and women. While it is true that few students do it between 1 and 2 days per week, this figure is higher than that found by other authors (16), who also reported higher alcohol consumption in men than in women. The results of this research are above those found by Castañeda-Vázquez & Romero-Granados (17), since more than one third of the population studied use alcohol on weekends and more than 40% do so occasionally. One of the main problems of university students is binge drinking, which has been described by several authors. (18,19)

In turn, tobacco is also used by one third of the students, a figure similar to that reported by Castillo-Viera & Sáenz-López (20) in students of the University of Huelva, although tobacco consumption in this age group is studied in a very superficial way. (3) In addition, prevention campaigns in this type of population are difficult and insufficient, so it is important to continue conducting research on lines of action and their effectiveness for controlling smoking at the youngest possible age.

Regarding transport, most of the students in this study move actively, whether by walking or cycling or any other means of transport. Comparing sexes, women show higher rates of active commuting than men, and they do it more frequently. There is evidence that active commuting to the educational center (school, institute, university, etc.) is an opportunity to increase PA levels in young people and prevent or mitigate the increase of body weight. (21-24) One of the main reasons found in this study for high mobility in bicycles is the orographic characteristics of Lleida, which is a small city without significant slopes, so it is not necessary to travel long distances to get anywhere. In consequence, some authors have considered developing strategies based on socio-ecological models (25), actions in relation to urban design, transport systems or resources for recreation and green spaces.

According to different studies, adults aged between 18 and 64 years should accumulate a minimum of 150 minutes per week of moderate aerobic PA or 75 minutes per week of vigorous aerobic PA (or the equivalent combination of both). The present study shows that 75% of university students are regularly active and that, of these, a large percentage have a high level of PA, so the majority are regularly active; this coincides with other studies conducted in university populations. (9,11) It was also found that most students who practice PA, do so two or more days a week, so the promotion and awareness campaigns towards the practice of PA should be directed towards a smaller group of students who do not carry out any PA at all.

PA practice had statistically significant differences between sexes. This is a constant pattern, since PA is one of the few health-related behaviors typically more prevalent in men than in women. (6,16,26) In this sense, activities that motivate university students to adhere to the practice of PA should be promoted.

Another variable studied was fruits and vegetables intake in students, but data were not encouraging, since only a third of the students consume fruits on a daily basis and only half do it between 3 and 6 days per week. The consumption of vegetables is much lower, since only 1 in 10 students interviewed here do it daily, being more frequent in women. Following the recommendations of the dietary guidelines for the Spanish population (27,28), which suggest the daily consumption of fruits and vegetables, the students of the UDL are still far below the established figures. (27,28)

These results show a progressive loss of adherence to the Mediterranean diet, characterized by a high consumption of vegetables and a abundant consumption of fresh fruits, as no student consumed these products. (29) The lack of consumption of fruits and vegetables could predict an increase in pathologies derived from poor diet, such as obesity or diabetes. (30,31)

University students are a key population to carry out health promotion and prevention activities, so it is necessary to create strategic education plans that improve the quality of life and promote the acquisition of good eating habits and the performance of PA. Based on the results, the UDL will propose specific strategies for the promotion of healthier lifestyles.

One of the main limitations of this study is that data related to alcohol consumption was self-reported and this means that, although data are reliable, could be biased despite having answered the test anonymously. Socio-economic data that could bias the results were not collected either. However, it is essential to be able to detect risk consumption early in order to modify consumption patterns in a population so vulnerable to its effects. Intervening the university population at risk may provide important benefits, not only in academic terms but in future pathologies derived from the consumption of alcohol and tobacco.

Conclusions

A high percentage of students use alcohol and tobacco regularly. The vast majority of students move actively, especially women. This study shows that a significant amount of university students are regularly active and that, of these, a high percentage has a high level of PA practice. According to the recommendations of different dietary guidelines, students of the UDL are far below in terms of consumption of fruits and vegetables.

Conflicts of interest

None stated by the authors.

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William Smellie, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

ORIGINAL RESEARCH

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Hypoxia-inducible factor HIF-1α modulates drugs resistance in colon cancer cells

Factor inducible por hipoxia HIF-1α modula la resistencia a drogas en células de cáncer de colon

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| Abstract |

Introduction: Drug resistance mechanisms may be associated with decreased cell death and its induction may depend on the response to oxidative stress caused by hypoxia. The correlation between hypoxia-inducible factor HIF-1α, the number of reactive oxygen species and their effect on cell survival has not yet been evaluated.

Objective: The purpose of this study was to evaluate the effect of HIF-1α activity and reactive oxygen species (ROS) accumulation in apoptosis of colon cancer cells.

Materials and methods: HT29 colon cancer cells were treated with Cobalt(II) chloride (CoCl2) or doxorubicin and the activity of HIF-1α was determined by ELISA assay. ROS were determined using fluorescence probe carboxy-H2DFFDA. Apoptosis was assessed by caspase-3 activation analysis, and PUMA and BAX mRNA levels by qRT-PCR. The reduction of the antiapoptotic effect due to hypoxia was attenuated by use of the endonuclease APE-1 (E3330) inhibitor. The endonuclease E3330 APE-1 inhibitor allowed evaluating the effect of ROS generated by doxorubicin and CoCl2 on apoptosis.

Results: Chemical hypoxia in combination with doxorubicin is an oxidative stressor in HT29 cells and induces a reduction in the apoptotic process in a time-dependent manner.

Conclusion: Resistance to hypoxia and doxorubicin-mediated cell death could be controlled by a mechanism related to the activity of HIF-1α and the amount of reactive oxygen species generated.

Keywords: Apoptosis; Cell Hypoxia; Colon Cancer; Doxorubicin (MeSH).

| Resumen |

Introducción. Los mecanismos de resistencia a drogas podrían asociarse con disminución en la muerte celular y su inducción podría depender de la respuesta al estrés oxidativo que origina la hipoxia. La correlación entre factor inducible por hipoxia HIF-1α, cantidad de especies reactivas de oxígeno y su efecto sobre la supervivencia celular aún no ha sido evaluada.

Objetivo. Evaluar el efecto de la inducción de la actividad de HIF-1α y la cantidad de especies reactivas de oxígeno sobre la apoptosis en células de cáncer de colon.

Materiales y métodos. Células de cáncer de colon HT29 fueron tratadas con cloruro de cobalto (CoCl2) o doxorrubicina; la actividad de HIF-1α se evaluó por ELISA. Las especies reactivas de oxígeno fueron determinadas con sonda fluorescente carboxi-H2DFFDA. La apoptosis fue evaluada por la actividad de caspasa-3 y los niveles de mRNA de los genes proapoptóticos PUMA y BAX por qRT-PCR. El inhibidor de la endonucleasa APE-1 E3330 permitió evaluar el efecto de las especies reactivas de oxígeno generadas por doxorubicina y CoCl2 sobre la apoptosis.

Resultados. La hipoxia química combinada + doxorubicina es estresor oxidativo en células HT29 e induce una reducción en el proceso apoptótico de manera tiempo dependiente.

Conclusión. La resistencia a la muerte celular mediada por hipoxia y doxorubicina podría estar controlada por un mecanismo relacionado con la actividad de HIF-1α y la cantidad de especies reactivas de oxígeno generadas.

Palabras clave: Apoptosis; Hipoxia celular; Cáncer del colon; Doxorrubicina (DeCS).

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Introduction

The development of resistance to chemotherapy remains one of the main drawbacks in the treatment of different types of cancer. The results of different studies suggest that reactive oxygen species (ROS) may play an important role in the regulation of drug resistance. (1-3) In addition, some authors have proposed that ROS may also have some effect on the regulation of hypoxia-inducible factor (HIF-1α) activity, which is one of the main transcription factors involved in cell signaling under hypoxic conditions. (4-6) Likewise, high levels of ROS under normoxic condition may increase the activity of HIF-1α; however its effect on hypoxia is still controversial, as some authors suggest that it would favor the degradation of HIF-1α and others point an increase in the expression of the transcription factor induced by the presence of ROS. (7,8)

Some of the mechanisms that explain the role of hypoxia in chemotherapy resistance in cancer include the dependence of many chemotherapeutic agents on the formation of free radicals derived from oxygen and the induction of HIF-1α, as these factors regulate the expression of various genes involved in tumorigenesis. (9) Hypoxia in colon cancer cells shows a decrease in the expression of pro-apoptotic proteins Bid and Bad, and HIF-1α is necessary to regulate Bid. A decrease in cellular apoptosis by chemotherapy has also been reported, suggesting that HIF-1α could be one of the factors involved in the development of hypoxia-induced chemoresistance in cancer cells. (10)

Doxorubicin is an anthracycline used regularly to treat different types of cancer and its mechanism of action involves the induction of ROS. (11) Breast, lung, gastric and ovarian cancer, among others, have shown resistance; however, its use in association with hypoxic effect has not yet been evaluated in colon cancer cells. Said resistance could be explained by a regulatory mechanism of apoptotic effectors. The PUMA pro-apoptotic protein (p53 upregulated modulator of apoptosis) belongs to the pro-apoptotic BH3 protein family. This group includes PUMA, Bid, Bad, Bim and Noxa proteins, which stimulate apoptotic pathways, as do other members of the Bcl-2 family such as Bax and Bak. (12) The expression of PUMA is regulated by the p53 tumor suppressor protein (13), although PUMA is thought to be involved in the p53-dependent/-independent pathways of apoptotic cell death through different signaling pathways and is regulated by a wide arrange of transcription factors. After its activation, the PUMA protein interacts with proteins that lead to Bax and Bak release, causing it to migrate from the cytosol to the mitochondria, and with subsequent induction of caspase activity to drive cell death. (14)

The objective of this study was to identify whether the regulation of PUMA by the combined use of hypoxia or doxorubicin decreases the apoptotic process through the activity of hypoxia-inducible factor HIF-1α and the generation of reactive oxygen species generated by said factors in the HT29 colon cancer cell line.

Materials and methods

Biological systems

The HT29 (ATCC® HTB38™) colorectal adenocarcinoma cell line, established from a primary human colon tumor with epithelial morphology and monolayer growth, was used for this study.

Cell culture

The cells were cultured at 37°C, 21% O_2 and 5% CO_2 in DMEM medium, supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin. Hypoxia conditions were chemically induced using 100 µM cobalt chloride ($CoCl_2$). Cells were treated with 100µM $CoCl_2$ or 5µM doxorubicin. The stimuli were applied for periods of 0, 12 and 24 hours.

Cell viability

Cells were subjected to the abovementioned conditions and the trypan blue exclusion method was used to determine their viability after the treatment. A 1:5 dilution of the cell suspension was prepared in trypan blue solution and mixed by pipetting. An aliquot of the mixture was then taken and placed in a Neubauer chamber to count viable (uncolored) and non-viable (blue-colored) cells, thus calculating the percentage of viable cells.

Determination of reactive oxygen species (ROS)

To determine the effect of different oxidative stress conditions on the cellular production of ROS, the 5(6)-carboxy-2,7-difluorodihydrofluorescein diacetate (H2DFFDA) fluorogenic marker (Invitrogen) was used. (12) The cells were cultivated in 96-well cell culture plates (Corning Costar®) and their growth was allowed for 24 hours, after this time treatments were carried out according to the condition to be studied: chemical hypoxia or doxorubicin. Then, they were rinsed with PBS 1x.

Cells were incubated at 37°C with the probe at a concentration of 10µM for 30 minutes and rinsed with PBS 1x. Subsequently, they were lysed with lysis buffer and 200µL of the cell lysate were transferred to a 96-well box for fluorescence reading at an excitation wavelength of 492nm and emission wavelength of 527nm, performed in the Cytation 3 Cell Imaging Multi-Mode Reader Imagine Reader (BioTek®). The fluorescence results obtained were normalized by microgram (µg) of protein using the bicinchoninic acid assay (BCA) method with the Pierce™ BCA Protein Assay Thermo Scientific Kit for quantification. 25µL of the protein extract or the blank were added to 200µL of working solution (50 parts of reagent and 1 part of reagent B) and incubated for 30 minutes at 37°C in a 96-well plate. The absorbance reading on the Cytation 3 Imagine Reader (BioTek®) was taken at an absorbance of 562nm. Protein concentration was determined using a calibration curve constructed with known concentrations of bovine serum albumin.

Activity of hypoxia-inducible factor HIF-1α

Nuclear proteins were extracted using a nuclear extraction kit (Active Motif) according to the manufacturer's recommendations. The cell suspension was centrifuged at 2 000 rpm at 4°C and the pellet was resuspended by pipetting in hypotonic buffer and transferred to a 1.5mL eppendorf tube, where the vortex suspension was mixed and incubated for 25 minutes on ice. The pellet was resuspended in lysis buffer (supplemented with Ditiotreitol [DTT] at a final concentration of 1mM) and an additional 2.5µL of detergent was added. This suspension was incubated for 30 minutes on a shaker platform at 150 rpm, after which it was centrifuged at 14 000 rpm for 10 minutes.

HIF-1 activity was evaluated from 20µg nuclear extract protein with the TransAM™ HIF-1 Transcription Factor Assay kit. To this end, the 20µg nuclear extract were diluted in lysis buffer (Trans AM™ lysis buffer, with 1mM DTT and protease inhibitor cocktail) up to a volume of 10µL. 40µL of binding buffer (AM4 Buffer and 1mM DTT) and 10µL of nuclear extract were added to wells previously coated with oligonucleotide containing the hypoxia responsive element (HRE).

This mixture was incubated for 1 hour under agitation at 100 rpm. Then three washes were performed with 1x wash buffer and anti-HIF1 antibody (1:500 dilution) was added and incubated for 1 hour in agitation. Incubation was performed with HRP (horseradish peroxidase) secondary antibody conjugate (dilution 1:1000) for 1 hour, after which washes were performed, and the wells were incubated with the dye solution for 10 minutes, then the reaction stopping solution was added. The absorbance reading was made at 450nm with a reference wavelength of 655 nm[160].

Caspase-3 Activity

The caspase-3 fluorimetric determination kit (Invitrogen) was used to evaluate apoptosis under different hypoxic conditions. The cells were incubated briefly at a confluence of 80% according to defined treatment times and untreated cells were used as negative control. Then, the medium was aspirated, the culture box was placed on ice and 200µL of lysis buffer (4-(2-hydroxyethyl)-1-piperazine-ethanesulfonic acid (HEPES) pH 7.4 200 mM, 3-[(3-Colamidopropyl)- dimethylammonium]-propane sulfonate (CHAPS) 25 mM and dithiotreitol (DTT) 25 mM) were incubated with this buffer for 10 minutes.

Subsequently, the adhered cells were scraped off and transferred to an eppendorf tube where they were centrifuged at 13 000 rpm for 15 min at 4°C, after which the supernatant was collected and the protein quantified by the BCA method. 20µg protein was mixed with 2.5µL Ac-DEVD-AMC (Acetyl-Asp-Glu-Val-Asp-7-amido-4-methylcoumarin) substrate in a final concentration of 20µM and assay buffer (HEPES 200 mM, pH 7.4 with 1% CHAPS, 50 mM DTT, 20 mM EDTA) to a final volume of 250µL. From this mixture, 200µL were transferred to a 96-well plate for fluorescence reading (λexcitation: 380nm /λemission: 460nm). Untreated cells were used as negative controls and cells treated with staurosporine (1 ug/ml) for 4 hours as positive controls of apoptosis. The results were expressed as times of change in fluorescence levels per µg of protein with respect to untreated cells.

mRNA expression of pro-apoptotic genes PUMA and BAX by RT-PCR

RNA extraction was performed after the treatments for each condition to be evaluated were completed. For this purpose, 1mL of Trizol® (Life Technologies) was added, removing the cells adhered by resuspension with this agent, and the suspension obtained was transferred to a 1.5mL eppendorf tube free of ribonucleases. 200µL of chloroform were added with inversion agitation and incubation for 3 minutes at room temperature, after which the mixture was centrifuged at 12 000g at 4°C for 15 minutes (Sigma Centrifuge 1-15K). The supernatant (aqueous phase) was transferred to a 1.5mL ribonuclease free eppendorf where RNA precipitation was performed with 500µL of cold isopropanol and incubation for 10 minutes. The mixture was centrifuged at 12 000g for 10 minutes at 4°C; the supernatant was discarded and the pellet was washed with 75% ribonuclease-free ethanol, and then centrifuged at 12 000g for 5 minutes at 4°C.

The supernatant was discarded and the pellet was resuspended in 50µL of molecular biology quality water (95284 Sigma-Aldrich®). RNA was quantified in the NanoDrop 2000 spectrophotometer (ThermoFisher Scientific®) and the 260/280 absorbance ratio was used to analyze the quality of the extracted RNA. Reverse transcriptase (Maxima First Strand cDNA Synthesis Kit for RT-qPCR - Thermo Scientific) was used for the synthesis of cDNA. For each cDNA synthesis reaction, 4µL of 5x reaction mix, 2µL of maxima enzyme mix, 11µL of RNA of 500 ng/µL concentration treated with DNAse I and 3µL of nuclease-free water were mixed to a final volume of 20µL. The mixture was incubated for 10 minutes at 25°C, followed by incubation for 15 minutes at 50°C, ending the reaction at 85°C for 5 minutes.

For the quantitative evaluation of the changes in mRNA levels of the PUMA and BAX genes, the qRT-PCR technique was used. Specific primers were used for each of these genes (Table 1) and the Platinum®SYBR® Green qPCR SuperMix-UDG cocktail was used, which comes in a 2x concentration and contains Platinum® Taq DNA polymerase, SYBR® Green I Tris-HCl dye, KCl, 6 mM MgCl2, 400µM dGTP (deoxyguanosine triphosphate), 400µM dATP (deoxiadenosine triphosphate), 400µM dCTP (deoxycitidine triphosphate), 800µM dUTP (deoxiuridine triphosphate), uracil-DNA glycosylase and stabilizers. For each gene to be evaluated, a reaction mixture was prepared and the specific qRT-PCR program was run in the DNA Engine Opticon® 2 System detection system.

Table 1. Description of specific primers for each of the genes, size and temperature used by the qRT-PCR technique.

Gene	Flow	Sequence 5′-3′	Size pb*	Standardized temperature °C
PUMA	Forward	GACCTCAACGCACAGTACGAG	98 pb	60°C
	Reverse	GACCTCAACGCACAGTACGAG		
BAX	Forward	CCCGAGAGGTCTTTTTCCGAG	155 pb	60°C
	Reverse	CCAGCCCATGATGGTTCTGAT		
B-actina	Forward	GCCAACACAGTGCTGTCT	113 pb	60°C
	Reverse	GGAGCAATGATCTTGATCTT		

Source: Own elaboration.

Inhibition of transcription factor HIF-1α

The effect of APE-1 E3330 endonuclease inhibitor on HIF-1α activity was evaluated. The cells treated with the inhibitor were used to evaluate the amount of ROS and the activity of HIF-1α. The cells were incubated with E3330 (10-30 µmol/L) in the presence or not of $CoCl_2$, previously described for the different study conditions.

Statistical analysis

At least three independent experiments were performed for each trial. The results were analyzed by unidirectional variance analysis (ANOVA). A $p<0.05$ was considered significant. The SPSS program was used for data analysis.

Results

$CoCl_2$-induced hypoxia generates a variation in the number of reactive oxygen species

HT29 cells were treated with $CoCl_2$ for 12 and 24 hours to induce HIF-1α activity. $CoCl_2$ 100uM increased 14 times the activity of HIF-1α at 24 hours compared to the control group (cells under normoxic conditions) with a $p<0.05$ (Figure 1). The combined treatment of $CoCl_2$ with doxorubicin showed that HIF-1α activity does not vary with respect to the control with a $p>0.05$ (Figure 1).

The E3330 inhibitor was used to demonstrate that HIf-1α activity depends on the oxidative stress generated by $CoCl_2$ and doxorubicin; it acts on the APE-1 endonuclease, has a redox regulatory activity and also modulates AP-1 transcription factor activity. (14) Thus, the use of E3330 inhibitor decreased HIF-1α activity modulated by $CoCl_2$ or the use of doxorubicin at around 24 hours compared to control (untreated) cells, $p<0.05$ (Figure 2).

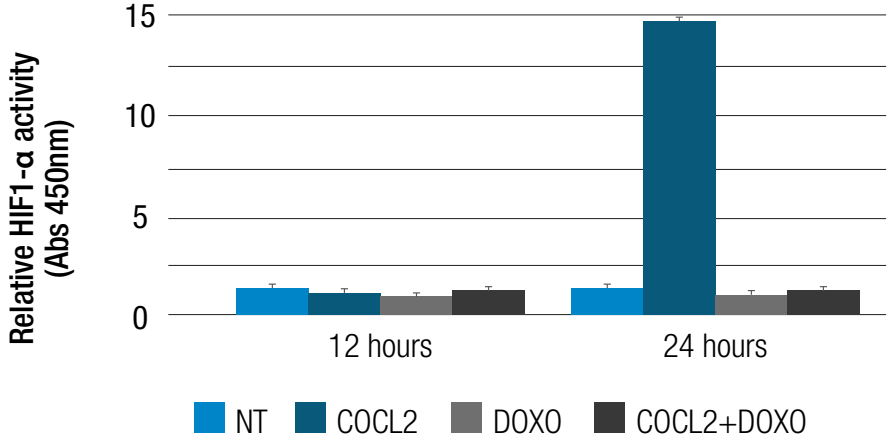

Figure 1. HIF1-α activity. HT29 cells treated with 100μM CoCl2 or 5μM doxorubicin (CoCl2 + Doxo).
Source: Own elaboration.

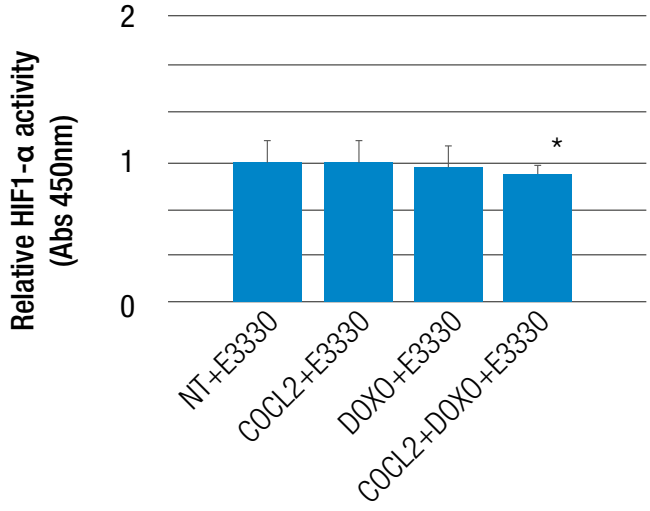

Figure 2. HIF1-α activity. HT29 cells treated with 100μM CoCl2 or 5μM doxorubicin (CoCl2+Doxo) treated with E3330 inhibitor and evaluated with the TransAM HIF-1a kit to determine the activity of HIF1-α.
Source: Own elaboration.

The modulation of oxidative stress could be involved in hypoxia-inducible factor activity

Treatment with $CoCl_2$ and doxorubicin separately generated an increase in reactive oxygen species at 12 and 24 hours. However, it is evident that the treatment with doxorubicin significantly increases the accumulation of reactive oxygen species compared with the control and with the use of $CoCl_2$. Combined treatment of $CoCl_2$ and doxorubicin has shown a significant increase in the amount of ROS and is similar at 12 and 24 hours ($p<0.05$ in both cases; Figure 3). Taking into account the previous result of HIF-1α activity due to the effect of $CoCl_2$ and doxorubicin, it could be said that the accumulation of ROS induced by the stimulation with these two agents may be more dependent on the use of doxorubicin than on HIF-1α activity generated by $CoCl_2$. This result may indicate a regulation of the transcription factor HIF-1α due to the accumulation of ROS generated by the use of $CoCl_2$ and doxorubicin.

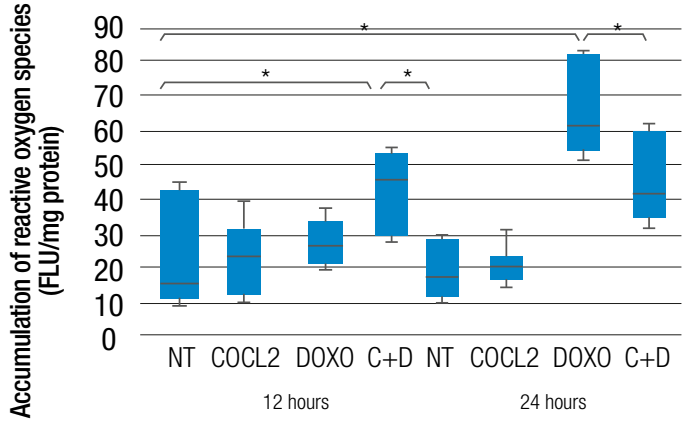

Figure 3. Relative levels of reactive oxygen species.
Source: Own elaboration.

Hypoxia-inducible factor HIF-1α does not alter cell viability in HT29 colon cancer line

It has been considered that an increase in the amount of reactive oxygen species could lead to cell death. For this reason, HT29 cells viability under chemical hypoxia conditions (100uM CoCl2) and the combination of treatments (100uM CoCl2 + 0.5 µM doxorubicin) (Figure 4) at different times (0-24h) was evaluated. The results show that there is no significant variation ($p>0.05$) in cell viability at different times and as a result of the aforementioned stimuli. Likewise, the treatment of HT29 cells with the combination of CoCl2 and doxorubicin treatment maintained cell viability at different times (0-24h), compared with untreated cells, with $p>0.05$ (Figure 4) and positive control H2O2 (200uM) $p>0.05$.

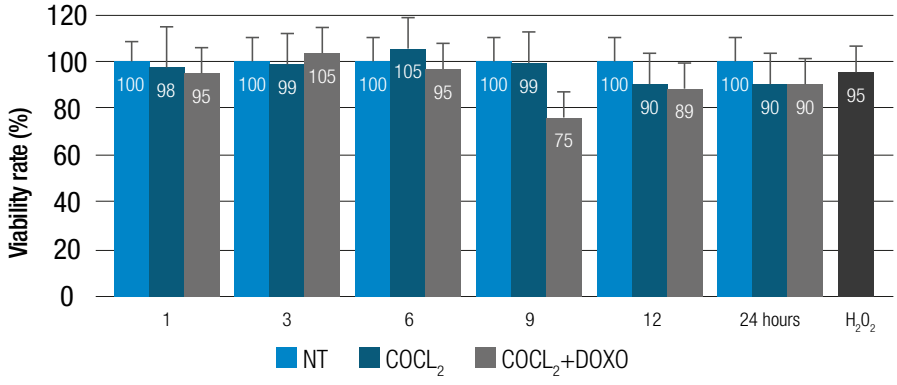

Figure 4. Percentage of cell viability.
Source: Own elaboration.

The process of apoptosis may be controlled by hypoxia

After 6 hours of incubation with $CoCl_2$ (100uM) under the conditions described above, caspase-3 activity decreased, which is attributed to increased HIF-1α activity over time. Caspase-3 activity decreased after 6 hours ($p<0.05$ relative to times of 1 and 3 hours) (Figure 5).

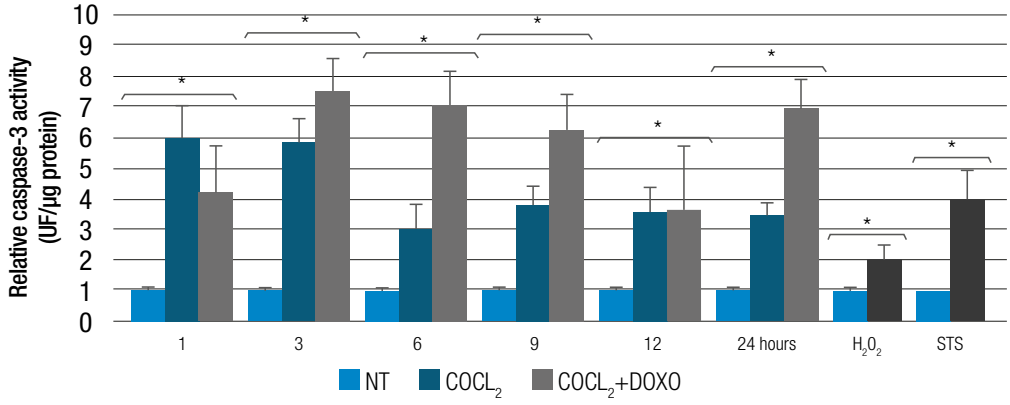

Figure 5. Caspase-3 activity.
Source: Own elaboration.

Figure 5 also shows how the effect of the combination of CoCl2 with doxorubicin decreases caspase-3 activity (p>0.05) compared with normal cells between hours 1 and 12. However, caspase-3 activity increases at 24 hours. It could be considered that the effect of these stimuli on caspase-3 activity is time dependent and could be caused by HIF-1α activity.

The expression of PUMA and BAX pro-apoptotic genes could be modulated by HIF-1α and ROS

The qRT-PCR technique allowed finding that treatment with 100uM CoCl2 significantly decreased PUMA mRNA expression (p<0.05); in turn, the combined treatment of CoCl2 or 5uM doxorubicin led to a significant increase (p<0.05) in PUMA mRNA expression, while BAX mRNA expression was significantly reduced (p<0.05) (Figure 6). The E3330 inhibitor led to a decrease in mRNA expression of the pro-apoptotic PUMA gene. This decrease is around 10 times lower, with a p<0.05 compared with cells without treatment (Figure 7).

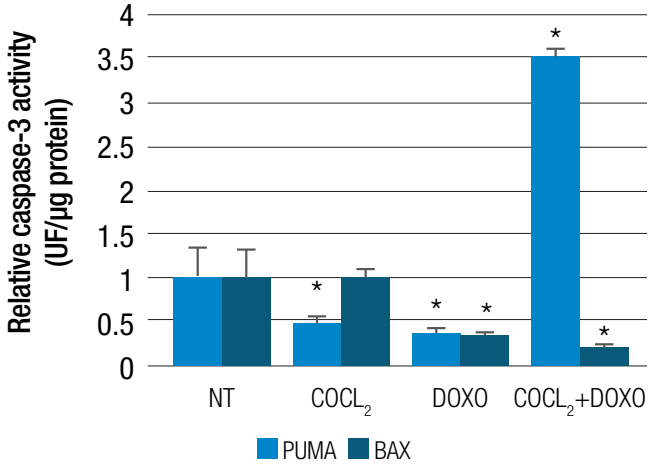

Figure 6. Relative PUMA and BAX mRNA expression. HT29 cells were treated with 100 µM CoCl2 or 5 µM doxorubicin ($CoCl_2$ + Doxo) for 24 hours.
Source: Own elaboration.

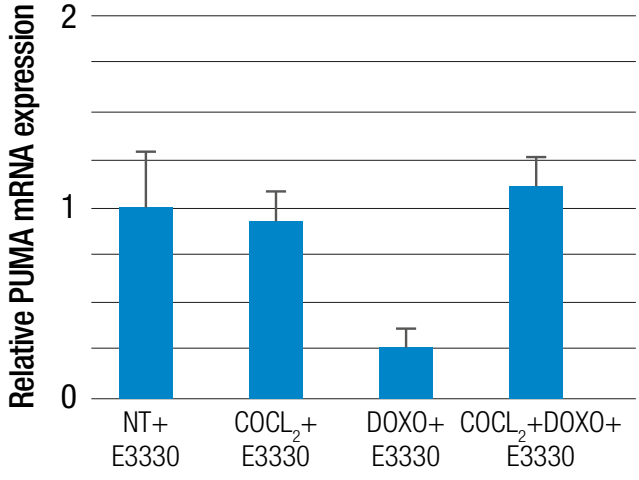

Figure 7. Relative PUMA mRNA expression. HT29 cells were treated with 100 µM CoCl2 or 5 µM doxorubicin (CoCl2 + Doxo) for 24 hours with E3330 inhibitor and evaluated by qRT-PCR technique.
Source: Own elaboration.

The expression of the PUMA pro-apoptotic gene could be modulated by the accumulation of ROS

One of the possible mechanisms by which oxidative stress can induce cell death is apoptosis; for this reason, PUMA mRNA levels were evaluated through conventional PCR. Hydrogen peroxide is a reactive species modulator that was used at a concentration of 200uM to determine the effect on the alteration of PUMA mRNA expression. This effect led to a decrease in PUMA mRNA expression (p<0.05) with respect to untreated cells (Figure 8 and 9). These results could indicate that the increase in the generation of ROS by hydrogen peroxide is comparable with the use of HIF-1α and doxorubicin separately, which significantly increases the amount of ROS and, in turn, significantly reduces the expression of PUMA mRNA.

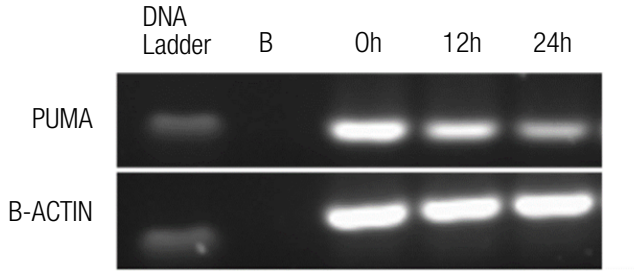

Figure 8. Relative PUMA mRNA expression. HT29 cells were treated with 200 µM H_2O_2 at different times, evaluated by conventional PCR for PUMA and compared to the b-actin gene expression in agarose gel.
Source: Own elaboration.

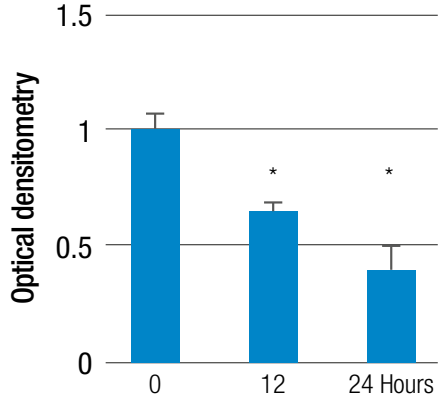

Figure 9. Relative PUMA mRNA expression. HT29 cells were treated with 200 µM H202 at different times and evaluated by conventional PCR for PUMA.
Source: Own elaboration.

Discussion

Resistance in cancer can be measured through different cellular mechanisms, including apoptosis. (15) A hypoxic tumor environment is considered as one of the critical factors that favor drug resistance through the MDR phenotype. (16) Likewise, it is known that there is a wide range of molecules that could be regulated by hypoxia, with HIF-1α being the main response factor that modulates several processes. (17)

A hypoxic environment can be comparable to the effect produced by the use of substances such as $CoCl_2$, which acts as an iron chelator necessary for prolyl-hydroxylases to act by hydroxylating HIF-1α and leading to the translocation of HIF-1α to the nucleus and its dimerization

with HIF-1β, forming HIF-1. On the other hand, doxorubicin exerts antitumor activity inhibiting the proliferation of different cancer cell types (18,19); its use has been limited by an increase of oxidative stress and because it is a transporter substrate associated with drug resistance such as Pgp. However, its action, considering the hypoxic tumor environment, has not yet been well documented.

Previous studies have shown that both HIF-1 and HIF-2 could modulate the response to Sunitinib treatment in colon cancer cells leading to a decrease in cell proliferation. (20,21) Therefore, it is important to consider hypoxia inducible factor-1alpha activity in different molecular events necessary to regulate tumorigenicity. The transcription factor HIF-1α may be associated with the control of cell death by regulating the expression of pro-apoptotic genes.

The correlation between HIF-1α and the PUMA and BAX genes as pro-apoptotic inducers is not clear yet. This study demonstrated that chemical hypoxia induced with $CoCl_2$ promotes a decrease in the expression of PUMA mRNA level and maintains the basal expression of BAX mRNA. The same situation was observed in the determination of the effector caspase-3 activity in the apoptotic process. On the other hand, using doxorubicin alone caused a significant decrease in the expression of PUMA and BAX mRNA. However, when treatment with $CoCl_2$ was combined with doxorubicin, the PUMA mRNA expression increased, but HIF-1α activity decreased, corroborating the correlation between this transcription factor and the PUMA gene.

It should be noted that many solid cancers are highly hypoxic, which would indicate that, in these zones, the expression of the transcription factor HIF-1α is critical for tumorigenicity, favoring a greater proliferation and decreasing the capacity of the apoptotic pathway. Therefore, hypoxia could mediate cell survival by reducing the expression of pro-apoptotic genes, increasing drug resistance of colon cancer cells.

Different studies have shown that redox state altered by hypoxia, anoxia, oxidative stress and generation of ROS could regulate the expression of the PUMA gene in vitro and in vivo. (22-24) Although ROS are generated during apoptosis mediated by oxidative stress, as a result of mitochondrial damage (25), PUMA induction by ROS could induce an upstream feeding mechanism that favors the apoptotic process.

In addition, it has been proven that, in a hypoxic tumor environment, the amount of ROS is high and can activate hypoxia-inducible factors (26), indicating a direct correlation between these factors and oxidative stress. This study showed that the greatest amount of reactive species was observed at 24 hours, when HIF-1α activity is much higher in the HT29 colon cancer cell line, using chemical hypoxia HIF-1α. On the other hand, resistance associated with cell death could be evidenced in this study, where the combination of HIF-1α + doxorubicin promoted the maintenance of cell survival by decreasing the expression of pro-apoptotic factors and keeping cells alive, in such a way that the action of the drug was attenuated.

It has been reported that HIF-1 and the p53 tumor suppressor protein are involved in the cellular response to hypoxia; however, the way these two transcription factors determine cell fate is still unknown. (27) PUMA may activate by being dependent on p53 or not, which could explain the increase when the combination of hypoxia and doxorubicin occurs at 24 hours.

The PUMA protein is a general sensor of cell death stimulation and a promising therapeutic target in cancer (27); therefore knowing the mechanisms associated with its regulation is of great importance. This is also a mediator of p53-dependent apoptosis in a large number of cell types. (28) For example, HCT116 PUMA-knockout colon cancer cells are highly resistant to apoptosis induced by overexpression of p53 or DNA-altering agents such as doxorubicin, 5-fluorouracil (5-FU), cisplatin, oxaliplatin, etoposide and camptothecin. (24,25)

Different cell lines have shown that, in response to DNA damage, p53 is activated and leads to an increase in the expression of pro-apoptotic genes such as Noxa, PUMA and Fas. Similarly, cancer cells resistant to cisplatin have shown that there is an alteration of the mechanisms mediated by p53 inducing a decrease in the pro-apoptotic genes Noxa and PUMA. (29)

This study showed that there is a decrease in PUMA mRNA expression associated with hypoxia, which in turn is maintained when doxorubicin is used in combination with chemical hypoxia. Therefore, it is possible to consider that there is a modulating effect of HIF-1α on p53 that would affect PUMA expression by altering the apoptotic process of HT29 colon cancer cells, even in the presence of doxorubicin, a drug aimed at DNA alteration. In addition, this research allowed demonstrating that both chemical hypoxia and the use of doxorubicin increase oxidative stress.

APE1 endonuclease (Human AP Endonuclease) participates in redox regulation influenced by stress response, DNA repair and other cellular functions such as angiogenesis, inflammation and cell survival. (30) However, some recent studies show that there is still a wide arrange of unknown activities of this factor. (31) Some APE1 redox signaling targets have been considered, namely p53, AP-1 and HIF-1α, which lead to establish that APE1 inhibition could be considered as therapeutic targets with important clinical potential. (32)

In this study, APE1 inhibition led to an even greater decrease in the PUMA mRNA expression level, which would confirm the ability of this endonuclease to directly or indirectly regulate the expression of this gene. It is important to consider that HIF-1α regulates the expression of APE1 levels and this, in turn, is regulated by APE1. (33) On the other hand, it is also important to consider that the expression of the pro-apoptotic protein PUMA is regulated by other mechanisms independent of p53, such as induction mediated by the transcription factors Sp1, E2F1 and FOXO3a; the latter involves the inhibition of the Akt survival pathway and the activation of the JNK pathway. (33-36) For this reason, factor HIF-1α inhibition does not a guarantee the activity of a drug, and it is necessary to take into account its capacity, in a hypoxic environment, to increase the reactive oxygen species and the alteration of factors that regulate the cellular redox state that may occur.

Conclusion

This study demonstrates that hypoxia could lead to maintain cell survival of the HT29 colon cancer line by keeping HIF-1α active. Hypoxia-inducible factor activity can be favored by the increase of reactive oxygen species and, thus, modulate the expression of the pro-apoptotic factor PUMA. However, the inhibition of this transcription factor does not guarantee an increase in the expression of PUMA mRNA, since this could be dependent on the generation of ROS and, in turn, the redox regulatory factor APE1. This factor may have an important role in the regulation of the transcription of pro-apoptotic genes. The results of this study suggest that the inhibition of factors such as hypoxia or ROS could be useful, as a therapeutic target, to enhance the effectiveness of drugs used in cancer.

Conflicts of interest

None stated by the authors.

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None stated by the authors.

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ORIGINAL RESEARCH

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Clinical inertia in insulin prescription for patients with type 2 diabetes mellitus at a primary health care institution of Cartagena, Colombia

Inercia clínica en la prescripción de insulina en pacientes con diabetes mellitus tipo 2 de una institución de baja complejidad en Cartagena de Indias, Colombia

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| Abstract |

Introduction: Evidence has demonstrated clinical or prescriptive inertia along with an increased prescription of insulin, causing a delay in the change of prescription.

Objective: To determine the prescription pattern and clinical inertia of insulin use in the treatment of patients with type 2 diabetes mellitus (DM2) enrolled in a diabetes program at a primary health care institution of Cartagena, Colombia.

Materials and methods: Pharmacoepidemiology study that addresses drug utilization based on data collected through a review of medical records of 331 patients with DM2, aged 18 and older, who had at least 6 months of control.

Results: 64.4% of patients were treated with long-acting insulin analogues and 18.4% used insulin; 52.7% of the patients in which insuline use was required did not have a prescription of this drug.

Conclusions: There is clinical inertia related to insulin prescription. Strategies should be implemented to overcome prescriptive inertia for people with DM2 in order to achieve therapeutic goals earlier and effectively prevent the development and progression of chronic complications.

Keywords: Diabetes Mellitus Type 2; Insulin; Therapeutic Uses; Drug Prescriptions; Drug-related side effects and adverse reactions (MeSH).

| Resumen |

Introducción. Paralelo al aumento de la prescripción de la insulina se ha demostrado la inercia clínica o prescriptiva, de tal manera que la demora en cambiar la prescripción es prolongada.

Objetivo. Determinar el patrón de prescripción y la inercia clínica en la utilización de insulina al momento de estar indicada en el tratamiento de los pacientes con diabetes mellitus tipo 2 (DM2) que acuden a un programa de diabetes en una institución de baja complejidad de Cartagena, Colombia.

Materiales y métodos. Estudio de farmacoepidemiología dirigido al campo de los estudios de utilización de medicamentos que se basó en datos recogidos mediante la revisión de historias clínicas de 331 pacientes con DM2, mayores de 18 años y que tuvieran mínimo 6 meses de control.

Resultados. El 18.4% de los pacientes utilizaron insulina. 64.4% fueron tratados con análogos de insulinas de acción prolongada. 52.7% de los pacientes con indicación de insulina no tenían prescrito el fármaco.

Conclusiones. Existe inercia clínica para la prescripción de insulina. Se deben implementar estrategias que superen la inercia prescriptiva para que las personas con DM2 alcancen tempranamente las metas terapéuticas y prevengan de manera efectiva el desarrollo y la progresión de complicaciones crónicas.

Palabras clave: Diabetes mellitus tipo 2; Insulina; Indicación Terapéutica; Prescripción de medicamentos; Inercia; Efectos colaterales y reacciones adversas relacionados con medicamentos (DeCS).

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Introduction

The International Diabetes Federation (IDF) estimated that the regional prevalence of diabetes in 2015 was 9.4% among adults aged between 20 and 79 years in South and Central America. The increase of number of cases expected for 2040 is greater in these countries than in other areas, since 48.8 million cases are expected by then. Prevalence for Colombia, as reported in the seventh edition of the IDF Diabetes Atlas for the age-group 20-79 years is 9.6%, which provides an approximate figure of 3.04 million people with diabetes mellitus type 2 (DM2). (1)

Diabetes mellitus is a chronic disease that, if not treated early and properly, generates complications basically because of the poor control of glycemia and the years of evolution of the disease. Good control of diabetes eliminates symptoms, avoids acute complications and reduces the incidence and progression of chronic microvascular complications. Adding adequate control of other associated problems, such as high blood pressure and dyslipidemia, also prevents macrovascular complications; such prevention has proven to be cost-effective. (2,3)

Along with the epidemic of diabetes observed nowadays around the globe, a remarkable increase in the use of anti-diabetic drugs has also been reported in the last decades. The 57% increase in the use of insulin reported by the Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency of Medicines and Medical Devices) in Spain between 2000 and 2014 is particularly striking. (4)

As the prescription of insulin increases, clinical or prescriptive inertia, understood as the delay in the modification of the pharmacological treatment when the recommended therapeutic goals are not met, has also been reported. In this regard, HbA1c ≥8% values prove that there is a delay in the change of prescription, amounting up to nearly 9 years when insulin is required. (5,6)

Most patients with DM2 are treated exclusively by general practitioners, with an average of eight consultations per year. Several studies have confirmed that the prescription of insulin in primary care services is very low, with a range of 6-20%, and that the combination of oral therapy with insulin is also underutilized between 0% and 6%. (7,8)

Although insulin therapy is the most effective therapy, and even treating physicians accept its benefits, there is reluctance to prescribe insulin and prefer to initiate this treatment only "when necessary or absolutely essential." The barriers reported by physicians for the initiation of insulin are: 1) concern about adverse events, 2) considerations about the difficulty of use by the patient, 3) limited time to provide education in insulin therapy, and 4) inadequate training to start and continue insulin treatment. (9-12)

Hypoglycemia is common in patients with DM2; about 90% of all patients receiving insulin have experienced an episode of this type. (13) In view of this adverse event, clinical inertia is demonstrated based on the low percentage of primary care physicians who intensify drug treatment due to the lack of achievement of the expected goals, and a lower tendency to initiate insulin, even with elevated HbA1c values, showing little familiarity with insulin prescription. (14)

Hypoglycemia caused by insulin can be potentially avoidable, since education can reduce this index; adequate monitoring of blood glucose is also crucial for safe prescription. (15) These episodes can lead to lack of adherence to the treatment, which implies greater likelihood of worsening of the disease, increased health expenses and decreased quality of life in chronic patients. (16)

The drugs included in the Health Benefits Plan of the country for patients with DM2 treated by general practitioners are only metformin, glibenclamide and insulins (human and analogous). With the advent of MIPRES (Application for Reporting the Prescription of Services and Technologies not Covered by the Benefit Plan), patients of the contributory scheme have access to medications that are not covered by the Capitation Payment Unit, while patients of the subsidized health scheme do not have access to this broad coverage.

All insulin analogues are available in Colombia and have new pharmaceutical forms in order to improve their administration and allow flexibility in daily administration, simplifying the dosage regimen.

The specific moment when insulin therapy should be initiated can be difficult to determine for each person, since there are no universal clinical guidelines. Indications for the initiation of insulin include non-achievement of goals with oral antidiabetics, contraindication of oral antidiabetics, ketonuria, ketoacidosis, acute hyperglycemic decompensation or marked hyperglycemia: fasting glycemia >250-300 mg/dL, HbA1c >9-10%. (17-22)

The objective of this study was to determine the prescription and clinical inertia pattern in the use of insulin at the time of indication in the treatment of patients with DM2 enrolled in a diabetes program of a primary health care institution of Cartagena de Indias, Colombia.

Material and methods

This is a pharmacoepidemiology study that specifically addresses descriptive studies on drug use, based on data collected after reviewing the medical records of patients with DM2, and over 18 years of age, who were enrolled in a diabetes care program during 2013 and 2014 for a minimum of 6 months of control in a primary health care institution. The population is composed of 1 340 patients and the investigation was approved by the Research Office of the Empresa Social del Estado Hospital Local Cartagena de Indias, which serves for the pertinent purposes as an institutional ethics committee by means of minutes issued on March 30, 2016.

With an expected prevalence of 50%, an error of 5% and a confidence interval of 95%, the sample obtained included 384 medical records. Since this was a finite population, the sample size was adjusted for a total of 299 clinical records. When adding 10% to cover losses, the final sample was 331. For sample selection, a simple random sampling of the list of patients was made using the tool Sample of Microsoft Excel. Data were collected through an instrument that investigated the pattern of insulin prescription and the adequacy of drug prescription, determining whether there was an indication for the use of insulin and prevention of adverse effects of the drug.

Based on the DM2 care guidelines of the Ministry of Social Protection, the institution defined that insulin prescription is indicated when the goals are not achieved using oral anti-diabetics, as a contraindication of anti-diabetics, in patients with weight loss or tendency to ketosis, when ketonuria or fasting glycemia >250 mg/dL and HbA1c >9%. (19,20,22-24)

The established target for glycemic control was HbA1c ≤7%, as defined in the DM2 care guidelines used in Colombia, adopted at the respective institution and in force at the time of care. (21,24) Education on hypoglycemia was considered as performed when two parameters were found in the clinical records: education on the identification of hypoglycemia symptoms and prescription of glucometer, strips and lancets.

The data were stored in a Microsoft Excel spreadsheet and the analysis was carried out using the statistical program SPSS version 21.0. Statistical analysis yielded tables reporting absolute and relative frequencies, as well as measures of central tendency and dispersion for quantitative variables.

Results

61.3% (n=203) of the study population were females and the average age was 54.3 years (σ=12.2). 73.7% (n=244) of patients with type

2 diabetes had BMI ≥25 kg/m^2 and only 1.5% (n=5) had BMI <18.5 kg/m^2. 63.1% (n=209) had data on HbA1c in their medical records and 20% had no urinalysis reports. Of 263 patients with urinalysis reports, none had ketonuria (Table 1).

Table 1. Characteristics of patients with type 2 diabetes mellitus included in the study. Cartagena de Indias, Colombia.

Characteristics		n	%
Sex	Female	203	61.3
	Male	128	38.7
Body Mass Index	Underweight	5	1.5
	Normal weight	82	24.8
	Obesity	117	35.3
	Overweight	127	38.4
Information on HbA1c	No	122	36.9
	Yes	209	63.1
Urinalysis report	No	68	20.5
	Yes	263	79.5
Total		**331**	**100**

Source: Own elaboration.

18.4% (n=61) of patients used insulin, regardless it was long-acting, intermediate-acting, rapid-acting or ultra-rapid. The most widely used basal insulin was glargine, as its use was reported in 57.6% (n=34) of the patients requiring this type of insulin. 62% (n=38) of patients were treated with long-acting insulin analogues (glargine and detemir), while 34% (n=21) received NPH insulin as basal insulin. Crystalline insulin was the most used as prandial insulin (Table 2).

Table 2. Prescription pattern in patients with type 2 diabetes mellitus included in the study. Cartagena de Indias, Colombia.

Type of prescription		n	%
Basal insulin	Detemir	4	6.6
	Glargina	34	55.7
	NPH	21	34.4
	No basal insulin	2	3.3
Prandial insulin	Aspart	3	4.9
	Crystalline	10	16.4
	Glulisine	5	8.2
	Non-prandial	43	70.5
Total		**61**	**100**

Source: Own elaboration.

It was found that 39% (n=129) of the clinical records evaluated showed some indication for the initiation of insulin treatment, either definitively or temporarily. Among patients with insulin indication, only 47.3% (n=61) were prescribed insulin.

In decreasing order, the main conditions indicated for the initiation of insulin therapy were: fasting glucose >250 mg% (54.3%), HbA1c >9% (24%), contraindicated oral anti-diabetics (17.9%), symptomatic patients with weight loss (15%) and failure to achieve HbA1c goals despite the use of the two oral anti-diabetics available in the mandatory health plan (metformin and glibenclamide) (11.6%) (Table 3).

Table 3. Conditions that indicate insulin prescription in patients with type 2 diabetes mellitus included in the study. Cartagena de Indias, Colombia.

Indications	n	%
Fasting glucose >250 mg%	70	54.3
HbA1c >9%	31	24.0
Oral anti-diabetics contraindicated	23	17.9
Symptomatic patients and weight loss	20	15.5
Failure to achieve HbA1c goals	15	11.6

Source: Own elaboration.

Of 61 patients with insulin prescription, only the clinical records of 52.5% (n=32) reported receiving education to identify hypoglycemia early and the prescription of the glucometer kit.

Discussion

Exposure to chronic hyperglycemia leads to glucotoxicity in several cells; there is a strong correlation between toxicity and vascular endothelial dysfunction, particularly damaging endothelial cells in the capillaries of the retina, the mesangial cells in the renal glomerulus, and the microvasculature that supplies the nerves. (25)

Strict glycemic control of diabetes is fundamental to prevent micro and macrovascular complications that increase the economic burden for the health system and affect healthy life years in these patients. (26) In addition, it has been evidenced that early and effective insulin intervention is important because inhibiting glucotoxicity and decreasing the onset of complications may be beneficial to preserve functional beta-cell mass. (27,28)

The percentage of patients who used insulin was 18.4%, which is relatively similar to the figures reported in Colombia by Villegas *et al.* (29) and Machado-Alba *et al.* (30): 19.6% and 23.5%, respectively; it is worth noting that these authors included patients with type 1 and type 2 diabetes (10.5% and 4.9%, respectively).

A figure of 18.4% of insulin use is higher than that found in Italy by Pellegrini *et al.* (31), who reported 15.3% among patients attended by general practitioners, but lower than Machado-Duque *et al.* (32) with 26.1% in Pereira in a retrospective cohort followed up for 5 years, and than Alba *et al.* (33), who reported a 54% use of insulin in a study conducted in Bogotá with patients of a university hospital program.

With this in mind, it can be said that due to the difference in the inclusion criteria, the follow-up time and the scope of the studies, an exact comparison cannot be performed. However, despite the difficulties, it is possible to conclude that there is a low prescription rate of insulin in the diabetes care program studied here.

Currently available insulin analogs offer the same clinical effectiveness as conventional human insulins, with benefits in terms of hypoglycemia and less weight gain. Basal insulin analogues are preferred over NPH insulin because a single dose of insulin provides a lower serum insulin concentration for about 24 hours, resulting in significantly less hypoglycemia. (18,34)

A change in the prescription pattern of insulins has been observed worldwide, as the use of long-acting drugs analogous has

increased, causing the detriment of intermediate-acting and human-derived insulins. (4,35) The use of long-acting insulin analogues is predominant with 64.4%, and an a significant use of ultrafast-acting insulin analogues is also observed, which shows that the percentage of use of insulin analogues is increasing since their introduction in the mandatory health plan.

To support the positive aspects of this change in insulin prescription trends, a reduction in the risk of nocturnal hypoglycemia with the use of long-acting insulin analogues compared to NPH insulin has been reported by the literature, as well as a lower risk of hypoglycemia with ultra-fast insulin analogs compared to crystalline insulins. (36,37)

Regarding the increase of anti-diabetics prescription, a greater percentage increase of oral anti-diabetics is observed in relation to insulin; this could be related to the clinical inertia of physicians, who unjustifiably delay the initiation of insulin therapy. Primary care physicians state that they feel safer using oral anti-diabetics; therefore the prescription of the hormone is late and at a very low percentage, as only 6-20% of patients with DM2 are treated with it. In addition, an average delay in the initiation of insulin between 7.7 and 9.2 years is observed in cases in which it is required. (5,38)

The United Kingdom Prospective Diabetes Study (UKPDS) revealed that only 33% of patients treated with metformin and sulfonylureas had HbA1c <7% after 3 years of treatment. (39) It reports 18.4% of patients with insulin prescription, but the most interesting thing about said study is that 52.7% of patients with some insulin indication had not been prescribed, proving the inertia in the prescription of this drug for the patients treated by the program.

The Collaborative Drug Therapy Management Service shows that the introduction of insulin in patients with HbA1c >9% improves glycemic control and that it is less frequent than recommended. (40) In the UKPDS, each year, about 3% of patients treated with insulin experience a severe episode of hypoglycemia; in addition, 40% had an episode of hypoglycemia of any degree of severity. (37) The prevention of hypoglycemia requires some major considerations, including the appropriate use of capillary blood glucose monitoring and self-management supported by education. Furthermore, the patient needs to be well informed about the risk factors for hypoglycemia, its symptoms, prevention and treatment, and must constantly monitor glucose; consequently, education on hypoglycemia is fundamental to prevent this complication. (13)

No information regarding education on hypoglycemia or prescription of a glucometer kit was found in 47.5% of the clinical records evaluated. It is necessary to consider the possibility that these activities have been carried out and not reported; however, it should be noted that the professionals of this institution have limited time for conducting these educational strategies and there is no educational support provided after the medical consultation.

Following this train of thought, and considering all the reasons for the low prescription of insulin, this scenario leads to inadequate control of diabetes and is one of the causes of the onset of complications. Insulin is traditionally the last therapeutic option, and once it is initiated, complications have already appeared. Therefore, it is necessary to sensitize clinicians on the importance of initiating insulin in a timely manner.

These findings confirm the need to implement strategies that overcome the prescriptive inertia for patients with DM2 to reach early therapeutic goals and effectively prevent the development and progression of chronic complications. Given that greater inertia in the prescription of insulin has been observed, these strategies should place special emphasis on their proper use in a timely manner.

A limitation of the study was that a significant percentage of patients did not have HbA1c or ketone urine tests, so the number of patients who would have an insulin indication for glycosylated hemoglobin >9% or ketonuria could be higher. The duration of the disease in patients attending this program is unknown. The longer it takes to diagnose the disease, the greater the need for insulin.

Conclusion

Adequate metabolic control in type 2 diabetic patients decreases the incidence of complications. Using all therapeutic options available is fundamental to achieve good control; insulin is the most effective medication and should be used without delay in all patients with this indication. Therefore, it is very important to educate primary care physicians on specific indications. It is imperative to provide training by disclosing the advantages that the Colombian health system has when making available all the types of insulin covered by the health plan.

Conflicts of interest

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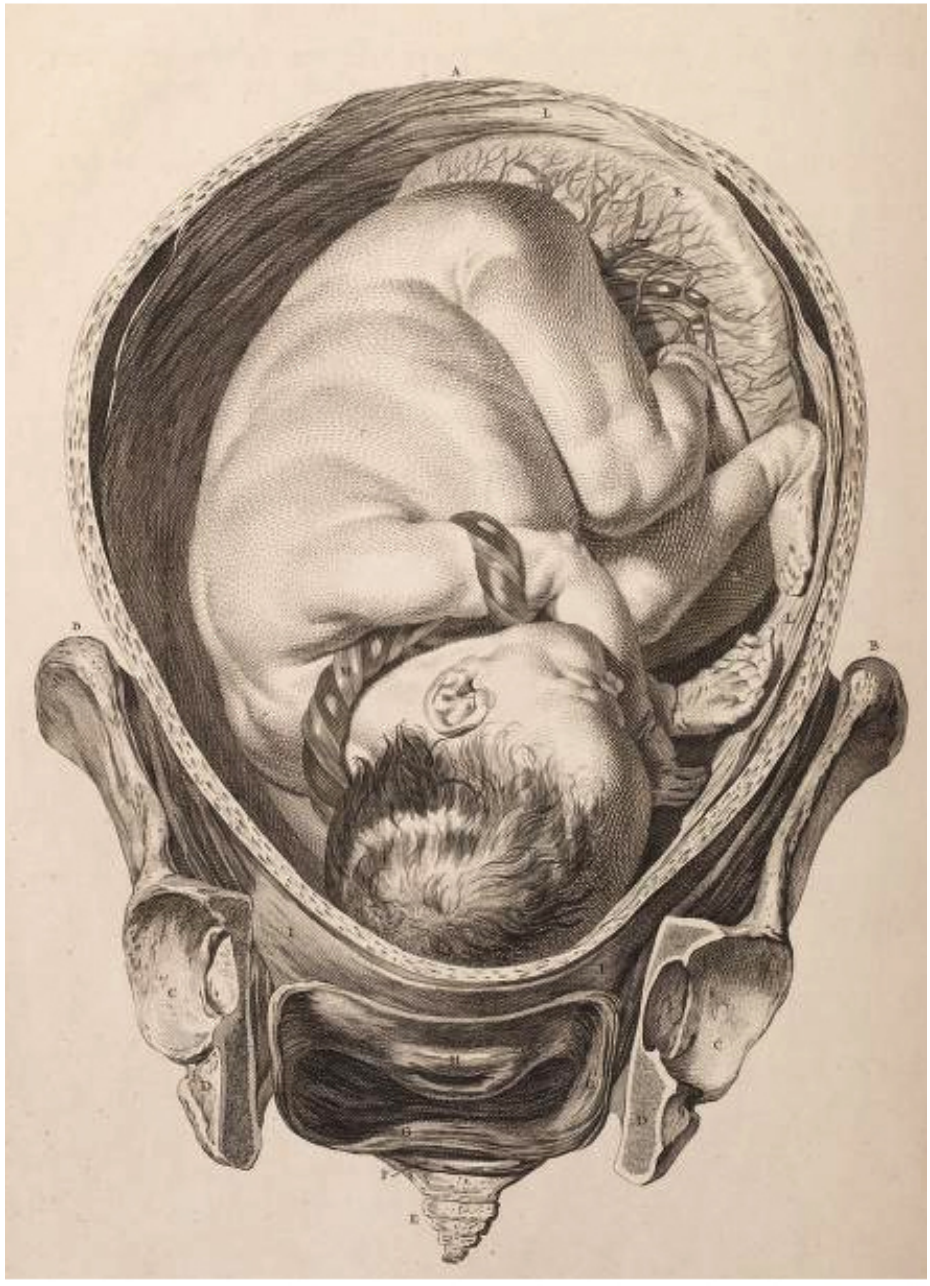

WILLIAM SMELLIE, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

ORIGINAL RESEARCH

DOI: http://dx.doi.org/10.15446/revfacmed.v66n4.65208

Scientific and academic production and visibility of the Faculty of Health Sciences of Universidad del Cauca

Producción y visibilidad científico-académica de la Facultad de Ciencias de la Salud de la Universidad del Cauca

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| Abstract |

Introduction: Bibliometric indexes are important indicators of the quality of the country's medical programs. There are few studies of this kind at the Universidad del Cauca.

Objective: To evaluate the scientific-academic activity of the Faculty of Health Sciences (FHS) of the Universidad del Cauca based on bibliometric production indicators of the authors, visibility and impact during the period 2010-2016.

Materials and methods: Descriptive, cross-sectional, bibliometric research. Different categories of the academic production of the FHS were identified (citation by authors, language of publication, areas of health sciences), and the main journals where the authors published. In addition, the metric indicators of the journals and citation indexes of the authors were determined, as well as their enrollment in research groups and the most cited publications according to SCOPUS.

Results: 183 articles were found. The main language of publication was Spanish and mainly in the clinical-surgical area. 60% of the articles of the main authors have some international collaboration. The Revista de la Facultad de Ciencias de la Salud of Universidad del Cauca had the largest number of articles published by authors of the same faculty during the period under study.

Conclusion: The scientific and academic production and visibility of the FHS of the Universidad del Cauca is low. The findings reveal the need for greater institutional support for research, and the creation and support of research groups and incubators. Therefore, this work seeks to encourage greater visibility of the FHS in the national and international scientific field.

Keywords: Bibliometrics; Medicine; Research; Colombia (MeSH).

| Resumen |

Introducción. Los índices bibliométricos son indicadores importantes de la calidad de los programas de medicina del país. En la Universidad del Cauca se cuenta con pocos estudios de este tipo.

Objetivo. Evaluar la actividad científico-académica de la Facultad Ciencias de la Salud (FCS) de la Universidad del Cauca a partir de indicadores bibliométricos de producción de los autores, visibilidad e impacto durante el período 2010-2016.

Materiales y métodos. Investigación bibliométrica descriptiva de corte transversal. Se identificaron diferentes categorías de la producción académica de la FCS (citación por autores, idioma de publicación, áreas de las ciencias de la salud) y las principales revistas donde publicaron los autores. Se determinaron los indicadores métricos de las revistas, los índices citacionales, la vinculación a grupos de investigación y las publicaciones más citadas de acuerdo a Scopus.

Resultados. Se encontraron 183 artículos. El principal idioma fue español y la mayoría de publicaciones eran del área clínico-quirúrgica. El 60% de los artículos de los principales autores tienen alguna colaboración internacional. La Revista de la Facultad de Ciencias de la Salud de la Universidad del Cauca presenta el mayor número de artículos publicados por autores de la misma facultad durante el periodo en estudio.

Conclusión. La producción y visibilidad científico-académica de la FCS de la Universidad del Cauca es baja. Los hallazgos encontrados revelan la necesidad de un mayor apoyo institucional para la investigación, la creación y el apoyo a grupos y semilleros de investigación. Con esto se pretende tener un grado mayor de visibilidad en el campo científico, tanto nacional como internacional.

Palabras clave: Bibliometría; Medicina; Investigación; Colombia (DeCS).

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Introducción

The dissemination of research results in health sciences is generally done by publishing scientific articles, essays, documents or books that facilitate the exchange of ideas and the use of scientific evidence among the different local, regional and world academic communities. (1)

The application of statistical methods, among others, to written communication products of research is known as bibliometrics. (2) This activity responds to the need to quantify scientific production in order to compare, measure and objectify it (3), and "also stands out for its maturity both in its praxis and in its conceptual theoretical development." (4, p11)

Bibliometrics is based on indicators and is defined as

> "[…]a set of methodological knowledge applied to measure the number of documents published and their citations, according to their origin and authors, which ultimately contributes to the evaluation of the outputs of science" (1, p44).

Indicators enable the characterization of scientific activity, academic productivity and the impact of research. By tradition, the fundamental criterion used to assess the success of a researcher is the number of published works; researchers with a large number of publications are considered highly productive, experienced and successful.

However, at present, one of the most used indicators is h-index, which indicates scientific performance by analyzing the number of times that an author, publication or journal has been cited. (5) H-index is considered an easily accessible indicator because it can be looked for in Google Scholar; it measures the global impact and represents the influence of the author in a specific field of research, that is, the degree to which his/her work has been useful for other researchers. (6) Even so, it has some disadvantages because it can be manipulated in highly cited articles and analyzes all kinds of products (original articles, systematic reviews), giving the same value to all of them, and is influenced by the number of years the researcher has been working on a specific area. (7)

Regarding journals, the SCOPUS database has the largest amount of abstracts and citations of peer-reviewed literature and has bibliometric tools to track, analyze and visualize research. (8) This instrument measures, on the other hand, the scientific prestige of the sources and classifies them by means of quartiles, being 1 (Q1) the highest impact score. SCOPUS has other scientific indicators that are used to evaluate and analyze publications, such as the SCImago Journal Rank (SJR), an indicator that provides a relative quality index of the journals included in the SCOPUS databases from 1996 onwards. (9) The SJR makes an estimation of the time an article of a journal has been cited over a period of 3 years and is useful to compare journals, since it classifies them according to their prestige. The Source Normalized Impact per Paper (SNIP) is another indicator that measures the impact of a journal citation based on the total number of citations in a given field of research. (10)

The bibliometrics of scientific production is also a benchmark for placing the faculties of medicine and health sciences in the national and international context. (5) The Universidad del Cauca is ranked ninth among Colombian universities in terms of scientific production (11); nevertheless, neither the university nor the Faculty of Health Sciences (FHS) have a system of permanent tracking of the production of their academic community nor of bibliometric indicators evaluating the volume and citations of their scientific production, which limits the information processes needed for accreditation and feedback of their research groups and their departments.

Quilindo C, Calvache JA, Delgado-Noguera M. [Producción y visibilidad científico-académica de la Facultad de Ciencias de la Salud de la Universidad del Cauca]. Rev. Fac. Med. 2018;66(4):557-63. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.65208.

A preliminary work conducted at the Universidad del Cauca (12), also in the Faculty of Health Sciences (FHS), evaluated scientific-academic production by departments in the period 2010-2016. This study characterized the main author by sex, profession, employment and academic attainment while establishing the type of journal or means of dissemination of the scientific and academic production, as wellas the collaboration percentage with entities external to the FHS. (12) Still, not only the faculty but the entire university lack internal bibliometric studies. Given the current situation of the institution, it is important to continue carrying out works in this area and, in consequence, the objective of this study was to evaluate the scientific-academic activity of the FHS of Universidad del Cauca based on bibliometric production indicators of authors, visibility and impact. In this way, this line of research is strengthened and may be an incentive for other faculties, libraries and the university itself to begin the process of measuring their contributions.

Materials and methods

This was a descriptive, cross-sectional bibliometric research that considered as population all the academic scientific production of the FHS of the Universidad del Cauca, represented in the publication of articles in journals and periodicals. Certified production in the period between January 2010 and April 2016 was selected as sample; 183 products met the inclusion criteria. Certified academic scientific production —with ISSN (International Standard Serial Number)— was included and classified into different typologies (original research, review or other).

The search and localization of the information was structured in two phases. During phase 1, a thorough search was performed in the PubMed, MEDLINE, ScienceDirect, Cochrane Library, SCOPUS, LILACS, Google Scholar databases, in the databases of the Vice-Rector's Office for Research of the Universidad del Cauca, and in CVLaC curriculums to identify the academic production of the faculty in the period under study. The common strategy for searching title, abstracts, affiliation and authors was: Filiation: Universidad del Cauca/University of Cauca Date: Jan 2010 to Apr 2016 (Annex 1). The total result of the searches was debugged manually using the EndNote software (Windows OS). In phase 2, after obtaining the results of the initial search, a statement was sent to the heads of each department of the faculty for socialization. The statement requested the review of the search results and adding the production that was not included.

The 183 articles found were classified by language of publication and related health sciences area (basic, clinical-surgical, public health and others), taking into account abstract and full text reading.

Regarding the production of authors of the FHS, the type of the product, the year of publication and the number of citations were established by means of SCOPUS. In case the article of any author was duplicated, it was excluded.

With respect to the visibility of authors, the h-index was identified using Google Scholar, and the category of the main author as a

researcher was established based on the system of the Administrative Department of Science, Technology and Innovation (Colciencias) through call 737 of 2015 (13), and classified as Junior, Senior, Associate, New, Not recognized or Other. The association of the main author with some research group of the Universidad del Cauca was established.

The 10 main journals included in the SCOPUS database, where the authors of the FHS made their publications, were identified. The quartile, SJR and SNIP indicators from these journals were obtained.

Qualitative variables were summarized with absolute frequencies and proportions, and quantitative variables by means of descriptive statistics and graphs. The statistical package R was used for the analysis and the graphs were designed using the free statistical package RStudio. (14)

Results

Phase 1 of the information search yielded 1 362 studies that met the inclusion criteria: 1 092 records were found in external databases and 270 in Latin American databases. 170 articles were excluded based on the evaluation of titles, 119 records based on the evaluation of the abstracts, and 865 records based on authors and affiliation, for a total of 1 154 articles excluded. Thus, 183 publications were included in the study after excluding 25 that were repeated or duplicated (Figure 1).

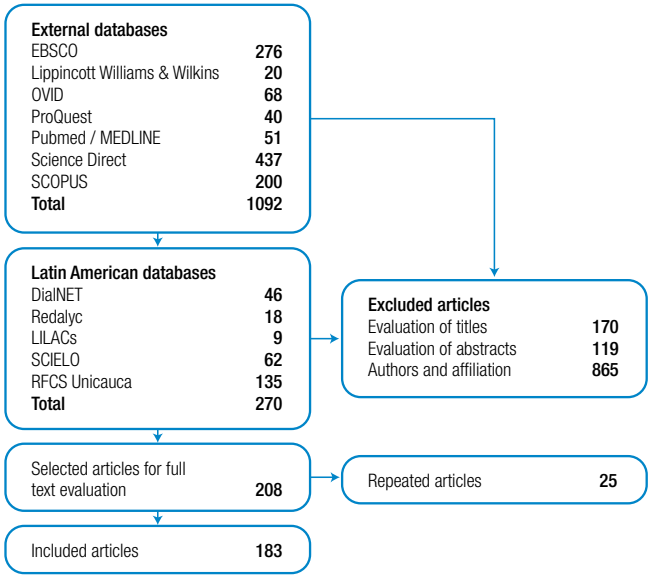

Figure 1. Search and selection flowchart of studies conducted in the Faculty of Health Sciences of the Universidad del Cauca. 2010-2016. Source: Own elaboration.

According to SCOPUS, the health area represents 11% of all the academic-scientific production of Universidad del Cauca, which places it in third, surpassed by computer sciences and engineering. (15)

Publication language

Of the total production found, 157 articles (85.7%) were originally published in Spanish and 26 (14.2%) in English.

Distribution of production by area of knowledge

Of 183 articles produced by the professors of the FHS, 104 (63.7%) were from the clinical-surgical area. The basic areas and those related to public health contributed with 26 (14.2%) and 20 (10.9%) products, respectively.

The main authors, according to the number of citations, are presented in Table 1. Half of the scientific-academic production of these authors corresponds to original articles; there are also systematic and narrative reviews and a case report. 60% of the articles of the main authors of the faculty have some international collaboration.

Table 1. Main authors of the Faculty of Health Sciences of Universidad del Cauca and number of citations, year of publication and type of product according to SCOPUS.

Study	Authors *	Number of citations	Type of product	International cooperation
Alonso-Coello *et al.* (16). 2010	Pablo Alonso Coello, Affan Irfan, Ivan Solà, Ignasi Gich, **Mario Delgado Noguera**, David Rigau, Sera Tort, Xavier Bonfill, Jako Burgers, Holger Schunemann.	123	Original article	Yes
Delgado-Noguera *et al.* (17). 2015	**Mario F Delgado Noguera, José Andrés Calvache**, Xavier Bonfill Cosp, Eleni P Kotanidou, Assiina Galli-Tsinopoulou.	45	Systematic review	Yes
Concha *et al.* (18). 2010	**Juan M Concha**, Alejando Sandoval, Philipp N Streubel.	27	Original article	Yes
Barajas-Nava *et al.* (19). 2010	Leticia Barajas Nava, Ivan Solà, **Mario Delgado Noguera**, Ignasi Gich, Carola Orrego Villagran, Xavier Bonfill, Pablo Alonso-Coello.	12	Systematic review	Yes
Calvache *et al.* (20). 2011	**José Andrés Calvache**, Manuel Felipe Muñoz, Francisco Javier Baron.	6	Original article	Yes
Correra-Correa *et al.* (21). 2010	Zamanda Correa Correa, **Isabel Muñoz Zambrano**, Andres Felipe Chaparro	5	Original article	No
Rendón-Becerra & Ortiz-Martínez (22). 2016	**César Augusto Rendón Becerra, Roberth Alirio Ortiz Martínez.**	4	Original article	No
Romero-Rojas *et al.* (23). 2013	Alfredo Romero Rojas, María Rosa Bella Cueto, **Ivone A Meza Cabrera**, Angeles Cabezuelo Hernández, Darío García Rojo, **Hernando Vargas Uricoechea**, José CameselleTeijeiro.	4	Case report	Yes
Sierra-Zúñiga *et al.* (24). 2013	**Marco Fidel Sierra Zúñiga, Oscar Eduardo Castro Delgado, Juan Carlos Caicedo, Ángela María Merchán Galvis, Mario Delgado Noguera.**	3	Original article	No

* The names in bold correspond to the authors of the Faculty of Health Sciences of Universidad del Cauca.
Source: Own elaboration.

Production and visibility of the main authors

Table 2 presents the top 10 authors by order of production according to the h-index found for the period 2010-2016. In addition, it also presents their category according to call 737 of 2 017 of Colciencias, the research group of Universidad del Cauca to which they belong, and the classification of the group.

Table 2. Characteristics of the main authors in terms of production of the Faculty of Health Sciences of Universidad del Cauca. 2010-2016.

Author	h-index *	Colciencias Category †	Research group ‡	Registration of the group in Colciencias VRI †
Mario Delgado -Noguera	11	Senior	Lactancia materna y alimentación complementaria (Breastfeeding and complementary feeding)	--
José Andrés Calvache	8	Senior	Investigación en anestesiología GRIAN (Research in anaesthesiology GRIAN)	C
Hernando Vargas-Uricoechea	3	NR	Endocrinología y metabolismo (Endocrinology and metabolism)	--
Tomás Omar Zamora	2	NR	SG	--
Nelson López	0	NR	SG	--
Guillermo Rivera	2	NR	SG	--
Pilar Mirely Chois	1	Junior	Comunicación humana y sus desordenes (Human communication and its disorders)	C
Juan Pablo Martínez	0	NR	SG	--
Jenny Arroyave	0	NR	SG	--
Edwin Muñoz	0	NR	SG	--

VRI: Vice-Rector's Office for Research; NR: non-registered researcher; SG: author not associated to a research group; --: research group not registered in Colciencias or not endorsed by the Universidad del Cauca.
* Data retrieved from Google Scholar.
† Data taken from call 737 of 2017 of Colciencias.
‡ Data according to the Vice-Rector's Office for Research, Universidad del Cauca.
Source: Own elaboration.

Citation indexes of the top 10 journals where authors published

Evaluation of citation indicators

Of the total of the journals or means of disclosure where the authors of the FHS of Universidad del Cauca published, 9 of them were found in SCOPUS (Table 3). The Cochrane Library and Burns belong to Q1 and have 4 and 2 products, respectively. The Revista de la Facultad de Ciencias de la Salud of Universidad del Cauca, which is not registered in the SCOPUS platform, has the largest number of articles published by the authors of the same faculty during the study period.

Table 3. Main journals or means of dissemination of scientific production of the Faculty of Health Sciences of Universidad del Cauca according to the SCOPUS quartile. 2010-2016.

Journal	Quartile according to SCOPUS	SJR	SNIP	Frequency
The Cochrane Library	Q1	2.3	18.6	4
Burns	Q1	0.895	1.174	2
Biomédica Revista del Instituto Nacional de Salud	Q2	0.280	0.447	2
Revista Colombiana de Anestesiología	Q3	0.151	0.410	9
Clínica e Investigación en Arteriosclerosis	Q3	0.195	0.165	2
Revista de Salud Pública	Q4	0.138	0.146	4
Revista Colombiana de Cardiología	Q4	0.114	0.096	2
Aquichán	Q4	0.136	0.183	2
Arete	Q4	0.101	0.00	2
Revista de la Facultad de Ciencias de la Salud de la Universidad del Cauca	--	--	--	103

SJR: Scimago Journal Rank; SNIP: Source normalized impact per paper.
Source: Own elaboration.

Discussion

Medical research is a fundamental pillar of knowledge and demands vocation and basic training in methodological and ethical aspects that undergraduate and postgraduate medical training does not always include in its programs. (25,26) In Latin America, about two thirds of the professionals do not carry out research, having as main barriers lack of time, lack of knowledge in research methodology and lack of institutional culture that incorporates research as an usual task. (25) Some subjects, such as Health Research (27), and scientific production itself are not paid enough attention by medical schools, particularly at Universidad del Cauca.

The production of the FHS during the period 2010-2016 was 183 studies. 157 articles (85.7%) were published in Spanish and were mainly related to the clinical area. Today, this result is a normal trend in Latin America, where many researchers do not write in English yet. The articles of the top 10 authors were mostly written in collaboration with international authors and in English. This collaboration is likely to be important when publishing in English-language journals, as they have greater visibility. (28)

According to the analysis carried out, the clinical-surgical area was the main area of publication (42.8%). In the study by Sisa *et al*. (29) in Ecuador, the main thematic area was the clinical-surgical area with 60%. This result demonstrates the low level of research and publication in the core areas in the FHC. (12)

The h-index is one of the most popular instruments for evaluating the impact and quality of a researcher's articles. Depending on the number of citations and the amount of scientific production, this index detects outstanding researchers within the area and measure their productivity; however, it should be considered that this index depends on the number of publications of the author, does not discriminate between the types of products, is strongly influenced by the age of the researcher, and does not allow comparing different areas of knowledge. (7,30,31)

Romero-Torres *et al.* (32) noted that the h-index was directly related to the years the author has devoted to research, but in Colombia this fact does not seem to be met given the relative science and technology backlog. The highest h-index found in this work was 11 and corresponds to Colciencias Senior Researchers, who usually have a PhD, have worked in international networks and have published in other languages.

Regarding the main authors of the FHS, only 30% of them were registered as researchers in Colciencias and were part of a research group registered in the Vice-Rector's Office for Research (VRI). These results show that most of the main authors of the FHS (70%) do not have any link to a group endorsed by Colciencias and their publications do not seem to come from a formal project registered in the VRI or have participated in any call. Today, the Universidad del Cauca has only two journals indexed in the Publindex registry of Colciencias, which makes evident the need for more publications of this type where both research groups and professors can publish.

Indirect measurement of academic quality can be done through intellectual and scientific production and bibliometric indicators that measure the quality and quantity of publications and allow evaluating individual researchers, journals and universities. (33) In 2010, Frenk *et al.* (34) published a study on barriers to research among orthopedists; it is important to note that this Spanish study has a short version. (35) This study found little literature on the subject, but at the same time pointed out the concern for a necessary change in medical education that favors research, writing and publication. For researchers, it is also essential to go beyond the departmentalization of the knowledge plan proposed by Flexner in 1910 and avoid the so-called "tribalism" of the professions, in this case the departments, that is, their tendency to act in isolation or even compete among them. (34)

Nowadays, 17 Colombian journals in the health area are registered in SCOPUS, but none of them belong to the Q1. (25) The Revista de la Facultad de Ciencias de la Salud of Universidad del Cauca, the local journal, has the largest number of articles published by the authors of the same faculty during the study period, which shows that the authors of the FHS prefer publishing locally, perhaps because of a close relationship with the Editorial Committee and because of the easy access to the language in which its contents are published. (12) However, it is possible for this trend to change due to the new classification policies of the journals registered in Colciencias, which leave local or regional journals without an important support although they seek to avoid inbreeding in the publication.

According to the study by Rodríguez-Morales (26) at Universidad Tecnológica de Pereira, of the total of publications, 45.5% were published in quartile I journals (Q1), while the present study only found 3.2% artciles published in Q1 journals. In that same study, of the total authors (n = 55) only one was classified in the Senior category, 10 in the Junior category and the others were not registered (26); these findings were similar to those of this investigation where only two authors were classified in said categories. These data clearly show that there are few researchers recognized by Colciencias in the FHS and that this seems to be a common reality in the faculties of health and medicine throughout the country. (36)

Sánchez-Bello *et al.* (37), in a study carried out between 2001 and 2015 in Colombia, highlight that the scientific production of a medical school can be considered essential, since new possibilities can be extended to improve the care provided to patients through innovation. In addition, the volume of scientific production of medical schools in Colombia is concentrated in a few universities, and may even appear to be null in other institutions. (38)

In a consensus article of orthopedists on the barriers to research in Latin America (35), the authors found research designs difficult to carry out, as well as little ability to read journals in English, lack of incentives or academic recognition, poor funding for research projects and weak publication in high-impact journals. The authors considered that a solution to these barriers is using medical teaching models based on evidence-based medicine (EBM), give residents feasible and manageable research questions, seek support through incentives or grants, partner with universities with access to journals, and use databases to directly access information. (33)

According to Sánchez-Bello *et al.* (37), of the few professionals who investigate, 61% do not go beyond presenting an abstract in oral format or poster in congresses, and in fact about 40% of them never become an article and, of course, are never published in indexed journals. Therefore, according to the current policies of Colciencias on visibility and productivity it is difficult to generate any impact in the field of research. (38)

However, many of the shortcomings exposed here can be solved by designing educational policies aimed at addressing the aforementioned barriers, promoting scientific culture, generating research groups or incubators and adopting the scientific method as the basis for medical research (26,39), but these policies also demand investment and interest. One of the implemented strategies has been the promoting the implementation of the scientific method in clinical practice, which, for nearly three decades, has fostered the EBM movement by promoting clinical actions based not only on experience but also on the critical reading of scientific publications. (40,41)

Research groups or incubators are another strategic way to favor health research at the undergraduate level, because they help to appropriate the academic and institutional culture of educational and scientific processes. They are also the place where methodological tools can be strengthened, research processes can be experimented, products can be socialized and academic learning spaces can be strengthened. (42)

Conclusion

These findings point out the need for greater institutional support for health research, the creation and support of research groups and incubators, and the promotion of academic programs for better proficiency in the English language to facilitate the production of new knowledge and, particularly, to ensure that the FHS and the Universidad del Cauca itself have a greater degree of visibility in both national and international scientific fields.

Conflicts of interest

None stated by the authors.

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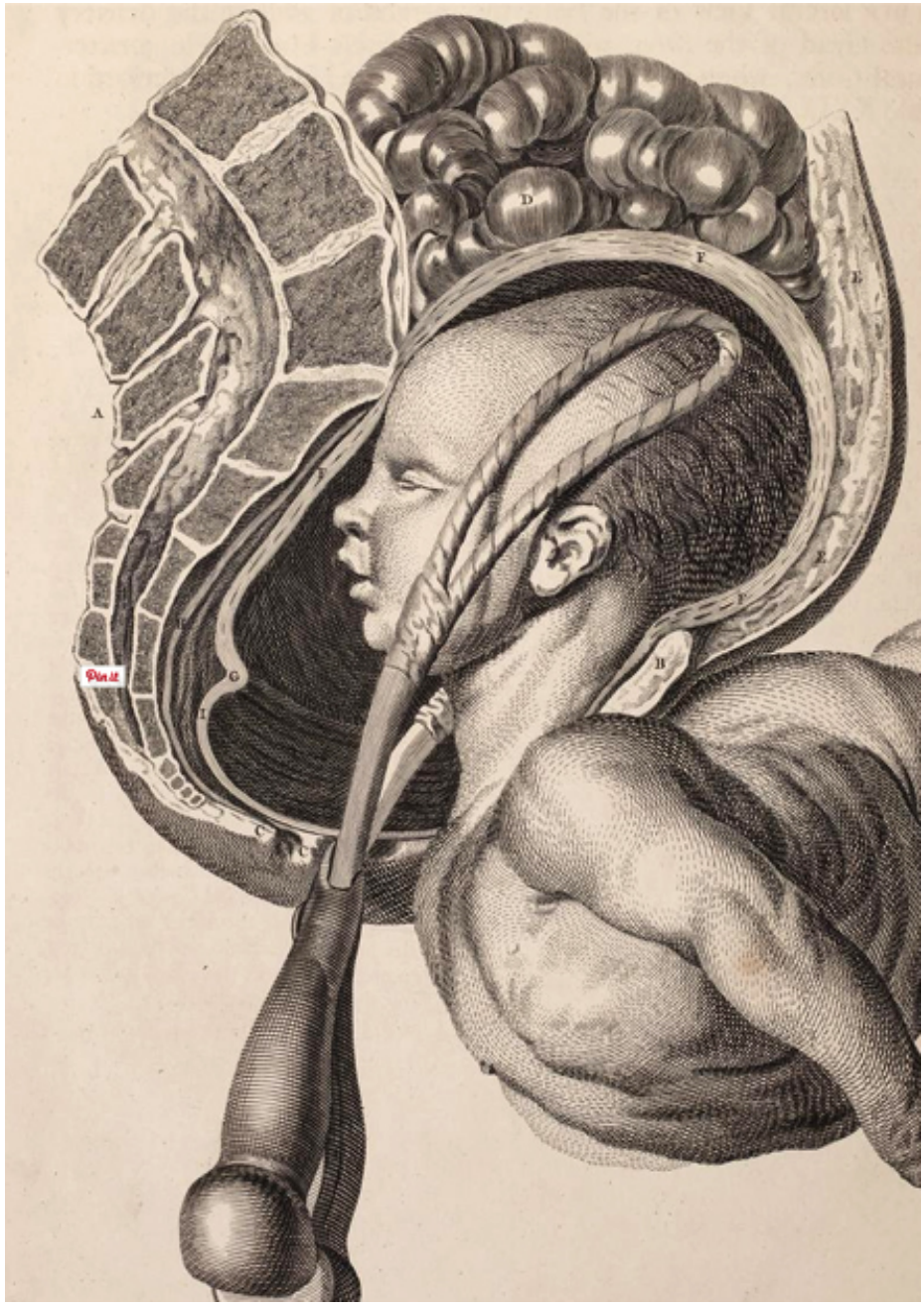
Annex 1. Information search strategies

Common strategy	Filiation: Universidad del Cauca / University of Cauca Date: Jan 2010 to Apr 2016
SCOPUS	AF-ID("Universidad del Cauca" 60051434) AND (LIMIT-TO(PUBYEAR,2016) OR (LIMIT-TO(PUBYEAR,2015) OR (LIMIT-TO(PUBYEAR,2014) OR LIMIT-TO(PUBYEAR,2013) OR LIMIT-TO(PUBYEAR,2012) OR LIMIT-TO(PUBYEAR,2011) OR LIMIT-TO(PUBYEAR,2010))
ScienceDirect	pub-date >2009 and pub-date <2016 and AFFILIATION (Universidad del Cauca) or (University of Cauca).
ProQuest	all(Universidad del Cauca) OR all(University of Cauca) Limites adicionales: Desde 01 January 2010 hasta 31 Abril 2016
EBSCO	TX Universidad del Cauca OR TX University of Cauca Limiters - Published Date: 20100101-20141231; Scholarly (Peer Reviewed) Journals; Hidden NetLibrary Holdings
PubMed	University of Cauca[Affiliation] OR Universidad del Cauca[Affiliation] AND ("2010/01/01"[PDAT] : "2016/04/31"[PDAT])
Ovid	Universidad del Cauca.in. or Universidad del Cauca.ab. or Universidad del Cauca *.au. or University of Cauca.in.
Wolkers Kluwer	Universidad del Cauca in Author Affiliation OR University of Cauca in Author Affiliation between years 2010 and 2016
Google Scholar	(Universidad del Cauca OR "University of Cauca") AND ("health sciences" OR "facultadcienciassalud")



WILLIAM SMELLIE, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

ORIGINAL RESEARCH

DOI: http://dx.doi.org/10.15446/revfacmed.v66n4.66132

Association between metabolic risk markers, body composition and different manifestations of strength in young adults

Asociación entre marcadores de riesgo metabólicos y diferentes manifestaciones de la fuerza en adultos jóvenes

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| Abstract |

Introduction: For decades, low levels of muscle strength (MS) have been associated with an increased risk of mortality from all causes.

Objective: To identify the correlation between values of different manifestations of MS and metabolic risk markers (MRM) in young university students.

Materials and methods: The study included 50 participants (37 men, 13 women), aged between 19 and 23 years. The grip strength of both hands and the muscular strength of upper and lower limbs were evaluated, as well as height, weight, body mass index (BMI), skin folds, HDL, cholesterol and triglycerides.

Results: No significant associations between MRM and the different manifestations of MS were found.

Conclusion: MS and MRM are separately associated with mortality risk factors and with suffering from cardiovascular diseases

Keywords: Triglycerides; Cholesterol; Lipoproteins, HDL; Muscle (MeSH).

Fernández-Ortega JA, Hoyos-CuartasLA, Ruiz-Arias FA. Association between metabolic risk markers, body composition and different manifestations of strength in young adults. Rev. Fac. Med. 2018;66(4):565-70. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.66132.

| Resumen |

Introducción. Desde hace varias décadas, los bajos niveles de fuerza muscular (FM) han sido asociados al incremento en el riesgo de mortalidad por todas las causas.

Objetivo. Identificar la relación entre los valores de diferentes manifestaciones de FM con biomarcadores de riesgo metabólico (BRM).

Materiales y métodos. El estudio estuvo compuesto por 50 participantes (37 hombres, 13 mujeres) con edades entre 19 y 23 años. Se evaluó la fuerza prensil de ambas manos, la potencia y la fuerza máxima de miembros superiores e inferiores, colesterol y triglicéridos. Además, se midió talla, peso, índice de masa corporal y pliegues cutáneos.

Resultados. No se identificaron relaciones significativas entre los BRM y las diferentes manifestaciones de la FM.

Conclusión. La FM y los BRM se relacionan con el riesgo de mortalidad y enfermedades cardiovasculares de forma separada.

Palabras clave: Triglicéridos; Colesterol; Lipoproteínas HDL; Fuerza muscular (DeCS).

Fernández-Ortega JA, Hoyos-CuartasLA, Ruiz-Arias FA. [Asociación entre marcadores de riesgo metabólicos y diferentes manifestaciones de la fuerza en adultos jóvenes]. Rev. Fac. Med. 2018;66(4):565-70. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.66132.

Introduction

Among physical characteristics, muscle strength (MS) has gained great importance within the context of health thanks to the progress made regarding knowledge of muscle functions, as it is considered an endocrine and immune organ and because of its role in metabolism. (1) At first, muscles were thought to be involved only in movement and regulation of energy metabolism; however, in the last decade, new evidence has suggested that skeletal muscle acts as an endocrine organ because it expresses and produces several cytokines and peptides in response to muscle contractions. (2,3)

Currently, there is sufficient evidence of the association between MS and the reduction of the risk of mortality from all causes. For decades, good levels of MS have been associated with a preventive

effect against chronic and metabolic diseases, while low muscle performance is associated with metabolic syndrome, cancer and increased risk of mortality from all causes, both in men and women. (4-7) This association has been confirmed in the meta-analyzes of Volaklis *et al.* (8) and Cooper *et al.* (9), who observed an inverse correlation between MS and mortality, even after adjusting factors for some confounding variables such as physical activity levels and cardiorespiratory fitness, both in adult and younger populations.

Timpka *et al.* (10) conducted a prospective study with 38 588 Swedish adolescents (16-19 years), and concluded that the risk of mortality from all causes decreased by 20% in participants with the best results in grip strength and leg extension, compared to those who obtained low MS results. Other studies (11-12) reported similar results and identified that subjects with moderate or high muscular capacity have a risk reduction of 35% and 44%, respectively, compared to those with low MS levels. However, up to date, few studies have evaluated the association between muscle strength and metabolic syndrome. (13)

The studies by Jurca *et al.* (14) and Aoyama *et al.* (15) reported an inverse correlation between MS and metabolic risk (β=-0.37; p<0.0001), which was marginally non-significant after further adjustment with aerobic fitness.

For this review, several search strategies were used including searches in specialized journals, in the Cochrane Central Register of Controlled Trials, and in the MEDLINE, PubMed, ProQuest, Hinari, SPORTDiscus, Embase, CINAHL, PsycINFO, PEDro and Ovid databases. After gathering all the data, it was observed that, until now, few studies have evaluated the association between MS and metabolic syndrome, and the results are contradictory. These observations were confirmed by Wijndaele *et al.* (13) and a recent meta-analysis conducted by Volaklis *et al.* (8)

In the Colombian context, several studies have addressed this issue. Ramírez-Vélez *et al.* (16), in a cohort study conducted with 6 095 adults aged between 18 and 40 years, observed that the group of participants with low and moderate levels of MS/body mass (BM) presented higher values in the cardiometabolic risk score index, regardless of their body mass index (BMI) (p<0.001). On the other hand, the group with high MS/BM values had higher levels of cardiometabolic protection.

On the other hand, García-Hermoso *et al.* (17) demonstrated that adults with good MS levels and low fat have significantly lower levels of metabolic risk compared to those with low MS levels. Ramírez-Vélez *et al.* (18) studied the association between MS and cardiovascular health in 1 199 children and young people and observed that high levels of MS (absolute or relative) are significantly (p<0.001) associated with better cardiovascular health.

The purpose of this study was to identify the correlation between the different manifestations of MS and the plasma concentrations of cholesterol, triglycerides, HDL-C and LDL-C in a group of young adults. This approach has been little studied, since most research works focus on the correlation between aerobic capacity and metabolic risk biomarkers, whose results are contrary to those related with MS, as concluded by Jurca *et al.* (14), who report that MS and cardiorespiratory fitness are independently and inversely related to metabolic syndrome.

Materials and methods

Design and population

This is an observational, descriptive and correlational cross-sectional study that was carried out in the Exercise Physiology Laboratory of Universidad Pedagógica Nacional in 2016. The group of participants consisted of 50 university students (37 men and 13 women) aged between 19 and 25 years, who participated voluntarily in the study. Inclusion criteria were: being a university student, men and women with low levels of physical activity and capable of performing physical exercise; exclusion criteria were: suffering from any type of pathology, being habitual smokers or drinkers, and having participated or being involved in structured programs of physical exercise or training in the last year.

This study was designed following the deontological norms recognized by the Declaration of Helsinki (19) and the Resolution 8430 of 1993 of the Ministry of Health of Colombia (20), which regulate clinical research in humans. The Research Ethics Committee of the Universidad Pedagógica Nacional (VGU-400, March 28, 2017) approved the study. In addition, all participants were informed of the details of the study and signed the informed consent.

Variables

For the development of the study, the following variables were evaluated:

Body composition

Anthropometric measurements were total BM, evaluated using an electronic scale (Healht Metter 599 KL with 0.50g precision); height, measured with a height rod (Detecto D52, USA); and BMI, estimated using the formula BMI=weight (kg)/size $(m)^2$.

Maximum strength

Days before the assessments, the procedure of each MS and peak anaerobic power test was carefully explained to the subjects. Six minutes of specific warming-up of the involved muscle groups was performed before the evaluations.

The maximum muscular strength of the upper limbs was evaluated using the bench press test on a Smith machine by directly determining the one-repetition maximum (1RM). The test began with a load of 40% of the body weight of each subject and the participants were asked to perform 4-6 repetitions (21); at the end, the OMNI-RES scale was applied. (22) According to the score assigned to the effort, progressive increases of 10% were made. Maximum strength was determined when the subjects were only able to perform one repetition-maximum with said load. There was a 3-minute recovery period between each series to avoid fatigue.

The maximum strength of the lower limbs was evaluated performing a half squat on a Smith machine, using the same upper limb protocol, but starting with a load of 60% of body weight.

Peak anaerobic power

Peak anaerobic power of upper limbs was assessed using the Wingate test on a Monark 871E bicycle (Monark exercice, Varberg Sweden). Height and distance between the subject and the pedals of the bicycle were adjusted in order to align the glenohumeral joint with the center of the pedals; then three warming-up rounds were performed at 40RPM with a load of 0.10% of body weight and a sprint was executed for 5 seconds at minutes 2, 3 and 4. After 3 minutes of recovery, the participants performed the test using a load of 4.5% of body weight for men and 3.5% for women. (23)

Peak anaerobic power of the lower limbs was assessed by using the Wingate test on a Monark 834E bicycle (Monark exercice,

Varberg Sweden). Previously, the participants warmed-up for 5 minutes at 40RPM, with a load of 0.30% of body weight and a sprint was executed for 5 seconds at minutes 2, 3 and 4. After 3 minutes of recovery, the participants performed the test using a load of 7.5% of body weight for men and 6.7% for women. Saddle height was adjusted to ensure that knee flexion was not greater than 5 degrees.

The Optojump Microgate® Germany was used to estimate flight times (precision of 1/1000 seconds) with two types of jumps: countermovement jump (CMJ) and squat jump (SJ). Two attempts of each type of jump were made at intervals of 6 minutes between both, selecting the best record for statistical analysis.

Isometric strength

Grip strength of both hands was assessed by dynamometry method, using a Takei Grip-A dynamometer T.K.K 5001 (Scientific Instruments Co. Ltd, Tokyo, Japan) with a measuring range of 0-100kg and precision of 0.5kg. Two attempts were made with each hand, with recovery periods of 3 minutes; the best result was recorded. Likewise, isometric leg strength was evaluated with a Takei Back-A dynamometer T.K.K 5002 (Scientific Instruments Co. Ltd., Tokyo, Japan) with a measuring range of 0-300kg and precision of 0.5kg, using the same procedure.

Metabolic biomarkers

The analysis of plasma concentrations of triglycerides, HDL and total cholesterol (TC) was carried out on an empty stomach, asking the subjects not to consume any food after 11:00 pm the night before taking the blood sample. Blood was extracted from the cephalic vein, placing the subjects in supine position. Triglycerides were analyzed using the lipase/glycerol kinase/glycerol phosphate oxidase enzymatic method. HDL-C cholesterol was analyzed using the polyanion/cholesterol esterase/homogeneous oxidase enzymatic method. Measurements were made on an Olympus AU5400 analyzer (Olympus Diagnostica, Hamburg, Germany).

Statistical analysis

The results were analyzed using the SPSS software (version 20.0, SPSS, Inc., Chicago, IL). For the anthropometric, clinical, biochemical and strength condition variables, mean, standard deviation and coefficient of variation were calculated for each study group. On the other hand, to determine the correlations between variables of MS and metabolic risk markers, bivariate correlations were calculated through the Pearson coefficient for the total number of participants in the sample. The normality of the variables was verified by Kolmogorov-Smirnov test, using a level of significance of 5%. A qualitative rating scale was used according to the magnitude of the correlation observed: weak for values >0.40; moderate, between 0.41 and 0.60; strong, between 0.61 and 0.80; and very strong, between 0.81 and 1.

Results

The population that participated in the study had an average age of 21.8±2.3 years and 74% were men. Table 1 shows the descriptive statistics of the general anthropometric, biochemical, strength and peak anaerobic power characteristics of the study population.

Table 1. Morphological, biochemical, strength and peak anaerobic power characteristics of the population evaluated.

Characteristic	Men		Women		Difference by sex	%
	(n=37)	CV	(n=13)	CV		
Age (years)	21.4±2.9	0.13	22.2±4.8	0.22	0.8	4%
Weight (kg)	64.7±6.3	0.1	57±6.3	0.11	7.7	12%
Height (cm)	171±0,5	0.03	160±10	0.04	0.11	6%
Body mass index (kg/m²)	22.2±2	0.09	22.1±1.9	0.09	0.1	0%
Sum of skinfolds (mm)	102.8±31.8	0.31	175±30	0.17	72.3	41%
Triglycerides (mg/dl)	103.7±63.9	0.62	89.9±48.9	0.54	13.8	13%
HDL (mg/dl)	43.4±8	0.18	53.9±11.2	0.21	10.5	19%
Cholesterol (mg/dl)	167.9±37.4	0.22	169±35.1	0.21	1.4	1%
Grip strength in left hand (kgf)	39.1±6.3	0.16	30.6±4.4	0.15	8.5	22%
Grip strength in right hand (kgf)	40.3±7.4	0.18	31.9±4.7	0.15	8.4	21%
Isometric strength of lower limbs (kgf)	145.9±35.5	0.24	111±32.2	0.29	34	23%
Half squat (kg)	116.6±17.4	0.15	85.2±18.3	0.22	31.4	27%
Bench press (kg)	61.7±9.9	0.16	36.2±10.1	0.28	25.5	41%
Peak anaerobic power upper limbs (watts)	250.6±50.7	0.2	136±33.2	0.24	114.2	46%
Relative peak power upper limbs (watts/kg)	3.7±0.9	0.24	2.3±0.4	0.19	1.4	38%
Peak anaerobic power lower limbs (watts)	513±87.7	0.17	360±69.8	0.19	152.3	30%
Relative peak power lower limbs (watts/kg)	7.7±1.3	0.17	6.1±1	0.17	1.6	21%
Countermovement jump (cm)	26.4±5.3	0.2	18.2±4.5	0.25	8.2	31%
Squat jump (cm)	33.1±4.1	0.13	25.7±3.9	0.15	7.4	22%

CV: covariance.
Source: Own elaboration.

Table 2 presents the partial correlations between HDL-C values and strength and power indicators. HDL-C values have low and negative correlations with values $p<0.01$ and $p<0.05$ for muscle strength and power tests. No sex differences were identified in the distribution of total cholesterol. A higher proportion of women with HDL-C values >40 mg/dL and triglycerides >200 mg/dL were observed ($p<0.05$). No strong associations of HDL-C with the strength and power variables were found in the group of men or women.

Table 2. Correlation of HDL cholesterol with strength and power indicators.

HDL cholesterol	Men and women
Grip strength in right hand (kgf)	r=-0.312 *
Bench press (kg)	r=-0.510 †
Grip strength in left hand (kgf)	r=-0.363 *
Half squat (kg)	r=-0.381 *
Peak anaerobic power upper limbs (watts)	r=-0.333 *
Peak anaerobic power upper limbs (watts/kg)	r=-0.351 *

* The correlation is significant at 0.05 (bilateral).
† The correlation is significant at 0.01 (bilateral).
Source: Own elaboration.

Discussion

The present study provides elements to discuss the relationship between different manifestations of MS and plasma values of triglycerides, total cholesterol, LDL-C and HDL-C. Evidence on this regard is scarce and contradictory, and the results of certain studies are difficult to interpret due to some weaknesses and the inadequate control of factors that may influence lipid metabolism and statistical power. (24) This statement is confirmed in the review carried out by Durstine *et al.* (25) and in the meta-analyzes of Kelley *et al.* (26) and Zhang *et al.* (27), who analyzed workout plans in different populations and found few interventions that used MS training as a physical activity strategy. Most studies used low intensity aerobic work.

Blood levels of HDL-C are 4-24 mg/dL, but they are higher in subjects who perform physically demanding work or perform resistance exercise on a regular basis, compared to less active people. The relative differences of HDL-C between these two groups range between 9% and 59%. (25,28) The same pattern is observed with TC and LDL-C. (26) However, this situation is not the same when MS is the physical activity performed.

Zhang *et al.* (27) observed, in a population of young adults, a low to moderate negative correlation between the different manifestations of strength and HDL-C, as well as a lack of correlations with triglycerides, TC and LDL-C. These results agree with the results of this study and the reports of most of the previous works.

Jurca *et al.* (14) identified a moderate inverse association between the prevalence of metabolic syndrome and MS (β=-0.37, $p<0.0001$), which decreases (β=-0.08, $p<0.01$) when it is adjusted with cardiorespiratory fitness. (29)

Wijndaele *et al.* (13) reported low inverse correlations in men and moderate correlations in women ($p<0.05$) between MS and triglycerides, cholesterol and HDL-C.

Artero *et al.* (30) identified moderate inverse correlations between grip strength and triglycerides ($p<0.01$), and HDL-C and cholesterol ($p<0.001$).

Steene-Johannessen *et al.* (31) conducted a study to identify the independence between MS and cardiorespiratory fitness for the risk of metabolic disease. The researchers evaluated standing long jump-explosive power, grip strength, abdominal strength and cardiorespiratory capacity directly using the peak oxygen uptake. The results indicate a negative association of MS and metabolic risk (β=-0.337, $p<0.001$), and a weak negative correlation of grip strength with triglycerides and positive with HDL-C.

Regarding the methodology, the most commonly used tests in previous studies for the assessment of maximum strength and peak power were hand dynamometry and long jump. For this study, dynamic strength tests were used based on the 1RM methodology, such as bench press or squats, and explosive tests such as the Wingate test, CMJ or SJ, which could make the results between the studies little comparable. For example, in this study, the best correlation of HDL-C was obtained with bench press and not with hand dynamometer, which had similar correlation values to power in upper limbs. This could indicate that the level of correlation between HDL-C and MS depends on the type of test used to assess the maximum strength.

Fernández *et al.* (32), in a study on the correlation between the different manifestations of strength, observed that although the musculature of the upper or lower limbs is under evaluation, there is great variability in the correlation between the tests. This difference could be explained by the contribution of the muscle groups involved in the movements to each of the tests, which may not be the same. This would indicate that the information provided in each of the tests is specific to the muscle group and movement, and cannot be extrapolated to another muscle group or movement. This difference can also be attributed to the neuromuscular implications of the different types of muscle actions involved in each test.

However, the reason why there are no positive correlations between high levels of strength and plasma levels of HDL-C, as is the case of cardiorespiratory capacity, remains unresolved. In this regard, Prabhakaran *et al.* (24) carried out an MS training for 14 weeks, with two sets of eight repetitions and bench press, leg extension and rowing workouts performed at 85% of 1RM. The results of the program led to significant reductions of cholesterol by 9% ($p<0.05$) and LDL-C by 14.3% ($p<0.05$) in the TC/HDL ratio. Triglycerides and HDL-C did not report significant changes.

Likewise, Kokkinos *et al.* (33) carried out a strength-training program in 37 subjects with three types of exercises. The results indicated that none of the proposed workout plans generated significant changes in plasma concentrations of triglycerides, total cholesterol, HDL-C and HDL2-C. Later, the same authors carried out another study with trained subjects performing strength work at 70% of 1RM and did not observe significant changes in plasma concentrations of triglycerides, TC, HDL-C or LDL-C. (34)

In the study by Manning *et al.* (35), 16 sedentary obese women trained 3 times a week for 12 weeks performing three sets of 6-8 repetitions at 60-70% of 1RM. No significant changes were observed in body weight, BMI or CT, HDL-C, LDL-C, TG, TC/HDL-c, apo AI or apo B-100 levels. (35)

Goldberg *et al.* (36) developed a free-weight workout plan for 16 weeks in a group of sedentary young men and women. Women presented a 9.5% reduction in cholesterol, 17.9% in LDL-C and 28.3% in triglycerides. The total cholesterol/HDL-C and LDL/HDL rates were reduced by 14.3% and 20.3%, respectively. In men, the LDL-C cholesterol was reduced by 16.2%, while the total cholesterol/HDL and LDL/HDL levels were reduced by 21.6% and 28.9%, respectively.

Only one study (37) that observed an increase in HDL-C and a decrease in TC and LDL-C in a similar way was identified; this study was conducted through strength training and resistance training. There, the results would indicate that, although participants presented significant gains in MS, strength training did not alter the plasma levels of TC, HDL-C, LDL-C, triglycerides, nor the TC/HDL-C ratio, as is the case of aerobic training programs. One possible explanation is the specificity of the adaptive response to physical activity, which, according to the level and type of stimulation, generates changes in hormonal profiles and inflammatory and immune parameters, as well as intrinsic changes in skeletal and cardiac muscles.

Although the mechanisms underlying the effect of physical activity on the lipid profile are not clear, one hypotheses raised several decades ago about the cause of the increase in plasma HDL-C due to the effects of aerobic exercise is related to the metabolic adaptations that the muscle undergoes due to an increase in enzymatic activity, which leads to an increase in the capacity to oxidize fatty acids in comparison with glycogen. This better use of plasma triglycerides occurs because of the increase in the lipoprotein lipase (LPL) activity that is located in the lumen of blood capillaries and hydrolyzes triglycerides, allowing the uptake of free fatty acids (FFA) and the increase in muscle angiogenesis. (38)

One of the possible mechanisms involved in HDL-C modulation is reverse cholesterol transport, which removes cholesterol from the circulation and distributes it to peripheral tissues and the liver. Two important events occur during aerobic exercise: 1) the increase of lecitin-cholesterol acyltransferase (LCAT), an enzyme responsible for ester transfer to HDL cholesterol, and 2) the reduction of cholesterol ester transfer protein (CETP), the enzyme responsible for the transfer of HDL cholesterol to the other lipoproteins. (39,40) This increases

the activity of lipoprotein lipase, although data on this issue are inconsistent. (41) All this increase in the degradation of lipoproteins rich in triglycerides, by means of apoproteins transfer could lead to an increase in the plasma concentration of HDL-C.

In physiological terms, aerobic physical activity performed for a long period creates resistance and keeps the cardiac pump elevated at a constant rate, which can boost cardiac function and increase HDL. (28)

This series of biochemical and physiological mechanisms is not activated in the same way during strength workout. Each type of workout poses a challenge for the organism's control systems to generate an adequate adaptive response. In this sense, and from a functional and metabolic point of view, muscle cells are not a homogeneous tissue and the cell signaling mechanisms and endocrine responses for the two types of workouts are different. Fatty acids are oxidized mostly in type I oxidative fibers that are primarily activated during low to moderate intensity physical activity. On the contrary, strength workout with moderate or high loads increases the activation of glycolytic fibers, therefore decreasing the participation of oxidative fibers. Similarly, cardiovascular function during SM workout is intermittent, since a high heart rate pump is not maintained at a constant rate, but for short periods (2-3 seconds) followed by recovery.

These statements are supported by the work of Aellen *et al.* (42), who studied the effects of anaerobic and aerobic training performed 4 times a week for 9 weeks on lipoprotein concentrations in a group of 62 healthy untrained men. 33 subjects performed physical activity at low intensity, 16 at an intensity above the anaerobic threshold (blood lactate concentration >4 mmol) and 12 served as controls. The caloric expenditure calculated from both training groups was similar; TC, HDL-C, the subtractions of HDL-C (HDL2-c, HDL3-c) and LDL-C were evaluated in the three groups. With anaerobic training, these variables turned to the opposite direction compared to aerobic training, which influenced the lipoprotein profile in the desired direction. The authors concluded that training above the anaerobic threshold has no effect on the blood lipoprotein profile and that changes are achieved with moderate training intensities. The study by Said *et al.* (43) obtained the same results. However, Lira *et al.* (44), in their study on acute response to different percentages of 1RM, observed that the concentration of HDL-C was significantly higher after training at 50% -1RM and at 75% -1RM compared to 110%.

Conclusions

This research identified a moderate to low inverse correlation between HDL-C and the different manifestations of MS. However, these results are preliminary and should be observed with caution due to several study limitations that may have generated a bias. Therefore, it is suggested to carry out studies with a larger sample size, but with the same participation of men and women to verify if similar responses are presented between them.

Along the same lines, a nutritional analysis should be included to quantify the energy expenditure of each subject, as well as the quantification of the level of physical activity and the determination of the ethnic group of each participant. With regard to women, it is important to know whether they are menstruating during the collection of the samples and which phase they are in due to the effect it has on the fluctuations of the lipid profile.

Due to the lack of evidence and the contradictory results of different works carried out on the subject, this study contributes to the consolidation of the evidence of the relationship between MS and metabolic risk markers and also indicates the need to establish this relationship from broader valuations of MS.

Conflicts of interest

None stated by the authors.

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ORIGINAL RESEARCH

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Risk of eating disorders in a group of high school students of a school in Bogotá D.C., Colombia. 2016

Riesgo de trastornos del comportamiento alimentario en un grupo de estudiantes de secundaria en un colegio de Bogotá D.C., Colombia. 2016

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| Abstract |

Introduction: According to estimations, eating disorders affect 1-4% of the general population. In Colombia, few studies address this issue; however it has been found that the percentage of women with anorexia in Bogotá D.C. is similar to figures worldwide.

Objective: To identify the risk of developing eating disorders (ED) in sixth through eighth grade students from a private school of Bogotá D.C.

Materials and methods: Cross-sectional quantitative study conducted in sixth through eighth grade students from a school of Bogotá D.C., who were applied the EAT-26 Test. Those with scores greater than 20 were classified as having symptoms of risk of ED, and parents were summoned to receive prevention education on this matter.

Results: 979 students were surveyed: 523 were boys and 456, girls, a 9.4% prevalence of ED risk was found. Male students of the lower grades had a higher risk of suffering from eating disorders; predominance was observed in the female sex as the grade level increased.

Conclusion: Men are more likely to develop risk symptoms for eating disorders, especially at early ages. Designing strategies to prevent the onset of this disorder in the school population is recommended.

Keywords: Anorexia; Bulimia; Prevalence; Students; Adolescent (MeSH).

| Resumen |

Introducción. Se estima que los trastornos alimentarios afectan el 1-4% de la población general. En Colombia son escasos los estudios al respecto, sin embargo en Bogotá D.C. se ha encontrado que el porcentaje de mujeres con anorexia es similar al que existe a nivel mundial.

Objetivo. Identificar el riesgo para el padecimiento de trastornos de conducta alimentaria (TCA) en estudiantes de sexto a octavo grado de un colegio privado de Bogotá D.C.

Materiales y métodos. Estudio cuantitativo transversal cuya muestra estuvo constituida por los estudiantes de grado sexto a octavo de un colegio en Bogotá D.C., a quienes se les aplicó el Test EAT-26. Se consideró que quienes obtuvieron puntaje >20 presentaban síntomas de riesgo de TCA, por lo que sus padres recibieron intervención educativa de prevención.

Resultados. Se encuestaron 979 estudiantes: 523 niños y 456 niñas, hallando una prevalencia de síntomas de riesgo de TCA de 9.4%. Los estudiantes de sexo masculino de los grados inferiores presentaron mayor riesgo de padecer TCA; se observó predominio en el sexo femenino a medida que aumentó el grado escolar.

Conclusión. Los varones tienen mayor tendencia a presentar síntomas de riesgo para padecer TCA, en especial en edades tempranas. Se recomienda diseñar estrategias para prevenir la aparición de este trastorno en la población escolar.

Palabras clave: Anorexia; Bulimia; Prevalencia; Estudiantes; Adolescente (DeCS).

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Introduction

Eating disorders (ED) are complex disorders that involve two types of behavioral disorders: some directly related to diet and weight, and others derived from the relationship with oneself and with others. These disorders have become an emerging pathology in developed and developing countries, being the third most common chronic disease among adolescents after obesity and asthma. (1) EDs caused by food restriction are classified as anorexia nervosa (AN), bulimia nervosa (BN) and disorders not otherwise specified in the DSM-5. (2)

AN is a psychiatric disease characterized by a significantly low body weight and fear of gaining weight. Its most important feature is an alteration in the way how an individual perceives self-image or weight; in fact, this distortion of body image is a diagnostic criterion. (3,4) For its part, BN is manifested by episodes of excessive food intake, followed by compensatory behavior in order to minimize or eliminate the effects of the excess, including purges, fasting or exercise. Unspecified behavioral disorders include binge eating disorder and other eating disorders that do not meet the clinical criteria of AN or BN. (4,5)

The causal risk factors of eating disorders are multifactorial, as they result from the complex interaction of psychological, physical and sociocultural factors that interfere with the behavior of the individual, making their etiology difficult to understand. (5) This makes them complex pathologies that require a multidisciplinary approach, involving professionals like psychologists, psychiatrists, doctors, nutritionists, among others. Likewise, research on ED has increased, perhaps due to the growing incidence reported in the last decade; the serious physical, psychological and social consequences that have caused these disorders (6), and because they involve mainly children and adolescents, who are going through a growing stage, developing their personality and self-esteem, and strengthening habits that will remain for a long time. 85% of EDs begin during adolescence (7), with serious repercussions for life.

According to estimates, eating disorders affect between 1% and 4% of the general population, especially adolescent and young adult women, with a distribution of 0.5% to 3% for AN and 1% to 4% for BN. 3.2% of women between the ages of 18 and 30 have some type of eating disorder regardless of their socioeconomic status. In addition, it has been found that EDs in men have a prevalence of 5% to 10% of that estimated for women (7); AN and BN affect about 3% of women throughout their lives and it could be said that 90-95% of cases occur in women. Regarding AN, most cases occur in young women, but men seek treatment more often (5-10%). (8) In teenagers, prevalence ranges between 0.3% and 2.2%, being higher in females. However, some studies in adolescents aged between 13 and 18 years have not found significant differences over time between both sexes. During middle and late adolescence, women are at greater risk. (5)

On the other hand, pilot tests done in schools of Bogotá D.C. have found that the percentage of girls with anorexia matched figures worldwide, that is, between 1% and 4%. (9) A prevalence of 17.7% was estimated in the university population of Medellín, where 0.8% is for AN, 2.3% for BN and 14.6% for non-specific ED. (7)

There are several questionnaires designed to screen and identify EDs, one of them is the Eating Attitudes Test (EAT), designed by Garner & Garfinkel (10) to assess abnormal feeding attitudes, especially those related to fear of gaining weight, the urge to lose weight and the presence of restrictive eating patterns. The EAT is an easy instrument to apply and correct, and is sensitive to symptomatic changes over time. At first, it was a 40-item instrument adapted to the Spanish language, and then, through a factor analysis, a 26-item version was developed, which is highly predictive and which, in turn, was adapted to Spanish. (10)

The purpose of this research was to identify the risk of suffering from eating disorders in sixth through eighth grade students of a private school in Bogotá D.C., Colombia, by applying the Eating Attitudes Test (EAT-26) for screening purposes. It is worth mentioning that this research addresses the issue of identifying the risk of suffering from eating disorders because it was determined using a validated survey; the disease was not diagnosed.

The research was carried out in sixth to eighth grade students considering the psychological and physical changes experienced by this population during their transition from elementary to high school, since they achieve more freedom at this point regarding food selection and parents may reduce supervision on this aspect. In addition, at this stage of life eating habits begin to consolidate and are closely linked to the environment of the children and their culture; during this period, the importance of self-esteem and self-acceptance regarding body image to feel accepted in their environment is evident. (11)

The identification of the risk of developing an ED is important to plan and carry out appropriate interventions that avoid the deterioration of the health condition of the subjects involved, taking into account the stage of development in which they are and the severity of the symptoms that they may present. (12)

Materials and methods

This was a quantitative and transversal study; the sample included sixth through eighth graders of a private school of Bogotá D.C. and was constituted by 990 students who, voluntarily, with prior informed consent by the legal guardian and with the child's consent, decided to participate in the study. The age range of the participants was 10 to 15 years.

The updated version of the study, as well as this article, were approved by the Ethics Committee of the Faculty of Medicine of the Universidad Nacional de Colombia through Act 013-238-18 of September 14, 2018 and followed the principles of the Declaration of Helsinki (13), the guidelines for good clinical practice and the ethical aspects specified in Resolution 8430 of 1993 of the Colombian Ministry of Health (14), Title II, Chapter I, where respect for dignity and protection of the rights and welfare of the participants prevailed. According to this resolution, this study was considered as a minimum risk investigation (14), once the instrument was applied during interviews. The parents of children with a certain risk were summoned to inform them of the results and possible options to follow.

The instrument used was the EAT-26 test, an attitudinal questionnaire that indicates the risk of suffering from an eating disorder that consists of 26 questions that inquire about the behaviors of people suffering from a disorder, among them, vomiting after eating, feeling guilty after eating high-calorie foods, exercising to burn calories, and others. The cut-off point for identifying the risk of suffering from an ED was a score $\geq$20; a higher score meant a greater number of abnormalities in the eating behavior. (15,16)

This instrument has been used and validated by several national and international studies to assess the presence of symptoms of eating disorders. In a validity study conducted by Constain *et al.* (17), the EAT-26 showed a 92% reliability; these authors concluded that the instrument was "appropriate for screening possible EDs, contributing to early detection in young women." Likewise, the study by Vera-Morejón (18) determined a test sensitivity of 48.5%, a specificity of 94% and a efficiency of 77%, concluding that the EAT-26 is a valid test for detecting EDs, which can be applied in mixed populations (composed of men and women) and with high specificity.

For this research, the information was analyzed using descriptive statistics in the Microsoft Excel 2010 program.

One of the limitations of this research is the fact that the responses of the test are self-reported, reason why the participants could have omitted or failed to tell the truth in order to conceal information when they were informed about the objective of the test and the possible social and family implications of completing it with honesty.

Results

The sample selected for the study was composed of 979 sixth to eighth grade students, 523 boys and 456 girls, of a school in Bogotá D.C.; the age range of the participants was 10 to 15 years. The distribution was made by grade as follows: 311 students of the sixth grade, 335 of the seventh grade and 333 of the eighth grade.

A 9.4% prevalence of risk of suffering eating disorders was found. Regarding the distribution by sex, it was slightly higher in boys (9.8%) in comparison with the prevalence observed in girls (9.2%) . The highest incidence of cases identified as having a risk of developing EDs was found in the sixth (44%) and seventh (31%) grades (Figure 1).

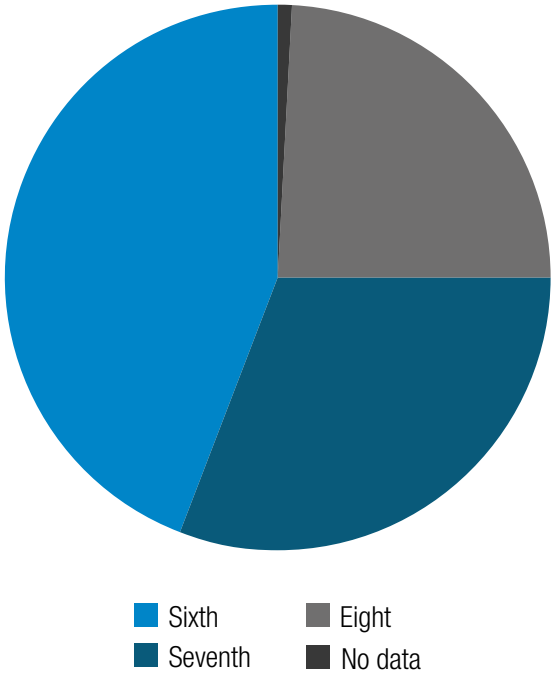

Figure 1. Students at risk of developing eating disorders by grade.
Source: Own elaboration.

In the lower grades, male students present a higher number of symptoms or risk behaviors for developing EDs, and as the school grade increases, there is a predominance of risk in the female sex (Figure 2).

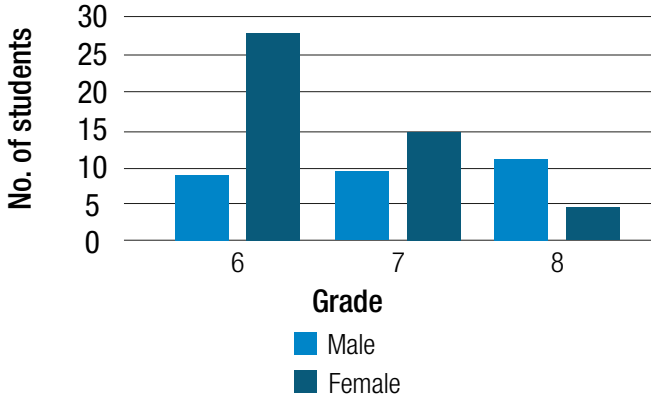

Figure 2. Distribution by sex and grade at risk for eating disorders.
Source: Own elaboration.

Discussion

The prevalence of EDs found in this investigation is higher compared to studies conducted in other schools of Colombia; for example, the risk found in Santander was 5.8% for bulimia and 1.7% for anorexia. (19) Another study conducted in Bucaramanga, which sought to determine the internal consistency and criterion validity of the eating behavior survey (Encuesta de Comportamiento Alimentario - ECA) in adolescents, reported the following prevalence figures: 1.6% for AN, 3.1% for bulimia and 2.75% for unspecified EDs. (19)

A study, conducted in a Mexican population with an average age of 16.71 years and from various communities of the municipality of Tejupilco, found that 14% of men and 20% of women were prone to develop EDs and related symptoms (4), figures higher than those found in this research, perhaps because the mean age was higher in the aforementioned study.

As reported by Moreno-González & Ortiz-Viveros (20) in another study on the relationship between EDs and self-esteem, a greater tendency to suffer from these disorders was observed in women, with a percentage of 12% in the reported clinical cases, compared to the 4% reported for men. Also, in an study carried out in Bogotá D.C. and in the central savannah of Cundinamarca in students aged between 12 and 20 years who responded the EAT-26 test and the Zung Self-Rating Anxiety Scale, the frequency of EDs found in the screening phase was 15.1%. This research clearly showed that EDs occur at an early age. (21)

On the other hand, a study carried out in Lima, Peru, in which 483 female students with an average age of 14 ± 3 years were included, found that 13.9% of the participants were at risk of developing EDs (22), a percentage higher than that reported by the present study, with the difference that the population was exclusively female in the Peruvian study.

Regarding men and women who are at risk of suffering from EDs, the results of this research are similar to those found in a study conducted by Unikel *et al.* (23) in Mexico to identify risk behaviors in students aged between 13 and 18 years. However, the same study showed that risk behaviors increase as age increases, which contrasts with this research, where a greater risk was found in students of lower grades, while a decrease in the number of cases with risk behaviors for EDs was observed as age increased.

In terms of sex comparison, the results of a study conducted in adolescent students from the metropolitan area of Bucaramanga show that the SCOFF questionnaire had an internal consistency of 0.521 in males and 0.584 in females. On the other hand, factor analysis showed a factor that explained 34.7% of the variance in males and a factor responsible for 37.5% of variance in females. (24)

EDs can negatively impact a child's health status and cognitive development, so, according to the results reported here, it is necessary to design different strategies to prevent the onset of this condition in school populations, as well as the inclusion of a food and nutrition education program in school curricula in order to improve nutritional and eating habits in this population; in this way, long-term complications will be avoided. In addition, it is essential to inform the parents of the students at risk of suffering from EDs about the nutritional behavior of their children, so that these disorders can also be prevented and treated at home.

Conclusion

This study found that the children at highest risk of suffering from EDs were males, especially at young ages, which corresponds to sixth grade students aged between 11 and 12 years. These results differ

from those reported by other studies because of the context and age of the participants. For this reason, future studies should be carried out in other private schools of Bogotá D.C. to have more elements of analysis on the prevalence of this type of EDs in this population.

Conflicts of interest

None stated by the authors.

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ORIGINAL RESEARCH

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Videoconferencing in occupational therapy in hospital contexts and palliative care

Videoconferencia en terapia ocupacional en contextos hospitalarios y cuidados paliativos

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| Abstract |

Introduction: Communication and information technologies in the health context allow optimizing inter-institutional activities in continuing education.

Objectives: To describe the activities performed by of the Special interest group on Occupational Therapy in hospital contexts and palliative care and to discuss the importance of videoconferencing in the continuing education process of Occupational Therapy students and health professionals in this field.

Materials and methods: A documentary, retrospective, and descriptive study was conducted. The special interest group was created through the Telemedicine University Network, which is a high-speed network connecting university hospitals and health teaching centers in Brazil. There are 34 operating centers from 15 Brazilian states and one Chilean university registered in the group.

Results: 36 videoconferences were made between August 2013 and December 2017, where relevant topics for the practice of occupational therapists in hospital contexts and palliative care were presented. Videoconferencing allows occupational therapists to access updating material on specific topics through interactive communication sessions in virtual spaces regardless of their current location, thus overcoming geographical barriers.

Conclusion: Videoconferencing contributes to the updating and spreading of knowledge and professional practices among students and occupational therapists in their professional field.

Keywords: Occupational Therapy; Telemedicine; Videoconferencing (MeSH).

| Resumen |

Introducción. Las tecnologías de la información y de la comunicación en la salud permiten la optimización de actividades interinstitucionales en educación a distancia.

Objetivos. Describir las actividades del Grupo de interés especial en terapia ocupacional en contextos hospitalarios y cuidados paliativos y discutir la importancia de la videoconferencia para la educación continua de los profesionales y estudiantes de terapia ocupacional en este ámbito.

Materiales y métodos. Estudio documental y retrospectivo-descriptivo. El grupo de interés especial fue creado a través de la Red Universitaria de Telemedicina, que consiste en una red de alta velocidad que conecta hospitales universitarios y centros de enseñanza de salud en Brasil. El grupo incluye 34 centros operativos registrados en 15 estados brasileños y una universidad de Chile.

Resultados. Se realizaron 36 videoconferencias entre agosto de 2013 y diciembre de 2017 con temas relevantes para la práctica de los terapeutas ocupacionales en contextos hospitalarios y cuidados paliativos. La videoconferencia permite la actualización científica de terapeutas ocupacionales en temas específicos de la especialidad a través de comunicaciones interactivas en espacios virtuales sin importar la distancia, superando así barreras geográficas.

Conclusión. La videoconferencia contribuye a la actualización y difusión de conocimientos y prácticas profesionales entre estudiantes y terapeutas ocupacionales en el ámbito profesional.

Palabras clave: Terapia ocupacional; Telemedicina; Videoconferencia (DeCS).

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Introduction

The emergence of modern interactive technologies has changed the conception of health care, especially when it comes to overcoming geographical barriers and achieving remote connectivity between users and health professionals. Information and communication technologies help optimizing services and processes that generate a convergence of technological solutions and quality health services, which enables improvements in activities related with health education, health logistics planning, teleassistance regulation, and the implementation of methods required to enable multi-institutional activities.

Teleconferencing or videoconferencing emerged in the 1960s as a business communication tool for facilitating remote business meetings. Nowadays it is widely used due to video technology development and the acceptability of international telecommunication standards.

The Brazilian National Research and Educational Network (RNP for its acronym in Portuguese) is an institution created by the Ministry of Science, Technology, and Innovation (Ministério da Ciência, Tecnologia e Informação - MCTI) in 1989 in order to promote integration and collaboration among health professionals working in institutions dedicated to telehealth, as well as to operationally support multi-institutional discussion groups and permanent education. In this sense, the Telemedicine University Network (Rede Universitária de Telemedicina - RUTE), a project created in Brazil in 2005, has allowed research groups to have exchange sessions between them through a high-speed network.

As of 2007, the National Telehealth Program was implemented as a Brazilian government intersectoral strategy (linking the MCTI, the Ministry of Health and the Ministry of Education) in order to coordinate tele-education and teleassistance initiatives, together with interconnection infrastructures of university hospitals and health teaching centers in Brazil. (1-3) By the end of the second semester of 2017, the RNP comprised 134 operating centers and over 300 institutions with approximately 50 full operation Special interest groups (SIGs) in several health professions, specialties, or subspecialties such as Psychiatry, Cardiology, Ophthalmology, Dermatology, Nursing, Occupational Therapy, and others. (4)

SIGs are virtual spaces where professionals from linked institutions promote activities such as debates, case discussions, lessons, diagnosis, researches, and distance assessment, by addressing several medical specialties and subspecialties for a number of health professionals in different levels of professional training. These groups provide the opportunity of interaction between partners involved in the implementation of computing and telecommunication technologies, thus promoting and supporting the application of telemedicine in their respective specialty.

The creation of SIGs is an interesting and effective strategy for disseminating information and producing exchange opportunities between professionals and students of Occupational Therapy. According to the Canadian Association of Occupational Therapists in British Columbia:

> "Special interest groups and practice networks provide a forum for sharing expertise and experience in occupational therapy in particular areas of professional interest [...] provide opportunities for [...] networking, information exchange, and resource sharing for occupational therapists through meetings, newsletters and document sharing. They promote and facilitate continued education through informal education events or conferences and publications." (5)

The SIG on Occupational Therapy in hospital contexts and palliative care was established in August, 2013. Its purposes consist of promoting technical and scientific knowledge and exchanging information, experiences and educational programs between professionals working in occupational therapy services of hospitals and universities in several states of Brazil, as well as between students, residents, and researchers interested in this health specialty. Presentations and discussions of topics, methods, technical and scientific approaches, clinical cases, researches, and issues on occupational therapy are held in monthly meetings through the RUTE. (4,6)

This SIG is an initiative of the Scientific Association of Occupational Therapy in Hospital Contexts and Palliative Care (Associação Científica de Terapia Ocupacional em Contextos Hospitalares e Cuidados Paliativos - ATOHosP), the first Occupational Therapy Specialty scientific society of Brazil, created in August, 2012. The professional specialty of occupational therapy in hospital contexts was officially recognized by the Federal Council of Physiotherapy and Occupational Therapy (COFFITO) by means of Resolution Nº 366 of May 2009, Resolution Nº 371 of November 2009, and is regulated by Resolution Nº 429 of July 2013. (7-9) Competences of this type of occupational therapist specialist include the direction, coordination and supervision of occupational therapy services, technical responsibility, leadership, counseling, auditing, teaching and research in general or specialized hospitals of medium or high complexity health care and in all phases of ontogenetic development.

The purpose of this study is to describe the operational dynamics of this SIG and the importance of videoconferencing for continuing education in occupational therapy in hospital contexts and palliative care.

Materials and methods

A documentary, retrospective, and descriptive study using RUTE electronic documents, ATOHosP records and the information available in both of their websites was conducted. (4,6)

Technological advances have allowed transmitting digital videoconferencing in narrower bands without losing image quality. Currently, it only requires a computer, a mobile phone or a tablet with internet connection and an internet browser, as well as a microphone and headphones set, to benefit from the integration and interactivity made possible by videoconferencing, since there is no need for additional hardware or software. This service also enables meetings recording, which are later made available for streaming or downloading in the website of RUTE.

Between August 2013 and December 2017, 36 video conferences were made on a monthly basis. These video conferences follow an annual scheduling, are carried out on the second Friday of each month, last 90 minutes, and involve the live participation of the operating centers registered in the SIG. The video conference signal is also open for internet users to watch it through the RUTE website connection tool, which enables any user to join the conference as a spectator, but not as a participant able to interact with the participating operating centers, for it is not possible to estimate the total number of virtual users.

Video conferences are performed as follows: during the first 15 minutes, representatives of all connected operating centers introduce the people participating in the conference; then, during 30 minutes, a professional occupational therapist explains the previously determined topic for the current month, and finally, for about 45 minutes, all participants are able to speak, raise questions, clarify doubts, make comments, and share experiences.

Results

Over its 4 years of existence, there has been a progressively increased interest in the activities of the SIG, which is evidenced when comparing the institutions registered (6) when it was established in August 2013 and the number of registered centers (34) by December, 2017, which are presented in Table 1.

Table 1. Registered institutions in the Special interest group of occupational therapy in hospital contexts and palliative care according to their place of origin (December, 2017)

Location / State	Number of institutions	Institutions registered at RUTE
Amazonas (AM)	1	Getúlio Vargas University Hospital - Federal University of Amazonas (UFAM);
Bahia (BA)	3	Roberto Santos General Hospital (HGRS);
		Ana Nery Hospital (HAN); Federal University of Bahia (UFBA);
Brasília - DF	1	University Hospital of Brasília (HU/UnB);
Ceará (CE)	1	General Hospital of Fortaleza (HGF);
Espírito Santo (ES)	1	Cassiano Antonio de Moraes University Hospital of the Federal University of Espírito Santo (HUCAM / UFES);
Maranhão (MA)	1	University Hospital of the Federal University of Maranhão (UFMA);
Mato Grosso do Sul (MS)	1	Maria Aparecida Pedrossian University Hospital (HUMAP);
Minas Gerais (MG)	3	Clinics Hospital of the Federal University of Minas Gerais (UFMG); Risoleta Tolentino Neves Hospital (UFMG); Clinics Hospital of the Federal University of Triângulo Mineiro (HC/UFTM);
Pará (PA)	3	Federal University of Pará (UFPA); João B. Barreto University Hospital - Federal University of Pará (HUJBB / UFPA); Santa Casa de Misericórdia do Pará (SCMPA);
Paraná (PR)	1	Clinics Hospital of the Federal University of Paraná (HC/UFPR);
Pernambuco (PE)	3	Osvaldo Cruz University Hospital of Recife (HUOC / PE);
		Cardiology Emergency Hospital of Pernambuco (PROCAPE); Clinics Hospital of Federal University of Pernambuco (UFPE);
Rio de Janeiro (RJ)	2	Galeão Air Force Hospital (HFAG); Bonsucesso Federal Hospital (HFB);
Rio Grande do Sul (RS)	3	University Hospital of Santa Maria (HU/UFSM); Franciscan University Center (UNIFRAN); University Hospital of the Federal University of Pelotas (HU/UFPel);
Santa Catarina (SC)	1	São José City Hospital of Joinville (HMSJ);
São Paulo (SP)	8	Clinics Hospital of the Ribeirão Preto Medical School of University of São Paulo (FMRP-USP): campus unit, Emergency Unit (UE) and Américo Brasiliense State Hospital (HEAB); Children's Institute of the Medical School of the University of São Paulo (ICr / FMUSP), in partnership with the Emílio Ribas Institute of Infectious Diseases (IIER); Hospital for Rehabilitation of Craniofacial Anomalies - University of São Paulo (HRAC-USP); Federal University of São Paulo (UNIFESP) Barretos Cancer Hospital (HC Barretos); Federal University of São Carlos (UFSCar); University Hospital of the Federal University of São Carlos (HU / UFSCar);
Chile	1	Central University of Chile (UCC).
Total:	34 operating centers	

Source: ATOHosP (6)

Therefore, this study covered three types of hospitals: general hospitals, university hospitals and specialized hospitals. Furthermore, operating centers from universities (not hospitals) are also registered members. The participating groups were composed of occupational therapists, residents enrolled in multi-professional health residency programs in hospitals accredited in the SIG, as well as faculty members and undergraduate students. It is also worth noting the wide reach this SIG has from a geographical point of view: its participating institutions represent 14 Brazilian states and Brazil's Federal District, besides it expanded its coverage to international dimensions when one video conference was held by a Chilean institution.

36 video conferences were carried out during the study period (Table 2); topics discussed were determined by the group responsible for each presentation and in agreement with the ATOHosP. Although video conferences are live streamed, presentations are publicly available on the website of RUTE, which contributes to continuing education.

The subjects related to the occupational therapy specialty in hospital contexts presented in said video conferences, as well as their work

fields, were as follows the skills and competences the occupational therapy specialist is required to have, the different practices in different hospital contexts and in palliative care, and the administration of occupational therapy services in hospitals.

Table 2. Topics discussed in the video conferences made by the Special interest group on Occupational Therapy in hospital contexts and palliative care through the tools provided by RUTE.

#	Topics	Responsible (*)
1	Presentation and planning of the activities of the Scientific interest group	FMRP-USP
2	Occupational therapy specialty in the hospital context	UNIFESP
3	Professional competence of the occupational therapist in hospital contexts and palliative care	UFPR
4	The grieving process in the hospital context, which included a debate on occupational therapeutic assistance	UFPA
5	Occupational therapy in palliative care	ICr-USP/ IIER
6	Occupational Therapy actions in a high complexity hospital - General Hospital of Fortaleza (HGF) challenges and limitations	HGF
7	Palliative care and rehabilitation: reviewing concepts and practices in the health care network	FMRP-USP
8	Occupational therapy in oncology	Barretos HC
9	Assessment of occupational therapy in hospital contexts	UnB
10	Elaboration and indicators of the Occupational Therapy Service in hospital contexts and palliative care	ICr-USP/ IIER
11	Early and intensive intervention of occupational therapy in the prevention of delirium in the elderly in intensive care units. A randomized clinical study	Universidad Central de Chile
12	Billing of occupational therapy procedures in hospital contexts at the Clinics Hospital of Federal University of Triângulo Mineiro (UFTM)	UFTM
13	Evaluation of the First congress on Occupational Therapy in hospital contexts and palliative care	FMRP-USP
14	Occupational therapy intervention in both an adult and a pediatric intensive care unit	ICr and IIER
15	Occupation and palliative care in geriatrics	UFPA
16	Occupational Therapy in Hospital Contexts	FMRP-USP
17	Systemization of the assistance to the Occupational Therapy Service in the A. C. Moraes University Hospital	HUCAM / UFES
18	Homecare program for discharging patients in the Clinics Hospital of Federal University of Triângulo Mineiro (HC-UFTM)	HC/UFTM
19	Occupational therapy in a hospital context and its implementation in multi-professional residency	HU/UnB
20	Occupational therapists involved in the production of health of the Bonsucesso Federal Hospital (HFB)	HFB
21	Occupational therapy clinical records: Indicators of the documentation in an ambulatory context	UFSCar
22	Using video conference for continuing education in Occupational Therapy specialty in hospital contexts	UFPR
23	From clinical practice to research and teaching and from research and teaching to clinical practice	UFMG
24	Thoughts on the practice of OT in a hospital context and the 445/ 2014 Resolution	UFTM
25	Occupational therapy in cardiology: focus on heart failure and cardiac surgery	IIER
26	Occupational therapy in a cardiology hospital	PROCAPE
27	Constructive process of indicators of occupational therapy	HU/UFSCAR
28	Multi-professional reception in oncology	UHB
29	Occupational therapy intervention in the Bone Marrow Transplant Unit	ICr-USP
30	Construction of the Wound protocol by the Occupational Therapy Service	HRTN/UFMG
31	Research in occupational therapy in hospital contexts and palliative care	FMRP-USP
32	Quality of life and use of alternative communication technologies in head and neck cancer cases	FMRP-USP
33	Prescription and wheelchair adaptation experience in a hospital context: challenges for its implementation	HUPES/BA
34	Occupational therapy approach in the Burn Treatment Center of the Galeão Air Force Hospital (HFAG)	HFAG
35	Occupational therapy intervention in congenital heart disease (Edwards syndrome)	PROCAPE
36	Grief and occupational therapy	HU/UFSCAR

(*) Acronyms have been previously described in Table 1
Sources: ATOHosP (6); RUTE (4)

The average number of operating centers participating in the video conferences is presented in Table 3:

Table 3. Average participation in the video conferences.

Period	Months	Participant groups (n)	Groups participation average
2nd semester, 2013	August September October November December	02 08 09 07 09	7
1st semester, 2014	March April May June	10 15 16 16	14.3
2nd semester, 2014	August September October	17 16 15	16
1st semester, 2015	March April May June	16 16 12 13	14.3
2nd semester, 2015	July September October November December	12 12 10 11 09	10.8
1st semester, 2016	March April May June	14 17 12 14	14.3
2nd semester, 2016	August September October November December	17 15 16 15 10	14.6
1st semester, 2017	May	15	15
2nd semester/2017	July August September November December	11 19 19 17 15	16.2
Total average			13.6

Source: Own elaboration.

Video conferences held from 2013 to 2017 were evaluated through an internet survey sent to those who had participated in any of the video conferences organized by ATOHosP. (10) 25 people from several states of Brazil completed the survey. 100% of the respondents considered that these video conferences had contributed to their professional training and practice through the updating process and the experiences exchange in occupational therapy care in different hospital contexts and in different regions of the country, which in turn strengthened their theoretical repertoire, and increased the possibilities of assistance protocols and management, and qualification of occupational therapy practices, among other benefits.

Discussion

An actions network can facilitate health care in Brazil through specialized remote assistance; furthermore, it has the potential to create spaces to carry out new distance and continuing education processes, as well as to promote the development of education and research activities. However, telehealth practices in occupational therapy are not common, for they require the systemization of the services that are offered.

In this sense, different concepts have been described in the literature addressing this topic (11-16):

1. Telemedicine is the use of medical information that is exchanged via digital communication means in order to promote health education, prevent and treat diseases, manage chronic illnesses and arrange rehabilitation procedures. (13) Telemedicine or Tele-assistance means the provision of healthcare services by health professionals in situations where distance is a critical factor; in addition, it is also used for health providers and health professionals' continuing education purposes. (17)
2. Telerehabilitation is a service model provided by means of interactive telecommunication technologies that helps delivering evaluation, preventative, diagnostic, and therapeutic services, and implementing assistive technologies and adaptive techniques, among other objectives;
3. Teleconferencing or videoconferencing is a tele-education or distance education modality that uses specific software to create virtual interaction channels to be used in in continuing education in health areas at both undergraduate and graduate levels. (18)
4. Telehealth encompasses both telemedicine and telerehabilitation to provide distanced based health-related services. This term describes the scope of occupational therapy, since it integrates a broad definition of distance based health care activities such as consultations through videoconferencing, image transferring, remote monitoring of chronic conditions, and continuing education.

Telemedicine and telehealth are interchangeable terms involving several actions based on information and communication technologies that are used in order to improve clinical health conditions of patients in hospitals, specialized health units, health care centers, private medical practices, at home, and in other assistance contexts.

According to the World Federation of Occupational Therapists, telehealth can be an appropriate service delivery model for occupational therapy, and may improve access to occupational therapy services (19-21).

On the other hand, the purpose of telerehabilitation is to improve access to rehabilitation services through the use of telehealth technologies; in addition, it also works as a basis to develop innovative tools and systems to facilitate access to rehabilitation and independent life support services. For its appropriate implementation and use it requires rehabilitation engineers, support technicians, rehabilitation doctors, occupational therapists, physiotherapists, speech-language therapists, educators, rehabilitation nurses, neuropsychologists, and specialists on health policies. (22)

Augestad and Lindsetmo (23) conducted a literature review in 2009 where they analyzed 51 manuscripts and concluded that videoconferencing is an educational tool widely used to overcome knowledge gaps and distance-based challenges among trauma surgeons, with a good cost-effectiveness outcome regarding the treatment and follow-up of surgical patients. (24)

Videoconferencing in occupational therapy includes the facilitation of aspects such as occupational performance, occupational adaptation, health care and well-being provision, disease prevention and a better quality of life. It also provides people living in remote or disadvantaged areas with access to occupational therapy services, and lets health providers and health specialists reach people who, otherwise, would be impossible to make contact with. Moreover, videoconferencing allows preventing unnecessary delays in the provision of care, reducing professional isolation through distance education, team research and team consultation, and other activities. (12,14,24)

To refine a low vision assessment, a study conducted in USA by Smith (25) examined video conferencing experiences of occupational therapists and occupational therapy students participating in online focus groups by using communications and information technologies. The focus group was conducted as an online discussion forum through interactive videoconferencing. Smith discussed the benefits and challenges derived from using these technologies and concluded that students had a satisfactory experience since communication was facilitated, as well as therapists, who valued communication with their peers as one of the most significant benefits of the experience. (25)

Further studies on learning, performance and satisfaction, as well as measures of quality and preferences, benefits and challenges, including privacy and safety practices during and after telehealth sessions, are necessary to determine the success rate of this type of programs. (26)

Results obtained in the present study are consistent with what the SIG has proposed regarding the discussion of topics, methods, and specific technical and scientific approaches of clinical cases, researches, and issues related with the occupational therapy specialty in hospital contexts and palliative care between the participating institutions.

Video conferences made through the SIG on occupational therapy in hospital contexts and palliative care have a major role in strengthening this profession, for they focus on promoting group actions between institutions offering occupational therapy education programs and hospitals, so that activities related with knowledge acquisition and professional practices in this context are encouraged.

Likewise, these video conferences have allowed occupational therapists and occupational therapy students from all over the country to meet, regardless of the distance between them, to discuss relevant topics in relation with their field of action.

Given that Brazil is a continental country (with a territorial area of 8 515 767.049 km^2) and that traveling long distances sometimes hinder participation in scientific events, a growing interest in continuing education activities through teleconference has been recently observed in occupational therapy students and professionals attending universities and hospital institutions in different states of Brazil. This type of knowledge sharing experience has also called the attention of occupational therapy scientific and professional associations, and federal and regional boards, for it favors national

integration, as well as the consolidation of the occupational therapy specialty in hospital contexts and palliative care.

Videoconferencing in telemedicine can be used as a strategy for reducing regional disparities in health care and health education, while in telehealth it can be used as a mean of approximation between professionals, institutions and services.

Conclusion

Videoconferencing through the SIG on occupational therapy in hospital contexts and palliative care allowed the progressive creation of a collaboration network made of occupational therapists working in general hospitals, specialized units and similar institutions, which has made possible the active interaction and participation between professionals from several institutions and services located in different parts of Brazil. In addition, this tool enabled enhancing clinical practices and stimulating social actors involved in teaching, care, and research in occupational therapy.

Occupational therapists and people in need of their services can benefit from the use of emerging communications and information technologies in different practical scenarios. By removing barriers to health care such as social stigmas, long distances and socioeconomic and cultural issues, videoconferencing in occupational therapy may lead to reduce the impact of staff scarcity in poor or disadvantaged areas.

Videoconferencing has a growing potential in terms of professional training and provision of services in hospitals and palliative care for occupational therapists working in different fields of action, such as mental health promotion, rehabilitation, occupational health, among others.

Limitations: Although this program has the potential to be expanded to several areas of knowledge in occupational therapy, there are some limitations, including the definition of the fixed weekly schedule for video conferences to be made and the lack of an effective system for keeping track of attendance and conducting a systematized evaluation. More systematized studies on the potentialities and weaknesses of this strategy on continuing education are required to show the potential and advantages videoconferencing in occupational therapy has to offer.

Conflicts of interest

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ORIGINAL RESEARCH

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Differential molecular approach and ESBL detection from *Klebsiella pneumoniae* and *Escherichia coli* isolated from the supraglottic region of patients undergoing mechanical ventilation in an intensive care unit

Aproximación molecular diferencial y detección de BLEES a partir de Klebsiella pneumoniae y Escherichia coli aisladas de la región supraglótica de pacientes sometidos a ventilación mecánica en una unidad de cuidados intensivos

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| Abstract |

Introduction: Given their ability for colonizing the supraglottic region, desiccation tolerance, resistance to β-lactam antibiotics, and adherence to both inert surfaces and epithelial cells, *Klebsiella pneumoniae* and *Escherichia coli* are potentially pathogenic microorganisms for patients undergoing mechanical ventilation in an intensive care unit (ICU).

Objective: To perform a molecular characterization and detection of extended spectrum β-lactamases (ESBL) in *K. pneumoniae* and *E. coli* strains isolated from the supraglottic region of patients undergoing mechanical ventilation in an ICU.

Materials and methods: A descriptive study was conducted in 18 isolates. Disk diffusion technique was used for detecting ESBL-producing bacteria. Molecular characterization was made by BOX-PCR technique, while ESBL production was confirmed by testing the isolates against cefotaxime and ceftazidime, alone and in combination with clavulanic acid.

Results: a *K. pneumoniae* strain and another *E. coli strain* were confirmed as ESBL producers. A divergence greater than 50% was observed in most of the strains; besides non-infectious origin strains resistant to third generation cephalosporins were found.

Conclusion: The polyclonality found in this study might indicate that most of the strains belong to each patient's microbiota.

Keywords: Beta-lactamases; Gram-Negative Aerobic Bacteria; Mechanical Ventilation; Antimicrobial Drug Resistances; Intensive Care Unit (MeSH).

| Resumen |

Introducción. Dada su capacidad para colonizar la región supraglótica, tolerar desecación, resistir los antibióticos β-lactámicos y adherirse tanto a superficies como a células epiteliales, la *Klebsiella pneumoniae* y la *Escherichia coli* son microorganismos potencialmente patógenos para los pacientes de la unidad de cuidados intensivos (UCI) sometidos a ventilación mecánica.

Objetivo. Realizar la caracterización molecular y la detección de β-lactamasas de espectro extendido (BLEES) a cepas de *K. pneumoniae* y *E. coli* aisladas de la región supraglótica de pacientes internados en UCI y sometidos a ventilación mecánica.

Materiales y métodos. Estudio descriptivo realizado en 18 aislamientos. Se utilizó la técnica de difusión en disco para detectar bacterias productoras de BLEES. La caracterización molecular se realizó mediante la técnica de BOX-PCR y la producción de ESBL fue confirmada mediante la prueba con cefotaxima y ceftazidima, solas y combinadas con ácido clavulanico.

Resultados. Una cepa de *K. pneumoniae* y otra de *E. coli* resultaron productoras de BLEES. La mayoría de cepas presentaron una divergencia superior al 50%, evidenciándose, además, cepas de origen no infeccioso resistentes a cefalosporinas de tercera generación.

Conclusión. La policlonalidad encontrada podría indicar que la mayoría de las cepas pertenecen a la microbiota de cada paciente.

Palabras clave: Inhibidores de beta-Lactamasas; Bacterias aerobias Gramnegativas; Ventilación mecánica; Resistencia microbiana a antibióticos; Unidad de cuidados intensivos; resistencia bacteriana a múltiples medicamentos (DeCS).

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Introduction

The admission of patients to the intensive care unit (ICU) has an effect on the frequency of infections caused by strains of multi-resistant Gram-negative bacilli (MRGN). Some risk factors increase the susceptibility to MRGN infections, including those caused by extended spectrum beta-lactamases (ESBL) producing strains. Some of these risk factors include immunosuppressive treatments in diseases such as cancer (1), transplant interventions (2), the implementation of central or urinary catheters (3), hemodialysis procedures (4), and mechanical ventilation devices. (5)

Klebsiella pneumoniae and *Escherichia coli* are Gram-negative bacilli that are present in the intestinal tract of mammals, and their colonization rates are trebled in hospital environments in a direct proportion to the length of the stay. Furthermore, their colonization degree has been associated with the selective pressure exerted by antibiotics on intestinal microbiota. (6,7)

These microorganisms are potentially pathogenic for ICU patients undergoing mechanical ventilation since, after colonizing the supraglottic region, they adhere to both inert surfaces and epithelial cells and trigger ventilator-associated pneumonia (VAP) in order to resist desiccation and β-lactam antibiotics respectively. (8,9)

Currently, four pathogenic pathways for VAP to occur have been described: by aspiring secretions through the oropharynx, by contiguity, by entering into contact with blood (hematogenous route), and through breathing circuits. Aspiration of secretions through the oropharynx is the most common pathway (10), therefore biofilms containing respiratory pathogenic microorganisms from the supraglottic region constitute a source of pneumonia associated with health care.

Microbiological analysis by molecular methods performed on the tongue and from bronchoalveolar lavage has evidenced the presence of a several bacterial species. (11) Some tests have suggested that these microorganisms are able to act as pathogens that affect the lower respiratory tract. (11) The isolation of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter spp*, and enterobacteria from dental plaque in patients with pneumonia associated with health care, indistinguishable of isolates obtained from bronchoalveolar lavage, reinforces this idea. (11)

This study was made from the data obtained in a prior research where the effectiveness of chlorhexidine mouthwash was compared to toothpaste mouthwash in terms of decontamination of the bacterial microbiota in the supraglottic region. In addition, reduction of the supraglottic region bacterial microbiota in patients undergoing mechanical ventilation at the ICU was evaluated. After 72 hours in the ICU, colonization of the oropharynx by normal microbiota was reduced, while pathogenic microbiota increased, being *K. pneumoniae* and *E. coli* the most common microorganisms. (12) Some of these strains were preserved in order to determine, as it is proposed here, their susceptibility against antibiotics, as well as their molecular profiles.

Considering the above mentioned, this study focused on the molecular characterization and detection of ESBL-producing *K. pneumoniae* and *E. coli* strains isolated from the supraglottic region of patients undergoing mechanical ventilation in an ICU.

Materials and methods

Type of study and sample unit

A descriptive study was carried out. Microorganisms were preserved in the Collection of Microorganisms of Universidad Católica de Manizales (CM-CUM).

The data was collected from a prior study conducted in patients undergoing mechanical ventilation at the ICU of a hospital in Manizales, Colombia), between 2013 and 2014. The sample consisted of 18 isolates of *K. pneumoniae* and 7 isolates of *E. coli* obtained from the supraglottic region of said patients. In addition, 5 isolates of *K. pneumoniae* obtained from blood cultures, external secretion and peritoneal fluid of patients admitted to the same ICU, but not included in the first study, were also considered for molecular analysis.

Assessment of response to antimicrobials and ESBL production

The preserved strains were initially grown on nutrient agar and were subsequently inoculated on a selective medium (MacConkey agar). These preserved strains were confirmed in terms of gender and species through the automated system VITEK® 2 compact (BioMérieux) at the UCM laboratory.

After confirming the identification, antimicrobial susceptibility was determined by means of the disk diffusion method on selective medium (Mueller Hinton Agar), in accordance with the recommendations of the Clinical and Laboratory Standards Institute (CLSI), (13) including the following antibiotics for detecting possible ESBL-producing strains: aztreonam, cefotaxime, cefotetan, ceftazidime and ceftriaxone.

For preparing the inoculum, 4 to 5 colonies of similar morphology were selected from each culture and were homogenized in 5mL of saline solution, while the resulting turbidity in the solution was adjusted by using sterile saline solution until a density equivalent to 0.5 on the McFarland standard was achieved. Within 15 minutes after adjusting the inoculum, the spread plate technique on a Mueller Hinton agar was performed by using a sterile swab, and then, antibiotic disks were placed on the surface of the inoculated agar through sterile forceps. The disks were distanced at a 24mm average length. Afterwards, plates were incubated at 37°C for 16 to 18 hours. Finally, diameters of inhibition zones were measured according to the CLSI criteria. (13) To confirm ESBL-producing strains, double-disk diffusion method was used in accordance with the the CLSI standard and the following breakpoints: cefpodoxime (≤22mm), aztreonam (≤27mm), ceftazidime (≤22mm), cefotaxime (≤27mm) or ceftriaxone (≤25mm) (13).

ESBL production by the strains studied was confirmed through growth measurement against cefotaxime and ceftazidime alone and in combination with clavulanic acid. A ≥5mm difference between the diameter of the disk where ceftazidime + clavulanic acid were used and the disk where only ceftazidime was used, or between the disk were cefotaxime + clavulanic acid were applied and the one where only cefotaxime was used, was considered as ESBL production.

Genotyping by BOX-PCR system

Bacterial DNA was extracted by using the UltraClean® Blood DNA Isolation Kit (NON-SPIN), which was provided by MOBIO laboratories, Inc. Subsequently, the DNA obtained was stored in Eppendorf tubes at -20°C until its amplification by polymerase chain reaction (PCR) was done.

BOX-PCR typing was performed with the AR1-5´-CTACGGCAAGGCGACGCTGACG-3´ primer under the following conditions: 100ng of DNA were amplified in a mini thermal cycler (Bio Rad®) and were arranged in a reaction volume of 25µL, (14,15) which contained 0.2mM of DNTPs, 2mM of $MgCl_2$, 1.5µM of primer, 0.10mg/mL of BSA, 10% of DMSO and 1U/µL of Taq DNA polymerase (BIOLINE®). For the BOX-PCR amplification, first the DNA was denatured for 5 minutes at 95°C and then underwent 30 denaturation cycles (92°C, 30 sec), an association cycle (60°C, 1 min), and one extension cycle (65°C, 8 min), which was followed by a final extension cycle at 65°C for 8 min. Amplified products were separated by electrophoresis on 2% agarose gel with 1.0 X TBE buffer, for 3.5 h at 4.6 V/cm. Banding patterns were recorded in photos (14,15).

Finally, visual inspection of electrophoretic profiles was done and matrices of presence and absence of bands for the *K. pneumoniae* and *E. coli* isolates were constructed by using Microsoft Office Excel software.

Statistical analysis

The analysis of the matrices was done by using NTSYSpc 2.2 version software. A dendrogram with the unweighted pair group method with arithmetic averages algorithm and Jaccard similarity coefficient was created.

The similarity coefficient (S) was obtained based on the following equation: $S=2*N_{ab}/a+b$, where N_{ab} is the total number of similar bands between 2 isolates and a+b is the total sum of the number of bands of isolates a and b.

Ethical considerations

The microorganisms used in this study were collected in a prior research that was approved by the Research Ethics Committee of the Universidad Católica de Manizales on April 18, 2012, this approval was updated in September 2018 by this committee, it should be noted that due to the university policies the approvals issued by said ethics committee are not numbered. In addition, participants' informed consent was duly obtained in said research.

Results

K. pneumoniae response to antimicrobials and ESBL production

Out of the 18 *K. pneumoniae* strains analyzed, sensitivity to aztreonam, cefotaxime, ceftriaxone, cefotetan and ceftazidime was observed in 11 (61%), while the 7 remaining strains (39%) were resistant to these antibiotics. Intermediate sensitivity was not observed in any of the isolations (Figure 1).

Then, 12 potentially ESBL-producing strains were selected and they were assigned the following GIBI codes: 104, 106, 162, 157, 335, 344, 330, 338, 340, 332, 331, and 343. Through the disk diffusion technique, an ESBL test was done for each of the strains, the results are as follows: 11 negative isolates and 1 ESBL-producing strain (Table 1).

E. coli response to antimicrobials and ESBL production

Out of 7 *E. coli* strains analyzed, 6 (86%) showed sensitivity to aztreonam, cefotaxime, ceftriaxone, cefotetan, and ceftazidime. Intermediate sensitivity was not observed in any of the isolations (Figure 2).

Later, 4 potentially ESBL-producing strains were selected and were given the following GIBI codes: 160, 169, 171, and 334. Results after performing the ESBL production confirmatory test were as follows: negative for 3 isolates, and positive for 1 strain (Table 2).

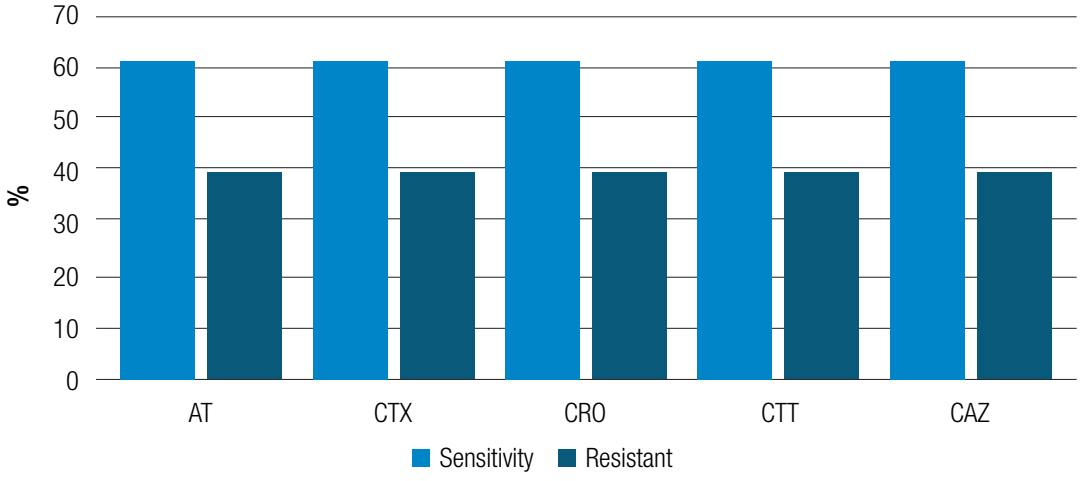

Figure 1. Percentage of sensitivity of *Klebsiella pneumoniae* strains against different antibiotics.
At: Aztreonam; CTX: Cefotaxime; CRO: Ceftriaxone; CTT: Cefotetan; CAZ: Ceftazidime.
Source: Own elaboration.

Table 1. ESBL production test performed on the 12 selected *Klebsiella pneumoniae* strains.

GIBI CODES	CTX	CTX-CA	CAZ	CAZ-CA
104	31mm	31mm	28mm	28mm
106	30mm	30mm	30mm	31mm
162	33mm	33mm	30mm	30mm
157	31mm	32mm	28mm	29mm
335	11mm	16mm	Resistant	10mm
344	28mm	29mm	28mm	29mm
330	<10mm	10mm	Resistant	Resistant
338	12mm	13mm	<10mm	10mm
340	23mm	25mm	18mm	21mm
332	<10mm	11mm	Resistant	Resistant
331	10mm	14mm	Resistant	<10mm
343	<10mm	11mm	Resistant	<10mm

CTX: Cefotaxime; CAZ: Ceftazidime; CA: Clavulanic acid.
Source: Own elaboration.

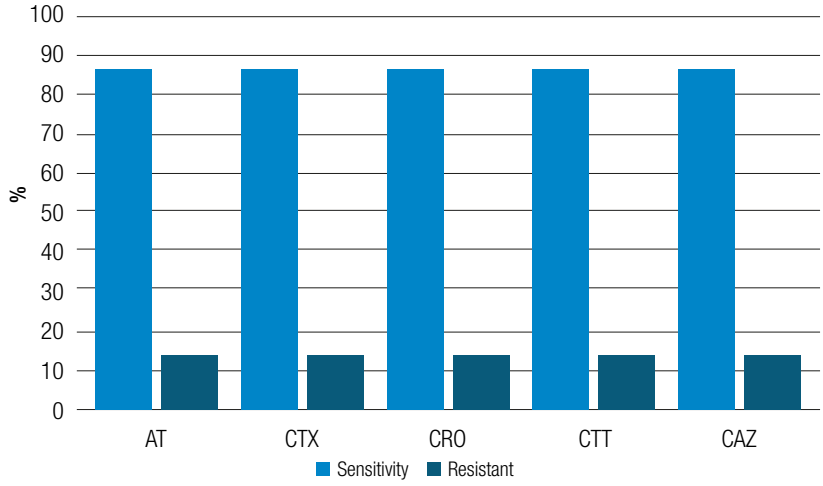

Figure 2. Percentage of sensitivity of *Escherichia coli* strains against different antibiotics.
At: Aztreonam; CTX: Cefotaxime; CRO: Ceftriaxone; CTT: Cefotetan; CAZ: Ceftazidime.
Source: Own elaboration.

Table 2. ESBL production test performed on the 4 selected *Escherichia coli* strains.

GIBI CODES	CTX	CTX-AC	CAZ	CAZ-AC
160	30mm	31mm	27mm	28mm
169	30mm	30mm	28mm	29mm
171	Resistant	20mm	15mm	21mm
334	28mm	28mm	27mm	28mm

CTX: Cefotaxime; CAZ: Ceftazidime; CA: Clavulanic acid.
Source: Own elaboration.

Electrophoretic profile of *K. pneumoniae* strains

Regarding the results obtained through the BOX-PCR fingerprinting technique, out of 23 *K. pneumoniae* isolates, 2 groups with a divergence greater than 50% were observed. In the first group, constituted by 12 isolates, 3 subgroups were identified: subgroup 1, with isolates 62 and 344; subgroup 2, with isolates 72 and 331, and subgroup 3, where isolates 73, 104, 102, 92, 332, 335, 330, and 112 were found. It is noteworthy that isolate 112 had a divergence greater than 50% in comparison with the other isolates of this subgroup. In addition, a 100% similarity between

isolates 73 and 104 was observed, as well as between isolates 92, 332, and 335, while similarity among other isolates was less than 90% (Figure 3).

On the other hand, in the second group, made up by 11 isolates, 3 subgroups were found: isolates 79 and 338 in subgroup 1, isolate 103 in subgroup 2, and strains 164, 168, 106, 157, 163, 162, 340, and 343 in subgroup 3. A 100% similarity between isolates 157 and 163 was observed, while similarity among other isolates in the remaining subgroups was less than 90% (Figure 3).

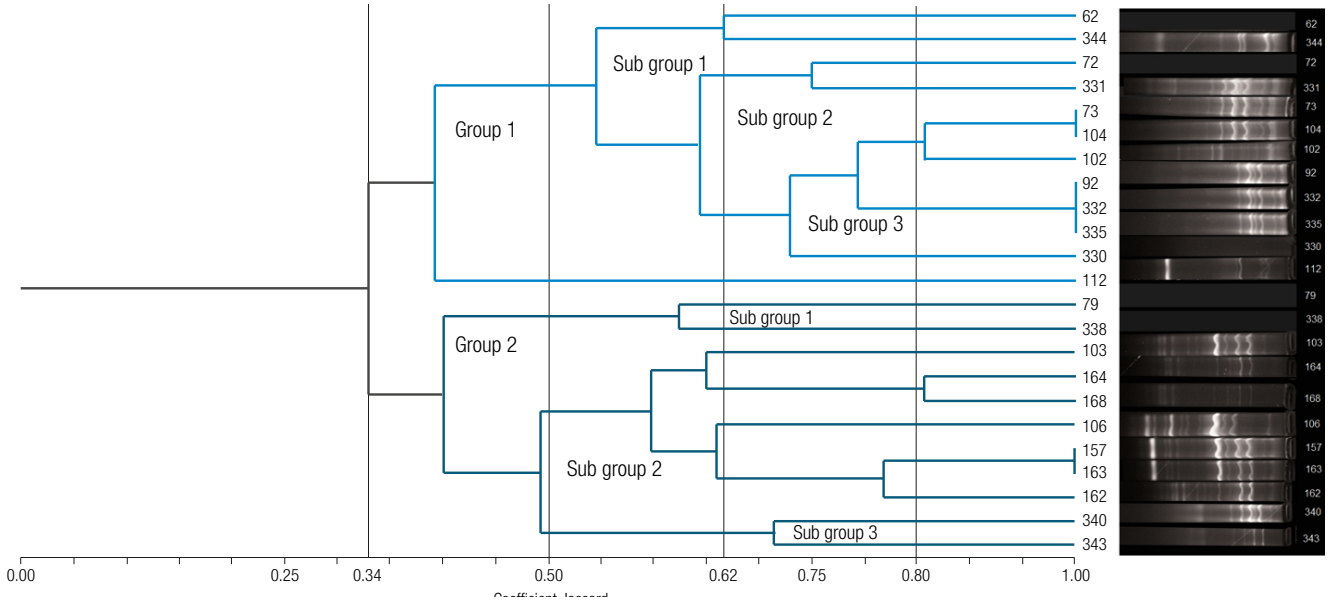

Figure 3. Cluster analysis to determine similarity among *Klebsiella pneumoniae* strains and electrophoretic profiles according to the BOX-PCR test. Source: Own elaboration.

Electrophoretic profile of *E. coli* strains

According to the results obtained after performing the BOX-PCR test, a divergence greater than 50% in the 7 isolates was found. A 92% similarity between isolates 159 and 160 was observed, while for isolates 161 and 334 a 91% similarity was reported (Figure 4).

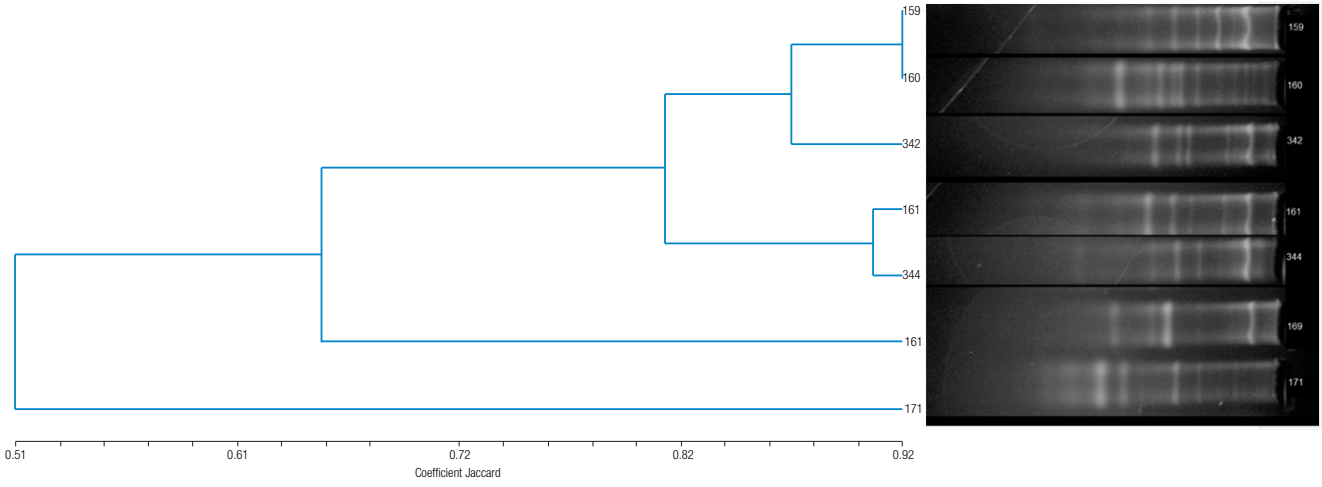

Figure 4. Cluster analysis to determine similarity among *Escherichia coli* strains and electrophoretic profiles according to the BOX-PCR test. Source:Own elaboration.

Discussion

In this study one type of ESBL-producing strain was identified. In Colombia, higher percentages of ESBL-producing *K. pneumoniae* and *E. coli* strains have been reported. For example, in a study conducted in 22 *K. pneumoniae* isolates obtained from patients with a hospital-acquired infection, 15 were resistant to ceftazidime, cefotaxime, ceftriaxone and aztreonam. Besides, all the 15 strains were confirmed as ESBL-producing. (16) Likewise, another research conducted on 144 isolates of *E. coli* and *K. pneumoniae*, obtained from patients staying at several hospitalization services, reported that 48.6% of the total sample were resistant to any cephalosporin, while 25.6% of the *E. coli* and 48.4% of the *K. pneumoniae* strains were ESBL-producing. (17) Another study carried out in a hospital in Valledupar (Colombia) reported a 12.3% ESBL-producing enterobacteria, with *E. coli* and *K. pneumoniae* as the most frequent strains (55.6% and 23.2%, respectively). (18)

Prior studies in Colombia have focused on strains with an infectious origin, while in this research isolates were obtained from the microbiota of the supraglottic region. Considering their origin, the isolates were not expected to be resistant to third generation cephalosporins or ESBL producers, which explains why the results obtained here indicate that the prevalence of ESBL-producing strains was lower than those reported in previous studies. Furthermore, resistance to third generation cephalosporins by strains from the supraglottic region may imply that there is a possibility of other resistance mechanisms such as alteration of target sites related to the penicillin-binding protein (PBP), reduction of porin-mediated outer membrane permeability, and efflux pumps. (9)

It has also been reported that dissemination in the hospital environment occurs mainly because of the presence of strains of endogenous origin that are associated with each patient's microbiota. (16) Moreover, the resistance observed in the strains obtained from the supraglottic region could be explained by the fact that treatments against various infections are made through empiric therapy, namely, without knowing the etiology and antimicrobial susceptibility of the pathogen involved in the infection. Likewise, other inappropriate practices such as self-medication promote the development of resistance mechanisms. When these factors come together, any type of resistance to be acquired will have an effect on the effectiveness of antimicrobial treatments, thus generating therapeutic limitations in hospitals.

On the other hand, the 100% genotypic similarity between some of the strains studied here suggests a common intrahospital contamination source, as well as some cross contamination events, since patients' dates of admission and stays at the ICU were different.

The results of this study indicate the need for controlling ESBL-producing strains from the supraglottic microbiota of patients referred to the ICU. One strategy to control said strains is to use routine surveillance cultures, which also includes an educational intervention for the staff involved. (19) Regarding this approach, it is necessary to raise the awareness on the possibility of using microbial culture on a regular basis as an alert tool, especially if there is enough evidence to consider that some patients may be hosts of ESBL-producing strains prior to their admission to the hospital or the ICU.

In this sense, Boyer *et al.* (20) reported the need to eliminate circulating strains in the environment. Therefore, monitoring potential sources of contamination that are usually underestimated, such as sinks, is an appropriate practice, for sometimes these sources may contain ESBL-producing bacteria and their elimination helps reducing the incidence of multiresistant strains in any ICU. (21) In that regard, the installation of self-disinfecting siphons in sinks of ICUs has been proved to remove biofilm formation and reduce transmission of ESBL-producing Gram negative bacteria. (22)

Experts on this matter agree that genotyping by BOX-PCR technique offers an adequate discriminatory power, as well as reproducibility, and that is a fast typing alternative to get fast results. Furthermore, it requires less investment in comparison with other techniques such as gel electrophoresis by pulsed fields (PFGE) and DNA sequencing. (3) Somehow, a more efficient approach involving the identification of differential resistance genes could include matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), considering the reduced times it requires and the possibility of obtaining specific mass spectra of genus and species it offers. (23)

Conclusions

A greater than 50% divergence in the molecular profiles among the strains groups of *K. pneumoniae* and among those of *E. coli* was determined. This polyclonality indicates that most of the strains belonged to the microbiota of each patient.

The isolation of *K. pneumoniae* and *E. coli* resistant to third generation cephalosporins and ESBL-producing strains in the ICU had as its main source the microbiota of each patient. Cases of genotypic similarity of 100% suggest a common intrahospital contamination source. These cases involved cross contamination events, since the date of admission and the time of permanence of patients in the ICU were different.

Considering their pathogenicity mechanisms, the presence of *E. coli* and *K. pneumoniae* resistant to β-lactam antibiotics strains in the supraglottic region could trigger persistent infections such as VAP, which is considered as a major financial challenge for the maintenance of public health.

Conflicts of interest

None stated by the authors.

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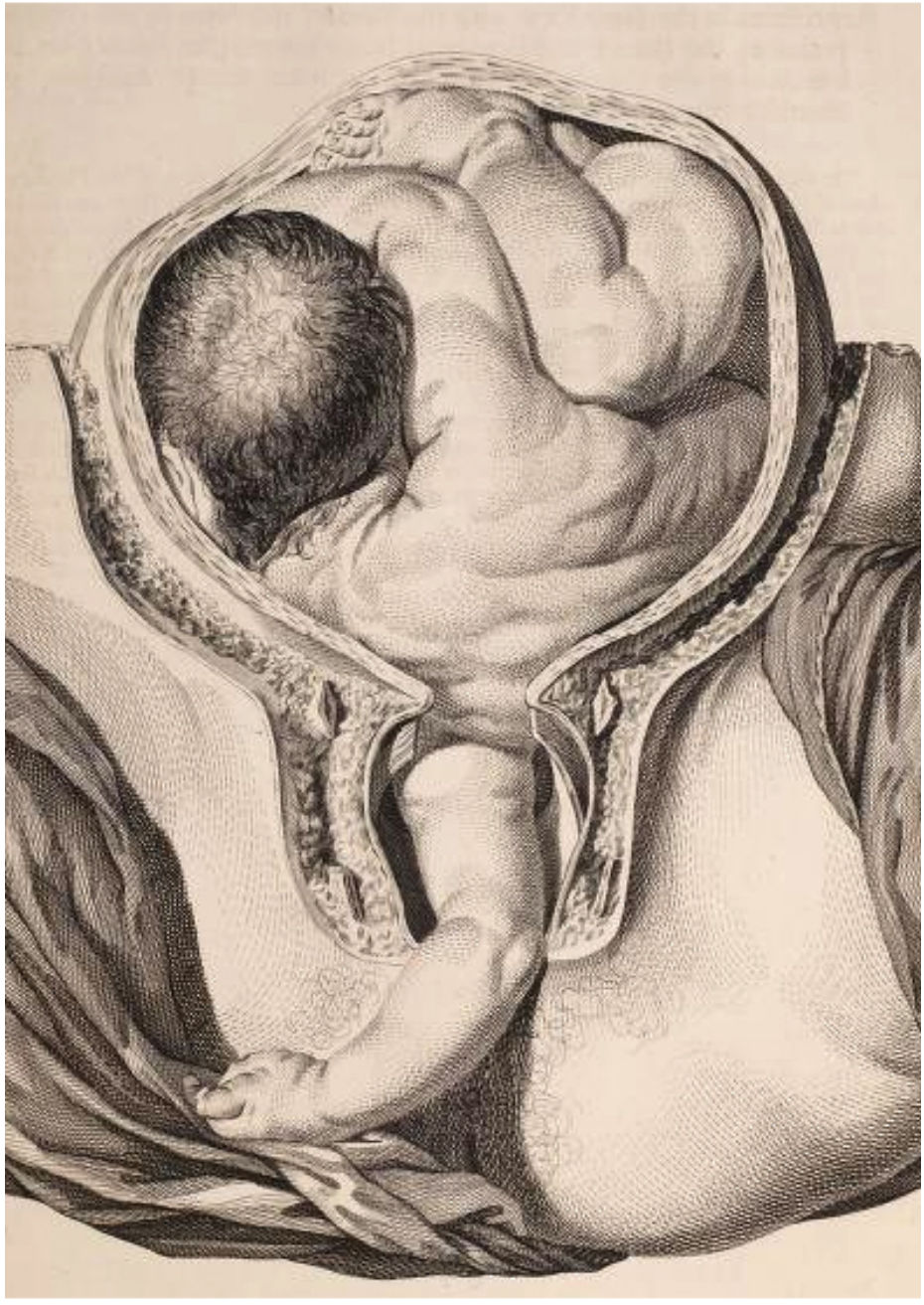

William Smellie, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

ORIGINAL RESEARCH

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Correlation between glycemic control and knowledge in patients with type 2 diabetes mellitus treated at the Family Health Center of the Araucanía region, Chile

Relación del control glicémico con el nivel de conocimientos en pacientes con diabetes mellitus tipo 2 pertenecientes al Centro de Salud Familiar de la región de la Araucanía, Chile

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| Abstract |

Introduction: Diabetes mellitus type 2 (DM2) is a public health problem considering its magnitude and repercussions.

Objective: To determine the correlation between glycemic control and the level of knowledge about their disease in patients with DM2.

Materials and methods: The sample consisted of 65 adults with DM2, aged between 55 and 74 years. The Michigan Diabetes Research and Training Center's Revised Diabetes Knowledge Test was applied to measure the level of knowledge about DM2. Glycemic control was determined based on the last glycosylated hemoglobin value. Information on educational attainment, years of diagnosis of the disease and use of insulin therapy was obtained from clinical records.

Results: Patients with a sufficient level of knowledge of their disease had better glycemic control than those whose knowledge was insufficient ($p<0.001$). There were no differences when comparing educational attainment ($p=0.201$), years of diagnosis of the disease ($p=0.126$) and insulin use ($p=0.108$) with glycemic control.

Conclusion: Glycemic control in DM2 patients can be improved by delivering tools that allow them to be empowered with knowledge about their disease, regardless of their educational attainment, the duration of the disease course or the type of treatment.

Keywords: Glycemic Index; Knowledge; Type 2 Diabetes Mellitus (MeSH).

| Resumen |

Introducción. La diabetes *mellitus* tipo 2 (DM2) es un problema de salud pública dadas su magnitud y sus repercusiones.

Objetivo. Determinar la relación entre el control glicémico y el nivel de conocimientos sobre su enfermedad en pacientes con DM2.

Materiales y métodos. Se seleccionó una muestra de 65 adultos con DM2 de entre 55 y 74 años de edad. Para medir el nivel de conocimiento sobre DM2 se aplicó el Michigan Diabetes Research and Training Center's Revised Diabetes Knowledge Test. El control glicémico fue determinado mediante el valor de hemoglobina glicosilada vigente. Nivel educacional, años de diagnóstico de la enfermedad y uso de terapia insulínica fueron obtenidos de la ficha clínica.

Resultados. Los pacientes con un nivel de conocimiento suficiente de su enfermedad presentaron mejor control glicémico que aquellos cuyo conocimiento era insuficiente ($p<0.001$). No existieron diferencias al comparar nivel educacional ($p=0.201$), años de diagnóstico de la enfermedad ($p=0.126$) y uso de insulina ($p=0.108$) con el control glicémico.

Conclusión. El control glicémico de pacientes con DM2 es mejorable mediante la entrega de herramientas que permitan empoderarlos de conocimientos acerca de esta patología, independiente de su nivel de instrucción, tiempo que llevan padeciendo la enfermedad o tipo de tratamiento.

Palabras clave: Glucemia; Conocimientos; Diabetes *mellitus* tipo 2 (DeCS).

Rosas-Muñoz M, Chávez-Sepúlveda C, Alarcón-Hormazabal M, Godoy F, Vázquez-Aguilar P, Cea-Leiva F. Correlation between glycemic control and knowledge in patients with type 2 diabetes mellitus treated at the Family Health Center of the Araucanía region, Chile. Rev. Fac. Med. 2018;66(4):589-93. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.60464.

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Introduction

Type 2 diabetes mellitus (DM2) is a chronic noncommunicable disease characterized by sustained hyperglycemia, which is caused by defects in insulin action or secretion. This pathology usually develops in people >40 years old, who have a sedentary lifestyle and poor eating habits, and is associated with family history. (1) Chronic hyperglycemia can manifest with damage to multiple organs, being the leading cause of blindness, kidney failure and amputations in adults; it is also one of the leading causes of heart disease and thrombosis. (2)

According to the International Diabetes Federation's 2015 report, an estimated 415 million adults between the ages of 20 and 79 worldwide have diabetes, of whom 193 million are undiagnosed. Another 318 million people have impaired glucose tolerance, putting them at high risk of developing the disease. If this increasing number is not stopped, an estimated 642 million people will be living with the disease by 2040. (3) In Chile, the prevalence of DM2 has increased from 6.3% to 9.4% according to the National Health Survey. (4)

Considering this world scenario, the American Diabetes Association recommends assessing the level of knowledge about DM2 and self-care skills, at least annually, and encouraging or providing tools for permanent education. (1) Health education in diabetic patients is an ongoing process that seeks to promote the knowledge, skills and self-care capacity of people diagnosed with DM2, which has a very positive impact on the reduction of unnecessary morbidity and mortality rates due to poor glycemic control. (5) Therefore, it is important for the patient to understand why good glycemic control should be maintained, know how to achieve it, and learn the appropriate strategies to solve any problem. To achieve this, there are international standards that define the characteristics that make up education in DM2 to be applied in the health system. (6)

In Chile, health promotion and education activities aimed at most patients with DM2 are the responsibility of primary care teams of the different health centers. These actions are fundamental to inform and motivate the population to adopt and maintain healthy practices and lifestyles, in addition to fostering environmental changes and directing human resource training and research in their own field. (7)

Several methodologies have been used to assess knowledge in patients with DM2. (1,8,9) In turn, different educational interventions that combine individual or group education have been made public, as well as the use of internationally validated instruments to measure the level of knowledge. (10) To select these instruments, linguistic validation should also be considered.

According to the available literature, having better knowledge of the disease is associated with a better level of self-care, thereby favoring glycemic control expressed in the reduction of glycosylated hemoglobin (HbA1c) and improving quality of life in these patients. (1,3,10-13)

Given the importance of the level of knowledge in the patient and its fundamental role in the proper management of the disease, the objective of this study is to determine whether glycemic control measured with HbA1c and the level of knowledge in patients with DM2 treated at a family health center in the region of Araucanía, Chile, are correlated or not.

Materials and methods

A cross-sectional correlational study in 65 adults diagnosed with DM2 (47 women and 18 men) was carried out using convenience sampling. The average age of the study participants was 62.8±6.22 years, all with recent HbA1c tests and users of the Cardiovascular Health Program of the Family Health Center (CESFAM) located in the commune of Padre Las Casas, Araucanía region, Chile. Participants were informed and made aware of the importance and objectives of the research and signed an informed consent. This research was approved by the Bioethics Committee of the Universidad Santo Tomás de Chile through Minutes CEC UST N°82/2015, issued on August 14, 2015. In addition, this work took into account the ethical principles for medical research involving human subjects of the Declaration of Helsinki. (14)

The instrument used to measure the level of knowledge was the Michigan Diabetes Research and Training Center's Revised Diabetes Knowledge Test, developed and validated by the Michigan Diabetes Training and Research Center. (15) This instrument consists of 23 questions that measure knowledge regarding the disease and has been translated into Spanish and adapted for studies in the Chilean adult population. (16) It is a multiple-choice test with only one true answer; the first 14 questions refer to general information about diabetes, symptoms, diet and exercise, while the remaining 9 are related to insulin-based treatment and should be answered only by those on insulin-based therapy.

In order to classify the level of knowledge of the patients, the authors of this study defined a score >60% for approval, which was interpreted as sufficient knowledge of the disease. It is worth noting that this is a validated questionnaire for patients with DM2, that its components refer to practical aspects of disease management and that it does not contain questions related to the physiopathology of the disease.

The test was applied in a written and individualized way, and was taken only once by each participant after being explained by a nutritionist.

Glycemic control in each patient was determined by means of the value of the last HbA1c test, which was obtained from the clinical records of CESFAM; the evaluation of this indicator was analyzed in the laboratory of the center. HbA1c <7% was considered adequate glycemic control and HbA1c >7% as uncontrolled blood glucose. This categorization was made based on the Clinical Guidelines for Diabetes Mellitus type 2 in force in national primary care centers. (7) In addition, the information of each patient such as age, insulin use, educational attainment and years of diagnosis of the disease, was obtained from the clinical records.

An exploratory data analysis was carried out to debug the information, thus determining the prevalence of the variables of the main study together with a descriptive analysis. The chi-square test was used to determine the association between two qualitative variables, and in case of obtaining one degree of freedom because both variables were dichotomous, the Fisher's exact test was preferred. Contrasts were significant with a value of $p<0.05$. All analyses were performed using the SPSS software, version 19, for Windows.

Results

Table 1 shows that the subjects participating in this study were characterized by having a higher percentage of elementary educational attainment, followed by secondary education. It is also evident that the largest amount of patients of both sexes was diagnosed between 1 and 5 years earlier. In addition, a higher percentage of men were on insulin therapy compared to women. It can be seen that women have more metabolic control than men, and a higher percentage in terms of knowledge sufficiency in the test.

Table 1. Characterization of the sample according to sex.

Characteristics		Women n=47	Men n=18	Total n=65
		n (%)	n (%)	n (%)
Educational attainment	Elementary	36 (76.6)	14 (77.8)	50 (76.9)
	Secondary and higher	11 (23.4)	4 (22.2)	15 (23.1)
Years of diabetes diagnosis	Between 1 and 5 years	27 (57.5)	10 (55.5)	37 (56.9)
	Between 5 and 10 years	9 (19.1)	3 (16.7)	12 (18.5)
	>10 years	11 (23.4)	5 (27.8)	16 (24.6)
	With insulin treatment	20 (42.6)	10 (55.5)	30 (46.2)
	Adequate metabolic control	16 (34.0)	4 (22.2)	20 (30.8)
	Sufficient knowledge	26 (55.3)	6 (33.3)	32 (49.2)

Source: Own elaboration.

Table 2 shows that the group with sufficient knowledge has, in a significant way, better glycemic control in comparison with the group with insufficient knowledge, which has higher rates of uncontrolled blood glucose ($p<0.001$). It is also evident that there were no statistically significant differences between the level of knowledge in relation with sex ($p=0.166$). In addition, there were no significant differences ($p=0.042$) regarding the level of knowledge about the disease among subjects who had higher educational attainment (secondary or higher education) when compared with those with a lower level of studies.

Table 2. Comparison of glycemic control, sex and educational attainment according to level of knowledge.

Characteristics	Sufficient knowledge (n=32)	Insufficient knowledge (n=33)	p
	n (%)	n (%)	
Glycemic control <7% HbA1c	17 (85.0)	3 (15.0)	0.000
Uncontrolled blood glucose ≥7% HbA1c	15 (33.3)	30 (66.7)	
Male sex	6 (33.3)	12 (66.7)	0.166
Female sex	26 (55.3)	21 (44.7)	
Subjects with primary education	21 (42.0)	29 (58.0)	0.042
Subjects with secondary or higher education	11 (73.3)	4 (26.7)	

Source: Own elaboration.

Table 3 shows that there were no statistically significant differences when comparing sex ($p=0.549$), educational attainment ($p=0.201$), years of diagnosis ($p=0.126$) or insulin use ($p=0.108$) with glycemic control.

Discussion

This research shows that most patients with DM2 who have sufficient knowledge of their disease (Table 2) have a normal glycemic control, as well as a significant difference when compared with patients whose knowledge was insufficient, where a lower percentage presented normoglycemia; all this evidence confirms that the level of knowledge does affect glycemic control.

Table 3. Comparison of educational attainment, years of disease progression and use of insulin therapy in relation to glycemic control.

Characteristics		Glycemic control <7% HbA1c (n=20)	Uncontrolled blood glucose ≥7% HbA1c (n=45)	p
		n (%)	n (%)	
Sex	Male	4 (22.2)	14 (77.8)	0.549
	Female	16 (34)	31 (66)	
Educational attainment	Subjects with primary education	13 (26)	37 (74)	0.201
	Subjects with secondary or higher education	7 (46.7)	8 (53.3)	
Years of diabetes diagnosis	Between 1 and 5 years	10 (27)	27 (73)	0.126
	Between 5 and 10 years	2 (16.7)	10 (83.3)	
	>10 years	8 (50)	8 (50)	
Treatment	Insulin	6 (20)	24 (80)	0.108
	No insulin	14 (40)	21 (60)	

Source: Own elaboration.

This finding is consistent with other studies that also state that glycemic control is achieved when patients' level of knowledge on DM2 is high. (1,3,10-12,17) Another research also exposes that poor patient education and low awareness of such issues in people with high blood pressure or diabetes mellitus can affect their level of control. (18) On the other hand, it has been documented that people with greater knowledge about their own health condition have greater adherence to the recommendations given by health professionals, which in the future represents a greater control of complications. (19)

It should be noted that the percentage of metabolic compensation (normoglycemia) in the subjects who had an adequate level of knowledge of their disease in this study is higher than the goal set by the Government of Chile through the National Health Strategy for meeting the Health Objectives of the 2011-2020 decade, which seeks to achieve metabolic compensation in at least 31.8% of patients with DM2. (20)

Thus, by analyzing the variables related to level of knowledge, it is evident that there is a need to continue strengthening the Cardiovascular Health Program, which has been the most important strategy for the management of DM2 in Chile since 2002, and includes actions related to health promotion and education as essential tools to control the disease. (7) It should be noted that all patients participating in this research are part of this health program, which includes pharmacological and non-pharmacological treatments provided by a multidisciplinary health team. These strategies, based on the need to provide permanent education to diabetic patients, are also a priority for updating the clinical guidelines for DM2 management published in Chile in 2010. (7)

Furthermore, this study found that low level of knowledge on DM2 is a determining factor for poor glycemic control, thus exposing patients with poor metabolic control to the onset of chronic complications, disability and premature death.

Metabolic control in patients with DM2 could be related to educational attainment, since a less educated population has limitations to identify the name of the medications, reading instructions, understanding an appointment card, monitoring glycemic figures

and keeping a record of them. (6,21) Regarding sex, some studies conclude that women have a greater number of non-clinical factors that help accepting self-care actions and prevent complications in DM2. (22) Despite this, no statistically significant differences were found in the present study in the level of knowledge about diabetes (Table 2) or glycemic control (Table 3) in subjects when compared by sex or educational attainment. This finding reveals the vulnerability of the patients treated at the Padre Las Casas Family Health Center in the Araucanía region, who, besides having elementary and secondary education, are residents of rural areas with a high or low degree of marginalization. Consequently, health teams face challenges related to generating effective strategies for education in DM2 based on the strengthening of the non-pharmacological treatment of this disease, emphasizing healthy eating habits and targeted physical activity for a population with low education.

As it has been shown in other works, patients who have suffered from DM2 for more years should have greater knowledge of it, which would be reflected in better glycemic control. (23) However, this research did not find significant differences when comparing the years of diagnosis of the disease with adequate glycemic control (Table 3). This proves the importance of maintaining long-term educational interventions to increase the level of knowledge and self-care skills and thereby achieve sustained improvement in metabolic control. (18,24-28)

When analyzing glycemic control in patients according to insulin use (Table 3), it was observed that, of those who were on insulin treatment, only 20% had an adequate glycemic control, being this percentage lower than that presented in patients that did not have this treatment, as only 40% had normal glucose levels. Although the difference was not statistically significant, it was expected due to a greater pathophysiological involvement in patients with DM2 who require insulin therapy, which explains their lower glycemic compensation. (29) This was also in line with a recent review that reported that most insulin users have high HbA1c levels, resulting in less metabolic control. (30)

The main limitation of this study is the lack of studies conducted at a local level applying the Michigan Diabetes Research and Training Center's Revised Diabetes Knowledge Test to measure the level of knowledge on diabetes mellitus. It would be interesting if national health programs addressing these patients implement locally-adapted instruments to measure their knowledge of their disease.

Conclusions

The results of this study are relevant to continue strengthening patient-centered educational processes at the onset and during the evolution of the disease, which should be addressed even from primary health care services.

A meta-analysis concludes that education on diabetes applied in any format, but performed on a regular basis, leads to glycemic improvement for patients. (31) Therefore, the health team should be trained with appropriate techniques, knowledge and skills to achieve adequate diabetes education in terms of improved quality of life and prevention of complications in these patients.

Conflicts of interest

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William Smellie, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

ORIGINAL RESEARCH

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Status of scientific production in Medicine in South America. 1996-2016

Situación de la producción científica en medicina en Sudamérica. 1996-2016

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| Abstract |

Introduction: One way to evaluate research function is analyzing the scientific production indexed in databases.

Objective: To evaluate the level of scientific production in medicine in South America using the SCOPUS database.

Materials and methods: Bibliometric, observational, descriptive and cross-sectional study based on Scopus database records of medical publications between 1996 and 2016.

Results: Brazil is the country with the highest volume of scientific production in South America and the Mercosur bloc with 210 969 publications over the period under study, followed by Argentina with 44 826. Bolivia and Paraguay are the countries with the lowest contribution, with 1 173 and 784 scientific papers, respectively.

Conclusion: The countries with the highest volume of scientific production in South America are Brazil, Argentina, Chile and Colombia, since their combined scientific production in Medicine accounts for more than 90% of the region's total production. Similarly, there are countries with low levels of scientific production, but with significant average annual growth rates.

Keywords: Medicine; South America; Bibliometrics; Science (MeSH).

| Resumen |

Introducción. Una forma de evaluar la función de investigación es mediante la producción científica que ha sido indexada en bases de datos.

Objetivo. Evaluar el nivel de producción científica en medicina en Sudamérica a través de la base de datos de Scopus.

Materiales y métodos. Estudio bibliométrico, observacional, descriptivo y de corte transversal que se basó en los registros de la base de datos Scopus de publicaciones médicas realizadas entre 1996 y 2016.

Resultados. Brasil destaca como el país con mayor volumen de producción científica a nivel de Sudamérica y dentro de los países miembros de Mercosur con 210 969 publicaciones a lo largo del periodo estudiado, seguido de Argentina con 44 826 publicaciones. Bolivia y Paraguay son los países que tienen menor contribución con 1 173 y 784 trabajos científicos, respectivamente.

Conclusión. Los países con mayor volumen de producción científica en Sudamérica son Brasil, Argentina, Chile y Colombia, mismos que contribuyen en conjunto con más del 90% del total de la región. Del mismo modo, se evidencia la existencia de países con niveles bajos de producción científica, no obstante con tasas de crecimiento promedio anual significativas.

Palabras clave: Medicina; Sudamérica; Bibliometría; Ciencia (DeCS).

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Introduction

In 1970, the Organization of American States suggested that it was necessary to study the volume of articles published in journals inside and outside the region to evaluate and promote Latin American scientific journals. This is not only useful for assessing and measuring the magnitude of regional scientific effort, but also for formulating, designing and implementing national and international policies to foster and promote scientific development and production. (1)

Similarly, in recent years, research has gained importance and has become the prelude to scientific production, impacting the academic, scientific, economic and social development of the countries in which

the research is carried out. (2) This last aspect brings with it the need for quantification and evaluation of scientific activity, its achievements and impacts.

Scopus is a database, shared with Science Citation Index (SCI), of great global relevance for citations and abstracts of peer-reviewed literature: scientific journals, books and conference proceedings. It has intelligent tools to search, analyze and visualize research works, giving an overview of scientific production around the world on science, technology, medicine, social sciences, arts and humanities.

It is important that researchers and editors of scientific journals become familiar with this database, and that academic institutions promote publication in journals indexed in Scopus (3), in order to make their academic productions visible worldwide. Therefore, the publication of articles in indexed journals is key for the evaluation of scientific production and, consequently, as an element of global scientific evaluation.

One of the many responsibilities that medical professionals, students and health personnel have is publishing the research they carry out during their training. (4-6) Only by publishing it is possible to know the impact factor, which is used to measure the number of articles published and the number of times these publications have been cited in other publications. (4) So, in this context, the question arises: why investigate?

In response to this question, research is fundamental in the training of individuals who wish to know more and be more creative, critical, persevering and passionate about solving problems and being part of the solution. (6) Thus, in a study addressing student scientific production in Latin America, the countries that had the most journals with student publications were Colombia, Chile and Peru (7), despite the fact that student contribution was not significant due to the large number of students. Based on these publications, students develop their first research tools and then consolidate themselves in the scientific production of their country and even their continent. They also contribute to the generation of knowledge, intelligent decision-making based on sound scientific results and beneficial changes of social impact.

The term "scientific production" refers to the number of publications containing results of scientific research from authors, institutions, regions and countries on different areas; these data are included in nationally and internationally recognized bibliographic indexes. (8,9)

In this context, this work aims to evaluate the level of scientific production in Medicine in South America using the Scopus database, in order to identify and compare the characteristics, variations, position and trends between countries and economic blocs (Mercosur and the Andean Community). To this end, information on scientific production of the main South American countries during the period 1996-2016 was considered.

In short, this study seeks to provide approximate data useful for a reflection on scientific production in the region and its analysis in future situations in time and space, in order to create beneficial strategies or activities in favor of scientific production in each country and as a region.

Materials and methods

This was a bibliometric, observational, descriptive and cross-sectional study based on records from publications indexed in the Scopus database in South America from 1996 to 2016. To this end, an analysis of scientific production and a comparison between countries and economic blocs was performed. Scopus data was obtained from Scimago Journal & Country Rank (SJR), a tool developed by the SCImago Research Group that offers scientific indicators of journals and countries from Scopus.

The main tools used for systematization, calculations on growth rates, participation structure and the elaboration of tables and output figures were the Scopus database and Microsoft Excel 2010.

All the countries in South America were considered as study variables: Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Paraguay, Peru, Uruguay and Venezuela. Additionally, overall production, average annual production, average growth rate per year and share of scientific production per country were taken into account.

Limitations

Regarding limitations, this work only evaluated scientific production in South America published in Scopus, considering that there are countries with scientific publications that are not included in this database. Therefore, it is expected that new studies look for similar results in other national and international indexes.

Although this study does not evaluate the quality of the published works and their analysis in each country, this factor should be considered in future studies in order to know their relationship.

Furthermore, several factors involved (political, academic, social) and other actions that promote research and publication in these countries and that may be reflected in scientific production should be considered.

Results

Table 1 shows that the accumulated production of research in Medicine in South America during the period 1996-2016 was 327 975 publications. Brazil stands out with 210 969 publications, followed, in order of relevance, by Argentina (44 826), Chile (27 716) and Colombia (19 753). The remaining countries have less than 10 000 publications, being Bolivia and Paraguay the countries with the lowest amount of publications with only 1 173 and 784, respectively.

With respect to average research production per year, South America has 15 618 publications; Brazil also stands out with 10 046 research works and Argentina with 2 135; the other countries have less than 1 500 publications, with the lowest number in Bolivia with 56 and Paraguay with 37.

Table 1. Overall production, annual average, growth rate and participation in research in South America per country. 1996-2016.

Country	Overall production n	Average annual production	Average growth rate per year	Production share per country	Position
Argentina	44 826	2 135	6.4%	13.7%	2
Bolivia	1 173	56	12.1%	0.4%	9
Brazil	210 969	10 046	10.3%	64.3%	1
Chile	27 716	1 320	8.8%	8.5%	3
Colombia	19 753	941	14.3%	6.0%	4
Ecuador	2 730	130	14.2%	0.8%	8
Paraguay	784	37	16.1%	0.2%	10
Peru	6 912	329	16.3%	2.1%	6
Uruguay	4 009	191	8.7%	1.2%	7
Venezuela	9 103	433	5.1%	2.8%	5
Total	327 975	15 618	9.6%	100.0%	

Source: Own elaboration.

However, the countries with less than 1 500 publications have a significant average annual growth, as in the cases of Peru (16.3%), Paraguay (16.1%), Colombia (14.3%), Ecuador (14.1%) and Bolivia (12.1%).

Considering growth levels in these countries, an upward trend in scientific production is expected in the coming years, provided that the entities linked to the promotion of research pay the necessary attention and provide support, particularly in Paraguay and Bolivia, which show the lowest levels of scientific production. The rest of the countries have an average annual percentage variation below 10.0%, the lowest being Venezuela with 5.1%.

Regarding the structure of participation in scientific production per country, Brazil stands out again with a contribution of 64.3% of the total number of South America, followed by Argentina with 13.7%; whie the other countries' share is below 10.0%. In other words, Brazil and Argentina contribute with 78.0% of the publications produced in the region, while the remaining 22.0% corresponds to other countries, of which Ecuador (0.8%), Bolivia (0.4%) and Paraguay (0.2%) have the lowest levels of contribution.

Figure 1 shows the trend in the levels of scientific production achieved by Bolivia, Paraguay, Ecuador, Uruguay and Peru, in which Peru stands out with an upward trend since 2002. In addition to this, Uruguay has had a growing trend since 2002 and Ecuador since the beginning of 2005, although a slight decrease is observed in 2007 before recovering its growth level. In the cases of Bolivia and Paraguay, there was a relatively static trend until 2005, but after 2006, they showed a slight recovery; as far as Bolivia is concerned, their level of growth is lower than that of Paraguay.

Figure 2 shows the trend in the volume of scientific production of Bolivia, Colombia, Venezuela, Chile, Argentina and Brazil, in which the latter stands out with a highly significant level compared to the rest of the countries, being more visible since 2002. Although Argentina and Chile have a slightly increasing trend, it is not as evident as the one of Brazil, which shows a vertiginous growth.

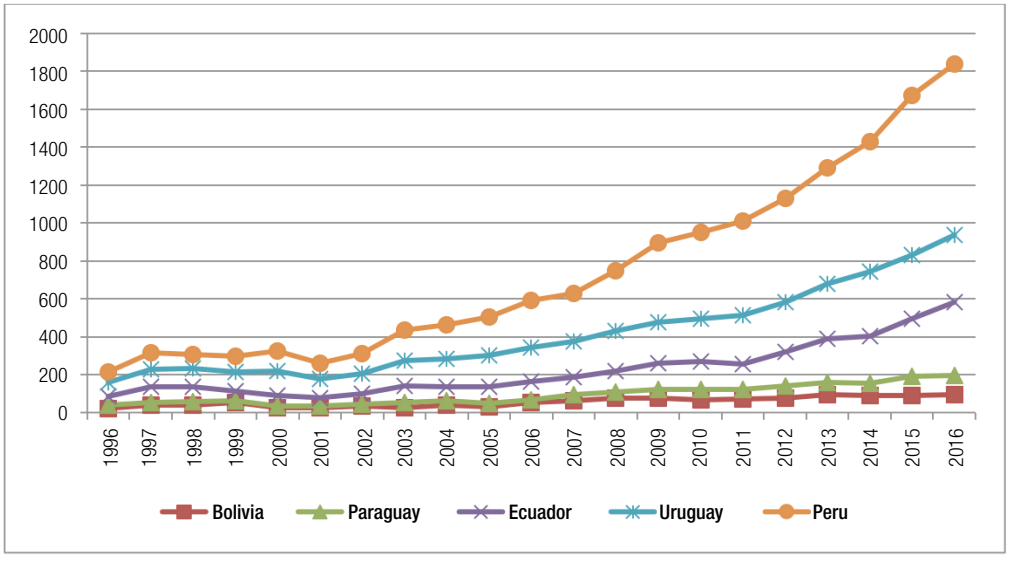

Figure 1. Comparison of the level of scientific production in Bolivia, Paraguay, Ecuador, Uruguay and Peru. 1996-2016. Source: Own elaboration.

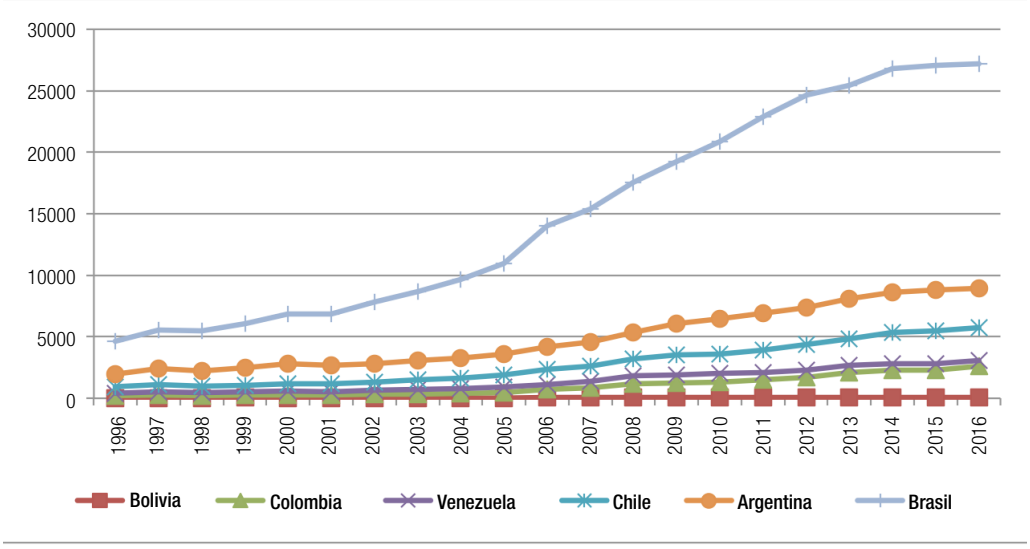

Figure 2. Comparison of the level of scientific production in Bolivia, Colombia, Venezuela, Chile, Argentina and Brazil. 1996-2016. Source: Own elaboration.

The economic bloc of the Southern Common Market (Mercosur), which includes Argentina, Brazil, Paraguay, Uruguay, Venezuela and Bolivia, has a scientific production with a volume of 270 864 publications, which represents 82.6% of the overall amount of South America (327 975) (Table 2). Within this bloc, Brazil stands out with 77.9% of participation, followed by Argentina with 16.5%; both represent 94.4% of the total of Mercosur and the remaining countries reach together 5.6%. This situation is evident when understanding that these two countries show a higher degree of economic and social development than the other members of the group.

Table 2. Overall production, annual average, growth rate and participation in research work in member states of Mercosur. 1996-2016.

Country	Overall production n	Average annual production	Average growth rate per year	Production share per country	Position
Argentina	44 826	2 135	6.4%	16.5%	2
Bolivia	1 173	56	12.1%	0.4%	5
Brazil	210 969	10 046	10.3%	77.9%	1
Paraguay	784	37	16.1%	0.3%	6
Uruguay	4 009	191	8.7%	1.5%	4
Venezuela	9 103	433	5.1%	3.4%	3
Total	270 864	12 898	9.3%	100,0%	

Source: Own elaboration.

On the other hand, the average scientific production per year in the member states of Mercosur was 12 898 publications, of which Brazil contributed with an average production of 10 046 works per year; the lowest figures correspond to Bolivia and Paraguay. However, taking into account the average growth rates per year by country, Paraguay (16.1%), Bolivia (12.1%) and Brazil (10.3%) stand out.

By analyzing the importance of scientific production within the framework of the Mercosur economic bloc, a positive and growing trend is observed in the 2002-2015 period, excluding 2016 as it presents a slight decrease in the volume of production.

Brazil is the main contributor to the growing trend of scientific production, with the highest proportion of research carried out within the framework of Mercosur; Argentina ranks second with a relatively significant contribution as well.

Table 3 depicts the scientific production within the framework of the Andean Community of Nations (CAN), which comprises the countries of Bolivia, Colombia, Ecuador and Peru, with a production volume of 30 568 works that, compared to the level of production of all South American countries, represents 9.32% and a 11.3% participation in relation to Mercosur (270 864 publications). In both the scientific contribution of members of the CAN is very low.

Colombia stands out among the CAN memberss with a total accumulated production in the study period of 19 753 papers, which represents a contribution of 64.6%, followed by Peru with 6 912 scientific papers, with a participation of 22.6%. The other member countries have less than 3 000 publications, with Bolivia being the lowest contributor with only 1 173 papers and a contribution below 10.0%.

Table 3. Overall production, annual average, growth rate and participation of research works according to member countries of the Andean Community of Nations. 1996-2016.

Country	Overall production n	Average annual production	Average growth rate per year	Production share per country	Position
Bolivia	1 173	56	12.1%	3.8%	4
Colombia	19 753	941	14.3%	64.6%	1
Ecuador	2 730	130	14.2%	8.9%	3
Peru	6 912	329	16.3%	22.6%	2
Total	30 568	1 456	13.8%	100.0%	

Source: Own elaboration.

As for the average growth rate of scientific production per year, the CAN countries show a significant increase of 13.8%, as opposed to the growth level of Mercosur, which is 9.3%. Although the member countries of the CAN present marked differences in their contribution to scientific production in Medicine, the levels of growth per country are quite significant, since they exceed their growth rate by more than 12%. This means that there is a significant increase in the levels of research, which, if maintained, would imply a recovery and contribution in the field of research, not only as members of the CAN but also of other economic blocs or integration agreements, as well as in South America.

With regard to the trend of scientific production in all the CAN member countries, a significant upturn since 2002 onwards is observed. In this context, the countries with the highest contribution to the growth of scientific production levels are mainly Colombia and Peru, although Ecuador is equally important with a significant contribution since 2009; however, in the case of Bolivia, its participation is imperceptible.

Discussion

Considering the results obtained, Aguado-López & Becerril-García (10) report a sudden fall in scientific production in Venezuela, represented by the Ibero-American scientific production of 2005, which went from 5.5% to 3% in 2014. This coincides with this work, where participation was 2.8% and the average annual growth rate was negative for South America.

In the case of Peru, the study by Arroyo-Hernández *et al.* (11), a bibliometric analysis of biomedical scientific production in the Ica region between 1998 and 2010, showed important evidence of student participation in the publication of scientific articles. These approaches add to Huamaní *et al.* (12), who described a 4.5% student participation in Peruvian medical journals indexed in SciELO-Peru between 1997 and 2005. This reflects the participation of undergraduate students in scientific publications in indexed journals. (13,14)

On the other hand, Eróstegui-Revilla *et al.* (15) state that Latin America contributes with 4% of the scientific production worldwide, and that Brazil ranks first with a contribution of more than 50% of said value, data that coincide with this work. Bolivia's contribution represents 0.3% of Latin America scientific production and 0.01% worldwide. Considering that there are scientific journals in this

country that are not indexed and others that do not have ISSN, much of its scientific production is not visible and therefore not quantified.

Likewise, according to a study addressing scientific production in PubMed database from 1999 to 2008 (16), the country with the largest scientific contribution in Ibero-America was Brazil, with more than 50% of the scientific production in health areas, followed by Mexico and Argentina, considered as large producers. Next were Chile, Colombia, Venezuela, Cuba, Puerto Rico and Uruguay with a contribution between 1% and 6%; these countries make up the group of medium-sized producers. Of a total of 20 countries studied, the remaining 11 (Peru, Costa Rica, Ecuador, Panama, Guatemala, Bolivia, Paraguay, Nicaragua, Honduras, Dominican Republic and El Salvador) were considered small producers for their contribution was <1% (16), a situation that reflects similar results in the present study.

Mayta Tristán *et al.* (17) report that 60.8% of the medical students surveyed in their study say that there are limitations for publishing at undergraduate level due to lack of teaching support and academic incentives. Considering that university training in research is perceived as deficient by undergraduate students in Latin America, 90% of these students did not consider the quality of their study as a limiting factor. (17) In this way, universities and other academic institutions linked to research should encourage and strengthen scientific production in students, in order to recover the culture of critical reading and writing. This should be done with students, teachers, university authorities and all those involved in this profession.

In Chile, ranked fourth in SCImago and with the highest number of scientific publications in the Latin American region, the participation of medical students in scientific production is relevant (18), which probably causes a positive effect that is reflected in its 8.5% contribution so Latin American scientific production, after Brazil and Argentina.

As for Colombia, the role of public universities in the scientific production indexed in Scopus in the area of medicine is notable, considering that 75.7% of its production comes from 6 public universities, whereas 69.9% of indexed scientific production comes from the same institutions. (19) This would weigh the country's position in South America, considering that, according to the data reported here, Colombia has an outstanding participation (64.6%) in comparison with the other CAN member countries. Regarding research policies in this country, it was found that "research incubators" are considered as a strategy of extracurricular pedagogical training and aim to promote research in undergraduate students (20,21); they also have a positive impact in terms of scientific participation, based on the results reflected in this study.

Conclusions

In South America, the scientific production shares of Brazil, Argentina, Chile and Colombia are highly relevant, since together they contribute with more than 90% of the overall production in Latn America. In addition, there is evidence of the existence of countries with low levels of scientific production; however, they have significant average growth rates per year, so their scientific contribution is expected to increase significantly in the coming years.

It is necessary to create scientific research networks in South America and the economic blocs by identifying and bringing together academic instances, collegial groups and scientific associations of undergraduate students, in order to promote and support those countries whose volumes of scientific production are currently low.

Strategic alliances of research groups should be established in each country and between countries with less developed scientific production activities in the field of Medicine. (22)

It is recommended that medical schools in countries with low levels of scientific production inplement in their curricula subjects such as research methodology, statistics, research ethics, scientific writing and publication or related policies to deepen and achieve greater knowledge regarding the use of tools that are necessary to keep a constant line of research. They should also promote, as a university policy that allows their production to be reflected, the indexation of their journals and publications in databases that are recognized worldwide. Student collaboration is essential to promote research, for it is a way to make possible the continuous training of researchers.

Conflicts of interest

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ORIGINAL RESEARCH

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Costs of health care in the last-year-of-life in Colombia: Evidence from two contributive regime health plans

Gasto en el último año de vida en Colombia: evidencia proveniente de aseguradores del régimen contributivo

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| Abstract |

Introduction: In USA, each year 5% of Medicare beneficiaries die, accounting for 25% of total Medicare health spending. Currently there are no studies addressing this issue in Latin American countries.

Objective: To estimate how much money do health care plans spend, in comparison with their total health spending, in the provision of health care to people in their last-year-of-life in Colombia.

Materials and methods: Based on claims data from two health plans with approximately 3.7 million people enrolled in the Colombian health system contributory regime, health care costs associated with patients in their last-year-of-life from 2011 to 2013 were estimated by using the decedent-survivor allocation method.

Results: Last-year-of-life health expenditure in people aged 65 and above accounted for 18% of total spending. The decedent-survivor ratio in this group age was 4.7. Last-year-of-life health spending in all age ranges was 6.2% while the decedent-survivor ratio was 15.1.

Conclusions: With the exception of USA, findings reported here suggest that last-year-of-life health care costs in Colombia are higher than those reported in other countries in the case of the elderly. Therefore, policymakers and health plans should work in strategies promoting palliative care programs in order to reduce these costs.

Keywords: Health Expenditure; Health Services for the Aged; Colombia (MeSH).

| Resumen |

Introducción. En EE. UU., el 5% de los beneficiarios del seguro Medicare mueren cada año y dan cuenta del 25% del gasto del seguro anual. No existen estudios al respecto para países latinoamericanos.

Objetivo. Estimar la proporción de recursos que destina un asegurador, en comparación con sus gastos totales, a personas que están en su último año de vida en Colombia.

Materiales y métodos. Usando los datos de facturación de dos entidades promotoras de salud del régimen contributivo con más de 3.7 millones de afiliados, se estimó el gasto en el último año de vida de sus afiliados con el método de asignación de gastos a fallecidos y sobrevivientes.

Resultados. El gasto en el último año de vida para población >65 años correspondió al 18% con una razón de gasto entre fallecidos y sobrevivientes de 4.7. Para todas las edades el gasto en el último año de vida fue 6.2% y la razón de gasto entre fallecidos y sobrevivientes fue de 15.1.

Conclusiones. En comparación con otros países, a excepción de EE. UU., el gasto en el último año de vida en Colombia para los adultos mayores es superior. Los hacedores de política y los gerentes de aseguradoras deben prestar mayor atención a incentivar programas de cuidado paliativo.

Palabras clave: Gastos en salud; Servicios de salud para ancianos; Colombia (DeCS).

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Introduction

There is a heated debate on the efficiency and effectiveness of using aggressive treatments for achieving health outcomes at the end of life. On the one hand, there is clinical evidence of cost-effective treatments that add years of life. (1) On the other hand, some state that the intensity of treatments provided in the last months of life can be considered as an indicator of the propensity health professionals have to use highly expensive technologies. (2) For example, it has been reported that in USA the use of intensive care units by Medicare

beneficiaries experienced a dramatic increase in the last decade, rising from 24.3% in 2000 to 29.2% in 2009. (2) Likewise, in the USA higher health spending levels in the last six months of life is not correlated with higher survival rates in patients who have suffered heart attacks, cardiac arrest, or gastrointestinal bleeding. (3)

The interaction between physicians' beliefs and patients' preferences have also been questioned in the available literature. In this sense, Cutler *et al.* (4) reported that 36% of health care spending at the end of life and 17 % of total health expenditures in the USA are associated with physicians' beliefs unsupported by clinical evidence. (4) In this regard, Meier (5), in a case study, describes the existing tension between a palliative care physician who is helping a cancer patient coping with her coming death and her oncologist, who opposes to the idea of quitting the treatment. (5) Similarly, in another study, Meier (6) argues that overtreatment in patients near their death is a major cause of low-value care. (6)

In recent years, several studies focusing on quantifying payments made by third party payers for the provision of health care to patients in their end of life phase have been published in order to illustrate this debate, in particular those made by Medicare in the USA. Some of these studies indicate that payments made by Medicare for the provision of care to patients in their last year of life (LYOL) account for 25% of its total expenditure involving the provision of health care to the elderly (aged 65 or older). (7-9) Somehow, studies addressing this topic in other developed countries are scarce (10-12), and nonexistent in Latin-American countries.

The purpose of this study is to estimate the proportion of payments made in health plans for the provision of health care to people in their LYOL in Colombia by using data on health expenditures from two health plans in the elderly and other age groups.

This is a topic of great importance for Colombian policymakers for at least two reasons. First, Colombia is a middle income country in which the proportion of people aged 65 or older is rapidly increasing. According to population projections made by the Colombian government, by 2020, 8.5% of the total population will be ages 65 or older, which almost doubles the 4.4% reported in 1985. Likewise, in terms of gender, by 2020, 9.4% of all women and 7.6% of all men in Colombia will be part of the elderly population (aged 65 or older). (13) In addition, according to the 2015 Colombian National Survey on Health, Wellness and Aging, 28% of the elderly need help in their activities of daily living (ADLs), including eating, taking a shower, or walking, while 2% are bedridden. (14) These data suggest that disability and chronic illness prevalence in the elderly in Colombian is increasing, and that both conditions are correlated. Besides, higher rates of hospitalization of elderly population and elder abandonment represent higher healthcare spending for the Colombian health system, which is worsened by the lack of trained caregivers for this population. (14).

The second reason is that in 2009 the Colombian health system was declared in a social emergency state by the Colombian government (15) due to a serious financial crisis that has not yet been resolved.

Although the present study addresses this issue in Colombia, its results cannot be used to characterize the general situation in the country for several reasons. First, people enrolled in the health plans analyzed here are employees or self-employed individuals who can afford being in the health care contributory regime, as opposed to those who are in the subsidized regime. Second, there are 12 health care plans in which Colombian employees can be enrolled, but the data analyzed here were obtained from only two of these health plans. Third, health plans in Colombia are free to structure their own provider networks and health care models, and therefore they are able to set certain limits to physicians and organizations that tend to overtreat patients.

Materials and methods

Medical costs were allocated in terms of survivors and decedents. (8) The reference period was from 2011 to 2013. Total health expenditure per year, which was used to estimate LYOL health costs, was distributed between survivors and decedents according the following rules:

- Health costs associated with individuals whose status was reported as alive on the 31st day of December of the year in which the expenditure took place were assigned to the **survivors group**.
- Health costs associated with any individual whose dead was reported in any day of the year in which health spending occurred were assigned to the **decedents group.**
- Health costs associated with patients that were alive in the year in which health care provision payments were made, but then died during the following year, were assigned to both groups by using the difference between the date of death and the date of the health service provision. For example, when a person died on June 30th of the year following the year in which health spending happened, health care costs between January 1st and June 30th were assigned to the survivors group, while health expenditure between July 1st and December 31st was assigned to the decedents group. Per capita payments were estimated by dividing total cost for decedents or survivors by the total number of person-days for decedents or survivors.

Data from 2011 to 2013 were used in this study. The following fields were available in each claim: location (department and municipality), ICD-10 diagnosis code, date of service, service code (CUPS, for its acronym in Spanish), type of service (outpatient, diagnostics, inpatient, emergency), type of payment made to the provider by the health plan (i.e., capitation, fee-for-service), units of services provided, payment amount, copayment amount, type of service (procedures or medicines) and service provider code. The following information of all members enrolled in both health plans was available: encrypted unique identifier, sex, date of birth. The date of death of individuals who died in 2011, 2012, and 2013 was also available. Costs were calculated in Colombian pesos (COP), but these amounts are presented in tables in USD currency using an average exchange rate of 1 838 COP/USD so that international comparisons are easier to make.

Results

Descriptive statistics of the analysis period are shown in Table 1. A higher death rate was observed in men, and approximately 65% of them died aged 65 or older. Concerning the average number of claims, the following values were found: 18 claims per user, 63 claims per decedent, and 17 per survivor. Finally, on average a survivor represented an average spending of USD 331, while a decedent, an average of USD 5.008.

Table 1. Descriptive statistics of claims registered between 2011 and 2013.

	All	Decedents	Survivors
Male (%)	44.91	51.22	44.88
Age (years)	31.61	65.87	31.44
Claims per user	18.09	63.69	17.87
Payments per user (USD)	354	5008	331

Source: Own elaboration.

LYOL average health spending by age group and sex based on pooled data from 2011 to 2013 is shown in Table 2. If all age groups are considered, LYOL health spending accounts for 6.25% of total spending. Average health costs associated with users who died were 15.11 times higher than those associated with survivors. Regarding age groups, the highest proportion of LYOL health spending was observed in those aged 65 or older (17.93%), followed by those in the 60 to 64 ages range (9.18%), which can be explained by the high risk of dying these age groups have.

Finally, LYOL health spending in members aged 65 or older based on gender is as follows: 16.2% in women and 20% in men; in addition, in this age group, health care costs associated with decedents were on average 4.7 times higher than those reported for survivors.

Table 2. Average 2011-2013 expenditure by sex and age (US dollars).

	Expenditure (in USD)			Enrollees (Users)		Expenditure per enrolee		
Age groups distribution	Total spending	Decedents	LYOL Spending (%)	Survivors	Decedents	Survivors	Decedents	D/S ratio
Total	1 077 634	67 301	6.25%	3 049 031	13 423	331	5 008	15.11
0-1	42 101	1 562	3.71%	88 669	116	460	13 609	29.59
1-17	140 751	2 099	1.49%	805 878	212	172	9 914	57.59
18-59	621 376	20 762	3.34%	1 872 265	3 414	321	6 077	18.94
60-64	70 125	6 438	9.18%	95 427	1 037	667	6 221	9.32
65+	203 281	36 440	17.93%	186 792	8 643	892	4 205	4.71
Women	615 788	32 178	5.23%	1 686 256	6 521	346	4 936	14.26
0-1	19 108	764	4.00%	42 858	53	429	14 566	33.92
1-17	66 000	851	1.29%	406 038	85	161	10 262	63.92
18-59	382 587	9 642	2.52%	1 077 149	1 468	346	6 565	18.96
60-64	37 029	2 887	7.80%	52 680	452	648	6 391	9.86
65+	111 065	18 034	16.24%	107 532	4 462	864	4 031	4.66
Total	461 847	35 123	7.60%	1 362 775	6 902	313	5 079	16.21
0-1	22 993	798	3.47%	45 811	63	489	12 848	26.30
1-17	74 752	1 249	1.67%	399 840	127	184	9 819	53.39
18-59	238 790	11 120	4.66%	795 116	1 946	286	5 715	19.95
60-64	33 096	3 551	10.73%	42 747	584	691	6 093	8.82
65+	92 216	18 406	19.96%	79 260	4 181	930	4 390	4.72

D/S: Decedent/Survivor.
Source: Own elaboration.

Discussion

LYOL health spending represents around 25% of total Medicare expenditure in the USA. (8) In addition, several authors argue that a part of this expenditure cannot be supported by clinical evidence and does not provide a better quality of life for terminally ill patients. (2-4,6)

To the best knowledge of the author of the present study, currently there are no studies addressing LYOL health care costs in any Latin American country, so this is the first one providing LYOL health spending estimations in Colombia based on the data of more than 3.7 million users enrolled in two different health plans and living in some of the most populated urban areas of the country (Bogotá, Medellin, Cali). According to the results reported here, LYOL health spending in Colombia regardless of age (6.25%) is higher than what other studies have reported for countries like South Africa (5.4%) (12) and the Netherlands (5%). (10,11) Regarding LYOL health care costs in people aged 65 or over, it accounted for a 17.9% of the total expenditure for the provision of health care to this population, which is significantly lower than the percentage reported by some authors for Medicare beneficiaries aged 65 or older in the USA. (7-9)

Results reported here are of great importance in Colombia, since this study addresses a rarely discussed topic in the literature, in particular in Latin America. Somehow these results are limited, as the data used in this study comprise near 3.7 million users, out of approximately 20 million, of the Colombian health system contributory regime, who were enrolled in two health plans, so they can't be extrapolated to all users of the contributory regime, or those enrolled in the subsidized regime. Also, there is risk selection from health plans trying to avoid very ill patients, and, adverse selection from very ill patients to try to enroll in health plans that have better health care models.

Conclusions

The fact that a higher amount of money is spent in the provision of care to patients in their LYOL is not surprising at all, but it raises the question of whether there are more efficient and more humane ways to

provide care at the end of life period. Health systems financial stability in developing countries is very weak, as there are other sectors in which already scarce financial public resources are also required. Findings reported here suggest the necessity to start discussing the role of palliative care in developing countries, including home care and advanced directives. Likewise, based on the findings described here, health insurers should focus on the prevention and early detection of disability in the elderly, as well as on the implementation of alternative ways to provide patients in their LYOL with a better quality of life. For example, in the USA, Medicare program allows all terminally ill patients (with a six months of life prognosis) to decide whether they want to quit curative care and rather being give home care based treatments focusing on being comfortable in the final moments of their life by means of services that include physical, emotional, social, and spiritual care for both, patients and their relatives, or not.

Conflicts of interest

None stated by the author.

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ORIGINAL RESEARCH

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Effect of a respiratory muscle training program on lung function, respiratory muscle strength and resting oxygen consumption in sedentary young people

Efecto de un programa de entrenamiento muscular respiratorio en la función pulmonar, la fuerza muscular respiratoria y el consumo de oxígeno en reposo en personas jóvenes sedentarias

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| Abstract |

Introduction: Physical inactivity is a risk factor for developing noncommnunicable diseases, as well as respiratory and cardiovascular disorders. To counter this, different types of interventions have been proposed, including respiratory muscle training (RMT).

Objective: To determine the effect of a respiratory muscle training program on respiratory muscle strength, lung function and resting oxygen consumption in sedentary subjects.

Materials and methods: Pretest-posttest experimental study conducted in sedentary students. Lifestyle and the level of physical activity was determined using the International Physical Activity Questionnaire (IPAQ) and the FANTASTIC questionnaire, while respiratory muscle strength was established by means of expiratory and inspiratory pressure using a Dwyer Series 477 meter, and lung function and oxygen consumption was determined by spirometry and indirect calorimetry whit Vmax Encore 29C® calorimeter. Respiratory muscle training was performed for eight weeks with Threshold IMT system. R software, version 3.1.2, was used for statistical analysis.

Results: Clinically and statistically significant improvements were found in maximal inspiratory pressure (MIP) (pre: 81.23±22.00/post: 96.44±24.54 cmH_2O; p<0.001); maximal expiratory pressure (MEP) (pre: 94.84±21.63/post: 107.39±29.15 cmH_2O; p<0.05); pulmonary function FEV_1 [(pre: 3.33±0.88/post: 3.54±0.90L) (p<0.05)]; and FEV_1/FVC ratio [(pre: 87.78±7.67/post: 93.20±6.02% (p<0.01)].

Conclusion: The respiratory muscle training protocol implemented for eight weeks using the Threshold IMT system improved strength and FEV_1. There were no significant changes in oxygen consumption.

Keywords: Sedentary Lifestyle; Muscle Strength; Oxygen Consumption; Spirometry; Indirect Calorimetry (MeSH).

| Resumen |

Introducción. El sedentarismo es un factor de riesgo para desarrollar enfermedades crónicas y generar alteraciones respiratorias y cardiovasculares. Para contrarrestar esto, se han planteado modalidades de intervención como el entrenamiento muscular respiratorio (EMR).

Objetivo. Determinar el efecto de un programa de EMR sobre fuerza muscular respiratoria, función pulmonar y consumo de oxígeno en reposo de sujetos sedentarios.

Materiales y métodos. Estudio experimental pre y post-intervención con estudiantes sedentarios. El nivel de actividad física y estilo de vida se determinó con el International Physical Activity Questionnaire y el cuestionario Fantástico, la fuerza muscular respiratoria por medio de presión inspiratoria y espiratoria máxima con medidor Dwyer Series 477 y la función pulmonar y el consumo de oxígeno mediante espirometría y calorimetría indirecta, con calorímetro Vmax Encore 29C®. Se realizó EMR durante ocho semanas con sistema Threshold IMT. El análisis estadístico se hizo con el software R versión 3.1.2.

Resultados. Se encontraron cambios clínicos y estadísticamente significativos en presión inspiratoria máxima (pre: 81.23±22.00/post: 96.44±24.54 cmH_2O; p<0.001); presión espiratoria máxima (pre: 94.84±21.63/post: 107.39±29.15 cmH_2O; p<0.05), función pulmonar VEF_1 (pre: 3.33±0.88/post: 3.54±0.90 litros (p<0.05), y relación VEF_1/CVF (pre: 87.78±7.67/post: 93.20±6.02% (p<0.01).

Conclusión. El protocolo de EMR de ocho semanas con sistema Threshold IMT mejoró los parámetros de fuerza y VEF_1, sin cambios significativos en el consumo de oxígeno.

Palabras clave: Estilo de vida sedentario; Fuerza muscular; Consumo de oxigeno; Espirometría; Calorimetría indirecta (DeCS).

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Introduction

According to the World Health Organization, sedentary lifestyle is one of the leading risk factors for developing noncommunicable diseases. It is presumed to be the fourth leading cause of death, accounting for 6% of deaths worldwide, and is also considered as a leading cause of 21-25% of breast and colon cancers, 27% of diabetes cases and 30% of the burden of ischemic heart disease. Furthermore, estimates are that 60% of the world's population is not physically active (PA), which is a major public health problem for the general population. (1)

In university students from Colombia, high values of sedentarism, ranging from 57% to 82%, have been reported (2,3); these values coincide with other reports around the world and even exceed the average. In this regard, Prieto-Rodríguez (4) observed that the level of sedentary lifestyle was close to 83% at Universidad Nacional de Colombia, Bogotá Campus, students. However, the study by Rodríguez *et al*. (5) established that about 70% of the evaluated students did not perform the recommended PA level, a figure that is significantly inferior; nevertheless, levels of inactivity are alarming.

That said, it has been observed that a sedentary lifestyle has a negative impact on lung function and maximal oxygen consumption (VO_{2max}); likewise, an average decrease of VO_{2max} of 0.26 mL/min/kg per year and of 0.23 mL/min/kg per year in men and women, respectively, has been described (6), which represents ~7% less in comparison with physically active subjects. (7) On the other hand, significant reductions have been reported ($p<0.05$) in relation to respiratory muscle strength (RMS), volume and lung capacity as representatives of the functionality of the respiratory system, leading to an alteration of the ability to generate pressure mediated by the modification of the relationship between length and contraction velocity; the former depends on the change of amplitude, which causes lower total lung capacity (TLC), while the latter relates to muscle fatigue during effort, which represents a decrease in pulmonary function and low tolerance to physical activity. (8)

In response to alterations in respiratory muscle and VO_{2max} decrease caused by a sedentary lifestyle, a hypothesis has proposed that the application of respiratory muscle training (RMT) improves RMS parameters, lung function and VO_{2max}. However, the use of this methodology in this population has not been widely described; on the contrary, it has been studied in clinical and sports settings in order to improve health condition and physical performance, finding significant changes in muscle strength (~10-55%) (9,10) and VO_{2max} (~1-4 mL/kg/min in patients). (11) These results correlate with possible adaptive changes, including an increase in the percentage of Type I fatigue-resistant fibers and an increase in the size of Type II fibers in respiratory muscles. (12) Therefore, the aim of this study is to determine the effect of an RMT program on RMS, lung function and resting oxygen consumption in sedentary subjects. (5,13-16)

Materials and methods

Type of study

This is a prospective, longitudinal, experimental study with pre and post-intervention measurements.

Participants

Students attending the Universidad Nacional de Colombia were included; they were aged between 15 and 35 years, sedentary and with a PA level <150 minutes per week, presenting associated risk factors such as overweight, unbalanced diet and consumption of alcohol and tobacco. Subjects who reported any type of previously diagnosed neurological, osteomuscular, metabolic or cardiopulmonary pathology and respiratory trauma that compromised the integrity of the rib cage were excluded. Subjects with a high or moderate level of PA according to the International Physical Activity Questionnaire (IPAQ), short version, were also excluded. The sample was probabilistic and the software G Power 3.1.9.2 for Windows was used (d=0.9; statistical power 1-β=0.99; probabilistic error α=0.05), n=21+4 (10% expected follow-up losses). (17,18)

Anthropometric variables and physical activity level

Sociodemographic variables were recorded and the short IPAQ and the FANTASTIC questionnaire were applied to measure PA level and lifestyles, respectively. If the interview met the criteria of the study, anthropometric characteristics were measured according to the International Standards for Anthropometric Assessment (ISAK). The measurements were taken between 08:00 a.m. and 4:00 p.m. in a comfortable place at the right temperature. A stadiometer was used to measure height (20-205cm, 1mm precision), body weight was measured with a digital scale (Kenwell®, 100g precision) and body mass index (BMI) was determined by using the Quetelet index. The measurements were taken twice and the average score was recorded for statistical analysis.

Respiratory muscle strength

RMS was determined by measuring maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) using a Dwyer Series 477 meter (±300mmHg), and following the American Thoracic Society/European Respiratory Society (ATS/ERS) protocol and what has been previously described by other authors. (5,8,19,20) Participants started the test in a seated position without further support and were instructed to exhale in a controlled manner as much air as possible to obtain inspiration from the residual volume (RV); then, they were instructed to put on a mouthpiece and nose clip and to take vigorous air through the mouth during the circuit. For the MEP, participants took in the largest amount of air in a controlled manner until they reached TLC and then exhaled vigorously through the meter. Three measurements were taken for MIP and three for MEP, spaced by 1-minute rest periods; the highest value obtained was recorded.

Oxygen consumption

Energy expenditure, VO_2 and carbon dioxide (CO_2) production at rest were measured by means of indirect calorimetry using the Vmax Encore 29C® calorimeter (Calorimetry Laboratory of the Department of Human Nutrition of the Faculty of Medicine of the Universidad Nacional de Colombia). The subjects, in a seated position, were

coupled to the flow sensor using a MicroGardR® disposable filter, a conventional FreeFlow™ mouthpiece and a nasal clip, and then breathed normally through the mouth avoiding inspirations or forced exhalations and changes of position for a period of 20 minutes, during which the system recorded the variables mentioned in real time. In order to avoid alterations during the measurement, participants were not allowed to see the recording monitor, so that they could not control the respiratory rate or volume per minute at any time. (21)

Pulmonary function tests

After the previous procedure was done, participants rested for 5 minutes and continued with lung function measurements, including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1) and FEV_1/FVC ratio, which were recorded using the same equipment (Vmax® Encore PFT system). Forced spirometry was performed following the ATS/ERS parameters described by Miller *et al.* (22) Three phases were considered during the maneuver carried out with the closed-circuit method: maximal inspiration, "forced" exhalation and continuation of exhalation until the end of the test.

Maneuver, posture, inhalation, placement of mouthpiece and nose clip and exhalation were instructed and demonstrated; participants were coupled to the circuit where they performed maximal inspiration with a pause of less than one second of TLC (phase 1), followed by exhalation until reaching the RV (phases 2 and 3).

During the whole process, participants were encouraged and the flow/volume curve was monitored in order to guarantee an ideal layout. An acceptable maneuver was required to meet the following criteria: 1) recording a satisfactory expiration; 2) not coughing, especially in the first second; 3) avoiding Valsalva maneuvers that could interrupt air flow; 4) preventing air leaks or losses; 5) not obstructing the circuit with the tongue or teeth or deforming the mouthpiece with a bite; 6) disregarding early termination; and 7) preventing re-inspiration. The test was repeated until three usable curves were achieved (meeting at least criteria 1 and 2), without exceeding eight repetitions, each with a rest period <1 minute. (22)

Training plan

An RMT period of 8 weeks was established. The initial load corresponded to 50% of the total resistance in cm of H_2O in the Threshold IMT system. Participants performed three sets of 10 repetitions a day and the weekly load progression was 7%. The performance was valid when the membrane was mobilized and maintained for at least 2 seconds during inspiration. Training sessions of each participant were recorded and follow-up was carried out every week in person, via email or telephone.

Statistical analysis

Data had a normal distribution, therefore, they are presented as means and standard deviation (σ). Mann-Whitney U test was used to confirm the heterogeneity of the pre- and post-intervention measurements. The level of significance was set at 0.05. R software, version 3.1.2, was used for statistical analysis.

Ethical considerations

The study was approved by the Ethics Committee of the Faculty of Medicine of Universidad Nacional de Colombia, through Minutes 16-155-15 issued on September 22, 2015. Its implementation took into account the guidelines established in the Declaration of Helsinki (23) and the Resolution 8430 of the Ministry of Health of Colombia (24) for biomedical research on human beings, thus this study can be considered as a minimum risk research for its participants, who signed an informed consent prior to their participation. Confidentiality and proper handling of personal data were preserved at all times.

Results

During the pre-intervention phase, 18 subjects were evaluated and, according to IPAQ, were classified as sedentary; of these, 56% were women. The age of the participants ranged between 17 and 32 years; the average body weight was 66.01kg, height 164cm, and BMI 24.55 kg/m² (Table 1).

Table 1. Anthropometric characteristics of pre-intervention assessment.

Parameters	Female (56%)	Male (44%)	Total (n=18)
Age (years)	21.14±2.77	21.82±4.14	21.44±3.380
Height (m)	1.583±0.03	1.71±0.06	1.64±0.08
Weight (kg)	59.25±8.95	74.61±9.94	66.01±12.04
Body Mass Index (kg/m²)	23.76±3.55	25.56±3.30	24.55±3.49

Source: Own elaboration.

For the post-intervention assessment, a sample of 15 subjects completed the 8 weeks training protocol+, of which 60% were women, with an average weight of 65.05kg, height of 1.64m and BMI of 24.14 kg/m².

The comparison of pressure, spirometry and pre-intervention calorimetry measurements is summarized in Table 2. Statistical analysis allowed establishing statistically significant differences in the following variables: MIP ($p<0.001$), RQ ($p<0.01$) and MEP, FEV_1 and FEV_1/FVC ($p<0.05$); on the other hand, measurements of FVC, VO_2, VCO_2 and resting energy expenditure (REE) did not show significant differences after performing the 8 RMT during 8 weerks.

Table 2. Comparison of changes in pre- and post-training pressure, spirometry and calorimetry measurements.

Parameters	Pre-measurement	Post-measurement	p-value
MIP (cm of H_2O)	81.23±22.00	96.44±24.54	0.000 ‡
MEP (cm of H_2O)	94.84±21.63	107.39±29.15	0.014 *
FVC (L)	3.79±0.88	3.80±0.93	0.388
FEV_1 (L)	3.33±0.88	3.54±0.90	0.032 *
FEV_1/FVC (%)	87.78±7.67	93.20±6.02	0.003 †
VO_2 (mL/kg/min)	4.39±0.75	4.39±0.90	0.489
VCO_2 (mL/kg/min)	3.33±0.60	3.18±0.60	0.909
RQ	0.75±0.07	0.71±0.05	0.011 *
REE (kcal/day)	1964.67±358.33	1946.27±413.8	0.681

MIP: maximal inspiratory pressure: MEP: maximal expiratory pressure; FVC: forced vital capacity; VEF_1: forced expiratory volume in 1 second; VO_2: resting oxygen consumption; VCO_2: resting carbon dioxide production; RQ: respiratory quotient; REE: resting energy expenditure.
* $p<0.05$.
† $p<0.01$.
‡ $p<0.001$.
Source: Own elaboration.

Measurement of respiratory muscle strength

Clinically and statistically significant increases in MIP values from 81.23±22.00cm to 96.44±24.54cm H_2O ($p<0.001$) and in MEP values from 94.84±21.63cm to 107.39±29.15 cm H_2O ($p<0.05$) were observed (Figure 1).

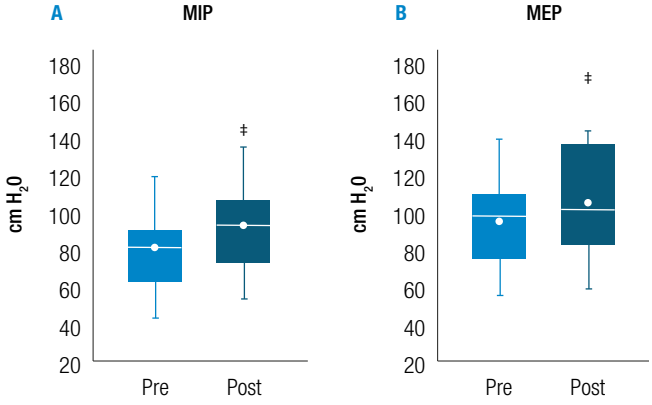

Figure 1. Pre and post-intervention measurements of maximal inspiratory pressure and maximal expiratory pressure.
Source: Own elaboration

Pulmonary function

No change in FVC values were observed after the intervention with the Threshold IMT system. In contrast, participants' ability to exhale the greatest amount of volume in the first second (FEV_1) increased significantly from 3.33±0.88 to 3.54±0.90 liters ($p<0.05$); FEV_1/FVC ratio went from 87.78±7.67% to 93.20±6.02% ($p<0.01$). In Figure 2, the dot represents the median, which is very similar in these variables to the mean of the majority, with the exception of pre-intervention FEV_1 where the mean is 0.47 liters greater.

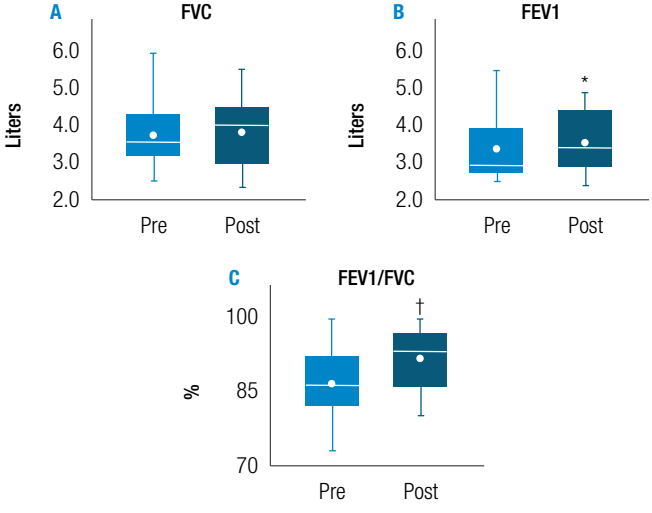

Figure 2. Pre and post-intervention measurements of lung function.
Source: Own elaboration.

VO_2, CO_2, RQ and REE at rest

Resting oxygen consumption and carbon dioxide production during the respiratory cycle remained the same after the RMT. Energy expenditure was similar during the pre- and post-intervention phases, while the respiratory quotient (RQ) showed a significant decrease, going from 0.75±0.07 to 0.71±0.05 ($p<0.05$) (Figure 3).

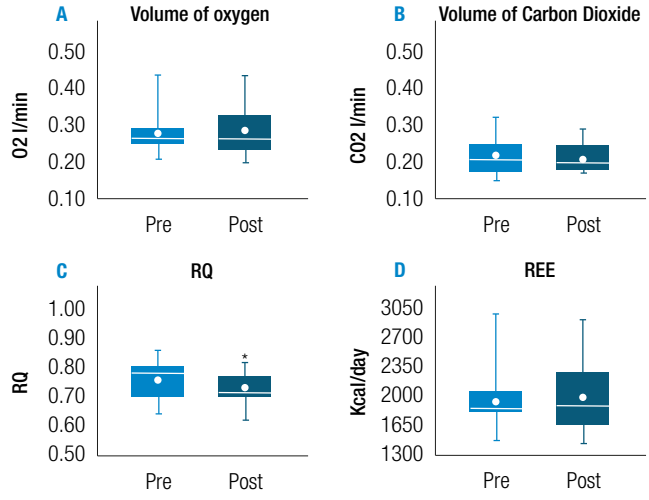

Figure 3. Pre and post-intervention measurement of metabolic variables.
Source: Own elaboration.

Discussion

The level of PA was determined using the IPAQ; 18 participants were classified as sedentary and were included in the study. Significant changes were observed in the RMS of MIP (from 81.23±22.00cm to 96.44±24.54cm of H_2O; $p<0.001$), MEP (from 94.84±21.63cm to 107.39±29.15cm of H_2O; $p<005$) and FEV_1 (from 3.33±0.88 to 3.54±0.90 liters; $p<0.05$).

RMT is one of the strategies used around the world in people with cardiopulmonary impairment or healthy individuals. The prescription of this procedure varies depending on the characteristics of the population and the presence or absence of deficiencies. For this study, the RMT period was established in accordance with previous investigations conducted in non-pathological populations. Enright *et al.* (25) established an 8-week training program with a 80% resistance of maximal inspiratory effort and a fixed volume of 36 repetitions; muscle recruitment intensity was defined by gradually shortening rest times between repetitions. With this form of prescription, statistically significant results were achieved for MIP, lung volumes and TLC.

In contrast, other authors have suggested that RMT at low intensities, such as 40% MIP, can generate significant changes. (11) In this regard, the intensity of the RMT used in the present study, which was implemented for 8 weeks, coincides with reports on the effects on RMS. Volume and training intensity allowed observing changes in respiratory pressure variables, although no significant changes in spirometric parameters and VO_2 were found.

The effect on RMS observed in each subject varied (Figure 1); in 50% of the participants MIP increases were <20%, while for the remaining participants, they were higher (20-59%). This was also observed in the MEP variable, although changes did not exceed 32%. Differences between subjects may be associated with lack of maintenance of muscle overload during the training period; authors have suggested that a person can reduce the training load by altering inspiratory flow between repetitions, leading to differences in strength. (25)

In spite of these differences, the changes in pressure values obtained here coincide with what other studies have reported. (13,14) In this study, with a progressive intensity that reached 60%,

improvements were achieved, representing 16% for MIP and 11% for MEP on average. Such changes may be associated with respiratory musculature, which is skeletal, responding to training in the same way as any muscle of the musculoskeletal system according to the theory of training: if intensities between 60% and 80% are applied, maximum effective strength or resistance is gained, and that condition can be maintained. (26)

Some authors have described that the adaptive mechanism to training depends on the increase in the proportion of Type I fibers and the size of Type II fibers that directly change the length-tension relationship on which force-generating mechanics of the respiratory system depends. (8,12,23) In addition, greater neural activation of the diaphragm and recruitment of the chest wall muscles are observed during a training program such as the one proposed here. (9)

Regarding spirometric parameters, their average values correlate with the reference values described for the Bogotá population. (27) In this study, no significant changes regarding FVC were observed after the intervention; this finding is not unexpected, since they were considered as normal values in the initial assessment considering the participants' anthropometric composition, therefore no major modifications were expected unless a significant decrease in pulmonary function was observed. (28) Another important change was seen in FEV_1, which also determines mathematically a better FEV_1/FVC ratio. This correlates with the marked improvement of muscle strength parameters, where expiratory muscles are able to generate more power and exhale about 90% of the FVC.

VO_2 is related to kinetics of oxygen transport (O_2), muscular work and the efficient use of O_2 by mitochondria; it is assumed that sedentarism can accelerate the reduction of O_2 intake, oxidative capacity and expenditure itself. (29) In this research, no significant differences were observed, which agrees with previous studies in which no increase in VO_2 was reported after the completion of an RMT program because the increase of this variable is related to adaptation during long periods of training and is directly proportional to the intensity of the activity, capillary density in the muscle, and number, size and increase of mitochondrial enzymes in the cells of large muscle groups, reaching improvements of up to 50% of VO_2 and only 15% in RMT. (30,31)

On the other hand, VCO_2 values show a 5% decrease, which may depend on the type of food consumed, body or environmental temperature and hormonal activity. RQ ranges from 0.71 to 0.75, indicating that resting energy expenditure occurs by metabolism of fatty substrates. (32) REE represents the number of calories needed for a 24-hour period in which no significant PA is performed. It has been found that, in sedentary people, EER accounts for most of the total caloric intake (60-70%). In indirect calorimetry, this variable depends on the values of O_2 and CO_2 gases, therefore, the absence of RMT effects, especially on O_2 consumption, reported in this study, explains the stability of energy expenditure. (33,34)

Conclusions

The 8-week RMT protocol using the Threshold IMT System improved RMS and FEV_1 parameters; however, no significant changes were observed in VO_2. The adaptive mechanisms that may interfere in the changes observed in muscle strength probably depend on the morphological adaptations of the muscle fibers and the optimization of the recruiting capacity of the chest wall muscles.

It is necessary, on the one hand, to apply RMT programs in combination with other modalities of physiotherapeutic intervention, such as the prescription of multimodal physical activity, to allow greater adherence to this type of treatment and, on the other, to carry out studies with a larger sample size to achieve a greater effect.

Some of the limitations of this study include the lack of follow-up of the participants (three in total), the fact that the Threshold system has a maximum resistance of 41cm H_2O —limiting the prescription of higher loads in participants with MIP values >90cm H_2O—, and that the training period can influence patterns of adaptation and improvements of lung function parameters. Despite this, this research is expected to provide information that will help further studies in this area.

Conflicts of Interest

None stated by the authors.

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ORIGINAL RESEARCH

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3D rendering as a tool for cardiac anatomy learning in medical students

El uso de render 3D como herramienta para el aprendizaje de anatomía cardiaca en estudiantes de medicina

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| Abstract |

Introduction: Teaching cardiac anatomy, due to its complexity, is a constant challenge for professors and students. This situation has led to the creation of new pedagogical strategies, including the use of 3D rendering, to improve learning.

Objective: To assess the impact of 3D rendering as a digital instrument on cardiac anatomy learning.

Materials and methods: An experimental study was carried out with two groups of students from a medical program randomly selected. Each group consisted of 40 students; one was the control group (3HB) and the other, the study group (3HA). Both groups attended lectures and practices in the dissection hall of the university, that is, they received training using the traditional methodology. The control group received training using the traditional methodology, as well as instruction using anatomy atlas texts, while the 3HA group received training using the 3D Heart-tomy software, a three-dimensional virtual instrument.

Results: Theoretical and practical tests were analyzed, and an opinion survey was conducted, which allowed finding that the students of the 3HA group had better academic performance in the theoretical test than the control group.

Conclusion: Didactic and digital 3D media facilitate the understanding of the location of the anatomical structure, and works as a pedagogical tool, although it does not replace practices in the dissection hall.

Keywords: Heart; Learning; Anatomy (MeSH).

| Resumen |

Introducción. La enseñanza de la anatomía cardiaca, por su complejidad, es un reto constante para docentes y estudiantes, lo que ha impulsado la creación de nuevas estrategias pedagógicas que mejoren su aprendizaje y por lo cual el uso del render 3D facilita su aprendizaje.

Objetivo. Evaluar el impacto del render 3D como instrumento virtual en el aprendizaje de la anatomía cardiaca.

Materiales y métodos. Se realizó un estudio experimental donde se seleccionaron dos grupos al azar de un programa de medicina; cada grupo estuvo constituido por 40 estudiantes, uno fue el control (3HB) y el otro el de estudio (3HA). Ambos grupos recibieron clases magistrales y prácticas en el anfiteatro, es decir la metodología tradicional. El grupo control siguió la metodología tradicional, instruyéndose con textos de atlas de anatomía y el grupo 3HA se instruyó, además, aplicando el software 3D Heart-tomy, instrumento virtual tridimensional.

Resultados. Se analizaron evaluaciones teóricas y prácticas, además se realizó una encuesta de opinión que evidenció que los estudiantes del grupo 3HA obtuvieron un mejor desempeño académico en la evaluación teórica que el grupo control.

Conclusión. Los medios didácticos y virtuales en 3D facilitan la comprensión de la ubicación de la estructura anatómica y funcionan como herramienta pedagógica, pero no sustituyen las prácticas en el anfiteatro.

Palabras clave: Corazón; Aprendizaje; Anatomía (DeCS).

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Introduction

Learning anatomy is an art. Centuries of curiosity, dedication and intelligence allowed our ancestors to learn, through anatomical dissection, about what today are the basics of medicine. (1) The traditional method of teaching and learning anatomy includes on-campus classes given by a professor with experience and knowledge on the subject. In addition, students receive classes in dissecting rooms using anatomical specimens, where they can perform identification and differentiation of structures, dissection and injection, relying on anatomy texts such as atlases that offer images in two dimensions (2D). (2)

Based on the international nomenclature, human anatomy has a great variety of structures, and three main methods used for their study are regional anatomy, systems anatomy and clinical anatomy. (3) Anatomical illustrations are fundamental for medicine learning. In the past, they were obtained by dissecting animals, given that the inspection and dissection of a human corpse was illegal and the person who engaged in this practice could be sentenced to death. The founder of modern anatomy, Andreas Vesalio, began to make illustrations based on direct observations and dissections on human cadavers in the 16th century, turning dissection into a fundamental part of the class for his students. The anatomist found errors in the information previously described by Galen regarding the anatomy and function of the human body (4), and although Leonardo da Vinci dissected human corpses before Vesalio, his findings were not disclosed because it was illegal. Perspective can be found in da Vinci's drawings, and this contributed to a three-dimensional approach to the body. (5)

Currently, in order to perform dissections and explorations of structures (6), texts such as anatomy atlas are used, as they offer 2D illustrations, although they do not allow perceiving their depth and do not provide enough perspective or detail to grasp correctly the structures. Learning should focus on personal development because it is an empirical process, making practices in the dissection hall fundamental; even so, difficulties in understanding continue to occur due to insufficient cadavers, deterioration of structures and ethical limitations. (7)

In this context, the most important historical achievement of anatomy has been the improvement of graphic tools. Several historical figures have concentrated their efforts on the development of new tools or methods that allow achieving greater realism in the illustrations; however, the lack of technology in certain places has limited the ability to progress significantly, reducing the learning options to the use of literary tools and cue cards. With the incorporation of virtual media in society, it is essential to continue with the efforts and create tools that increase the similarity of the anatomical graphic resources with reality.

Two-dimensional illustrations and the ability of the draftsman were the only tools available in the past; today three-dimensional resources allow for spatial understanding and the analysis of a complete structure with only one graphic resource, compared with the illustrations that need many images to analyze only one structure without preserving spatial comprehension. Digital tools, along with traditional learning methods, optimize the understanding of cardiac anatomy. The main evolutionary objective of the study of anatomy is, then, to ensure that multimedia tools bring the student closer to reality. (8)

In this regard, multiple strategies have been developed with new software technologies that have proven to be very useful for increasing educational performance, particularly in specialties related to health sciences, because computational tools have the ability to create very similar scenarios that complement the learning process, although they can never replace direct experience with reality. (9)

This study was formulated from the perspective of a student when realizing that the hours in the dissection hall were not enough to study and review the structures, because that is the only place where teaching with a three-dimensional approach can occur, achieving greater spatial location with respect to orientation, relationship and nomenclature. In this context, the following questions arose: if the basis of the anatomy begins with dissection, why not using software with the structures found? Can traditional teaching in cardiac anatomy be optimized?

Interactivity and multimedia tools in education are of great importance. Studies show a marked increase in the interpretative capacity of students when they are involved in an educational model equipped with interactive multimedia tools. (10) One of these tools is called Anatomage, which consists of a digital table for virtual 3D dissection. Its implementation has shown favorable outcomes in 63% of students, who claim to have increased their knowledge; in addition, 78% stated that the interactivity of the tool has more impact. (11)

Technological alternatives with greater acceptance include 3D software, which, compared with anatomy atlases, have an unlimited number of perspectives that facilitate perception thanks to the interaction with the rendered model. (12) Another study reported greater facility to understand two-dimensional images after studying with 3D web tools. (13)

One of the greatest challenges of teaching consists in identifying the methods preferred by the students, since it is important to develop the appropriate didactic approach to involve students with the information taught. This is important in subjects that require great memory effort, for which generating dynamics that are pleasant enough to prevent information from being forgotten is also recommended. After making a 3D model of the larynx, a satisfaction survey found that 93% of the students preferred the technological tool and 87.4% recognized greater facility to understand its anatomy. (14,15)

Taking this into account, the objective of this research was to evaluate the impact of using 3D rendering as a digital tool on cardiac anatomy learning.

Materials and methods

This is an experimental study that included third-semester students of a medical program as study population. The population was divided into two groups consisting of 40 students each: the 3HA group, which corresponded to the study or intervention group, and the 3HB or control group. At the time of the study, participants were taking the subject Anatomy II, in the specific context of cardiac anatomy learning.

The selection of students for each group was random, for a total population of 80 students. Those who failed the subject and were enrolled in a program other than Medicine were excluded. Academic performance analysis was not performed according to sex or age.

Both groups attended lectures and practices in the dissection hall, that is, they used the traditional methodology. The 3HB group only followed the traditional methodology, which corresponds to 6-hours lectures and classes in the dissection hall for 4 hours, using texts of anatomy atlases. The 3HA group received traditional instruction and also 2 hours of class in which digital pedagogical strategies applying the 3D Heart-tomy program in the computer room were used, in order to support the theoretical and practical components. The 3D Heart-tomy file used was run using the Blender v2.78 software, which is open source. The file was prepared by the company Botero Mechatronics SAS based on real hearts obtained in the dissection hall.

The digital didactic instrument consisted of an interactive three-dimensional projection, as shown in Figure 1. This interactive learning tool frames and splits each of the structures to understand their relationship and the composition of the heart.

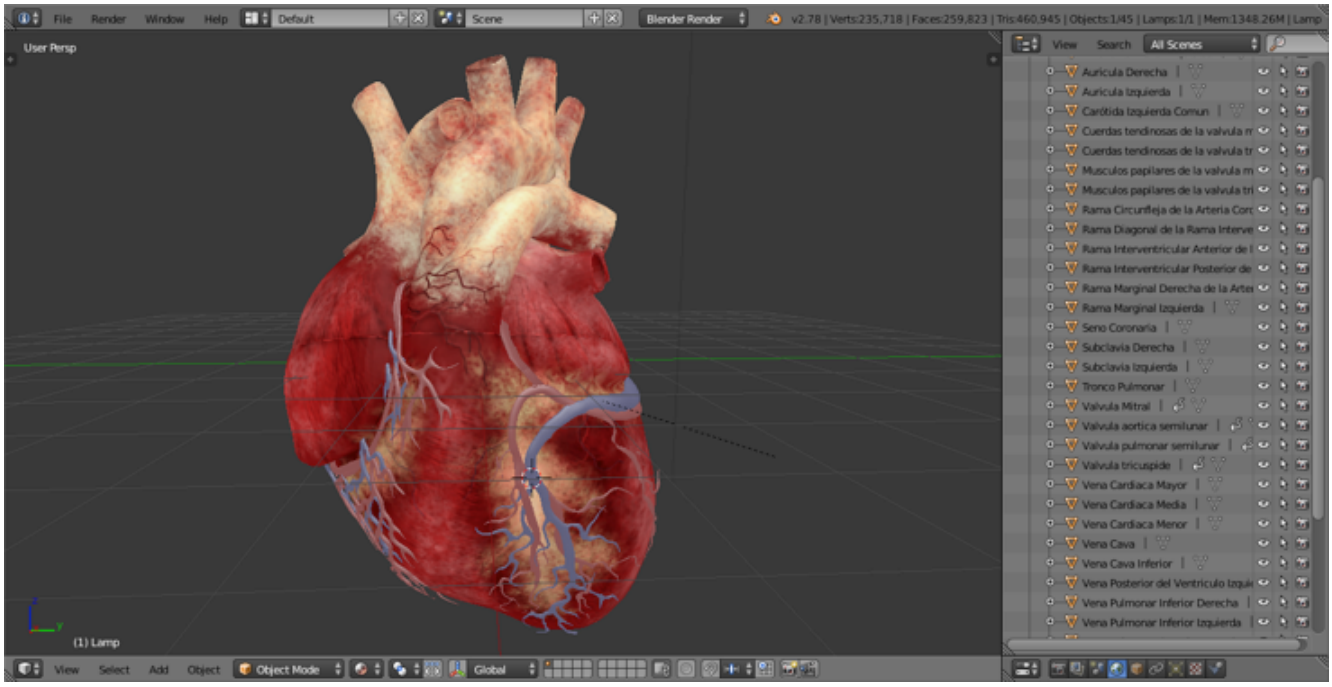

Figure 1. 3D Heart-Tomy anatomy file.
Source: Document obtained during the study.

The 3D Heart-tomy allows identifying the structure with its name, moving it, separating it and analyzing its unions and direction. Students can also see all the structures through real-time manipulation. This program has the option of orbiting the 3D model, allowing any perspective as desired, has a list of the nomenclature of each structure, and highlights the name. In the same way, it is possible to hide some sections to visualize the inner part of the heart and there is an Rx option to visualize its interior without hiding the exterior. Finally, a file contains a self-qualifying test that allows students to analyze what structures are being forgotten.

Classes were taught by the same professor and the heart related topics addressed during the virtual based classes were as follows: external configuration and large vessels, internal configuration, epicardium, myocardium, endocardium, electrical system, coronary circulation, innervation and images.

The objective of the theoretical tests in the classroom and the practical test in the dissection hall was to measure the conceptualization of the topic related to cardiac anatomy, with an approval score of at least twelve correct questions (60%), equivalent to a passing grade of 3.0.

Five independent evaluators and experts in the field reviewed these tests and validated the relevance of the questions in relation to the educational level of the groups under study and the requirements on heart knowledge for medical students of the subject Anatomy II.

To avoid bias while grading, the students were identified through their student identification number and the group to which they belonged was only known when the grades were entered into the system, after the tests had been graded.

In addition, an opinion poll was conducted to evaluate the students' opinion of the impact of 3D Heart-tomy as an implementation of new technologies for teaching and learning about cardiac anatomy.

Information was obtained strictly based on the criteria defined for carrying out a medical-legal autopsies contained in Decree 786 of 1990. (16) In addition, all the principles of the Declaration of Helsinki 2013 for medical research were followed (17), thus ensuring respectful treatment of the pieces obtained during the study and maintaining the confidentiality, dignity and integrity of the deceased person. According to the parameters established by the Resolution 8430 of 1993 of the Ministry of Health of Colombia (18), this investigation was presented before the Ethics Committee on Human Research of the Faculty of Health Sciences of Universidad de Ciencias Aplicadas y Ambientales (UDCA), which granted its approval through Minutes 20160401, issued in April 2016. Informed consent was obtained from all participants.

Results

The results obtained were compared after being typed in a table. The amount of grades <3.0, the amount of grades between 3.0 and 3.9 and the amount of grades ≥4.0, both in the theoretical test and the practical test in the dissection hall, were retrieved (Table 1).

Table 1. Statistical results of the theoretical and practical tests of the study group and the control group.

Characteristics	Theoretical exam		Practical exam in the dissection hall	
	3HA Group	3HB Group	3HA Group	3HB Group
Arithmetic mean	4.3	3.6	2.75	2.66
Mode	4.5	4.5	2.5	2
Students mode	19 (47.5%)	13 (32.5%)	11 (27.5%)	8 (20.0%)
Minimum grade	0.0	0.0	1.0	0.5
Maximum grade	5.0	5.0	5.0	4.5
Passed	39 (97.5%)	30 (75.0%)	18 (45.0%)	18 (45.0%)
Failed	1 (2.5%)	10 (25.0%)	22 (55.0%)	22 (55.0%)
Number of students who obtained 5	9 (22.5%)	3 (7.5%)	1 (2.5%)	0 (0%)
Grades ≤1	1	1	1	4
Grades ≥4	28	16	5	7

Source: Own elaboration.

The results show a difference between both groups. The average grade of the 3HA group was 4.3 compared to the 3HB group, which had an average grade of 3.6. In this case, a favorable result can be seen in the group that used the 3D tool, which is 14% higher than the result of the group that did not use it.

Regarding the proportion of students who passed the test, the 3HA group obtained a percentage of 97.5%, while the 3HB group obtained 75%. This showed that 25% of the control group failed and only 2.5% of the group that used the digital tool failed the subject.

There were also positive results for the 3HA group in terms of the number of students who achieved the highest score, 22.5%, while only 7.5% obtained it in the control group, which shows results that favor by 15% the group that used the technological tool.

After analyzing the last result, most grades greater than or equal to 4.0 were obtained by the 3HA group and 70% of the students in this group are in the mentioned range; meanwhile only 40% of the students in the control group obtained a 4.0 or higher grade. A 30% difference in favor of the members of the 3HA group.

Data of the theoretical test were organized according to the distribution to find the value of X^2, which sought to prove the hypothesis that the traditional method of learning and the use of technology strengthen learning of cardiac anatomy, as described in Table 2.

Table 2. Passing and failing grades obtained in the theoretical test.

Group	Passed	Failed	Total
3HA Group	39	1	40
3HB Group	30	10	40
Total	69	11	80

Source: Own elaboration.

The results were obtained through OpenEpi. The value was compared with the table of critical values of the distribution X^2 having 0.005 as margin of error. The value of X^2 in the table for this margin is 8.5, which is greater than the calculated value and allows concluding that the hypothesis for the theoretical test can be accepted.

The odds ratio (OR) is 13 (lower limit: 1 576, upper limit: 107.2), which means that students who used the software are 13 times more likely to pass the theoretical test. Although the interval is wide, the confidence interval is greater than 1.

The differences in the practical tests were not significant between the groups, being 2.75 the average grade in the intervention group and 2.5 in the control group. It should be noted that the result was low for both groups, but a little higher for the group that used the 3D tool.

The results of the practical test were organized to determine the corresponding value of X^2, which was 0 and can be seen in Table 3.

Table 3. Passing and failing grades obtained in the practical test.

Group	Passed	Failed	Total
3HA Group	18	22	40
3HB Group	18	22	40
Total	36	44	80

Source: Own elaboration.

The alternative hypothesis cannot be accepted for the practical test, because the OR is 1, so there is no statistical significance in passing the practical test using the software.

Each grade of the theoretical test obtained by a specific student was typed in a Microsoft Excel sheet, by means of which Figure 2 was generated; it is possible to see that the results of the 3HA group are notoriously higher than those of the 3HB group.

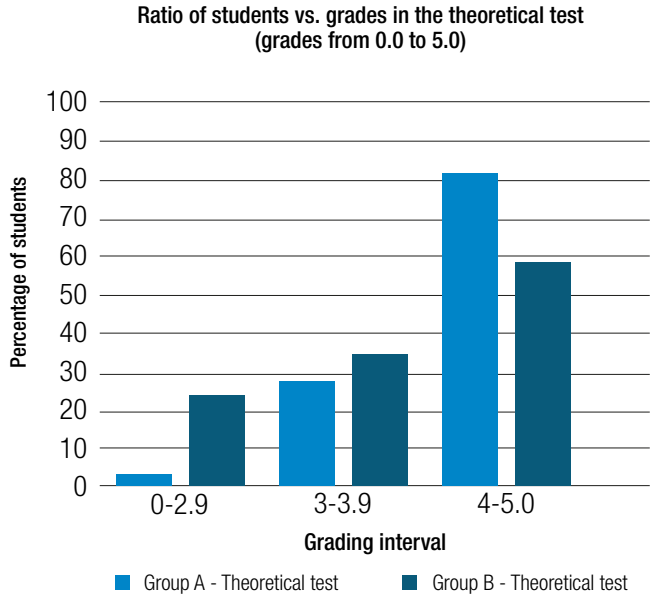

Figure 2. Results obtained by the students in the theoretical exam.
Source: Own elaboration.

The results of the practical test did not differ much in both groups; however, students in the control group obtained grades below the minimum grades obtained by those in the intervention group, which evidences a better performance in the latter, as it can be seen in Figure 3.

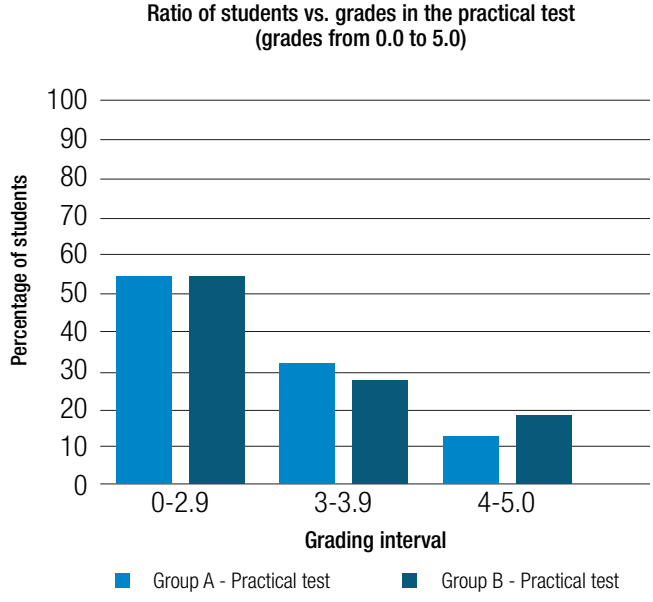

Figure 3. Results of the students in the practical test.
Source: Own elaboration.

The survey yielded satisfactory results; the percentages of passing and failing grades obtained by students for each question asked, together with the percentage of unjustified questions can be seen in Table 4 and Figure 4.

Table 4. Results of each question in the opinion survey

Question	Yes	No	Unjustified
1. Do you recommend the use of 3D software for cardiac anatomy learning?	97.5%	2.5%	20.0%
2. Do you think that there is an academic and learning advantage compared to the students who did not use the tool?	95.0%	2.5%	20.0%
3. Do you think that the use of the 3D Heart-tomy virtual tool facilitated learning and academic performance in cardiac anatomy?	90.0%	7.5%	20.0%
4. In your opinion, do you think that using virtual tools is convenient for learning about cardiac anatomy?	87.5%	7.5%	37.5%
5. Does learning with interactive tools replace practice in the dissection hall?	67.5%	22.5%	35.0%
6. Did the 3D Heart-tomy tool help you reinforce what you learned in theoretical and practical classes of cardiac anatomy?	95.0%	2.5%	27.5%
Men	27.5%		
Women	72.5%		
Total average of approval	88.75%		
Total average of failing	7.5%		
Overall average of unjustified questions	26.5%		

Source. Own elaboration.

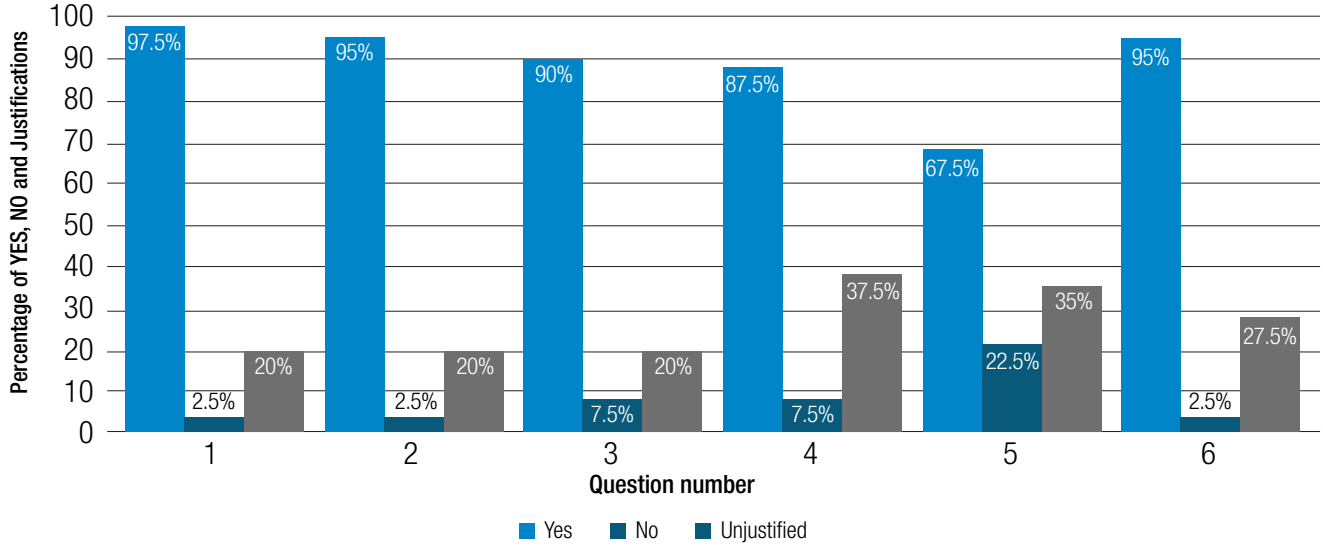

Figure 4. Software satisfaction results according to the opinion survey.
Source: Own elaboration.

Discussion

A new field of medical education was born with the advent of new technologies. In recent years, the several benefits that digital media can provide and how much they could improve the learning process have been explored. For the specific case of anatomy, this research has similar results to other studies conducted on the use of 3D tools, which confirm that they are very useful as an additional means of teaching subjects on anatomy.

When analyzing the data and Figure 2, it can be seen that the trend line in the 3HA group is constantly above the trend line observed in the control group. The performance of students who use digital tools has been higher in multiple studies than in students who use non-technological means; computer-based instruction allows the student to be more actively involved, facilitating the achievement of effective learning.

There are few comparative studies; however this study is similar to those performed by Lim *et al.* (14) and Hopkins *et al.* (19), who took 3 groups of people made up of 74 students who were enrolled in the pre-test, laboratory session and post-test (pro sections n=26, 3D model n=23, hybrid n=25) in 17 separate group learning sessions, where each participant attended a single lab session. Students showed a significant improvement of knowledge in the post-test. Although the difference in the results was not that high, there was a better performance in those who used the 3D tool, which correlates with what is reported here. The students then responded to a questionnaire in which 82% preferred to have the usual study tools together with the 3D tool. Observations from the Lim *et al.* study (14) ensure that 3D tools do not replace any other study method and may work better if used as a complement, which is consistent with the results obtained here.

A similar study (20) compares whether a three-dimensional presentation is more effective for teaching than a presentation

supported by a traditional book or not. This research involved 46 students who were divided into two groups, one that participated in the interactive computer-based learning module with 3D images and another that received their lessons in computers using non-interactive 2D images. After each teaching module, students completed a satisfaction survey and nine points of anatomical knowledge after the test. The group that used the 3D tool scored higher in the post-test than the group that used the 2D tool, with an average score of 74% and 64%, respectively; these results were similar to those obtained in the present study (20).

In the post-test satisfaction survey, the group that used the 3D tool expressed higher satisfaction and showed significantly higher figures compared to the students in the control group that used the 2D tool. After verifying the pre-test and post-test analysis, although a higher score was found, it was not statistically significant. Like other authors, in this study, the satisfaction survey showed that students preferred using three-dimensional tools for learning.

In the opinion poll, six questions were asked to students who used 3D software in order to evaluate the impact of the implementation of a digital didactic tool for teaching cardiac anatomy on learning in third-semester students. The result in terms of student satisfaction with the software was quite positive and in line with other studies that found great satisfaction in the use of digital tools for the study of anatomy.

Use of render, as a cognitive tool, facilitates the learning of human cardiac anatomy. (21) In most studies, as found here, the use of digital environments proves to be efficient for learning cardiac anatomy. (22)

Conclusions

Participating students agreed that the 3D rendering tool facilitates the learning of cardiac anatomy and improves theoretical academic performance due to the interactivity they are given by it. This opinion resembles statements from other studies and shows an increase in learning capacity thanks to the implementation of new digital technologies.

Didactic and digital 3D media facilitate the understanding of the location of the structure and works as a pedagogical tool; however, it does not replace practices in the dissection hall.

Conflicts of interest

None stated by the authors.

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ORIGINAL RESEARCH

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Use of sexual health services at hospitals by cleaning workers in Bogotá D.C. 2016

Uso de los servicios de salud sexual por parte de trabajadoras de servicios generales en hospitales en Bogotá D.C. 2016

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| Abstract |

Introduction: Poverty and social inequalities together with sexually transmitted diseases have a negative impact on women's health, which is considered to be a public health problem.

Objective: To analyze barriers to accessing sexual and reproductive health services in cleaning workers.

Materials and methods: A survey was administered to a sample of 37 female cleaning workers at a hospital in Bogotá D.C. A bivariate analysis was performed with chi-square test, as well as a multivariate analysis with binomial logistic regression.

Results: Need factors showed greater association with non-use of sexual health services. All married women had accessed the service over the past 12 months, but there were 5.9 less possibilities of using sexual and reproductive health services when there was no awareness about risk behaviors of sexually transmitted diseases.

Conclusion: The determining factor for the utilization of sexual health services is the health care need factor. Variables such as perception of risk behaviors and appropriateness of health care significantly influence the use of the service.

Keywords: Housekeeping Hospital Service; Sexually Transmitted Diseases; Accessibility of Health Services; Sexual Health; Gender Identity; Women (MeSH).

| Resumen |

Introducción. La pobreza y las desigualdades sociales, junto a infecciones de transmisión sexual, tienen un impacto negativo en la salud de la mujer, lo que se considera un problema de salud pública.

Objetivo. Analizar las barreras de acceso para la utilización de servicios de salud sexual de las mujeres trabajadoras en servicios generales.

Materiales y métodos. Se aplicó una encuesta a una muestra de 37 mujeres trabajadoras en servicios generales en un hospital de Bogotá D.C. Se realizó análisis bivariado con prueba chi cuadrado y multivariado con regresión logística binomial.

Resultados. Los factores de necesidad tuvieron mayor asociación con la no utilización de los servicios de salud sexual. Todas las mujeres casadas accedieron al servicio en los últimos 12 meses y existe 5.9 menos posibilidades de utilizar los servicios de salud sexual y reproductiva si se desconocen las conductas de riesgo de las infecciones de transmisión sexual.

Conclusión. El principal factor determinante para la utilización de los servicios de salud sexual es el factor de necesidad de atención en salud, cuyas variables, como la percepción de conductas de riesgo y la pertinencia de la atención en salud, influyen significativamente en la utilización del servicio.

Palabras clave: Servicio de limpieza en hospital; Enfermedades de transmisión sexual; Accesibilidad a los servicios de salud; Salud sexual; Identidad de Género; Mujeres (DeCS).

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Introduction

In recent history, women have legitimized sexual rights as human rights, promoting gender equity as a determining factor for sexual and reproductive health research and public policy planning. (1,2) The Colombian health care model is strongly influenced by the competition within the supply and demand of health services; moreover, market laws compromise the equality and universality of these services. (3)

According to a systematic review of studies on access to health services in Colombia, access has not increased as there are barriers associated with insurance, economic income, educational attainment and geographical, organizational and quality-service accessibility. (4) In this regard, the efforts of national and international health organizations to fight the occurence of sexually transmitted diseases (STDs) specifically have not prevented persistent reproductive and sexual health risks. (5)

UNAIDS estimates show that although the incidence of HIV has decreased in recent decades, it is still a public health problem. (6,7) Both women and men living with HIV and receiving treatment have increased significantly (8); it is also a matter of concern that around 1.4 million maternal infections and 520 000 congenital infections caused by syphilis have been reported worldwide, including 304 000 perinatal deaths from 2009 to 2012 among working populations and disadvantaged social classes of Latin America. (9,10) Furthermore, the people most prone to contract these diseases are the most disadvantaged human groups. (10,11)

It should be noted that barriers to accessing sexual health services are determined by internal factors that depend on each person's perception and decision while looking for a health service, as well as external factors that can derive from administrative, legal and structural difficulties, lack of awareness about the health system, socio-economic situation, culture, communication and education. (12-14) Identifying the barriers to accessing health services largely contributes to monitor inequalities and generate proposals to mitigate impacts on their health condition. (15)

The utilization of health services comes from the interaction of three main factors: 1) predisposing factors: they are inherent to the patient, do not depend on the pathology and evaluate the perception of health and disease related to socioeconomic and demographic variables (age, sex, occupation, ethnicity, etc.) (16); 2) mediating or capacity factors: they can facilitate or limit access to services and are subject to changes in health policies, and 3) need factors: they include aspects related to the health-disease process and address the need in two ways, namely, the patient's perspective and the evaluation by the health staff. (17-19)

Therefore, the objective of this study was to analyze the barriers to accessing sexual and reproductive health services by female cleaning workers at a hospital center in Bogotá D.C. in 2016; these women are one of the most marginalized human groups given their low educational attainment, low income and lack of knowledge about their health rights.

Materials and methods

The study was developed under an observational, descriptive cross-sectional design. A survey was conducted based on the behavioral model of health services proposed by Aday & Andersen and adapted for sexual health. (17) Need factor variables were: knowledge of sexual health services, sexual and reproductive rights, STDs, contraception and quality of health care received. The predisposing factor variables were: age, marital status, ethnicity, educational attainment, socio-economic level and social support. Finally, capacity factor variables were: family income, commuting time and location of the Healthcare Service Provider (IPS by its acronym in Spanish), out-of-pocket expenses, among others. The query "sexual health services over the past 12 months" was established for the exposure variable.

Similarly, a pilot study (10 surveys) was conducted to check whether the questionnaire was understood, as well as the coherence and relevance of questions concerning the topic under evaluation.

The inclusion criteria used were: women who were not pregnant, female hospital cleaning workers hired by the JDR company (contracting party) at Fundación Hospital San Carlos, an institution where 37 women work in cleaning services. It was relevant to conduct the study in this vulnerable population because there was no prior record.

Frequency measurements were performed to determine the sample distribution based on age, marital status, ethnicity, employment status, educational attainment and socio-economic level. Predisposing, capacity and need factors concerning the use of sexual and reproductive health services were identified through bivariate and multivariate analyses; the goal was to develop an explanatory model based on the individual determining factors of the Aday & Andersen model.

The chi square test was performed in the bivariate analysis, where the significant statistical evidence were values of $p<0.10$. Effect confusion and modification were assessed through a multivariate analysis by selecting the variables with values $p<0.25$ in the bivariate analysis; this analysis was performed using the logistic regression model. The Wald test was used to establish statistical significance and measure the strength of association with the odds ratio (OR) values. The process was executed in the SPSS® software version 14.

The study was approved by the Research Committee of the Master's Degree in Public Health and Social Development of Fundación Universitaria del Área Andina and all the participants signed and informed consent. On the one hand, the research followed the guidelines of the Declaration of Helsinki (20) on the participation of the subjects and the researcher's confidentiality duties both at the beginning of and during the study; on the other, the research followed the guidelines established in the Resolution 8430 of the Colombian Ministry of Health (21), which sets forth the scientific, technical and administrative standards for health research.

Results

Regarding predisposing factors, 18.9% of the sample had not completed secondary studies, and only 2.7% had completed higher education studies, thus confirming that most of them have a low educational attainment; no participant was identified within an ethnic group (Table 1). 35.1% of the respondent women were 21 to 40 years old and the bivariate analysis showed that age influenced the utilization of sexual health services before the 12 months; for example, 21 to 30-year old women used the service the most (66.7%), while 41 to 50-year old women used it less (12.5%). The marital status variable showed that 100% of married women attended the appointments, while only 14.3% of unmarried women attended the appointments (based on the p-value of the chi square test); 40.5% of the interviewed population lived in cohabitation. Finally, the multivariate analysis did not find any variables of predisposing factors that were closely related to the utilization of health services.

Table 1. Determining factors for the utilization of sexual and reproductive health services by cleaning workers at a hospital in Bogotá D.C.. 2015.

Factor	Variables		n	%	P
Predisposing factors	Age (years)	≤20	6	16.2%	0.094
		21-30	6	16.2%	
		31-40	13	35.1%	
		41-50	8	21.6%	
		>50	4	10.8%	
	Educational attainment	Illiterate	0	0.0%	0.206
		Incomplete primary	3	8.1%	
		Completed primary	4	10.8%	
		Incomplete secondary	7	18.9%	
		Completed secondary	22	59.5%	
		Higher education	1	2.7%	
	Marital Status	Single	14	37.8%	0.087
		Married	2	5.4%	
		Cohabitation	15	40.5%	
		Widow	1	2.7%	
		Divorced	5	13.5%	
Capacity factors	Socio-economic level	1	16	43.2%	0.625
		2	20	54.1%	
		3	1	3.7&	
		4	0	0.0%	
	Income	1 CLMW	37	100.0%	0.973
		From 1 to 2 CLMW	0	0.0%	
		More than 2 CLMW	0	0.0%	
	Additional support	Yes	6	16.2%	0.633
		No	31	83.8%	
Need factors	Knowledge about sexual and reproductive rights	Yes	21	26.8%	0.143
		No	16	43.2%	
	Condom use	Yes	10	27.0%	0.539
		No	14	37.8%	
		Sometimes	13	35.1%	
	Partner interested in using a condom	Yes	12	32.4%	0.123
		No	19	51.4%	
		Sometimes	6	16.2%	
	Appointment allocation time	Low	37	100.0%	0.152
		Normal	0	0.0%	
	Discrimination	Yes	4	10.8%	0.230
		No	33	89.2%	
	General quality of care	Low	14	37.8%	0.137
		Normal	22	59.5%	

CLMW: Current legal minimum wage
Source: Own elaboration.

With respect to capacity factors, 54.1% of the respondents belonged to the socio-economic level 2, 100% had an income of one current legal minimum wage, 59% had 1 to 2 children, 83% did not have any additional financial support and 89.2% considered that their income was insufficient to cover their monthly expenses. Moreover, 48.6% mentioned that the IPS was close to their workplace. It is worth mentioning that 67.6% stated that they have economic difficulties to use health services and nobody mentioned any difficulties related to work for such access (Table 1). The bivariate analysis showed that family income is related to lack of attendance to health services in 75.7% of the sample and that no variables in the multivariate analysis were strongly associated with the use of services.

Need factors showed that 43.2% is not aware of their sexual and reproductive rights and 64.9% is not aware of the sexual health services offered by their health promotion organization. Concerning knowledge about STDs, it was observed that 91% know what STDs are, since most of them have received information directly from health professionals at their workplace. It was evident that the respondents associate infidelity and having multiple sexual partners to a risk behavior leading to HIV infection (45.9%), as well as not using condoms (67%).

Concerning quality of health care, 100% of the participants gave a low rating to the opportunity they have to get appointments and the explanations given by health care professionals, 10.8% felt discriminated and 13.5% felt judged during the appointment; in short, the quality of health care in general had a low rating from 37.8% of the respondents.

Moreover, only 27% use condoms on a regular basis during their sexual relations, 24.3% did not consider it necessary and 21.6% did not like it. 54% had taken an HIV test, the majority (27%) had been tested more than 3 years before the execution of the study and did not deemed it necessary to repeat it. 89% had undergone a cytology test; however, 78.4% had not taken this test in the last year. Taking into account the time of the last appointment for sexual health services, it was found that 37.8% had never accessed these services and that 37.8% had not used them in the last 12 months (Table 1).

Multivariate analysis showed that the need factors related to knowledge about STDs, purchase of condoms and problems related to access to sexual health services have a statistically significant correlation with the utilization of sexual and reproductive health services by women. That is to say, those who do not have proper knowledge about HIV/AIDS risk behaviors use sexual health services 5.9 times less than women with such knowledge. Furthermore, purchasing condoms in places such as pharmacies and supermarkets has an impact on access to the services, since those buyers access the services 0.8 times less than those who get condoms at their IPS. Finally, when there are issues to make sexual health appointments, women access 2.1 times less than those who do not have any difficulty in doing so (Table 2).

Table 2. Logistic regression analysis. Explanatory model of self-perception of sexual health and its correlation with quality of life among female cleaning workers.

Factor	Variable		OR *	CI95%	p
Need factors	HIV risk behavior		5.9	0.764-46.4	0.089
	Place of condom purchase		0.76	0.02-2.40	0.143
	Issues to make an appointment		2.16	0.038-121.5	0.092
	Adjustment quality	Nagelkerke R2	0.467		
		Hosmer-Lemeshow test	0.89		

* OR adjusted by variables of knowledge about HIV transmission behaviors, issues to request for services, and place where condoms are purchased.
Source: Own elaboration.

Discussion

The state of the art of research on access to health services in Colombia shows that Colombians experience mainly administrative, economic and cultural barriers, where the perception of health condition and the need for care together with a low educational attainment and the lack of information on matters related to the right to health play a key role in the utilization of health services. (22,23) This study demonstrated that the perception of risk in health care is related to the utilization of services and is influenced by the social and economic context of the individual, as well as by variables such as age, marital status, educational attainment and ethnicity.

The above has been shown in research on access to health services, mostly among women who suffer a high-cost disease such as cervical cancer or breast cancer. (24-31) It is also essential to recognize the role of social support in the utilization of health care, since it was demonstrated that married women accessed services more frequently than unmarried women or women in cohabitation. In contrast to these results, a research on taking Pap test stated that one of the main factors that limits access to said test is the pressure that women are subjected to by their partner. (32)

Geographic and travelling access barriers have also been identified, particularly in rural areas (24); this demonstrates that the use of health services in cities is not linked to the travelling time, since the servicing IPS are located close to the participants' residence or workplace. (12,33,34)

Out-of-pocket expenditure represents an economic burden that the most vulnerable populations are not able to afford. (35) In the case of Colombia, this translates into not guaranteeing full access to services due to factors such as copayment, travelling and treatments that are not covered by the Mandatory Health Plan (POS for its acronym in Spanish). The bivariate analysis of this research showed that capacity factors are related to and represent barriers to accessing sexual health services; however, they are not the most representative factors.

STDs have been studied in depth worldwide, demonstrating that they are preventable diseases transmitted primarily by sexual contact (36); nevertheless, STDs and their negative impacts on health, which may include chronicity, infertility, cancer or even death, have not been controlled. (37,38) Consequently, STDs continue to be a priority for public health and a change that focuses on preventing contagion and providing timely treatment (39-41) that encompasses the perception of risk is required, since there is a higher probability of non-access to health services when risk behaviors related to STD transmission are not known, condoms are purchased in commercial places and issues arise while making an appointment.

Furthermore, some research studies have found a correlation between the social stigma generated by HIV in communities and the access to and effective use of health services for the diagnosis and treatment of the disease. (42) Also, gender status is considered to be one of the factors that lead to health inequalities, since it has been defined as a social construction that takes the female and male concepts beyond biological characteristics, relates to all economic, social and private aspects of life of individuals, and determines features and roles depending on sex or on how society sees the subject. (1,43-46)

Access to health services has been studied throughout the world; however, the lack of a specific characterization of populations is evident; although population groups with similarities are addressed, it is not possible to extrapolate their special features. (47) This study allows advancing in knowledge about access barriers and determining factors that influence access to sexual health services by a group of women that has not been extensively studied nor intervened in a timely manner by the health system, even less when they are immigrants, considering essential variables such as predisposing factors, capacity factors and need factors to evaluate the utilization of health services, which are modified over time. Thus, it is imperative to generate continuous monitoring to determine the actual needs of the population.

Identifying access barriers contributes largely to monitor inequalities and generate proposals to mitigate impacts on health condition. (48) Therefore, one of the limitations of this study lies on the fact that the results obtained show a correlation between the perceived need to attend health services, the knowledge about sexual health rights and the risk behaviors of STD transmission; these are, however, not enough to demonstrate the cultural, social, political and economic reasons influencing the use of health services. Therefore, it is advisable to perform a qualitative study to identify and go in depth regarding other determining factors related to women's sexual health.

Conclusion

The determining factor identified for the utilization of sexual health services by female cleaning workers at a hospital in Bogotá D.C. is health care need; associated variables such as perception of risk behaviors and appropriateness of health care significantly influence the use of the service.

Conflicts of interest

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From substance fermentation to action potential in modern science (part two)

De la fermentación de sustancias al potencial de acción en la ciencia moderna (segunda parte)

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| Abstract |

Introduction: After conducting a bibliographical review on the works of various researchers at different times to explain the phenomenon of the transmission of nerve impulses, it is observed that since the eighteenth century, when modern science was born, scientific knowledge in the field of physiology had an accelerated development following the creation of new research techniques and the application of the scientific method. Thus, the philosophical theory of "animal spirits" led to the current concept of action potential, understood as a merely electrochemical phenomenon.

Discussion: The establishment of the scientific method and the development of new research techniques led several researchers at different times to unravel the molecular mechanisms involved in the transmission of nerve impulses, which took two and a half centuries to reach the current concept about the origin of action potential.

Conclusion: The notion "animal spirits" was valid for many centuries, while modern science took a little more than two centuries to understand the phenomenon of nerve impulse transmission.

Keywords: History; Physiology; Action Potentials; Science (MeSH).

| Resumen |

Introducción. Después de una revisión bibliográfica sobre los trabajos de diversos investigadores en distintas épocas para explicar el fenómeno de la transmisión nerviosa, se observa que a partir del siglo XVIII, cuando surge la ciencia moderna, el conocimiento científico en el campo de la fisiología tuvo un desarrollo acelerado por la creación de nuevas técnicas de investigación y la aplicación del método científico. Así, de la teoría filosófica de los "espíritus animales" se llegó al concepto actual del potencial de acción, entendiéndose este como un fenómeno meramente electroquímico.

Discusión. Con el establecimiento del método científico y el desarrollo de nuevas técnicas para la investigación, diversos investigadores en distintas épocas fueron desentrañando los mecanismos moleculares implicados en la transmisión de los impulsos nerviosos, por lo que solo bastaron dos siglos y medio para llegar al concepto actual sobre el origen del potencial de acción.

Conclusión. La teoría filosófica de los espíritus animales perduró por muchos siglos, mientras que a la ciencia moderna le tomó poco más de dos siglos para entender el fenómeno de la transmisión nerviosa.

Palabras clave: Historia; Fisiología; Potenciales de acción; Ciencia (DeCS).

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Introduction

Before the birth of modern science, the concepts issued by researchers were accepted almost as dogmas, without being proven by other researchers. Following the scientific revolution, knowledge began to acquire a new dimension, slowly detaching itself from religious influence, leading to dispute and question the concept of animal spirits that controlled our nervous system.

Modern science, an era for reason

The first part of this article, entitled *From animal spirits to scientific revolution in Medicine (first part)*, published in volume 66 issue 2 of this journal, presented a historical review of the way how the functioning of the nervous system based on animal spirits was formerly conceived. This idea prevailed until the seventeenth century, during the scientific revolution, when Giovanni Alfonso Borelli demonstrated that such spirits did not exist. (1)

This literature review of the period between the eighteenth century, when modern science was born, and the first half of the twentieth century, when the phenomenon of nerve impulse transmission was clarified, presents the most outstanding characters and events that prompted knowledge about the way how nerve information is transmitted through neurons and, consequently, the physiology of the nervous system.

Revolution of thought

Although many historians state that the scientific revolution began during the Renaissance, modern science took on its avant-garde role and detached itself from any religious influence only until the eighteenth century. Since then, science developed a way of interpreting the reality that is attempted to be demonstrated by means of the verification of observed facts or data, that is to say, applying the scientific method proposed by Descartes.

Until the eighteenth century, two hypotheses had been proposed to explain that the brain was the place where consciousness, sensation and understanding were located (2), and that many bodily structures were controlled through nerves. The first hypothesis emerged in the sixth century BC and prevailed until the first half of the seventeenth century; it proposed the presence of "animal spirits" that were transported by nerves to make organs work. The second hypothesis, raised in the second half of the seventeenth century, based on the experimental work of Giovanni Alfonso Borelli, an advocate of the scientific method, showed that animal spirits were not transported by the nerves and proposed that muscles contract due to the fermentation of chemical substances. (3)

At the dawn of modern science, a third hypothesis arose to explain the phenomenon of nerve conduction. In 1713, the physicist, mathematician and alchemist Sir Isaac Newton (1642-1727) proposed that the animal spirits promulgated by Galen were actually "ethereal vibrations" that originated in the brain and ran through the nerves to reach the muscles to generate mechanical actions. (4)

In 1752, the Swiss physician and anatomist Albrecht von Haller (1708-1777), considered as the father of modern physiology, based on his experimental work on animals, concluded that only some parts of the body showed sensitivity and that it was a specific property of the nerves, while other parts showed irritability and responded to different stimuli, such as electricity, by contracting; this property is exclusive to the muscles. (5,6) In 1756, the Italian anatomist Leopoldo Caldani (1725-1813), captivated by Haller's work, designed an experiment to verify this theory, for which he used an electric current obtained from a Leyden jar (a device used to store electric charge) for the first time to stimulate muscle tissue in experimental animals, proving that the muscles reacted by contracting. (7) Therefore, the thought that still prevailed over the presence of spirits transported by the nerves began to change to give way to the idea of "electric fluid", whose flow could be controlled by the power of the mind. At this point, the fourth hypothesis arose, which states that nerves transmit electricity.

Animal electricity

Luigi Galvani (1737-1798), Italian doctor and disciple of Caldani, was also interested in the phenomenon of electricity and showed that applying a small electric current on the spinal cord of a dead frog generated abrupt muscle contractions in its limbs. In 1780, Galvani concluded that it was the result of a phenomenon he called "animal electricity" and that the electricity necessary to cause the contractions did not come from the outside but from the inside of the living organism (8,9), apparently from the brain. He also inferred that, after death, the nerves could still retain the ability to drive the electrical impulse and transfer it to the muscle fibers to react to it. (8)

Years later, in 1841, the German physician and physiologist Emil du Bois-Reymond (1818-1896), at the request of his professor Peter Johannes Müller (1801-1858), who was not interested in the field of electricity, confirmed and expanded the findings reported by Matteucci in 1840 on the existence of an electric current that appeared between a damaged segment and another intact part of a muscle. In fact, du Bois-Reymond proved the existence of a current in the injured muscle which he called Muskelnstrom and observed, furthermore, that the amplitude of said current decreased by stimulating the nerve; he called this "negative variation". (10,11) Later, the researcher attached the electrodes of a galvanometer to a nerve and saw the same phenomenon. These works allowed establishing the basic principles of nerve impulse.

In 1850, the German physician and physicist Hermann Ludwig Ferdinand von Helmholtz (1821-1894), who was interested in nerve transmission, which was thought to be impossible to estimate at that time because of the speed at which it was transmitted, designed an experiment to measure said speed. For this purpose, he used the newly dissected sciatic nerve of a frog and the corresponding muscle it innervated, and coupled a clock that started when the nervous stimulus appeared and stopped at the moment of the contraction. After several measurements at different temperatures, Helmholtz was able to calculate that the speed was 27-30 m/s. (8,12) Then, he made some measurements on human subjects and found that the driving speed was much faster, about 60 m/s. (13)

Wilhelm Friedrich Kühne (1837-1900), a German physiologist, used fixation and staining and, in the 1870s, described that nerve endings reached a small formation on the muscle membrane, calling this entire structure "neuromuscular junction". (14) Kühne proposed that the current produced by the nervous impulse excited the muscle fibers in this junction. A few years later, Du Bois-Reymond suggested that the nervous transmission could be of chemical nature, where nerve endings could secrete some chemical agent that excited the muscle causing its contraction. (15)

At that time, the relationship between nerve fibers and nerve cells was not clear, as it was believed that they were two distinct anatomical entities. However, Jan Evangelista Purkinje (1787-1869), a Czech anatomist and physiology professor, and Gabriel Valentin (1810-1883), a German physician and physiologist, believed that these two nervous elements were fundamental in the organization of the central nervous system and that they could be associated, but without an apparent physical connection. (16)

Later, Robert Remak (1815-1865), a Polish embryologist and physiologist, showed that nerve cells were connected to the fibers and that they were extensions of the cell body (17); he further proposed that such cells provide the energy necessary for the transmission of the nervous impulse. But it was Louis Antoine Ranvier (1835-1922), a French histologist, who in 1875 demonstrated the anatomical connection between nerve cells and T-shaped fibers in the dorsal roots of the spinal ganglia. Also, Ranvier explained that one of the two branches of the fiber was directed towards the spinal cord and the other towards the periphery. (18) However, many physiologists of the time still believed that nerve cells were of little importance for the conduction of nerve impulses, including the neurophysiologist Augustus Volney Waller (1816-1870); moreover, such cells were believed to be passive repeating stations.

In 1860, the German neuroanatomist Otto Friedrich Karl Deiters (1834-1863) developed a microdissection technique to isolate nerve cells under the microscope. This researcher was able to obtain clear images of these cells and found that they had two different types of

branching processes connected to their body: one, a tree type, with thin and short branches which he called "protoplasmic processes" —later called dendrites by Wilhelm His (1831-1904) in 1889—, and a long fiber with a smaller number of branches that he called "axis cylinder" —later named axon by Rudolph Albert von Kölliker (1817-1905) in in 1891. (19)

A characteristic of nerve physiology that drew the attention of researchers in the late nineteenth century was the relationship between the intensity of stimulation of multiple nerve fibers and the possible responses of the electric potential. In 1871, Henry Bowditch (1840-1911), an American physician and physiologist, demonstrated that a stimulus may or may not cause muscle contraction, and that it depends on the threshold potential of the stimulus applied. This is considered to be the first demonstration of the all-or-none law. (20)

Neural doctrine

By the end of the nineteenth century, it was known that the nerve was made up of multiple fibers. With the establishment of the neuron doctrine, it was understood that the nerve impulse travelled from one nerve cell to another through the axon and that this potential for action occurred quickly and was, perhaps, of the all-or-none type. Meanwhile, since 1888, the Spanish histologist Santiago Felipe Ramón y Cajal (1852-1934) devoted himself to conduct a detailed study of the cellular architecture of a large part of the nervous system, including all its connections, in which he identified the dendritic spines and suggested that they could be involved in learning and memory processes. (21) For this, he used the histological staining technique developed by Camilo Golgi (1842-1926), which consisted in treating the sample with silver solution to impregnate the neurons and visualize them under the microscope; however, only a few cells were stained due to the presence of myelin. Cajal used the same technique to prepare his samples, but he made modifications to the staining method and applied it to cuts of young brains that did not have yet abundant myelin in their structure. The result was surprising, because he managed to see clearly the morphology of nerve cells (22) and then made his famous drawings. The German pathologist Heinrich Wilhelm Gottfried von Waldeyer (1836-1921) coined the term "neurons" in 1891 to name these cells, and also formulated the hypothesis that neurons are the basic structural units of the nervous system, a hypothesis that was demonstrated shortly after by Cajal.

Cajal also developed the neuron doctrine, which stated that neurons are discrete entities that are genetically, morphologically and physiologically independent, and that are also able to communicate with each other, without forming a diffuse reticulum. (23) These postulates went against what many historians of his time thought, among them Camilo Golgi, who defended at all costs the reticular theory, proposed in 1858 by the German anatomist Joseph von Gerlach (1820-1896), who stated that nerve cells were not separate but connected forming a continuous network. (24)

Nevertheless, recent studies have shown that large groups of neurons that establish extensive networks connected by electrical synapses to process neural information can be found in certain parts of the brain, and that such synapses are more common than previously thought. Cajal also observed that dilations were formed in the terminal end of stained axons, which were later called synaptic boutons; in addition, he proposed the law of dynamic polarization to explain that nerve impulse is transmitted unidirectionally from the dendrites to the end of the axon. (25,26) Therefore, Cajal established the basic principles of neuron and nervous tissue functioning, for which he was awarded, along with Camilo Golgi, the Nobel Prize in Medicine in 1906.

Consistent with neuron doctrine, the concept of "histological continuity" with "functional continuity" was established. To name these "contacts" that form between neurons, the English Arthur Woollgar Verral (1851-1912) proposed the name "synapse", a word of Greek origin meaning "conjunction". That name was accepted and introduced by Charles Scott Sherrington (1857-1952) in 1897. The concept of synapsis allowed explaining the phenomenon of delay in nerve impulse conduction, which varies in duration between 0.3 and 1 millisecond. Sherrington further observed that the histological substrate for the integrative action of the nervous system was related to multiple synaptic interconnections. (27)

Although electrical theory was used for a long time as an explanation to support the conduction of action potentials by nerves to the muscles, the work done by the German doctor and pharmacologist Otto Loewi (1873-1961) led the idea towards a biochemical explanation. In fact, in 1921, Loewi designed an experiment that occurred to him, in his own words, while sleeping. He dissected two frog hearts, leaving the vagus nerve in one of them, and immersed them separately in saline solution so that they continued beating for a while. Then, he stimulated the vagus nerve in one of the hearts and saw that the heartbeat slowed down. Finally, he took the saline solution in which the heart had been immersed and applied it to the second heart, noting that it also reduced its heart rate. Loewi concluded that the vagus nerve should have released a chemical at the level of the parasympathetic synapse, which he called vagus substance, and which caused the same response in the second heart.

Five years later, Loewi and his collaborator, E. Navratil, proved that the vagal substance was acetylcholine (28), thus becoming the first neurotransmitter identified; they also demonstrated that this substance was rapidly degraded by the enzyme cholinesterase and concluded that the transmission of nerve impulses was of a neurohumoral type. Loewi's works were widely known and he was awarded the Nobel Prize in Medicine in 1936, which he shared with Henry Hallett Dale (1875-1968), discoverer of acetylcholine in 1913.

Joseph Erlanger (1874-1965), American chemist and physician, and Herbert Spencer Gasser (1888-1963), American physiologist, designed an experiment in which they adapted a cathode ray oscilloscope to amplify the electrical potentials of nerves. These researchers obtained for the first time an exact image of action potentials and discovered that these potentials were formed by waves that moved at different speeds along nerve fibers and that the speed varied in direct proportion to the diameter of the fiber. (29) This way, they established a classification of the fibers as a function of speed: Group A fibers (motor and some sensory), Group B fibers (visceral sensory) and Group C fibers (unmyelinated). They also demonstrated that different nerve fibers can perform different functions. For this work they were awarded the Nobel Prize in Medicine in 1944.

Interested in the electrochemical mechanisms of synaptic transmission, Bernard Katz (1911-2003) and Paul Fatt (1924-2004) proposed the quantal hypothesis of neurotransmitter release of acetylcholine in the motor end plate, which means that acetylcholine is not released continuously by nerve terminals but in small amounts or quanta, where each quantum causes a small signal in the muscle fiber. They also said that acetylcholine binds to specific membrane receptors that act as ionic channels through which ions flow to create an electric current. (30) For his work in nerve physiology and biochemistry, Katz was awarded the 1970 Nobel Prize in Medicine, which he shared with Julius Axelrod (1912-2004) and Ulf von Euler (1905-1983), who also worked on the chemical transmission of nerve endings and the mechanism of storage and inactivation of neurotransmitters.

The invention of the electron microscope, designed by Max Knoll (1897-1969) and Ernst Ruska (1906-1988) in 1931, allowed cell

biology to enter a period of intense research activity, which began by interpreting what all those blurred spots that showed the first images obtained meant. With the improvement of the techniques for the preparation of samples that allowed obtaining images of greater quality, the puzzle of that marvelous ultrastructure that shapes the cells was put together.

The American neuroscientist Sanford Louis Palay (1918-2002), using an electron microscope, took on the task of unraveling the ultra-structural details of the synapse in the central nervous system. In 1953, he expanded this knowledge by demonstrating with his images that there is a gap (the synaptic cleft) between the pre- and postsynaptic cells. This definitively validated Cajal's neuron doctrine. (17) In 1954, Palay and his colleague George Emil Palade (1912-2008), a Romanian physician, reported the presence of mitochondria and membranous vesicles in nerve terminals.

In 1947, the Argentine physician Eduardo De Robertis (1913-1988), who was also interested in understanding neuronal ultra-structure by means of electron microscopy, observed for the first time the presence of microtubules inside axons devoid of myelin. But it was until 1954 when he made a momentous discovery: while working in a team with George Bennett, he saw membranous spheres inside the presynaptic terminals, similar to what Palay and Palade saw, and named them synaptic vesicles. De Robertis and Bennett suggested that such vesicles were involved in the storage of neurotransmitters and their transport to the presynaptic membrane. (31)

Ionic flow, the explanation of the problem

As progress was made on the knowledge of the microscopic anatomy of the nervous system, other researchers from different latitudes were striving to unravel the physiological mechanisms involved in the transmission of nerve impulses. In 1952, Alan Lloyd Hodgkin (1914-1998) and Andrew Fielding Huxley (1917-2012), British physiologists and biophysicists, proposed a mathematical model to explain how nerve impulses start and propagate in neurons. This model consists of a series of non-linear differential equations that explain the ionic mechanisms involved in the origin and propagation of action potentials. The researchers used the giant axon of squids as an experimental model, which allowed them to use the voltage clamp technique (32), due to its size, to record the internal ionic currents by means of electrodes.

Thus, according to Hodgkin and Huxley, nerve impulse consists of a rapid and coordinated sodium ion influx and the subsequent potassium ions exit through the membrane of the excitable cells. (33) Thanks to this important work, the British scientists were awarded the Nobel Prize in Medicine in 1963, which they shared with the Australian neurophysiologist John Carew Eccles (1903-1997) for his research on the ionic mechanisms of excitation and inhibition of synapses.

In 1949, Eccles thought that the transmission of nerve impulses in the synapses was strictly electrical. To prove this, he designed an experiment where he took the knee stretching reflex as a model, since only two neurons, one sensitive and the other motor, are involved. In the early 1950s, Eccles realized that his initial assessment was wrong, corroborating what Loewi and Dale had discovered years earlier: when the nerve impulse reaches the end of an axon, a chemical that causes the nerve impulse to pass to the next neuron is released. However, Eccles went further and determined that neurotransmitters opened a channel that causes an influx of sodium ions in the postsynaptic membrane. (15,34)

The conclusions reached by Hodgkin and Huxley led them to hypothesize about the possible existence of ionic channels in the membranes of excitable cells, a fact that was confirmed a few decades later by the physicist and physician Erwin Neher (1944) and physician Bert Sakmann (1942), both of German origin, who developed the patch clamp technique that allows the measurement of the function of ion channels in cell membranes (35); for this work, they were awarded the Nobel Prize in Medicine in 1991.

Discussion

René Descartes (1596-1650), an outstanding French philosopher, mathematician and physicist, defined the rules of the method for "rightly conducting one's reason and of seeking truth in the sciences" (36) in his work Discourse on the Method. Consequently, since the seventeenth century, the implementation of the scientific method as a basic tool and path for the process of research allowed separating scientific knowledge from authority, dogmatic tradition and faith. In addition, the influence of subjectivity on a researcher's work was greatly minimized. Evidently, from then on, researchers in the field of medical sciences assumed an analytical-deductive reasoning in their observations and experiments, as was the case of Giovanni Alfonso Borelli. He was one of the advocates of the scientific method, whose reasoning, detached from any religious and dogmatic influence, led him to conclude that there were no animal spirits transporting themselves through the nerves to control body parts. (3)

After the establishment of modern science in the eighteenth century, scientific knowledge, particularly physiology, underwent an accelerated development driven by the creation of new laboratory tools and techniques, but also by more objective thinking, detached from religious authority and its inquisitorial apparatus. Speculative theories and the subordination of science to religious beliefs had been left behind, and now new knowledge had to be verified and validated by the scientific community. This objective reasoning was evident in the type of theories that have been postulated since then to try to explain the phenomenon of nerve impulse transmission, since they were more coherent with the reality of the moment and easier to measure and verify using the appropriate instrumentation.

Therefore, only two and a half centuries were necessary to unravel the molecular mechanisms involved in the transmission of nerve impulses through the nerves, while the philosophical theory about animal spirits that prevailed until that time was valid for about 23 centuries; it was almost a dogma.

Conclusions

A historical analysis of the evolution of human thought and the events involved in the establishment of a more objective truth makes evident that believing in myths and the fear of questioning paradigms cloud reason and slow down the normal rhythm of knowledge. However, with the development of new research techniques and with the support of the scientific method, researchers in the field of the physiology of the nervous system managed to determine, in a relatively short time, the molecular mechanisms that underlie nerve fibers for transmission of nerve impulses in the form of action potentials.

Conflicts of interest

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William Smellie, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

REVIEW ARTICLE

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Prevalence of metabolic syndrome among university students: A systematic review

Prevalencia de síndrome metabólico en estudiantes universitarios, una revisión sistemática

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| Abstract |

Introduction: Metabolic syndrome (MS) is defined as a set of conditions including high blood pressure, dyslipidemia, glucose intolerance and visceral obesity. In recent years, an increase of obesity in university students has been observed, although the accurate prevalence of MS is unknown.

Objective: To determine the prevalence of MS in university students between January 2000 and January 2016.

Materials and methods: A systematic review of studies published in the PubMed, LILACS, ScienceDirect, UpToDate, Imbiomed, SciELO and Google Scholar databases was performed. To ensure the highest number of papers, different combinations of words related to MS were used in Spanish, English, and Portuguese.

Results: A total of 16 studies met the inclusion criteria. Students from different health, social and human sciences careers from America, Asia and Europe participated in said studies. The prevalence of MS ranged from 0 to 19.2% according to NCEP-ATP III.

Conclusions: The prevalence of MS varies widely across studies. It is important to expand MS research, as this would allow designing specific interventions for high-risk groups in the university context.

Keywords: Prevalence; Metabolic Syndrome X; Students; Universities; Review (MeSH).

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| Resumen |

Introducción. El síndrome metabólico (SM) se define por la coexistencia de hipertensión arterial, dislipidemia, intolerancia a la glucosa y obesidad visceral. En años recientes, se ha observado incremento de la obesidad en universitarios, pero no se tiene precisión sobre la prevalencia de SM.

Objetivo. Determinar la prevalencia de SM en estudiantes universitarios entre enero de 2000 y enero de 2016.

Materiales y métodos. Revisión sistemática de estudios publicados en PubMed, LILACS, ScienceDirect, UpToDate, Imbiomed, SciELO y Google Schoolar. La búsqueda usó diferentes combinaciones de palabras relacionadas con SM en español, inglés y portugués.

Resultados. 16 estudios reunieron los criterios de inclusión e incluyeron la participación de estudiantes de distintas carreras de ciencias de la salud, sociales y humanas, además eran provenientes de América, Asía y Europa. La prevalencia de SM observada estuvo entre 0% y 19.2% según los criterios NCEP-ATP III.

Conclusiones. La prevalencia de SM varía ampliamente en los diferentes estudios. Es importante extender la investigación del SM, esto permitiría el diseño de intervenciones para grupos de alto riesgo desde el contexto universitario.

Palabras clave: Prevalencia; Síndrome X metabólico; Estudiantes; Universidades; Revisión sistemática (DeCS).

Campo-Arias A, González-Guerrero JL, Peñaloza-Vázquez C, Tatis-González JF. [Prevalencia de síndrome metabólico en estudiantes universitarios, una revisión sistemática]. Rev. Fac. Med. 2018;66(4):629-33. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.60658.

Introduction

Today, metabolic syndrome (MS) is one of the biggest public health concerns worldwide. (1) The International Diabetes Federation states that the frequency of this syndrome is high in the global context, and is also parallel and congruent with the high frequency of type 2 diabetes and cardiovascular disease in the general population. (1,2)

MS is also known as plurimetabolic syndrome, insulin resistance syndrome, or metabolic X syndrome and is defined as the presence or coexistence of high blood pressure, dyslipidemia, insulin resistance, glucose

intolerance and visceral obesity. (3) This set of risk factors significantly increases the likelihood of long-term cardiovascular disease. (4)

In the past years, university students have shown higher obesity figures. (4,5) Young adults starting college are at a transition age, which is critical to the consolidation of health-related behaviors or habits. (6) For example, first-year college students experience faster weight gain than the average adult at another stage of life. (7) This relates to lifestyle choices, including poorly balanced diet, lack of physical activity or regular exercise, tobacco use, and excessive consumption of alcoholic beverages. (8) It has been fully established that these factors, together with obesity, contribute to increased risks of suffering from MS, regardless of age and educational or vocational level. (9)

Early detection of MS in young adults in the university context may guide the design of preventive programs or specific interventions to reduce the onset of the syndrome and associated medical and psychosocial complications that often become chronic. (10)

It is important to know the prevalence of MS in university students in order to take measures from a public health perspective and design strategies for early identification. This design is done using different screening techniques of possible cases in the academic context, and aims to reduce or minimize the problems associated with MS and the subsequent deterioration in the quality of life once current students are part of the country's productive system. (11,12)

To date, there is no systematic review summarizing the observed prevalence of MS in university students in different contexts. Systematic reviews in other age groups showed striking values and a systematic review including obese adolescents revealed a mean prevalence of 31.2% ranging from 2.1% to 58.3%. (13) A similar review, including adults aged between 18 and 65 years, apparently healthy, from Latin American countries, found an adjusted prevalence of 24.9%, with a range between 18.8% and 43.3%. (14)

The objective of this systematic review was to establish the prevalence of MS in the university population as reported in studies published between January 2000 and January 2016.

Materials and methods

A systematic review of studies published in the PubMed, LILACS, ScienceDirect, UpToDate, Imbiomed, SciELO and Google Scholar databases between January 2000 and January 2016 was carried out to review the prevalence of MS in university students.

"Metabolic syndrome", "Cardiovascular risk factors", "University students" and "Students" were included as keywords. In order to ensure the largest number of publications, different word combinations were used in Spanish, English and Portuguese. This process was complemented by a manual review of the references of articles initially identified in the database search. Studies that evaluated the presence of MS according to the criteria of the National Cholesterol Education Program and the Adult Treatment Panel III (NCEP-ATP III) were included. (15) Figure 1 presents the flowchart of the selection of the reviewed studies.

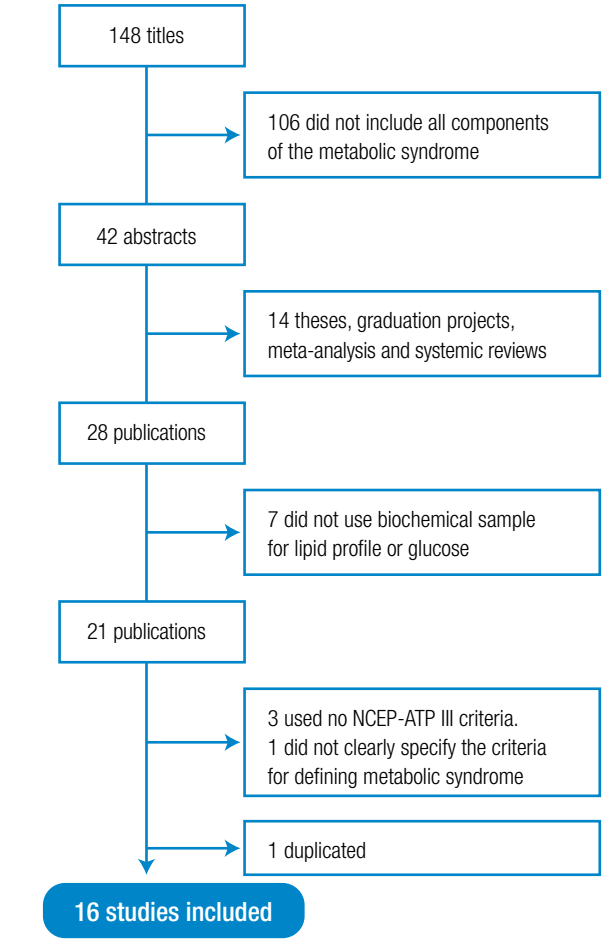

Figure 1. Flowchart of research inclusion.
Source: Own elaboration.

NCEP-ATP III defines MS as the coexistence of at least three of the following factors: increased abdominal perimeter (≥102cm in men and ≥88cm in women), hypertriglyceridemia (≥150 mg/dl), decreased HDL (<40 mg/dl in men and <50 mg/dl in women), fasting hyperglycemia (≥110 mg/dl) and altered blood pressure (systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg). (15,16) Narrative reviews, graduation projects, theses and studies carried out in the university context in which professors or administrators were mixed and the prevalence in the student group that could not be discriminated were excluded.

First, the titles were reviewed, then the abstracts and finally the full version of the articles that met all the inclusion criteria. A descriptive analysis of the publications was carried out and the country in which the study was conducted, year of publication, sample size, major/program, academic level of the population studied, and observed prevalence of MS in percentages were specified. For a more accurate observed prevalence, 95% confidence intervals were found for each of the frequencies reported in the articles.

The quality of the studies was evaluated using the questionnaire for observational analytical studies proposed by du Prel *et al.* (17). This instrument consists of 12 points that collect the most important aspects of the design and non-experimental observational studies analysis, as proposed by the instrument *Strengthening the Reporting of Observational Studies in Epidemiology*. (18)

Results

148 titles were identified, of which 120 were discarded since 106 did not include all the components of the MS and 14 were theses, graduation projects, meta-analyses or systemic reviews. Of the 28 pre-selected abstracts, 7 investigations that did not use biochemical tests to define MS were eliminated, as well as 3 that used criteria other than NCEP-ATP III, finally 1 study that did not clearly specify the criteria used to define MS, and 1 duplicated were also excluded. 16 studies m*et all* the criteria for this review. (19-34) Regarding the quality of study reports, all met at least 11 of the 13 criteria assessed (10 met 13, 5 met 12, and 1 met 11). The articles with the lowest scores usually had smaller samples.

In general, studies conducted in different parts of the world, most of them from Latin America or Brazil, were included. In terms of the major or program to which the students were enrolled, the largest selection was made randomly from all programs (10 studies). The age of the participants ranged approximately between 17 and 26 years, and both men and women participated. The prevalence range of MS ranged from 0% to 19.2%. Table 1 summarizes the information on the findings of the studies in chronological order.

Discussion

This study shows a high variation in the prevalence of MS in university students, which is between 0% and 19.2% according to the NCEP-ATP III criteria. In this sense, 10 studies found a prevalence of MS of <5.0%, 3 between 5.1% and 15%, and 3 of >15%, and this is somehow different from what has been reported in other systematic reviews in children, adolescents and adults.

Friend *et al.* (35) made a systematic review with 85 published studies in children and adolescents between 2003 and 2010 and found an average prevalence of MS of 3.3%. Other systematic reviews of findings in adult populations show a substantially higher prevalence. For example, Oguoma *et al.* (36), in 32 published studies between 2002 and 2013 worldwide, with a total sample of 10 854 subjects, found that the average prevalence is 27.9% according to NCEP-ATP III. De Carvalho-Vidigal *et al.* (37) reviewed 10 articles in Brazilian subjects, published until May 2013, with a total participation of 8 505 people, and found an average prevalence of MS of 28.9% according to the same criteria.

Table 1. Prevalence of metabolic syndrome in university students (NCEP-ATP III).

Authors, year	Country	n	Sampling	Prevalence % (CI95%)
Huang *et al.* (19), 2004	USA	163	Random	0.6 (0.0-1.7)
Palomo *et al.* (20), 2006	Chile	783	Random	1.0 (0.3-1.7)
Oviedo *et al.* (21), 2008	Venezuela	120	Non-random*	3.3 (0.1-6.5)
Nillakupt & Viravathana (22), 2010	Thailand	96	Non-random*	1.0 (0.0-3.1)
Fernandes & Lofgren (23), 2011	Jamaica	189	Random	3.7 (1.0-6.4)
Dalleck & Kjelland (24), 2012	USA	207	Non-random	6.8 (3.3-10.3)
de Freitas *et al.* (25), 2012	Brazil	702	Random	1.7 (0.7-2.6)
Martínez *et al.* (26), 2012	Chile	385	Random	4.9 (2.7-7.1)
Topè & Rogers (27), 2013	USA	376	Random	16.0 (12.2-19.8)
Maldonado-Villalón *et al.* (28), 2013	Mexico	141	Random*	7.8 (3.4-12.2)
Arnold *et al.* (29), 2014	USA	109	Non-random†	0.0
Zea-Robles *et al.* (30), 2014	Colombia	193	Random	16.6 (11.3-21.9)
Vilarouca-da Silva *et al.* (31), 2014	Brazil	550	Random	3.5 (2.0-5.0)
de Carvalho *et al.* (32), 2015	Brazil	968	Random	19.2 (16.7-21.7)
Alarcón *et al.* (33), 2015	Colombia	177	Random	9.6 (5.2-14.0)
Mee-Kyung *et al.* (34), 2015	Korea	151	Random	4.0 (0.9-7.1)

Source: Own elaboration.
* Medical students only.
† African-American students only.

Certainly, the differences in the prevalence percentages and variables associated with MS observed between the studies reviewed in this research and previous systematic reviews may be explained by the variety of demographic and cultural characteristics of the participants. (38) Likewise, social and economic inequalities should be considered, not only those that occur between countries, but also those that are found in different regions of the same country. The prevalence of obesity and, consequently, of MS tends to be higher in developed or high-income countries. (4)

It is relevant to know the prevalence of MS in university youth, both for education and public health. This information about the frequency in university institutions is fundamental to encourage, based on the best evidence, the promotion of healthy lifestyles that include non-pharmacological measures such as diet and exercise at this stage of life. (39) Moreover, these measures may need to be implemented at elementary and secondary education levels (40-42) due to the increasing prevalence of obesity in the early years of life, which is the main component of MS. (43-45)

From a public health perspective, this prevalence is relevant for promoting metabolic disorders, and control and reducing associated long-term morbidity and mortality. (46) It is important to promote preventive actions based on a healthy lifestyle that include a balanced

diet —for example, the Mediterranean diet, which has demonstrated to be helpful to reduce and prevent metabolic disorders— and habits such as regular physical activity. (47) These actions can be included in the curricular and extracurricular components of vocational training programs as ways to promote self-care. (48,49) Similarly, it is necessary to work for the promulgation of public policies more aligned with a healthy lifestyle from the early stages of life. (50-52)

The strength of this systematic review is that it summarizes the research done in the university population of the last years to date, which were not included in any systematic review. The search also included articles in Spanish and Portuguese that are not usually considered in English-language publications. However, there are some limitations, including that the participating populations showed high heterogeneity in their characteristics and in the quality of the studies, which greatly limits the generalization of any conclusion.

Conclusion

Prevalence of MS in university students is high when compared to that observed in children and adolescents; therefore, further research with more representative or stratified samples is needed to know the frequencies in different sectors or subgroups of university populations, which will allow the design of specific interventions for high-risk groups in the university context.

Conflicts of interest

A preliminary analysis of this work was presented at the IV Congreso de Salud Integral, Universidad del Magdalena, held in Santa Marta on October 28 and 29, 2016 and appears in the form of a summary in the report of said event.

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WILLIAM SMELLIE, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

CASE REPORT

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Bilateral fracture of corpora cavernosa with complete rupture of the anterior urethra: Case report and review of recent findings for surgical management

Fractura bilateral de cuerpos cavernosos con sección completa de uretra anterior. Reporte de caso y revisión de conceptos actuales sobre el manejo quirúrgico

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| Abstract |

Introduction: Penile fracture is a rare urological emergency associated in up to 30% of cases with injury to the anterior urethra. Recent data suggest that early surgical intervention is the best treatment strategy. This investigation describes a case of bilateral corpora cavernosa injury associated with complete rupture of the anterior urethra and presents current concepts about its management.

Case presentation: 39-year-old man with bilateral corpora cavernosa injury and complete rupture of the anterior urethra, who received early surgical treatment with satisfactory early clinical outcomes. A literature review was made in PubMed and Embase, limiting the search to scientific articles published in the past 10 years using the MeSH terms "Penile diseases", "Genital diseases, male", "Wounds and injuries". Some references were included given their clinical relevance. In this case, similar to international experiences, early surgical management of corpora cavernosa fractures allowed achieving adequate clinical outcomes in the patient.

Conclusions: The diagnosis of penile fracture is based on clinical findings. Early surgical management should be considered as a therapy of choice. Conservative management has a higher complication rate versus early surgical management. The case described here had an adequate clinical evolution after 3 months of follow-up.

Keywords: Penile Diseases; Genital Diseases, Male; Wounds and injuries; Penis (MeSH).

| Resumen |

Introducción. La fractura de cuerpos cavernosos es una urgencia urológica que se asocia hasta en 30% de los casos a lesión de la uretra anterior. Datos recientes postulan la intervención quirúrgica temprana como la mejor estrategia de tratamiento. La presente investigación describe un caso de lesión bilateral de cuerpos cavernosos asociada a sección completa de uretra anterior y define conceptos actuales sobre su manejo.

Presentación del caso. Hombre de 39 años con fractura bilateral de cuerpos cavernosos y sección completa de uretra anterior, quien recibió tratamiento quirúrgico temprano con resultados clínicos tempranos satisfactorios. Se realizó una revisión de la literatura en PubMed y Embase limitando la búsqueda a artículos científicos publicados en los últimos 10 años y utilizando los términos MeSH "Penile diseases", "Genital diseases, male", "Wounds and injuries". Algunas referencias fueron incluidas dada su relevancia clínica. De forma similar a experiencias internacionales, el manejo quirúrgico temprano de la fractura de cuerpos cavernosos en este caso permitió desenlaces clínicos adecuados en el paciente.

Conclusiones. El diagnóstico de la fractura de pene se basa en hallazgos clínicos; el manejo quirúrgico temprano debe considerarse como la terapia de elección para esta entidad. El tratamiento conservador presenta una mayor tasa de complicaciones versus el manejo quirúrgico temprano. El caso descrito presenta buenos desenlaces post-operatorios a corto plazo.

Palabras clave: Enfermedades del pene; Heridas y lesiones; Enfermedades de los genitales masculinos; Pene (DeCS).

Castañeda-Millán DA, Manrique-Mejía O, Capera-López C, Donoso-Donoso W. Bilateral fracture of corpora cavernosa with complete rupture of the anterior urethra: Case report and review of recent findings for surgical management. Rev. Fac. Med. 2018;66(4):635-8. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.65917.

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Introduction

Corpora cavernosa fracture is a urological emergency, generally associated with sexual activity, which requires early surgical intervention to avoid possible functional sequelae in the penis (erectile dysfunction, abnormal curvature, painful erection, fibrotic plaque, among others). Some characteristic clinical findings of this type of fracture include hematoma and edema of the penis; sudden pain and rapid detumescence after trauma; and a "crack" sound at the time of trauma. The literature describes complex cavernous injures associated with urethral injury in up to 38% of cases (1), although there is no general consensus on the management of this type of rupture. This article presents the case of a bilateral fracture of the corpora cavernosa associated with complete rupture of the anterior urethra, and describes the most recent findings in the literature on the management of this entity.

In addition, this clinical case report presents a brief literature review performed in PubMed and Embase, using the MeSH terms "Penile diseases", "Genital diseases, male", "Wounds and injuries", which was limited to scientific articles published in the past 10 years. 119 articles were retrieved, and after reviewing the abstracts, 104 articles were excluded as they were not related to penile fracture. The analysis was carried out in 15 articles. Some references were included given their clinical relevance.

Case presentation

39-year-old man with no relevant medical history, who consulted a tertiary care teaching university hospital in Bogotá D.C., Colombia due to penile trauma during intercourse. During the sexual act, the patient heard a "crack" and felt intense pain of sudden onset with immediate detumescence of the penis. He consulted the emergency service 40 minutes after the event.

Physical examination showed a large hematoma and edema that involved the penis with the characteristic "eggplant deformity", as well as urethral bleeding, which led to immediate surgical exploration due to suspicion of concomitant urethral injury. The patient did not report desire to void and abdominal palpation did not show urinary retention.

Subcoronal incision with penile denudation was performed and the tunica albuginea was ruptured bilaterally on the ventral side of the corpora cavernosa, with complete rupture at the junction of the proximal-middle third of the penile urethra (Figure 1).

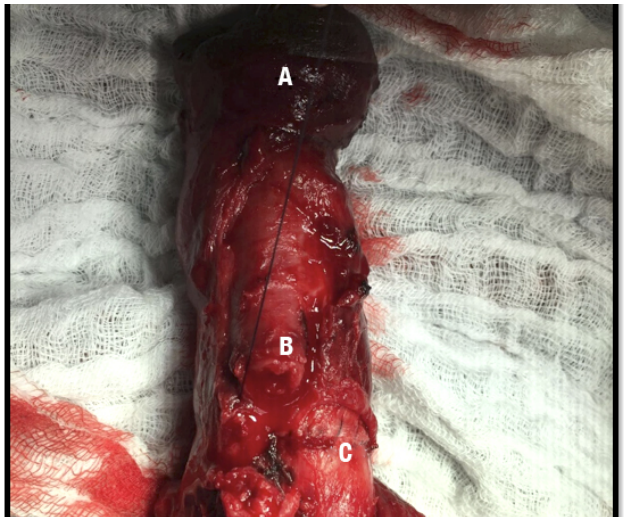

Figure 1. Intraoperative findings. A) Buck's Fascia hematoma; B) complete rupture in anterior urethra; C) rupture line in tunic albuginea.
Source: Own elaboration.

The hematoma surrounding the injury was evacuated and the tunica albuginea was continuously sutured with 3/0 resorbable material. A Foley 18 Fr probe was placed to perform urethral anastomosis, and the devitalised edges were resected. Tension-free urethral anastomosis was constructed with a four-quadrant excisional approach and spatulated ends, using vicryl 5/0. Suture was performed by quadrants in the spongy body using vicryl 4/0 and, finally, a circumcision was performed following the dorsal slit-sleeve technique. The patient was discharged 48 hours after the intervention and the urethral catheter remained for 21 days. After 3 months of follow-up, the subject did not present complications, de novo urinary obstructive symptoms, abnormal curvature of the penis or deficiency in the quality of his erections (Figure 2).

Figure 2. Appearance 2 weeks after surgery.
Source: Own elaboration.

Discussion

Penile fracture is a rare urological entity, with an incidence close to 1 case per 175 000 inhabitants; between 2006 and 2007, 1 043 cases were reported in the USA. (2) This entity is associated in most cases with sexual activity and requires early therapeutic measures; however, scientific production in Latin America is quite limited: only two scientific works are available in Colombia (3-4) and some descriptive works in Latin America have been conducted, which include reports of associated urethral injury. (5-8)

Pavan *et al.* (9) reported that clinical diagnosis is achieved in 90% of cases. The most common signs and symptoms in their series of 41 patients were penile hematoma (82.6%), detumescence (82.6%) and pain (60.9%). They also described urethral involvement (25%) and bilateral fracture of the corpora cavernosa (20%). Within the group that received early surgical treatment, 36.8% presented some complication, while all patients who received late management presented complications, being the most frequent abnormal curvature of the penis (77.8%), palpable plaques/nodules (44.4%) and erectile dysfunction (33.3%). The findings of these researchers, in terms of complications in the conservative management group, are similar to those described by Yapanoglu *et al.* (10), who reported a general complication rate of 80% in patients treated with this approach.

Estimates are that up to 16% of patients with a history of fracture of the corpora cavernosa have erectile dysfunction. In this regard, El-Assmy *et al.* (11) described age >50 years and bilateral involvement

of the corpora cavernosa as risk factors for erectile dysfunction after penile fracture.

Swanson *et al.* (12) report 18.5% urethral involvement and a general posttraumatic erectile dysfunction rate of 29.2%, which decreases to 20% in patients undergoing early surgical correction. They also state that the use of complementary images is not mandatory to diagnose penile fracture. These data contrast with Nason *et al.* (13), who described difficulties to maintain an erection in only 12.5% of the patients included in their series.

Pariser *et al.* (14) performed a 9-year retrospective analysis and found an annual incidence of 459 cases per year in the USA, which occurred mostly in summer and on weekends, a higher probability of urethral injury as age increases (age >41 years OR: 2.25, 95%CI: 1.25-4.05, p=0.07), and increased risk of concomitant urethral injury in patients with urethral bleeding (OR: 17.03, 95%CI: 3.2-90.5, p=0.01). On the other hand, Kramer (15) described penile fracture as a more frequent event in patients who have sexual intercourse under stress (extramarital relationships and in places other than beds). Barros *et al.* (16) associated the risk of penile fracture during intercourse with position: 41% "doggy style", 25% male-superior position and 10% female-superior position.

Koifman *et al.* (17) presented one of the most significant experiences in Latin America: in their series of 150 cases, they used complementary diagnostic images in 39.3% of the patients, being ultrasound the most used study (24.6%); the use of nuclear magnetic resonance was reserved only for 0.6% of patients. In their casuistry, they described the use of retrograde urethrography in all cases with suspected urethral injury (14% of cases). According to clinical findings, the researchers classified the cases as high vs. low probability of penile fracture; in all low probability cases (absence of early detumescence after trauma, edema and mild-moderate hematoma and palpation of the corpora cavernosa without pathological findings), they used ultrasonography as a complementary test, while complementary imaging tests were used only in 9.6% of cases with high probability of fracture of the corpora cavernosa.

Several authors (18-20) state that the diagnosis of penile fracture is clinical and support early surgical management when there is clinical diagnostic suspicion, especially if the patient presents urethral bleeding as a warning sign considering possible urethral involvement. In general terms, they support early surgical approach due to the good clinical outcomes obtained and the lower percentage of long-term complications.

Kozacioglu *et al.* (21) found no significant differences in erectile dysfunction and abnormal curvature of the penis rates in patients who were taken to early surgical correction of penile fracture compared to those who were taken to delayed surgery 11.3±8.5 hours after the onset of the trauma. Ibrahiem *et al.* (22) found a greater proportion of palpable scar/fibrosis (71.4%) in patients who underwent tunica albuginea defect repair with non-absorbable material (p=0.01).

A recent meta-analysis (23), which included 58 studies with 3 213 patients, revealed that 46% of penile fractures occurred during intercourse, 18% due to masturbation, and 8.2% to rolling over in bed. No statistically significant relationship was found between the position during the sexual act and the relative risk of suffering penile fracture (5 studies, n=76, p=0.53, I2=42%); 95.4% of patients with penile fracture received surgical management, while only 4.6% underwent conservative management. The percentage of complications was higher in patients with conservative management (46% vs. 20.6% surgical management), and the most common were: erectile dysfunction (37%), palpable plaques/nodules (33%) and abnormal curvature of the penis (23%). Complications in the surgical treatment group were palpable plaque/nodule (13.9%), abnormal curvature of the penis (2.7%) and erectile dysfunction (1.94%). Only 6.1% of patients with a fracture of the corpora cavernosa presented concomitant urethral involvement (23).

When comparing early and late surgical management, the former presented a lower rate of general complications (p<0.00001) and abnormal curvature of the penis (p<0.0004). No results were obtained with statistical significance for erectile dysfunction and the presence of palpable plaques/nodules, and no significant differences in clinical outcomes were observed in patients who underwent surgical correction of the tunica albuginea with resorbable suture versus non-resorbable suture. However, a greater possibility of painful fibrotic plaque with non-absorbable suture was considered (23).

Falcone *et al.* (24), in their most recent systematic review, found that the use of diagnostic imaging is not mandatory; however, such aids (ultrasound and nuclear magnetic resonance) can help the surgeon to choose the type of surgical approach: subcoronal with denudation of the penis for exploration or incision in the area with cavernous or urethral involvement. The authors did not find relevant clinical differences between the use of absorbable sutures versus nonabsorbable sutures, although, similar to Amer *et al.* (23), they describe a greater possibility of postoperative pain in the area of injury with the use of nonabsorbable sutures.

Wong *et al.* (25) conducted a systematic review to evaluate the outcomes of patients undergoing early surgical management (<24 hours) versus patients undergoing deferred surgical management (>24 hours). The results showed erectile dysfunction in 6.6% vs. 4.5% (OR: 0.58, 95%CI: 0.24-1.37, p=0.213), palpable scar 5.4% vs. 4.5% (OR: 0.59, 95%CI: 0.18-1.98, p=0.393), and abnormal curvature of the penis 1.8% vs. 4.5% (OR: 0.33, 95%CI: 0.12-0.92, p=0.034). These results did not show significant differences in the occurrence of erectile dysfunction and symptomatic scars, but they support early surgical management as the line that generates a lower percentage of abnormal curvature of the penis.

According to the data described in the literature, it can be inferred that the standard management for penile fracture is surgical and that early intervention produces fewer complications. Currently, there are no data available that show significant statistical weight to establish differences between the types of sutures and the types of surgical knots to be used. Although the use of diagnostic imaging is not mandatory, it can help to define the type of surgical approach or, in cases of low clinical probability of penile fracture, to rule out the diagnosis.

Post-operative functional results in the described case are correlated with the aforementioned global experiences. After receiving early surgical management, the patient did not present any type of complication at 3 months of follow-up.

Conclusions

Penile fracture is a rare entity and, to date, there are no estimates of its incidence in Latin America. The diagnosis of this entity is clinical and it is only necessary to resort to diagnostic images in cases of low probability of fracture of the corpora cavernosa; however, the use of these diagnostic aids should not delay surgical exploration. Early surgical management is the current standard treatment, since it has a lower incidence of complications compared to long-term deferred or conservative management. The case presented here had a good post-operative evolution in the short term.

Ethical considerations

This manuscript complies with the principles established in Resolution 8430 of 1993 issued by the Colombian Ministry of Health (26) and,

according to said principles, it can be considered as non-risk research. Furthermore, this study was approved by the Subcommittee on Ethics of the Urology Unit of the Faculty of Medicine of Universidad Nacional de Colombia.

Conflicts of interest

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CASE REPORT

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Empyema necessitatis due to *Citrobacter freundii:* Case report

Empiema necessitatis por Citrobacter freundii. Reporte de caso

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| Abstract |

Introduction: This paper presents the first case of empyema necessitatis secondary to infection with *Citrobacter freundii* (according to the databases consulted), and one of the few reports of this pathology in Colombia.

Case presentation: This is the case of a 26-year-old patient from a rural area, with a history of severe cognitive deficit, who was taken to the emergency department due to a clinical picture of 15 days of evolution consisting of neurological deterioration associated with asthenia, adynamia, fever and cough with purulent expectoration. On admission, a chest x-ray was taken, finding pneumonia of the middle lobe with associated pleural effusion, for which empirical antibiotic management was initiated. The patient presented clinical deterioration and appearance of right pectoral mass, so a computed tomography of the thorax was performed, revealing empyema necessitatis. Close drainage and culture of the collection were made, with negative mycobacteria culture and positive report for *C. freundii*. The patient received specific antibiotic treatment for 8 weeks, with complete improvement of his clinical condition.

Conclusion: Besides being the first case of empyema necessitatis by *C. freundii* that has been reported, this case is important because of the low amount of reports on this pathology in Colombia, considering that its main cause is tuberculosis, which is endemic in the country.

Keywords: Empyema Pleural; Pneumonia; *Citrobacter freundii* (MeSH).

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| Resumen |

Introducción. Según lo encontrado en las bases de datos consultadas, el presente es el primer caso de empiema necessitatis secundario a *Citrobacter freundii*. Además, constituye uno de los pocos reportes de esta patología en Colombia.

Presentación del caso. Se trata de un paciente de 26 años procedente de área rural, con antecedente de déficit cognitivo severo, quien fue llevado al servicio de urgencias por cuadro clínico de 15 días de evolución consistente en deterioro neurológico asociado a astenia, adinamia, fiebre y tos con expectoración purulenta. Al ingreso se tomó radiografía de tórax, encontrando neumonía del lóbulo medio con derrame pleural asociado, por lo que se inició cubrimiento antibiótico empírico. El paciente presentó deterioro clínico y aparición de masa pectoral derecha, por lo que se realizó tomografía computarizada de tórax, evidenciando empiema necessitatis. Luego, se hizo drenaje de la colección, con cultivo negativo para micobacterias y aislamiento de *C. freundii*. Se dio tratamiento guiado por antibiograma durante ocho semanas, con posterior recuperación completa del cuadro clínico.

Conclusión. Además de ser el primer caso de empiema necessitatis por *C. freundii*, este es importante por la escasa cantidad de reportes en Colombia, considerando que su principal causa es la tuberculosis, la cual es endémica en el país.

Palabras clave: Empiema pleural; Neumonía; *Citrobacter freundii* (DeCS).

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Introduction

Empyema necessitatis or empyema necessitans is a complication of pleural empyemas in which the infection extends out of the pleural cavity, involving the soft tissues of the thoracic wall or other body segments. (1,2) It is mainly caused by *Mycobacterium tuberculosis* infection, followed by *Actinomyces spp.* (3) This paper reports the case of a patient with empyema necessitatis secondary to *Citrobacter freundii* infection, which is the first of its kind reported so far in the literature, as seen after a search in PubMed, BIREME and SciELO databases is made.

Case presentation

A 26-year-old Caucasian patient, from a rural area, with a history of severe cognitive deficit secondary to cerebral palsy, was taken by his

father to the emergency department due to a clinical picture of 15 days of evolution consisting of neurological deterioration evidenced by decreased contact with his environment, and greater difficulty to perform the basic activities of daily living (eating and dressing). These symptoms appeared along with asthenia, adynamia, fever and cough with greenish phlegm.

Physical examination showed a patient with blood pressure of 100/68mmHg, heart rate of 76 beats per minute, respiratory rate of 17 breaths per minute and oxygen saturation of 94% to the environment. He also had multiple caries and gingivitis, drowsiness, hypoprosexia and diminished lung sounds in the right base. Hypochromic microcytic anemia, leukocytosis with neutrophilia, elevated C-reactive protein and normal renal and hepatic function were found in the paraclinical tests taken to the patient on admission (Table 1).

Table 1. Paraclinical tests on admission.

Paraclinical test	Results
Complete blood count	**Leukocytes**: 20300/µL. **PMN**: 84.4%. **Lymphocytes**: 6.5%. **Monocytes**: 7.9%. **Hemoglobin**: 11.5 g/dL. **MCV**: 76fL. **MCH**: 25.6 pg. **Platelets**: 546000
C-reactive protein	92.8 mg/dL.
Liver function tests	**Bilirubin**: total: 0.75 mg/dL; direct: 0.32 mg/dL. **AST**: 39 U/L **ALT**: 51 U/L
Kidney function tests	**Creatinine**: 1.0 mg/dL **BUN**: 8 mg/dL

PMN: polymorphonuclear leukocyte; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen.
Source: Own elaboration.

Sputum smears were taken, which were negative for acid-fast bacilli. The chest x-ray showed consolidation in the middle lobe associated with pleural effusion, leading to a diagnosis of community-acquired pneumonia. Empiric management with ampicillin/sulbactam and clarithromycin was initiated. Despite having received a 5-day course of antibiotics and the improvement of respiratory and neurological symptoms, febrile peaks persisted, so new laboratory tests were taken, revealing persistence of leukocytosis and neutrophilia, and elevated C-reactive protein (Table 2). Ultrasonography of the right pleural cavity showed free-flowing pleural effusion (339.4cm^3).

Table 2. Control paraclinical tests on day 6.

Paraclinical test	Results
Complete blood count	**Leukocytes**: 17100/µL. **PMN**: 84%. **Lymphocytes**: 9.1%. **Monocytes**: 5.5%. **Hemoglobin**: 11.2g/dL. **MCV**: 74fL. **MCH**: 25.1 pg. **Platelets**: 528000
C-reactive protein	128.4 mg/dL

PMN: polymorphonuclear neutrophils; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin.
Source: Own elaboration.

A diagnostic thoracentesis was performed, which allowed obtaining clear fluid with characteristics of simple parapneumonic effusion (Table 3). Culture of this sample was taken for common germs, which was negative.

Given the persistence of systemic inflammatory response signs, the antibiotic treatment was changed to piperacillin/tazobactam and acquired immunodeficiency was ruled out as a causal factor of poor response to treatment by negative HIV ELISA test. During the following 4 days of therapy, the patient developed a mass on the anterior right thorax, of about 4 cm in diameter, without local inflammatory changes.

Computed tomography of the thorax was performed, revealing consolidation of the middle lobe and ipsilateral pleural effusion, along with hypodense mass projected on the pectoral muscular plane (Figure 1) and extension from the fourth to the seventh intercostal space, leading to diagnose empyema neccesitatis.

Table 3. Cytochemical and cytological study of pleural fluid and paired blood samples.

Pleural fluid	pH	8.0
	Aspect	Slightly turbid
	Proteins	46.8 g/dL
	Glucose	85.79 mg/dL
	Lactic dehydrogenase	427.3 U/L
	Leucocytes	203 leucocytes (100% neutrophils)
	Red blood cells	3-5 per field, 100% fresh
	Adenosine deaminase	10.5 U/L
Blood	Lactic dehydrogenase	413 U/L
	Glycemia	74.5 mg/dL
	Total proteins	8.1 g/dL

Source: Own elaboration.

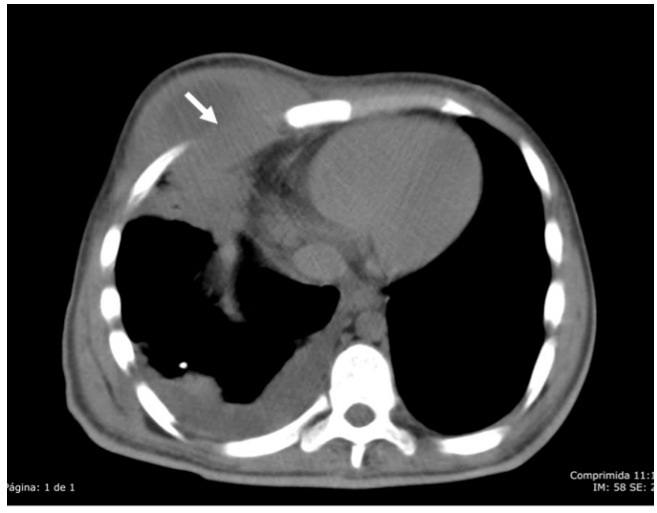

Figure 1. Computed tomography of the thorax. Axial section.
Source: Document obtained during the study.

Figure 1 shows consolidation of the middle lobe and ipsilateral pleural effusion, along with hypodense mass projected on the pectoral muscular section. The arrow indicates the point where pleural collection passes through the muscular section of the chest wall into the subcutaneous cellular tissue of the right pectoral region.

Percutaneous drainage was established for treating and diagnosing the collection. ADA (adenosine deaminase) and culture were performed for mycobacteria, which were negative, as well as a culture for common germs with *C. freundii* isolate with hyperproduction of class C chromosomal beta-lactamase and sensitive to aminoglycosides and fluoroquinolones (Table 4). Cefepime was administered for four weeks and the scheme was completed with oral ciprofloxacin for four weeks more. Respiratory and neurological symptoms completely resolved, and the thoracic mass disappeared.

Table 4. Antibiogram of microorganism isolate.

Pleural fluid culture	*Citrobacter freundii*. Amikacin ≤2 S. Cefepime ≤1 S. Cefoxitin ≥4 R. Ceftazidime 16 R. Ceftriaxone 4 R. Ciprofloxacin ≤0.25 S. Doripenem ≤0.12 S. Ertapenem ≤0.5 S. Gentamicin ≤1 S. Imipenem ≤0.25 S. Meropenem ≤0.25 S. Piperacillin/Tazobactam ≤4 S. Tigecycline ≤0.5 S.

S: Sensitive; R: Resistant.
Source: Own elaboration.

Discussion

First described in 1640 by Guillan de Baillon (2,4), empyema necessitans or empyema necessitatis is a pleural empyema complication, in which infection extends towards the pleural cavity and involves the soft tissues of the chest wall (1) or other body segments. This occurs more frequently through the less resistant area, which is usually located between the second and sixth intercostal space and between the midclavicular line and the anterior axillary line. In less frequent cases, the abdominal wall, paravertebral space, vertebrae, esophagus, bronchi, mediastinum, diaphragm, pericardium, flank, breast and retroperitoneum may be involved. (1,2,4) Another manifestation may include the formation of pleurocutaneous or bronchopleurocutaneous fistulas. (3)

Empyema necessitans is more common in adults. Chronic alcoholism, cachexia, chronic obstructive pulmonary disease, tuberculosis, poor oral hygiene and bronchiectasis have been found to be risk factors. (5)

In this case, the extension of pleural empyema occurred through the fourth to seventh intercostal space with involvement of the soft tissues of the thoracic wall; the risk factor of this adult patient was having poor oral hygiene.

To establish a diagnosis, it is necessary to confirm the continuity of the pleural collection with the thoracic wall or the affected body segment. (5)

The most frequent etiological agents and mortality rates have changed with the advent of antibiotics. In 1940, Sindel (6) published a review of cases in which he found that the most frequent cause was *M. tuberculosis* (73% of cases), followed by *Streptococcus pneumoniae*, and a total mortality rate of 66%, of which 87% were related to tuberculosis.

After the development of antibiotics, Freeman *et al.* (4) conducted a case review from 1966 to 2004 and found that 50% of these infections were secondary to tuberculosis and 24% to actinomycosis. Then, Llamas *et al.* (5), in a review of cases published between 2004 and 2010, found that *M. tuberculosis* and actinomycosis (mainly *Actinomyces israelii* and *Actinomyces odontolyticus*) remained the main causes (35% and 20%, respectively). In both studies, the reported mortality was 0%. Following these publications, case reports were reviewed, finding only one case of mortality related to infectious empyema. (7)

In addition to the microorganisms described, cases have been reported involving *Klebsiella corrodens, Streptococcus milleri, Burkholderia cepacia, Fusobacterium nucleatum, Mycobacterium avium intracellulare, Aspergillus fumigatus, Zygomycetes, Blastomyces spp, Peptostreptococcus, Bacteroides, Propionibacterium, Coccidiodes immitis, Streptococcus agalactiae, Nocardia asteroides* and *Corynebacterium jeikeium*. (2,3,8-10)

Differential diagnoses should consider traumatic causes (pulmonary herniation), neoplasms (mesothelioma, lymphoma, malignant fibrous histiocytoma, among others) and inflammatory processes in the chest wall. (3) In the case described here, the patient did not report a traumatic history, so pulmonary herniation was not considered as a possibility. On the other hand, the clinical picture and the paraclinical symptoms suggested an infectious pulmonary process, which, added to the neutrophilic exudate within pleural fluid, which is more frequently associated with parapneumonic effusion (11-13), led to consider a neoplasm as unlikely. Furthermore, the most common finding in a neoplastic exudate is the presence of lymphocytes >50%. (13)

Treatment consists of broad-spectrum antibiotic therapy until a culture-directed therapy can be administered and, in most cases, the collection is drained. (2)

Regarding surgical approach to drainage, Akgül *et al.* (7) conducted a study in seven patients with empyema necessitatis of various etiologies. These authors concluded that surgical techniques may include chest tube, decortication or open drainage of the collection, and that they should be chosen taking into account the physical condition, age, the duration of symptoms, the etiology and the existence of a parenchymal pathology in each patient. (7) In this case, the management of the collection was limited to percutaneous drainage because the patient's caregivers refused more invasive surgical procedures.

This case is important given that, after conducting a search, it is the first report of this pathology by *C. freundii*, which broadens the spectrum of clinical pictures that can occur due to this microorganism. This bacterium is part of the genus *Citrobacter* (member of the *Enterobacteriaceae* family), which are facultative, mobile and oxidase-negative anaerobic gram-negative bacilli that use citrate as the sole source of carbon. In the environment, citrobacteria are commonly found in water, soil and food; they are also occasional colonizers of the gastrointestinal tract in humans and, although the strains involved are considered to be of low virulence, they can be the origin of multiple types of infections (urinary, respiratory, intra-abdominal, surgical site, bone, central nervous system and bacteremia), representing 3-6% of all infectious diseases due to enterobacteria. They can cause community-acquired infections and infections associated with health care, affecting, especially, neonates (meningitis and brain abscesses), elderly and immunocompromised patients.

Along with *Citrobacter koseri, C. freundii* is one of the species most associated with infections. (14-15) Regarding its susceptibility profile, *C. freundii* has natural resistance to amoxicillin, amoxicillin/clavulanate, ampicillin, ampicillin/sulbactam, cephamycins and first and second generation cephalosporins. Its acquired resistance to other β-lactams is given by the presence of ampC, extended spectrum β-lactamases and carbapenemases; resistance to fluoroquinolones and aminoglycosides has also been reported. (15)

In this case, the infection occurred in a patient in whom acquired immunodeficiency was ruled out and who is outside the common age groups. For this reason, the possibility of developing the infection due to an episode of bronchoaspiration secondary to severe cognitive deficit that facilitated the passage of this germ from the gastrointestinal tract to the respiratory tract was considered. Regarding antibiotic therapy, empirical intra-hospital treatment with ampicillin/sulbactam and clarithromycin was initiated, following the recommendations of the Colombian guidelines for the treatment of community-acquired pneumonia in immunocompetent adults (16), in the context of a patient with a CURB-65 Severity Score of 1, with distant housing as a socioeconomic risk factor and with risk factors for gram-negative bacteria. Using ampicillin/sulbactam may explain the therapeutic failure of the first scheme due to the inherent resistance of *C. freundii* to this antibiotic. On the other hand, with the isolate of an ampC-producing and fluoroquinolone-sensitive strain, intra-hospital treatment with cefepime and outpatient scheme with ciprofloxacin was decided.

Conclusion

This is a clinically relevant case, since it is one of the few reported in Colombia of this entity (17) and the first one described by *C. freundii.* The absence of reports of cases of empyema necessitans in the country is noteworthy, given that, a higher incidence would be expected since this is an endemic area for tuberculosis. This observation could be explained by underreporting in the country or could be an indicator of a good effectiveness of the diagnosis and treatment of infections due to *M. tuberculosis.* Finally, this case is useful to illustrate the importance of considering this pathology in patients with pneumonia and parapneumonic effusions with poor response to treatment or with the appearance of associated pectoral mass, since this implies a change in the diagnostic and therapeutic approach, which may significantly affect the prognosis of patients.

Ethical considerations

The case presented here was published prior the informed consent of the patient's relatives was obtained.

Conflicts of interest

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CASE REPORT

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Late diagnosis of pseudohypoparathyroidism in adulthood. Case series

Pseudohipoparatiroidismo diagnosticado tardíamente en la adultez, una serie de casos

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| Abstract |

Introduction: Pseudohypoparathyroidism (PHP) is a rare hereditary disease, characterized by hypocalcemia/hyperphosphatemia secondary to peripheral resistance to parathyroid hormone (PTH). PHP diagnosis is usually precluded since hypocalcemia is considered as the primary diagnosis, thus delaying further diagnostic studies and preventing an adequate management of this clinical condition.

Materials and methods: Retrospective review of the databases of the Endocrinology departments of two tertiary care centers of Medellin, Colombia from January 2012 to December 2016. Patients diagnosed with PHP based on clinical presentation and confirmatory laboratory values were included.

Results: Four patients met the inclusion criteria. All PHP cases were diagnosed in adulthood despite strong early clinical and laboratory evidence of the disease. Three patients were diagnosed with Fahr's syndrome and two with Albright's hereditary osteodystrophy. The mean values obtained were PTH of 376.8 pg/mL, calcium of 6.17 mg/dL and phosphorus of 6.55 mg/dL.

Conclusions: PHP is a rare disorder. This paper describes four PHP cases diagnosed during adulthood. Emphasis should be placed on the judicious approach to the patient with hypocalcemia and hyperphosphatemia with increased PTH and normal renal function, since these symptoms strongly suggest a diagnosis of PHP.

Keywords: Pseudohypoparathyroidism; Parathyroid Diseases; Hypocalcemia; hyperphosphatemia (MeSH).

| Resumen |

Introducción. El pseudohipoparatiroidismo (PHP) es una condición rara caracterizada por hipocalcemia e hiperfosfatemia secundarias a resistencia periférica a la hormona paratiroidea (PTH). Es frecuente que la hipocalcemia sea establecida de forma equivocada como diagnóstico primario y que el diagnóstico definitivo de PHP sea tardío, difiriendo los estudios y el manejo específico que exigen estos pacientes.

Materiales y métodos. Se revisaron de forma retrospectiva las bases de datos de endocrinología de dos centros terciarios de Medellín, Colombia, desde enero de 2012 a diciembre de 2016. Se incluyeron pacientes con diagnóstico de PHP por presentación clínica y valores confirmatorios de laboratorio.

Resultados. Cuatro pacientes cumplieron los criterios de inclusión. Todos los casos fueron diagnosticados en la adultez a pesar de tener evidencia temprana, clínica y bioquímica de la enfermedad. Tres pacientes tenían síndrome de Fahr y dos tenían osteodistrofia hereditaria de Albright. Los valores medios registrados fueron PTH de 376.8 pg/mL, calcio de 6.17 mg/dL y fósforo de 6.55 mg/dL.

Conclusiones. El PHP es un trastorno raro; se describen cuatro casos diagnosticados de forma tardía en la adultez. Se enfatiza en el enfoque juicioso del paciente con hipocalcemia, la cual, en presencia de hiperfosfatemia con PTH elevada y función renal normal, debe hacer sospechar el diagnóstico de PHP.

Palabras clave: Seudohipoparatiroidismo; Enfermedades de las paratiroides; Hipocalcemia; hiperfosfatemia (DeCS).

Trejo MC, Román-González A, Ruíz S, Tobón C, Castaño P, Arango C, *et al*. Late diagnosis of pseudohypoparathyroidism in adulthood. Case series. Rev. Fac. Med. 2018;66(4):643-49. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.66940.

Trejo MC, Román-González A, Ruíz S, Tobón C, Castaño P, Arango C, *et al.* [Pseudohipoparatiroidismo diagnosticado tardíamente en la adultez, una serie de casos]. Rev. Fac. Med. 2018;66(4):643-49. English. doi: http://dx.doi.org/10.15446/revfacmed.v66n4.66940.

Introduction

Pseudohypoparathyroidism (PHP) is a rare, heterogeneous and hereditary condition characterized by peripheral resistance to parathyroid hormone (PTH). (1) Its onset usually occurs during childhood with clinical manifestations of hypocalcemia and laboratory studies that reveal hypocalcemia and hyperphosphatemia. These studies, added to elevated serum PTH concentrations, allow establishing the initial diagnosis. Some patients are diagnosed earlier through genetic studies because they have a close relative affected by this condition.

Although the role of PHP in the diagnostic approach to hypocalcemia is clear (2), it often goes unnoticed even when frankly suggested by symptoms, laboratory tests, and neuroimaging findings. This situation delays studies, counseling, and the specific management of this entity.

The biochemical profile is the same in all PHP cases, but its clinical presentation may vary according to the specific genetic defect and the imprinting pattern. Albright's hereditary osteodystrophy (AHO) is a phenotype that consists of skeletal anomalies including rounded facies, obesity, short stature, subcutaneous ossifications and brachydactyly, which are observed in types 1a and 1c, as well as pseudo-pseudohypoparathyroidism (PPHP), which is absent in types 1b and 2. (1)

Other clinical manifestations, besides those associated with the typical phenotype, are derived from hypocalcemia and elevated calcium-phosphorus product, such as Fahr's syndrome, which consists of secondary gangliobasal calcifications.

This paper presents four cases of patients with a late diagnosis of PHP despite long-standing symptomatic hypocalcemia and clear evidence of the disease reported in their clinical history; two of them had AHO, three presented Fahr's syndrome, and pathological fractures were present in one of the cases.

This series of cases intends to call the attention of emergency physicians and outpatient consultation doctors regarding the mandatory character of a judicious approach to hypocalcemia, which is a finding but not a diagnosis. In addition, it also seeks to highlight the relevance of knowing how to interpret the biochemical profile of calcium-phosphorus metabolism in a specific clinical setting and highlight PHP as a diagnostic possibility for all patients with hypocalcemia, regardless of its severity and presentation.

Materials and methods

The inter-consultation and consultation databases of the Endocrinology Service of two tertiary care hospitals of Medellín, Colombia, were reviewed retrospectively from January 2012 to December 2016. The institutions were Hospital Universitario San Vicente Fundación and Hospital Pablo Tobón Uribe.

Patients diagnosed with PHP due to clinical presentation and confirmatory laboratory values (PTH, calcium and phosphorus levels) were included. Patients with other parathyroid diseases such as primary, secondary or tertiary hyperparathyroidism and all hypoparathyroidism cases were excluded. A database was designed including the most important clinical variables of PHP, finding four cases (Table 1). The IBM SPSS Statistics V21 software and Microsoft Excel 2016 were used to analyze the data obtained. The study was approved by the Research and Ethics Committee of Hospital Pablo TobónUribe (Minutes 12/2018 of June 28 2018) and the Research Ethics Committee of the Hospital Universitario San Vicente Fundaciòn (Minutes 21-2918 of july 13 2018).

Continuous variables are presented as mean and standard deviations (σ), while categorical variables are presented as frequencies and proportions.

Table 1. Relevant diagnostic information.

Information	Case 1	Case 2	Case 3	Case 4	Final aggregate
Reason for consultation	Hypocalcemia	Convulsion	Convulsion Pathologic fracture Hypocalcemia	Hypocalcemia	Hypocalcemia (100%) Convulsion (50%)
History	Epilepsy	Epilepsy	Mother with AHO	Hypothyroidism	-
AHO	No	No	Yes	Yes	AHO 50%
Age	22	23	21	25	-
PTH pg/mL	373.3	416.4	398	319.7	376.8 (σ=41.99)
Calcium mg/dL	5.8	5.2	5	8.68	6.17 (σ=1.70)
Phosphorus mg/dL	8.85	6.5	6.2	4.66	6.55 (σ=1.73)
25(OH)D ug/dL	-	34	-	19.6	26.8 (σ=10.18)
Magnesium mg/dL	1.92	1.65	1.72	-	1.76 (σ=0.14)
TSH mU/mL	5.02	3.63	2.89	5.58	4.2 (σ=1.23)
Free T4	1.16	0.85	1.14	1.97	1.28 (σ=0.48)
Magnetic resonance	Bilateral and symmetric intracranial calcifications Predominance in basal ganglia/normal EEG			-	Calcifications 75%
Diagnostic	PHP 1B/2 Fahr's syndrome RTH	PHP 1B/2 Fahr's syndrome Tubulopathy	PHP 1A/1C Fahr's syndrome	PHP 1A/1C; Hypothyroidism	-

AHO: Albright's hereditary osteodystrophy; PTH: intact parathyroid hormone; TSH: thyroid stimulating hormone; PHP: pseudohypoparathyroidism; RTH: resistance to thyroid hormone.
Source: Own elaboration.

Case presentation

Case 1

22-year-old man referred by the Neurology service to the Endocrinology service to conduct studies of hypocalcemia, with no perinatal neuroinfection or neurotrauma history, and neurodevelopment referred to as normal. The patient was diagnosed with epilepsy at 13 years of age after an episode of generalized tonic-clonic seizure and therapeutic failure with valproic acid, gabapentin and levetiracetam. Also, the subject had a presumptive diagnosis of Fahr's disease with extrapyramidal symptoms managed with risperidone.

During consultation with Endocrinology, the patient reported symptoms of anxiety, paresthesia and involuntary movements in the lower limbs. Physical examination showed normal vital signs; AHO, Trousseau's and Chvostek's signs were negative. Paraclinical tests revealed hypocalcemia and persistent hyperphosphatemia with elevated PTH, and normal magnesium and renal function, which led to the diagnosis of PHP. Other hormonal axes were studied; subclinical hypothyroidism was reported given the discrete elevation of TSH with FT4 in normal range, and the corticotropic axis was normal. The patient did not have an AHO phenotype, so partial resistance to thyroid hormones was considered as possible and a PHP type 1b as more likely (Table 2).

Table 2. Classification of pseudohypoparathyroidism and differential diagnosis.

Classification	Hormone resistance	AHO	GNAS defect	PTH infusion
PHP 1a	Multiple: PTH, TSH, Gn, GnRH	Yes	Maternal mutation	↓cAMP ↓Phosphaturia
PHP 1b	PTH, TSH *	No	Imprint	↓cAMP ↓Phosphaturia
PHP 1c	Multiple: PTH, TSH, Gn	Yes	Maternal mutation	↓cAMP ↓Phosphaturia
PHP 2	PTH	No	Unknown	Normal cAMP ↓Phosphaturia
PPHP	No	Yes	Paternal mutation	Normal

PHP:pseudohypoparathyroidism; AHO: Albright's hereditary osteodystophy; PTH: parathormone; TSH: thyroid-stimulating hormone; Gn: gonadotropins; GnRH: gonadotropin-releasing hormone; GNAS: guanine nucleotide binding protein, alpha stimulating; PPHP: pseudo-pseudohypoparathyroidism.
* Some cases
↓ Low/decreased
Source: Own elaboration based on Tafaj *et al.* (3).

Magnetic resonance imaging (MRI) revealed hyperintensity of the putamen and head of the caudate on the FLAIR sequences, and hyperintensity in the pulvinar of the thalamus. Gradient echo sequences showed a tendency to calcification of the deep cerebellar gray nuclei, the pale globe and some subcortical regions. Given the recent diagnosis of alterations of calcium metabolism secondary to PHP, these findings were clearly compatible with Fahr's syndrome. Treatment with calcium carbonate and calcitriol was prescribed, as well as joint follow-up by Neurology and Endocrinology.

Four years after his diagnosis, the patient remains adherent to medical management and has not presented new convulsive episodes, although some extrapyramidal symptoms still persist. The most recent known laboratory tests reveal acceptable levels of calcium (8.7 mg/dL) and phosphorus (4.38 mg/dL), as well as persistent elevated PTH (460 pg/mL).

Case 2

23-year-old woman with a history of epilepsy since she was 15 years old, who reported presenting five generalized tonic-clonic convulsive episodes and no medical treatment. At the age of 20, hypocalcemia of unknown etiology was discovered through routine laboratory studies, so calcium carbonate was prescribed, which the patient took intermittently. The woman had no relevant family history and was admitted to the emergency department due to a new generalized tonic-clonic seizure episode; during the review of systems, she described suffering from generalized paresthesia for several months.

Physical examination showed tongue with a fissure in the right lateral region due to bite and erythema in the right patella due to contusion, both secondary to the convulsive episode; Trousseau's and Chvostek's signs were negative. Paraclinical tests taken on admission —which included hemoleucogram, ionogram, renal and hepatic function— revealed hypokalemia (2.8 meq/L) and hypocalcemia (5.2 mg/dL; corrected with albumin 5 g/dL), and normal magnesium and renal function, for which substitution was initiated with potassium gluconate and calcium carbonate. A CT brain scan was performed, exposing multiple supra and infratentorial calcifications, predominantly in the bilateral basal ganglia region and the thalami; these findings were confirmed by a brain MRI that suggested Fahr's disease as a diagnostic possibility.

Considering this clinical scenario, in-hospital endocrinology assessment was requested to study hydroelectrolytic alterations associated with a possible Fahr's syndrome. Endocrinology requested more laboratory studies that showed hypocalcemia and hyperphosphatemia with elevated PTH, normal 25-hydroxy vitamin D and normal renal function, leading to a diagnosis of PHP. Other relevant laboratory tests included normal thyroid profile and phosphaturia in inappropriately normal levels (phosphorus in urine) over a 24-hour period: 0.51gr; reference value 0.4-1.3; phosphaturia 23.1 mg/dL).

Regarding the classification of PHP (Table 2), given that the patient did not have an AHO phenotype, it was likely to be type 1B or 2; evidence of non-resistance to other hormones supported type 2. On the other hand, brain imaging findings in the presence of calcium metabolism alterations, convulsive syndrome and secondary extrapyramidal symptoms make up Fahr's syndrome.

In addition, the Nephrology service was asked to expand the study of hypokalemia, regarded as secondary to loss of kidney function. Associated tubulopathy was proposed as etiology, although a definitive diagnosis was not established.

During hospitalization, the patient remained asymptomatic, received oral supplementation with calcitriol 0.5µg every 12 hours and calcium carbonate 600mg every 8 hours until stable concentrations of calcium and phosphorus were achieved. She was discharged with prescription for outpatient treatment that included oral potassium supplement intake. The patient remained adherent to medical management, without new convulsive episodes, calcium in 8.3 mg/dL and potassium in 3.8 mg/dL as goals, but with persistent elevated phosphorus (5.3 mg/dL), and constant joint follow-up by the Endocrinology and Nephrology services.

Case 3

21-year-old man with no significant personal or perinatal history, and without previous neuroinfection or neurotrauma. Relevant family history included short stature and shortening of the fourth and fifth metacarpal and metatarsal on the part of the mother.

The patient was taken to the emergency service after experiencing a tonic-clonic seizure episode, falling from his own height, and

inability to walk after the event. On admission, fracture of the right hip was documented, which was managed with osteosynthesis without complications. Paraclinical tests taken on admission (complete blood count, ionogram, renal and hepatic function) showed severe hypocalcemia (5 mg/dL), which required a referral to the Endocrinology service.

During the endocrinology consultation, the patient reported general malaise and generalized paresthesia over the last week prior to the consultation. Physical examination revealed as important findings short stature, overweight, shortening of the fourth and fifth metatarsal and metacarpal (Figure 1) and positive Archibald's and Trousseau's signs.

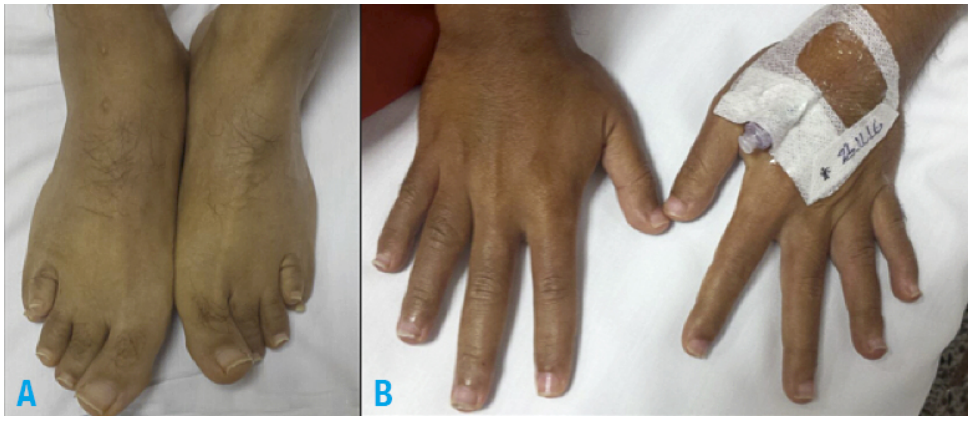

Figure 1. Phenotypic features of Albright's hereditary osteodystophy, case 3. A) shortening of the fourth and fifth metatarsal; B) shortening of the fourth and fifth metacarpal.
Source: Documents obtained during the study.

In addition, a brain tomography was performed, which revealed bilateral calcifications in the basal, thalamic and subcortical nuclei compatible with Fahr's syndrome.

These phenotypic clinical findings of AHO, in the context of hypocalcemia and hyperphosphatemia with elevated PTH, are compatible with the diagnosis of PHP type 1a/1c (Table 2).

During his hospitalization, the patient remained asymptomatic and received supplements with calcium and calcitriol orally, with daily biochemical monitoring until stable levels were achieved. He was discharged with prescription for outpatient treatment and follow-up with Endocrinology. During his last appointment, two years after the diagnosis of PHP, he reported remaining asymptomatic; calcium (10.9 mg/dL) and phosphorus (4.46 mg/dL) levels were found within target, so it was decided to continue the same medical management.

Case 4

25-year-old woman referred to the Endocrinology service for evaluation of hypocalcemia with a history of hypothyroidism treated with levothyroxine, as well as treatment with calcium, vitamin D and calcitriol supplementation due to hypocalcemia and vitamin D deficiency detected in ambulatory paraclinical tests requested by a general practitioner. No relevant family history was reported.

The patient denied symptoms that could suggest hypocalcemia and Fahr's syndrome. Physical examination showed normal vital signs and, as positive findings, short stature, overweight and shortening of the third and fourth metacarpal and metatarsal (Figure 2); Trousseau's and Chvostek's signs were negative. Her medical history included a paraclinical test taken one year before consultation in which hypocalcemia, 25-hydroxy vitamin D deficiency and elevated PTH were reported, findings compatible with a diagnosis of PHP, which suggested subtype 1a/1c in the presence of phenotypic traits of AHO and resistance to thyroid hormones (Table 2). Additional studies showed normal gonadotropic axis, normal karyotype and normal thyroid ultrasound. The patient continued in follow-up with Endocrinology, and remained adherent to medical management and asymptomatic.

Discussion

PHP is comprised of a heterogeneous group of rare diseases and has an estimated prevalence of 0.79 per 100 000 inhabitants. (3) It is characterized by peripheral resistance to the action of PTH, a hormone produced and secreted by the parathyroid glands in response to low serum calcium levels, whose main function is to maintain the homeostasis of calcium-phosphorus metabolism. (4)

Figure 2. Phenotypic traits of Albright's hereditary osteodystophy, case 4. A) shortening of the third and fourth metatarsal; B) shortening of the third and fourth metacarpal.
Source: Documents obtained during the study.

PHP is an entity with autosomal dominant inheritance and genomic imprinting. The defect that prevents the action of PTH derives from genetic or epigenetic alterations in the GNAS (guanine nucleotide binding protein, alpha stimulating) locus (5) and in the long arm of chromosome 20 (20q13.3), which encodes the alpha subunit of the Gs protein (G stimulator) to which the PTH receptor is coupled (PTHR1). (3,6,7)

Laboratory tests show hypocalcemia and hyperphosphatemia, with normal renal function and elevated serum concentrations of PTH. (4) In PHP, the main site of resistance to PTH is the proximal renal tubule and, as a direct result, hyperphosphatemia and low concentrations of 1,25 dihydroxyvitamin D (1,25(OH)2 D) are observed, the latter being the main cause of hypocalcemia; this, in turn, increases the PTH and worsens hyperphosphatemia. Since PTH responses in the bone and distal renal tubule are preserved, high levels of PTH could partially prevent symptomatic hypocalcemia by mobilizing calcium from the bone and increasing renal calcium reabsorption. (8)

Clinical manifestations may vary according to the genetic defect and the imprinting pattern under which this is expressed. (9) A phenotype compatible with AHO may be observed, characterized by rounded facies, obesity, short stature, ectopic ossification and brachydactyly. (6) Other clinical manifestations, besides those related to the typical phenotype, are derived from hypocalcemia and the high calcium-phosphorus product.

PHP is classified into different subtypes based on the phenotype, the hormonal resistance pattern, the genetic defect and the renal response to exogenous PTH infusion. (Table 2) The phenotype is defined by the presence or absence of AHO, and hormone resistance is determined by the resistance to other hormones dependent on the Gsα protein system, such as TSH, gonadotropins or GH. (10) PPHP presents the typical AHO phenotype in an isolated manner, without biochemical alterations in the phosphocalcic profile since there is no resistance to the action of PTH. (4)

The renal response to PTH infusion is explained by the normal capacity of formation of cyclic adenosine monophosphate (cAMP) before the stimulation of the PTHR1 receptor, which is coupled to Gs proteins with high concentrations of expected cAMP in healthy subjects. In PHP, this response is variable: it is preserved in type 2 and absent in type 1, despite the fact that the phosphaturic response is deficient in both types, indicating a defect distal to the generation of cAMP in PHP2. (7,8)

In general, patients with PHP first experience signs and symptoms of hypocalcemia, which depend on its chronicity and severity. Hypocalcemia is usually established as a primary diagnosis, which delays the diagnosis of PHP, even in the presence of suggestive clinical evidence and secondary Fahr's syndrome in up to 80% of patients. This syndrome consists of the presence of brain calcifications, predominantly in the basal ganglia, in the context of an alteration of calcium metabolism; it also manifests with convulsive syndromes, extrapyramidal symptoms and neuropsychiatric disorders. (11-13) Ectopic calcifications may develop as a consequence of late diagnosis and treatment, being the presence of cataracts, cochlear and subcutaneous calcifications more commonly observed.

The four cases described here correspond to adult patients (Table 1) whose reason for initial consultation, despite being associated with symptomatic hypocalcemia, did not lead to an assertive diagnosis. The definitive diagnosis of PHP was made years after the clinical onset of the disease in tertiary care institutions with an Endocrinology service. Of the cases reported, three (cases 1, 2 and 3) met the criteria for Fahr's syndrome, which emphasizes the late nature of the diagnosis. (14) The diagnostic approach of each case was made based on hypocalcemia (Figure 3) (2,15), which suggests the diagnosis of PHP when associated with hyperphosphatemia and elevated PTH.

PHP is diagnosed after other conditions have been discarded, and PHP1 and PHP2 have been classically differentiated based on the renal response to the exogenous PTH infusion. Urinary phosphate excretion is altered in both types, while cAMP is only decreased in PHP1. However, because of the lack of availability of this measurement in our context, resistance to TSH could guide the classification in the absence of the AHO phenotype. PHP classification does not change the therapeutic behavior.

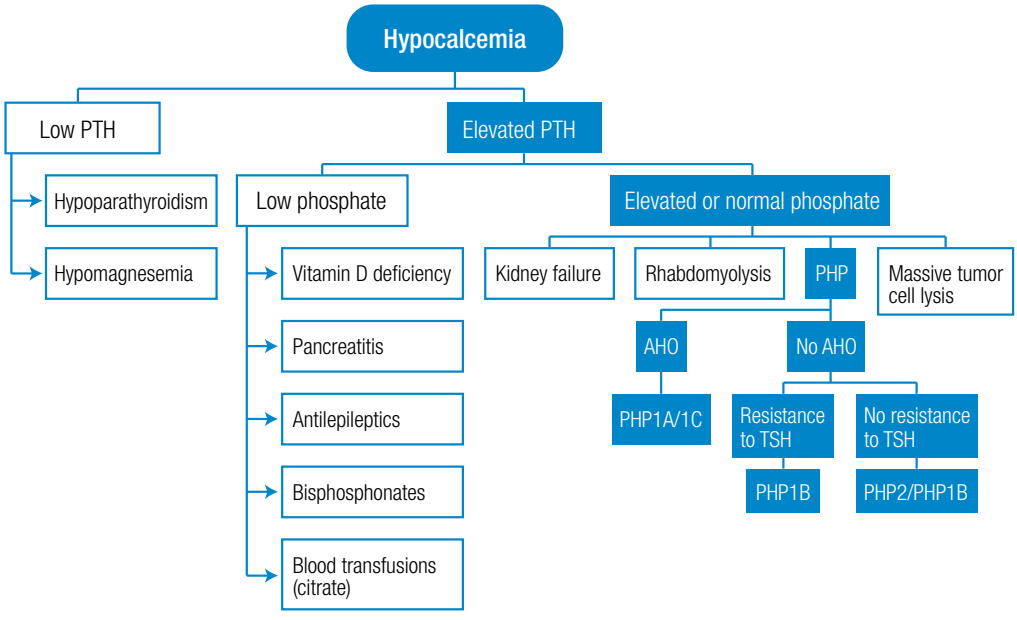

Figure 3. Diagnostic approach to PHP.
PTH: parathormone; PHP: pseudohypoparathyroidism; AHO: Albright's hereditary osteodystrophy; TSH: thyroid stimulating hormone.
Source: Elaboration based on Tafaj *et al.* (3).

Differential diagnosis includes other entities with a laboratory profile similar to PHP such as renal disease (whether chronic or acute), which is easily discarded by measuring creatinine, and osteomalacia, which presents with hypocalcemia and PTH elevation; contrary to this, PHP occurs with hypophosphatemia.

With respect to the PHP subtype (Figure 3 and Table 2), although urinary cAMP measurement or genetic studies were not carried out in any of the patients described, it was possible to achieve an initial approximation based on the phenotype and the hormonal resistance profile. In this regard, cases 3 and 4 present phenotypic features of AHO (short stature and round face), while case 3 shows shortening of the fourth and fifth metacarpals, and case 4, brachydactyly. In the presence of resistance to PTH and AHO, the probable diagnosis is PHP type 1a or 1c; however, for a definitive classification, it is necessary to carry out genetic studies that are not available in Colombia. On the other hand, cases 1 and 2 present a PHP biochemical profile without signs compatible with AHO, suggesting PHP type 1b or 2. The definitive classification requires genetic studies; however, the profile of multiple hormonal resistance of case 1, resistance to PTH and TSH, supports the diagnosis of type 1a.

The treatment of PHP consists in the administration of active metabolites of vitamin D, ideally calcitriol, with or without oral calcium supplement and with dose adjustment until achieving a calcium level in the normal range. (16) Because some tissues are not resistant to PTH, elevated PTH levels may be sufficient to maintain normal calcium levels in some patients with PHP1; however, as far as possible, the treatment should be aggressive enough to normalize PTH levels and avoid the potential effects of bone demineralization. (17) In the reported cases, all patients received calcium and calcitriol supplementation, which led to achieve normal calcium levels and symptomatic improvement.

As mentioned above, the aim of this series of cases is to describe the clinical diversity of PTH and to emphasize the importance of the basic approach using laboratory tests in patients with symptomatic hypocalcemia; a calcium-phosphorus profile properly interpreted should lead to an accurate diagnosis and timely treatment of PHP.

There are only two publications available in the literature in Colombia. The first is a report by Ucros *et al.* (18) about a family of three siblings with AHO phenotype, hypocalcemia and lack of response to PTH, which was published in 1957, and the second is a manuscript by Bernal *et al.* (19) that describes the case of a 5-year-old girl with short stature, AHO phenotype, cataracts, neurodevelopmental delay, seizures and hypocalcemia. In Latin America, after a search in LILACS, 41 reported cases were found, 5 of which were described in a Brazilian publication (20); other cases have been reported in Chile, Mexico and Venezuela. In world literature, Underbjerg *et al.* (21), reported in 2016 a series of 60 cases, the largest on PHP published; the median age at which the diagnosis was established in this series was 13 years, much lower than the age of the 4 cases presented here, which was 22.5 years.

This report, besides being the largest series of cases published in Colombia, is interesting because it presents patients who were diagnosed with PHP in adulthood, even though this is an inherited disorder with early clinical onset. This proves that there are shortcomings in the diagnostic approach to patients with hypocalcemia and, perhaps, that calcium disorders are underdiagnosed and sometimes overlooked as a differential diagnosis of frequent clinical expressions, such as seizures and other neuromuscular symptoms.

Conclusions

Hypocalcemia is not a diagnosis, but a laboratory finding that requires optimizing efforts to find its etiology. Although PHP is a rare possibility, it should be considered in the diagnostic algorithm. The diagnosis of PHP can be achieved based on a judicious approach to hypocalcemia.

Hypocalcemia along with hyperphosphatemia in the presence of elevated PTH with normal renal function are findings that confirm PHP. Although its strict classification requires genetic studies, the phenotype and the profile of the associated hormonal resistance allow a first approximation. Therefore, it is essential to rule out a calcium disorder in all patients with convulsive syndrome or calcifications in the basal ganglia using central nervous system imaging.

Conflicts of interest

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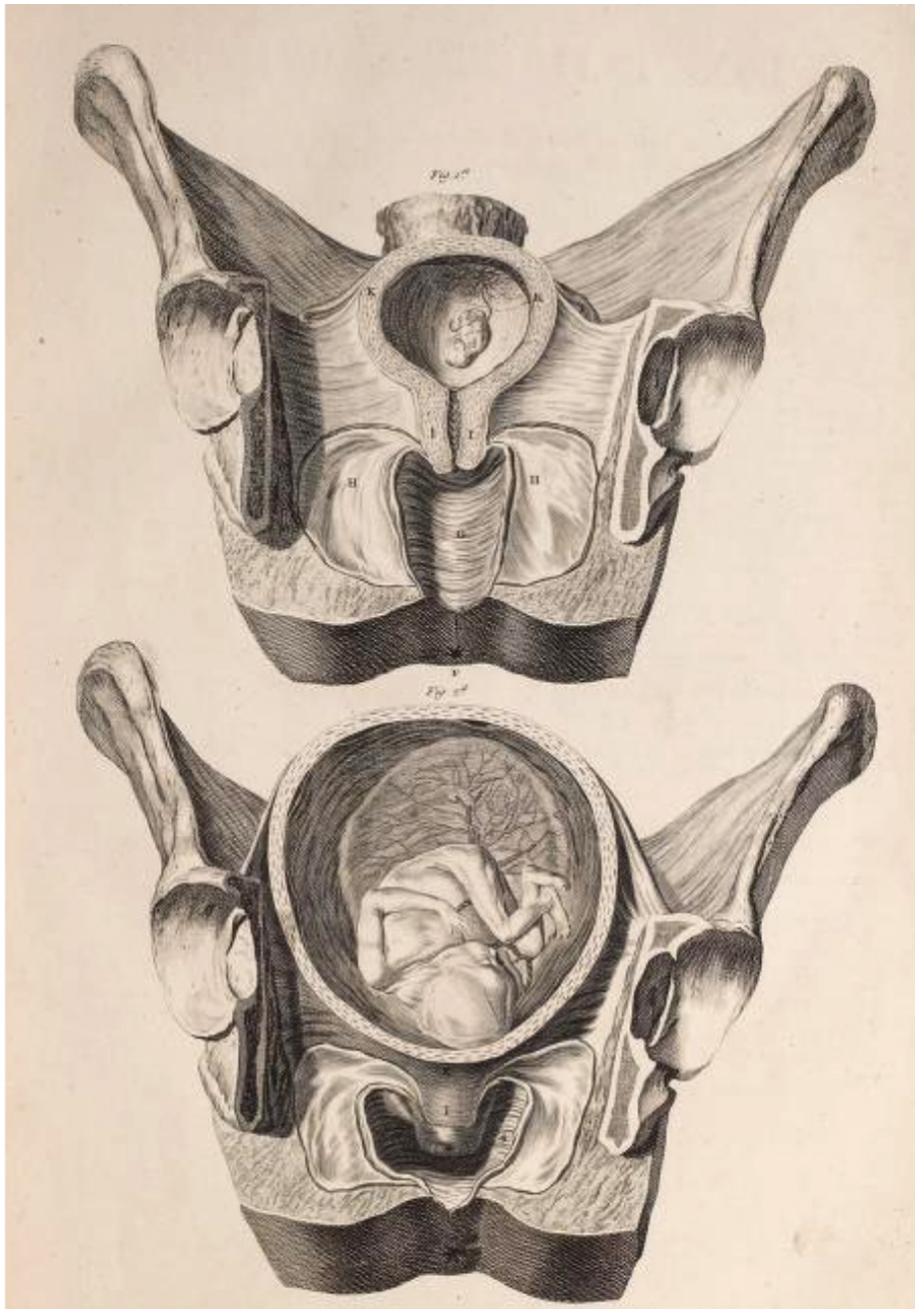

WILLIAM SMELLIE, M.D. (1754)
"A Sett of Anatomical Tables with explanations and an abridgement of the Practice of Midwifery"

Índices

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Vernaza Pinzón Paola	Departamento de Fisioterapia, Facultad Ciencias de la Salud, Universidad del Cauca	Colombia
Vernetta Santana Mercedes	Departamento de Educación Física y Deportiva, Facultad de Ciencias del Deporte, Universidad de Granada	España
Vidal Martí Cristina	Universidad de Barcelona	España
Villafañe Ferrer Lucy Margarita	Programa de Bacteriología, Corporación Universitaria Rafael Núñez	Colombia
Villalobos Aremis Litaí	Dirección de Salud Reproductiva, Centro de Investigación en Salud Poblacional, Instituto Nacional de Salud Pública	México
Villalón Urrutia Hernán	Servicio de Neonatología, Departamento de Pediatría, Clínica Las Condes Facultad de Medicina, Universidad de Chile	Chile
Villamil Gómez Wilmer Ernesto	Programa de Medicina, Universidad de Sucre	Colombia
Villegas Arenas Oscar Alberto	Facultad de Medicina, Universidad de Manizales	Colombia
Villegas Múnera Elsa María	Departamento de Medicina Preventiva y Salud Pública, Facultad de Medicina, Universidad de Antioquia	Colombia
Vilte Ona Mockus Sivickas Ismena	División de Lípidos y Diabetes, Departamento de Ciencias Fisiológicas, Facultad de Medicina, Universidad Nacional de Colombia	Colombia
Witanco Martínez Luz Maira	Escuela de Medicina y Ciencias de la Salud, Facultad de Ciencias Naturales y Matemáticas, Universidad del Rosario	Colombia
Yamazaki Nakashimada Marco Antonio	Instituto Nacional de Pediatría	México
Yoshie Toyoda Cristina	Departamento de Terapia Ocupacional, Universidade Estadual Paulista	Brasil
Yupanqui Concha Andrea	Departamento de Terapia Ocupacional, Facultad de Ciencias de la Salud, Universidad de Magallanes	Chile
Zapata Albán María del Pilar	Escuela de Rehabilitación Humana, Universidad del Valle	Colombia
Zenteno Juan Carlos	Departamento de Investigación Genética, Instituto de Oftalmología Fundación Conde de Valencia IAP	México
Zerpa Rangel Olga Rengina	Emerson Clinical Research Institute	USA

Temáticos

Editores de la Revista de la Facultad de Medicina Universidad Nacional de Colombia

Años	Volumen	Editor
1932 - 1941	Vol. 1 al 10	Dr. Jorge E. Cavelier
1942 - 1943	Vol. 11 No. 1 al 12	Dr. Marco A. Iriarte
1944	Vol. 12 No. 9- 10	Dr. Julio Aparicio
1944 - 1945	Vol. 12 No. 11 al 12	Dr. Darío Cadena M.
1946	Vol. 15 al 16	Dr. Manuel Antonio Rueda Vargas
1947 - 1949	Vol. 17 No. 2 al 12	Dr. Arturo Aparicio Jaramillo
1950 - 1951	Vol. 18, 19	Dr. Alfredo Luque
1952 - 1958	Vol. 20 al 26	Dr. Carlos Vásquez Villegas
1959	Vol. 27	Dr. Raúl Paredes
1960 - 1964	Vol. 28 al 32	Dr. Guillermo Fergusson Manrique
1965	Vol. 33	Dr. Alejandro Jiménez Arango
1966 - 1967	Vol. 34 al 36	Dr. Rafael Casas Morales
1968	Vol. 36	Dr. Enrique Carvajal Arjona
1971 - 1972	Vol. 37	Dr. Alfonso Vargas Rubiano
1972	Vol. 38 No. 1 y 2	Dr. Carlos Cuervo Trujillo
1972 - 1973	Vol. 38 No. 3 y 4	Dr. Alfonso Tribín Piedrahita
1974 - 1980	No se publicó la revista	
1981	Vol. 39 No. 1	Dr. Gerardo Aristizábal A.
1985, 1986	Vol. 40 No. 1, 2	Dr. Álvaro Murcia Gómez
1987 - 1992	No se publicó la revista	
1993 - 2003	Vol. 41 al 51	Dr. Álvaro Rodríguez Gama
2004 - 2012	Vol. 52 al 60 No.1, 2, Supl	Dr. Germán Enrique Pérez
2012 -	Vol. 60 No. 3,4	Dr. Franklin Escobar Córdoba

Contenido Revista Facultad de Medicina Volumen 66

Vol. 66 No. 1

Editorial

Investigación original

Artículo de reflexión

Artículo de revisión

Reporte de caso

Carta al editor

Vol. 66 No. 2

Editorial

Original research

Reflection paper

Review article

Case report

Letter to the editor

Vol. 66 No. 3

Editorial

Investigación original

Artículo de reflexión

Artículo de revisión

Case report

Vol. 66 No. 4

Editorial

Original research

Reflection paper

Review article

Case report

Author Guidelines

The Revista de la Facultad de Medicina (Journal of the Faculty of Medicine) adheres to the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals del International Committee of Medical Journal Editors (ICJME) (http://www.icmje.org/icmje-recommendations.pdf).

General guidelines

A. Submission of articles to the Revista de la Facultad de Medicina (Journal of the Faculty of Medicine)

Articles shall only be received at our OJS (Open Journal System) website (http://goo.gl/rsVzGU). Submission must include: article, metadata and complementary files (assignment of copyright https://goo.gl/EfWPdX and authorship responsibility https://goo.gl/6zztk4)

B. Languages of submission and language of publication

As of January 10, 2018 and in accordance with what the editorial of V65N2 (https://goo.gl/HaZ37B) states, all articles received shall begin a transition process for being published in English. In consequence, articles shall be received in English, Spanish and Portuguese, provided that the following terms are fulfilled:

I. Submissions in English

Articles written in English prior to its submission must be accompanied by a letter signed by an official translator or an English Language specialist (professional level) with a certified English language proficiency (C2) in which he or she states that the article has been reviewd or checked by him/her and that it complies with the minimum academic standards of language. Each submission will be reviewed and may be rejected if the journal staff concludes that it does not meet the minimum language requirements.

II. Submissions in Spanish and Portuguese

Authors shall attach (step 4 of the submission process) the Publication in English Commitment Letter (https://goo.gl/4rhxxh) signed by them in which they commit to translate the text into English, if the article is approved for publication. The project will be undertaken by one of the official translators of the journal, whose contact details will be provided by the Journal staff in a timely manner when the document reaches this stage of the process. Once the selected translator has received the payment (all of them will charge the same fee), the journal will be notified in order to submit the final version of the article for translation, after being proofread. Such version will be reviewed and approved by both the authors and the Journal. Current translation rate is 120 Colombian pesos per original word to be translated (roughly 0.06 USD per word), the list of references will not be included in this service as it does not require to be translated. Exceptions will be considered for those authors who prove to experience difficulties regarding the payment of this service, for example, authors residing in countries such as Venezuela or Cuba due to the exchange rate in theese countries.

C. Authorship

Those appointed as authors of articles submitted to our Journal must fully comply with the authorship criteria established in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals del International Committee of Medical Journal Editors (ICJME), setction II, subsections A and B (http://www.icmje.org/icmje-recommendations.pdf)

D. Structure of articles – General sections

In accordance with the ICJME recommendations, before submitting an article, authors must verify it has the following general structure (please, keep in mind that according to the type of article an specific structure will also be required, for further details please see Section E of these guidelines)

I. Title page:

1. Provide a title in the language in which the article is written
2. Provide a title in a second language (English or Spanish depending on which language is written the article)
3. Provide a short title no longer than 40 characters (including blank spaces)
4. All authors' full names and last names must be stated; their institutional affiliation must be identified with superscript Arabic numerals.
5. Institutional affiliation for each author must be presented without specifying positions, only institutions and sections/departments within them shall be included.
6. Provide the ORCID number for each author.
7. Complete contact details of the main author or the corresponding author must be provided (name, institutional address, telephone, city, country, email).
8. Word count: please state the total number of words that make up the article without taking into account words included in titles, abstracts, acknowledgments, tables, figures, and the list of references. The number of words must not exceed the maximum allowed for each the type of article (see Section F)
9. Number of figures and tables: please state the total number of tables and figures included in the article. The maximum numbers of tables and figures allowed is 6.

II. Abstract (in Spanish)

1. It must not exceed 200 words.
2. References must not be included.
3. In case of experimental studies, protocol (clinical trial) registry number must be included in the last line of the abstract, example: https://www.ncbi.nlm.nih.gov/pubmed/29791437
4. Original research articles, review articles and short communications must have an abstract made up the following sections: "introduction", "objective", "materials and methods", "results" and "conclusions".
5. For case reports, abstracts shall be presented in accordance with the CARE checklist of information to include when writing a case report (http://www.care-statement.org/resources/checklist), item 3, Abstract.
6. Keywords (in Spanish): Include 3 to 6 exact descriptors from DeCS Bireme (http://decs.bvs.br/).

III. Abstract

1. It must not exceed 200 words.
2. References must not be included.
3. In case of experimental studies, protocol (clinical trial) registry number must be included in the last line of the abstract, example: https://www.ncbi.nlm.nih.gov/pubmed/29791437
4. Original research articles, review articles and short communications must have an abstract made up the following sections: "introduction", "objective", "materials and methods", "results" and "conclusions".
5. For case reports, abstracts shall be presented in accordance with the CARE checklist of information to include when writing a case report (http://www.care-statement.org/resources/checklist), item 3, Abstract.
6. Keywords: Include 3 to 6 exact MeSH descriptors (http://www.nlm.nih.gov/mesh/).

IV. Introduction

The summarized rationale of the study must be included in this section. Furthermore, at the end of this section, the purpose of the study must be clearly stated. Only the references required to support the ideas depicted here are to be included.

V. Materials and methods

The type of study and the methodology used (sample identification, selection criteria, statistical methods, etc.) shall be described here. If the procedures performed during the study involved humans or animals, authors must explicitly state that they followed the ethical principles for medical research on humans of the Declaration of Helsinki (2013) and any other applicable national regulations, said documents must be duly referenced. Additionally, it must be clearly expressed that the study was approved by the ethics committee of the institution or institutions where it was carried out, and the corresponding letter of approval from the ethics committee must be enclosed.

In case of experimental studies, registration of clinical trials in a public trials registry at or before the time of first patient enrollment as a condition of consideration for publication is mandatory. An example of a public trial registry can be found at https://clinicaltrials.gov. The clinical trial registration number must be included in the last line of the abstract.

VI. Results

The results obtained in the study must be presented in a logical and coherent way. Data can be shown in tables or figures, but not simultaneously in both. Avoid repeating the data presented in tables and figures within the body of the article, and do not combine the presentation of results with your discussion, as the latter has its own section.

VII. Discussion

In this section, results obtained in the study must be addressed without making a general review of the subject. Authors must only discuss the new and most relevant aspects presented by the study and the conclusions proposed from them. Limitations of the research and the agreement or disagreement of findings reported in the article with other studies on the subject, duly referenced, must be reported.

VIII. Conclusions

Conclusions must be related to the objectives of the study described in the "introduction" section. Do not draw conclusions that are not supported by the findings of your study or that are supported by a work that has not yet been finalized. If appropriate, create new hypotheses but present them as such. Propose your recommendations.

IX. Conflict of interests

Please state, based on the funding sources of the study or any other reason, whether the authors have a conflict of interest or not. Authors must complete and sign the Conflict of Interest Disclosure Form of the ICJME (http://www.icmje.org/about-icmje/faqs/conflict-of-interest-disclosure-forms) and attach it to the submission (step 4).

X. Funding

Please state if the study was funded by external sources and if they influenced its completion.

XI. Acknowledgment

Express your gratitude only to people and institutions that have contributed substantially to your work. Authors are responsible for acknowledging the people or institutions that could be recognized as contributors to the results of the work and its conclusions by the readers.

XII. Tables, figures and references

1. Tables

A maximum of 6 tables and/or figures is allowed. Tables shall be editable, have a title, be listed in order of appearance, be mentioned within the body of the article and be included immediately after the paragraph in which they are first mentioned. If abbreviations are used, they must be clarified in table footers. If a table already published is partially or totally reproduced, the corresponding reference must be added and a letter of permission for its reproduction must be

attached. If a table is created by the authors, the legend "Source: own elaboration." must be included.

2. Figures

A maximum of 6 tables and/or figures is allowed. Figures must be editable and have a minimum 72 dpi resolution. Figures include any type of illustration other than tables (graphics, x-rays, photographs, etc.) and must be listed in order of appearance. Every figure shall be mentioned within the body of the article and included immediately after the paragraph in which it is first mentioned. If abbreviations are used, they must be clarified in figure footers. Titles and legends must not be included in the figure but below it. If a figure already published is partially or totally reproduced, the corresponding reference must be added and a letter of permission for its reproduction must be attached. If a table is created by the authors, the legend "Source: own elaboration." must be included.

Please refrain from including any description in figures footers, such explanations shall only be included in the main text of the article.

XIII. References

Both in-text and end references must conform strictly to the Vancouver style adopted by the ICJME in its recommendations. References must be introduced in order of appearance and identified by Arabic numerals in parentheses, without superscripts, at the end of the sentence or paragraph where they are alluded to. For a complete guide on the Vancouver system, please go to https://goo.gl/XdCdmS or https://goo.gl/8DJ5Er.

E. Type of articles accepted – Specific structure

In addition to the general structure described above, each type of article must meet the following requirements:

I. Editorial

An editorial is a paper written by the editor, by a member of the Editorial Board or by a guest researcher on orientations in the subject domains of the journal.

The maximum number of words allowed for Editorials, excluding abstracts, tables and figures, and references, is 1000.

II. Original research

Original research articles are papers that present in detail the original results of both research projects already finished and biomedical researches. It is an unpublished text that provides new information on specific aspects, as well as relevant contributions to scientific knowledge.

Original research articles shall have a structured abstract and must comply with the general structure for writing articles required by the Revista de la Facultad de Medicina (see Section D).

If the procedures performed during the study involved humans or animals, authors must explicitly state that they followed the ethical principles for medical research on humans of the Declaration of Helsinki (2013) and any other applicable national regulations, said documents must be duly referenced. Additionally, it must be clearly expressed that the study was approved by the ethics committee of the institution or institutions where it was carried out, and the corresponding letter of approval from the ethics committee must be enclosed.

In case of experimental studies, registration of clinical trials in a public trials registry at or before the time of first patient enrollment as a condition of consideration for publication is mandatory. An example of a public trial registry can be found at https://clinicaltrials.gov. The clinical trial registration number must be included in the last line of the abstract, for example: https://www.ncbi.nlm.nih.gov/pubmed/29791437

Articles reporting results of clinical trials in "Materials and methods" must include a data sharing statement that complies with the provision of the ICMJE recommendations, Section II, Subsection L, paragraph II (Data Sharing).

The maximum number of words allowed for Original Research articles, excluding abstracts, tables and figures, and references, is 3500.

III. Short communication

It's a brief article reporting final, partial or preliminary original results of a technologic or scientific research that usually requires a rapid dissemination.

Short communications shall have a structured abstract (in English and Spanish) and must comply with the general structure for writing articles required by the Revista de la Facultad de Medicina (see Section D).

If the procedures performed during the study involved humans or animals, authors must explicitly state that they followed the ethical principles for medical research on humans of the Declaration of Helsinki (2013) and any other applicable national regulations, said documents must be duly referenced. Additionally, it must be clearly expressed that the study was approved by the ethics committee of the institution or institutions where it was carried out, and the corresponding letter of approval from the ethics committee must be enclosed.

The maximum number of words allowed for Short communications, excluding abstracts, tables and figures, and references, is 1500.

IV. Systematic Review

Review articles are the result of a research where the results of published or unpublished researches on a field of science or technology are analyzed, systematized and integrated in order to report development trends and the progresses that have been made in the field the review addresses. This type of paper is characterized by a careful literature systematic review of at least 50 references.

- Only systematic reviews are to be submitted. Narrative or literature
- reviews will not be accepted anymore, unless the editor asksauthors to submit this type of article to start the publication process
- Systematic reviews shall have a structured abstract and must comply with the general structure for writing articles required by the Revista de la Facultad de Medicina (see Section D).
- At least 50 references shall be included.
- Systematic reviews must strictly comply with all the items established in the PRISMA checklist: http://prisma-statement.org/PRISMAStatement/Checklist
- Systematic reviews must comply with the following structure: Introduction, Materials and methods, Results (where the PRISMA based studies selection flowchart (https://goo.gl/hD7PWq) should be included), Discussion and Conclusions, this in line with the structure

established in the PRISMA checklist: http://prismastatement.org/PRISMAStatement/Checklist

The maximum number of words allowed for Systematic reviews, excluding abstracts, tables and figures, and references, is 4000.

V. Reflection paper

When writing reflection papers authors shall present the results of a research from their analytical, interpretative or critical perspective on a specific topic and using original sources. Essays and reflection papers on topics related to medicine and health areas are to be included in this section.

Reflection papers must have the following structure: "Introduction", "other sections of the article", "conclusions".

The maximum number of words allowed for Reflection papers, excluding abstracts, tables and figures, and references, is 3500.

VI. Case report

A case report is an article where the results of a study on a particular situation are presented in order to make known the technical and methodological experiences considered in a specific case. It includes a brief review of the literature related to the condition being reported.

Case reports submitted to the Journal must follow all the items of the CARE checklist for writing case reports (http://www.care-statement.org/resources/checklist).

When submitting a case report, the informed consent signed by the patient(s), or legal representative(s), whose data and/or experience was used for writing the report must be uploaded as a supplementary file in step 4 of the submission process.

The maximum number of words allowed for Case reports, excluding abstracts, tables and figures, and references, is 2000.

VII. Letter to the editor

A document presenting critical, analytical or interpretative stances on documents published in the Journal that, in the opinion of the Editorial Board, constitute an important contribution to the subject discussion by the scientific community of reference.

The maximum number of words allowed for Letters to the editor, excluding abstracts, tables and figures, and references, is 1000.

F. Assignment of rights, responsibility of authorship and translation commitment letter

All submissions must be accompanied by the assignment of rights, responsibility of authorship and translation commitment letter forms, duly completed and signed by all authors. The forms are available in https://goo.gl/EfWPdX, https://goo.gl/6zztk4 and https://goo.gl/4rhxxh, respectively. These forms can be loaded during step 4 of the submission.

G. Similarity and plagiarism report

Once received, articles will be analyzed, using the TurnItin Software, to generate a similarity and plagiarism report. If the article exceeds 15% of similarity, and if said similarity is not derived from a thesis (be aware this report does not take into account references and less than 7 words matches), it will be sent back to the authors for modification or rejected as appropriate.

H. Ethics and transparency

The Revista de la Facultad de Medicina accepts and adheres to the "Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals" issued by the International Committee of Medical Journal Editors (ICMJE) (www.icmje.org) and to the guidelines established by the Equator (Enhancing the QUAlity and Transparency Of health Research) Network (http://www.equator-network.org/) and the Committee on Publication Ethics (COPE) (http://publicationethics.org/) in order to guarantee the quality of scientific publications, their transparency, integrity and respect for the ethical principles that govern biomedical research. In consequence, the works sent to the Journal must be adjusted to these guidelines.

When procedures have been carried out on humans or animals, the ethical principles for medical research on humans of the Declaration of Helsinki 2013 (https://goo.gl/C5BPi3) and any other applicable national regulations must be explicitly stated and duly referenced. Additionally, the study must be approved by the ethics committee of the institution or institutions where it was carried out, and the respective letter of approval issued by the ethics committee must be enclosed.

If personal images or data are used during the study, the identity and the privacy of the people involved must be protected by editing the images included in the article and using terms and conventions to refer to their data or names.

The articles (or important parts of them) sent to the Revista de la Facultad de Medicina must be unpublished documents that do not correspond to translations or adaptations of other sources already published. By submitting the article together with the assignment of rights (https://goo.gl/EfWPdX) and authorship responsibility (https://goo.gl/6zztk4) forms duly completed, the authors state that:

1. They grant an exclusive license to publish and reproduce their work to the Revista de la Facultad de Medicina in case the article is accepted.
2. They assume full responsibility for the content of the document, as well as legal and moral responsibility to ensure that matters relating to the accuracy or integrity of any part of the article are properly investigated and resolved.
3. The document has not been previously published under any modality, has not been submitted to another journal and that it will not be sent to other journals while waiting for acceptance or rejection.
4. They accept that the Journal reserves the right to make modifications to the original text during the proofreading and layout processes and to only accept the changes suggested by the authors that the journal team considers pertinent.

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. The article (or most of it) has not been published, is not in the process for publication in another journal and will not be sent to other journals while waiting for acceptance or rejection.
2. The text is typed and double-spaced on letter-sized sheets, with margins of 2.5x2.5x2.5x2.5, and 12-point Verdana font. Unless the paper is an Editorial or Letter to the Editor, its writing style does not use any first person (plural or singular) form of conjugation.
3. The maximum limit of words allowed by the journal has been preserved, excluding the abstracts, tables, figures and references: 4 000 for "Systematic Reviews"; 3 500 for "Literature reviews", "Original Research" and "Reflection articles"; 2 000 for "Case Reports", and 1 000 for "Letter to the Editor" and "Editorial".
4. An abstract in Spanish and one in English, of maximum 200 words each, have been included. Three to six keywords were added, both in Spanish and English, taken from the DeCS and MeSH descriptors, respectively.
5. All the indications for the submission of articles, as established in the "Guidelines for authors", have been met. In case of breaching 4 or more items, the article will be rejected.
6. The article is organized according to the structure required for each type of article, as established in the "Guidelines for authors".
7. The references strictly follow the Vancouver style, as required by the journal, and were chosen as recommended in the "Guidelines for authors", including DOI where applicable. For further examples, please visit https://goo.gl/XdCdmS.
8. References include all material published in widely circulated journals, books, official information available online and other types of information that can be cited according to the Vancouver system. Abstracts of papers presented at congresses or symposia can only be referenced when they are published in widely circulated journals.
9. If this study involved humans or experimental animals, the "Materials and methods" section explicitly states that the applicable international ethical standards were met and that the study was approved by the ethics committee of the institution or institutions where it was made. The respective letter of approval issued by the ethics committee is enclosed.
10. The tables and figures are editable, respect the maximum allowed (6) and were made considering the amount of data they contain and the parameters established in the "Guidelines for authors".
11. If tables or figures already published are reproduced, written authorization of their authors or copyright owners is attached, as appropriate.
12. Photographs, figures (x-rays, etc.) and data respect the anonymity and privacy of the people involved.
13. Metadata (author contact details, title, abstract, keywords, references, etc.) are duly entered in step 2 of the submission.
14. The assignment of rights (https://goo.gl/EfWPdX), authorship responsibility (https://goo.gl/6zztk4) and translation commitment letter (https://goo.gl/4rhxxh) forms were completed and signed by all the authors to be loaded in step 4.

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The letter of copyright transfer and the letter of authorship responsibility must be submitted along with the original paper through the Journal OJS platform. These files are available in https://goo.gl/EfWPdX y https://goo.gl/6zztk4 and must be uploaded in step 4 (supplementary files).

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Directrices para autores/as

La Revista de la Facultad de Medicina (RFCM) se adhiere a las "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals del International Committee of Medical Journal Editors (ICJME) (http://www.icmje.org/icmje-recommendations.pdf).

A. Envío de artículos a la Revista de la Facultad de Medicina

Solo se recibirán artículos a través del portal OJS (Open Journal System) en el link http://goo.gl/rsVzGU, donde se deberá realizar el envío completo: artículo, ingreso de todos sus metadatos y archivos complementarios (cesión de derechos https://goo.gl/EfWPdX y responsabilidad de autoría https://goo.gl/6zztk4)

B. Idiomas de recepción e idioma de publicación

A partir del 10 de enero de 2018 y de acuerdo con en el editorial del V65N2 (https://goo.gl/HaZ37B), se empezará un proceso de transición de publicación en inglés, por lo cual se recibirán artículos en inglés, español y portugués siempre que se cumplan las siguientes condiciones:

I. Envío en inglés

Deberá ir acompañado de una carta firmada por traductor oficial o personal especializado (certificado este último con nivel C2 en inglés) en la que afirme que ha escrito o ha revisado el artículo y que el mismo cumple con las reglas de redacción de dicho idioma. Todo envío será revisado de forma y de concluirse que no cumple con los requisitos mínimos de idioma, será rechazado.

II. Envíos en español y portugués

Los autores adjuntarán firmado el oficio de compromiso de publicación en inglés (https://goo.gl/4rhxxh) en el que, siempre que el artículo apruebe el proceso editorial de publicación, se comprometen a traducirlo al inglés con uno de los traductores oficiales de la revista, cuyos datos les serán suministrados. Este proceso estará a cargo de la Revista y los detalles se informarán cuando documento llegue a esta etapa del proceso. Una vez los autores realicen el pago al traductor seleccionado (quienes manejarán una misma tarifa), este último informará a la revista para proceder al envío final del artículo con corrección de estilo para realizar su traducción al inglés, versión que revisarán y aprobarán los autores y la revista. La tarifa actual de la traducción es de 120 pesos colombianos por palabra original traducida (aproximadamente 0.06 usd por palabra), no se contará la lista de referencias para estos efectos. Se tendrán en cuenta excepciones para quienes demuestren dificultades para el pago de este servicio, por ejemplo autores que residan en países como Venezuela o Cuba debido a la compleja tasa cambiaria.

C. Autoría

Quienes figuren como autores de los artículos enviados deberán cumplir en su totalidad con los criterios de autoría establecidos en Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals del International Committee of Medical Journal Editors (ICJME), sección II, subsecciones A y B, http://www.icmje.org/icmje-recommendations.pdf.

D. Presentación del artículo - Secciones generales

De acuerdo a las recomendaciones de ICJME los artículos deben cumplir con la siguiente estructura general (según el tipo de artículo se requerirá una estructura específica, al respecto ver la sección F de estas indicaciones):

I. Página de portada

1. Título en el idioma en que se presente el artículo (Español, Inglés, Portugués).
2. Título en segundo idioma (inglés o español según idioma de presentación del artículo).
3. Título corto que no exceda 40 caracteres contando espacios (inglés y español).
4. Nombres completos de autores con filiación identificada por número arábigo en superíndice.
5. Filiación completa de cada autor sin especificar cargos, solo instituciones y secciones dentro de las mismas.
6. Identificación ORCID de cada autor. Esta información también debe incluirse en los metadatos del envío (paso 2 del envío en el portal OJS).
7. Correspondencia completa del autor principal (nombre, dirección institucional, teléfono, ciudad, país, correo electrónico).
8. Recuento de palabras: indique el número total de palabras en el texto sin tener en cuenta las palabras de títulos, resúmenes, agradecimientos, tablas y figuras, ni listado de referencias. El número de palabras no debe exceder el máximo permitido según tipo de artículo (ver Sección E).
9. Número de figuras y tablas: indique el número total de tablas y figuras en el artículo. No debe exceder el máximo permitido: 6.

II. Resumen

1. No debe superar las 200 palabras.
2. No debe incluir referencias.

3. En caso de estudios experimentales, incluir el registro del protocolo (ensayo clínico) en la última línea del resumen, ejemplo: https://www.ncbi.nlm.nih.gov/pubmed/29791437
4. Para *Investigación original, Artículo de revisión,* y *Comunicación breve* debe estructurarse en "Introducción", "objetivo", "materiales y métodos", "resultados", "conclusiones".
5. Para reportes de caso debe estructurarse de acuerdo con los lista de comprobación CARE para presentación de reportes de caso (http://www.care-statement.org/resources/checklist), ítem 3 Resumen.
6. Palabras clave: Incluir 3 a 6 descriptores exactos que se encuentren DeCS Bireme (http://decs.bvs.br/).

III. Abstract

1. No debe superar las 200 palabras.
2. No debe incluir referencias.
3. En caso de estudios experimentales, incluir el registro del protocolo (ensayo clínico) en la última línea del resumen, ejemplo: https://www.ncbi.nlm.nih.gov/pubmed/29791437
4. Para Investigación original, Artículo de revisión, y Comunicación breve debe estructurarse en "Introduction", "objective", "materials and methods", "results", "conclusion".
5. Para reportes de caso debe estructurarse de acuerdo con los lista de comprobación CARE para presentación de reportes de caso (http://www.care-statement.org/resources/checklist), ítem 3 Resumen.
6. Keywords: Incluir 3 a 6 descriptores exactos que se encuentren en MeSH (http://www.nlm.nih.gov/mesh/).

IV. Introducción

Sintetice la racionalidad del estudio y, al final de esta sección, indique el objetivo del mismo. Cite solo las referencias estrictamente necesarias.

V. Materiales y métodos

Describa el tipo de estudio y la metodología empleada en la realización del artículo (identificación de la muestra, criterios de selección, métodos estadísticos, etc.). Si se realizaron procedimientos en seres humanos o animales debe expresarse de forma explícita que se respetaron los principios éticos para las investigaciones médicas en seres humanos de la Declaración de Helsinki (2013) y cualquier otra normativa nacional que aplique, debidamente referenciadas, y que el estudio fue aprobado por el comité de ética de la institución o instituciones donde fue realizado, acompañando el envío con la respectiva carta de aprobación por parte del comité de ética. En caso de estudios experimentales se requiere que el protocolo del estudio (ensayo clínico) haya sido registrado previamente en una base de datos de registro de protocolos, se sugiere consultar https://clinicaltrials.gov, Incluir el registro en la última línea del resumen.

VI. Resultados

Presente de forma lógica y coherente los resultados obtenidos. Los datos se pueden mostrar en tablas o figuras, pero no de forma simultánea en ambas. Evite repetir en el texto los datos presentados en tablas y figuras y no combine la presentación de los resultados con su discusión, pues esta última tiene su propia sección.

VII. Discusión

Aborde los resultados obtenidos en el estudio sin realizar una revisión del tema en general. Discuta únicamente sobre los aspectos nuevos e importantes que aporta su trabajo y las conclusiones propuestas a partir de los mismos. Indique las limitaciones de la investigación y las concordancias o discordancias de sus hallazgos con los obtenidos en otros estudios sobre el tema, debidamente referenciados.

VIII. Conclusiones

Deben estar relacionadas con los objetivos del estudio que fueron descritos en "introducción". No formule conclusiones que no estén respaldadas por los hallazgos del estudio o que se apoyen en otros trabajos aún sin finalizar. Si lo considera pertinente, plantee nuevas hipótesis pero califíquelas como tales. Cuando sea apropiado, proponga sus recomendaciones.

IX. Conflicto de intereses

Indique si a partir de la financiación del estudio o por otro motivo los autores presentaron o no conflicto de intereses en la realización del artículo. Debe diligenciarse el formato de divulgación de conflicto de intereses del ICJME (http://www.icmje.org/about-icmje/faqs/conflict-of-interest-disclosure-forms) y adjuntarse como archivo complementario (paso 4 del envío).

X. Financiación

Señale si el estudio contó con financiación externa y si esta influenció su realización.

XI. Agradecimientos

Agradezca solo a personas e instituciones que hayan contribuido sustancialmente a su trabajo. Los autores son responsables por la mención de personas o instituciones a quienes los lectores podrían atribuir un apoyo a los resultados del trabajo y sus conclusiones.

XII. Tablas, figuras y referencias

1. Tablas

Deben ser editables. Se permitirá un máximo de 6 tablas y/o figuras. Deberán tener título, enumerarse en orden de aparición, mencionarse en el texto e incluirse inmediatamente después del párrafo en que son nombradas. Si se utilizan abreviaturas han de ser aclaradas en forma de pie de tabla. Si una tabla ya publicada es reproducida parcial o totalmente indíquelo referenciándolo y adjuntando en el envío carta de permiso para la reproducción de la misma. Si una tabla es creación de los autores indíquelo con la leyenda Fuente: elaboración propia.

2. Figuras

Deben ser editables y tener una resolución mínima de 72 dpi. Denomine como figura cualquier tipo de ilustración que no sea tabla (gráficos, radiografías, fotografías, etc.) y enumérelas en orden de aparición. Toda figura deberá mencionarse en el texto e incluirse inmediatamente después del párrafo en que es nombrada. Si se utilizan abreviaturas, las

mismas tienen que ser aclaradas en forma de pie de figura. Los títulos y leyendas no deben aparecer en la figura, sino abajo de la misma. Si una figura ya publicada es reproducida parcial o totalmente indíquelo referenciándolo y adjuntando en el envío carta de permiso para la reproducción de la misma. Si una figura es creación de los autores indíquelo con la leyenda Fuente: elaboración propia

No incluir descripciones en los pies de figura, estas explicaciones deben incluirse en el cuerpo del documento.

XII. Referencias

La citación de referencias, tanto in texto como en el listado final, debe ajustarse estrictamente al formato Vancouver aprobado por el ICJME en sus recomendaciones . La enumeración debe realizarse en orden de aparición y debe identificarse mediante números arábigos entre paréntesis, sin superíndice, ubicados al final de la frase o párrafo en donde se les alude. Para una guía sobre el sistema Vancouver ir a https://goo.gl/XdCdmS o https://goo.gl/8DJ5Er.

E. Tipos de artículo, estructura y máximo de palabras

Además de la estructura general antes descrita, cada tipo de artículo debe cumplir con los siguientes requisitos:

I. Editorial

Documento escrito por el editor, un miembro del Comité Editorial o un investigador invitado sobre orientaciones en las áreas de especialidad de la revista.

Máximo permitido de palabras 1000, sin contar títulos, resúmenes, tablas y figuras y referencias

II. Investigación original

Artículo que presenta, de manera detallada, los resultados originales de proyectos de investigación ya terminados, así como de investigaciones biomédicas. Es un trabajo inédito que aporta nueva información sobre aspectos específicos y contribuye de manera relevante al conocimiento científico.

Debe incluir resumen estructurado y cumplir con la estructura general requerida por la revista (ver Sección D).

Si se realizan estudios en o con datos de seres humanos o animales deben haberse tenido en cuenta los principios éticos de investigación de la Declaración de Helsinki y la normativa nacional que aplique (debidamente referenciadas), indicar que fue aprobado por comité de ética institucional y acompañar el envío con la carta de aprobación por parte de dicho comité.

En caso de estudios experimentales se requiere que el protocolo del estudio haya sido registrado previamente en una base de datos de registro de protocolos, se sugiere consultar https://clinicaltrials.gov, Incluir el registro en la última línea del resumen, ejemplo: https://www.ncbi.nlm.nih.gov/pubmed/29791437.

Si la investigación reporta resultados de ensayos clínicos debe incluirse (en materiales y métodos) una declaración sobre la divulgación de datos que cumpla con lo establecido por en las recomendaciones del ICMJE, Sección III, Subsección L, literal II (Data Sharing).

Máximo permitido de palabras 3500, sin contar títulos, resúmenes, tablas y figuras y referencias

III. Comunicación breve

Documento breve que presenta resultados originales finales, preliminares o parciales de una investigación científica o tecnológica que, por lo general, requiere de una pronta difusión.

Debe incluir resumen estructurado y cumplir con la estructura general requerida por la revista (ver Sección D).

Si se realizan estudios en o con datos de seres humanos o animales deben haberse tenido en cuenta los principios éticos de investigación de la Declaración de Helsinki y la normativa nacional que aplique (debidamente referenciadas), indicar que fue aprobado por comité de ética institucional y acompañar el envío con la carta de aprobación por parte de dicho comité.

Máximo permitido de palabras 1500, sin contar títulos, resúmenes, tablas y figuras y referencias

IV. Artículo de revisión (categoría general):

Documento resultado de una investigación donde se analizan, sistematizan e integran los resultados de investigaciones publicadas o no publicadas sobre un tema específico con el fin de dar cuenta de los avances y tendencias de desarrollo en este campo. Se caracteriza por presentar una cuidadosa revisión sistemática de la literatura médica de por lo menos 50 referencias.

- Solo se aceptarán revisiones sistemáticas. Las revisiones narrativas no serán aceptadas, a menos que exista invitación previa por parte del Editor para su presentación a proceso de publicación
- La revisión sistemática debe incluir resumen estructurado y cumplir con la estructura general requerida por la revista (ver Sección D)
- Mínimo de referencias a incluir: 50
- Debe cumplir estrictamente con todos los ítems de la lista de comprobación PRISMA: http://prisma-statement.org/PRISMAStatement/Checklist
- Debe estructurarse en Introducción, Materiales y métodos, Resultados (donde debe incluirse el flujograma formato PRISMA https://goo.gl/hD7PWq), Discusión y conclusiones, esto en línea con la estructura de la lista de comprobación PRISMA: http://prisma-statement.org/PRISMAStatement/Checklist
- Máximo permitido de palabras: 4000, sin contar títulos, resúmenes, tablas y figuras y referencias

V. Artículo de reflexión

Documento que presenta los resultados de una investigación, desde una perspectiva analítica, interpretativa o crítica del autor, sobre un tema específico en el que se recurre a fuentes originales. En esta sección también se incluyen aquellos ensayos y artículos de reflexión sobre temáticas relacionadas con la medicina y el área de la salud.

Deberá estructurarse en “Introducción”, “texto del artículo”, “conclusiones” Máximo permitido de palabras 3500, sin contar títulos, resúmenes, tablas y figuras y referencias

VI. Reporte de caso

Documento que presenta los resultados de un estudio sobre una situación particular con el fin de dar a conocer las experiencias técnicas y metodológicas consideradas en un caso específico; incluye una revisión breve de la literatura relevante.

La estructura y presentación de los reportes de caso deben cumplir todos los ítéms del checklist de los líneamientos CARE (http://www.care-statement.org/resources/checklist) para presentación de casos.

El envío debe estar acompañado del consentimiento informado del o los pacientes o sus representantes objeto del caso (paso 4 del envío, archivos complementarios)

Máximo permitido de palabras 2000, sin contar títulos, resúmenes, tablas y figuras y referencias

VII. Carta al editor

Texto en el que se expresan posiciones críticas, analíticas o interpretativas sobre los documentos publicados en la Revista que, a juicio del Comité Editorial, constituyen un aporte importante a la discusión del tema por parte de la comunidad científica de referencia.

No requiere estructura.

Máximo permitido de palabras 1000, sin contar títulos, resúmenes, tablas y figuras y referencias

F. Formatos de cesión de derechos, responsabilidad de autoría y compromiso de traducción

Todo envío deberá ir acompañado de los oficios cesión de derechos, responsabilidad de autoría y compromiso de traducción debidamente diligenciados y firmados por todos los autores, los cuales están disponibles para descarga en https://goo.gl/EfWPdX, https://goo.gl/6zztk4 y https://goo.gl/4rhxxh, respectivamente. Dichos oficios podrán cargarse en el paso 4 del envío.

G. Informe de similitud y plagio

Una vez recibidos, los artículos serán analizados con el Software TurnItin, donde se generará un informe de similitud y plagio, en caso de superar 15% de similitud y no derivarse de un trabajo de grado o tesis de postgrado dicha similitud (no se tienen en cuenta referencias ni coincidencias menores a 7 palabras), el artículo será devuelto para modificación o rechazado según sea el caso.

H. Declaración de ética y transparencia

La Revista de la Faculta de Medicina acepta y se adhiere a las "Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals" del International Committee of Medical Journal Editors (ICMJE) (www.icmje.org) y a los lineamientos establecidos por Equator (Enhancing the QUAlity and Transparency Of health Research) Network (http://www.equator-network.org/) y por el Committee on Publication Ethics (COPE) (http://publicationethics.org/) con el fin de garantizar la calidad de las publicaciones científicas, su transparencia, integridad y debido respeto de los principios éticos que rigen la investigación biomédica. De acuerdo a lo anterior, los trabajos enviados a la Revista de la Facultad de Medicina se deben ajustar a dichos lineamientos.

Además, cuando se hayan realizado procedimientos en seres humanos o animales debe expresarse de forma explícita que se respetaron los principios éticos para las investigaciones médicas en seres humanos de la Declaración de Helsinki de 2013 (https://goo.gl/C5BPi3) y cualquier otra normativa nacional que aplique, debidamente referenciadas, y que el estudio fue aprobado por el comité de ética de la institución o instituciones donde fue realizado, acompañando el envío con la respectiva carta de aprobación por parte del comité de ética.

En caso de utilizarse imágenes o datos personales en la realización del estudio se debe proteger la identidad y privacidad de estas personas mediante la edición de las imágenes incluidas en el artículo y el uso de términos y convenciones para referirse a sus datos o nombres.

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4. Incluye un resumen en español y uno en inglés de máximo 200 palabras cada uno. Se indican 3 a 6 palabras claves, tanto en español, como en inglés, tomadas de los descriptores DeCS y MeSH, respectivamente.
5. Cumple con todas las indicaciones para la presentación y envío de artículos informadas en las "Directrices para autores". En caso de incumplir 4 o más ítems el artículo será rechazado.
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8. Incluye como referencias material publicado en revistas de circulación amplia, en libros, información oficial disponible en línea y otros tipos de información citable según el sistema Vancouver. Los resúmenes de trabajos presentados en congresos o simposios solo pueden referenciarse cuando estén publicados en revistas de circulación amplia.
9. Si este estudio comprometió seres humanos o animales de experimentación, en "Materiales y métodos" se ha expresado explícitamente que se cumplieron las normas éticas exigidas a nivel internacional y que el mismo fue aprobado por el comité de ética de la institución o instituciones donde fue realizado, acompañando el envío con la respectiva carta de aprobación por parte del comité de ética.
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