



Anais da Faculdade de Medicina de Olinda  
*Annals of Olinda Medical School*

# HEALTH SOCIAL RESPONSIBILITY



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**Inácio de Barros Melo Neto**

*Diretor-geral da Faculdade de Medicina de Olinda*

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## **Letter to the editors of the Anais da Faculdade de Medicina de Olinda**

Dear Editors

**T**he management of the Faculdade de Medicina de Olinda (FMO) congratulates them for sharing the thought that imagination is more important than science, and the resilience of the visionary materializes into a product. This is the expression of an Institution that, although not formally a University, conducts activities as if it were. It is in this sense that the support of FMO management emphasizes the non-separability of teaching, research, and extension as a guiding principle for a strong and quality Academy.

The journal is intended as a repository of new knowledge to be continuously stimulated at the Institution. In this thought, seeds are being planted, and they will be watered to produce knowledge as an unquestionable asset. The Institution will ensure that the journal, now in its infancy, follows the path of evolution into a permanent vehicle for transmitting knowledge. It is the imagination that grows without diminishing science. It is resilience asserting itself when life requires a cherished dream to become a reality. The creation of the FMO marked the realization of the dream of a family with an academic tradition characterized by flashes of boldness and determination. There was no shortage of obstacles to overcome, but they were. The creation of the new journal evidences the determination of the management to create academic facts that will foster the best concept of accreditation with the Ministry of Education.

You can be sure that today's support will last forever. We are partners who will walk together along the same path in the search for the quality of meritocracy of the FMO family. We are fighting brothers, and we will fight the good fight.

Congratulations on the release of the first issue of the first volume. It is the baptism of this partnership that the management hopes will be permanent. It is a revealed truth that fulfills another dream cherished in the imagination of FMO managers. Let us welcome you to the heart of this repository, and may it represent looking to the future with determination and courage.

Congratulations to you and all the authors who contributed to this endeavor. Let us move towards the future.



# EDITORIAL

Carlos Teixeira Brandt<sup>1</sup>, Maria Cecília Santos Cavalcanti Melo<sup>2</sup>

<sup>1</sup> Editor-in-chief, <sup>2</sup> Deputy Editor, Faculdade de Medicina de Olinda

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## A dream come true

*Nascimento de realidade sonhada*

The launch of a new scientific journal is always something to be greeted with enthusiasm, mainly because it is an additional contribution to alleviating the loneliness of those who dedicate themselves to intellectual work, the accumulation of knowledge, and the disclosure of what they have accumulated and transmitted. In essence, a journal of this nature is, above all, an invitation to expose the results of studies and research for public debate to achieve the main aim of the Academy: a dialogue that produces dissent and consensus, based on scientific principles and methods, with the main purpose of improving the quality of health care, particularly for those who need it most. Social responsibility must be an active part of the Academy in the training of new professionals.

The chosen name, “Anais da Faculdade de Medicina de Olinda,” expresses the aspiration to constitute a repository of new knowledge produced in this fledgling institution, idealized by visionary management with the decisive support of its highly qualified teaching staff. Now, those who conceived and planned this journal can consider themselves accomplished. The idea was immediately matured, as were the actions conceived by management and those who wear and will wear the same shirt. It is worth having them, developing them positively for years to come. It is born, consequently, reflected, debated, as a collective fruit of an academic community that listens and makes itself heard in the world of science. Biannual, with a global health focus, determined by the nature of the Web, it is guided by a high-level Editorial Board that is renewed every two years.

The journal will publish texts in Portuguese, English, and Spanish, and aims to maintain a high editorial quality. Regarding the content, an ad hoc

body of experts will evaluate and select the works that are submitted, independently and anonymously. The entire editorial process will be controlled and transparent, ensuring it is recognized as an academic journal of excellence, particularly in the Health Sciences and areas of study and research. The journal was born with the commitment to make clear the inherent nature of the one trio of the Academy: the production of new knowledge that sits alongside teaching and extension as an indivisible core.

The inaugural texts of the journal honor the academic environment due to the magnitude of the topics covered and the authors who author them. As can be seen, authors with a recognized level of reflection and high theoretical knowledge in the fields in which they work. Reading them means following paths of intellectual enrichment, exploring new fields of knowledge, visiting luminous spaces of discovery, and advancing into the future. Ethics is urgently needed as a science that studies morality. Scientific research, as the structuring foundation of human curiosity, makes good practice in individual and collective health the cornerstone of the proposed journal.

Advancing the state of knowledge appreciation for its production enables educational institutions to leverage quality, exemplify, and perpetuate new directions in the academic scenario. May the Anais of the Faculdade de Medicina de Olinda be like this.

Furthermore, it is a process of learning by dreaming, doing, listening, avoiding mistakes, and venerating success, with the wisdom that it is probabilistic.

Always visit us at our address: [revistaanaisfmo@fmo.edu.br](mailto:revistaanaisfmo@fmo.edu.br)



# THE IMPORTANCE OF ROUTINE SCREENING FOR MACROPROLACTIN IN SYMPTOMATIC PATIENTS WITH IDIOPATHIC HYPERPROLACTINEMIA

A IMPORTÂNCIA DO RASTREAMENTO DE ROTINA DA MACROPROLACTINA EM PACIENTES SINTOMÁTICAS COM HIPERPROLACTINEMIA IDIOPÁTICA

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## ABSTRACT

**Objective:** To evaluate the importance of screening for macroprolactin in symptomatic patients with apparent idiopathic hyperprolactinemia. **Methods:** The prevalence of macroprolactinemia, never systematically evaluated, was assessed during 20 months in consecutive symptomatic female patients with apparent idiopathic hyperprolactinemia routine and followed in two neuroendocrinology reference centers. **Results:** A total of 82 patients (mean age:  $36.1 \pm 7.3$  years, ranging from 25 to 50) were included, 69 (84.1%) were treated with cabergoline. The screening for macroprolactin was positive in 22 patients (26.8%), and 15 (68.2%) received incorrect long-term treatment with cabergoline. The clinical and demographic characteristics and baseline prolactin levels were compared in patients with true idiopathic hyperprolactinemia and in those with macroprolactinemia. **Conclusion:** Macroprolactinemia was observed in approximately 25% of patients with apparent idiopathic hyperprolactinemia. The findings highlight the importance of routine screening for macroprolactin in patients with idiopathic hyperprolactinemia, regardless of their clinical characteristics, to avoid misdiagnosis and unnecessary treatment with dopamine agonists.

**Keywords:** Macroprolactin; Screening; Macroprolactinemia; Idiopathic hyperprolactinemia.

## RESUMO

**Objetivo:** Avaliar a importância do rastreamento de rotina de macroprolactina em mulheres sintomáticas com aparente hiperprolactinemia idiopática. **Métodos:** Durante 20 meses, a prevalência de macroprolactinemia foi avaliada entre pacientes sintomáticas com aparente hiperprolactinemia idiopática rotineiramente seguidas em dois centros de referência de neuroendocrinologia de Recife. Esta prevalência nunca fora sistematicamente avaliada. **Resultados:** Um total de 82 mulheres (média das idades,  $36,1 \pm 7,3$  anos, faixa etária de 25 a 50) foram incluídas; 69 delas (84,1%) foram tratadas com cabergolina. A pesquisa para macroprolactina se mostrou positiva em 22 pacientes (26,8%), 15 das quais (68,2%) equivocadamente foram tratadas a longo prazo com cabergolina. As características clínicas e demográficas, bem como os níveis basais de prolactina, foram comparáveis em pacientes com hiperprolactinemia idiopática verdadeira e naquelas com macroprolactinemia. **Conclusão:** Macroprolactinemia foi encontrada em cerca de um quarto das pacientes com aparente hiperprolactinemia idiopática. Os resultados destacam a importância da pesquisa de rotina para macroprolactina em todas as pacientes com hiperprolactinemia idiopática, independentemente de suas características clínicas, a fim de se evitar diagnóstico incorreto e tratamento desnecessário com agonistas dopaminérgicos.

**Palavras-chave:** Macroprolactina; Pesquisa; Macroprolactinemia; Hiperprolactinemia idiopática.

## INTRODUCTION

Hyperprolactinemia is the most common endocrine disorder of the hypothalamic-pituitary axis<sup>1,2</sup>. Idiopathic hyperprolactinemia presents with increased serum prolactin (PRL) levels in the absence of known pituitary or central nervous system disease and other recognized causes<sup>1,3,4</sup>.

The molecular size of circulating PRL is heterogeneous. The predominant form in healthy individuals and patients with prolactinomas is the monomeric PRL (molecular weight of 23 kDa). In contrast, the dimeric (4560 kDa) and macroprolactin (150170 kDa) forms correspond to less than 20% of the total PRL<sup>5,6</sup>. Macroprolactinemia occurs when the hyperprolactinemia serum contains mostly macroprolactin<sup>1,7</sup>, which is formed by a complex of an IgG and a monomeric PRL in approximately 90% of cases<sup>1,8</sup>. Macroprolactin causes hyperprolactinemia due to low renal PRL clearance and decreased stimulation of the dopaminergic tonus<sup>8</sup>. In addition, macroprolactin has a high molecular mass and low biological activity and bioavailability<sup>8,9</sup>, which explains why patients with macroprolactinemia often lack typical symptoms associated with hyperprolactinemia<sup>8,11</sup>. Therefore, macroprolactinemia patients do not need to be treated<sup>10,12</sup>, unlike those with idiopathic hyperprolactinemia<sup>3</sup>.

The screening for macroprolactin has been considered for asymptomatic patients<sup>2,3,8,12</sup>. However, the presence of galactorrhea, menstrual disorders, or erectile dysfunction does not exclude the diagnosis, as shown in clinical studies<sup>10-16</sup>. This finding could be explained by the concomitance of macroprolactinemia with other disorders, such as polycystic ovary syndrome, non-functioning pituitary adenomas, prolactinomas, or other causes of monomeric hyperprolactinemia<sup>1,10,15-17</sup>.

This study aimed to determine the prevalence of macroprolactinemia during 20 months among symptomatic female patients with apparent idiopathic hyperprolactinemia, which was never systematically evaluated. Misdiagnosis in these cases could lead to unnecessary treatment with dopamine agonists.

## METHODS

The study was performed in two neuroendocrinology centers at Recife, Pernambuco, Brazil (Endocrine Research Center of Pernambuco and Di-

vision of Endocrinology of *Hospital das Clínicas*, Federal University of Pernambuco). The clinical, laboratory, and demographic data were compared in patients with and without macroprolactinemia.

PRL was measured using a chemiluminescence immunoassay (Immulite 2000®, Diagnostic Products Corporation, California, USA). Macroprolactin was determined by measuring the serum PRL level before and after polyethylene glycol (PEG) precipitation, with a reference ranged of 2.8 to 29.2 ng/mL. The criteria for diagnosis of macroprolactinemia and monomeric hyperprolactinemia were based on the study of Vieira et al.<sup>18</sup>, with PRL recoveries < 40% and > 60% after PEG precipitation, respectively.

Results were expressed as percentages and mean values ± standard deviation (SD), unless otherwise stated. Categorical variables were compared using the chi-squared or Fisher's exact test when appropriate. A paired Student's t-test was performed for the comparative analysis of two means, and a p-value < 0,05 was considered statistically significant.

The study was approved by local ethics and scientific committees, and all patients signed the informed consent form.

## RESULTS

A total of 82 patients (mean age: 36.1 ± 7.3 years; ranging from 25 to 50) were included in the study; 69 (84.1%) were treated with cabergoline.

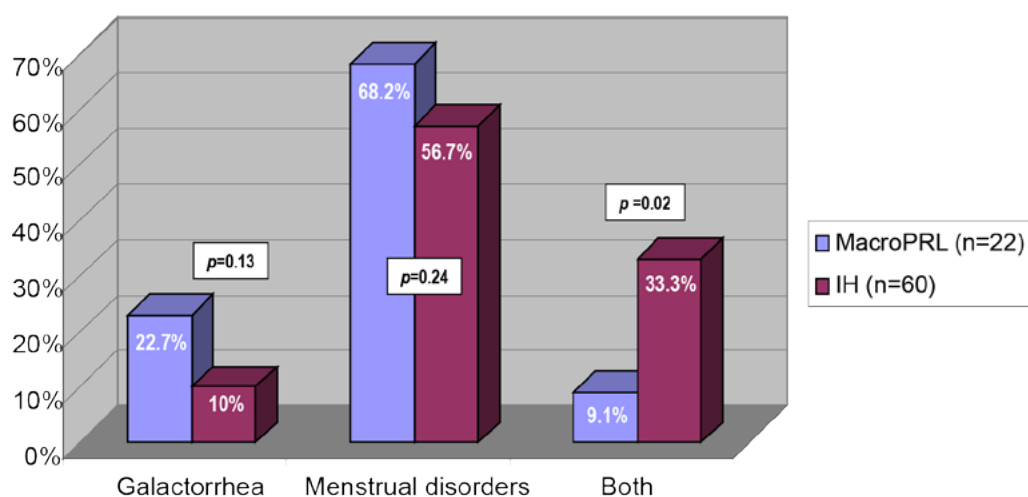
The screening for macroprolactin was positive in 22 patients (26.8%), and 15 (68.2%) received long-term treatment with cabergoline.

The clinical and demographic data were compared in patients with true idiopathic hyperprolactinemia and in those with macroprolactinemia (Table 1). However, the rate of patients experiencing menstrual disorders (oligomenorrhea or amenorrhea) and galactorrhea was significantly higher in the idiopathic hyperprolactinemia group (33.3% vs. 9.1%; p = 0.02). In contrast, the rates of patients presenting symptoms of isolated menstrual disorders or galactorrhea were similar in both groups (Table 1 and Figure 1).

**Table 1.** Comparison of clinical, demographic, and laboratory characteristics at diagnosis in symptomatic female patients with macroprolactinemia and idiopathic hyperprolactinemia.

Characteristics	Macroprolactinemia (n = 22)	Idiopathic hyperprolactinemia (n = 60)	p -value
Age (years)	37.30 ± 9.65	35.70 ± 6.51	0.11
Mean PRL levels (ng/mL)	137.05 ± 72.12 (70 to 295)	156.45 ± 65.07 (75 to 286)	0.15
Isolated galactorrhea (%)	22.70 (n=5)	10.00 (n=6)	0.13
Isolated menstrual disorders (%)	68.20 (n=15)	56.70 (n=34)	0.24
Menstrual disorders and galactorrhea (%)	9.10 (n=2)	33.30 (n=20)	0.02
PRL normalization during CAB treatment (%)	40.00(n=6/15)	81.40 (n=44/55)	<0.01

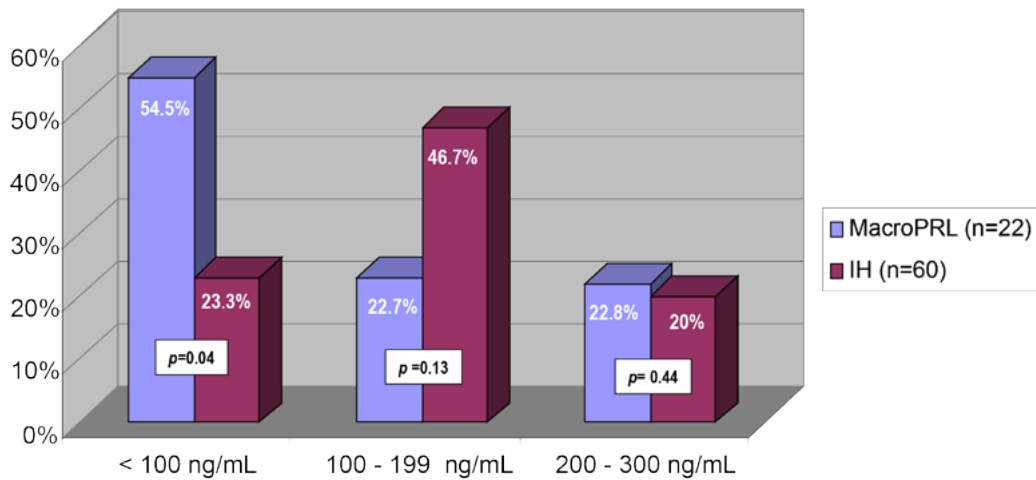
CAB: cabergoline; PRL: prolactin

**Figure 1.** Presenting clinical characteristics of female patients with macroprolactinemia (MacroPRL) and idiopathic hyperprolactinemia (IH). The combination of galactorrhea and menstrual disorders was significantly lower in the macroPRL group than among IH patients (9.1% vs 33.3%, p = 0.02).

PRL levels did not significantly differ in patients with macroprolactinemia (70 to 295 ng/mL; mean of 137.05 ± 72.12) and in those with true idiopathic hyperprolactinemia (75 to 286 ng/mL; mean of 156.45 ± 65.07; p = 0.15). However, PRL levels lower than 100ng/mL were more frequent in the macroprolactinemia group (Figure 2). After PEG

precipitation, all patients with macroprolactinemia had monomeric PRL levels within the normal range.

During cabergoline treatment, PRL normalization was achieved in 40% of patients with macroprolactinemia and in 81.4% of those with true idiopathic hyperprolactinemia (p < 0.01) (Table 1).



**Figure 2.** Distribution of patients with macroprolactinemia (MacroPRL) or idiopathic hyperprolactinemia (IH) according to their baseline prolactin (PRL) levels. Mean PRL levels were similar in both groups ( $p = 0,15$ ).

## DISCUSSION

This prospective study demonstrated positive macroprolactin in 26.8% of 82 symptomatic female patients with a previous diagnosis of idiopathic hyperprolactinemia. Other studies observed a prevalence of macroprolactinemia in individuals with idiopathic hyperprolactinemia ranging from 34.2% to 68.3%; however, the clinical profile was not mentioned<sup>16,19</sup>.

Macroprolactinemia has been recognized in asymptomatic patients and volunteers in studies<sup>1,5,6</sup>. Macroprolactin was shown to exhibit low bioactivity and bioavailability<sup>8,9</sup>, which may explain the lack of symptoms associated with hyperprolactinemia in most patients<sup>10-15</sup>. Accordingly, the 2011 Endocrine Society guidelines suggest screening for macroprolactin only in the investigation of asymptomatic hyperprolactinemic patients<sup>2</sup>. However, recent studies demonstrated galactorrhea and hypogonadism symptoms (oligo- and amenorrhea, infertility, and erectile dysfunction) often observed in patients with macroprolactinemia<sup>10-15,19,20</sup>.

Macroprolactinemia was asymptomatic in 36 (56.3%) of 64 patients; the others presented hypogonadism symptoms and galactorrhea<sup>20</sup>. Conversely, only 11.5% with monomeric hyperprolactinemia were asymptomatic ( $p < 0.001$ ). The frequency of galactorrhea (12.9% vs. 28.6%,  $p = 0.690$ ), menstrual disturbances (24.1% vs. 25.7%,  $p = 0.834$ ), and erectile dysfunction (50% vs. 42.3%,  $p = 0.722$ ) did not show a significant difference between groups. However, the combination of galactorrhea and menstrual disturbances was significantly more frequent in women with monomeric hyperprolactinemia

(34.3% vs 1.8%,  $p < 0.001$ )<sup>20</sup>. Menstrual disorders or galactorrhea were equally prevalent in patients with or without macroprolactinemia, whereas the combination of these characteristics predominated in the idiopathic hyperprolactinemia group.

The results of this study corroborate literature<sup>11-16,19</sup> since among macroprolactinemia women, menstrual disturbances were observed in 12.4%, infertility in 4.9%, and galactorrhea in 1.8%<sup>11-16,19</sup>. Moreover, 50.7% of men with macroprolactinemia complained of erectile dysfunction<sup>13,14</sup>.

Symptoms that motivate measurement of PRL are nonspecific and may occur coincidentally in patients who present hyperprolactinemia due to macroprolactin and associated conditions, such as idiopathic galactorrhea<sup>21</sup>, chronic anovulation (e.g., polycystic ovary syndrome)<sup>22</sup>, psychogenic erectile dysfunction<sup>23</sup>, or non-functioning pituitary tumors<sup>1,24</sup>. Furthermore, macroprolactinemia patients may present prolactinomas or other causes of monomeric hyperprolactinemia<sup>1,16,19</sup>, with PRL levels above the normal range after PEG precipitation<sup>1,8</sup>.

Idiopathic hyperprolactinemia probably occurs from small prolactinomas that escape detection using magnetic resonance imaging<sup>1,4</sup>. Additionally, an autoimmune mechanism<sup>25</sup> and hypothalamic regulatory dysfunction<sup>1,8</sup> could be involved in some cases. Last, familial idiopathic hyperprolactinemia is a very rare condition that may result from abnormalities of the PRL gene, the secretion of biologically inactive forms of PRL, or PRL insensitivity due to a mutation of the PRL receptor gene<sup>26</sup>.

The prevalence of idiopathic hyperprolactinemia and macroprolactinemia is not established in

the literature. In a Brazilian cohort of 115 hyperprolactinemic patients, 8 (7%) were classified with idiopathic hyperprolactinemia<sup>17</sup>. In two large European studies, 10%<sup>27</sup> and 29%<sup>28</sup> of patients with hyperprolactinemia had idiopathic hyperprolactinemia. Macroprolactinemia prevalence ranged around 18.5% when samples from reference laboratories were assayed<sup>1,29,30</sup>. A lower prevalence (10% to 26.1%) was observed in patients from four endocrinology departments<sup>11-17</sup>. Moreover, a prospective study diagnosed macroprolactinemia in 19 of 115 (16.5 %) consecutive patients with hyperprolactinemia<sup>17</sup>.

Although most patients with macroprolactinemia presented PRL levels under 100 ng/mL<sup>1,10-16</sup>, results vary and may reach 404 ng/mL or more<sup>1,10,13-15</sup>. In the present and previous studies<sup>10,12,16</sup>, mean baseline PRL levels were similar in patients with idiopathic hyperprolactinemia or macroprolactinemia. Therefore, patients may not be distinguished based on clinical criteria and increased PRL levels, indicating a need for a mandatory routine screening for macroprolactin in patients with apparent idiopathic hyperprolactinemia.

Dopamine agonists, particularly cabergoline, are the choice treatment for idiopathic hyperprolactinemia and prolactinomas<sup>2,3</sup>, although macroprolactinemia does not need to be treated<sup>2,11,15</sup>. In the present study, 22 macroprolactinemia patients (26.8%) were misdiagnosed, and 15 (68.2%) submitted to long-term cabergoline therapy. The rate of PRL normalization was lower in patients with macroprolactinemia compared with those with monomeric hyperprolactinemia (40.0 vs 81.4%,  $p = 0.02$ ), corroborating other studies<sup>11</sup>.

In conclusion, our findings demonstrated that macroprolactinemia is often observed in patients with an apparent idiopathic hyperprolactinemia. Thus, this study highlights the importance of routine screening for macroprolactin in all patients with idiopathic hyperprolactinemia to avoid misdiagnosis and unnecessary treatment with dopamine agonists, regardless of their clinical characteristics.

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# CARDIOSPERMUM CORINDUM L. (SAPINDACEAE) HAS GASTROPROTECTIVE AND ANTISPASMODIC EFFECTS IN RODENT MODEL

CARDIOSPERMUM CORINDUM L. (SAPINDACEAE) TEM EFEITO PROTETOR GÁSTRICO E ANTIESPASMÓDICO EM MODELO DE ROEDORES

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## ABSTRACT

**Objectives:** To investigate the effects of the hydroethanolic extract of aerial parts of *Cardiospermum corindum* (Cc-EtOH) in the ethanol-induced gastric ulcer assay in rats, its oral toxicity in mice, and its antispasmodic activity in isolated rat ileum *in vitro*. **Methods:** The anti-ulcerative activity of Cc-EtOH was evaluated in ethanol-induced rat gastric lesions. Oral toxicity was assessed in mice following a single acute treatment and monitored for 14 days. The antiespasmotic effect of Cc-EtOH in isolated rat ileum was analyzed *in vitro*. **Results:** Ethanol-induced gastric lesions in rats (ulcer index =  $367.5 \pm 89.3$  mm<sup>2</sup>) were prevented by 50, 150, and 500 mg/kg Cc-EtOH (ulcer index =  $210.0 \pm 55.8$ ,  $119.2 \pm 39.3$ , and  $47.7 \pm 13.2$  mm<sup>2</sup>, respectively), with efficacy comparable to omeprazole. Histological findings corroborated these results. A single oral dose of 2 g/kg Cc-EtOH induced transient sedation in mice after 60 min (n = 5), which was reversed within 30 min. No acute toxicity was observed, as evidenced by the absence of animal mortality, changes in body weight, or alterations in water or food intake over 14 days. Cc-EtOH reduced *in vitro* phasic contractions of isolated rat ileum elicited by carbachol or KCl (IC<sub>50</sub> =  $236 \pm 59$  and  $201 \pm 43$  mg/mL, respectively). **Conclusion:** The aerial parts of *C. corindum* contain bioactive compounds that exert effective gastric protection in rats, show no evidence of acute toxicity, and display antispasmodic effect *in vitro*.

**Keywords:** Medicinal plant; Plant extract; Anti-ulcer Agent; Antispasmodic effect; Toxicity

## RESUMO

**Objetivos:** Investigar os efeitos do extrato de etanol bruto obtido das partes aéreas *C. corindum* (Cc-EtOH) sobre o teste de úlcera gástrica induzido pelo etanol em ratos, sua toxicidade aguda oral em camundongos e sua atividade antiespasmódica em íleo isolado de rato. **Métodos:** O Cc-EtOH foi avaliado em lesões gástricas induzidas por etanol. Para verificar a segurança deste extrato *in vivo*, o teste de toxicidade aguda foi realizado durante 14 dias em camundongos. Finalmente, os efeitos do extrato no íleo do rato foram analisados. **Resultados:** O extrato Cc-EtOH (50, 150 e 500 mg/kg) protegeu significativamente a camada de mucosa gástrica do rato (área da úlcera =  $210,0 \pm 55,8$ ;  $119,2 \pm 39,3$  e  $47,7 \pm 13,2$  mm<sup>2</sup>, respectivamente) das lesões induzidas pelo etanol (área da úlcera =  $367,5 \pm 89,3$  mm<sup>2</sup>), tão efetivamente como omeprazol. As análises histológicas também corroboraram seu efeito protetor. Além disso, tratamento de 60 minutos com uma dose única de 2g/kg v.o., o extrato de Cc-EtOH promoveu a sedação dos camundongos (n = 5), que se reverteu após 30 minutos, sem causar nem a morte do animal, nem a massa corporal, a ingestão de água, nem as alterações da alimentação, durante 14 dias, mostrando não toxicidade aguda. O efeito antiespasmódico do extrato Cc-EtOH foi evidenciado no componente fásico das contrações induzidas por CCh e KCl (IC<sub>50</sub> =  $236 \pm 59$  e  $201 \pm 43$  mg/mL, respectivamente) em íleo isolado do rato. **Conclusão:** As partes aéreas do *C. corindum* contêm compostos químicos que são capazes de promover proteção gástrica efetiva em ratos, na ausência de qualquer toxicidade aguda, combinada com o efeito antiespasmódico *in vitro*.

**Palavras-chave:** Planta medicinal; Extrato vegetal; Agente anti-úlcera; Efeito antiespasmódico; Toxicidade

## INTRODUCTION

Gastric hyperacidity and gastroduodenal ulcers are frequent conditions that currently represent a major worldwide public health concern<sup>1</sup>. *Cardiospermum corindum* L. (*Sapindaceae*), popularly known as *balãozinho*, occurs in the northeastern, southeastern, and southern regions of Brazil<sup>2</sup>. In traditional medicine, particularly in the Brazilian northeast, infusions prepared from *C. corindum* are used to treat liver disorders and rheumatism, as a memory tonic, diuretic, and emmenagogue<sup>3</sup>. Several compounds have been isolated and chemically identified from the leaves and other aerial parts of *C. corindum*<sup>4,5</sup>. Despite its widespread folk use for stomach ailments, the biological activity of its compounds has not yet been scientifically described.

The present study aimed to investigate the effects of the hydroethanolic extract obtained from the aerial parts of *C. corindum* on ethanol-induced gastric ulcers in rats, its acute toxicity in mice, and its antispasmodic activity in isolated rat ileum.

## METHODS

The aerial parts of *Cardiospermum corindum* L. were collected during the flowering period at the base of Pico do Jabre, Paraíba, Brazil. The plant was identified, and a voucher specimen (No. M.F. Agra et al. 6898) was deposited in the Prof. Lauro Pires Xavier herbarium at Universidade Federal da Paraíba. The crude hydroethanolic extract (Cc-EtOH) was prepared according to previous report<sup>5</sup>.

The Cc-EtOH extract was dissolved in Tween-20 (0.32 mg/mL) and diluted in distilled water to final doses. Wistar rats (200 - 300 g) were stratified into six groups (n = 5) and pretreated with 50, 150, 250, or 500 mg/kg Cc-EtOH extract (gavage), 4 mg/kg omeprazole (intraperitoneal), or vehicle (distilled water-Tween-20, 10 mL/kg). One hour later, 1 mL of absolute ethanol was orally administered to each animal. After one hour, animals were euthanized in a CO<sub>2</sub> chamber, and their stomachs were collected and dissected along the greater curvature<sup>6</sup>. The ulcer index (UI) was assessed by quantifying the extent of erosion and experimental gastric lesions<sup>7</sup>. Samples were processed for histological analysis and stained with hematoxylin and eosin. This protocol was approved by the ethics committee on animal use of Universidade Nove de Julho (opinion AN 0002/11).

Swiss male mice (25 - 30 g) were divided into two groups (n = 5) and orally treated with either a single dose of 2 g/kg Cc-EtOH extract ("treated-group") or vehicle (10 mL/kg distilled water-Tween-20; "control group"). Animals were observed for 120 min at 30 min intervals to assess toxicity signs and motor activity (spaces roamed [S]). Reflexes (grooming or piloerection) were assessed after 24 h. Mortality, body weight, and water and food intake were concurrently monitored for 14 days. At the end of this period, animals were euthanized in a CO<sub>2</sub> chamber, and the heart, lung, liver, and kidney of animals were dissected and weighed (normalized to body weight<sup>9</sup>), and processed for hematoxylin-eosin histological analysis. Histopathological images were obtained using a camera-equipped microscope and analyzed with NS-Elements D software. This study was approved by the ethics committee on animal use of Universidade Nove de Julho (opinion # AN 0003/11).

Fasting (18 h) Wistar rats (250 - 350g) were decapitated, and the ileum was carefully isolated and dissected<sup>8</sup>. Tissue strips (1.5 cm) were mounted in organ baths containing 5 mL of modified Krebs-Henseleit solution at 37 °C with 11.0 mM glucose, and continuously aerated with O<sub>2</sub><sup>10</sup>. Strips were connected to a force transducer and amplifier, and contraction data were recorded using AQCD software. A Cc-EtOH stock solution (10 mg/mL) was prepared in 0.1% cremophor and diluted in Mili-Q water. After 30 min of equilibration period, strips were contracted with 1 μM carbachol (CCh) or 40 mM KCl, following 15 min of incubation with Cc-EtOH (27-730 μg/mL) or vehicle. Contractile responses to CCh or KCl were compared in the absence and presence of Cc-EtOH extract. The IC<sub>50</sub> of the Cc-EtOH extract in CCh- or KCl-induced contraction were calculated by non-linear regression<sup>11</sup>. This protocol was approved by the ethics committee on animal use of the Universidade Federal de São Paulo (opinion number 4295060514/14).

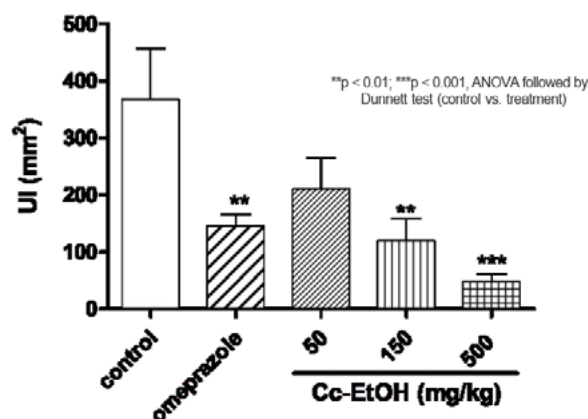
Results were expressed as mean ± SEM. Student T-test or one-way ANOVA test followed by post-hoc Dunnett test for multiple comparisons were used when applicable. Differences were considered significant at p < 0.05.

## RESULTS

Oral administration of ethanol induced stomach lesions (UI = 368 ± 89 mm<sup>2</sup>; Figure 1). Pretreat-

ment with 50 mg/kg Cc-EtOH extract (UI =  $210.0 \pm 55.8$  mm<sup>2</sup>) did not prevent the ethanol-induced lesions compared with the control group. However, treatments with 150 and 500 mg/kg Cc-EtOH pre-

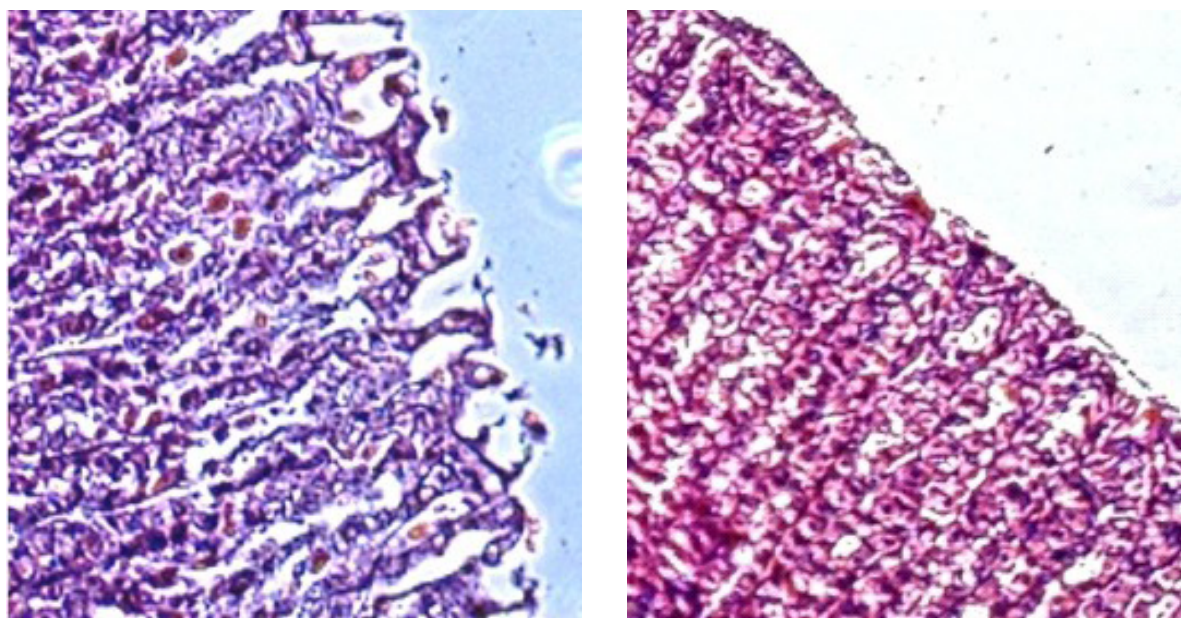
vented ethanol-induced lesions in a dose-dependent manner (UI =  $119 \pm 39$  and  $48 \pm 13$  mm<sup>2</sup>, respectively), similar to the effect observed with 20 mg/kg omeprazole (UI =  $146 \pm 20$  mm<sup>2</sup>).



**Figure 1.** Ethanol-induced lesions (control) in the presence of omeprazole (20 mg/kg) or Cc-EtOH extract (50, 150, and 500 mg/kg) on rat stomachs (n = 6).

Histological analysis confirmed epithelial damage and inflammatory infiltration in the control group (Figure 2A), consistent with the characteristic mucosal injury in the ethanol-induced ulcer lesion model. However, the single-dose treatment with 500 mg/kg Cc-EtOH extract prevented ethanol-induced gastric lesions (Figure 2B). Pretreatment also attenuated the inflammatory response, suggesting regeneration and re-epithelization of the gastric mucosa.

In subsequent experiments, oral administration of 2 g/kg Cc-EtOH extract did not induce mortality or changed body weight, water or food intake (data not shown). However, treated animals showed significantly reduced ambulation between 30 and 60 min after treatment ( $S = 47.8 \pm 4.4$  and  $34.4 \pm 3.1$  units, respectively) compared with the control group (Figure 3). Normalized organ weights are presented in Table 1.

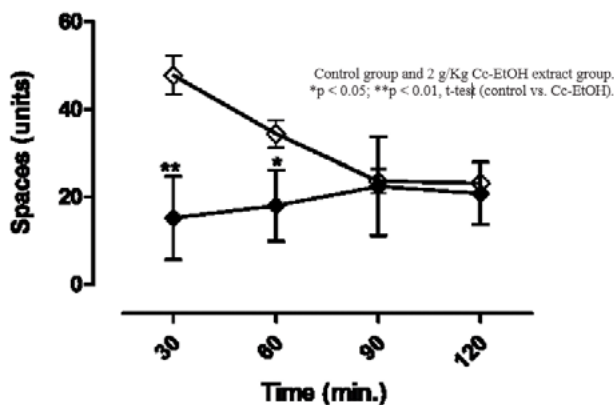


**Figure 2.** Effects of Cc-EtOH on ethanol-induced rat gastric lesions stained with hematoxylin and eosin. Panel A shows a photomicrograph (100 x) of epithelial lesion and inflammatory cell infiltration in the gastric mucosa after oral administration of ethanol. Panel B shows the effect of pretreatment with 500 mg/kg Cc-EtOH extract, preventing the instauration of epithelial lesions or inflammatory infiltration in the gastric mucosa.

**Table 1.** Weight of the indicated organs isolated from mice treated or not (control) with Cc-EtOH extract.

Treatment	Weight ± SEM (mg/g)			
	Liver	Heart	Lung	Kidney
Control	7.7 ± 0.7	0.9 ± 0.1	1.9 ± 0.1	2.2 ± 0.1
Cc-EtOH	6.5 ± 0.3	0.6 ± 0.1*	1.0 ± 0.2**	2.0 ± 0.1

Data are presented as mean ± SEM. (n = 5, t-test \*p < 0.05; \*\*p < 0.01)

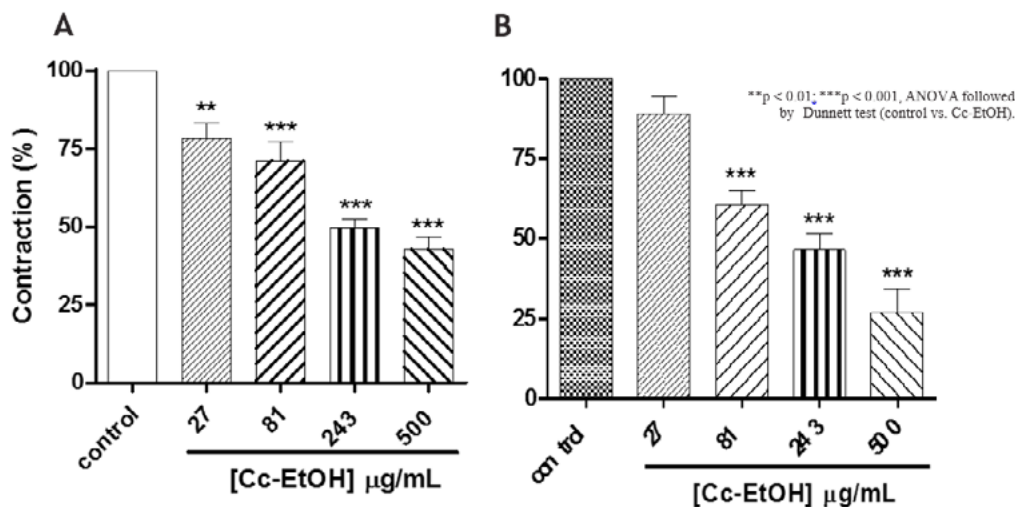


**Figure 3.** Effect of Cc-EtOH extract on mice ambulation from 30 min to 120 min of Cc-EtOH treatments (n = 5).

No significant changes were observed in liver or kidney weights, whereas heart and lung weights were reduced in treated animals compared with control group.

Preincubation with Cc-EtOH extract equipo-

tently antagonized the CCh- and KCl-induced phasic contractions (Figure 4A and B, respectively). No significant differences were observed between the calculated IC<sub>50</sub> for the Cc-EtOH extract in CCh-induced contraction (236 ± 59 µg/mL) and KCl-induced contractions (201 ± 43 µg/mL).



**Figure 4.** Effects of Cc-EtOH extract on phasic contractions induced by 1 µM CCh (panel A) or 40 mM KCl (panel B) of rat isolated ileum (n = 4).

**DISCUSSION**

The Cc-EtOH extract exhibited anti-ulcer activity in rats, showed no acute toxicity in mice, and presented antispasmodic effects in isolated rat ileum *in vitro*.

Considering the traditional use of *C. corindum* (*balãozinho*) in Bahia, Brazil, for its anti-ulcerative properties, we investigated its activity using an

ethanol-induced stomach ulcer model in rats<sup>8</sup>. The Cc-EtOH extract protected the gastric mucosa from ethanol-induced lesions with efficacy comparable to omeprazole, a proton pump inhibitor (Figure 1). This protective effect is consistent with previous findings in *C. halicacabum*<sup>11</sup> and *Serjania caracasana*, two other *Sapindaceae* species<sup>13</sup>. Thus, the anti-ulcer properties of *C. corindum* may be associated with

its chemical composition, including triterpenes, flavonoids, and steroids<sup>4,5</sup>, also reported in related species<sup>13</sup>.

No toxicological data were previously available for *C. corundum*, underscoring the need for *in vivo* assays. In the present study, acute oral toxicity of Cc-EtOH extract was investigated in mice, an appropriate model for initial toxicity screening<sup>14</sup>. No toxicity was detected, as no mortality or tissue damage was observed during the 14-day evaluation period. However, transient sedative effects were evidenced by decreased locomotor activity (Figure 3), consistent with earlier reports of central nervous system effects of this plant<sup>15</sup>. Nevertheless, this reduction in ambulation was limited to the first 60 min following oral administration. Organ weight analysis revealed decreased heart and lung weights (Table 1), although no histological alterations were observed. While the physiological relevance of these evidence remains unclear, the absence of morphological changes supports the safety of a single 2 g/kg oral dose of Cc-EtOH extract. Notably, this dose was four-fold higher than the effective anti-ulcer dose (500 mg/kg; Figure 1) and did elicit putative toxicity.

Further investigation in the gastrointestinal tract demonstrated that Cc-EtOH extract inhibited CCh- or KCl-induced phasic contractions in isolated ileum strips *in vitro* with similar potency, suggesting effects on two distinct transduction pathways involved in intestinal contraction. These contractile responses, whether pharmaco-mechanical or electromechanical couplings rely on Ca<sup>2+</sup> influx through voltage-dependent Ca<sup>2+</sup>-channels<sup>16</sup>.

The observed *in vivo* gastroprotective may, at least in part, rely on the antispasmodic proprieties of Cc-EtOH extract *in vitro*, similar to agents such as atropine (i.e., reducing gastrointestinal motility) and prostaglandins (i.e., protecting gastric mucosa)<sup>17</sup>.

In conclusion, Cc-EtOH extract promoted gastric protection in rats and antispasmodic effects *in vitro*, without evidence of acute toxicity. Together, these findings strongly support the traditional use of *balãozinho* in folk medicine for the treatment of gastric ulcers.

## CONFLICTS OF INTEREST

Nothing to declare.

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## **ORIGINAL ARTICLE**

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# STATE OF ACADEMIC HONESTY REGARDING UNAUTHORIZED ACQUISITION OF ASSESSMENT ANSWERS AMONG MEDICAL STUDENTS

ESTADO DE HONESTIDADE ACADÊMICA PELA OBTENÇÃO NÃO AUTORIZADA DE RESPOSTAS AVALIATIVAS ENTRE ESTUDANTES DE MEDICINA

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## ABSTRACT

**Introduction:** The evaluation of the ethical and moral behavior of individuals in the teaching-learning process is a problem that needs to be investigated. The purpose was to evaluate the status of academic honesty, with reference to the use of the cheat, among students of different levels in medical graduation. **Methods:** The prospective, observational, cross-sectional, and analytical study was conducted at the Olinda Medical School (FMO), including undergraduate students, of both genders and all ages who, randomly, answered a questionnaire about aspects involved in cheat practice. The study was approved by the Human Research Ethics Committee. The quantitative variables were expressed by their means and standard deviations and the qualitative ones, by their absolute and relative frequencies. The Chi-square test was used to evaluate associations. The value of  $p < 0.05$  was considered for rejection of the null hypothesis. **Results:** A total of 147 students from the second, third and fourth periods were evaluated, being 53% males, with a mean age of  $24.2 \pm 5.6$  years. Thirty-five (23.8%), 39 (26.5%) and 73 (49.7%) were second, third and fourth periods, respectively. It was observed a greater representativeness of the knowledge lack about the concepts of cheat practice in the students of the third period ( $p=0.0146$ ) and the academic honesty state was significantly lower among the students of the second period ( $p=0.0172$ ). **Conclusion:** There was persistence of dishonest academic practices throughout the student training in the health information acquisition and ignorance of ethical and moral concepts.

**Keywords:** Culture; Behavior; Ethics; Medical students

## RESUMO

**Introdução:** A avaliação do comportamento ético e moral de indivíduos no processo ensino-aprendizagem é um problema que suscita investigações. A proposta do estudo foi avaliar o estado da honestidade acadêmica, com referência à utilização da “cola”, entre alunos de diferentes níveis na graduação em Medicina. **Métodos:** O estudo prospectivo, observacional, transversal e analítico foi realizado na Faculdade de Medicina de Olinda (FMO), incluindo os graduandos do curso de Medicina da FMO, de ambos os gêneros e todas as idades que, de forma aleatória, responderam a um questionário sobre aspectos envolvidos na prática da “cola”. O estudo foi aprovado pelo Comitê de Ética de Pesquisa em Seres Humanos. As variáveis quantitativas foram expressas por suas médias e desvios-padrão e as qualitativas, por suas frequências absolutas e relativas. Foi utilizado o teste do Qui-quadrado para avaliação de associações. Foi considerado o valor de  $p < 0,05$  para rejeição da hipótese de nulidade. **Resultados:** Foram avaliados 147 alunos do segundo, terceiro e quarto períodos, com 53% do gênero masculino, com média das idades de  $24,2 \pm 5,6$ . Onde 35 (23,8%), 39 (26,5%) e 73 (49,7%) eram dos segundos, terceiros e quartos períodos, respectivamente. Foi observada maior representatividade do desconhecimento sobre conceitos éticos e morais da prática da cola nos alunos do terceiro período ( $p = 0,0146$ ) e o estado de honestidade acadêmica foi significativamente menor entre os alunos do segundo período ( $p = 0,0172$ ). **Conclusão:** Existe persistência de práticas acadêmicas desonestas ao longo da formação de estudantes na área da saúde e desconhecimento de conceitos éticos e morais de forma significativa.

**Palavras-chave:** Cultura; Comportamento; Ética; Estudantes de medicina

## INTRODUCTION

Academic dishonesty practices among university students, such as unauthorized access to exam answers or “cheating”, raise several reflections<sup>1</sup>. Its complexity is discussed by educators, who consider it to be frequent and cultural not only in Brazil but worldwide<sup>2-4</sup>. Academic behavior was associated with an impact on professional life in several areas of knowledge<sup>5-8</sup>. The damaging consequences of these behaviors among medical students include impacts on decisions and actions regarding human health, and may extend to medical residency and professional practice<sup>7-9</sup>. A lack of knowledge about ethics or morals in dishonest student practices demands investigations in Brazil, and above all, actions that can assess academic honesty as a characteristic of an ethical construct<sup>10</sup>. Thus, a lack of integrity can have repercussions on professional life<sup>11-14</sup>. This study aimed to evaluate the state of academic honesty, regarding the use of “cheating,” among students at

different levels of a medical school.

## METHODS

This prospective, observational, cross-sectional, and analytical study was conducted at the Faculdade de Medicina de Olinda (FMO). Undergraduate medical students of both genders and all ages randomly responded to a questionnaire on aspects involved in the practice of “cheating”. The only information registered about the participants was their current semester in medical school; those who did not respond adequately to the questions were excluded.

A questionnaire concerning the general understanding of the practice of “cheating” (Figure 1) was applied individually. A score was assigned to each answer of the questionnaire, which was omitted from the participants<sup>1</sup>. This score allowed for the leveling of the categories discriminated in Chart 1.

## QUESTIONNAIRE

PERÍODO FIRST ( ) SECOND ( ) THIRD ( ) FOURTH ( )

AGE YEARS OLD

GENDER M ( ) F ( )

A. WHAT IS YOUR OPINION ON THE “CHEATING” PRACTICE? ARE YOU FOR OR AGAINST IT?

1. ( ) DEFINITELY IN FAVOR. 00
2. ( ) IN FAVOR, BUT... 05
3. ( ) IMPOSSIBLE TO DECIDE FOR OR AGAINST IT. 10
4. ( ) AGAINST, HOWEVER. 15
5. ( ) UNQUESTIONABLY AGAINST. 20

B. “CHEATING” IS:

1. ( ) AMORAL 15
2. ( ) UNETHICAL 15
3. ( ) MORAL 00
4. ( ) ETHICAL 00
5. ( ) AMORAL E UNETHICAL 20

C. HAVE YOU EVER BEEN THE TARGET OR AGENT OF REQUESTS FOR “CHEATING”? (IF YES, ANSWER FROM D TO F).

1. ( ) YES 00
2. ( ) NO 10

D. FREQUENCY:		
1. ( ) RARE		20
2. ( ) FREQUENT		10
3. ( ) ALWAYS		00
E. INTIMACY DEGREE:		
1. ( ) UNKOWN	05	
2. ( ) FRIEND		00
3. ( ) BOTH		05
F. ANXIETY AND DAMAGE DEGREE:		
1. ( ) LOW		00
2. ( ) HIGH		10
3. ( ) VERY HIGH		20

Figure 1. "Cheating" practice questionnaire

Chart 1. Academic honesty score among undergraduate students in the FMO medical program.

Category	Score	Representation
1	41 a 100	Strong and moderate academic honesty
2	1 a 40	Poor academic integrity and academic dishonesty

Table 1. Knowledge about the ethical and moral concepts of "cheating" among students in the second, third, and fourth semesters of the FMO.

	Cheating Unethical practice		Cheating Ethical practice		Subtotal	Subtotal
	n	%	n	%		%
second semester	34	97.1	1	2.8	35	23.8
third semester	32	82.0	7	17.9	39	26.5
fourth semester	70	95.8	3	4.1	73	49.7
Subtotal	136		11			

N = absolute frequency X<sup>2</sup> = 8.452 – df = 2 (p = 0.0146)

Table 2. Academic honesty levels among students in the second, third, and fourth semesters of the FMO.

	Strong and moderate academic honesty		Poor academic integrity and academic dishonesty		Subtotal	Total (%)
	n	%	n	%		
second semester	22	62.8	13	37.1	35	23.8
third semester	34	87.1	5	12.8	39	26.5
fourth semester	61	83.5	12	16.4	73	49.7
Subtotal	117	30				

N = absolute frequency X<sup>2</sup> = 8.125- df = 2 (p = 0.0172)

The sample considered only students present in the classrooms during data collection. Quantitative variables were expressed by means and standard deviations, and qualitative variables by absolute and relative frequencies. The Chi-Square test ( $\chi^2$ ) was used to verify differences in frequencies between qualitative variables. Statistical significance was set at  $p < 0.05$ .

The study was approved by the research ethics committee of the FMO, and all participants provided a written consent form that ensured no penalties or risks of exposure.

## RESULTS

A total of 147 students from the second, third, and fourth semesters were evaluated, with 53% being male, with a mean age of  $24.2 \pm 5.6$  years. The number of participants was significantly different between semesters ( $p = 0.02$ ), with 35 (23.8%), 39 (26.5%), and 73 (49.7%) participants from the second, third, and fourth semesters, respectively.

A greater ignorance about the concepts of cheating was observed among students in the third semester, and a significantly lower level of academic honesty was registered for students in the second semester (Tables 1 and 2). Only one participant (0.6%) reported never having asked for or offered to “cheat”. The difference in frequencies regarding the degree of intimacy between participants in different semesters was not significant ( $p = 0.58$ ). However, the degree of anxiety was significant, with the fourth semester obtaining a high level of anxiety in the score when “cheating” ( $p = 0.03$ ).

## DISCUSSION

Behavioral questions about ethics and morals are increasingly becoming contemporary dilemmas in all areas of human existence. Academic training of health students, based on respectful foundations, such as the acquisition of scientific knowledge and its practical application, should be prioritized<sup>15</sup>. Physicians are expected to develop attributes beyond technical boundaries, performing actions that require emotional intelligence and universal ethical behaviors in line with established and agreed-upon morals.

This study provided reflective data for educators by transparently listing, in the early stages of the undergraduate course, concerns about the integrity of the ethical, moral, and humanistic academic train-

ing for the future profession. It is true that “one cannot teach ethics,” but one can provide moral support for its development.

Referring to obtaining unauthorized answers, “cheating” is an amoral academic practice, since it contradicts the rules of most educational institutions. In this study, the high frequency of the answer “Against, however.” concerning “cheating” expresses that the practice is inadequate but it may be justified. The lack of time to study the vast amount of content and the requirement to obtain minimum performance coefficients to progress in the course were exemplified, as seen in other studies<sup>5,7</sup>.

Participants were unaware of the moral and ethical concept of “cheating” based on institutional rules; the unethical concept was more frequent, and was not considered amoral. Additionally, these answers highlight a historical misunderstanding of the ethical and moral terms, as they are considered synonyms in many situations<sup>16</sup>. This complex conceptual confusion may contribute to the violation of rules, amorality, and the deconstruction of voluntary human acts of respect, freedom, care, limits, and actions with consequences. This confusion is combined with abominable modern attitudes that may seem, at first, to have no repercussions and should be banned from academic training.

Most academics responded positively to the act of “cheating,” corroborating other studies<sup>6</sup>. The degree of intimacy between people in the act of “cheating” had no significant association with the semesters. This result may be implicated in future professional corporatism for fraudulent acts. Significant levels of anxiety occurred in students in the more advanced semester, which may imply more conscious attitudes. Although the study has sample limitations, the comparisons between the semesters were significant.

## CONCLUSION

The state of academic honesty at a moderate level was the most frequent among students in the second semester of the FMO.

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# PROFILE OF POSTPARTUM ADOLESCENTS AND THEIR NEWBORNS ATTENDED AT THE REFERENCE MATERNITY IN ABREU E LIMA, PERNAMBUCO

*PERFIL DAS PUÉRPERAS ADOLESCENTES E SEUS CONCEPTOS ATENDIDOS NA MATERNIDADE DE REFERÊNCIA EM ABREU E LIMA, PERNAMBUCO*

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## ABSTRACT

**Purpose:** To describe the characteristics of adolescent mothers and their concepts attended in public maternity in Abreu e Lima - Pernambuco. **Methods:** Exploratory and analytical study. The sample was census in the year 2017. The parameters of the quantitative variables were expressed by their means and standard deviations and median. The parameters of the qualitative variables were expressed by their frequencies. T-test was used to verify differences between means. The correlation test was used between the parameters of the maternal and newborn variables.  $p \leq 0.05$  was considered for rejection of the null hypothesis. The project was approved by the Human Research Ethics Committee. **Results:** The mean age of pregnant adolescents was  $17.3 \pm 1.4$  years. There was a predominance of the: brown color, condition of being single and domestic. Seventy-six (23.5%) had leukorrhea, 13 (4.0%) were serological positive for syphilis and five (1.5%) had systemic arterial hypertension. The mean gestational age of these adolescents at the end of gestation was  $39.2 \pm 1.5$  weeks. The majority of the concepts was sent to the joint accommodation. There was no correlation between the characteristics of pregnant women and their concepts. **Conclusions:** The profile of pregnant adolescents enrolled in the investigation was 12 to 19 year old, with a predominance of 15 to 19 year old, mostly single, low schooling, brown, with a high prevalence of leukorrhea and syphilis. No relationship was found between the characteristics of adolescents and characteristics of their concepts.

**Keywords:** Teenage pregnancy. Adolescent health. Newborn. Pernambuco. Brazil

## RESUMO

**Objetivo:** Descrever as características das mães adolescentes e seus conceitos atendidos em maternidade pública de Abreu e Lima, em Pernambuco. **Métodos:** Estudo analítico. A amostra foi censitária no ano de 2017. Os parâmetros das variáveis quantitativas foram expressos por suas médias, desvios-padrão e medianas. Os parâmetros das variáveis qualitativas foram expressos por suas frequências. Foram utilizados teste para verificação de diferenças entre médias e teste de correlação entre os parâmetros das variáveis maternas e dos recém-nascidos. Foi considerado  $p \leq 0,05$  para rejeição da hipótese de nulidade. O projeto foi aprovado pelo Comitê de Ética de Pesquisa em Seres Humanos. **Resultados:** A média das idades das adolescentes gestantes foi de  $17,3 \pm 1,4$  anos. Houve predomínio da cor parda, do estado civil solteira e da condição de ser “do lar”. Setenta e seis delas (23,5%) apresentavam leucorreia, 13 (4,0%) eram portadoras sorológicas de sífilis e 5 (1,5%) apresentavam hipertensão arterial sistêmica. A média das idades gestacionais dessas adolescentes no término da gestação foi de  $39,2 \pm 1,5$  semanas. A maioria dos conceitos foi encaminhada para o alojamento conjunto. Não foi observada correlação entre as características das gestantes e dos seus conceitos. **Conclusões:** O perfil das adolescentes grávidas atendidas é de jovens de 12 a 19 anos, predominantemente as de 15 a 19 anos, na sua maioria solteira, baixa escolaridade, parda, do lar, com prevalência importante de leucorreia e sífilis. Não foi observada relação entre as características das adolescentes e as dos seus conceitos.

**Palavras-Chave:** Gravidez na adolescência; Saúde da adolescente; Recém-nascido; Pernambuco

## INTRODUCTION

Adolescent pregnancy occurs abruptly, is often unexpected, modifies the family environment<sup>1,2</sup>, and is most observed among less educated and poorer populations<sup>3</sup>. These young women face conflicts and need global and compassionate understanding. Concerning family structure and social context, the challenges involved with pregnancy in adolescence are not commonly considered<sup>4</sup>.

In Brazil, the prevalence of pregnancy among adolescents is about 19%, despite educational campaigns designed with clear and accessible language to enhance reproductive health. However, family stressors, limited opportunities, low educational level, inadequate use of contraceptive methods, and significant hormonal changes often drive young women to seek independence, which may manifest in the pursuit of consensual partners, culminating in early pregnancy<sup>2,5-16</sup>.

Recurrent pregnancy generates problems that may affect the mother and newborn, including increased morbidity, mortality, and hinder the entry of the adolescent into the job market<sup>3</sup>. Furthermore, the shorter stature of adolescents from socioeconomically disadvantaged settings is associated with lower mean height in newborns. Conversely, newborns from adolescents in less structured societies experience a greater impact on their health status<sup>7</sup>.

The influence of maternal age and related anthropometric and socioeconomic factors has been studied. However, the relationship between maternal age-related variables and neonatal outcomes (e.g., prematurity, low birth weight, and Apgar scores) has not been frequently investigated in Brazilian adolescent mothers<sup>6</sup>.

This study aimed to describe the characteristics of postpartum adolescents and their newborns receiving care at a public referral maternity hospital in the city of Abreu e Lima, Pernambuco.

## METHODS

The present study is an exploratory study, conducted at the public referral maternity hospital in the city of Abreu e Lima, Pernambuco, and at the Faculdade de Medicina de Olinda. The study included postpartum adolescents with normal-risk pregnancies who delivered at this facility. Those unable to complete the required data for additional analysis were excluded.

The postpartum adolescents were allocated into group I (12 to 14 years) and group II (15 to 19 years). The participants were assessed regarding ethnicity, marital status, occupation, comorbidities (systemic arterial hypertension, diabetes mellitus, sexually transmitted infections, and physical or psychological violence), and type of delivery. For the newborns, the following variables were recorded: birth weight, length, gestational age, Apgar score, head circumference, and hospital outcomes. All data (mothers and newborns) constituted the analytical component of the study.

The sample was census-based for the year 2017. Quantitative variables were expressed as means, standard deviations, and medians. Qualitative variables were expressed as absolute and relative frequencies. Student's t-test was used to verify differences between means. Pearson's correlation coefficient was used to analyze relationships between maternal and neonatal variables. A significance level of  $p \leq 0.05$  was adopted for rejection of the null hypothesis.

The study was approved by the research ethics committee on human subjects and authorized by the director of the public maternity hospital in Abreu e Lima, Pernambuco, and by the General Director of the Faculdade de Medicina de Olinda.

## RESULTS

In 2017, 1,492 pregnant women were admitted to the maternity unit where the study was conducted; 361 (24.2%) were aged between 12 and 19 years, 1,002 were between 20 and 34 years, and 139 were 35 or older. Of the 361 pregnant adolescents, 324 were eligible for inclusion in the study. Reasons for exclusion included complete or incomplete miscarriage ( $n = 23$ ), presence of cystocele ( $n = 1$ ), myomectomy procedure ( $n = 1$ ), and incomplete medical records ( $n = 12$ ).

Table 1 presents the absolute and relative frequencies of maternal sociodemographic characteristics. The mean gestational age at delivery among the adolescents was  $39.2 \pm 1.5$  weeks, with a median of 39 weeks and a range from 30 to 42 weeks. The data did not meet the criteria for normality.

Table 2 presents the mean birth weights, lengths, head circumferences, Apgar scores (at one and five minutes), and neonatal outcomes.

The mean birth weight of newborns in group I was  $3.134 \pm 0.442$  kg, and in group II was  $3.260 \pm$

0.397 kg ( $p = 0.2466$ ).

No strong correlations were observed between maternal age, marital status, comorbidities, and gestational age with the neonatal birth weight ( $r = 0.09$ ;  $r = 0.06$ ;  $r = 0.01$ ;  $r = 0.01$ ; and  $r = 0.28$ , respectively), neonatal length ( $r = 0.08$ ;  $r = 0.02$ ;  $r = 0.08$ ;  $r = 0.02$ ; and  $r = 0.28$ , respectively) or head circumference (maternal age:  $r = 0.10$ ; marital status:  $r = 0.12$ ; comorbidities:  $r = 0.01$ ; gestational age:  $r = 0.023$ , respectively).

## DISCUSSION

The assessment of adolescent characteristics in a small maternity hospital located in the metropolitan area of Recife is relevant because it has not been previously described and may reflect features representative of other localities within this region. However, these findings do not represent the characteristics of postpartum adolescents assisted in the larger maternity hospitals of Recife, which provide care within the Brazilian Unified Health System, because the former do not admit high-risk pregnant adolescents. In this sense, large maternity hospitals, by admitting younger and higher-risk pregnant adolescents, are more likely to generate newborns with lower birth weights, higher comorbidity rates, and increased morbidity and mortality. In Fortaleza<sup>6</sup>, in Northeastern Brazil, this information has not yet been evaluated.

The exclusion of 12 postpartum adolescents due to incomplete medical records may reflect difficulties in completing medical documentation properly within the institution where the study was conducted. The lower frequency of admissions among adolescents aged 13 to 15 years may account for the reduced occurrence of low-birth-weight newborns, small-for-gestational-age infants, and fewer morbidities. Regarding the variable younger maternal age, the proportion was lower than observed in Fortaleza<sup>6</sup>. The mean age of the adolescents included in the present study was similar to that reported in a larger study conducted at a nationally recognized referral institution in the South of Brazil<sup>5,17</sup>. However, in the present study, the representation of brown adolescents with low educational attainment and unemployment was more significant.

A high prevalence of single mothers ( $\pm 95\%$ ) was observed. In Fortaleza, this prevalence corresponds to the combined prevalences of single and consensual unions<sup>6</sup>, information that was not availa-

ble in the medical records of postpartum adolescents from our study.

The prevalence of syphilis among adolescents in this study was considerably higher than the reported prevalence among postpartum women in Brazil<sup>15</sup>, which may be associated with the higher levels of poverty in the Northeast compared with the South and Southeast regions<sup>5,6,10,17</sup>.

The frequency of vaginal delivery was higher than that of other adolescents assisted in Brazil<sup>5,10,17</sup> and abroad<sup>3,9,12,16</sup>, probably because the public health policy promoted by the Brazilian Ministry of Health encourages it.

The absence of a correlation may explain the lack of association between the characteristics of postpartum adolescents and newborns. Also, this finding may be attributed to the limitation of the sample to older adolescents and exclusion of high-risk pregnancies, which might have required admission to a neonatal intensive care unit, an unavailable resource at the institution where the study took place.

**Table 1.** Characteristics of postpartum adolescents attended at the maternity hospital of Abreu e Lima, Pernambuco, 2017.

Variables	Absolute frequency (n)	Relative frequency (%)
<b>Age (years)</b>		
12 to 14	15	4.6
15 to 19	309	95.4
<b>Ethnicity</b>		
White	30	9.3
Brow	290	89.5
Black	4	1.2
<b>Marital status</b>		
Single	308	95.1
Married	12	3.7
Divorced	4	1.2
<b>Occupation</b>		
Housewife	226	69.7
Student	86	26.5
Self-employed	12	3.7
<b>Comorbidities</b>		
Systemic arterial hypertension	5	1.5
leukorrhea	76	23.5
STI- Syphilis	13	4
<b>Type of delivery</b>		
Vaginal delivery	292	90.1
Cesarean section	32	9.9
Forceps-assisted vaginal delivery	1	0.3

Caption: n: number of adolescents.

**Table 2.** Characteristics of adolescent mothers and their newborns at the Abreu e Lima Maternity Hospital – PE, in 2017.

	Mean +/- SD	Median	Variation (minimum/maximum)	Frequency	
				Absolute (n)	Relative (%)
Birth weight (grams)	3,255±399	3,240	1,980 a 4,650		
Length (cm)	48.7±2.0	49	40 a 56		
Head circumference (cm)	34.3±1.3	34	31 a 38		
Apgar					
1° minute	8.3±1.2	9	3 a 10		
5° minute	9.5±0.8	10	5 a 10		
Destination of the NB					
Romming-in				314	96.4
High-risk nursery				10	3.1

Legend: n: number of concepts. RN: newborn.

## CONCLUSION

The profile of postpartum adolescents assisted at the Abreu e Lima Maternity Hospital aged 12 to 19 years, predominantly between 15 and 19 years, mostly single, with low educational level, brown, homemakers, and with an important prevalence of leukorrhea and syphilis. No association was found between the characteristics of postpartum adolescents and their newborns.

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# AXILLARY WEB SYNDROME AND ITS ASSOCIATION WITH LYMPHEDEMA AND RANGE OF MOTION REDUCTION IN WOMEN SUBMITTED TO BREAST CANCER SURGERY: A CROSS-SECTIONAL STUDY

*SÍNDROME DA REDE AXILAR E SUAS ASSOCIAÇÕES COM LINFEDEMA E DÉFICIT DE AMPLITUDE DE MOVIMENTO EM MULHERES SUBMETIDAS À CIRURGIA DO CÂNCER DE MAMA: ESTUDO TRANSVERSAL*

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## ABSTRACT

**Introduction:** Breast cancer is the most frequent neoplasm in Brazilian women and control of post treatment morbidities has stimulated investigations for a better quality of life. **Objectives:** To determine the frequency of axillary web syndrome (AWS) and the association with lymphedema and range of motion (MAD) of the shoulder joint after axillary surgery. **Methods:** Between December 2011 and September 2012, 97 women surgically treated for breast cancer were enrolled at the Cancer Hospital of Pernambuco, Brazil. The search for axillary cords, goniometry of the shoulder joint and perimetry of the ipsilateral and contralateral upper limbs of the affected breast were performed. For comparison between goniometric and perimetric values, Student's t-test and Lévené variance analysis were used. Chi-square and Fisher's exact tests were used to compare proportions. The significance level  $p \leq 0.05$  was adopted. The work was approved by Human Research Ethics Committee. **Results:** AWS was diagnosed in 28 (28.86%) women, of whom 15 (53.57%) had lymphedema. There was a significant reduction in most movements in the ipsilateral limb compared to its contralateral limb. **Conclusions:** There were expressive numbers of women diagnosed with AWS and association with early onset of perimetry changes, in addition to a significant reduction in shoulder range of motion.

**Keywords:** Postoperative complications; Goniometry; Axilla; Lymphadenectomy; Lymphedema

## RESUMO

**Introdução:** O câncer de mama é a neoplasia mais frequente na mulher brasileira, e o controle das morbididades pós-tratamento tem estimulado investigações para melhor qualidade de vida. **Objetivos:** Determinar a frequência da síndrome da rede axilar (SRA) e a associação com linfedema e déficit na amplitude de movimento da articulação do ombro após abordagem cirúrgica da axila. **Métodos:** Entre dezembro de 2011 a setembro de 2012, foram incluídas 97 mulheres tratadas cirurgicamente para câncer de mama no Hospital de Câncer de Pernambuco, Brasil. Foram realizadas busca pelos cordões axilares, goniometria da articulação do ombro e perimetria dos membros superiores ipsilateral e contralateral à mama afetada. Para comparação entre valores goniométricos e perimétricos, usou-se o teste t de Student e análise de variância Levene. Os testes Qui-quadrado e exato de Fisher foram utilizados para comparação de proporções. Adotou-se nível de significância de  $p \leq 0.05$ . O trabalho foi aprovado pelo Comitê de Ética de Pesquisa em Seres Humanos. **Resultados:** SRA foi diagnosticada em 28 (28,86%) mulheres, destas, 15 (53,57%) apresentavam linfedema. Houve redução significativa na maioria das movimentações no membro ipsilateral comparado com o seu contralateral. **Conclusões:** Houve expressivo número de mulheres diagnosticadas com SRA e associação com início precoce de alterações na perimetria, além de redução significativa da amplitude de movimento dos ombros.

**Palavras-chave:** Complicações pós-operatórias; Goniometria. Axila; Linfadenectomia; Linfedema

## INTRODUCTION

Breast cancer is the most frequent neoplasm among women, with an incidence of 55.7 per 100,000 individuals in the United States, 96.0 per 100,000 in Canada, and 52.5 per 100,000 in Brazil<sup>1-3</sup>. Surgical treatment or radiotherapy may cause functional motor deficits, such as reduced range of motion (ROM), pain, lymphedema, seroma, axillary web syndrome (AWS), and intolerance to daily activities<sup>4-6</sup>.

AWS is one of the leading causes of pain after axillary dissection and its characterized by a stretched band underneath the skin, often called cord<sup>7</sup> or lymphedema cord<sup>8</sup>, which may be localized in the medial upper arm and the anterior elbow. The dissection of axillary or sentinel lymph nodes, tissue damage, or cancer itself may cause the AWS<sup>7</sup>.

Many aspects of AWS remain undefined<sup>9</sup> and an adequate guideline for therapeutic interventions is required<sup>10</sup>.

This study aimed to determine the frequency of AWS and the association with lymphedema and reduced ROM of the shoulder joint after axillary surgery.

## METHODS

This analytical study was conducted between December 2011 and July 2012 in the Mastology Department of the Cancer Hospital of Pernambuco, Brazil. Women, aged 18 or older, treated for unila-

teral breast cancer and with two or fewer physical therapy sessions were included. Exclusion criteria comprised cases of recurrent breast cancer, missing medical records, and people with physical trauma or conditions preventing adequate movement of the ipsilateral upper limb. The centimeter staging was performed between the perimeters of the contralateral and ipsilateral limbs; the goniometry measured the maximum angles of the shoulder joints in flexion, extension, adduction, abduction, external rotation, and internal rotation<sup>11</sup>; detection of reduced ROM in shoulder joint, defined as a reduction of 10° or more in the ipsilateral limb compared to the contralateral limb<sup>12-13</sup>; breast laterality; and identification of AWS (presence of palpable cords with the patient seated during abduction, flexion, and external rotation of the ipsilateral shoulder).

The probabilistic sample included 97 patients, assuming an AWS incidence between 6% and 28.1%<sup>8,14,15</sup>.

Student's t-test with Levene's test for variance analysis compared goniometric and perimetric measurements of the ipsilateral and contralateral limbs. Chi-square and Fisher's exact tests were used to compare proportions. Statistical significance was set at  $p \leq 0.05$ .

## RESULTS

Results are presented in Tables 1-4.

**Table 1.** Distribution of tumor- and treatment-related information in 97 women with breast cancer – Cancer Hospital of Pernambuco, Brazil - December 2011 to July 2012.

Variables related to the tumor	AWS (cords)				Total (n=97)		p-value
	present (n = 28)		absent (n = 69)				
	n	%	n	%	n	%	
Breast laterality							0.701 <sup>†</sup>
Right	13	46.43	35	50.72	48	49.49	
Left	15	53.57	34	49.28	49	50.51	
Clinical staging of breast cancer at diagnosis							0.910 <sup>†</sup>
Initial	19	67.86	46	66.67	65	67.01	
Advanced	9	32.14	23	33.33	32	32.99	

For the variables, only sentinel lymph node biopsy and axillary dissection were considered. AWS: axillary web syndrome.

**Table 2.** Comparison of goniometric measurements in degrees between ipsilateral and contralateral limbs, according to breast laterality and the presence of AWS (cords) in 97 women with breast cancer– Cancer Hospital of Pernambuco, Brazil – December 2011to July 2012.

Goniometria (degrees)	Right breast			Left breast		
	Right limb	Left limb	p-value	Right limb	Left limb	p-value
Active shoulder flexion goniometry with AWS	112.85±6.98	162.38±4.80	< 0.001	162.20±4.23	102.40±9.35	< 0.001
No AWS	126.20±4.91	157.14±3.48	< 0.001	157.48±3.44	105.21±5.76	< 0.001
Active shoulder extension goniometry with AWS	46.08±5.07	50.92±3.17	0.109	58.80±3.21	48.80±5.09	0.058
No AWS	45.11±1.96	51.11±12.14	0.004	52.15±2.05	45.42±2.14	0.002
Active shoulder abduction goniometry with AWS	103.84±7.09	152.92±7.94	< 0.001	153.47±5.51	94.00±7.89	< 0.001
No AWS	122.57±5.57	156.23±3.79	< 0.001	154.88±4.02	99.45±5.98	< 0.001
Active shoulder adduction goniometry with AWS	27.46±3.70	36.85±2.42	0.014	37.07±2.32	27.33±3.54	0.014
No AWS	25.34±1.94	34.37±1.74	< 0.001	33.39±1.82	26.42±2.69	0.017
Active shoulder internal rotation goniometry with AWS	49.84±7.76	69.92±5.66	0.011	64.67±5.32	60.53±4.81	0.268
No AWS	57.17±3.66	64.20±3.59	0.008	60.13±3.61	57.47±4.57	0.548
Active shoulder external rotation with AWS	85.38±2.54	92.38±2.19	0.007	91.20±2.52	77.87±6.29	0.048
No AWS	83.31±2.58	88.20±2.34	0.090	87.91±2.88	78.94±3.76	0.026
Passive shoulder flexion goniometry with AWS	121.31±7.94	166.77±6.07	< 0.001	156.80±10.72	108.40±8.58	0.001
No AWS	133.69±4.84	165.29±2.46	< 0.001	164.85±3.23	117.15±5.69	< 0.001
Passive shoulder extension goniometry with AWS	46.31±4.40	54.23±3.06	0.022	62.13±3.32	54.40±4.24	0.066
No AWS	49.29±2.18	55.20±2.33	0.001	57.88±3.86	50.10±2.46	0.050
Passive shoulder abduction goniometry with AWS	109.23±8.19	157.92±7.84	< 0.001	158.53±11.44	98.07±7.74	0.004
No AWS	126.97±5.81	161.86±20.24	< 0.001	154.94±5.93	105.06±5.96	< 0.001
Passive shoulder adduction with AWS	28.62±3.29	36.00±2.08	0.025	39.60±1.91	28.53±3.19	0.002
No AWS	29.74±2.00	35.69±1.89	0.001	33.94±1.47	26.54±2.53	0.008
Passive shoulder internal rotation with AWS	58.38±6.40	74.46±5.56	0.011	71.60±4.51	65.87±5.34	0.359

**Table 3.** Comparison of perimetric measurements between ipsilateral and contralateral limbs, according to breast laterality and the presence of AWS, in 97 women with breast cancer – Cancer Hospital of Pernambuco, Brazil – December 2011 to July 2012.

Perimetry measurements (centimeters)	Right breast		p-value	Left breast		p-value
	Right limb	Left limb		Right limb	Left limb	
Palmar crease perimetry AWS						
AWS	18,71±0,27	18,45±0,17	0,176	18,94±0,32	18,64±0,29	0,300
no AWS	18,90±0,20	18,63±0,21	0,071	18,24±0,34	18,24±0,40	0,984
Wrist perimetry						
AWS	15,58±0,22	15,35±0,22	0,021	16,05±0,31	16,06±0,32	0,958
no AWS	15,68±0,21	15,61±0,17	0,589	15,50±0,38	15,40±0,38	0,248
Forearm perimetry, 7 cm from the elbow crease						
AWS	23,51±0,54	23,32±0,50	0,338	24,19±0,82	23,97±0,86	0,453
no AWS	23,25±0,55	22,89±0,56	0,069	23,51±0,44	23,24±0,44	0,100
Forearm perimetry, 14 cm from the elbow crease						
AWS	18,11±0,38	18,19±0,39	0,658	19,74±0,78	19,67±0,75	0,799
no AWS	18,57±0,64	18,32±0,63	0,146	19,40±0,44	19,16±0,45	0,230
Upper arm perimetry, 7 cm from the elbow crease						
AWS	26,81±0,62	26,40±0,67	0,143	27,28±1,27	27,89±1,29	0,131
no AWS	27,95±0,70	27,28±0,68	0,069	27,36±0,58	27,68±0,60	0,137
Upper arm perimetry, 14 cm from the elbow crease						
AWS	30,58±1,53	30,38±1,45	0,549	30,02±1,78	30,48±1,82	0,386
no AWS	30,68±0,82	30,35±0,82	0,109	30,05±0,73	30,33±0,73	0,199
axilla perimetry						
AWS	41,75±1,40	41,21±1,49	0,464	40,83±1,50	40,84±1,82	1,000
no AWS	41,62±0,88	41,02±0,70	0,217	42,04±0,95	42,71±1,04	0,148

**Table 4.** Association between lymphedema topography in the upper limb and AWS diagnosis (cords) in 97 patients with breast cancer – Cancer Hospital of Pernambuco, Brazil – December 2011 to July 2012.

Lymphedema topography	AWS (cords)				p-value
	Present		Absent		
	n	%	n	%	
Palmar crease					0,319
No	25	92,6	66	97,0	
Yes	2	7,4	2	3,0	
Wrist					0,716
No	27	100,0	67	98,5	
Yes	-	-	1	1,5	
Forearm, 7 cm from the elbow crease					0,592
No	25	92,6	62	91,1	
Yes	2	7,4	6	8,9	
Forearm, 14 cm from the elbow crease					0,042
No	27	100,0	59	86,8	
Yes	-	-	9	13,2	
Arm 7 cm from the elbow crease					0,173
No	25	92,6	56	82,4	
Yes	2	7,4	12	17,6	
Arm 14 cm from the elbow crease					0,429
No	22	81,5	58	85,2	
Yes	5	18,5	10	14,8	
Axilla					0,083
No	13	48,1	45	66,2	
Yes	14	51,9	23	33,8	

Loss of two samples with AWS. AWS: axillary web syndrome.

## DISCUSSION

AWS frequency was 28.8%, consistent with literature, which varies from 6% to 48.3%, due to variability in the definition criteria and methodological differences across studies<sup>8,14,17-18</sup>.

Significant decreases in ROM might be related to the post-surgery convalescence, as these limitations were observed regardless of AWS presence.

Considering breast laterality in relation to active and passive shoulder ROM, a greater reduction was observed when the left breast was affected, reflecting the predominance of right-handed patients. Muscles associated with hand dominance are more used in daily activities that require strength and more developed, leading to morphophysiological adaptations, such as muscle hypertrophy and greater motor unit recruitment<sup>19</sup>.

Regarding bilateral involvement, the frequency observed in this study corroborated previous li-

terature, although differences were observed in the ipsilateral limb topography. These differences were attributed to the time interval between surgery and measurements<sup>21</sup>.

A limitation of this study was the cross-sectional design and the lack of preoperative evaluation of patients<sup>17,22-24</sup>, which may have restricted the detection of preexisting ROM reductions or upper-limb circumference differences before surgery<sup>25</sup>.

The early onset of perimetric alterations in AWS highlights the need for appropriate treatment in the immediate post-operative period. Currently, literature lacks standardized therapeutic approaches for AWS and management strategies focusing on addressing associated morbidities.

## CONCLUSIONS

A significant number of women diagnosed with AWS were associated with early onset of pe-

rimetric alterations and a significant reduction of shoulder ROM.

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# FEEDBACK IN PROBLEM-BASED LEARNING AS A TEACHING-LEARNING INSTRUMENT: EFFECTIVENESS OF THE EVALUATION TOOL

*O FEEDBACK NA APRENDIZAGEM BASEADA EM PROBLEMAS COMO INSTRUMENTO DE ENSINO-APRENDIZAGEM: EFICÁCIA DA FERRAMENTA DE AVALIAÇÃO*

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## ABSTRACT

**Introduction:** The search for qualified professionals motivates the development of innovative teaching methods, such as problem-based learning (PBL). **Objective:** To analyze the effectiveness of the feedback on the PBL method in the evaluation of medical students. **Methods:** A descriptive study was conducted with 60 medical students, divided into six groups, using interviews to gather feedback on the PBL method. The research ethics committee approved the study, and the qualitative variables were expressed as frequencies. **Results:** Fifty-eight students (98.3%) had their first contact with the PBL in the Faculdade de Medicina de Olinda, and 54 students (90.47%) acknowledged the feedback as an important tool in the learning process. In addition, 12 students (20%) reported a lack of homogeneity in the feedback application. **Conclusion:** Tutorial feedback proved to be an effective evaluation tool in the teaching-learning process of medical students. Higher education institutions should encourage frequent use of tutors.

**Keywords:** Evaluation; Formative feedback; PBL

## RESUMO

**Introdução:** A importância da formação de profissionais cada vez mais capacitados estimula o desenvolvimento de novos métodos de ensino, onde a Aprendizagem Baseada em problemas (ABP) se insere. **Objetivo:** Analisar a eficácia do feedback da metodologia de ensino ABP no processo de avaliação dos estudantes de Medicina. **Métodos:** Foi realizado um estudo descritivo, constituído por uma amostra de 60 voluntários, estudantes de Medicina, divididos em seis grupos focais, através de entrevista com perguntas sobre a cerca do feedback realizado nos grupos de ABP. Os resultados das variáveis qualitativas foram descritos por frequências. O trabalho foi aprovado pelo comitê de ética da Instituição. **Resultados:** Foi observado que 58 estudantes (98.3%) tiveram seu primeiro contato com o método ABP após o ingresso na Faculdade de Medicina de Olinda. O feedback no ABP foi destacado por 54 (90,47%) dos entrevistados como um instrumento importante na aquisição do conhecimento. Falta de homogeneidade na aplicação do feedback no grupo tutorial foi referida por 12 estudantes (20%). **Conclusão:** O feedback tutorial apresentou eficácia como um instrumento de avaliação no processo de ensino-aprendizagem do estudante na formação médica. Existem tutores que não o aplicam com frequência, onde as Instituições de Ensino Superior devem estimular os profissionais para esse instrumento.

**Palavras-chave:** Avaliação; Feedback formativo; ABP

## INTRODUCTION

Medical education in Brazil raises concerns about the growing number of new medical schools in recent decades. Focusing on the need for qualified professionals with scientific knowledge and skills, the necessity of developing new teaching methods was observed<sup>1</sup>.

Problem-based learning (PBL) is a formative teaching-learning method, not a quantitative instrument with assigned grades, which is often observed in teaching and learning processes that use exams as an evaluation tool<sup>2,3</sup>.

As an active method, PBL stimulates students to search for knowledge, playing a main role in their

training, unlike traditional methods that involve passive students who only receive information. A new strategy was necessary to improve medical education, transmitting a holistic view of health problems<sup>4,5</sup>.

The student receives a grade related to their performance at the end of a PBL tutorial. Ideally, the tutor should give feedback related to the grade, a crucial tool in the teaching and learning process. In this formative assessment, the tutor and the student score positive points and areas for improvement in the daily performance. Thus, the tutor and student discuss the activities and skills, encouraging reflection and promoting a self-assessment<sup>6</sup>.

The feedback regarding difficulties and skills in the learning process helps students outline strategies to overcome failures that influence the knowledge production of the individual and the group<sup>3,6,7,8</sup>.

Thus, PBL enables students to actively produce knowledge, develop a critical sense, and engage in study using problems proposed by the tutor. The student becomes aware of the results of their practices, what was missed to improve skills, and outlines strategies to meet these needs<sup>4,5,9</sup>. Last, the feedback

work the criticism of the tutor on the performance of the student, which helps develop metacognition - a debated skill among educators<sup>6</sup>.

However, studies regarding the perception of medical students of tutorial feedback are scarce. Thus, this study aimed to analyze and reflect on the effectiveness of feedback as a teaching and learning tool for medical students within the tutorial group.

## METHODS

This qualitative and cross-sectional study was conducted at the Faculdade de Medicina de Olinda in Pernambuco, Brazil. The convenience sample of 60 medical students was divided into six groups.

Students without experience in PBL and those with cognitive deficits that prevented them from answering adequately to the interview were excluded from the study.

After approval by the research ethics committee, the students were invited to participate in the study. All stages and purposes were explained, and after signing the informed consent form, the interviews were performed (Table 1).

**Figure 1.** Questions of the established script of the interview:

**Introductory question: What was your first contact with the method (PBL)?**  
 In the current course at the FMO  
 In another course external to FMO

*Transition question:* Think about your experiences with the PBL method. How would you rate the impressions of the PBL methodological experience?  Good  Bad  Indifferent

**Key Questions**

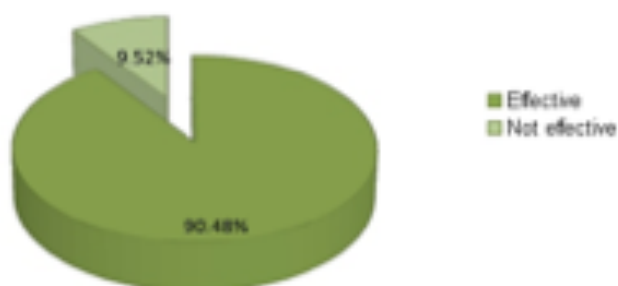
1. What is your opinion on the evaluation in the tutorial group?  Effective  Ineffective
2. What do you think about the feedback provided by the tutor at the end of the tutorial group?  
 Important  Unimportant
3. What do you think about the feedback as a tool in the teaching-learning process?  
 Essential  Unimportant
4. In your opinion, has the PBL method contributed to your medical training?  
 Efficient  Inefficient  Indifferent
5. In your opinion, has the feedback contributed to your medical training?  
 Yes  No
6. Did all tutors provide feedback at the end of the tutorial group?  Yes  No
7. Is there uniformity in the performance of the feedback among tutors?  Yes  No

Qualitative variables were expressed as absolute and relative frequencies. FMO: Faculdade de Medicina de Olinda.

## RESULTS AND DISCUSSION

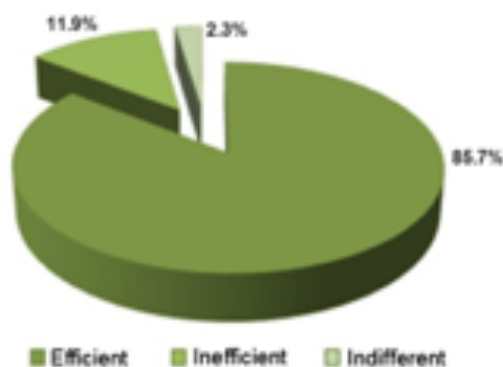
Most students (98.3%) had their first contact with the PBL method at FMO, including those from other higher education.

Of the 60 students, 54 (90.47%) highlighted feedback as fundamental instrument for evolving and revisiting their behavior, leading to reflection, modulating learning processes, and improving their medical training. Only six students (9.52%) did not consider feedback as an essential tool in the teaching-learning process (Figure 2).



**Figure 2.** Classification of feedback as an instrument of the teaching-learning process according to the students.

Additionally, 51 (85.71%) students considered the PBL method important for academic training, and 7 (11.90%) did not consider it a fundamental experience for learning and medical training. Moreover, 2 (2.38%) students reported that the method was indifferent to their training (Figure 3).



**Figure 3.** Classification of the efficiency of the PBL method on the perception of students.

The present study observed flaws in the feedback process in the tutorial groups. In this sample, 48 students (80%) received individual and group feedback at the end of PBL sessions. Those who did not receive feedback expressed dissatisfaction, reporting that feedback was applied only in groups, without individual feedback. In addition, students reported that despite training and institutional regu-

lations, tutors did not evaluate their groups uniformly, which impaired comprehension of students. This bias was considered a limitation in this study, which may indicate the need for regulation in the use of this assessment tool.

Students who received individual feedback were more satisfied, even when the score was insufficient, and they had better group and tutoring adaptation, as the feedback guided their performance evolution. Studies have shown that feedback stimulates metacognition, enabling students to revisit the error scenario, device a plan of correction, and improve their skills<sup>6</sup>.

Students were satisfied with the feedback and highlighted that the instrument contributed to academic training, as it stimulated group and individual learning, triggering an integration process important to their professional life. In addition, feedback encouraged students to seek reliable and update sources of research. Thus, this evaluation tool contributed to the development of skills essential to good doctors, such as knowing how to position themselves and making placements in a group. Additionally, feedback contributed to individual knowledge of their cognitive processes and self-regulating academic development and learning.

Feedback provided by tutors increased, with at least 80% of students receiving feedback in the second period, as in focal group 1 (Table 1).

Among interviewed students, 56 (92.85%) reported that feedback enriched the learning process, allowing them to visualize their academic performance, identify mistakes, receive guidance for correction, and improve their qualities. These data corroborate the study of Souza and Dourado<sup>8</sup>, who described how feedback reorients the student to the content studied, correcting misunderstandings, enabling a return to the desired learning path, and developing their skills<sup>9</sup>.

Moreover, studies confirmed that the competencies development such as decision making, communication, leadership, and management notions are important to meet the needs of professionals in the Unified Health System; thereby overcoming its deficiencies<sup>11</sup>.

Thus, feedback is important to activate cognitive and metacognitive processes, promoting conscious control of learning processes. In addition, the student improves their self-esteem and becomes more motivated<sup>8,12</sup>. This was evidenced in the pres

ent study, as most students were satisfied receiving feedback in the tutorial group.

**Table 1.** Representativeness of feedback provided by tutors in the first period and in the progress of the second period.

Focus groups	Feedback in the first period	Feedback on the progress of the second period
FG1	40%	80%
FG2	20%	100%
FG3	10%	100%
FG4	50%	100%
FG5	0 %	100%
FG6	10%	100%

## CONCLUSION

The tutorial feedback on the PBL method was considered an important evaluation tool in the teaching-learning process, in the perception of students, and was considered an effective instrument to improve medical training.

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# POSTOPERATIVE OUTCOME EXPECTATIONS OF AN OLDER ADULT PATIENT WITH EXPERTISE IN MEDICAL LITERACY SUFFERING FROM DRY EYE SYNDROME AND CATARACT - ETHICS AND EVIDENCE: A CASE REPORT

*EXPECTATIVA DO RESULTADO PÓS-OPERATÓRIO PELA ÓTICA DO IDOSO INFORMATIZADO COM SÍNDROME DO OLHO SECO E CATARATA - ÉTICA E EVIDÊNCIA: RELATO DE CASO*

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## ABSTRACT

**Introduction:** To explore the relationship of the ophthalmologist with an elderly and intellectually differentiated patient from the scientific point of view, about dry eye syndrome and cataract surgery results. **Case report:** Physician, researcher, white, 74.5 year-old, suffering from cataract and dry eye syndrome, anxious to obtain information in databases on the risk of increased postoperative dry eye syndrome symptoms after phacotomy. He was adequately evaluated by the specialist, as well as had a good communication with the candidate for the procedure in a free and spontaneous way. **Comments:** As technical information by the specialized professional with good knowledge in based evidence medicine and ethic, giving support to reduce the patient anxiety. There is a need for specialist preparation to deal with the elderly patients of the new millennium, updated in the cyber age.

**Keywords:** Physician-Patient Relation; Ethics; Medical information; Cataract; Dry Eye Syndrome

## RESUMO

**Introdução:** Explorar a relação do oftalmologista com o paciente idoso e intelectualmente diferenciado, do ponto de vista científico, sobre síndrome de olho seco e resultados de cirurgia de catarata. **Relato do caso:** Médico, pesquisador, branco, 74,5 anos, portador de catarata e olho seco, ansioso por ter obtido informações, em bases de dados, sobre riscos do aumento dos sintomas da síndrome de olho seco no pós-operatório da facectomia. Foi adequadamente avaliado pelo especialista, assim se candidatando ao procedimento de forma livre e espontânea. **Comentários:** As informações técnicas pelo profissional especializado tiveram seu cerne em medicina baseada em evidência e ética, dando suporte para redução da ansiedade do paciente. Há necessidade do preparo do especialista para lidar com os pacientes idosos do novo milênio, atualizados na era cibernética.

**Palavras-chave:** Relação médico-paciente; Ética; Informática médica; Catarata; Síndrome do olho seco

## INTRODUCTION

The age of information technology has brought about a break with operations<sup>5</sup>. The medical relationship, characterized by identification, empathy, safety, and reliability, has become a tool for enhancing professional performance paradigms, particularly in the inclusion of older adult populations in knowledge acquisition, appreciation of work activities, and interpersonal relationships<sup>1</sup>. Despite these advantages, they can cause new health problems in the population, generating diseases, including tho-

se ophthalmic, such as computer vision syndrome, which aggravates dry eye syndrome, a condition considered a public health problem<sup>2-5</sup>.

Cataracts are a natural part of aging, and their management often requires high-tech surgery in specialized centers. However, cataract surgery, even if uncomplicated, can cause dissatisfaction in patients with associated dry eye, necessitating clarification and management within the healthcare context<sup>6</sup>.

The etiology of worsening dry eye after cataract surgery remains unclear; however, pre- or perio-

## CASE REPORT

perative factors may be associated, such as the use of eye drops with preservatives, topical anesthetics, focal illumination of the surgical microscope, and corneal denervation, which can lead to damage to the external surface of the eye<sup>7,8</sup>. The case proposes aspects that should be part of the medical routine, supported by scientific rationality and ethics.

### CASE REPORT

CTB, 74.5 years old, white, male, doctor, researcher, highly educated, knowledgeable in evidence-based medicine, user of electronic technologies for a long time, healthy, complained about a progressive reduction in visual acuity and a foreign body sensation in the eyes for about a year. His apprehension about the information acquired on maleficence, beneficence, and justice was key to relieving his anxiety. Focusing on the fact that the worsening of dry eye symptoms is usually transient and can be minimized with reduced surgical time, and databases indicating a possible increase in inflammation control<sup>11</sup> due to dry eye after cataract surgery, he decided to consult an ophthalmologist. The diagnosis of moderate dry eye syndrome and bilateral cataract was confirmed, with an indication for surgery using the phacoemulsification technique with intraocular lens implantation associated with the femtosecond laser. He was advised on the factors involved in dry eye syndrome, including pre-existing diseases, lifestyle habits, the time spent using a computer, and the use of eye drops with preservatives during the preoperative period. Based on meta-analyses, the physician determined the surgical technique, the use of preservative-free artificial tears, and local corticosteroid therapy to manage potential adverse effects in the postoperative period.

The patient, duly informed, felt confident about having his procedures conducted and booked them with confidence in the specialist, as well as good expectations about undergoing surgery.

### COMMENTS

With the increase in life expectancy, chronic non-communicable diseases are growing exponentially, combined with the new habits of an increasingly informed population. Several of these diseases affect vision and can be a major economic and social burden for developing countries<sup>3,8</sup>.

Obtaining health information must be carefully evaluated, even among highly intellectual

people, and it is the responsibility of the assistant physician to empathize with the patient and provide communication skills to establish a good doctor-patient relationship<sup>9</sup>.

The post-operative management of the association of cataract and dry eye is still a challenge, as it is multifactorial, and the physician must be alert to patients with prior knowledge and their anxieties<sup>10</sup>. The intraoperative use of hydroxypropyl methylcellulose (HPMC 2%) after cataract surgery can improve the tear film on the ocular surface in the immediate postoperative period<sup>11</sup>.

The attitude of the assistant doctor, based on the ethical principle of autonomy, was not fundamental to resolving the “apparent conflict”. In other words, the physician was responsible for reducing ethical conflicts<sup>12</sup>. In the study, the well-informed patient felt satisfied with the care he received, which involved pillars of theoretical rationality, ethics, and emotional intelligence.

Evidence-based medical clarification, combined with professional experience and good listening skills, can foster a harmonious and welcoming relationship. Listening attentively to the patient and interacting at an appropriate level can make the difference between a satisfied patient and one who complains during the mid- to late follow-up<sup>12</sup>. Focusing on a good doctor-patient relationship can be a decisive tool for minimizing conflictual relationships and the causes of medical litigation.

### CONFLICTS OF INTEREST

Nothing to declare.

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# ANESTHESIA FOR CESAREAN DELIVERY IN A PATIENT WITH LYMPHANGIOLEIOMYOMATOSIS: A CASE REPORT

ANESTESIA PARA CESARIANA EM PACIENTE COM LINFANGIOLEIOMIOMATOSE: RELATO DE CASO

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## ABSTRACT

**Introduction:** Lymphangiomyomatosis (LAM) is a rare disease of unknown etiology, classically described in reproductive age women and, occasionally, reported in postmenopausal. Gestation in these patients is high risk, since the physiological changes of gestation add to those of LAM, worsening maternal cardiorespiratory status. **Case Report:** A 29-year-old pregnant woman with LAM and collapsing segmental and focal glomerulosclerosis (ESRF) diagnosed two years before had an indication of interruption of pregnancy during the 35th gestational week, due to worsening renal function. Spirometer examination revealed significant restrictive disorder. She was hospitalized during the 34th week of gestation and underwent steroid therapy for fetal lung maturation, when worsening of renal function and cesarean section were indicated. Combined regional anesthesia was chosen. **Comments:** LAM has a prevalence of 1 to 2.6 / 1,000,000 women. It is associated with Tuberous Sclerosis or idiopathic one.. Combined regional anesthesia was adopted because of the difficulty in managing the airway. Hormonal factors appear to play a role in the initiation and progression of LAM.

**Keywords:** Lymphangiomyomatosis. Obstetric anesthesia. Regional anesthesia.

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## RESUMO

**Introdução:** A linfangioleiomiomatose (LAM) é uma doença rara de etiologia desconhecida, classicamente descrita em mulheres em idade reprodutiva e, ocasionalmente, na pós-menopausa. A gestação nessas pacientes é de alto risco, pois as alterações fisiológicas somam-se às da LAM, agravando o status cardiorrespiratório materno. **Relato de caso:** Gestante, 29 anos, portadora de LAM e glomeruloesclerose segmentar e focal colapsante diagnosticadas há dois anos, teve indicação de interrupção da gestação no decorrer da 35ª semana por piora da função renal. Espirometria revelou importante distúrbio restritivo. Internada no curso da 34ª semana de gestação, submeteu-se a corticoterapia para a maturação pulmonar fetal, quando apresentou piora da função renal e foi indicada a cesárea. Optou-se pela anestesia regional combinada. **Comentários:** A prevalência da LAM em mulheres varia de 1 a 2,6/1.000.000 de mulheres e surge associada à esclerose tuberosa ou de forma idiopática. No caso, adotou-se a anestesia regional combinada em virtude da dificuldade no manejo da via aérea na gestante. Fatores hormonais parecem ter papel na iniciação e progressão da LAM.

**Palavras-chave:** Linfangioleiomiomatose; Anestesia obstétrica; Anestesia regional

## INTRODUCTION

Lymphangiomyomatosis (LAM) is a rare disease of unknown etiology, often described in women of reproductive age and less common in postmenopausal women. This condition is characterized by the hamartomatous proliferation of smooth muscles in the bronchioles, arterioles, and pulmonary lymphatic vessels, leading to airway narrowing, obs-

truction, and air trapping. Associated alveolar damage results in the development of pulmonary cystic lesions and lymphatic vessels involvement (lymphangiomyomas) over time<sup>1,2</sup>. LAM may also be associated with an extrapulmonary lesion, such as a renal angiomyolipoma<sup>2</sup>.

Pregnancy in patients with LAM is a high-risk condition because of the physiological cardiorespi-

ratory changes of gestation, added to the existing structural alterations, and is poorly tolerated<sup>3</sup>.

This study is a case report of a patient with LAM who underwent a cesarean delivery under combined regional anesthesia (epidural and spinal).

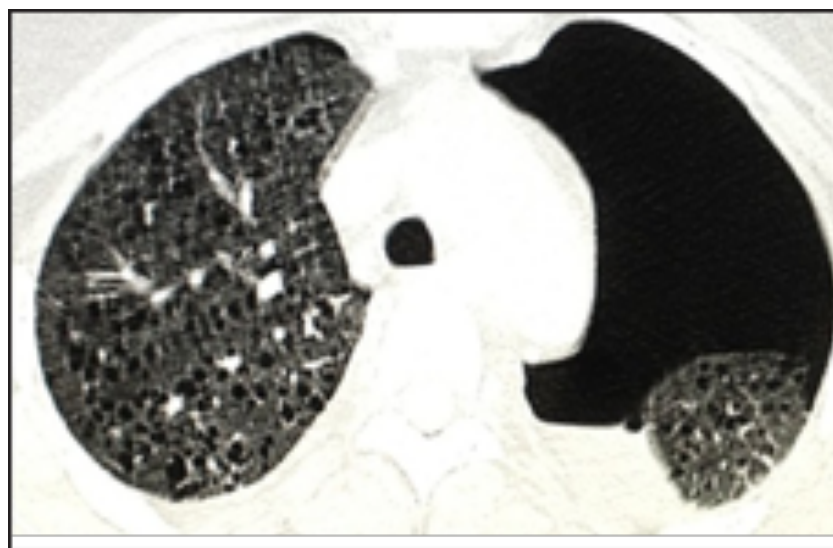
### CASE REPORT

A 29-year-old pregnant woman at 35 weeks of gestation was indicated for pregnancy termination due to clinical complications. At the age of 27, she was admitted to the nephrology department of the Hospital das Clínicas de Pernambuco, presenting with nephrotic syndrome and progressive worsening of renal function. A renal biopsy revealed collapsing focal segmental glomerulosclerosis. Her condition improved after treatment with prednisone (1 mg/kg) and furosemide. After one month, the patient experienced two episodes of pleuritic pain and sudden dyspnea secondary to pneumothorax, occurring 15 days apart and involving both lungs, as shown on chest X-ray. She underwent closed chest drainage, and due to recurrence, a computed tomography scan

of the chest was performed, which showed multiple thin-walled cysts in both lungs and a clear left pneumothorax (Figure 1). Another drainage procedure was performed, and the pulmonary condition was further investigated. The previous medical history of the patient included the use of oral contraceptives for 10 years and intermittent asthma with the use of a beta-2 agonist inhaler about twice per month.

The patient underwent pleurodesis and left pulmonary segmentectomy by video-assisted thoracoscopic surgery for diagnostic biopsy in April 2012. Histopathological findings confirmed LAM, and a spirometry showed a substantial restrictive disorder.

At age 28, the patient became pregnant and remained under follow-up in the nephrology outpatient clinic, with stable renal function and a reduction of prednisone dosage (50 mg/day). An ultrasound of the urinary tract highlighted findings consistent with parenchymal nephropathy. At 34 weeks of pregnancy, the patient was admitted for corticosteroid therapy to accelerate fetal lung development. During this period, elevated nitrogenous waste levels were observed, and pregnancy termination was indicated.



**Figure 1.** Computed tomography of the chest showing pneumothorax on the left and multiple cysts in both lungs.

During the pre-anesthetic evaluation, no findings were suggestive of a difficult airway, and the patient was classified as Mallampati class II. Preoperative arterial blood gas analysis showed pH = 7.37; pO<sub>2</sub> = 93 mmHg; pCO<sub>2</sub> = 29 mmHg; HCO<sub>3</sub><sup>-</sup> = 19.3 mmol/L; BE = -7.3 mmol/L; SatO<sub>2</sub> = 97%; and lactate = 1.2 mmol/L.

The anesthetic technique chosen was epidural at the T9-T10 interspace combined with spinal anesthesia at the L3-L4 level, with the administra-

tion of 8 mg of hyperbaric bupivacaine and 80 mcg of morphine into the subarachnoid space. Sensory block reached the T4 dermatome within three minutes. The surgery lasted 30 minutes without complications, and arterial hypotension was corrected with titrated doses of 50 mg of ephedrine and increased infusion of crystalloid solution. Postoperative arterial blood gas analysis showed pH = 7.29; pO<sub>2</sub> = 124 mmHg; pCO<sub>2</sub> = 32 mmHg; HCO<sub>3</sub><sup>-</sup> = 17.1 mmol/L; BE = -9.6 mmol/L; SatO<sub>2</sub> = 98%; and lactate = 2.1

## CASE REPORT

mmol/L.

The newborn had an Apgar score of 7 at one minute and 8 at five minutes. After surgery, the patient was referred to the intensive care unit. No hemodynamic alterations or signs of respiratory distress were observed. The patient was discharged on the eighth postoperative day.

## COMMENTS

LAM in women has a prevalence of 2.6 per 1,000,000. However, the limited awareness of the disease causes often misdiagnosis as asthma, chronic obstructive pulmonary disease, or bronchitis<sup>1</sup>.

The most common symptoms are exertional dyspnea and pneumothorax. The latter is frequently recurrent, even in patients with a normal chest X-ray, with a reported incidence of 40% to 80%<sup>1</sup>.

The patient presented with episodic dyspnea that has been diagnosed as intermittent asthma. However, after three spontaneous pneumothoraces (two on the left lung), the possibility of another primary pulmonary disease was considered.

The choice of the anesthetic technique must be guided by weighing risks and benefits for each patient. In this case, the severe pulmonary condition and the physiological changes of pregnancy were considered. The anesthetic blockade at a high spinal level was concerning, as it could hinder the lung function of a patient who was already dependent on accessory muscles. General anesthesia was also considered, as it offers more precise ventilatory control regardless of patient effort. Nevertheless, airway management in pregnant patients is challenging due to worsening Mallampati classification, soft tissue edema (e.g., pharynx and larynx), friable mucosa, reduced glottic area, and enlarged breasts<sup>4</sup>.

A combined blockade technique was chosen to allow the administration of low doses of anesthetic into the subarachnoid space and the insertion of an epidural catheter for titration. The aim was to avoid airway manipulation with positive-pressure ventilation, given the substantial pulmonary restrictive disease and multiple cysts of the patient, which increased her susceptibility to pneumothorax.

Hormonal factors may contribute to the initiation and progression of LAM, which is more prevalent in women, as hormone receptors are found in some LAM cells. Exogenous estrogen use and pregnancy may worsen the disease<sup>5,6</sup>. In this case,

a possible risk factor for the patient was the 10-year use of oral contraceptives. These patients should be advised against pregnancy due to maternal and fetal risks<sup>5-7</sup>. A study by Urban et al. (1999)<sup>8</sup> described that 23% of patients presented their first pulmonary event during pregnancy, although only two showed clinical worsening related to pregnancy.

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# METASTATIC BREAST CARCINOMA FOR OPTIC NERVE: CASE REPORT

CARCINOMA METASTÁTICO DE MAMA PARA NERVO ÓPTICO: RELATO DE CASO

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## ABSTRACT

**Introduction:** Ocular metastases are underreported and, in addition, some presentations are less frequent and should be screened in an interdisciplinary way. **Case report:** This is a 59-year-old white woman, with a history of unilateral breast cancer, whose symptoms and ophthalmologic signs were manifestations that led to the diagnosis of recurrence of the disease due to ocular metastasis. **Comments:** Due to the possible asymptomatic presentation, location of the lesion and absence of a screening protocol for ocular metastases in oncological diseases, many cases of intraocular metastatic tumors are not diagnosed. After a period considered free of the disease, the patient complaints served as a stimulus for ophthalmologic evaluation. Although, many advanced intraocular tumors may be asymptomatic, this contributes to increased ocular morbidity. Ocular rare sites of metastasis may be predictor of disease severity, where, in the study, the optic nerve involvement can be observed, a rare focus of dissemination in breast cancer.

**Keywords:** Breast neoplasms; Tumor metastasis; Screening; Eye

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## RESUMO

**Introdução:** Metástases oculares são subnotificadas e, adicionalmente, algumas apresentações são menos frequentes, devendo ser rastreadas de forma interdisciplinar. **Relato de caso:** Trata-se de mulher de 59 anos, branca, com história pregressa de câncer de mama unilateral, onde sintomas e sinais oftalmológicos foram as manifestações que levaram ao diagnóstico de recidiva da doença por metástase ocular após seis anos de tratamento. **Comentários:** Devido a possível apresentação assintomática das lesões, localização e ausência de protocolo de rastreamento para metástases oculares em doenças oncológicas, muitos casos de tumores metastáticos intraoculares não são diagnosticados. Após período considerado livre da doença, as queixas da paciente serviram de estímulo para avaliação oftalmológica, embora, muitos tumores intraoculares avançados podem ser assintomáticos, o que contribui para maior morbidade ocular. Sítios raros de metástase ocular pode ser fator preditor de gravidade da doença.

**Palavras-chave:** Neoplasias da mama; Metástase tumoral; Rastreamento; Olho

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## INTRODUCTION

The detection of ocular metastatic tumors from breast cancer is underreported, as the eye is an uncommon site compared with bone, lung, and liver; this issue may be associated with insufficient interdisciplinary assessment of these cancers<sup>1</sup>. Considering that breast cancer accounts for 28% of new cases per year in Brazil and worldwide<sup>2,3</sup>, routine screening for ocular tumor involvement or for adverse side effects of systemic treatment is not common among specialists dealing with this serious condition<sup>4</sup>.

The most frequent primary sites of ocular metastases are malignant breast tumors in women (28.6%), and lung tumors in men (23.8%)<sup>5</sup>. Uveal metastasis is the most common, especially to the choroid due to the rich vascularization of the site (88.0%), and is less frequent in the orbit and optic disc. Choroidal metastases usually appear as a whitish or yellowish creamy mass, often associated with subretinal fluid<sup>5</sup>. Other metastasis sites, such as the brain and liver, are common and associated with disease prognosis<sup>6</sup>, in which invasive ductal carcinoma is the histological subtype most often associated with systemic spread. The literature lacks informa-

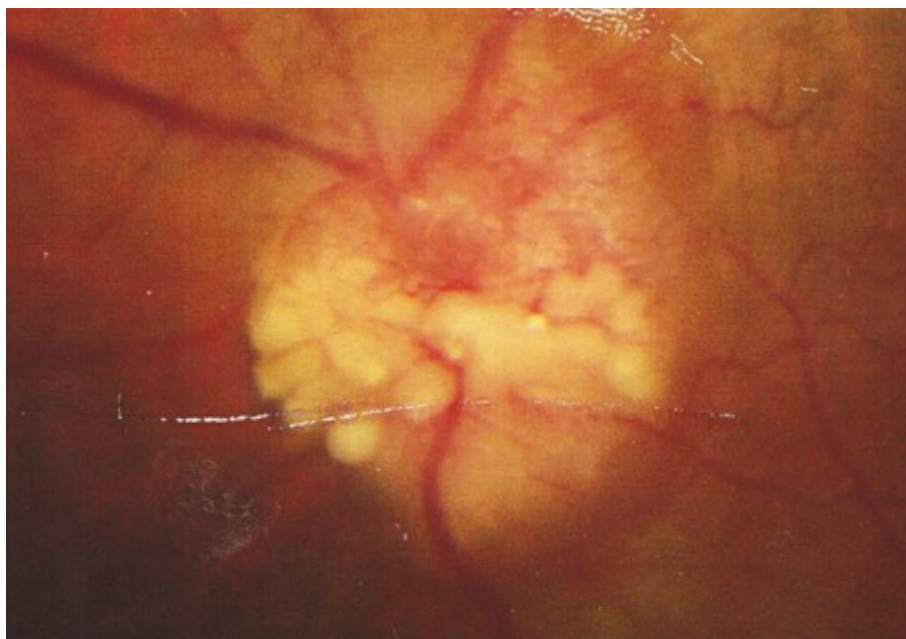
## CASE REPORT

tion regarding characteristics of breast cancer metastases in the eye, and invasive lobular cancer is the one with the highest association with orbital metastases<sup>7</sup>. This case report presents a rare manifestation of breast cancer metastasis that was not diagnosed early, highlighting the need for stronger interdisciplinary management.

### CASE REPORT

N.M.S.S.S., a 59-year-old white woman, was referred by her oncologist for an ophthalmic assessment due to progressive visual impairment in the right eye (RE) and headaches for the past three months. She had a history of unilateral radical mastectomy with lymph node dissection, followed by chemotherapy and radiotherapy for breast carcinoma six years earlier. The tumor presented the histologic subtype of papillary ductal cancer, positive for estrogen (assessed by immunohistochemistry). She was treated for five years with tamoxifen and remained under semi-annual follow-up. She also reported passive smoking exposure for 25 years. Ophthalmologic

ectoscopy revealed no abnormalities in the ocular adnexa. Best corrected visual acuity (Snellen chart): RE counting fingers at 50 cm; left eye (LE) at 20/20. Biomicroscopy: incipient nuclear sclerosis in both eyes. Intraocular pressure by applanation tonometry: 12x12 mmHg (at 2 p.m., without medication). Fundus examination: 1) RE showed a whitish, vascularized lesion with regular margins at the optic disc topography, with disruption of the lamina cribrosa and tissue protrusion into the vitreous cavity, but without distortion of the retinal vascular emergence, while the macula was unremarkable; 2) LE showed a normal optic disc color and margins, normal vessels and macula. Additional ophthalmic diagnostic tests were performed (Figure 1), and the patient was referred back to her oncologist with a counter-referral describing the ocular findings and requesting further investigation for central nervous system metastases. On oncologic reevaluation, brain magnetic resonance imaging revealed multiple images consistent with brain metastatic lesions. Palliative treatment for metastatic disease was proposed, but the patient died two months later.



**Figure 1.** Color retinography. Lesion indicating metastatic carcinoma in the optic nerve.

## COMMENTS

Intraocular metastases are often undiagnosed, and they may represent the initial manifestation of primary tumors<sup>2,5,6</sup>. Breast cancer accounts for most ocular metastases in women<sup>2-8,9</sup>. The site of the lesion may delay diagnosis and the timing of symptom onset. In our report, the patient reported visual impairment for over two months; this period may not correspond to the actual duration of optic nerve involvement, but served as a warning sign prompting further investigation. The lack of routine ophthalmic evaluation in cases of breast cancer highlights the limited interaction between specialists and the absence of screening protocols for ocular metastases, leading to missed opportunities for early detection<sup>10,11</sup>. Optic nerve involvement is uncommon, and when associated with brain lesions, it suggests metabolic similarities between these tissues, indicating greater disease severity. Although the tumor type was the most common form of breast cancer, metastasis to the optic nerve remains rare<sup>9,11</sup>. Early diagnosis and identification of lesion sites may enable the combination of ophthalmic interventions with oncologic management of the primary disease, potentially improving visual outcomes and survival<sup>12,13</sup>. However, brain metastases carry a poor prognosis, which in this case prevented timely ophthalmologic treatment due to the fatal outcome. The literature lacks information on ophthalmologic presentations that may serve as prognostic markers for this disease, highlighting the need for randomized clinical studies to assess possible associations between intraocular metastasis and factors, such as age, histological subtype, therapy received, follow-up duration, and primary tumor stages. The symptoms of the patient were paramount for the ophthalmic referral, emphasizing the importance of considering these complaints in multidisciplinary follow-up.

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# CYTOREDUCTIVE SURGERY/HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY PROGRAM AT THE HOSPITAL UNIVERSITÁRIO DE PERNAMBUCO: AN EXPERIENCE REPORT

*PROGRAMA DE CIRURGIA CITORREDUTORA/QUIMIOTERAPIA INTRAPERITONEAL  
HIPERTÉRMICA EM HOSPITAL UNIVERSITÁRIO DE PERNAMBUCO: RELATO DE EXPERIÊNCIA*

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## ABSTRACT

Several surgical approaches to oncology are being used, especially Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in the last decade in Brazil. However, the population access to this technique is limited. The technical report is about the findings in cancer patients after starting the HIPEC in the Cytoreductive Surgery (CCR) program in a public care hospital, Pernambuco-State, Brazil. Completed three years program-CCR / HIPEC of the Oncology Center of the University of Pernambuco (CEON-UPE), this program has been successful. Currently, enrolling patients from the state of Pernambuco and surrounding areas that do not have such therapeutic modality.

**Keywords:** Cytoreduction Surgical Procedures. Drug therapy. Unified Health System.

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## RESUMO

Diversas abordagens cirúrgicas oncológicas estão sendo empregadas, destacando-se a quimioterapia intraperitoneal hipertérmica (HIPEC) na última década no Brasil. No entanto, o acesso da população a essa técnica é limitado. Este relato de experiência versa sobre os achados em pacientes oncológicos após instituição da HIPEC no programa de cirurgia citorrredutora (CCR) de um hospital de atendimento público em Pernambuco. Completados três anos do programa CCR/HIPEC do Centro de Oncologia da Universidade de Pernambuco, é possível dizer que ele vem sendo bem-sucedido, matriculando atualmente pacientes do estado de Pernambuco e circunvizinhos que não dispõem dessa modalidade terapêutica.

**Palavras-chave:** Procedimentos cirúrgicos de citorredução; Quimioterapia; Sistema Único de Saúde

## INTRODUCTION

Hyperthermic intraperitoneal chemotherapy (HIPEC) was standardized and disclosed by Paul Sugarbaker in 1995<sup>1</sup>. In Brazil, this procedure was only introduced after 2001 by Ademar Lopes<sup>2</sup>. Still, this and other healthcare initiatives in the country have occurred almost exclusively in private or philanthropic institutions.

To date, the Brazilian Medical Association has not included a specific code for HIPEC in the list of procedures; in addition, this surgery has not yet

been regulated by the National Health Surveillance Agency.

Despite the lack of regulatory actions, hundreds of patients in Brazil require this surgery every year, and most die due to the lack of access to this treatment. Some patients turn to legal action and, when successful, undergo HIPEC in private or philanthropic centers.

Given the barriers experienced by patients within the public healthcare system, the Oncology Center of the University of Pernambuco (OC-UPE) implemented in March 2015 the cytoreductive sur-

gery (CRS)/HIPEC program to meet public demand.

## COMMENTS

A total of 37 CRS/HIPEC procedures were performed at the Hospital Universitário Oswaldo Cruz. All patients signed an informed consent form for surgical and anesthetic procedures.

Of the 37 patients, 32 (86.4%) were women. Among those, 16 (50%) had stage III-c ovarian cancer. Across both sexes, 17 (81.0%) had appendix cancer or pseudomyxoma peritonei; 2 (9.5%) had peritoneal mesothelioma; 1 (4.7%) had gastric cancer; and 1 (4.7%) had colorectal cancer (Table 1).

The mean surgery-anesthesia time for the group was  $5 \pm 1.8$  hours. The median postoperative intensive care unit stay was 2.4 days, and the median hospital length of stay was 7 days. The decreased hospital length of stay has been attributed to the

adoption of interventions suggested by the ERAS protocol<sup>3</sup> and the ACERTO program<sup>4</sup>, in addition to new protocols developed within the center, such as the use of intraperitoneal ropivacaine and the antibiotics metronidazole and gentamicin.

Two (5.4%) surgery-related deaths occurred in 30 days, and four (10.8%) additional deaths within 90 days, caused by severe clinical complications or progression of the underlying cancer. These outcomes are similar to those reported by international reference centers<sup>5,6</sup>.

After enrollment in OC-UPE, all patients were followed by a multidisciplinary team from the preoperative period through late postoperative care. After three years of the CRS/HIPEC program, the initiative can be considered successful, currently providing care to patients from the state of Pernambuco and neighboring states who lack access to this surgery.



**Figure 1.** Patient being prepared for CSR/HIPEC surgery.

## EXPERIENCE REPORT

**Table 1.** Characteristics of patients followed by the CSR/HIPEC program of the Oncological Surgery Service at the Hospital Universitário Oswaldo Cruz, Pernambuco, Brazil, from 2015 to 2018.

Characteristics of patients	Frequency		Mean	Standard deviation	Median (minimum and maximum)
	Absolute	Relative			
Sex	(n)	(%)			
Female	32	86.4	-	-	-
Male	05	13.6	-	-	-
Type of cancer					
Stage III-C ovarian cancer	16	50.0	-	-	-
Appendix cancer or Pseudomyxoma Peritonei	17	81.0	-	-	-
Peritoneal mesothelioma	02	9.5	-	-	-
Gastric cancer	01	4.7	-	-	-
Colorectal cancer	01	4.7	-	-	-
Surgical-anesthetic times (hours)	-	-	5	1.8	-
Intensive care unit stay (days)	-	-	-	-	2 (1–37)
Hospital length of stay (days)	-	-	-	-	7 (4–37)
Surgical complications					
Grade I. II	8	29.6	-	-	-
Grade III	2	7.4	-	-	-
Postoperative death (days)					
30	2	5.4	-	-	-
90	4	10.8	-	-	-

**Source:** The authors.

**Legend:** CCR/HIPEC: cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. n: number of patients. ICU: intensive care unit.

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# ANATOMIC STUDY OF THE DISCOMALLEOLAR LIGAMENT: A TOPOGRAPHIC DESCRIPTIVE CONTRIBUTION FOR IMAGE CAPTURING

*ESTUDO ANATÔMICO DO LIGAMENTO DISCOMALEOLAR: CONTRIBUIÇÃO DESCRITIVA TOPOGRÁFICA PARA CAPTURA DE IMAGENS*

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## ABSTRACT

**Introduction:** The obtaining of reliable structures that form the temporomandibular joint (TMJ) images has always been a challenge for professionals who work in the study and treatment of the problems that affect this joint. **Objective:** Since the discomalleolus ligament can promote a union between a temporomandibular joint and the middle ear, and that auditory disorders are usually related to the temporomandibular disorders, which makes it difficult to diagnose it, this study proposes anatomically an orientation for identification of the ligament for the guidance control to capture images of the discomalleolus ligament in the petrotympanic fissure. **Methods:** Subsidized by cadaveric dissection a measurement of planes through sections in dry skull through the formation of a three-dimensional prototype was performed. The study had the release from the anatomy department from the Federal University of Pernambuco. **Conclusion:** The guidelines generated from the topographic-anatomical study are effective in determining the discomalleolus ligament in radiological images.

**Keywords:** Temporomandibular Joint; Dysfunction Syndrome Temporomandibular; Middle Ear; Radiology

## RESUMO

**Introdução:** A obtenção de imagens confiáveis das estruturas que formam a articulação temporomandibular sempre foi um desafio para os profissionais que trabalham no estudo e tratamento dos problemas que acometem essa articulação. **Objetivo:** Tendo em vista que o ligamento discomaleolar pode promover a união entre a articulação temporomandibular e a orelha média, e que distúrbios auditivos geralmente estão relacionados aos quadros de disfunções temporomandibulares promovendo dificuldade em diagnosticá-la, este estudo concerne em propor anatomicamente, uma orientação para identificação do ligamento que servirá de orientação para captura de imagens do ligamento discomaleolar na fissura petrotimpânica. **Métodos:** Subsidiada por dissecação cadavérica, a mensuração de planos através de secções em crânio seco através da formação de um protótipo tridimensional foi obtida. O estudo teve liberação do Departamento de Anatomia da Universidade Federal de Pernambuco. **Conclusão:** As linhas de orientação geradas a partir do estudo anatômico-topográfico são eficazes na determinação do ligamento discomaleolar em imagens radiológicas.

**Palavras-chaves:** Articulação Temporomandibular; Síndrome da disfunção temporomandibular; Orelha média; Radiologia

## INTRODUCTION

In dental radiology, image interpretation is based on anatomical knowledge of the bones and adjacent soft tissues of the maxilla and mandible. Anatomical dissections of human cadavers verified a specific relationship between the temporomandibular joint (TMJ) capsule, articular disc, sphenomandi-

bular ligament, and middle ear, a connection formed by the discomalleolar (DML) and anterior malleolar ligaments that join the malleus<sup>1,2</sup>.

A temporomandibular disorder may change the position of the ossicles and the tympanic membrane through joint movements, causing hearing loss and related non-otological aural symptoms<sup>1-3</sup>.

## **ANATOMICAL-TOPOGRAPHIC STUDY**

The development of the TMJ and middle ear in humans is complex and still controversial<sup>4-7,9-13</sup>.

The DML is an embryonic remnant of the lateral pterygoid muscle<sup>11</sup>. Although its existence has been demonstrated, it is not mentioned in anatomy textbooks. Several authors have described it as a fibroelastic structure, inserted into the anterior process of the malleus and lateral to the chorda tympani nerve, which establishes an anatomical relationship between the TMJ, the middle ear, and Huguier's canal<sup>2,12,13</sup>.

The most frequent signs and symptoms presented by patients with TMD are pain in the masticatory muscles and TMJ, cervical pain, noises during mandibular movements, limitations or asymmetries in these movements, otological symptoms, fracture of restorations, and dental sensitivity. Auditory symptoms can be related to TMD or other auditory diseases, which confirms the possible coexistence of auditory impairments and highlights the need to define audiological conditions in TMD<sup>8,9</sup>. A study described that the movement of the capsular ligament and disc oscillated the tympanic membrane and the middle ear ossicular chain, which can generate otological symptoms related to TMD<sup>2</sup>.

Obtaining reliable images of the structures that form the TMJ has always been a challenge for specialists. Anatomical characteristics and the overlapping of adjacent structures are the primary causes of difficulties in clear visualization, which hinder diagnosis<sup>14</sup>.

Radiological examinations of the TMJ are intended to identify or confirm morphological or functional anomalies, provide diagnostic information for disc structures, and prevent inadequate treatments<sup>14,15</sup>.

Since the DML links the TMJ to the middle ear, and auditory disorders are often related to difficult-to-diagnose TMD, this study proposed a three-dimensional boundary to identify the location of the DML via imaging examinations.

## **METHODS**

The study was conducted at the Department of Anatomy of the Federal University of Pernambuco (UFPE) and was divided into two stages. The first stage involved cadaveric dissection to identify the DML.

A suitable cadaveric specimen containing the

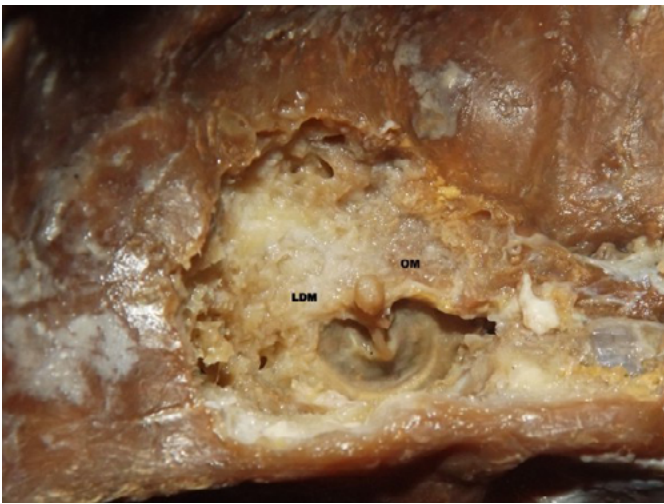
superficial and deep tissue layers arranged by anatomical planes was selected from the anatomy department collection. To visualize the DML in the tympanic cavity, an osteotomy was performed on the anterior wall of the petrous part of the temporal bone, and the superior wall of the tympanic cavity was removed to expose the malleus and the DML (Figure 1).

In the TMJ cavity, a retroauricular dissection of the superficial and deep layers of the TMJ was performed to visualize the neck of the mandibular condyle. Then, the condyle was sectioned for lateral rotation to expose the posterior part of the articular capsule, and the DML was visualized (Figure 2).

In the second stage, a cadaveric bone specimen was selected, and lines were traced to delimit the DML region, creating a three-dimensional plane as a reference for image acquisition, followed by the resection of the three-dimensional block.

## **RESULTS**

A topographical study was conducted on a dry skull to identify measurement planes and delimit the region containing the DML. In the anteroposterior position, a line was drawn from the inferior border of the maxillary process of the zygomatic bone to the mastoid process (L1), and another from the superomedial border of the infraorbital foramen to the base of the sphenoidal spine (L2) (Figure 3). In the lateromedial position, a line was drawn from the center of the articular eminence of the zygomatic bone to L2 (L3), and another connecting the anterior border of the mastoid process of the temporal bone to the extension of L2 (L4) (Figure 4). To measure height, a line from the zygomatic crest of the maxillary bone to the inferior border of the external acoustic meatus served as the inferior limit (L5), while an imaginary line passing transversely through the frontozygomatic suture, parallel to Camper's plane, served as the superior limit (L6) (Figure 5). This process created a three-dimensional plane used as a reference to delimit an area containing the petrotympanic fissure and the potential location of the DML (Figure 6).



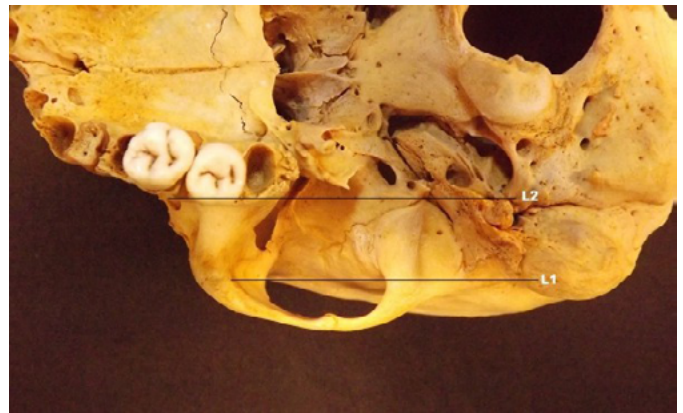
**Figure 1.** View of the MDL and the malleus bone.



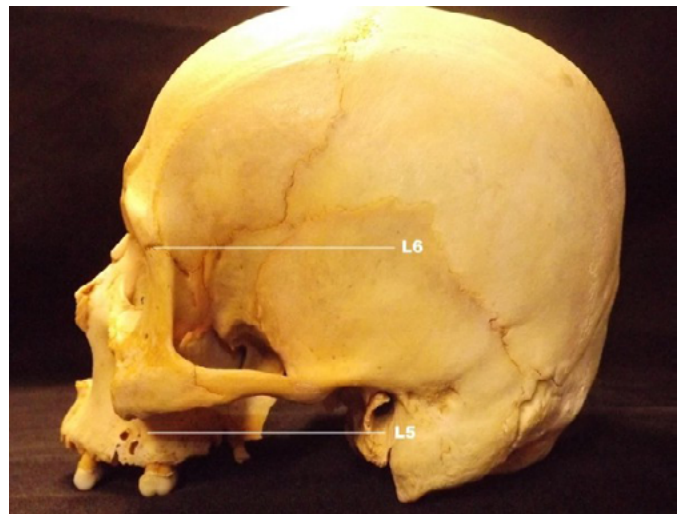
**Figure 2.** View of the DML.



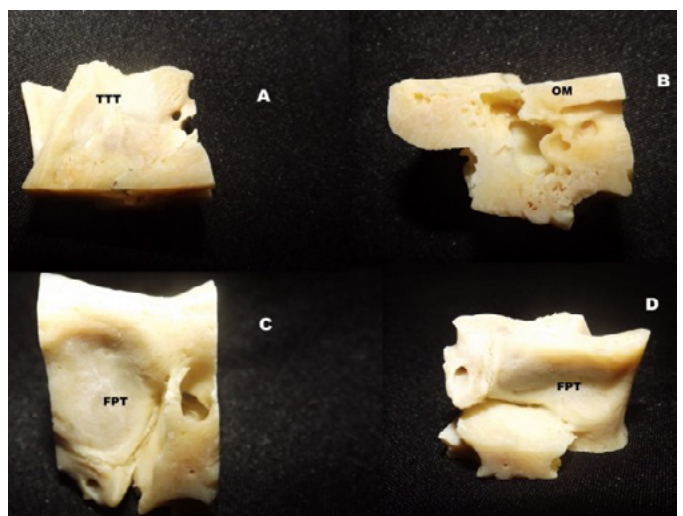
**Figure 3.** Line from the inferior border of the maxillary process of the zygomatic bone to the mastoid process (L1) and a line from the superomedial border of the infraorbital foramen to the base of the sphenoidal spine (L2).



**Figure 4.** Line (L3) from the center of the articular eminence of the zygomatic bone to L2, and another line (L4) that connects the anterior border of the mastoid process of the temporal bone to the extension of L2.



**Figure 5.** Line from the zygomatic crest of the maxillary bone to the inferior border of the external acoustic meatus (L5), and an imaginary line (L6) passing transversely through the frontozygomatic suture, parallel to Camper's plane.



**Figure 6.** A: tegmen tympani (TTT) - superior view; B: Middle ear (ME) - posterior view; C: petrotympanic fissure (PTF) - lateral view; D: petrotympanic fissure (PTF) - inferior view.

**COMMENTARY**

Several authors describe the DML extending posteriorly from the TMJ disc and capsule, passing through the petrotympanic fissure, and joining the malleus. The findings showed that the DML inserts into the posterior portion of the disc and articular capsule, originating from the anterior region of the malleus and passing through the petrotympanic fissure, corroborating the literature<sup>2,7</sup>.

Dissections have shown that the anterior malleolar ligament is present in the petrotympanic fissure<sup>12</sup>. Another study describes the DML as originating in the tympanic cavity and extending toward the lateral portion of the tympanic fissure<sup>13</sup>. Through the study of a dry skull and the measurement of the planes bordering this fissure, an image for the visualization of the DML may be created.

Detailed dissections of postmortem specimens using a superior approach through the middle cranial fossa, rather than the classic lateral approach, have been described<sup>2</sup>. In these dissections, the tissue was limited posteriorly by an imaginary line between the internal and external auditory meati, medially by a line between the internal auditory canal and the foramen ovale, anteriorly by a straight line passing mediolaterally through the foramen ovale perpendicular to the anterior line, and laterally by another straight line from the external acoustic meatus joining the anterior line. This imaginary rectangle formed within the middle cranial fossa contains part of the middle ear, the TMJ, and related structures. The floor of the middle cranial fossa and the roof of the tympanic cavity were carefully removed to expose the TMD meniscus, the chorda tympani nerve, middle ear ossicles, the external pterygoid muscle, tympanic membrane, auditory tube, and other structures in the region<sup>2</sup>. In the cadaveric dissection, a petrous approach was chosen to observe the structures of the middle ear and TMJ, enabling visualization of the DML, the capsule and meniscus of the TMJ, and the malleus bone.

In the topographical study using a dry skull and cadaveric dissection, a three-dimensional bone structure containing the petrotympanic fissure, the passage site of the ligament, was delimited. The tracings resulted in a region defined by an anterior coronal section at the geometric center of the articular eminence of the mandibular condyle and a posterior coronal section tangent to the lateromedial depth of the auditory canal. The region was also delimited by

two transverse sections: one tangent to the superior border of the petrous temporal bone, and the other tangent to the neck of the mandibular condyle. This bone block was created to guide the sections used for image acquisition and to capture the DML path from the middle ear to the posterosuperomedial border of the TMJ articular capsule.

**CONCLUSION**

This study proposed that the DML may be identified in imaging examinations by a three-dimensional plane, containing the petrotympanic fissure, formed by tracing lines L1, L2, L3, L4, L5, and L6.

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# MANAGEMENT OF UNCOMPLICATED ACUTE APPENDICITIS IN CHILDREN: REVIEW OF EVIDENCE PUBLISHED IN 2017-2018

MANUSEIO DE APENDICITE AGUDA NÃO COMPLICADA EM CRIANÇAS:  
REVISÃO DA EVIDÊNCIA PUBLICADA EM 2017-2018

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## ABSTRACT

**Objective:** To review and disseminate evidence from 2017 and 2018 on the use of nonoperative treatment for children with uncomplicated acute appendicitis. **Methods:** A literature search for 2017 and 2018 was performed using the following descriptors: uncomplicated acute appendicitis, children, pediatric appendicitis, management, medical treatment, clinical treatment, antibiotic treatment, nonoperative treatment, surgical treatment, and appendectomy. Randomized controlled trials were prioritized. **Results:** Nonoperative treatment for uncomplicated acute appendicitis in children presents similar outcomes for length of hospital stay, duration of antibiotic, pain intensity and duration, and perioperative complication rates; however, it may lead to higher rates of readmissions undetected diseases compared to surgical treatment. Nonetheless, this approach reduces the rate of negative appendectomy and sick leave days, speeds the return to school and daily activities, and reduce hospital costs and risk of long-term complications. **Conclusion:** Antibiotic therapy is a safe first-line option for children with uncomplicated acute appendicitis, and randomized controlled trial should be performed in tertiary hospitals in Brazil. Patients requiring future appendectomy do not experience significant complications. A multicenter Brazilian trial comparing antibiotic therapy with appendectomy, including outpatient treatment, should be conducted to assess the efficacy and safety of this strategy.

**Keywords:** Uncomplicated acute appendicitis; Children; Medical treatment; Antibiotics treatment; Appendectomy.

## RESUMO

**Objetivo:** Revisar a evidência existente em 2017-2018 e divulgar informações, com base científica sólida, no que se refere ao tratamento clínico para crianças com apendicite aguda sem complicações. **Métodos:** Foi realizada pesquisa de literatura para os anos 2017/2018 utilizando os seguintes descritores: apendicite aguda sem complicações, crianças, apendicite pediátrica, tratamento, tratamento médico, tratamento clínico, tratamento com antibiótico, tratamento não cirúrgico e tratamento cirúrgico, apendicectomia. Os ensaios controlados randomizados constituíram a melhor fonte de informação. **Resultados:** Na literatura revisada, pode-se dizer que a abordagem clínica para a apendicite aguda sem complicações em crianças apresenta resultados semelhantes quanto a permanência hospitalar, dias de antibioticoterapia, menor intensidade e duração da dor e taxas de complicações primárias perioperatórias, podendo haver mais readmissões para pacientes internados e outras doenças concomitantes quando comparadas com o tratamento cirúrgico. No entanto, esta nova abordagem (tratamento clínico) reduz a taxa de apendicectomia negativa, abrevia o tempo de licença por doença e cuidados médicos, promove o retorno mais breve da criança à escola e outras atividades normais, diminui o custo hospitalar e complicações à longo prazo. **Conclusão:** O tratamento com antibióticos isoladamente parece ser terapia segura de primeira linha em crianças selecionadas com apendicite aguda sem complicações e merece estudo randomizado controlado em hospitais terciários no Brasil. Aqueles pacientes que necessitarem de apendicectomia no futuro não apresentarão complicações significativas. Estudo multicêntrico brasileiro que compare o tratamento inicial com antibióticos versus apendicectomia, incluindo abordagem ao nível ambulatorial, deverá ser realizado para avaliar a eficácia e a segurança desta nova abordagem.

**Palavras-chave:** Apendicite aguda não complicada; Criança; Tratamento médico; Tratamento com antibióticos; Apendicectomia.

## INTRODUCTION

Nonoperative treatment for appendicitis has a success rate exceeding 85%, with supporting evidence emerging over the past decade. In such cases, cost-effectiveness supports the clinical approach, as the length of hospital stay is comparable to that of surgical treatment, and complications are generally fewer. However, recurrence of appendicitis occurs in approximately 4% to 20% of patients at long-term follow-up. Overall failure of nonoperative treatment, including early failure and recurrence, occurred more frequently among patients with appendicoliths than without appendicoliths and in those with misdiagnosis of uncomplicated appendicitis. A normal appendix is found in approximately 15% of children undergoing surgery. Patient satisfaction is slightly higher with surgical treatment<sup>1-15</sup>. Early appendectomy is more cost-effective among children with perforated appendicitis<sup>16</sup>.

Currently, laparoscopic appendectomy remains the preferred choice among pediatric surgeons<sup>17,18</sup>. This procedure can be performed safely in adults, even on an outpatient treatment, making it more attractive than seeking what remains a hypothetical treatment approach in tertiary hospitals of developed countries<sup>18-20</sup>.

Despite evidence supporting the feasibility of a randomized controlled trial, already conducted in some countries<sup>7,18,19</sup>, pediatric surgeons in Brazil are reluctant to offer antibiotic therapy for children with uncomplicated acute appendicitis, even in selected cases, when proposing options to parents. The choice for antibiotics and a critical analysis of the cost-benefit can be barriers to changing the traditional paradigm<sup>21</sup>. Thus, this study aimed to review and disseminate the evidence on the use of nonoperative treatment for children with appendicitis.

## METHODS

A literature search covering the years 2017 and 2018 was performed using the following descriptors: uncomplicated acute appendicitis, children, pediatric appendicitis, management, medical treatment, clinical treatment, antibiotics treatment, nonoperative treatment, surgical treatment, and appendectomy. Inclusion criteria were randomized controlled trials and cohort studies involving children treated

nonoperatively for uncomplicated appendicitis, with a minimum follow-up of one year. Two authors independently extracted data and assessed quality. Primary outcome was the percentage of children experiencing complications after treatment. Secondary outcomes were early failures, recurrent appendicitis and appendectomies, and length of hospital stay. The null hypothesis was that clinical outcomes, length of hospital stay, and hospital readmission rates would be unchanged after clinical and surgical treatments.

## RESULTS

Twenty-two studies were included. Regarding perioperative outcomes, survival rates and major complications were similar between surgical and nonoperative treatments. Length of hospital stay was longer in the antibiotic therapy compared with surgical treatment; however, this had been predefined in the protocols to allow closer monitoring of children and ensure patient safety. Since none of the children initially treated with antibiotics who later required appendectomy experienced serious complications, the length of hospital stay related to antibiotic therapy may be reduced. A disadvantage of antibiotic therapy for acute appendicitis is the possible bias introduced by spontaneously resolved cases of appendicitis in children.

Decreased hospital charges were observed in children with uncomplicated acute appendicitis who received only antibiotics<sup>19</sup>.

Same-day discharge for uncomplicated appendicitis was safe and feasible with laparoscopy, with the potential for significant healthcare cost savings<sup>21</sup>.

## DISCUSSION

Robust evidence supports antibiotics over surgery for treating children with uncomplicated acute appendicitis. Although non-inferiority of antibiotic therapy over appendectomy was demonstrated, approximately 75% of children with uncomplicated acute appendicitis can be successfully treated with only antibiotics. Moreover, long-term side effects of this approach are significantly lower than surgery. On the other hand, intraluminal appendicoliths may predict failure of nonoperative treatment and progression to complicated acute appendicitis in children and adults.

Appropriate clinical practice, along with adequate laboratory and ultrasound examinations for

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children with suspected acute appendicitis, can improve patient care by reducing unnecessary surgery and promoting more efficient use of hospital resources. These are important outcomes for developing countries such as Brazil.

For successful antibiotic therapy, it must provide broad coverage against all potential pathogens causing appendicitis. To overcome this limitation, agents such as ertapenem, ceftriaxone combined with metronidazole, or cefoxitin offer broad spectrum activity and advantage of once daily dosing, making them effective options for serious intra-abdominal infections, including appendicitis<sup>20</sup>. Future studies on antibiotic therapy for appendicitis should demonstrate efficacy while employing agents with a narrower antibacterial spectrum. Currently, ceftriaxone plus metronidazole represents a streamlined and cost-effective regimen for the treatment of non-perforated, perforated, and abscessed appendicitis in children.

Relapses can occur during life, which supports early surgical intervention to prevent complications and unnecessary costs. However, our hypothesis was that most children treated with only antibiotics would not experience recurrence in the following years.

Data interpretation is crucial in this type of review. For example, the one-year recurrence rate of appendicitis after antibiotic therapy was reported as 22.6%, which is a compelling finding. Additionally, the risk of undetected diseases in this group is a concern<sup>15</sup>.

Overall, nonoperative treatment for uncomplicated acute appendicitis in children yields similar outcomes in terms of length of hospital stay, duration of antibiotics, pain intensity and duration, and perioperative complication rates. However, this strategy may be associated with higher rates of readmissions and undetected diagnoses. Nonetheless, this approach reduces the rate of negative appendectomy and sick leave days, speeds the return to school and daily activities, and reduces hospital costs and long-term complications<sup>8</sup>. Double-blind randomized controlled trials are needed to differentiate these effects<sup>22</sup>.

If a surgical resident trainee is asked about the best option for treating children with uncomplicated acute appendicitis, the unquestionable answer would

be surgical treatment combined with perioperative antibiotics<sup>11</sup>. This view is also shared by most pediatric surgeons in Brazil.

This review complements the literature on the comparison between antibiotic therapy and surgical treatment for uncomplicated acute appendicitis in children, emphasizing the need for unbiased interpretations and proper use of available evidence.

Finally, pediatric surgeons must determine the best strategy for each patient with uncomplicated acute appendicitis, using evidence, clinical judgment, and available resources. The decision should prioritize patient safety and incorporate shared decision-making between surgeon, patient, and family<sup>14</sup>.

## CONCLUSION

Antibiotic therapy is a safe first-line option for children with uncomplicated acute appendicitis, and randomized controlled trials in tertiary hospitals in Brazil should be implemented. Patients requiring future appendectomy generally do not experience significant complications. A multicenter Brazilian trial comparing antibiotic therapy with appendectomy, including outpatient management, is feasible to assess the efficacy and safety of this strategy.

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# FEASIBILITY OF NILE TILAPIA (*OREOCHROMIS NILOTICUS*) SKIN AS A BIOLOGICAL DRESSING FOR BURN TREATMENT: A LITERATURE REVIEW

VIABILIDADE DA PELE DE TILÁPIA DO NILO (*OREOCHROMIS NILOTICUS*) COMO CURATIVO BIOLÓGICO NO TRATAMENTO DE QUEIMADURAS: REVISÃO DA LITERATURA

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## ABSTRACT

The use of biological occlusive dressings should prevent hydroelectrolytic losses, prevent bacterial contamination, promote epithelization or assist in the formation of granulation tissue for grafting. Recent studies point to the use of biological dressing based on aquatic animals as biomaterial in regenerative medicine. It is reviewed the state of the art of using Nile Tilapia (*Oreochromis niloticus*) as a biological dressing in the treatment of burns. Comparative researches between human skin and Nile Tilapia show favorable results regarding histological, histochemical, tensiometric and handling properties related to the characteristics of this material.

**Keywords:** *Oreochromis niloticus*. Nile Tilapia. Burns. Occlusive dressings.

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## RESUMO

O uso de curativos oclusivos biológicos deve prevenir as perdas hidroeletrólíticas, evitar a contaminação bacteriana, promover a epitelação ou auxiliar na formação do tecido de granulação para enxertia. Estudos recentes apontam a utilização de curativo biológico com base em animais aquáticos como biomaterial na medicina regenerativa. Neste artigo, é feita uma revisão bibliográfica, descrevendo o estado da arte do uso da pele da Tilápia do Nilo (*Oreochromis niloticus*) como curativo biológico no tratamento de queimaduras. Pesquisas comparativas entre a pele humana e a da Tilápia do Nilo comprovam resultados favoráveis quanto aos aspectos histológicos, histoquímicos, propriedades tensiométricas e manuseio relacionados às características desse material.

**Palavras-chave:** Tilápia do Nilo; *Oreochromis niloticus*; Queimadura; Curativo biológico

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## INTRODUCTION

The Brazilian Society of Burns defines burns as traumatic injuries often caused by thermal, chemical, electrical, or radioactive agents. These injuries affect organic tissues and may trigger systemic responses proportional to their extent and depth.

Management of second- and third-degree burns requires an interdisciplinary approach, encompassing fluid resuscitation, enteral nutritional support, analgesia, and antibiotic therapy. Dressings also play a crucial role in the surgical management of burn injuries.

Biological dressings prevent hydroelectrolytic loss, reduce bacterial contamination, and promote epithelialization or facilitate granulation tissue for-

mation for grafting. Animal-derived biological tissues, including porcine or frog skin, bovine pericardium, and porcine intestinal submucosa, are used for dressings<sup>1</sup>.

Recent studies have explored the use of Nile Tilapia (*Oreochromis niloticus*) skin, an aquatic animal-derived biological dressing, as a biomaterial in regenerative medicine, demonstrating good adherence to wounds in experimental rat models<sup>1,2</sup>. Comparative analyses with human skin showed favorable biological behavior regarding histological, histochemical, and tensile properties<sup>2</sup>.

Each year, about one million people suffer burn injuries in Brazil, and the Unified Health System allocates around 55 million reais annually for their treatment<sup>3</sup>.

Tilapia skin is typically discarded as waste, with only 1% used in handicrafts. The durability and sensitivity of tilapia skin for accessory production have prompted researchers to investigate its potential as a substitute for human skin in burn treatment.

According to the Brazilian Agricultural Research Corporation, tilapia accounts for 45.4% of the total fish production in Brazil, representing 68,000 tons. Between 2005 and 2015, the production increased by 223%, highlighting the abundance of this raw material<sup>4</sup>.

This literature review aimed to describe the current research on using Nile Tilapia skin as a biological dressing in burn treatment.

## METHODS

The present study is a narrative, exploratory, and secondary literature review. The bibliographic search was conducted using national and international indexed journals. Relevant literature was identified using the Virtual Health Library, a database aggregator.

The search strategy included the descriptors “queimaduras,” “curativos,” and “Tilápia do Nilo” from the Health Sciences Descriptors to broaden the identification of studies addressing the topic. Selected studies were critically evaluated for their direct relevance to the theme.

The present review did not follow a chronological order of publication. Instead, it presents a logical and coherent synthesis and integrates perspectives from different authors to enhance understanding of the theme.

## COMMENTS

Burn injuries represent a significant public health challenge, and their physical, psychological, and social consequences affect the patient and their family. Awareness campaigns and educational programs grounded in epidemiological principles should be integrated into public health policy<sup>3,5</sup>.

In Brazil, of the one million annual burn victims, about 10% require hospital care; most belong to low-income populations and rely on public healthcare services<sup>1,6</sup>.

Burn treatment is costly and involves prolonged rehabilitation, primarily affecting children and young adults, with a mean age between 25 and 26 years. Among younger individuals, alcohol is the

leading etiological agent, and the upper limbs are the most affected body region<sup>1,5</sup>.

Burn incidents in economically active individuals aged 20 to 30 often occur in the workplace, particularly during activities involving high-voltage electricity<sup>7</sup>.

At the tissue level, burns trigger a cascade of physiological responses aimed at restoring integrity. This process begins with acute inflammation, followed by cellular regeneration and tissue remodeling, culminating in the recovery of tensile strength. Effective wound management requires a multidisciplinary team within a hospital.

Various occlusive dressings are available, including silver-based dressings, hydrogels, and others<sup>8</sup>.

Silver dressings may accelerate healing, possess antimicrobial properties, and promote faster reepithelialization. Hydrogels have bactericidal effects, enhance wound healing, and reduce the risk of hypertrophic scarring, which improves aesthetic and functional outcomes. Their high moisture content also contributes to pain reduction by creating an optimal environment for tissue repair<sup>8</sup>.

The other dressings include foam, moist, petrolatum gel-based, and skin substitutes, which contribute to reduced healing time. Foam dressings are recommended for joint areas due to their flexibility and support for mobility. The moist environment accelerates reepithelialization. Petrolatum gel-based dressings are indicated for superficial partial-thickness burns<sup>8</sup>.

Although research indicates that an ideal temporary skin substitute has yet to be developed, biological skin alternatives have shown promising aesthetic results in the treatment<sup>1,8</sup>. However, they must undergo rigorous scientific validation to assess their biological behavior in human applications.

Human and animal-derived biological materials require thorough evaluation to ensure efficacy and biocompatibility as burn dressings. Studies comparing human skin with Nile Tilapia skin have demonstrated favorable results regarding histological and histochemical properties, tensile strength, and handling characteristics<sup>1,2,8</sup>.

Tilapia skin exhibits morphological similarities to human skin, including compact, long, and organized collagen bundles, as well as a predominance of type I collagen. These characteristics provide sa-

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tisfactory elasticity and facilitate surgical manipulation<sup>1,9-11</sup>.

Burn management involves local and systemic care, depending on the depth, location, and extent of the injury<sup>8</sup>. Burned skin is highly susceptible to contamination, and biological dressings must possess antimicrobial properties to prevent infection.

Animal skin may harbor microorganisms with pathogenic potential, necessitating strict disinfection and sterilization protocols that preserve its microscopic and mechanical properties. Recent research supports the effectiveness of chemical and radiation sterilization methods in preparing Nile Tilapia skin for clinical use<sup>10</sup>.

In private burn treatment centers, biosynthetic and artificial skin substitutes are commonly used, but they are expensive. In contrast, public healthcare centers typically employ sequential debridement, topical antimicrobials, and wound bed preparation for skin grafting<sup>1,2,6</sup>.

Conventional burn treatment using antimicrobial creams or ointments often causes discomfort and pain during dressing changes. Daily dressing replacement requires the complete removal of the ointment, causing pain and delaying healing.

Tilapia skin dressings provide wound protection and reduce the need for frequent dressing changes, as they remain in place until complete healing.

A comparative analysis of analgesic use in patients treated with silver sulfadiazine versus Tilapia skin showed reduced pain and decreased analgesic requirements in 20 patients at a burn center in Fortaleza<sup>12</sup>. These findings underscore the importance of pain management in burn care, a key goal for all healthcare professionals involved in the treatment.

A holistic approach to burn patient care should prioritize comfort and quality of life. Humanized care and the accessibility of Tilapia skin reflect on treatment costs.

The skin adherence to the wound bed further supports patient comfort. This treatment prevents external contamination and fluid loss, and the patient remains in place until complete healing, as demonstrated in a 2016 study conducted at the Dr. José Frota Institute<sup>6</sup>.

Tilapia skin used for dressings is prepared by the Drug Research and Development Center at the Federal University of Ceará, where it undergoes cleaning, cutting, and sterilization. Additional irra-

diation is performed at the Nuclear and Energy Research Institute in São Paulo<sup>1,6</sup>.

Each fish yields two skins measuring 15 cm by 5 cm, and the amount required depends on the wound size. Given the substantial Tilapia production in Brazil, its use in medical applications is feasible, provided that industrial-scale processing is implemented for broader social benefit.

Several medical specialties have begun exploring the use of Tilapia skin beyond burn treatment, including urology, dentistry, and gynecology<sup>6</sup>.

## CONCLUSION

Ongoing research efforts<sup>1,2,6</sup> continue to support the widespread adoption of Nile Tilapia skin as an innovative, safe, domestically sourced, and cost-effective dressing for burn patients, coming as an ideal wound care solution.

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**AUTHOR GUIDELINES**

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**SCOPE**

The Journal Annals of Olinda Medical School reflects the thinking and commitment to the production of knowledge based on the social responsibility that we assume as protagonists, and as part of the Institutional Development Project of the Faculdade de Medicina de Olinda (FMO). Aiming to strengthen the inseparability of teaching, research and extension, in addition to consolidating quality education, anchored in scientific bases and ethical values, the journal was created in light of an editorial line committed to a sustainable world and focused on medicine as a profession with a strong social and humanized component.

**The Journal Annals of Olinda Medical School - Health Social Responsibility**, was created in 2018. Since then, it has been the official vehicle of the Olinda School of Medicine to support its principles, especially those related to encouraging research, teaching, and professional medical practices. It is an important instrument for disseminating knowledge, allowing exchange with other areas that favor medicine and the community, and enabling improvement of the standard care provided to the population. Since its inception, Anais FMO has faithfully complied with the requirements for biannual online and printed periodicity for scientific publication, following the recommendations of the International Committee of Medical Journal Editors ([www.icmje.org](http://www.icmje.org)), which are commonly used in the areas of medicine and related sciences. Currently, Anais FMO is duly registered as a journal in the ISSN system. Articles are published in a continuous flow and all are free and open access, offered through the link <https://afmo.emnuvens.com.br>. By publishing their article in Anais FMO, authors transfer copyright to the journal and grant it the right of first publication. Manuscripts are submitted online through the platform, available at <https://afmo.emnuvens.com.br/afmo/about/submissions>.

**POLICIES OF THE JOURNAL ANNALS OF OLINDA MEDICAL SCHOOL****Research Ethics Committee Approval**

All publications submitted to the Annals of Olinda Medical School must have followed the research ethics recommendations of the Declaration of Helsinki and the standards of Resolution no. 466/2012 (<http://conselho.saude.gov.br/resolucoes/2012/Reso466.pdf>) and Resolution no. 510/2016 (<http://conselho.saude.gov.br/resolucoes/2016/Reso510.pdf>) of Brazilian National Health Council. Studies that analyze aggregated data without identifying participants, such as those available in official databases in the public domain are exempt from research ethics committee approval.

Following the guidance of the National Research Ethics Commission, National Health Council, Ministry of Health (CONEP/CNS/MS), no institution is superior to the research ethics committee to analyze the nature of research proposals. The research ethics committee that approves the research must be registered with CONEP.

Research ethics committee must also approve case reports, following the provision no. 166/2018, of the Research Ethics Committee/ CONEP/CNS, (<http://conselho.saude.gov.br/images/comissoes/conep/documentos/CARTAS/CartaCircular166.pdf>).

Case reports involving cadaveric parts must also have a research ethics committee approval. Reports that use parts from cadavers destined for medical schools or similar areas for teaching and research purposes, in addition to ethical approval, must have authorization from the responsible institution to conduct the research.

It is mandatory to send a copy of the research ethics committee approval before submission.

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Annals of Olinda Medical Schools recognizes that peer review is important in the publication process.

Therefore, we analyze the submitted manuscripts with ethics and maximum scientific rigor, following the steps below:

Every manuscript received is analyzed for suitability to the scope of the journal, its contribution to knowledge advancement, its originality, the methodological rigor with which the study was conducted, and the adequacy of the conclusions in relation to the results presented. In addition, the formatting is evaluated according to the standards of the journal. If any inaccuracy is identified, the manuscript is returned to the corresponding author, indicating the necessary adjustment. Only manuscripts that meet all the criteria described in the "Author Guidelines" undergo peer review.

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The editorial decision is made based on the comments from the reviewers. It may follow one of the following outcomes: (1) rejection, (2) new submission chance by addressing the comments received, or (3) approval with or without changes.

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The final editorial decision is recorded and is the responsibility of the editorial board. The manuscript content is the sole responsibility of the authors.

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**Original article:** a full paper of a clinical or experimental investigation with unpublished research results (limit of 3,400 words, seven authors, and 30 references).

**Integrative, systematic review, and meta-analysis:** they should address topics of interest in health. Narrative reviews will not be accepted. Authors must include the study motivation in the Introduc-

tion. Summary and abstract must be formatted as a single paragraph in a block format with up to 250 words (limit of 3,400 words, seven authors, and 45 references).

**Short Communication:** short communication of original research results. In general, short communications are leaner analyses with a brief discussion of the results (summary and abstract must be formatted as a single paragraph in a block format with up to 120 words; the manuscript must be up to 1,000 words with Introduction, Methods, Results, and Discussion sections; up to two tables/figures can be included in up to three pages combined; references are limited to six).

**Case reports:** description of clinical cases of interest due to their rarity, presentation, innovative diagnosis, or treatment (summary and abstract must be formatted as a single paragraph in a block format with up to 120 words; the manuscript must be up to 2,000 words with Introduction, Case Report, and Discussion sections; up to two tables/figures can be included in up to three pages combined; references are limited to fifteen; limit of seven authors).

**Experience reports:** detailed description of a successful or unsuccessful experience of an author or a team, which contributes to the discussion, exchange, and proposition of ideas for improving health care. It must include an introduction with a theoretical framework for the experience, objectives of the experience, methodologies used (including a description of the context and procedures), results, and final considerations. Summary and abstract must be formatted as a single paragraph in a block format with up to 120 words; the manuscript must have up to 2,000 words and up to two tables/figures; limit of 15 references and seven authors).

**Methodological paper and theoretical/technical essays:** manuscripts that deal with techniques or theories used in epidemiological studies or that portray an original clinical observation or description of technical innovations. Manuscript should be concise, limited to 1,500 words, five references, two illustrations, four authors, summary and abstract in must be formatted as a single paragraph in a block format with up to 120 words.

**Critical review:** restricted to a book or film in the medical field and related sciences. Argumentative manuscript in which the author describes and analyzes a social production aiming to influence his readers by recommending the work for its qualities

## INSTRUCTION TO AUTHORS

or rejecting it for its flaws. It must be presented as follows: (1) presentation - summary of the work analyzed with both technical information and information about the book or film content; (2) analysis – interpretation and analysis of the work highlighting its main points, whether positive or negative, and the critical analysis from the author; (3) conclusion - opinion on the work, resuming the main points analyzed (up to 1000 words and two authors);

**Letters to the Editor:** comments from readers on works published in the Annals of Olinda Medical School (500 to 700 words).

**Editorial:** It is the initial article of a volume and is generally requested by the Chief and Deputy Editors to guests with recognized technical and scientific skills.

The word count includes Introduction, Methods, Results, and Discussion (title page, summary, abstract, references, tables, and figures are not included in the word count).

Manuscripts submitted must be intended exclusively for the Annals of Olinda Medical School, and simultaneous submission to another journal is prohibited. The information and concepts presented in the manuscript, as well as the veracity of the research content, are the sole responsibilities of the author(s).

## FORMATTING

Manuscripts are accepted in Portuguese or English and must have an abstract in the original language of the manuscript and English. Manuscripts in English must have an abstract in English and Portuguese.

Manuscripts must be sent in Word, double-spaced, and Arial font size 12. Do not use line breaks. Do not use force manual hyphenations. The full term must follow abbreviations cited for the first time in the document. Title and abstract must not contain abbreviations.

## TITLE PAGE

**Title of the manuscript in Portuguese and English** (up to 25 words for each title);

**Author information** (full name, email, ORCID, affiliation, city, state, and country — do not include title and position);

**Indication of the corresponding author**, with their full address and email;

**Conflicts of interest**, in accordance with the Resolution of the Federal Council of Medicine (CFM) no. 1595/2000, which prohibits the publication of works for advertisement purposes of medical products and equipment, available at <https://sistemas.cfm.org.br/normas/visualizar/resolucoes/BR/2000/1595>. Conflicts of interest must be presented as follows: “The author(s) (name them) received financial support from the private company (mention its name) to conduct this study”. If there are no conflicts of interest, the authors must declare: “The authors have no conflicts of interest to declare”.

**Source of financing**, stating whether public or private; if there is none, mention that the study was not funded;

**Number of the Certificate of Presentation for Ethical Assessment (CAAE) or number of Research Ethics Committee approval;**

**Authors contribution to the manuscript.**

On the following pages, always starting on a new page, the following sections must be presented:

## SUMMARY AND ABSTRACT

Summaries must comply with the recommendations for each category of manuscript. In general, it must contain up to 250 words and be in structured format, covering the sections Objective, Methods, Results, and Conclusion. The same rule applies to the abstract.

Authors must include a minimum of four and a maximum of six keywords in both English and Portuguese regardless of the language in which the manuscript was submitted. The keywords must be standardized according to the Health Sciences Descriptors (DeCS), available at <http://decs.bvs.br/>.

## REFERENCES

References must be numbered consecutively according to the first mention in the manuscript and using superscript Arabic numerals in accordance with Vancouver style ([www.icmje.org](http://www.icmje.org)). The reference list must follow the numerical order of the manuscript, ignoring the alphabetical order of authors. Journal titles must follow the Index Medicus/ Medline. The name of the first six authors must appear, followed by the expression et al. when this number is exceeded. Whenever available, the Digital Object Identifier (DOI) must be provided (see examples below). Personal communications, unpu-

work, citations from books, thesis, and dissertations should be avoided. The accuracy of references is the responsibility of the authors.

## EXAMPLES

### Reference to a journal publication:

Ng OT, Marimuthu K, Koh V, Pang J, Linn KZ, Sun J, et al. SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study. *Lancet Infect Dis*. 2021 Mar; 21(3):333-343. doi: 10.1016/S1473-3099(20)30833-1

Jardim BC, Migowski A, Corrêa FM, Azevedo e Silva G. Covid-19 no Brasil em 2020: impacto nas mortes por câncer e doenças cardiovasculares. *Rev Saude Publica*. 2022; 56:22. <https://doi.org/10.11606/s1518-8787.2022056004040>.

### Reference to a World Health Organization Report

World Health Organization. Clinical Care for Severe Acute Respiratory Infection—Toolkit— Update 2022. Geneva: World Health Organization; 2022.

### Reference to electronic documents

Brasil. Casos de aids notificados no SINAN, declarados no SIM e registrados no SISCEL/SICLON, segundo capital de residência por ano de diagnóstico. Brasil, 1980-2021 [Internet]. 2021 [acessado em 12 abr. 2022]. Available at: <http://www2.aids.gov.br/cgi/deftohtml.exe?tab=net/br.def>

## FIGURES AND TABLES

Figures and tables must be inserted at the end of the manuscript, followed by their respective captions. Submission in separate files is not permitted. There must be page breaks between each one, respecting the maximum number of three pages for tables and figures combined. Do not format tables using the TAB key.

Figures must be up to 15 cm wide in Portrait orientation and 24 cm wide in landscape orientation and be presented within the requested margin (Normal Word setting). Colored figures are accepted. Figures must be provided in high resolution, plots in editable format, and tables, equations, charts, and flowcharts must be sent in an editable file (Word or Excel), never as an image.

published or on-going **CONTACT METHODS**



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