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JOURNAL OF MEDICAL RESIDENT RESEARCH

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1. Medical Residency I. Conselho Regional de Medicina do Estado de São Paulo
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JMRR
JOURNAL OF MEDICAL RESIDENT RESEARCH

GUIDE FOR AUTHORS

The **Journal of Medical Resident Research** (JMRR), previously called *Revista do Médico Residente* (RMR), is an official scientific publication of the Regional Council of Medicine of the State of São Paulo (Cremesp), focused on the publication of medical articles by medical scientists, who are at the begining of their careers. Its main objective is to disseminate medical-scientific knowledge, especially among doctors in training and residency programs.

To this end, contributions of this target audience in technical, ethical, bioethical and deontological articles are encouraged.

Each manuscript, in English and/or Portuguese, must clearly indicate an objective or hypothesis; the design and methods, including the characteristics of the institution where the research took place, criteria for the selection and exclusion of participants, and data sources; essential points of the interventions and analyses; main results of the study and its limitations; "discussion" section that interacts with the scientific literature; and conclusions.

Except when explicitly indicated, JMRR complies with rules and similar standards in the area, such as the Brazilian Federal Law Nº 6,932, of July 7, 1981, which provides for the activities of medical residents; those of the National Medical Residency Committee; and CNS Resolution Nº 466/12, of the Brazilian National Health Council (CNS), which establishes guidelines for research involving human beings.

For the preparation/submission of articles, authors are suggested to follow the standards of the EQUATOR Reporting Guidelines (Enhancing the Quality and Transparency Of Health Research), an organization that brings together researchers, editors of medical journals, reviewers, developers of guidelines on scientific texts, among others.

Other recommendations also include those of the International Committee of Medical Journal Editors, a group of editors of medical journals and related organizations that work together; the Committee on Publication Ethics (COPE); the Council of Science Editors (CSE); and the World Association of Medical Editors (WAME).

These standards aim to improve the quality of research, journals and medical science in general;

In addition to EQUATOR, the following are mentioned in this Guide:

CONSORT – *Consolidated of Reporting Trials*
MOOSE – *Meta-analyses Of Observational Studies in Epidemiology*
PRISMA – *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*
STARD – *Standards for Reporting of Diagnostic Accuracy Studies*
ARRIVE – *Animal Research: Reporting of In Vivo Experiments*

After all the stages of preparation, realization and concretization of the final version have been completed, the manuscripts must be submitted to **jmrr@cremesp.org.br**.

BRIEF INDEX OF TERMS

For better understanding and standardization, some terms mentioned in this **Guide for Authors** are presented below:

Case-control studies – Study design in which participants are selected from those who have a certain disease (cases) and those who do not (controls) to compare the odds of exposure to a particular variable between groups.

Cohort studies – Observational surveys in which individuals are classified or selected according to exposure status, and the incidence of a disease or condition is compared.

Experimental study (intervention) – One in which the researcher, in an intentional and controlled way, manipulates the exposure factor (intervention) to investigate its effects. They investigate hypotheses previously made, or look for factors that contribute to the onset of a certain disease.

Clinical trial – Experimental study with human volunteers, used to evaluate the safety and efficacy of treatments or interventions against diseases and health conditions of any nature and determine the pharmacological and pharmacokinetic and pharmacodynamic effects of new therapies.

Randomized clinical trial – In general, it is a clinical trial that compares two or more interventions, which are controlled by the researchers and applied randomly to a group of participants.

Quasi-experimental study – A study that does not contemplate all the characteristics of a "true" experiment, as a complete experimental control is not always possible, especially with regard to the randomization and application of the intervention.

Observational study – Conducted without the action of the investigator, who simply observes and measures the object of study (patients, the characteristics of the disease, etc.), without intervening or modifying any aspect being studied.

Prevalence or cross-sectional study – The measurement of the risk factors and the analyzed outcome occur concomitantly, not allowing inferring what came first (exposure or outcome).

Keywords – Section of the scientific article composed of three or four words, used for indexing it in databases. (Bireme Health Descriptors are suggested).

Qualitative research – It does not stick to numerical representativeness: in this approach, researchers seek to explain the reason for things, working with the universe of meanings, motives, aspirations, beliefs, values and attitudes.

Quantitative research – Its results can be quantified. As the samples are generally large and considered "representative", the statistically significant results are taken as if they constitute a real picture of the entire target population.

Abstract – Its main purpose is to provide an overview of the research. To this end, the objective, method, results and conclusions must be highlighted. Abstracts are classified in *Structured* – formed by "strata", i.e., items or sections –, each preceded by a subtitle, and *Unstructured* – presents information in running text, usually in a single paragraph. (See more about the topic in Requirements for the Preparation and Submission of Articles > Structure).

Case report and series – Corresponds to the detailed description of clinical cases, containing important characteristics about the signs, symptoms, and other characteristics of the patient, the therapeutic procedures used, as well as the outcome. *Case reports* usually comprise no more than three cases, while case series comprise three to ten cases.

Systematic review with meta-analysis – The object of analysis are not the study participants, but previous studies on a particular research object. *Meta-analysis* is understood as a statistical technique that is especially suitable for combining results from different independent studies, identifying and comparing, for example, the risks involved in two different treatments.

ARTICLE CATEGORIES

1. ORIGINAL RESEARCH

1.1 Original Articles

Usually include experimental, quasi-experimental or observational studies, program evaluations, randomized clinical trials, intervention studies, cohort studies, case-control studies, epidemiological studies, other observational studies, cost-effectiveness analyses, decision-making analyses, screening studies, and diagnostic tests. See specific guidelines for each type of study on the EQUATOR website.

Each article should contain its objectives and hypotheses, designs and methods, results, discussion and conclusions, which should be as timely and current as possible. A clear explanation of the methods and results is essential to make it easier to review the articles and to ensure the replicability of the results.

Original articles also involve theoretical essays (critiques and formulation of relevant theoretical knowledge), focused on the presentation and discussion of methodological aspects and techniques used in medical research.

Requirements:

- Maximum of 3,000 words
- Maximum of five tables and/or figures
- Structured abstract with no more than 350 words
- Up to 60 references
- Keywords

1.1.1. Clinical trials or studies

Any research project with participation of human beings inserted in groups for intervention and comparison, aiming to study the cause-effect relationship and the health outcome.

Interventions include (but are not limited to) experiments with drugs, surgical procedures, equipment, behavioral treatments, educational programs, dietary interventions, quality of life improvements, changes in the care process, and the like.

Articles that present partial or integral results of clinical trials must be accompanied by the number and the agency of registration, as recommended by the Latin American and Caribbean Center on Health Sciences Information (BIREME); the Pan American Health Organization (PAHO); the World Health Organization (on the Register of Clinical Trials to be published based on WHO guidelines); and the International Committee of Medical Journal Editors (ICMJE).

Requirements:

- Maximum of 3,000 words
- Maximum of five tables and/or figures, including a CONSORT flowchart
- Structured abstract with no more than 350 words
- Keywords
- Registration number of the Clinical Trials in a database (e.g., clinicaltrials.gov)
- CONSORT checklist
- In accordance with EQUATOR guidelines
- Up to 60 references

1.2 Special Articles

1.2.1. Methodological Articles

These articles feature new, improved, or noteworthy comments on techniques or methods deemed as relevant to basic, clinical, or treatment studies.

Requirements:

- Maximum of 2,000 words
- Maximum of two tables and/or figures
- Structured abstract with no more than 350 words
- Up to 30 references

1.2.2. Short communications

Short reports of findings of interest, but which do not include a more comprehensive analysis and discussion.

Requirements:

- Maximum of 1,200 words
- Maximum of three tables and/or figures
- Structured abstract with no more than 250 words
- Keywords
- Up to 15 references
- In accordance with EQUATOR guidelines

2. EDUCATION AND LITERATURE REVIEW

2.1 Systematic Reviews (without meta-analyses)

It aims to answer a specific question by synthesizing results from original quantitative or qualitative studies, according to PRISMA guidelines, with evaluation of the scientific literature and data sources on a clinical topic, emphasizing factors such as cause, diagnosis, prognosis, therapy or prevention, and describing in detail the process of searching for original studies; the inclusion criteria; and how the results of these studies were synthesized.

Requirements:

- Maximum of 3,500 words
- Maximum of five tables and/or figures, including a PRISMA diagram
- Structured abstract with no more than 350 words
- Up to 100 references
- Keywords
- In accordance with PRISMA guidelines and submitted to the PRISMA Checklist

2.2 Narrative review

Up-to-date review on a topic of interest from the perspective of renowned experts, which addresses an issue that is relevant to clinical practice.

It may include (but does not require) a systematic review of the literature.

Conclusions can be based on recent evidence and guidelines, with an emphasis on factors such as cause, diagnosis, prognosis, therapy or prevention.

Requirements:

- Between 2,000-3,500 words
- Maximum of five tables and/or figures
- Structured abstract
- Up to 100 references
- Keywords

2.3 Meta-analyses

Systematic and critical evaluations of the literature and data sources, referring to clinical topics, with emphasis on factors such as cause, diagnosis, prognosis, therapy or prevention.

In research with meta-analysis, a statistical technique is adopted to quantitatively combine the results of more than one study into a single total estimate.

For each specific type of article or data source, the methodology, population, intervention, exposure and tests must be described.

They must be submitted to the PRISMA checklist, and present the PRISMA flowchart used for the selection of articles. Authors of meta-analyses of observational studies should submit them to the MOOSE checklist and follow EQUATOR guidelines.

Requirements:

- Maximum of 3,500 words
- Maximum of five tables and/or figures, including a PRISMA diagram
- Structured abstract with no more than 350 words
- Keywords
- In accordance with EQUATOR guidelines, especially PRISMA and MOOSE
- Up to 100 references

3. OPINIONS

3.1 Editorial

Article presenting JMRR's opinion on a given subject, reflecting the point of view of the majority of the editorial board and the journal's administrative body – therefore, it is not signed by a particular editor. In essence, it is an opinionated and objective report on a specific article – or a review of some relevant articles – in the issue of the journal in question.

Doctors who are not involved in the journal's editorial board and administrative staff may be invited by the editors to write it, depending on the subject at hand.

3.2 Letter to the Editor

Related to the methods used to obtain or interpret data presented in an article published in the latest issues of JMRR. It may perform a new analysis of these data based on other scientific articles and/or methods and/or journals. It can also include a case report that is capable of illustrating new information.

When justified, a response from the author(s) of the study in question is requested.

Requirements (Letter to the Editor) :

- Maximum of 400 words
- Maximum of three authors
- Up to five references (one of which must be the article in question)

Requirements (Response from the author(s):

- Maximum of 500 words
- Up to six references

3.3 Point of view

External manuscript that is well-focused, academic and clearly presented, generally not linked to a specific article. It can address any important topic in Medicine, Medical Residency, Research, New Discoveries, Public Health, Prevention, Ethics and Bioethics, and Health Policies or Standards.

Requirements:

- Maximum of 1,200 words (or 1,000 if accompanied by a small table or figure)
- Maximum of three authors, with no more than two affiliations per author
- Up to seven references

REQUIREMENTS FOR THE PREPARATION AND SUBMISSION OF ARTICLES

1. PREPARATION

1.1 Structure

The structure of an original article or a review consists of pre-textual, textual and post-textual elements.

The **mandatory structural elements** are the *Title, Abstract and Submission and Approval Dates.* Title and Abstract in other language(s) are optional.

The **textual elements** are mandatory, and correspond to the elements usually standardized in scientific articles, as follows: *Title, Name of authors, Keywords, Abstract, Introduction, Materials and Methods, Results, Discussion, Conclusions and Bibliographic References.*

As for the **post-textual elements**, the References are mandatory, whereas the *Glossary, Appendix, Annex,* and *Acknowledgments* are optional.

It is recommended that the Abstract highlights the objective, method, results and conclusions of the document; that it is written in the active voice, third person singular; and that it is composed of a sequence of concise, affirmative sentences, in a single paragraph. The first sentence should be significant, explaining the main theme, followed by information about the research category (case study, analysis of the situation, etc.)

It is also suggested that the *Introduction* provides a brief narrative, indicating the objectives/hypotheses of the current study. It should not include the results. As for the *Materials and Methods* section, it must include enough details to allow other researchers to disseminate and/or replicate the study.

Attention: The maximum word limits of articles submitted to JMRR exclude Abstracts, Tables and Figures.

1.2 Formatting

The *Title* of the article and the subtitle (if any) must appear on the title page, in Portuguese or English, and be typographically differentiated or separated by a colon. Including the title in another language just below the original title is optional; additionally, centering it at the top of the title page and writing it in bold is recommended.

The name of the *Authors* must be inserted directly: first name (abbreviated or not) and last name, and it is suggested that they are written in full, each separated by a comma, in the same way as the names of the *Institutions.*

If there is more than one author, the names can be written on the same line, separated by commas, or on different lines. A succinct resume of each author must be included, with corporate association and contact address.

The *Keywords* must appear just below the abstract, preceded by the term "Keywords". Each of them must be separated and finalized by a period.

It is suggested adopting the Health Descriptors of the Latin American and Caribbean Center on Health Sciences Information (Bireme), which correspond to a translation of the Medical Subject Headings (MeSH) of the U.S National Library of Medicine, used by databases such as Scielo, Lilacs, VHL, MEDLINE and Pub Med.

These descriptors contain terms in English, Portuguese and Spanish.

JMRR recommends the articles to be arranged in a *Single Column*, in an *A4 Sheet, Portrait Format.* Font: Times New Roman, with the title in 14 pt; the subtitles and body text in 12 pt; the abstract in 11 pt; and citations with more than three lines in 10 pt, with four cm indentation from the left margin.

Additionally, 1.5 spacing and justified alignment should be used for paragraphs in the text, marked with a 1.5 indentation. There must be no blank line between paragraphs.

Page numbers need to be inserted in the upper right margin, with the exception of the first. Margins: left and top: three cm / right and bottom: two cm (do not include frames).

It is also recommended to start all sections on separate pages and divide the sections and subsections by assigning them Arabic numerals, aligning the section code with the left margin, preceding the title and separated from it by a space. Numbering should be progressive up to the quinary section, e.g.:

Primary section "1"
 Secondary section "1.1"
  Tertiary section "1.1.1"
   Quaternary section "1.1.1.1"
    Quinary section "1.1.1.1.1".

1. 3 Bibliographical references and citations

References are a a standardized set of essential elements that allow identifying or locating a document or part of it, published in different platforms or formats.

They must be presented in a standardized manner, according to the guidelines of specific organizations. Complementary elements can be added, whenever necessary, to facilitate the identification of the document.

The extraction of text citations from other studies can be done directly (literal transcription) and indirectly (paraphrase), duly documented with the name of the author of the original source.

JMRR adopts the standards established by the International Committee of Medical Journal Editors (ICMJE, which adopts **Vancouver**). These standards govern all citations in the body text.

For example, in articles written by between **one and six authors**, the references will obey the following form:

Author AA, Author BB, Author CC, Author DD. Title of the article. Short name of the journal. Publication date YYYY ddd; issue number: page numbers.

João GR, Maria JC, Antônio LC. Como resistir a um assédio moral durante a fase de internato. Rev. bioet. 2018 Dez; 54(1):111-4.

Articles with more than six authors are referenced as follows:

Author AA, Author BB, Author CC, Author DD, Author EE, Author FF, *et al*. Title of the article. Short name of the journal. Publication date YYYY ddd; issue number: page numbers.

João GR, Maria JC, Antônio LC, Joaquim KK,Rita OPG, Clara BO, *et al*. Relação do preceptor com os residentes e seus conflitos éticos. Saúde Soc. 2017 Jun; 200(6):
869-75

* Learn more about the Vancouver standard at Samples of Formatted References for Authors of Journal Articles, NIH U.S. National Library of Medicine

1.4 Figures and tables

In general, figures and tables are the fastest way to communicate large amounts of information, which would be complicated to explain in text.

Figures are ideal for displaying images, data graphs and layouts.

Images can help achieve the precision needed for a scientific manuscript: when choosing, the author must make sure to include scale bars, highlight important items, and identify the meaning of the different colors and symbols used.

Data graphs demonstrate the functional or statistical relationship between two or more items. In them, the axes must be highlighted, as well as the units for quantities, the curves, and the data sets, with legible font and size.

As for **schemes**, they correspond to the visual representation of abstract or immaterial concepts that relate to each other, forming a symbolic figure. Scientific and/or material schemes are used for investigative and theoretical purposes, and respond to a demonstrative or hypothetical objective to theorize about some aspect of science or logic.

Tables represent an objective way of presenting large amounts of data and communicating the results of studies. Thus, among other requirements, they must have clear and concise legends; data divided into categories; sufficient spacing between columns and rows; specification of units; and legible font and size.

Additionally, they must be cited in the text and numbered consecutively (i.e., 1, 2, 3) in the order in which they are mentioned, and must be provided in an editable format (Word or Excel). They can be included at the end of the manuscript's file or sent individually, but not both.

When the researcher plans to include tables in the manuscript, s/he must determine: 1) the details necessary for readers to understand the discussion; 2) a sufficient set of statistics that is capable of supporting the inferential methods used; 3) how to define it so that it can be understood in isolation.

For the preparation of tables, try to limit their content to essential materials: those with excess information become less effective. Although supplementary tables may be longer and more detailed than text tables, their role is to be directly and clearly related to the content and to be an integral part of the text.

The basic components of the table

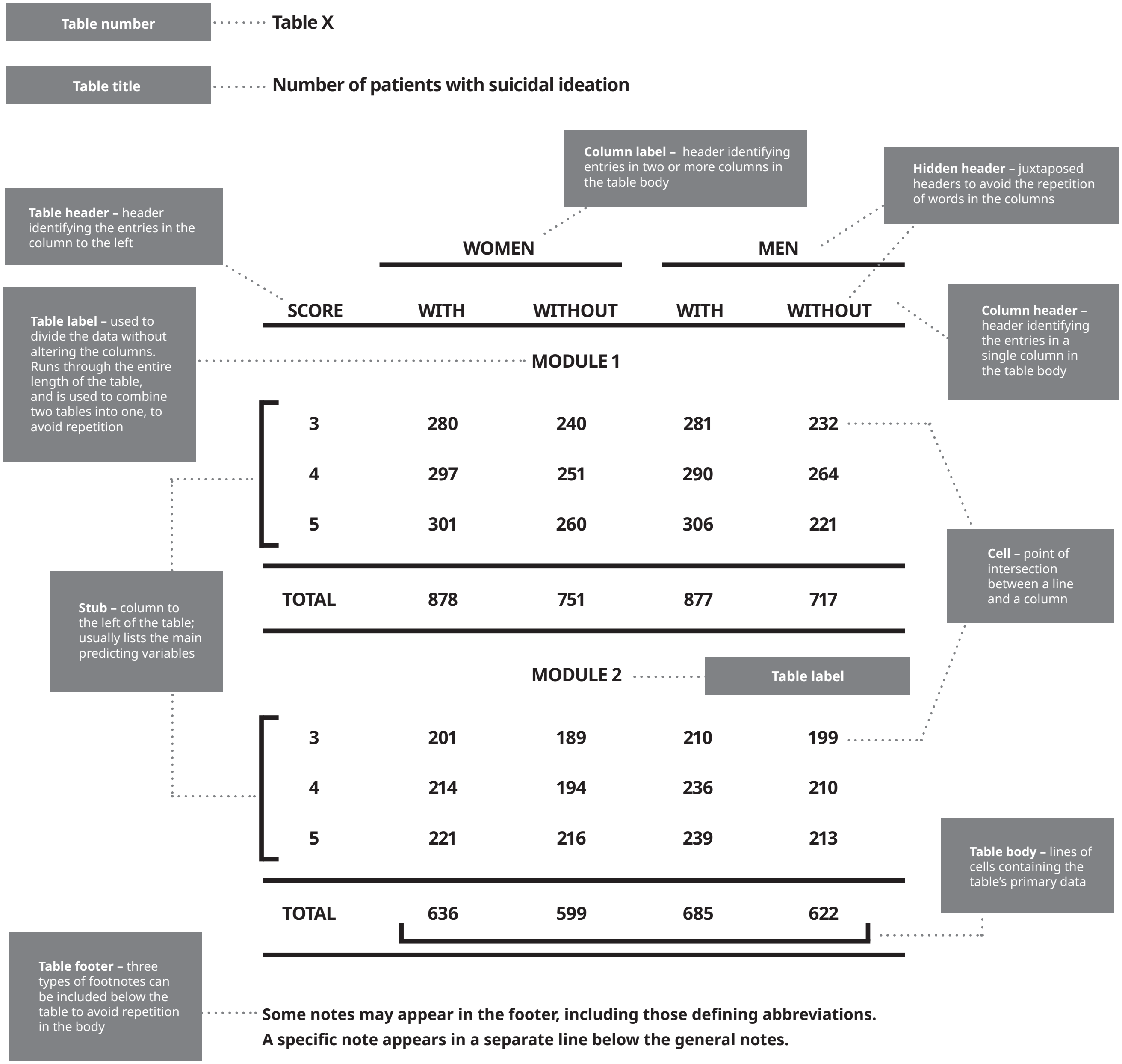

Table X

Number of patients with suicidal ideation

	WOMEN		MEN	
SCORE	WITH	WITHOUT	WITH	WITHOUT
		MODULE 1		
3	280	240	281	232
4	297	251	290	264
5	301	260	306	221
TOTAL	878	751	877	717
		MODULE 2		
3	201	189	210	199
4	214	194	236	210
5	221	216	239	213
TOTAL	636	599	685	622

Some notes may appear in the footer, including those defining abbreviations.
A specific note appears in a separate line below the general notes.

Table number

Table title

Column label – header identifying entries in two or more columns in the table body

Hidden header – juxtaposed headers to avoid the repetition of words in the columns

Table header – header identifying the entries in the column to the left

Table label – used to divide the data without altering the columns. Runs through the entire length of the table, and is used to combine two tables into one, to avoid repetition

Column header – header identifying the entries in a single column in the table body

Cell – point of intersection between a line and a column

Stub – column to the left of the table; usually lists the main predicting variables

Table label

Table body – lines of cells containing the table's primary data

Table footer – three types of footnotes can be included below the table to avoid repetition in the body

prototype are shown above, including the technical terms, the location of the items, and the definition of each element.

The layout must be logical and easily understandable to the reader. Table entries with data comparisons must be close to each other. Following this principle, in general, different indices (e.g., means, standard deviations, sample sizes) have to be segregated into different parts or lines.

Tables are designed to show something specific. For example, those with the purpose of communicating quantitative information will be effective only when they seem obvious to the reader at a glance. The same data can be organized in different ways, in order to emphasize the different characteristics of each datum.

An informational table complements the text, rather than duplicating it, leading readers to what to look for: if it is necessary to search for each item in the text, then the table will be unnecessary. Likewise, if additional tables are included in supplementary online files, they must be mentioned briefly in the article's printed version. Additionally, tables designated as "supplementary materials" must be accompanied by sufficient information to be understood by themselves.

Expressions such as "the table above", "below", or "the table on p. 45" should be avoided, because the tables' placement is not defined until the layout has been designed.

Following the logic of objectivity, authors may consider combining tables with repeated data. In general, identical columns and rows do not appear in two or more tables in the same article. The presentation of all tables in the manuscript should be consistent to facilitate comparisons, using similar formats and titles and the same terminology (e.g., response time or reaction time – not both).

Examples of figures and tables can be obtained in the manual of the Public Health School of the University of São Paulo (FSP-USP). Another suggestion is the Manual of the American Psychological Association.

2. SUBMISSION

Before submitting an article, all authors must have approved the final version to be submitted. The full manuscript or data must not have been previously published (except in summary or pre-printed form) or be currently under evaluation for publication elsewhere.

All manuscripts must be sent to jmrr@cremesp.org.br, indicating a valid email address of all authors.

To ensure transparency, the authors are expected to declare other articles that have used the same dataset or sample, in addition to identifying tables, figures and/or data that have been published in another journal, being responsible for obtaining permission from the copyright owner(s) if they decide to reproduce and/or modify any previously published material.

At the end of the submission, the person designated in the system as the "corresponding author" (responsible for the intermediation with the editorial team of JMRR) will receive an email notification stating that the text was received by the Editorial Office. If this does not happen, it means that there was a problem during the submission process, which should be informed to JMRR. Any manuscripts that do not comply with these guidelines will be returned to the author for correction.

Once processed, the submission will receive a number. Throughout the process, the status of the article will be available to the corresponding author, who is allowed to upload the entire submission (except the cover letter) in a single file when sending it, with numbered pages, in Word or PDF.

Tables and figures can be placed in the body of the manuscript or presented separately at the end. The authors must ensure that all elements are clearly legible to editors and reviewers.

EDITORIAL POLICIES

Authorship

To qualify as an "author", the individual must have participated sufficiently in the study, assuming public responsibility for all or part of the content after it has been submitted, approved and published. "Participating" here means making substantial intellectual contributions to the study, in the form of: 1) conception and design and/or acquisition of data and/or data analysis; and 2) writing of the article and/or critical review in search of important intellectual content.

All individuals who meet the criteria for authorship must be nominated as "authors". If the authorship is being assigned to a group, all of its members must meet the criteria described above.

Additionally, being an author also means agreeing to answer questions pertaining to the completeness of the article so that issues related to the accuracy or integrity of any part of it may be properly investigated and resolved.

Any changes in authorship after the initial submission, such as additions, exclusions, and reordering, must be approved in writing by the group, which may indicate the contribution of each author at the end of the article if they so wish.

When approving and finalizing the submission of a manuscript, JMRR assumes its recognition and acceptance, committing itself to reviewing and correcting the articles and ensuring that all individuals who meet the criteria for authorship are included on the title page, as well as that the submitted version is the one approved by all.

Disclosure of Financial Interests and Potential Conflicts of Interest

JMRR requires the authors of any type of articles to fully disclose possible conflicts of interest, including financial ones, in addition to specifying their nature. This is the responsibility of the entire group, under penalty of the article being returned, delaying the evaluation process.

Disclosure includes direct or indirect financial or personal relationships, as well as interests and affiliations that are relevant to the subject of the manuscript established in the last two years, or even those expected in the foreseeable future. It also covers (but is not limited to) grants or funding, affiliations, intellectual property/patents (in preparation, filed or granted), inventions, remuneration, consultancy and royalties.

Financial: financing and other payments, goods and services received or expected by the authors related to the subject of the study, or granted by an organization with an interest in the results.

Affiliations: being an employee, on the advisory board or a member of an organization with an interest in the results.

Intellectual property: patents or trademarks owned by someone or his/her organization.

Personal: friends, family, relationships and other close personal connections.

Ideological: beliefs or activism, for example, political or religious, that are relevant to the study.

Academic: competitors or someone whose study is criticized.

If an author has "nothing to declare", this should be made explicit.

The sources of financing, such as research grants from private and public institutions (development agencies), must be indicated at the end of the article.

Ethical Considerations

The authors should consider all ethical issues that are relevant to their research.

For example, in the Materials and Methods section, the institutional and/or licensing committee that approved the experiment(s) should be identified, confirming that the study was carried out in accordance with the relevant guidelines and regulations.

Studies involving human subjects must include detailed information about the informed consent process, including the method(s) used to assess the participants' ability to consent, the protection criteria included in the study, and relevant follow-up data, when available.

Among the ethical guidelines, JMRR follows those established by the Ministry of Health of Brazil, through the CEP/CONEP system (CNS Resolution Nº 466/12), and the International Committee of Medical Journal Editors, although it reserves the right to take alternative actions if necessary, including contacting the authors' institution, funding agency, or other appropriate research authority.

Studies involving human beings must be submitted to the Research Ethics Committees (CEPs) of the institution where they will be carried out, and if necessary, to the National Research Ethics Commission (CONEP), through the "Plataforma Brasil", an electronic system created by the Federal Government of Brazil to systematize the receipt of research projects by CEPs across the country. When analyzing and deciding, the CEP/CONEP system becomes co-responsible for ensuring the protection of the participants.

When reporting experiments on animals, the authors should indicate that the institutional and national guidelines for the care and use of laboratory animals, such as ARRIVE, have been followed.

JMRR takes its responsibility for scientific integrity seriously, and will verify any allegations of misconduct, such as plagiarism, duplicate submission or publication, fabrication or falsification of data, unethical treatment of research subjects, authorship disputes, and undisclosed conflicts of interest.

Any corrections to the literature will be treated on a case-by-case basis, through errata or retractions.

Peer review

All submissions, with the exception of editorials, comments and correspondence, will be subject to peer review or refereeing, a process used in the publication of scientific articles that consists in passing them on to the evaluation of one or more more specialists with an advanced degree and expert level of knowledge on the subject addressed by the author.

These evaluators are supposed to make comments and suggest revisions, with the aim of contributing to the quality of the publication. JMRR excludes reviewers who work at the same institution or with any other conflicts of interest. The identity of the individual reviewers remains confidential to all parties except JMRR's scientific and technical editors.

Submission processing

After the article has been submitted, it is previously analyzed by the editors of JMRR. If approved, it is passed on to external reviewers, after which the editorial decision and the reviewers' suggestions/corrections will be sent by email to the corresponding author.

In case the opinion of the reviewers differs, the editors reserve the right to invite an additional reviewer. Opinions may decide for accepting or rejecting the study, and suggest small or major changes. Rejected studies may be resubmitted if the authors believe that an important reformulation has been carried out or new findings have been included, in which case they must resubmit the article, including a letter to the Editor-in-Chief, justifying the resubmission. It will be up to the editorial board to accept it or not.

In the final phase, the article will be submitted to proofreading, the author being responsible for making final changes as requested and approving the final version.

JMRR will guide authors who submit their articles in Portuguese on English translation services.

After final acceptance, the article will be published online, becoming citable through the number assigned to the digital object identifier (DOI). The final written version will be published according to the journal's periodicity, in an issue selected by the Editorial Board, which will also define its circulation.

The authors are responsible for carefully reviewing the entire article in relation to precision. Once a corrected article is published online, additional corrections cannot be made without an errata.

Registration of Clinical Trials

As a condition for publication, in accordance with ICMJE, JMRR requires prospective registration of all clinical trials. Therefore, the name of the study, the name of the repository and the registration number must be included at the end of the abstract.

Observational-only studies will not require registration.

Return of articles and printing policies

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A brief summary of the articles published in this issue of the *Journal of Medical Resident Research*

Epidemiological analysis of laryngeal cancer hospitalizations in the Brazilian public health system between 2013 and 2023

Laryngeal neoplasms are the third most common type of head and neck cancer worldwide, excluding non-melanoma skin cancer. Its incidence is strongly associated with smoking and excessive alcohol consumption. Brazil is the country with the highest mortality from the disease in Latin America, and, among all countries, is behind only the United States, China, and India. Considering the impact of this problem on public health, the objective of this study was to analyze the number of hospitalizations of patients with laryngeal cancer in the Brazilian Public Health System (SUS), providing data to support programs aimed at improving care. To this end, an ecological, cross-sectional, quantitative, and descriptive approach was used, with data obtained from the SUS's hospital information system (SIH/SUS) over a decade.

Evaluation of diabetes mellitus and its complications as contributing causes of mortality in a general hospital (2016–2019)

Diabetes Mellitus (DM) is considered a syndrome with multiple etiologies, resulting from insulin deficiency or the inability of insulin to perform its functions adequately (insulin resistance). Once the disease is diagnosed, the strategy is to prioritize glycemic control, avoiding, among others, macrovascular and microvascular complications. Studying DM as a possible cause associated with death in diabetic patients is relevant, since most deaths result from a multicausal pathological process. This approach facilitates the evaluation of the disease's impact and its complications at the time of death, providing deeper insights into its effects on population health. However, DM is often underreported in death certificates, which makes this analysis difficult. This study sought to assess this issue by analyzing death certificates from a sample of patients from a general hospital.

Pain, knowledge, and support: the experience of a multidisciplinary team in an oncology outpatient clinic in Brazil

The concept of total pain is used to understand the pathophysiological mechanism of pain in cancer patients, proposing that pain relief can only be optimized by addressing its physical, psychological, social, and spiritual aspects. The care of these patients and their unique needs should adopt a holistic approach and, ideally, be delivered by a multidisciplinary team. This approach expands the focus of care to encompass not only the patients themselves but also their family members and the healthcare team as a whole. This qualitative study aimed to explore the meanings that professionals at a specialized outpatient clinic attribute to pain in adult oncology patients.

Acute myocardial infarction and non-obstructive coronary arteries: a case report

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a rare event that is difficult to diagnose. It is a syndrome caused by a set of conditions that affect the structure of the coronary microcirculation, culminating in an acute myocardial infarction (AMI), but without evidence of significant obstructive coronary artery disease on angiography. In this report, a group of surgeons and an intensive care physician present a case of MINOCA, highlighting key aspects of its diagnosis and treatment.

The relationship between endometriosis and malignant thyroid neoplasms: a systematic review

Endometriosis is a chronic inflammatory disease that affects approximately 10 to 15% of women of reproductive age. Thyroid cancer is a condition that predominantly affects women, with the highest incidence occurring between the ages of 45 and 64. Given this epidemiological overlap, recent studies have sought to analyze the potential association between endometriosis and thyroid cancer. Here, the authors present a systematic review of the literature, which aims to further explore this association and provide valuable insights for professionals managing these conditions.

JMRR
JOURNAL OF MEDICAL RESIDENT RESEARCH

EDITORIAL

JMRR and the resident physician

Since its inception, *JMRR* has been committed to fostering scientific research. The journal was born from the vision of its founder, Prof. Dr. João Carlos Simões, who was driven by a strong desire to provide resident physicians and physicians in training with a platform to publish their research and experiences in a scientific publication. Recognizing that young physicians often have limited opportunities to publish their work—given that many journals prioritize contributions from more experienced authors—Simões sought to create a space where emerging medical professionals could gain entry into the scientific community.

A resident physician undergoes rigorous theoretical and practical training during medical residency, which aims to prepare them to practice their chosen specialty after finishing the program. However, within this learning environment, scientific research should also be an integral part of this journey and should be actively encouraged by preceptors. Engaging in research within residency programs not only contributes to the advancement of medical science but also enhances the understanding of outcomes and clinical decision-making within a local context.

Researchers should strive to conduct studies with scientific rigor and a high level of evidence. Due to the inherent curiosity of an individual in training, resident physicians often develop a thorough clinical and scientific understanding of their patients in both inpatient and outpatient settings who presented with atypical manifestations or conditions rarely described in the literature. This curiosity and insight serve as important attributes and motivational factors for creating scientific knowledge. One of the most accessible ways to embark on a scientific journey is through the publication of a case report, as demonstrated by the authors of the manuscript *"Acute Myocardial Infarction and Non-Obstructive Coronary Arteries: A Case Report,"* featured in this third edition of *JMRR*. Case reports represent a valuable form of scientific contribution, offering a potentially high-quality publication opportunity with a relatively shorter preparation process.

Even after achieving specialization, science remains an integral part of a physician's career, continuously guiding their practice through evidence-based medicine. Thanks to science, medical advancements occur in leaps and bounds, providing a platform for critical discussions, particularly in times of public health crises. Scientific research should be a cornerstone of medical training, with scientific publications serving as the culmination of this process. Since its inception, *JMRR* has remained steadfast in its mission to promote science and foster a spirit of scientific inquiry, providing publication opportunities and paving the way for young physicians to embark on academic careers.

Dr. Douglas Kamei
Dr. Edoardo Filippo de Queiroz Vattimo
Editors of the Journal of Medical Resident Research

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JMRR
JOURNAL OF MEDICAL RESIDENT RESEARCH

EDITORIAL

Humanization in Medical Residency

> ***"First the patient, second the patient, third the patient, fourth the patient, fifth the patient, and then maybe comes science."***
> **Bela Schick (1877 -1967)**
> **Aphorisms and Facetiae of Bela Schick**

The commitment to humanizing medicine, particularly within the practice during medical residency, remains a fundamental concern in teaching hospitals and medical schools. The key discussion, pragmatically, revolves around how to carry out this process in a natural yet systematic manner.

The interaction between a resident physician and their patient must extend beyond formal, technical, or purely academic aspects. It is essential to recognize that this human connection should be built on respect, meaningful rapport, and a sense of responsibility. Resident physicians must never forget that medicine is, at its core, a profoundly human and compassionate science.

A resident physician with a true vocation should take genuine satisfaction in helping others. Medicine harnesses technological advances in the biological sciences to fulfill this humanistic mission. However, a physician with a strong humanistic foundation is not only a more skilled clinician but also a better person.

Humanism in the doctor-patient relationship is one of the greatest virtues of humanity and a fundamental tool for professionals who care for those in pain and suffering. It must be taught through practice, just as one learns to conduct an anamnesis or perform a thorough physical examination. A humane approach begins the moment a patient is first welcomed—with a warm handshake, addressing them by their name, having a compassionate gaze, and calm, reassuring words. It is reflected in the physician's ability to recognize the patient's vulnerability, respect their dignity, and foster a sense of trust and comfort.

Knowing how to convey confidence is an art rooted in the understanding that words can sometimes wound more deeply than a scalpel. When communicating with patients, it is essential to eliminate any trace of arrogance, vanity, or self-interest. A genuinely skillful resident physician is one who is available, attentive, and fully receptive to patients' concerns, never dismissing or underestimating their complaints.

I consider it absolutely essential that preceptors and medical school professors teach compassion and empathy as the most accessible and effective form of medicine. These values serve as the cornerstone of humanism in contemporary medicine.

Prof. Dr. João Carlos Simões
Editor Emeritus of JMRR
Professor Emeritus of Oncology at Faculdade Evangélica Mackenzie do Paraná (FEMPAR)

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JMRR
JOURNAL OF MEDICAL RESIDENT RESEARCH

EDITORIAL

A didactic journal for aspiring physician-scientists

About four years ago, the Regional Council of Medicine of the State of São Paulo (Cremesp) took its first steps toward launching its inaugural scientific journal, the Journal of Medical Resident Research (JMRR). Since then, this pioneering initiative has provided young physicians with a valuable opportunity to enter the academic field—an arena that often seems inaccessible—with greater confidence. With its strong educational mission, *JMRR* offers medical students, resident physicians, and early-career doctors essential feedback, guidance, and support at the most critical stage of their academic journey: the beginning. Moreover, with its bilingual edition, the journal enhances the visibility of published work, extending its reach to an international audience.

Since then, we have witnessed a continuous evolution in the quality of submitted manuscripts, along with a growing interest from medical residents and students. These works explore important topics that are not only relevant to those entering the medical profession but also to more experienced colleagues across a wide range of specialties. More importantly, they highlight the immense potential of the new generation of physicians, who require only encouragement, support, and opportunities to thrive in their careers, as many already possess the intellectual capacity, scientific spirit, academic curiosity, and dedication needed to make meaningful contributions to the field of medicine.

In this edition, as expected, we present papers of high scientific relevance. The articles explore topics that have a significant impact on fields such as public health and palliative care—both of which are crucial to modern medicine. Additionally, this issue includes a compelling case report detailing the authors' experience in managing a challenging diagnosis: acute myocardial infarction without coronary obstruction. The high caliber of these contributions underscores the success of JMRR in fulfilling its core mission—nurturing the scientific spirit of new generations of physicians.

The direction taken by *JMRR* has inspired us to develop additional initiatives focused on medical residency, including dedicated panels at the 1st and 2nd Cremesp Medical Congress—both of which were highly successful in terms of audience engagement and organization. Cremesp has also spearheaded pioneering events aimed at young doctors, such as the Introduction to Research Symposium, designed to guide them through the initial steps of scientific article writing. Given the great success of this initiative, we plan to hold it again in the future, reinforcing our commitment to fostering scientific development among early-career physicians.

JMRR and these other initiatives reflect Cremesp's steadfast commitment to upholding and promoting science. As Albert Szent-Györgyi, the Hungarian-born physiologist and naturalized American who won the 1937 Nobel Prize for his discovery of vitamin C as a catalyst, aptly stated: *"Research is seeing what everyone else has seen, and thinking what no one else has thought."*

Angelo Vattimo
President of the Regional Council of Medicine of the State of São Paulo

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JMRR

EPIDEMIOLOGICAL ANALYSIS OF LARYNGEAL CANCER HOSPITALIZATIONS IN THE BRAZILIAN PUBLIC HEALTH SYSTEM BETWEEN 2013 AND 2023

Análise epidemiológica dos pacientes internados por neoplasia maligna de laringe no Sistema Único de Saúde entre 2013 e 2023

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ABSTRACT

Objectives: Laryngeal cancer represents a significant public health problem, with more than 180,000 cases and 100,000 deaths per year worldwide. In Brazil, approximately 8,000 cases are diagnosed every year, causing 5,300 deaths. Considering this impact on public health, this study aims to analyze the number of hospitalizations of patients with this disease in the Brazilian Public Health System (SUS), providing data to support programs aimed at improving care for these patients. In addition, these data could also shed light on the strain laryngeal cancer places on the hospital network, which often falls short of meeting the demand for beds within the SUS. **Methods:** Using an ecological, cross-sectional, quantitative, and descriptive approach, data were gathered from the hospital information system (SIH/SUS) from 2013 to 2023. The TABNET tool, developed by the Department of Information Technology of SUS (DATASUS), was used for the analysis. The variables analyzed included the total number of hospitalizations, age group, region of the country, and sex. **Results:** From January 2013 to October 2023, a total of 131,021 hospitalizations for laryngeal cancer were recorded in Brazil. The Southeast region accounted for the highest proportion of hospitalizations (48.1%), followed by the Northeast (23.3%), South (19.1%), Central-West (6.2%), and North (2.9%). Of these hospitalizations, 85.4% involved male patients, with the most affected age group being 60 to 69 years, totaling 46,698 cases. There was no significant increase in hospitalizations during the COVID-19 pandemic. **Discussion:** The analysis identified a predominant profile among patients with laryngeal cancer admitted to the SUS, characterized by a higher proportion of male patients, primarily in the 60-69 age group and concentrated mainly in the Southeast region. The high number of hospitalizations relative to the disease's incidence in Brazil underscores the need for initiatives promoting early diagnosis, along with the development of effective prevention and treatment strategies to enhance patient care for this condition.

Keywords: laryngeal cancer, epidemiology, hospitalizations, SUS

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INTRODUCTION

Globally, more than 180,000 cases of laryngeal cancer are reported each year, resulting in approximately 100,000 deaths annually. In Brazil, around 8,000 cases and 5,300 deaths from laryngeal cancer occur each year. The country has the highest mortality rate for laryngeal cancer in Latin America and ranks fourth in incidence worldwide, following the United States, China, and India[1].

Laryngeal cancer predominantly affects men, most of them in their seventh decade of life. Ranked as the third most common head and neck cancer, excluding non-melanoma skin cancer, its incidence is intrinsically associated with smoking and excessive alcohol consumption. Moreover, laryngeal cancer stands out as the ninth leading cause of death in men and the 20th in women[2].

Anatomically and clinically, the larynx is divided into three regions: glottic, supraglottic, and subglottic. Each region has distinct lymphatic drainage patterns, differing both in quantity and drainage pathways, which can affect the progression of laryngeal cancer based on the tumor's location[3]. Approximately two-thirds of laryngeal cancer cases involve the glottic region, about one-third affect the supraglottic region, and only a small fraction occur in the subglottic region. Squamous cell carcinoma is the most common histological type of laryngeal cancer, accounting for over 85% of cases. Symptoms vary based on tumor location, with dysphonia being the most frequent, though dysphagia and odynophagia are also significant.

Several risk factors are associated with laryngeal cancer, including smoking, alcohol consumption, HPV infection, gastroesophageal reflux disease (GERD) with laryngopharyngeal manifestations, and a nutrient-poor diet[3].

The tumor, node, and metastasis (TNM) staging system, established by the American Joint Committee on Cancer and the Union for International Cancer Control, is the gold standard for staging laryngeal tumors[4].

Treatment choice is determined by factors such as the tumor's size, extent, location, and patient-specific characteristics like age, overall health, comorbidities, and psychosocial support. Additional considerations include laryngeal, pulmonary, and swallowing functions, the clinical expertise of the medical team, and access to rehabilitation services. Treatment-related toxicity and morbidity from chemoradiation or surgery must also be taken into account[5].

Given the public health challenges posed by the significant annual incidence of laryngeal cancer in Brazil, it is essential to monitor its epidemiological trends nationwide. The number of hospitalizations for laryngeal cancer within the Brazilian Public Health System (SUS) serves as a key indicator, potentially offering insights to inform targeted programs aimed at improving patient care. These hospitalization figures also shed light on the strain laryngeal cancer places on the hospital network, which often falls short of meeting the demand for beds within the SUS. Therefore, this study aims to conduct an epidemiological analysis of laryngeal cancer hospitalizations within the SUS over the past decade (2013-2023).

METHODS

This study is an ecological, cross-sectional, quantitative, and descriptive analysis. Data were obtained from the Hospital Information System (SIH/SUS) via the Department of Information Technology of SUS (DATASUS), utilizing the TABNET tool, covering the period from 2013 to 2023. The inclusion criteria consisted of patients hospitalized with malignant laryngeal neoplasms, classified under the code "C32" of the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Variables analyzed included the number of hospitalizations, age group, country region, and sex. Ethical approval was not required for this research, as it relied solely on publicly available data.

RESULTS

Between January 2013 and October 2023, a total of 131,021 hospitalizations for laryngeal cancer were recorded in Brazil. The Southeast region had the highest number, with 63,129 hospitalizations (48.1%), followed by the Northeast with 30,589 (23.3%), the South with 25,139 (19.1%), the Central-West with 8,225 (6.2%), and the North with 3,889 (2.9%).

Men accounted for most cases, with 111,988 hospitalizations (85.4%), while women accounted for 19,033 (14.6%). In the Southeast, 54,886 (86.9%) of hospitalizations involved male patients, compared to 8,525 (13.1%) female patients.

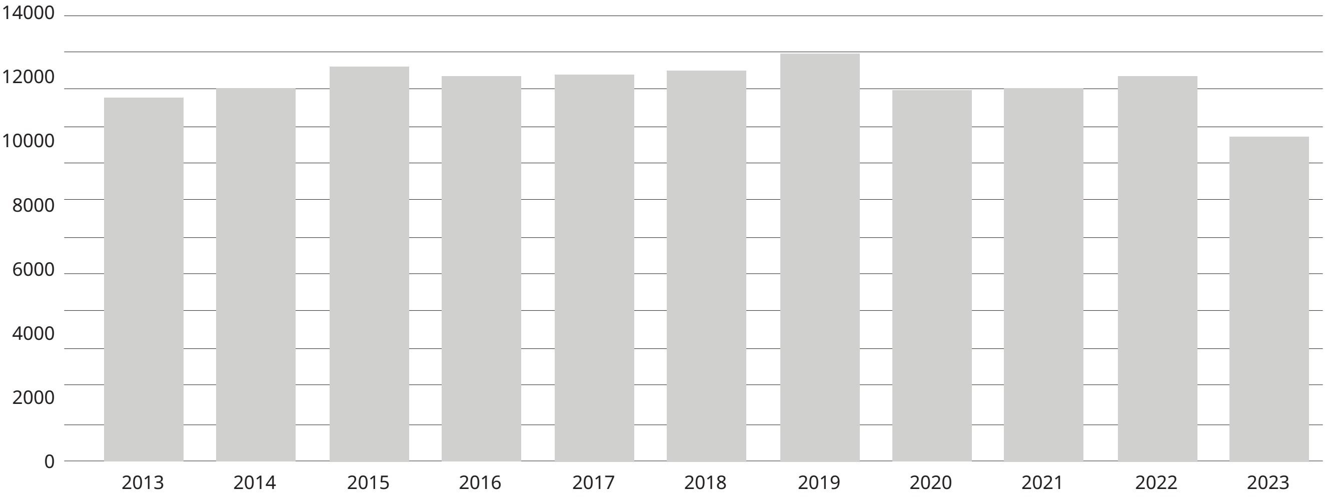
Hospitalizations spanned all age groups but were most prevalent among

TABLE 1 - Hospitalizations due to laryngeal cancer in Brazil between 2013 and 2023

AGE RANGE	MALE	FEMALE	TOTAL
TOTAL	**112,029**	**19,036**	**131,065**
Less than one year	46	20	66
1 - 4 years	75	61	136
5 - 9 years	56	77	133
10 - 14 years	28	52	80
15 - 19 years	92	75	167
20 - 29 years	309	195	504
30 - 39 years	1,507	569	2,076
40 - 49 years	10,684	1,930	12,614
50 - 59 years	34,224	5,303	39,527
60 - 69 years	40,418	6,299	46,717
70 - 79 years	19,558	3,356	22,914
80 years and more	5,032	1,099	6,131

Source: Brazilian Health Ministry - Public Health System Hospital Information System (SIH/SUS)

CHART 1 - Hospitalizations due to laryngeal cancer in Brazil between 2013 and 2023



Source: Brazilian Health Ministry - Public Health System Hospital Information System (SIH/SUS)

those aged 60 to 69, with 46,698 cases. A notable increase in cases was observed across all regions of the country from this age onward.

During the COVID-19 pandemic, hospitalizations due to laryngeal cancer declined, with the lowest numbers recorded in 2020 (11,693) and 2021 (11,737). However, in the last five years (2019-2023), there were 59,603 hospitalizations (53.22%), with the highest annual figures in 2019 (12,852) and 2022 (12,139).

DISCUSSION

The larynx, positioned anteriorly in the median plane, at the level of the third to sixth cervical vertebrae and situated between the carotid sheaths[6], serves as the continuation of the airway that links the pharynx to the trachea. Besides facilitating airflow during breathing, its several functions include preventing food and liquids from entering the trachea and lungs during swallowing and producing vocal sounds.

Approximately two-thirds of laryngeal cancers originate in the true vocal folds, with some arising in the anterior commissure of the glottis. These tumors are typically associated with persistent dysphonia, which often emerges early in the disease course. Advanced tumors may present with symptoms such as dyspnea, dysphagia, referred otalgia, odynophagia, chronic cough, hemoptysis, and stridor[7]. In contrast, one-third of laryngeal tumors affect the supraglottic region. These are generally more aggressive and often diagnosed at later stages, as dysphonia is not an early symptom, making early detection more difficult. Furthermore, the supraglottic region, as opposed to the glottis, is rich in lymphatic vessels, which facilitates lymphatic spread of the cancer. In these cases, patients may present with signs of airway obstruction, such as stridor or dyspnea on exertion, along with dysphagia, pain, and metastatic lymphadenopathy[9]. Finally, subglottic tumors are rare, often asymptomatic initially, and usually detected only when locally advanced, frequently necessitating laryngectomy as a first-line treatment[10].

Squamous cell carcinoma is the predominant histological type in laryngeal tumors across all anatomic regions[11]. However, the larynx can also be affected by various other benign and malignant tumors, with truly benign tumors representing 5% or fewer of all cases. Indirect laryngoscopy is essential to evaluate suspected laryngeal cancer, followed by biopsy under direct laryngoscopy if a suspicious lesion is identified. Squamous cell carcinomas typically manifest as mucosal lesions, easily visualized during laryngoscopy, while non-squamous tumors are often submucosal, requiring further evaluation with imaging techniques such as computed tomography or magnetic resonance imaging[12].

Smoking is a major risk factor for head and neck cancer, increasing the risk by 5- to 25-fold compared to non-smokers[13]. A dose-response relationship has been observed, as demonstrated by a study that included 605 head and neck cancer cases and 756 controls, both drawn from the same population-based cohort. Among smokers, the relative risk for laryngeal cancer was 7.5, with risk increasing alongside greater smoking exposure. However, the risk decreased following smoking cessation and returned to baseline levels after 20 years of abstinence[14]. Similar studies also found that individuals who started smoking before age 18 and those with heavier smoking histories have a higher risk[15].

According to the 2013 Brazilian National Health Survey in Households, the Southern Region of Brazil had the highest smoking rate, with 16% of adults (over 18 years) smoking, while the Southeast, the most populous region of the country, had a rate of 15%. In the last survey, in 2019, the South continued to have the highest percentage, with 14.7%, compared to 13.5% in the Southeast[16]. This pattern may partly explain why the South Region recorded the highest number of hospitalizations, adjusted by population according to the 2022 census[17], with 0.84 hospitalizations per 1,000 inhabitants. In comparison, the Southeast recorded 0.74 hospitalizations per 1,000 inhabitants; the Northeast, 0.56; the Central-West, 0.5; and the North, 0.22.

It is also noteworthy that tobacco production is predominantly concentrated in Brazil's South Region, likely impacting the social, political, and economic landscape and contributing to greater acceptance and consumption of tobacco in this area. Additionally, the high presence of European immigrant descendants in southern Brazil and its sociocultural influences may be linked to smoking behaviors observed in this region[18]. Regarding gender distribution, smoking rates in 2013 were estimated at 18.9% for men and 11.0% for women[19], which may partly explain the higher rates of hospitalization among men in this study.

In terms of alcohol consumption, Brazil's annual per capita intake of pure alcohol among individuals over 15 years old surpasses the average observed in the Americas[20]. It is estimated that men consume two to ten times more alcohol than women[21]. Considering that alcohol consumption and smoking have an interactive and multiplicative effect on the risk of developing head and neck cancer, these figures may also account for the higher hospitalization rates for laryngeal cancer among men in this study.

Despite these conclusions, it is not possible to definitively establish an association between laryngeal cancer and smoking or alcoholism based solely on the data from this study, as it only accounts for hospitalizations related to the disease. Nevertheless, the findings align with existing literature, suggesting that men have higher exposure to these risk factors than women, as discussed earlier. Future research using longitudinal data and direct measures of exposure will be crucial to explore further the potential correlation between smoking, alcohol consumption, and the risk of hospitalization for laryngeal cancer.

Another important risk factor for laryngeal cancer is infection with human papillomavirus (HPV), a sexually transmitted disease that causes anogenital and oropharyngeal conditions in both men and women[22]. Epidemiological and molecular evidence has confirmed HPV's causal role, particularly type 16, in head and neck cancer. A comprehensive meta-analysis of 148 studies, covering 12,163 cases of head and neck squamous cell carcinoma, found HPV DNA in 22.1% of laryngeal tumors, compared to 45.8% in oropharyngeal cancers and 24.2% in oral cavity cancers[2]. An observational study using the National Cancer Database (NCDB), which included over 24,000 patients with head and neck squamous cell carcinoma, detected HPV DNA in 11% of laryngeal tumors[24]. In Brazil, the SUS offers the HPV vaccine to males and females aged 9 to 14 years, as well as to transplant recipients, patients undergoing chemotherapy or radiotherapy, people living with HIV/AIDS, and victims of sexual violence[25]. While HPV vaccination has been linked to a reduction in oral HPV infections, there is still no conclusive evidence of its impact on decreasing the risk of head and neck cancer. In this study, we observed a decline in hospitalizations among female patients with laryngeal cancer aged 10 to 30 years, with 47 cases in 2013 compared to ten in 2023. Despite the limitations mentioned earlier and the inability to make causal inferences, this trend could suggest a possible protective effect of vaccination in this subgroup, which was among the first to be vaccinated by the SUS. Additionally, the risk of HPV-related head and neck carcinoma outside the oropharynx, particularly laryngeal cancer, remains lower than that seen in oropharyngeal cancers[27].

GERD, a well-established risk factor for esophageal cancer, may also be linked to laryngopharyngeal tumors through laryngopharyngeal reflux, as indicated by studies using 24-hour pH monitoring[28]. GERD is one of the most common gastroenterological diagnoses, affecting around 12% of the Brazilian population, with similar prevalence in men and women[29]. Although findings in the literature are conflicting, the proposed pathophysiological mechanism suggests that gastric acid reaching the upper airways induces chronic inflammation by generating reactive oxygen and nitrogen species and intracellular acidification. This process may activate proliferative signaling pathways and cause cellular damage in the laryngeal epithelium, potentially leading to malignant transformation and the development of laryngopharyngeal squamous cell carcinoma[28]. Additionally, alcohol consumption can lower the tone of the lower esophageal sphincter, making it a dose-dependent risk factor for GERD30 and suggesting an interaction between risk factors for laryngeal cancer. Despite the potential role of GERD in the pathophysiology of laryngeal cancer, this study could not provide further conclusions on this association, given that the data were limited to hospitalizations and did not account for patients' comorbidities.

During the COVID-19 pandemic, delays in cancer screening and diagnosis became evident across several countries, leading to an increase in late-stage diagnoses, many of which were made in emergency settings. Additionally, significant delays were noted in initiating treatment for patients recently diagnosed with laryngeal cancer[31]. These trends align with the findings of this study, which showed a decline in hospital admissions for laryngeal cancer in 2020 and 2021.

Since Theodor Billroth's first total laryngectomy in 1879, treatment approaches have advanced considerably. Modern options include endoscopic laser laryngectomy for early-stage tumors and radiation therapy, which can be used alone in early cases or as adjuvant therapy in more advanced stages[3]. Currently, even for many patients with locally advanced laryngeal cancer (stages III or IV), organ-preserving strategies involving chemoradiotherapy are often preferred over total laryngectomy, as they offer better functional outcomes, although they do not provide a survival advantage compared to total laryngectomy[32]. With proper treatment, five-year disease-specific survival rates are high, reaching 100% and 96% for stages I and II, respectively, in leading centers[33]. Furthermore, care by a multidisciplinary team specialized in head and neck cancer has been associated with better outcomes, especially concerning vocal and swallowing rehabilitation[34].

This study, however, did not include data on treatment modalities or their potential outcomes. Generally, non-surgical cancer treatments can be administered on an outpatient basis, which tends to result in lower hospitalization rates, except in cases of complications. Analyzing the therapeutic modalities used could help explain trends in hospitalization rates over time. Additionally, examining treatment-related complications, including the number of hospitalizations, could enable comparisons of the morbidity linked to each therapeutic strategy. Common complications include xerostomia, dental disease, hypothyroidism, and osteoradionecrosis. Other critical outcomes to monitor post-treatment are voice and swallowing rehabilitation, nutritional status, continued use of alcohol and tobacco, depression, and other comorbidities.

This study was also unable to obtain data on relapse and recurrence rates among hospitalized patients, which are key contributors to hospital admissions. Understanding these rates is essential for evaluating treatment effectiveness and informing clinical follow-up strategies. Most recurrences (around 90%) occur within the first three years after curative treatment, underscoring the need for more frequent follow-up during this period. However, maintaining long-term monitoring, even at reduced frequency, is beneficial due to the potential for late recurrence and the development of new primary head and neck cancers, which share common risk factors[35].

Despite the study's limitations, some preliminary conclusions can be drawn regarding the profile of laryngeal cancer patients hospitalized at the SUS over the past decade. The predominance of male patients (85.4%) and those aged 60-69 can be attributed to higher rates of tobacco use and alcohol consumption in this population. While the Southeast region recorded the highest absolute number of hospitalizations of patients with laryngeal cancer, the South had the highest rate of hospitalizations adjusted for population size.

This study was limited to data from public hospitals, a significant constraint since private hospitalizations were not accounted for. Additionally, the data do not allow for statistical correlations with risk factors, habits, or comorbidities. Nonetheless, the findings provide insights that can inform future research using other databases, such as those from the National Cancer Institute (INCA) and the Global Cancer Observatory (GCO), which offer more detailed information on risk factors.

Finally, it is also crucial to emphasize the importance of health promotion in preventing laryngeal cancer, particularly by reducing smoking and alcohol consumption. Educating the public about the symptoms of laryngeal cancer is equally important, as it encourages patients to seek medical care at early stages, which is critical for timely diagnosis and better treatment outcomes.

CONFLICT OF INTEREST

The authors attest they have no conflict of interest to declare.

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EVALUATION OF DIABETES MELLITUS AND ITS COMPLICATIONS AS CONTRIBUTING CAUSES OF MORTALITY IN A GENERAL HOSPITAL (2016–2019)

Avaliação do diabetes mellitus e suas complicações como causa associada ao óbito, no período de 2016 a 2019, em um hospital geral

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ABSTRACT

Objectives: To evaluate diabetes mellitus (DM) as the underlying and contributing cause of death, as well as its main comorbidities in patients who died at Hospital Edmundo Vasconcelos (HEV). **Methods:** This is an observational and retrospective study. We analyzed all death certificates at HEV from January 2016 to June 2019. Of these, 26 certificates were excluded. We evaluated sociodemographic characteristics, the prevalence of DM, and its macro and microvascular complications. The same variables were reviewed in the electronic medical records of patients. **Results:** No significant associations were detected between the sociodemographic variables and the prevalence of DM. According to the electronic medical record, we found that 138 individuals had DM, but only 77 of these had a death certificate that mentioned the presence of this disease. Diabetic patients were also more likely to develop coronary artery disease, peripheral arterial disease, and hypertension. **Conclusion:** DM was listed in the death certificate, either as the underlying or associated cause, in 18.5% of deaths, while the medical records showed a prevalence of 33.3% among deceased patients. This discrepancy underscores the underestimation of DM's contribution to mortality in death certificate data.

Keywords: diabetes, mortality, death certificate.

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INTRODUCTION

The World Health Organization (WHO) defines diabetes mellitus (DM) as a syndrome with multiple etiologies resulting from either a deficiency of insulin or an inability to perform its functions effectively. Insulin, a hormone produced by pancreatic β cells, is crucial for carbohydrate metabolism, as it facilitates the transport of glucose into cells to be converted into energy. A lack of insulin or resistance to its action leads to elevated blood glucose levels, resulting in hyperglycemia[1].

In 2021, over 537 million people worldwide were estimated to be living with DM, with approximately 90% of cases being type 2 DM[2]. In Brazil, the prevalence of DM is particularly concerning as the country undergoes epidemiological transitions, with chronic diseases related to aging, including DM, becoming increasingly prominent in public health[3].

Morbidities associated with DM are often due to a combination of disease duration and poor glycemic control. Following diagnosis, achieving glycemic control is the primary goal of treatment, as it can help prevent or delay both acute and chronic complications, improve quality of life, and reduce mortality[1,4].

Despite being a significant and growing health problem worldwide, approximately 75% of cases of DM occur in developing countries, including Brazil, where the prevalence of DM is expected to rise over the coming decades[2]. Additionally, DM is the third leading cause of premature mortality, surpassed only by systemic arterial hypertension and tobacco use[4]. Thus, DM is extremely important for public health, given its high prevalence and resulting macrovascular (such as cardiovascular, cerebrovascular, and peripheral vascular diseases) and microvascular complications (including retinopathy, nephropathy, and neuropathy).

Currently, the Brazilian Institute of Geography and Statistics (IBGE) and the Mortality Information System (SIM) of the Brazilian Ministry of Health, which was established in 1975, collect mortality data for the Brazilian population. Although SIM serves as the primary source of mortality data in Brazil and has expanded its scope significantly over the years, challenges remain in enhancing data quality, mainly due to the inadequate completion of the Death Certificate (*Declaração de Óbito* - DO), the system's standard document. The DO consists of three self-copying, sequentially prenumbered copies provided by the Ministry of Health and distributed by State and Municipal Health Departments according to a standardized nationwide flow[5].

DM can be recorded on the DO in three ways: in part I, as either an underlying cause of death or an antecedent condition, and in part II, as a condition that contributed to death but did not result in the underlying cause listed in part I6. However, mortality statistics are based solely on the underlying cause of death, which the WHO defines as "the disease or injury that initiated the chain of pathological events that led directly to death, or the circumstances of the accident or violence that produced the fatal injury[7]." While the underlying cause of death is a valuable indicator for public health, studying this variable alone does not capture the impact of other conditions that may have contributed to the death, such as DM[8,9].

Thus, analyzing mortality through multiple causes, rather than only the underlying cause, is essential, as most deaths result from a multicausal pathological process. Understanding all diseases and complications present at the time of death enables a more comprehensive profile of the population's health. Moreover, analyzing mortality due to multiple causes offers valuable insights for public health professionals, as it provides a richer dataset that better reflects disease prevalence within the population[10].

DM is estimated to contribute to 14.5% of global mortality from all causes—a number greater than the combined deaths from infectious diseases such as HIV/AIDS, tuberculosis, and malaria4. However, accurately estimating DM-related mortality remains challenging, as approximately one-third of countries lack quality epidemiological data on DM. Moreover, where data exists, mortality due to DM is often underestimated due to frequent omission of this diagnosis on death certificates. Possible reasons for such an omission include the physician's unawareness of the patient's DM diagnosis prior to death, a low suspicion of DM's contribution to death, or physical space limitations on the DO[6]. As a result, when only the underlying cause of death is considered, diabetes ranks between the 4th and 8th leading cause of death. However, studies analyzing multiple causes of death have shown that the actual number of DM-associated deaths may be up to 6.4 times higher[4]. This suggests that the contribution of DM to overall mortality is significantly underestimated when only underlying causes are assessed[6].

In this context, the primary objective of this study is to evaluate DM as both an underlying and contributing cause of death in patients who died between January 2016 and June 2019 at Hospital Edmundo Vasconcelos (HEV) in São Paulo, Brazil. Additionally, the study aims to analyze the presence of DM-related comorbidities, including macrovascular and microvascular complications such as coronary artery disease (CAD), cerebrovascular disease, peripheral arterial disease (PAD), diabetic retinopathy (DR), nephropathy, and neuropathy, in this patient group. By examining these factors, the study seeks to assess the extent to which DM-related mortality may be underestimated when it can be considered both an underlying and an contributing cause of death.

METHODS

This observational, retrospective study was conducted based on death certificates issued by HEV. The study sample includes patients who were hospitalized at HEV and died between January 2016 and June 2019. We analyzed all DOs from this period obtained through the hospital's Mortality Review Commission. Based on these DOs, we reviewed electronic medical records to identify the presence of DM in the patients' histories and/or as a primary diagnosis, as well as its major macrovascular and microvascular complications, including CAD, stroke, PAD, DR, diabetic nephropathy, and neuropathy and assessed their impact on the primary outcome (mortality).

All medical records were reviewed to account for cases where DM may not have been listed as the underlying or contributing cause of death on

FIGURE 1 - Flowchart describing the study's methods.

the DOs despite the presence of this comorbidity. Additionally, we collected sociodemographic data such as sex, race, age group, profession, education, and marital status. We examined a total of 440 DOs, excluding three of these due to incomplete data, and 23 pertained to patients referred to the Death Verification Service (Serviço de Verificação de Óbitos - SVO), which uses different documentation, potentially resulting in interpretation difficulties due to inconsistent information.

We performed descriptive statistics for all variables. For categorical variables, we used measures of complete cases, frequency, percentage, and cumulative percentage. For continuous variables, such as age, we used measures of complete cases, mean, standard deviation, maximum, and minimum.

The inclusion criteria for this study encompassed all deaths occurring at HEV during the specified period. Exclusion criteria included patients referred to the SVO or Legal Medical Institute (Instituto Médico Legal—IML) and those for whom complete information could not be obtained from the electronic medical records or DOs. **Figure 1** provides a flowchart illustrating the process performed in this study to analyze these deaths.

Descriptive statistics were obtained for all variables. For categorical variables, we reported counts, frequencies, percentages, and cumulative percentages. For continuous variables, such as age, we calculated the number of complete cases, mean, standard deviation, maximum, and minimum values.

To investigate whether DM is underestimated as a cause of death, we analyzed the frequency of various conditions potentially associated with DM (DR, diabetic nephropathy, neuropathy, CAD, PAD, and stroke) in patients with and without a DM diagnosis. We used a contingency table for this analysis and applied the Chi-square (χ^2) Association Test with Fisher's Correction, appropriate for cases with cell frequencies below 5. Statistical significance was set at 5% ($p < 0.05$).

The objective of this analysis was to determine whether the frequencies of specific causes of death differ between patients with and without DM. If no significant association is found, it suggests that the observed frequencies vary by chance. Conversely, a significant association would indicate that a DM diagnosis influences the distribution of these causes of death. We calculated the Odds Ratio (OR) to assess this possible association. When calculating the OR was not feasible, such as when variables had more than two categories, we interpreted the association based on the relative frequencies in the contingency table. Lastly, to determine whether DM was accurately identified in medical documentation, we compared the diagnosis in the DOs with that in the medical records, using the contingency table and the χ^2 test.

The project was approved by the Ethics Committee of the HEV/Fundação Instituto de Moléstias do Aparelho Digestivo e da Nutrição under the number 23949019.5.0000.0090/2019.

RESULTS

The study sample consisted of 440 individuals, with 26 excluded based on the criteria described above, resulting in a final sample of 414 patients. The mean age of the participants was 73.5 years (see **Table 1**), and 53% were women.

Regarding race, 82.8% were white, 7.5% were Asian, and 5.1% were Black (see **Table 2**). Regarding marital status, 46.8% were married, and 31.4% were widowed. Additionally, 28.9% of the sample had completed higher education.

Among diabetic patients identified in their medical records, 55.7% were male, and approximately 25.4% had

TABLE 1 - Age of deceased patients at Hospital Edmundo Vasconcelos in São Paulo, Brazil, between January 2016 and June 2019.

	AGE RANGE	STANDARD DEVIATION
Age	0,5 -105	18,26

Source: death certificates.

TABLE 2 - Race of deceased patients at Hospital Edmundo Vasconcelos in São Paulo, Brazil, between January 2016 and June 2019.

RACE	NUMBER OF PATIENTS	PERCENTAGE (%)
White	342	82.81
Asian	31	7.51
Black	21	5.08
Brown (*Pardo*)	16	3.87
Native-Brazilian	0	0
Unknown	3	0.73

Source: death certificates.

TABLE 3 - Diagnosis of Diabetes Mellitus according to different sources of data.

	ELETRONIC MEDICAL RECORD		
DEATH CERTIFICATES	NO	YES	TOTAL
Yes	2	75	77
No	274	63	337
Total	276	138	414

Source: death certificates and electronic medical records.

completed higher education. No significant associations were found between sociodemographic variables and the presence of DM ($p > 0.05$).

Considering only the DOs, DM was mentioned anywhere in the certificate of 77 patients (18.6%). Among these cases, CAD showed a statistically significant association ($p < 0.01$), with an Odds Ratio (OR) of 3.10 (95% CI = 1.52 to 6.19), indicating a 3.10 times greater likelihood of CAD in diabetic patients. A similar trend was observed for PAD, with a statistically significant χ^2 value ($p < 0.01$) and an OR of 3.83 (95% CI = 1.50 to 9.54), suggesting a 3.83 times greater likelihood of PAD in patients with DM. Additionally, diabetic patients were found to be 7.79 times more likely to have hypertension as a comorbidity (95% CI = 4.38 to 13.99).

DR was not documented in any cases, while nephropathy had a prevalence of 1.9% within the sample, although its etiology was undetermined in all cases. Diabetic neuropathy had a prevalence of approximately 0.7%.

A review of medical records revealed that 138 patients (33.3%) in the sample had a diagnosis of DM, compared to only 77 patients whose DO indicated DM, as shown in Table 3. This difference suggests that in 14.8% of cases, DM was not included in the DO despite being present in the patient's medical history.

Among the 138 patients with DM identified in the medical records, 19.1% had CAD as a complication, 15.9% had experienced at least one stroke (unspecified if ischemic or hemorrhagic), and 9.9% had been diagnosed with PAD.

In this analysis, the association between DM and CAD was statistically significant ($p < 0.01$), with an OR of 2.81 (95% CI = 1.66 to 4.81), indicating a 2.81 times greater likelihood of CAD in diabetic patients. A similar trend was found for PAD, with an OR of 4.53 (95% CI = 2.20 to 9.73), reflecting a 4.53 times higher likelihood of PAD in those with DM. The likelihood of stroke was also elevated in patients with DM, with an OR of 1.99 (95% CI = 1.12 to 3.52). Additionally, diabetic patients were 4.96 times more likely to have hypertension as a comorbidity (95% CI = 3.09 to 8.12).

Regarding microvascular complications, DR was not documented in the medical records of any patients. On the other hand, nephropathy was documented in 9.2% of patients, although the renal disease's etiology was unclear in 4.8% of cases. Diabetic neuropathy was identified in only 1.9% of cases.

DISCUSSION

Significant issues exist regarding the reliability and validity of cause-of-death information on DOs. These challenges stem from diagnostic inaccuracies, variations in causal interpretation, and identifying the conditions that contributed to death[8]. Additionally, the Brazilian DO provides only four lines for part I and two lines for part II, which can restrict space, particularly for patients with multiple chronic conditions, such as many patients with DM. As a result, other conditions, including hypertension, dyslipidemia, and chronic kidney disease, may compete for space on the DO due to the lack of a clear hierarchy among these comorbidities.

Consequently, DM is frequently omitted from DOs, as demonstrated in this study's sample, where DM was recorded in only 18.6% of cases on DOs, compared to 33.3% in medical records. This finding is even lower than that reported in a U.S. study by McEwen *et al.*[6], who documented DM in 39.0% of the death certificates analyzed, though DM was listed as the cause of death in only 10% of cases. That study concluded that death certificates underestimate the prevalence of diabetes among deceased patients, resulting in a biased representation of the causes of death for individuals with DM. In our study, however, the prevalence of DM in medical records was closer to that found on death certificates analyzed by McEwen *et al.*

Unfortunately, mortality statistics based solely on death certificates fail to reflect the actual mortality rate due to DM[12]. In another study by McEwen *et al.*[13] focusing on patients with type 1 DM, the disease was mentioned in any part of the death certificate in only 46% of cases and listed as the cause of death in just 16%. In another sample that included patients with both type 1 and type 2 DM, McEwen *et al.*[6] found an association between the likelihood of DM being mentioned on the death certificate and factors such as insulin use and disease duration, although no significant differences were noted between DM types. In our study, however, it was not possible to identify insulin-dependent diabetics or determine disease duration, as many medical records listed only the DM diagnosis without details on treatment or duration of the disease. This limitation restricts our ability to accurately detail the characteristics of patients whose DM diagnosis is reported on the DO and compare them to those not mentioned in their death certificates.

Chronic complications of DM are increasingly common as the incidence of this metabolic disorder rises. In our study, macrovascular complications were noted in 24.1% of medical records, whereas microvascular complications were documented in only 9.4%. This disparity may stem from a tendency not to investigate or document microvascular diseases, compared to macrovascular diseases such as CAD and cerebrovascular disease, as these conditions are often linked to acute events and death. These findings differ from those of Santos *et al.*[14], who reported a prevalence of microvascular complications in 53.8% of patients with type 2 DM, significantly higher than in our study. However, it is essential to note the different patient profiles in the two studies: while Santos *et al.* conducted telephone interviews with patients registered with the Diabetic Association of Maringá and Region (ADIM), this study evaluated patients who had recently died.

In our study, no cases of DR were reported, which contrasts with existing literature showing that the natural progression of DM generally involves the development of microvascular complications across multiple sites simultaneously. However, in clinical practice, retinal changes, for example, do not necessarily imply concurrent renal impairment, and vice versa. Studies, however, indicate that when diabetic nephropathy is present, it is common to find some degree of DR in the same patient[15].

Our study also found that 19.1% of diabetic patients had CAD as a complication of DM (classified as ischemic cardiomyopathy). CAD is known to be a complex condition influenced by multiple inflammatory, metabolic, and genetic factors. Extended follow-up in the Diabetes Control and Complications Trial (DCCT) demonstrated a 57% reduction in cardiovascular mortality with intensive glycemic control during the initial study years[16]. This association appears relevant, as diabetic patients in our sample were found to be 2.81 times more likely to be diagnosed with CAD compared to non-diabetic patients.

Our results indicated a 4.96-fold higher likelihood of hypertension in diabetic patients compared to those without DM. This finding aligns with previous studies that reported a 2.4-fold increased prevalence of hypertension in diabetic patients. This association is significant, as hypertension is linked to various acute cardiovascular events, which are the leading cause of death in patients with type 2 DM4. It is worth noting that the stronger association observed in this study could be attributed to the sample consisting of recently deceased patients who likely had more severe conditions.

In summary, our study supports the hypothesis that data recorded on death certificates underestimates the contribution of DM to overall mortality. Furthermore, diabetic patients in our study exhibited a higher likelihood of macrovascular complications, such as CAD and PAD, as well as hypertension. However, this trend was not observed for microvascular complications, possibly due to limited investigation or documentation of these conditions in the medical records of critically ill patients. For instance, DR was not reported in any cases, suggesting that its prevalence, like that of DM, is underestimated.

To improve the reliability of death certificate data, a potential solution would be to add a dedicated field for recording major comorbidities, such as DM, hypertension, and smoking, regardless of their direct causal relationship with death[17]. Without such an intervention, death certificates will remain an unreliable source for estimating the association between DM and various causes of death. As a result, death certificates will not accurately measure DM's impact on life expectancy.

CONFLICT OF INTEREST

The authors attest they have no conflict of interest to declare.

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PAIN, KNOWLEDGE, AND SUPPORT: THE EXPERIENCE OF A MULTIDISCIPLINARY TEAM IN AN ONCOLOGY OUTPATIENT CLINIC IN BRAZIL

Dor, conhecimento e acolhimento: experiência de uma equipe multidisciplinar em um ambulatório oncológico no Brasil

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ABSTRACT

Pain is one of the most feared symptoms by adult cancer patients. However, it is also one of the most frequent. In the healthcare field, meanings influence teamwork and patient adherence to treatments. This issue highlights the importance of research investigating meanings related to complex human phenomena, such as pain. The main objective of this study was to understand the meanings attributed to pain in adult cancer patients by professionals from a specialized outpatient cancer clinic. Developed following the principles of the clinical-qualitative method, this study interviewed 20 professionals from an outpatient clinic specializing in health care for adult cancer patients. The number of participants was defined by using the inductive thematic saturation criterion. The instrument used was a semi-structured interview. Data collection was performed individually and recorded in audio. The corpus of this study was composed of literal and complete transcripts of the audio recordings of the semi-structured interviews and was subjected to clinical-qualitative content analysis. Field notes provided additional input for this purpose. The validity of the categories resulting from the clinical-qualitative content analysis was confirmed through a meeting with other researchers from the research group, predominantly postgraduate students. The results were organized around reports that highlight the importance, for the participants, of specialized professionals, who must be both welcoming and supported, favoring the care of adult cancer patients with pain. These findings can be used in different initiatives to improve health care offered in specialized outpatient clinics.

Keywords: Pain, Perception, Patient Care Team, Qualitative Research.

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INTRODUCTION

The concept of "total pain" is used to capture the multifaceted pathophysiology of pain experienced by cancer patients, emphasizing that adequate pain relief requires addressing its physical, psychological, social, and spiritual dimensions[1]. Caring for these patients should involve a holistic approach, ideally delivered by an interdisciplinary team. Such a team brings together diverse areas of expertise, aiming to broaden the scope of care to encompass not only patients but also their peers and the healthcare team as a whole[2].

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage"[3]. This definition, endorsed by the World Health Organization (WHO), is widely accepted among healthcare providers and researchers focused on pain.

Cancer, a chronic degenerative disease, is responsible for approximately 12% of deaths globally and accounts for around 15 million new cases each year, causing a significant public health impact that ultimately influences public policies. Therefore, these statistics highlight the need for policies that encourage scientific research and economic investment in developing alternative strategies for patient support, monitoring, treatment, and care[4].

Clinical expertise is now recognized as equally essential as values, attitudes, and behaviors in healthcare[5], especially in cancer care. Humanized care integrates a scientific understanding of the health-illness-treatment process with an individualized view of each patient[6]. This approach should be a central consideration in the educational curriculum and training of healthcare professionals[7,8].

Finally, it is essential to mention that, in healthcare, the work team itself can be a significant source of professional satisfaction, particularly when each member contributes with unique knowledge and individual experience to benefit patients[6]. Similarly, a willingness to collaborate is highly valued and fosters a positive, supportive environment.

In this context, this study aimed to explore the meanings that professionals in a specialized outpatient clinic attribute to pain in adult cancer patients and to examine how these insights relate to applying skills gained through their clinical experiences.

METHODS

Methodologically, this study employs a qualitative research design. Such type of research focuses not on phenomena per se but rather on the meanings these phenomena hold for individuals or groups[9]. Thus, regardless of the specific objective, qualitative research seeks to describe and understand human experiences in their most subjective aspects, prioritizing the perspectives of participants[10].

Participants in this study were healthcare professionals over 18 years old who had been working in the same healthcare service for at least one month at the time of data collection. To ensure anonymity, participants were given pseudonyms inspired by the names of galaxies and constellations, while any patients they mentioned were assigned pseudonyms based on comets.

The study setting was an outpatient clinic specializing in adult cancer care within a public hospital in a medium-sized city in southeastern Brazil[11]. This hospital exclusively serves patients through the Unified Health System (*Sistema Único de Saúde* - SUS) and is a regional reference center for approximately 500,000 people, providing a range of clinical and surgical services. Additionally, it is certified as a High Complexity Oncology Care Unit (*Unidade de Assistência de Alta Complexidade em Oncologia* - Unacon) by the Brazilian Ministry of Health, being equipped with the human and technological resources necessary for the diagnosis and treatment of various types of cancer.

The hospital provides inpatient beds and emergency, urgent, and outpatient care to meet the diverse needs of adult cancer patients, specifically in Breast Surgery, Gynecology, Urology, and Coloproctology. The outpatient clinic operates Monday through Friday from 7 am to 7 pm, excluding holidays, and is staffed by a multidisciplinary team of 41 professionals. This team includes 12 doctors (three oncologists, two urologists, two general surgeons specializing in the digestive system, an anesthesiologist, a cardiologist, a breast cancer specialist, a gynecologist, and a palliative care specialist), five nurses, two nursing technicians, one nursing assistant, two pharmacists, two pharmacy technicians, a psychologist, a social worker, a nutritionist, a clinical laboratory technician, three receptionists, two cleaning assistants, a pantry and kitchen assistant, and seven security guards.

The primary data collection tool for this study was a semi-structured interview. This method, well-suited for clinical-qualitative research, allows participants to freely express their personal perspectives and meanings regarding the topic defined by the researcher[12].

The thematic guide for this study included the following questions: (1) What does pain mean to you? How does it manifest in adult cancer patients? (2) In your opinion, is pain in adult cancer patients different from pain in other patients? If so, in what ways?; (3) In your opinion, what factors improve or worsen the pain of adult cancer patients?; (4) In your opinion, how should pain in adult cancer patients be assessed in terms of cause and intensity?; (5) In your opinion, what should the goals of care be for adult cancer patients experiencing pain?; (6) What is it like for you to care for adult cancer patients with pain complaints? Do you see positive and negative aspects? If so, which ones?; (7) Has your perspective on this topic changed over time? If so, how?; (8) In your opinion, what could be done to improve the care of adult cancer patients with pain?; (9) Do you have any notable examples from your professional experience involving caring for adult cancer patients in pain?

Of the 41 professionals at the outpatient clinic, 27 were invited to participate in this study, with no refusals or withdrawals. However, two participants were unavailable due to health-related work absences. Not all eligible professionals were contacted because the sample size was determined using the saturation criterion rather than the exhaustion criterion. This approach was selected as it is widely accepted for scientific validity in qualitative research[13]. Specifically, the inductive thematic saturation criterion was used, as the number of participants was defined once the themes identified in the initial data analysis were deemed sufficient to address the research objective[14].

The corpus of this study consisted of complete, verbatim transcriptions of the audio recordings from the semi-structured interviews, which were then analyzed using clinical-qualitative content analysis, following the methodological framework developed by Faria-Schützer *et al.*[15]. This approach builds on Bardin's[16] original content analysis method. Therefore, the first step is to perform a preliminary immersive reading of the material (or a "floating reading" if literally translated from the term lecture flottante used by Bardin in her original work in French). This step aims to connect the reader with latent meanings and construct units of analysis related to the research focus, a recommended practice in clinical-qualitative content analysis in the health field that is useful to interpret underlying meanings within individual interviews[15]. The validity of the analytic categories — ensuring they were mutually exclusive, thematically cohesive, and aligned with research objectives — was confirmed in a second meeting involving additional researchers from the group, primarily postgraduate students.

This study received approval from an Ethics Committee and followed ethical standards outlined in Brazilian legislation. All participants signed an informed consent form before data collection, formally explaining the study's objectives and procedures. It was clearly stated that all eligible participants were free to decline involvement without consequence and could withdraw their consent at any time, even after data collection was complete. The researcher's commitment to maintaining participant confidentiality was also formalized within this document.

RESULTS

The study involved 20 professionals from diverse roles within an outpatient clinic specializing in adult cancer care, including doctors, nursing staff, pharmacists, psychologists, social workers, nutritionists, receptionists, security personnel, and environmental services/cleaning staff, as detailed in **Table 1**.

Twelve participants emphasized that caring for adult cancer patients requires specialized technical knowledge, linking this need to their understanding that pain tends to be more intense in this population. Seven participants mentioned they had studied or sought additional information on the topic since beginning their work at the Oncology Outpatient Clinic. Antila's account illustrates this sentiment:

> *"If you don't have a prepared team, with knowledge, they won't be able to understand what they [the patients] are saying [...]. Perhaps a trained professional will understand it perfectly. They will be able to see them [the patients] in their entirety within their [the professional's] knowledge. Something that I think other professionals will have this difficulty with".*

Seyfert highlighted the importance of ongoing education for healthcare providers:

> *"The palliative [care] course, these courses that we have been doing [...], really opened my mind. [...] I think that people [professionals] should have more knowledge, you know? More closely, about the oncology patient. About the phases of their treatment, the phase of life that they are in. Because I only had this vision when I got closer, when I started working with this. So I see that, I think that many people do not have this knowledge and treat them as a normal patient who is there, who is hospitalized, the same treatment for everyone. So I think that is lacking".*

Half of the participants emphasized the importance of understanding each patient's unique needs and offering a welcoming attitude, often through simple gestures, aligning with the view of pain as a subjective experience, which is central to the second category. Seyfert shared an example from a consultation to illustrate this approach:

> *Met "I think that what makes [pain] better is when you understand them [patients]. Listen to what they want to say; sometimes, if they are upset, understand that moment and respect it. So much so that I respect it a lot. Just today, a patient's daughter said: 'Oh, I want her to eat fish.' A daughter told her mother, who was there in a wheelchair: 'I want her to eat fish because fish is good. Because someone at the other hospital sees the nutritionist, and she eats a lot of fish, and my mother has to eat fish.' So I said: 'Look, but if she doesn't like fish, we have to respect her, she can eat other things.' Then the lady made such a happy face, like: 'Someone understands me.' You know? 'Phew! I won't have to eat fish.' So I felt that she was relieved. Because, in addition to all the pressure of the treatment, the pain she is feeling, the surgery she had, she also had a daughter pressuring her to eat the fish she doesn't like [laughs]. So I feel that just by the fact that the patient is respected, they already feel more relieved".*

Pegasus similarly highlighted the importance of building trust with patients:

TABLE 1 - Distribution of Participants by Sex and Position within the Multidisciplinary Team

PARTICIPANT	POSITION	SEX
Cartwheel	Nursing Technician	Female
Antila	Registered Nurse	Female
Lacerta	Psychologist	Female
Redshift	Front Desk Staff	Female
Hoag	Registered Nurse	Masculino
Columba	Pharmacy Technician	Female
Hydra	Cleaning/Environmental Services Associate	Female
Mice	Oncologist	Female
Magalhães	Security Guard	Masculino
Messier	Registered Nurse	Female
Andromeda	Front Desk Staff	Female
Lyra	Social Worker	Female
Seyfert	Nutricionist	Female
Phoenix	Front Desk Staff	Female
Aquila	Pharmacist	Female
Pegasus	Registered Nurse	Female
Centaurus	Pharmacy Technician	Female
Sagitta	Nursing Technician	Female
Cassiopeia	Pharmacist	Female
Markarian	Registered Nurse	Female

* To preserve their anonymity, participants were identified by pseudonyms, referring to the nomenclature of galaxies and constellations.

> *"I think that, in addition to the physical exam, an anamnesis of everything that has happened [is necessary]. You must have the means, and the person must have the confidence to tell you. Because many times they don't trust you and they don't tell you everything that has happened. And we try as if it were building blocks, like this, to put it together, to be able to understand. So, I think that's it, you have the trust of the person, you can get them to tell you everything. [...] What has been happening to them over the course of these days".*

Cartwheel shared a story that illustrates the impact of a welcoming approach in easing pain-related symptoms:

> *"We have a patient here, an old one, not a new one. She was terrified of the Portocath®. When the Portocath® was implanted, she felt sick, very sick. She vomited, and when it was time to get it, you know, to put the little needle in there, she felt pain. The smell of chlorhexidine [...]. What did I do one day? I put makeup on her. I said: 'Look, let's do this?' I said to Antila: 'Antila, swap the chlorhexidine for alcohol,' and she went there and swapped it [winking one eye as if to imply that we were just pretending]. Then I started putting makeup on her. I said: 'We're going to put makeup on you and you're not going to look. Let's agree on this? You're not going to look?' I started putting makeup on her, and playing around, and putting makeup on her. So Antila punctured her, the medications started to run, she didn't feel it, she didn't feel sick. Do you understand? She didn't even feel the prick".*

Cassiopeia, on the other hand, recalls the importance of complementary therapies:

> *"Using complementary therapy techniques, which we talk about, integrative medicine. Maybe a massage, acupuncture, aromatherapy, right? Complementary therapies that also take the patient out of the cold environment of the hospital. [...] The goal would be not only to improve the pain itself, but to treat it, which I repeat because, from my experience, I see that sometimes it is a palliative, a word. The goal would be not only to focus on the pain, but on the patient's quality of life as a whole. This will directly influence them. Their perception of pain".*

Antila, conversely, emphasized the importance of promptness in care delivery, resonating with the theme of prioritizing cancer patients experiencing pain, as discussed in the second category:

> *"If everything happens quickly, I think it gets better, right [...]. And then, sometimes, what makes it worse is the delay, right? I think that makes it worse. It increases their pain. And then it gets better when we see them, and we do it faster. We feel it, that it improves. The delay in seeing them, the delay in medicating them [...]. Because we see, for example, when they [the patients] arrive here, we welcome them, we put them [in the bed]. It's not that they are not in pain, they are, but then, the speed at which we address their discomfort, we prepare the medication and follow the prescription to alleviate it; I believe it improves. When they are in pain and they haven't even managed to get a bed or be seen, I think it gets much worse".*

Cartwheel seems to agree with this position:

> *"The patient shouldn't feel pain in the hospital. [If] the patient is in pain, I think you have to put them first, see them first, medicate them [...]. You can't feel pain in a hospital. I think that's the end, in my opinion. You can't understand that. You see the person in pain and waiting there, right? I think you have to see them first".*

Hoag further discussed possible side effects of medication and stressed the importance of non-pharmacological approaches to pain management:

> *"We still have the false impression that medication solves everything. If you are in pain, you will take painkillers, you will take, I don't know, sedatives, and you will solve the pain, right?[...] We forget about care that can also reduce pain. [...] There are several factors that improve pain before you have to overload an organism with medications when it is already overloaded with other things. [...]. That is why I say that pain is unique, each patient is unique. Each patient is unique. And there is no one-size-fits-all recipe, so we need to work as a team. And learn a lot about this problem of pain, right? [...] Every day we are learning new ways of dealing with pain [...]"*

Hoag also highlighted the importance of a supportive, multidisciplinary approach to pain management:

> *"I think we need a cohesive team, right? That's what we call a multidisciplinary team. So we have the nutritional part, with the nutritionist, who can use foods that do not interfere so much in the body's cycle, in order to reduce the potential for pain. The psychologist, who works a lot with this acceptance phase. Nursing, in the aspect of dealing with the other person's pain and respecting the other person's pain limit. The medical team, right? Preparing this patient for a very difficult issue, which is palliative 'supportive', right? So, pain doctors are extremely important professionals because they are the reference, not only to prescribe the painkiller but also to guide the patient on how all of this will work. [...] The oncology patient wants very little from you. From the moment you open your ears to hear what they have to say and so on, look the person in the eye like that, you are already giving the first medication".*

Cassiopeia proposed expanding the care environment to better accommodate oncology patients:

> *"Here at the hospital we don't have a [specific] oncology inpatient ward. And I think that mixing patients with those from general internal medicine is very wrong. Because there are patients with many types of pathologies, viruses and bacteria, etc. And the oncology patient already has an extremely depressed immune system. The treatment is difficult, right? And exposing the patient, putting the patient in, carrying the patient upstairs, doing all that, that transportation, is what I think you end up contaminating everything. And staying there, together with the other patients, without having an exclusive place? I think that's what's needed".*

Messier, meanwhile, linked quality of life with the dignity of death when asked about ways to improve care for patients experiencing pain.

> *"I believe that these are palliative care beds. There are no vacancies for the people*

> *we deal with. Not to mention that when cancer patients become terminally ill, they can stay at home with their families, but no one is prepared for that. So what is the other option? Unfortunately [admission to a hospital]. But if they have access to a multidisciplinary palliative care team, explaining to the family what their role is... And [explaining] that the patient will be receiving care there. I think they would have a good quality of death. I think one could say with dignity. Because they will be speaking the same language there."*

The need to acknowledge the emotional burden on the multidisciplinary team was highlighted, although subtly, by several participants, including Markarian:

> *Sometimes you don't see many results. The patient has chronic pain, and sometimes you don't see much improvement, right? I think this also brings discomfort as a team. For example: 'Oh, what could we do?' Sometimes we've tried everything, and this patient doesn't get better. There's all this. I think this is frustrating for us [professionals] too, often."*

Similar reflections can be seen in the following report by Hoag:

> *"The loss of a patient in oncology is very painful for the team. We also need to deal with this, and also accept the loss of our patient, right? [...] So I had to talk to a lot of people to learn that the people we care for also pass away, right? [...]. And each patient will have a different impact on our lives too. Because they are human beings who lived with us for six months, a year, ten years, whatever. So when they stop being in the service, it is remarkable in some way, right? [...] And we need to deal with it".*

Although essential to achieve the goals of care for patients and family members, the role of public policy and political investment in establishing a national palliative care program was mentioned by only two participants, including Antila:

> *"How are we going to treat pain if we see that the national palliative care policy is also not implemented within the hospitals? So, they [the patients] arrive, but there is no national palliative care policy on where these patients will be cared for. Where they will be admitted to? There is not even [...] sometimes there is not even a bed for them. That is what we see, right? It may not be just like this in Brazil in general. Maybe in other hospitals it may be different. But I see it as a general problem, because of the service regulations, so all of this makes things difficult for them [patients]. So we watch them die".*

Magellan echoed these concerns, stressing the importance of political commitment to address these challenges:

> *"We see the government out there, they say they do it, do it, do it, but they are very negligent, they do not provide the assistance they should [...]. Whether you like it or not, it is a disease that has a death sentence, right? Many are cured, but most are not. What we can do, in the case of you guys, health professionals, is to alleviate the pain, most of the time. [...] So it has to start at the top. They [politicians] must see the situation of these patients and must really invest, invest heavily in it. Because there may not be a cure, but if there is survival, right? They say: 'Look, you will live another ten years'. Then the patient will [get better]. But that has to be a heavy [government] investment."*

DISCUSSION

Most participants emphasized the importance of technical knowledge for adequately managing patients with chronic, difficult-to-control cancer pain. Some healthcare professionals expressed frustration stemming from insufficient specialized training in chronic pain management, a sentiment documented in prior research[17,18]. In many cases, this frustration is internalized as guilt when treatments for complex cases are unsuccessful, with certain professionals even describing feelings of fear and stress upon recognizing the names of these patients on their clinic schedules[19,20].

However, the humanistic complexity inherent in caring for patients with cancer-related pain highlights the limitations of a purely technical approach. Consequently, the curricular guidelines for healthcare training should emphasize developing a critically reflective, humanistic skillset to address health promotion, prevention, recovery, and rehabilitation from a comprehensive perspective on the health-disease continuum[21]. This dimension of affective-social care aligns with institutional and governmental policies that advocate for humanization in healthcare, aiming to foster meaningful, empathetic relationships between patients and professionals[22].

To cultivate such humanistic skills in training, educators must recognize the depth and complexity of the concept of humanization. The formation of values, attitudes, and behaviors during professional training must be an intentional process facilitated through thoughtful planning and discussion in immersive teaching and learning environments. This approach requires implementing both formal and informal curricular strategies to nurture sensitivity, commitment, and respect for each patient's unique identity and humanity[23].

Participants in this study reported that comorbidities frequently accompany pain, including depression, anxiety disorders, loss of appetite, edema, and wounds, all of which negatively impact quality of life. The involvement of non-medical professionals—such as psychologists, nutritionists, nurses, and physiotherapists—is invaluable in providing holistic care that incorporates diverse coping strategies to support health. It is evident that an expanded, patient-centered approach, which transcends a purely disease-focused perspective, is the most effective way to achieve patient satisfaction[24].

Many participants also emphasized the importance of legitimizing patients' pain, even when it is not visibly apparent. Recognizing and validating a patient's pain relies on the strength of the bond between the professional and the patient with chronic pain, which is essential for a supportive approach and promoting health and well-being. When this professional-patient relationship is well-established, it often yields benefits beyond the accuracy of diagnosis[25].

Nonverbal communication is as significant as spoken words in the professional-patient relationship. Actions such as making eye contact, sitting at the patient's level, creating a welcoming environment, ensuring the patient and their family understand the information provided, allowing the patient to ask questions, repeating the patient's words as a form of validation, and minimizing external interruptions are all crucial elements in building trust and rapport, as noted by the study's participants[26].

Establishing a strong professional-patient relationship enables a deeper understanding of pain—a symptom as frequent as it is complex—and its profound impact on a patient's quality of life[27]. As the professionals interviewed described, this nuanced perception is essential to enhancing the quality of this interaction and recognizing certain behaviors repeatedly employed by the healthcare team.

Multiprofessional care fosters adaptive, contemporary healthcare systems that reflect the specific realities of each service, as highlighted by Hoag. This welcoming approach to care nurtures trust and commitment in the relationships between patients and professionals, facilitating advancements in health solutions and strengthening connections between teams and services in implementing public policies that support the SUS. This requires an ethical-political stance grounded in recognizing and valuing diversity, fostering collective agency, and ensuring living conditions that promote health[28].

The National Humanization Policy (*Política Nacional de Humanização* - PNH) advocates for structural changes in the management of health services through expanded democratic spaces for discussion, listening, exchanges, and collective decision-making. This approach includes not only welcoming patients and their families but also supporting the professionals who make up the multidisciplinary team. This support is essential, as it allows for a shared evaluation of the challenges in meeting the needs of the population—challenges reported by many professionals in the field[29].

PNH also outlines various approaches to creating a welcoming environment, including adapting physical spaces so that healthcare services align with care demands, reorganizing workflows, managing local teams to prioritize compassionate care, fostering humanized work relationships, restructuring management practices in healthcare units, building therapeutic bonds, and encouraging interdisciplinary practices[28]. These recommendations were echoed by participants in this study when asked about possible strategies for enhancing care for cancer patients with pain.

Complementary treatments, recognized in Ordinance Nº. 1,083 of the Brazilian Ministry of Health from October 2nd, 2012[30], were also widely recommended by participants as beneficial supplements to traditional pharmacological pain treatments, including for cancer pain[31]. Such approaches offer supportive options that can work alongside conventional treatments.

As the study's participants emphasized, the potential for pharmacological pain management side effects should be anticipated, prevented, and effectively managed. Nonetheless, adverse symptoms associated with analgesic medications remain common, often dose-dependent, and influenced by factors such as individual biological variations, the presence of comorbidities, and concurrent treatments—factors that are especially relevant in cancer patients[32].

Caution in pharmacological treatment is essential to avoid prescribing medications that contradict treatment objectives. One common misunderstanding, as highlighted by a participant, involves the misuse of hypnotic and sedative drugs for their assumed analgesic effects—a misconception prevalent among the lay population. Sedatives and hypnotics primarily affect the level and content of consciousness rather than addressing the underlying mechanisms of physical pain. Yet, some healthcare professionals may still misuse them, aiming to achieve pain relief through sedation. Adhering to the ethical principle of "do no harm"[33] requires recognizing that administering consciousness-depressing medications to patients in physical pain can lead to an unpleasant, unrelieved sleep state, leaving patients unable to adjust their position or perform self-care to ease their discomfort that remains unaddressed. Therefore, consciousness and analgesia, while interrelated, are distinct processes and should be treated with medications from different pharmacological classes as appropriate.

Participant Pegasus emphasized the importance of accurately interpreting patients' expressions to tailor care effectively. Her remarks highlight a commitment to understanding each patient's unique perspective within their social and personal context. This approach respects the values attributed to the patient's choices and the responsibilities that accompany them, enhancing the likelihood of successful treatment outcomes. Such a patient-centered approach is well-supported in scientific literature and has proven effective[34].

Pain is one of the primary reasons for suffering and seeking healthcare, with substantial economic implications for public health and wide-ranging biopsychosocial effects, as highlighted in this study. Timely, effective, and appropriate pain management directly affects both the perceived intensity of pain and overall quality of life[35]—a point well-recognized by the participants in this study.

In the state of São Paulo, Brazil, State Law Nº. 17,832, enacted on November 1st, 2023[36], recently guaranteed the prioritization of care for cancer patients. Nationally, Bill Nº. 4,890, introduced in 2020, which seeks to ensure preferential care for cancer patients in public services, is still under review in the Brazilian Chamber of Deputies[37].

Participant Cartwheel expressed a moral concern regarding the suffering of patients in pain within a hospital environment, considering such occurrences unacceptable. As a nursing professional in the Oncology Outpatient Clinic, Cartwheel's concerns are supported by scientific literature: numerous triage tools are available for the emergency setting, enabling nurses to prioritize immediate care based on severity[38]. Given that pain is widely recognized as the fifth vital sign[39], it should not be neglected.

Further concerns were raised about whether the multidisciplinary team at the Oncology Outpatient Clinic is sufficiently staffed to meet the needs of adult oncology patients experiencing pain, as well as about the organization of workflows. Ideally, this team would include clinical and surgical oncologists, palliative care and pain specialists, psychologists, nutritionists, physiotherapists, pharmacists, dentists, nursing staff, social workers, and chaplains, along with essential administrative personnel (such as receptionists, security, cleaning staff, kitchen and pantry staff, warehouse workers, human resources personnel, and lab/imaging technicians). The number of professionals should be sufficient to accommodate the rising demand of patients diagnosed with cancer, aligning with the Brazilian Constitution, which asserts that health is a universal right and a State obligation[40,41]. Moreover, although there is no set limit on the number of patients each professional should see per shift, staffing levels should always ensure quality and safety in patient care, as underscored in healthcare policies and guidelines[29].

Concerns about the adequacy of staffing in the multidisciplinary team at the Oncology Outpatient Clinic are closely linked to burnout among healthcare professionals. The scientific literature shows that burnout cases have risen significantly in recent years, primarily driven by work overload. In sectors like Oncology, this is compounded by a heightened self-demand among healthcare providers, stemming from the emotional strain of recognizing that curative outcomes may be unachievable in treating chronic diseases[42,43]. This theme emerged in several participant accounts, including those of Markarian and Hoag.

In cancer patients, community or hospital-acquired infections have a high risk of progressing into severe clinical forms, often leading to poorer prognoses and elevated morbidity and mortality rates. This vulnerability is influenced by factors such as cancer staging, length of hospitalization, febrile neutropenia, use of invasive devices, age, comorbidities, and microbial resistance[44]. Participant Cassiopeia highlighted this perspective, stressing the importance of a dedicated hospitalization environment for cancer patients, separate from units housing patients with other diagnoses.

Participants like Cartwheel voiced concerns about adapting physical spaces to align the supply of healthcare services to demand and shared ideas for enhancing service quality. She expressed a desire to create a game room to encourage patient socialization and plans to present this project to her supervisor. Cartwheel's focus on effective use of space, fostering humanized work relationships, and creating therapeutic bonds aligns closely with the principles outlined in the PNH[28].

Another critical consideration raised by participants, with clear applicability to clinical practice, is the need to view pain as a complex, multidimensional phenomenon. This approach aligns with the previously discussed need for comprehensive education and training across healthcare specialties that recognizes that pain arises from an interplay of biological, psychological, spiritual, and social factors. Fully addressing this perspective still requires expansive efforts in public policy and civic initiatives, updated institutional guidelines, and effective regulations from the Brazilian Ministry of Education to enhance both basic and professional training standards. Additionally, an empathetic commitment from caregivers and all those involved in health promotion is essential.

A limitation of this study is that the participants represent a wide variety of professions, encompassing different technical levels and specialties, as shown in **Table 1**. However, this diversity also brings valuable different perspectives. In this regard, the multidisciplinary team should work cohesively, collaborating with patients and their families and extending their knowledge to the community to improve the quality of life of health system users. Interdisciplinary health education and continuing education initiatives—particularly those focused on teamwork—foster shared responsibilities, helping to ease the burden associated with the expectation to meet the various needs of patients with life-threatening illnesses and their caregivers, whether formal or informal.

Another limitation is that this study was conducted in a single healthcare institution, with all participants working at the same location, which may restrict the generalizability of the findings. Environmental triangulation across multiple healthcare settings would be beneficial to enhance the validation of these observations.

CONCLUSION

The organization of both outpatient and hospital care for patients with cancer pain is crucial in promoting health and quality of life. Beyond professional considerations, the institutions' characteristics—including their management models, whether private or public, municipal, state, national, or even international—also play a foundational role. Additionally, cultural and social perceptions of these services influence care outcomes.

This article compiled the perspectives of professionals from a specialized outpatient clinic on the meanings attributed to pain in adult cancer patients, revealing a range of different insights. While participants shared their subjective views, many converged on key themes, including the importance of humanistic training for healthcare professionals, the need to legitimize patient-reported pain, and the value of an empathetic, welcoming, and compassionate approach in caring for patients with cancer pain. Multidisciplinary care was also highlighted as essential. Technical aspects of pain management, such as the sometimes inappropriate use of hypnotics, as well as concerns about the high incidence of burnout in this field, were noted. Other concerns included the need to achieve more effective pain control in healthcare services. These reports illustrate that public policies and cultural and institutional ideologies significantly shape healthcare professionals' experiences, ultimately influencing patient care and management.

CONFLICT OF INTEREST

The authors attest they have no conflict of interest to declare.

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JMRR

ACUTE MYOCARDIAL INFARCTION AND NON-OBSTRUCTIVE CORONARY ARTERIES: A CASE REPORT

Infarto agudo do miocárdio e artérias coronárias não obstrutivas: um relato de caso

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ABSTRACT

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a rare event that is difficult to diagnose. Given the rarity of this condition, we report the case of a 61-year-old patient who was treated in the intensive care unit of the Padre Bento Hospital Complex in Guarulhos, Brazil, who developed a rare case of MINOCA syndrome during hospitalization for subarachnoid hemorrhage. Coronary angiography did not show significant coronary artery obstruction. The patient showed clinical improvement and was discharged after 48 hours, with recommendations for outpatient cardiology follow-up and cardiac magnetic resonance imaging.

Keywords: acute myocardial infarction, non-ST elevation myocardial infarction, MINOCA, coronary angiography.

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INTRODUCTION

Myocardial infarction with nonobstructive coronary arteries (MINOCA) is a syndrome resulting from a set of conditions that affect the structure of the coronary microcirculation, culminating in acute myocardial infarction (AMI), but without evidence of significant obstructive coronary artery disease on angiography[1].

Given the complexity associated with MINOCA syndrome, the challenges for its correct and early diagnosis are significant. Much of this complexity arises from the wide range of possible etiologies for the syndrome, which include coronary spasm, microvascular dysfunction, coronary embolism, and inflammatory conditions. Furthermore, there are still no treatment guidelines for MINOCA. As a result, many patients do not receive an accurate diagnosis nor appropriate and timely treatment[2].

Thus, considering the uncertainties and the knowledge gap surrounding this subject, this study presents a clinical case of MINOCA and discusses essential aspects of its diagnosis and treatment. This aims to increase awareness, particularly among emergency physicians, allowing early recognition and more effective treatment of MINOCA.

CLINICAL CASE PRESENTATION

The case involves a 61-year-old female patient, N.S.S., of mixed race, from Guarulhos, State of São Paulo, Brazil, with a history of smoking, systemic arterial hypertension, type II diabetes mellitus, and prior coronary artery angioplasty with stent placement. The patient was admitted to the intensive care unit at the Padre Bento Hospital Complex in Guarulhos on April 24, 2019, due to subarachnoid hemorrhage (Fisher grade II) with associated abnormalities within the brain parenchyma. The patient was hemodynamically stable, conscious, and oriented. On May 13, 2019, cerebral angiography showed irregular intracranial artery contours but no significant stenosis or aneurysms.

The next day, in the morning, the patient experienced severe left-sided chest pain radiating to the back and left arm, accompanied by sweating and uncontrollable vomiting. This presentation was identified as type B precordial anginal pain. She was given 300 mg of acetylsalicylic acid and underwent a 12-lead electrocardiogram that showed ST-segment elevation in AVR and ST-segment depression in V6, prompting the initiation of the high-risk coronary syndrome protocol.

Cardiac markers of myocardial necrosis were slightly elevated six hours after symptom onset, with creatine kinase MB (CK-MB) increasing from 21 U/L to 33 U/L (normal < 25 U/L) and troponin rising from 1.25 mg/dL to 1.55 mg/dL (normal < 0.1 mg/dL), indicating AMI.

The patient's pain subsided with morphine and nitroglycerin. On the same day, coronary angiography revealed a dominant right coronary circulation pattern, irregular coronary arteries, and a patent stent in the anterior interventricular artery but no significant stenosis or obstruction.

After 48 hours of clinical stabilization, troponin levels normalized, and the patient was discharged from the ICU with referrals for outpatient follow-up care with cardiology and cardiac magnetic resonance imaging (MRI).

DISCUSSION

MINOCA accounts for approximately 5-6% of AMI cases[3-6]. Patients' demographic and clinical characteristics differ from those with AMI due to obstructive causes. MINOCA patients tend to be younger (average age 58) compared to those with obstructive AMI (average age 61)[7-10] Furthermore, women with a diagnosis of AMI are twice as likely to experience MINOCA compared to men, and higher incidences are observed among Black and Hispanic populations in the U.S5,11. However, despite these epidemiological differences, it is not possible to differentiate between AMI caused by MINOCA and obstructive mechanisms based solely on clinical or epidemiological features, making coronary angiography essential for this differential diagnosis[5].

Diagnostic criteria for MINOCA are[5]:

1. Classic AMI criteria (elevated cardiac markers of myocardial necrosis, suggestive clinical presentation, ECG changes such as ST-segment elevation or new left bundle branch block, myocardial changes on cardiac perfusion scan, or new ventricular wall motion abnormalities).
2. Absence of ≥50% coronary artery obstruction on angiography[9];
3. Exclusion of other clinically evident causes that could result in the observed acute clinical presentation.

It is important to emphasize that MINOCA is a working diagnosis with multiple underlying etiologies that require further work-up to be identified[5,12]. This process involves thoroughly reviewing the patient's history and physical examination, looking for factors suggesting conditions such as viral infections, drug use, increased thrombotic risk, or significant psychological stress (which could indicate Takotsubo cardiomyopathy). However, if a specific etiology is established (e.g., recent cocaine use causing artery coronary spasm), MINOCA should not be the primary diagnosis[3].

However, if the cause remains unclear, further diagnostic evaluation is critical. The initial step involves a detailed analysis of coronary angiography, which may uncover alternative causes of AMI other than ≥ 50% obstruction, such as coronary dissection or plaque instability. The latter, despite having an atherothrombotic mechanism, might not obstruct the main coronary arteries but instead potentially lead to distal embolization of thrombi resulting from plaque erosion or rupture[3]. Techniques such as optical coherence tomography or intracoronary ultrasound can help identify these conditions[3], while cardiac MRI is highly valuable for MINOCA evaluation, especially when myocarditis or structural abnormalities are suspected[3,13]. When coronary spasm is on the differential, a spasm provocation test can be a useful diagnostic adjunct, while echocardiography has lower specificity in this context[5]. **Table 1** outlines the potential causes of MINOCA and the recommended work-up evaluation.

In addition to cardiac causes, further investigation may be indicated to rule out non-cardiac causes of elevated cardiac markers of myocardial necrosis, such as chronic kidney disease and pulmonary thromboembolism, depending on clinical suspicion[5]. For instance, if a patient presents with unilateral lower limb edema, a workup for pulmonary embolism may be indicated, including tests such as D-dimer and chest CT with pulmonary angiography. In cases where thrombophilia is suspected, additional tests for specific conditions, such as Factor V Leiden, may be indicated.

While it is crucial to exclude non-cardiac causes of false-positive results for AMI, the absence of coronary obstruction on angiography should not be interpreted as the absence of myocardial injury. Instead, a thorough evaluation to determine the specific etiology of MINOCA is essential to avoid overlooking a serious cardiovascular event. Furthermore, accurate diagnosis is critical for guiding targeted treatment, preventing recurrence, and reducing mortality. For instance, if coronary spasm is identified, treatment with calcium channel blockers should be initiated, as this approach is linked to better outcomes[5,13].

The case of patient N.S.S. illustrates the typical epidemiological profile for patients at increased risk for MINOCA, meeting all clinical diagnostic criteria. Although she received AMI treatment according to standard guidelines, the institution where she underwent coronary angiography did not adhere to the recommended diagnostic algorithm for MINOCA following confirmation of the absence of coronary obstruction[14].

The MINOCA syndrome remains relatively under-recognized, even among specialists. Although the syndrome is increasingly described in the literature, this limited awareness often impedes diagnostic evaluation and patient follow-up. As a result, many patients continue to receive treatment based on traditional AMI protocols, which may not be optimal for MINOCA. To improve patient outcomes, it is crucial to enhance physician awareness of MINOCA, particularly among those working in emergency settings.

In the case presented, a complete etiological investigation was not possible due to limited resources, reflecting a common challenge in many healthcare facilities in Brazil resulting from insufficient resources. This case underscores the need to establish efficient referral and counter-referral workflows to facilitate the proper investigation and management of MINOCA.

CONFLICT OF INTEREST

The authors attest they have no conflict of interest to declare.

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TABLE 1 - Differential diagnosis of MINOCA etiologies and diagnostic work-up

POSSIBLE ETIOLOGIES OF MINOCA		RECOMMENDED DIAGNOSTIC TESTS
Myocardial causes	Cardiomyopathies (Takotsubo, hypertrophic, dilated)	Cadiac magnetic resonance imaging, ventriculography
	Miocarditis	C-reactive protein, erythrocyte sedimentation rate, cadiac magnetic resonance imaging, and myocardial biopsy
	Trauma	History and physical exam
	Acute myocardial infarction induced by tachyarrhythmia	Monitorization
Coronary causes	Coronary artery dissection	Echocardiogram and coronary computed tomography angiography
	Coronary spasm induced by sympathomimetics	Toxicology tests
	Epicardial coronary artery spasm	Intracoronary acetylcholine provocation testing
	Coronary microvascular spasm	Intracoronary acetylcholine provocation testing
	Coronary microvascular disease	Coronary flow reserve calculation
	Coronary slow flow phenomenon	Angiography with TIMI frame count
	Thrombosis secondary to plaque instability (erosion or rupture)	Optical coherence tomography and intravascular ultrasound
	Coronary emboli	Echocardiogram

Adapted from Pasupathy *et al.* 2016[10] and Tamis-Holland *et al.* 2019[12].

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JMRR

THE RELATIONSHIP BETWEEN ENDOMETRIOSIS AND MALIGNANT THYROID NEOPLASMS: A SYSTEMATIC REVIEW

A relação entre endometriose e neoplasia maligna da tireoide: uma revisão sistemática

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ABSTRACT

Objectives: endometriosis is a chronic inflammatory disease affecting an estimated 10-15% of reproductive-aged women. Thyroid cancer, predominantly occurring in women, most commonly presents between the ages of 45 and 64. In the context of this gender overlap, existing evidence suggests a potential relationship between endometriosis and thyroid cancer. This study aims to explore this possible relationship. **Methods:** this systematic review followed the structured approach outlined in the PRISMA 2020 checklist for study selection. Inclusion criteria focused on studies examining the association between endometriosis and thyroid cancer, excluding case reports and retrospective studies with fewer than ten cases. PubMed was the primary database used for the search, employing the terms "endometriosis," "thyroid cancer," and "endometriosis and thyroid cancer." The studies were evaluated between October 2023 and April 2024. **Results:** the PubMed search yielded 20 studies, with an additional eight studies identified from the reference lists of previously included studies. Following a comprehensive review, 12 articles met the eligibility criteria and were included in the review. Data primarily derived from two meta-analyses and one large retrospective study converged on an estimated 33% to 39% increased risk for women with endometriosis to develop thyroid cancer later in life. **Discussion:** although evidence points to a possible association between endometriosis and thyroid cancer, potentially influenced by female sex hormones, the observed increase in non-gynecological cancers among endometriosis patients suggests additional factors may contribute to the elevated cancer risk. Study limitations, including a predominance of retrospective and cross-sectional designs, significant risk of bias, and high heterogeneity, limit definitive conclusions and causal interpretations. Further research using robust prospective designs is needed to clarify the underlying mechanisms and to guide clinical protocols for improved management of patients with endometriosis.

Palavras-chave: endometriosis, thyroid cancer, female sex hormones, systematic review.

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INTRODUCTION

Endometriosis is a chronic inflammatory disease that affects an estimated 10-15% of reproductive-aged women. It is caused by the presence of tissue similar to the endometrium, including glandular and stromal components, outside the uterine cavity. The disease is classified into four stages, ranked according to severity: stage I includes mild cases, while stage IV indicates the most severe forms[1].

Thyroid cancer is a condition that mainly affects women, with a female-to-male ratio of 3:1, most commonly occurring between the ages of 45 and 64. Over the last three decades, there has been a 300% increase in the incidence of this cancer, mainly due to a rise in cases of papillary thyroid cancer[2].

Due to this epidemiological overlap, recent studies have sought to analyze the potential relationship between endometriosis and thyroid cancer[3-5]. This possible association may have important clinical implications, such as a potential indication to investigate thyroid nodules in patients with endometriosis thoroughly. This study aims to explore this association further and to provide valuable insights for physicians managing these conditions.

METHODS

This study is a structured literature review conducted using PubMed as the database for study search and selection. The search terms were "endometriosis," "thyroid cancer," and "endometriosis and thyroid cancer." No time restrictions were applied to the search. The articles identified were screened in three stages: title review, abstract review, and full-text review. Additional studies were included by reviewing the reference list of a previously included study. Studies without available full-text manuscripts, case reports, and retrospective studies with fewer than 10 cases were excluded. There were no language restrictions for study search or selection.

Data were extracted from three studies: two meta-analyses and one retrospective study. The remaining selected studies provided additional information to discuss the topic further and explore this systematic review's academic and clinical significance.

Two medical students (in their third and 11th periods, respectively) and a head and neck surgeon and professor of medicine with 36 years of experience reviewed and analyzed the articles between October 2023 and April 2024.

RESULTS

Twenty studies, all in English, were retrieved from PubMed searches covering the 16 years from 2007 to 2023. Eight more were identified from the reference list of full-text manuscripts. During the screening process, 16 studies were excluded, resulting in 12 studies being included in this review (see **Figure 1** for the PRISMA flowchart of study selection and **Table 1** for a list of included studies).

Kvaskoff *et al.*'s[3] meta-analysis, which included five studies about thyroid cancer, reported a Standardized Rate Ratio (SRR) of 1.39 (95% CI: 1.24–1.57), indicating that patients with endometriosis have a 39% increased risk of developing malignant thyroid neoplasms later in life compared to women without endometriosis. Likewise, Gandini *et al.*'s[4] meta-analysis found an SRR

TABLE 1 - List of studies included included in the review of endometriosis and thyroid cancer association

STUDY'S AUTHORS	STUDY DESIGN	SAMPLE SIZE/ NUMBER OF STUDIES INCLUDED (META-ANALYSIS)	YEAR OF PUBLICATION
Mehedintu *et al.*[1]	Review	N/A	2014
Seib *et al.*[2]	Review	N/A	2019
Kvaskoff *et al.*[3]	Systematic review and meta-analysis	5 studies	2021
Gandini *et al.*[4]	Systematic review and meta-analysis	5 studies	2019
Melin *et al.*[5]	Retrospective study	63,630	2007
Saunders *et al.*[6]	Review	N/A	2021
Bouic *et al.*[7]	Review	N/A	2023
Chmielik *et al.*[8]	Review	N/A	2018
Huang *et al.*[9]	Cross-sectional (genetics)	989	2022
Lamartina *et al.*[10]	Review	N/A	2020
Braganza *et al.*[11]	Prospective cohort	70,047	2014
Kvaskoff *et al.*[12]	Systematic review	N/A	2015

of 1.38 (95% CI: 1.17–1.63), representing a 38% increased risk of thyroid cancer in patients with endometriosis.

Additionally, Melin *et al.*'s5 retrospective study found a Standardized Incidence Ratio (SIR) of 1.33 (95% CI: 1.02–1.70), indicating a 33% higher incidence of thyroid cancer in the study sample compared to what would be expected in the general population.

DISCUSSION

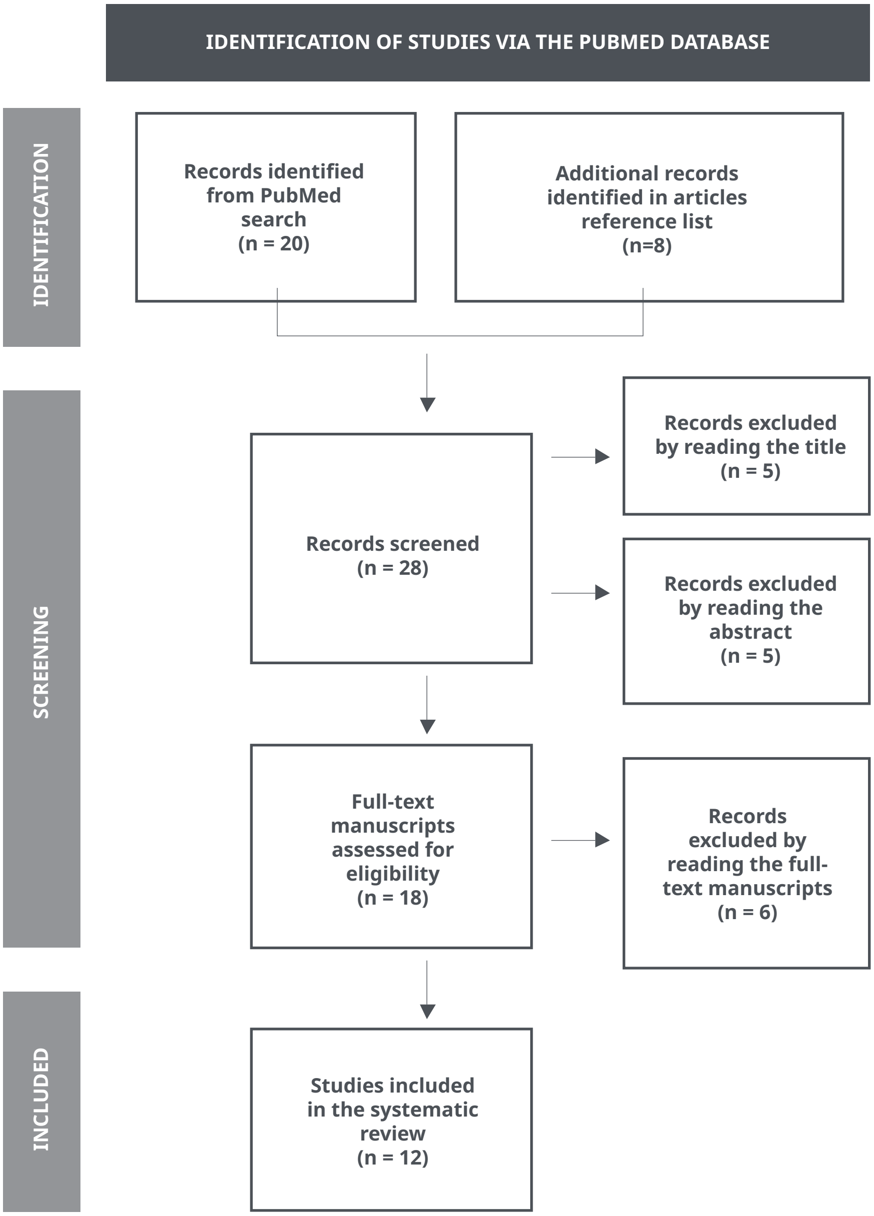
Endometriosis is a chronic condition characterized by the dissemination of endometrium-like tissue to locations outside the uterine cavity. The most common sites of ectopic tissue implantation include the ovaries, cul-de-sac, and uterosacral ligaments[1,6]. Surgery remains the gold-standard method for categorizing the disease into four stages of severity[6].

Current treatments of endometriosis have significant limitations in effectiveness. Therapeutic approaches include surgery to excise ectopic endometrial lesions, along with medications aimed at hormonal modulation. However, these interventions do not reliably prevent disease recurrence[6,7]. Repeated surgeries may be necessary in cases of recurrence, which can negatively impact patients' quality of life[7].

The etiology of endometriosis remains unclear. Several theories have been proposed, including the roles of lifestyle factors, environmental influences, celomic metaplasia, and immune system dysfunctions[1,7]. This uncertainty highlights the need for future research aimed at improving the prognosis and management of the disease.

Thyroid cancer, on the other hand, is the most common endocrine malignancy worldwide, with incidence rates increasing in recent decades[2,8]. It predominantly affects women, with a female-to-male ratio of 3:12. The five main types of thyroid tumors are papillary, follicular, poorly differentiated, anaplastic, and medullary carcinomas[8]. Known risk factors for thyroid cancer include obesity, certain benign thyroid conditions (e.g., chronic thyroiditis and goiter), female sex hormones, growth factors (e.g., insulin-like growth factor and chronic thyroid-stimulating hormone hyperstimulation), dietary factors (e.g., low iodine intake), smoking, physical inactivity, and childhood exposure to ionizing radiation[9,10].

FIGURE 1 - PRISMA 2020 flow diagram showing the process for study selection



Screening approaches to each type of thyroid cancer vary. For medullary thyroid cancer, genetic testing is recommended primarily in cases where multiple endocrine neoplasia type 2 (MEN2) is suspected, due to its association with RET gene mutations. For well-differentiated thyroid cancers, such as papillary and follicular thyroid carcinoma, the U.S. Preventive Services Task Force does not recommend routine screening, as the potential risks outweigh the benefits[11]. Lamartina *et al.*[10] suggest that neck palpation by a skilled physician could serve as an intermediate approach between no screening at all and highly sensitive ultrasonography. However, further large-scale studies are needed to support this recommendation.

As a higher incidence of thyroid cancer has been observed in women with an earlier onset of menarche and late menopause, female sex steroid hormones may be involved in the elevated occurrence of thyroid cancer in these patients. Experimental studies have shown that estradiol can promote the proliferation of thyroid cells in vitro. Additionally, individuals diagnosed with thyroid cancer have shown elevated post-diagnosis serum estradiol levels and decreased progesterone blood concentrations[12].

Braganza *et al.*[12] investigated the association between benign breast and gynecological conditions, reproductive and hormonal factors, and the risk of thyroid cancer. The study included 70,047 women aged 50 to 78, which were followed over 11 years, during which 127 women were diagnosed with thyroid cancer. The results indicated that older age at natural menopause, a higher estimated number of lifetime ovulatory cycles, a greater number of childbirths, and the presence of uterine fibroids were associated with an increased risk of thyroid cancer. However, although the study employed a prospective design, endometriosis was not isolated as the primary exposure variable. Nonetheless, these findings provide insights into the potential effects of female sex hormones on thyroid cancer, even though they do not specifically address the impact of endometriosis.

The evidence that gynecological diseases and female sex hormones may be linked to thyroid cancer raises the question of whether endometriosis, a common benign gynecological condition, might also affect the incidence of thyroid cancer. As mentioned, a retrospective study by Melin *et al.*[5] investigated the incidence of various cancers in 65,349 patients with endometriosis. In addition to finding a SIR of 1.33 for thyroid cancer, the authors reported a higher incidence of other non-gynecological cancers in patients with endometriosis, including renal cancer, brain tumors, and malignant melanoma. These findings suggest that women with endometriosis may be at an elevated risk of various cancer types, not only gynecological tumors or cancers with a known higher incidence in women. Therefore, factors beyond female sex hormones may contribute to this increased risk of thyroid cancer.

Although the meta-analysis by Kvaskoff *et al.*[3] reported a strong association between endometriosis and increased risk of thyroid and ovarian cancer—suggesting a possible role of sex hormones given the disproportionately higher incidence of thyroid cancer in women—the authors also noted an increase, although minimal, in the risk for other non-gynecological cancers, such as cutaneous melanoma. However, the authors highlighted that most studies included in the meta-analysis had a severe or critical risk of bias and high heterogeneity. These limitations significantly hinder definitive conclusions about the relationship between endometriosis and cancer risk, particularly regarding the influence of sex hormones.

In contrast to the other two studies, Gandini *et al.*'s[4] meta-analysis reported no increase in melanoma risk while finding a moderate positive association with thyroid and endometrial cancer. The authors also observed no between-estimates heterogeneity ($I^2 = 0\%$) for thyroid cancer studies and no publication bias, further strengthening the evidence for an association between endometriosis and thyroid cancer. However, the reliance on data primarily from retrospective or cross-sectional studies makes it challenging to draw definitive conclusions and establish causality.

Besides its association with various cancers, including thyroid cancer, endometriosis has also been linked to benign conditions such as autoimmune diseases and allergies[13]. However, evidence from a previous cross-sectional study indicates that benign thyroid conditions, such as autoimmune thyroid disorders, hypothyroidism, and hyperthyroidism, are not more frequent in patients with endometriosis than in the general population[14].

This study has several significant limitations. First, the small number of studies included - only 12 - highlights the need for further research to better elucidate the association between endometriosis and thyroid cancer. This limited number poses challenges in building a robust dataset for a comprehensive systematic review. Moreover, specific data on different types of thyroid cancer associated with this increased risk are still not available. Second, only one study employed prospective designs[12] but did not focus on endometriosis as the primary exposure variable. This is a significant limitation, as prospective studies are essential for establishing causality. On the other hand, retrospective studies may be prone to biases such as recall bias, which complicate the ability to draw definitive conclusions.

In summary, this review's main finding suggests an association between endometriosis and thyroid cancer. Studies converged on a 33% to 39% increased risk for women with endometriosis to develop thyroid cancer later in life. Understanding the relationship between these two conditions could ultimately benefit patients by creating enhanced clinical protocols and improving outcomes. However, given the limited data on this subject, more research is needed to fully understand this association and its underlying mechanisms.

CONFLICT OF INTEREST

The authors attest they have no conflict of interest to declare.

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