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BREAST CANCER IN MEN: PREVALENCE AND ITS MAIN CHARACTERISTICS - A REVIEW OF CURRENT LITERATURE

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ABSTRACT

Breast cancer is widely recognized as a major public health concern worldwide, predominantly affecting women. However, although it is relatively rare, breast cancer can also occur in men, accounting for a significant portion of cases diagnosed annually. Although less common, male breast cancer presents unique challenges in diagnosis, treatment, and clinical management, requiring a specific and personalized approach to ensure optimal patient outcomes. Understanding the prevalence and characteristics of breast cancer in men is critical to guide effective public health policies, prevention strategies, and clinical interventions. The general objective of this study is to discuss the prevalence and clinical, histopathological and therapeutic characteristics of breast cancer in men, in order to consolidate existing knowledge and identify gaps that can guide future research. The methodology of this work is the Literature Review. It is concluded that studies on breast cancer in men have provided a comprehensive view of this condition, from its prevalence to its main clinical characteristics and challenges associated with diagnosis and treatment.

Keywords: Male Breast Cancer. Breast Neoplasm in Men. Diagnosis of Breast Cancer in Men.

INTRODUCTION

Male breast cancer is a rare condition, accounting for less than 1% of all breast cancer cases diagnosed worldwide¹. Despite its low incidence compared to female breast cancer, male breast cancer presents unique particularities and challenges that deserve attention. Between 2004 and 2014, 19,795 cases were diagnosed in the United States, with an increase in the incidence rate from 7.2% to 10.3%¹.

The mortality associated with male breast cancer significantly decreased during the same period, from 11% to 3.8%¹. Several factors contribute to this mortality rate, including income, type of health insurance, tumor characteristics, and comorbidities, as measured by the Charlson-Deyo Score². Additionally, age, tumor size, hormone receptor expression, and the stage of cancer at diagnosis directly influence mortality. Hazard ratios (HR) vary significantly according to cancer stage, with higher HRs associated with more advanced stages of the disease².

Studies indicate that men are generally diagnosed at more advanced stages than women, which may be attributed to a lack of awareness and lower rates of preventive screening. As a result, survival rates for men with breast cancer tend to be lower than those for women, highlighting the importance of early diagnosis and appropriate treatment strategies.

The treatment for male breast cancer is similar to that used for women, involving surgery, radiotherapy, chemotherapy, and hormone therapy. However, there is a growing need for treatment protocols specifically for men, due to biological and clinical differences between the

sexes. Clinical trials that include men are essential for developing more effective and personalized therapeutic approaches.

In conclusion, male breast cancer, although rare, represents a significant area of concern in public health. A detailed understanding of its incidence, risk factors, clinical characteristics, and response to treatment is crucial for the development of clinical strategies and public health policies aimed at reducing mortality and improving the quality of life of patients.

METHODS

The present study is characterized as a bibliographic literature review of a descriptive nature. The type of study adopted aims to synthesize and critically analyze pre-existing scientific literature to identify, evaluate, and interpret all relevant research available on the topic under study, namely, male breast cancer. This review was conducted globally, without geographical restrictions, considering the universality of the phenomenon investigated.

The population of interest for the review includes male individuals diagnosed with breast cancer, with no delimitations by age, ethnicity, or socioeconomic conditions, as the goal is to encompass the broadest spectrum of available scientific evidence. The sampling process for this bibliographic review was intentional and non-probabilistic, selecting relevant scientific articles on the topic, available in the PubMed, Medline, and Lilacs databases.

The initial search in the PubMed database returned 7,239 articles without applying filters. After applying the temporal filter considering the last ten years and the language filter for English and Portuguese, the number was reduced to 3,284 articles. With the requirement of full-text availability, the total decreased to 2,072 articles. Finally, by applying the methodology type filter, 368 articles remained.

Similarly, in the Medline database, the initial search generated 6,806 articles. The application of the language filter reduced the set to 6,208 articles. With the inclusion of the ten-year temporal criterion and the requirement of full-text availability, the number was reduced to 1,551 articles. Selecting the methodology type, 206 articles remained.

In the Lilacs database, 252 articles were initially found. With the application of the language filter, the total became 134 articles. After the methodology, time, and full-text availability filters were applied, 40 articles remained.

The inclusion criteria for the final selection of articles encompassed documents in English and Portuguese, published in the last ten years, and fully available in open-access databases. The search terms used included keywords pertinent to the topic, such as "male breast cancer," "male breast neoplasia," "diagnosis of male breast cancer," among others, in English and Portuguese.

The methodology employed in the articles was qualitative, aiming to include only review articles and clinical studies. Articles that did not meet these criteria were excluded. Regarding ethical aspects, the literature review does not involve direct risks to participants as there is no primary data collection.

The data analysis was conducted through a qualitative approach to identify patterns, themes, similarities, and differences in the results of the selected studies. After applying all the mentioned inclusion and exclusion criteria, the research resulted in a final sample of 19 articles for detailed analysis.

RESULTS

Prevalence of Breast Cancer in Men:

Male breast cancer is a rare disease, accounting for approximately 1% of all breast cancer cases worldwide. Epidemiological studies indicate that prevalence varies geographically, with

higher rates observed in regions with higher overall cancer incidences. In the United States, the annual prevalence is estimated at about 2.5 cases per 100,000 men, while in European countries such as France, the prevalence ranges from 0.5 to 1 case per 100,000 men. This pattern of low prevalence is consistent globally, reflecting a continuous need for awareness and deeper scientific investigation ¹.

Temporal Trends in the Incidence of Male Breast Cancer:

Analysis of temporal trends reveals a gradual increase in the incidence of male breast cancer over the past decades. Data from the National Cancer Institute of the United States show that the incidence rate increased from 0.86 per 100,000 men in 1975 to 1.44 per 100,000 men in 2015¹. This increase can be partially attributed to improvements in diagnostic methods and greater awareness of the disease. However, factors such as population aging and changes in risk factors also contribute to this upward trend. Understanding these trends is crucial for developing more effective prevention and treatment strategies³.

Geographic Distribution of Male Breast Cancer:

The geographic distribution of male breast cancer varies considerably between different regions of the world. In North America and Europe, incidence rates are relatively higher, while in Asian and African countries, rates tend to be lower. This geographic variation can be influenced by genetic, environmental, and socioeconomic factors. For example, in the United States, the incidence is higher among white men compared to African American and Asian men. Studies suggest that differences in exposure to risk factors, such as diet and hormone levels, may explain some of these disparities⁴.

Risk Factors Associated with Male Breast Cancer:

Several risk factors have been associated with the development of breast cancer in men. Among the main ones are advanced age, family history of breast cancer, genetic mutations (such as BRCA1 and BRCA2), and exposure to estrogens. Other factors include obesity, chronic liver diseases, and Klinefelter syndrome. Epidemiological studies show that men with BRCA2 gene mutations have up to an 80 times higher risk of developing breast cancer compared to the general population. In addition, prolonged exposure to female hormones, whether through medical therapies or endocrine conditions, also significantly increases the risk².

Histopathological Characteristics of Male Breast Cancer:

Male breast cancer shares many histopathological characteristics with female breast cancer, although there are some notable differences. Most tumors in men are invasive ductal carcinomas, with a small proportion of ductal carcinoma in situ and other histological types. Studies show that tumors in men tend to be diagnosed at more advanced stages, often due to lack of awareness and screening. In terms of molecular characteristics, the expression of hormone receptors (estrogen and progesterone) is common, and about 10-15% of tumors are HER2-positive. These characteristics directly influence treatment options and patient prognosis⁵.

Surgery in the Treatment of Male Breast Cancer:

Surgery is one of the main treatment options for male breast cancer, with mastectomy being the most common procedure. Clinical data indicate that modified radical mastectomy, which involves the removal of breast tissue and axillary lymph nodes, is frequently performed due to the late presentation of the disease6. In addition to surgery, adjuvant treatment, including radiotherapy, chemotherapy, and hormonal therapy, is often used to improve clinical outcomes. Studies show that surgery combined with adjuvant therapies can significantly increase the five-year survival rate, especially in early stages of the disease⁷.

Radiotherapy as a Therapy for Male Breast Cancer:

One of the main benefits of radio therapy is its ability to provide localized treatment, concentrating the radiation on the specific area where the tumor was located. This minimizes the impact on surrounding healthy tissues, thus reducing the risk of adverse side effects. However, precision in delivering radiation is crucial to ensure that only cancer cells are affected while preserving the integrity of normal tissues⁴. It has been shown to be an effective therapeutic modality that can be used both as adjuvant treatment and as an integral part of managing advanced-stage cancer⁸. The decision to use radio therapy as part of the treatment plan for male breast cancer is based on several factors, including: tumor size and location, disease stage, presence of metastases, and patient preferences⁹. In most cases, radio therapy can be combined with other treatments, such as surgery and chemotherapy, to achieve the best possible outcomes⁸.

Chemotherapy and Hormonal Therapy in the Treatment of Male Breast Cancer:

Chemotherapy is a systemic approach that uses cytotoxic drugs to destroy cancer cells, either by preventing their cell division or damaging their DNA. It can be administered before surgery (neoadjuvant) to reduce the tumor size and facilitate surgical removal, or after surgery (adjuvant) to eliminate remaining cancer cells and reduce the risk of recurrence. Additionally, chemotherapy may be indicated to control metastases in advanced stages of the disease¹⁰.

Chemotherapy and hormonal therapy play fundamental roles in the treatment of male breast cancer, although the incidence of this disease is considerably lower compared to women. These therapeutic modalities aim to reduce tumor size, control its spread, and prevent recurrences, contributing to improved clinical outcomes and quality of life for affected patients¹⁰.

Chemotherapy regimens for male breast cancer are generally based on protocols similar to those used for female breast cancer, taking into account the tumor's sensitivity to different chemotherapeutic agents, disease stage, and the patient's individual characteristics. The most common drugs include anthracyclines, taxanes, antimetabolites, and alkylating agents. The choice and combination of these agents are determined by the oncologist based on a comprehensive evaluation of the clinical case.

However, it is important to note that chemotherapy is associated with significant side effects, such as nausea, vomiting, fatigue, hair loss, bone marrow suppression, and increased risk of infections. These adverse effects can negatively impact the patients' quality of Hormonal therapy aims to block the effects of hormones that stimulate tumor growth or reduce their production in the body. Aromatase inhibitors, such as letrozole, anastrozole, and exemestane, are frequently used in hormonal therapy for male breast cancer, especially in men with estrogen receptor-positive tumors. These drugs work by inhibiting the aromatase enzyme, responsible for converting androgens into estrogen, thus reducing estrogen levels in the body and inhibiting tumor growth¹¹. Another option for hormonal therapy is tamoxifen, a selective estrogen receptor modulator (SERM), which blocks estrogen receptors in cancer cells, preventing their stimulation by the hormone. Tamoxifen can also be an option for men with estrogen receptor-positive breast cancer, especially in cases of advanced or metastatic tumors. Like chemotherapy, hormonal therapy may be associated with side effects, including hot flashes, changes in libido, erectile dysfunction, weight gain, and increased risk of blood clots. However, these adverse effects tend to be less severe compared to chemotherapy and can be managed with additional medications

or dose adjustments.¹²

Careful monitoring of the treatment response is essential to evaluate the effectiveness of therapeutic interventions and make adjustments when necessary. Regular imaging exams, such as mammograms and MRIs, along with clinical evaluations and laboratory tests, are important for early detection of any signs of recurrence or disease progression.²

DISCUSSION

Over the past few decades, there has been increasing awareness about breast cancer, particularly among women. However, many are unaware that this disease can also affect men, although to a much lesser extent. Discussing male breast cancer, its prevalence, and distinctive characteristics is crucial for a comprehensive understanding of this condition¹³.

Male breast cancer is a rare condition, representing less than 1% of all breast cancer cases diagnosed. Although the incidence is low, its significance cannot be underestimated, as it can have significant implications for the health of affected men. The prevalence of breast cancer in men varies by geographic region and demographic factors, but studies indicate that the incidence rate is gradually increasing worldwide ⁶.

One of the distinctive features of breast cancer in men is that it is often diagnosed at more advanced stages compared to breast cancer in women. This is partly due to the lack of awareness about the possibility of men developing the disease and reluctance to seek medical attention for breast-related symptoms. As a result, early diagnosis is challenging, and many cases are discovered when the cancer has already spread to other parts of the body⁷.

Symptoms of breast cancer in men may include a lump or thickening in the breast, changes in the nipple, nipple discharge, breast or axillary pain, and changes in the appearance of the breast. However, it is important to note that these symptoms may also be related to benign and non-cancerous conditions, highlighting the importance of a proper medical evaluation for an accurate diagnosis¹.

Known risk factors for breast cancer in men include older age, family history of breast cancer, genetic mutations, exposure to ionizing radiation, use of hormone therapy, obesity, and chronic liver disease. Understanding these risk factors can help identify men at higher risk of developing the disease and implement strategies for prevention and early detection¹⁴.

The diagnosis of breast cancer in men typically involves a combination of clinical examinations, imaging tests such as mammography and ultrasound, and biopsy for tissue analysis. Once the diagnosis is confirmed, treatment will depend on the stage of the cancer, the overall health of the patient, and other individual factors. Treatment options may include surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapies³.

Although survival rates for male breast cancer have improved over the years, there are still significant challenges to be addressed. The lack of awareness about the possibility of men developing breast cancer can lead to delays in diagnosis and treatment, negatively affecting outcomes. Additionally, men often face stigmas and taboos associated with the disease, which can hinder seeking the necessary support and assistance¹⁵.

Ongoing research is essential for improving the understanding of breast cancer in men and developing more effective prevention, diagnosis, and treatment strategies. This includes studies on the underlying mechanisms of the disease, identification of specific biomarkers, development of screening approaches tailored to men, and evaluation of new therapies and interventions¹⁶.

Therefore, while male breast cancer is a rare condition, its prevalence is increasing, and its importance should not be underestimated¹⁷. It is crucial to raise awareness about the possibility of men developing the disease, promote early detection, and provide appropriate support to

affected men¹⁸. With continued efforts in research, education, and awareness, it is possible to improve outcomes and quality of life for men with breast cancer¹⁹.

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