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Breast cancer mortality in Brazilian men: an age-period-cohort study

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ABSTRACT

Introduction: Male breast cancer is a rare malignancy whose health impacts remain unknown, notably in countries like Brazil. The purpose of this article was to evaluate breast cancer mortality in Brazilian men by an age-period-cohort study. **Methods:** This ecological study evaluates the mortality of Brazilian men due to breast cancer using an age-period-cohort model. Data were sourced from the public, open-access Brazilian database DATASUS, available at https://datasus.saude.gov.br, covering the period from 1996 to 2021. Demographic data represent the total population of Brazilian males, while clinical data focus on patients whose cause of death was coded as 175 (ICD-9) or C50 (ICD-10). The age-period-cohort effects were analyzed following the classic model and its adaptations. The analysis was performed using R 4.4.0. Alpha® software. **Results:** It was noted an increasing mortality trend with aging, peaking in men over 80 years old. From 1996 to 2009, no statistically significant changes were observed in the hazard ratio (HR). However, from 2010 onward, a significant increase in HR was found, reaching a peak in 2020–2021 (HR 2.79634; 95%CI 2.37121–3.29770). A total of 34 birth cohorts (1919–2011) were analyzed. Cohorts from 1919–1964 and 1981–2011 did not show statistically significant results, while those from 1966–1979 exhibited a decreasing HR, with the lowest HR seen in the 1979 cohort (HR 0.91323; 95%CI 0.83545–0.99825). Conclusions: This study identifies a growing trend in male breast cancer mortality in Brazil, particularly after 2010, with variations across birth cohorts.

KEYWORDS: epidemiology; breast cancer; age-period-cohort.

INTRODUCTION

Male breast cancer (MBC) is a rare malignancy, representing less than 1% of all breast carcinomas diagnosed annually in the United States[1]. The lifetime risk of a man developing breast cancer is estimated to be approximately 1 in 1,000, significantly lower than the 1 in 8 observed in women[1,2].

Some risk factors associated with MBC include a family history of breast cancer, black ethnicity, exposure to radiation, genetic mutations (such as the breast cancer genes BRCA1 and BRCA2), use of exogenous estrogen, and conditions like Klinefelter's syndrome, which are linked to elevated estrogen levels[1-3].

Globally, the incidence of MBC remains much lower than that of female breast cancer (FMC)[2]. Data from population-based studies in countries such as Denmark, Finland, Norway, and Sweden have shown world-standardized incidence rates of 0.40 per 100,000 person-years for men, in stark contrast to 66.7 per 100,000 person-years for women[2-5].

In Brazil, the epidemiology of MBC mirrors global trends, but with notable regional variations. Between 2005 and 2015, 1,521 deaths were attributed to MBC, with the most significant rise in mortality seen among patients aged 80 years or older[6].

Despite the growing recognition of MBC in Brazil, data on mortality and disease trends remain limited[6]. The paucity of comprehensive mortality data in Brazil presents a significant challenge in understanding the full scope of the disease[6]. Expanding research efforts to capture and analyze more robust mortality data is crucial for developing effective public health strategies[6].

Therefore, this research was developed with the aim to evaluate breast cancer mortality in Brazilian men by an age-period-cohort (APC) study.

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METHODS

Study characterization

This study employs an ecological approach to evaluate mortality among Brazilian men due to breast cancer, utilizing an APC modeling framework to explore temporal and generational effects on mortality rates.

Data source

Data for this analysis were extracted from DATASUS, an open-access and publicly available Brazilian health information database, accessible at https://datasus.saude.gov.br. The dataset was categorized into two components: demographic data, which includes the total male population in Brazil during the study period, obtained from the Brazilian Institute of Geography and Statistics (IBGE) census data and demographic projections; and, clinical data, whose records pertain to male individuals whose cause of death was attributed to breast cancer, identified using the International Classification of Diseases in its ninth edition (ICD-9) code 175 and the ICD-10 code C50. Variables analyzed included age at death, year of death, and cause of death.

Temporal classification

To assess temporal trends, data were stratified by birth cohorts and defined periods. The periods were categorized as 1996–1999, 2000–2004, 2005–2009, 2010–2014, 2015–2019, and 2020–2021. Age groups were arranged at five-year intervals, ranging from 10–14 to 75–79 years, with a final category for individuals aged 80 years and older. Finally, birth cohorts were calculated by subtracting the age at death from the year of death, adhering to the classical Lexis diagram framework.

Statistical modeling

Given that mortality data represent count-based outcomes, they were modeled using a Poisson regression framework, suitable for count data[7-9]. The APC model was constructed to disentangle age, period, and cohort effects, incorporating the following equation[7-9]:

$$log\,(\lambda ijk) = \mu + \alpha i + \beta j + \gamma k$$

Where: the mortality rate (λijk) for age (i), period (j), and cohort (k) was modeled and μ represents the global average mortality rate; α represents the average age effect; β represents the average period effect, and γ represents the average cohort effect[7-9].

Recognizing that Poisson regression assumes the equality of the mean and variance, the presence of overdispersion was assessed using a likelihood ratio test comparing the Poisson model to a negative binomial model[7-9]. Where overdispersion was detected, adjustments were made by employing the negative binomial model to provide robust standard error estimates, ensuring the validity of the results.

Submodels were sequentially tested to assess the relative contributions of age, period, and cohort effects using likelihood ratio tests and the Akaike Information Criterion for model selection. The final model was evaluated for goodness-of-fit through deviance statistics. All statistical analyses were conducted using R (version 4.4.2), with the Epy package facilitating APC modeling.

APC interactions were analyzed within the broader epidemiological and societal context. For instance, age effects were interpreted in light of physiological vulnerability, while period effects considered advancements in diagnostic technologies and healthcare access. Cohort effects were evaluated for their potential linkage to generational exposures, such as environmental or occupational risks.

Hazard ratios (HRs) and their 95% confidence intervals (CIs) were calculated and reported with precision. An HR between 0 and 1 suggests that independent variables (age, period and/or birth cohorts) act as a protective factor for the dependent variable, in this case, MBC mortality, thereby reducing the likelihood of its occurrence. An HR equal to 1 indicates that the independent variable has no measurable impact on MBC mortality, reflecting a neutral association. Conversely, an HR greater than 1 implies that the independent variable functions as a risk factor, increasing the likelihood of mortality from MBC. The CIs of the HR provide insight into its statistical significance and precision. If the entire CI falls below 1 (e.g., 0.5–0.9) or above 1 (e.g., 1.2–1.8), the result is considered statistically significant. In contrast, a CI that crosses 1 (e.g., 0.8–1.2) indicates a lack of statistical significance, as it includes the possibility of no effect.

RESULTS

A total of 3,913 deaths were observed along the evaluated time. In all age subgroups assessed, the number of deaths showed a growing absolute pattern; that is, the number of deaths increased as age increased.

An increasing trend in mortality rates of Brazilian men from breast cancer was observed with individual aging, with mortality peaks reached in men after 80 years old (Table 1; Figures 1 and 2).

The years between 1996 and 2009 did not demonstrate statistical significance in their mortality HR. Since 2010, a growing and statistical significant HR has been observed, with HR peaks identified in the final evaluated period, 2020 to 2021 (HR 2.79634; 95%CI 2.37121–3.29770) (Table 2; Figure 3).

A total of 34 cohorts were analyzed, from 1919 to 2011. The cohorts born between 1919 and 1929, as well as between 1944 and 1964, and from 1981 onwards did not present statistical significance in their HR. On the other hand, the cohorts from 1966 to 1979 showed a decreasing HR with a peak of lower HR observed in the 1979 cohort (HR 0.91323; 95%CI 0.83545–0.99825) (Table 3; Figure 4).

Table 1. Brazilian men's breast cancer mortality rates for 100,000 individuals by age groups.

Age groups (years)	Mortality rates for 100,000	95% Confidence interval
10–14	0.00135	0.00092–0.00198
15–19	0.00255	0.00181–0.00359
20–24	0.00478	0.00352–0.00650
25–29	0.00899	0.00686–0.01179
30–34	0.01690	0.01333–0.02143
35–39	0.03177	0.02583–0.03908
40–44	0.05972	0.04980–0.07161
45–49	0.11225	0.09535–0.13213
50–54	0.20719	0.17758–0.24173
55–59	0.34308	0.29437–0.39984
60–64	0.47872	0.40243–0.56948
65–69	0.63591	0.51314–0.78805
70–74	0.91911	0.71637–1.17922
75–79	1.44000	1.08386–1.91314
Over 80	2.35234	1.72271–3.21209

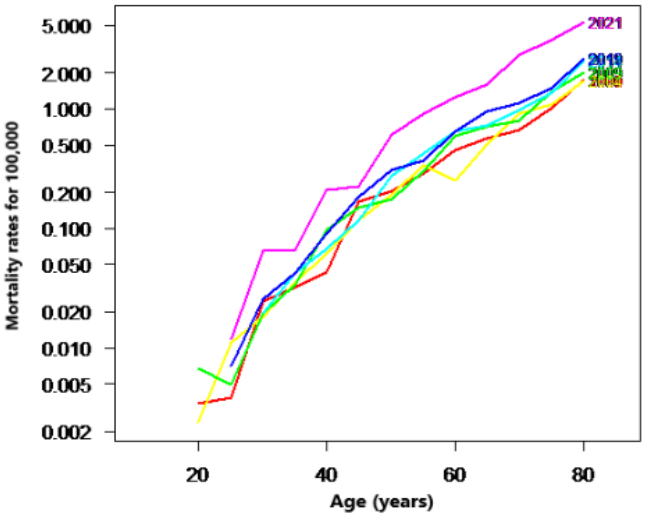

Figure 1. Brazilian men's breast cancer mortality rates for every 100,000 individuals by age and period.

Figure 5 summarizes the main results of this study; that is, an increase in mortality with population aging, especially among those who died over 80 years. In addition, since 2010, an increase in HR was noted, with a peak in the period 2020–2021. Finally, during the cohorts from 1966 to 1979, a progressive reduction in HR was noted among the evaluated groups.

The figure shows on its Y-axis (vertical) the mortality rate due to MBC for every 100,000 individuals. The X-axis (horizontal) specifies the age at which individuals died. Each line on the

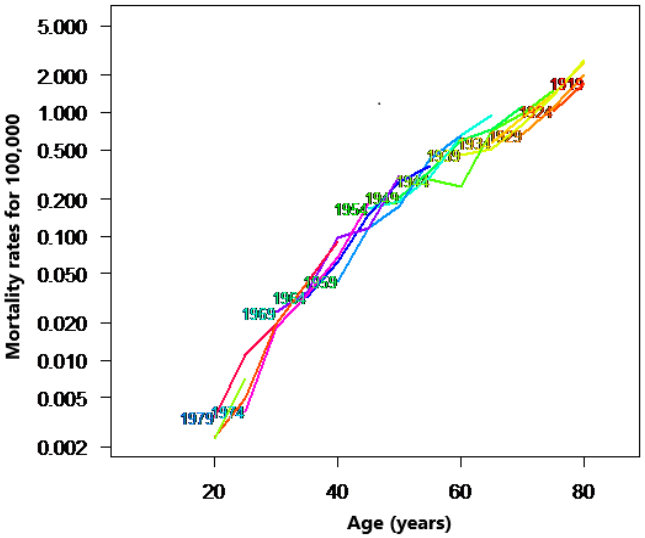

Figure 2. Brazilian men's breast cancer mortality rates for every 100,000 individuals by age and birth cohort.

Table 2. Brazilian men's breast cancer hazard ratio by evaluated periods.

Period	Hazard ratio	95% Confidence interval
1996–1999	0.99486	0.97560–1.01450
2000–2004	1.02082	0.94405–1.10384
2005–2009	1.11184	0.96396–1.28241
2010–2014	1.25725	1.08620–1.45523
2015–2019	1.35218	1.15330–1.58536
2020–2021	2.79634	2.37121–3.29770

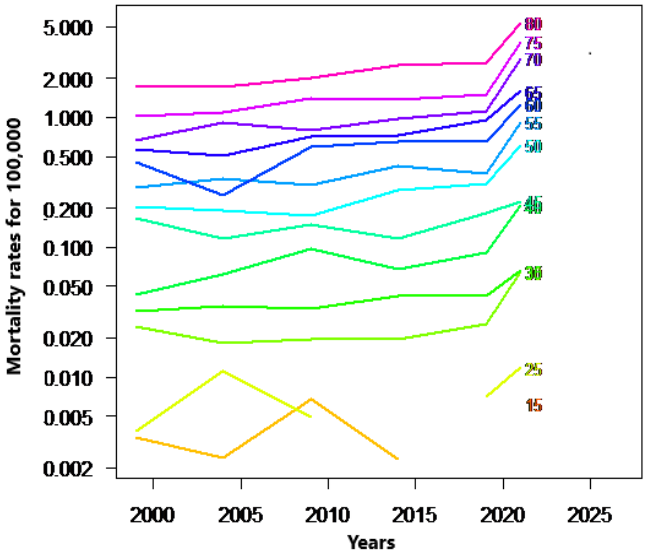

Figure 3. Brazilian men's breast cancer mortality rates for every 100,000 individuals by the evaluated years.

Table 3. Brazilian men's breast cancer hazard ratio by evaluated cohorts.

Cohort	Hazard ratio	95% Confidence interval
1919	0.76110	0.53993–1.07287
1924	0.77237	0.57619–1.03535
1929	0.78381	0.61167–1.00439
1934	0.79541	0.64376–0.98280
1939	0.81451	0.67595–0.98147
1941	0.83231	0.69732–0.99343
1944	0.87588	0.74373–1.03151
1946	0.91115	0.77802–1.06707
1949	0.96061	0.82907–1.11301
1951	0.98371	0.86503–1.11868
1954	1.00220	0.92114–1.09038
1956	1.00585	0.95581–1.05850
1959	1.00256	0.99344–1.01177
1961	0.99693	0.99041–1.00350
1964	0.98530	0.97008–1.00076
1966	0.97613	0.95783–0.99478
1969	0.96143	0.93280–0.99094
1971	0.95159	0.91342–0.99136
1974	0.93702	0.88380–0.99345
1976	0.92743	0.86423–0.99526
1979	0.91323	0.83545–0.99825
1981	0.90389	0.81671–1.00037
1984	0.89005	0.78931–1.00364
1986	0.88094	0.77152–1.00588
1989	0.86745	0.74555–1.00928
1991	0.85857	0.72872–1.01157
1994	0.84543	0.70415–1.01505
1996	0.83678	0.68823–1.01738
1999	0.82396	0.66501–1.02091
2001	0.81553	0.64996–1.02328
2004	0.80305	0.62802–1.02685
2006	0.79483	0.61381–1.02924
2009	0.78266	0.59308–1.03284
2011	0.77465	0.57965–1.03525

graph represents a specific time. From the figure, it is possible to observe that MBC mortality increases with age, regardless of the evaluated period. It is worth noting that 2021 presents the highest mortality rates.

The figure shows on its Y-axis the mortality rate due to MBC for every 100,000 individuals. The X-axis specifies the age at which individuals died. Each line on the graph represents a specific birth cohort. From the figure, it is possible to observe that MBC

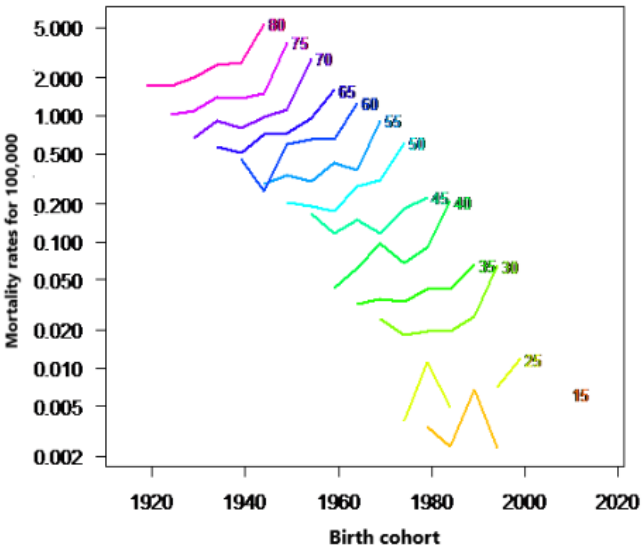

Figure 4. Brazilian men's breast cancer mortality rates for every 100,000 individuals by birth cohort.

mortality increases with age, regardless of the birth cohort. It is worth noting that more recent birth cohorts present lower mortality rates than older birth cohorts.

The figure shows on its Y-axis the mortality rate due to MBC for every 100,000 individuals and on the X-axis, the evaluated periods. Each line on the graph represents a specific age group. From the figure, it is possible to observe that MBC mortality is greater in older individuals and that they maintained a practically constant trend throughout the entire evaluated period.

The figure shows on its Y-axis the mortality rate due to MBC for every 100,000 individuals and on the X-axis, the birth cohorts. Each line on the graph represents a specific age group. From the figure, it is possible to observe that MBC mortality is higher in older individuals, which corresponds to older birth cohorts, whereas MBC mortality is lower in younger individuals, which represents more recent birth cohorts.

The figure is composed of two distinct parts. On the left, the mortality rate for MBC for every 100,000 individuals (Y-axis) is evaluated according to the age group (X-axis), and an increase in the mortality rate can be observed as age progresses. On the right, it is possible to observe the relative risk (Y-axis) between each birth cohort and period evaluated. Since the unit of measurement for both variables is years (X-axis), they can be represented together. It can be abstracted from the graph that from 1996 to 2009, no statistically significant changes in the HR were observed. However, from 2010 onward, a significant increase in HR was found, reaching a peak in 2020–2021. As previously indicated in the results section and Table 3 many birth cohorts did not present a statistically significant HR. However, among the statistically significant cohorts, the ones from 1966 to 1979 demonstrated a decreasing HR with a peak of the lowest HR observed in the 1979 cohort.

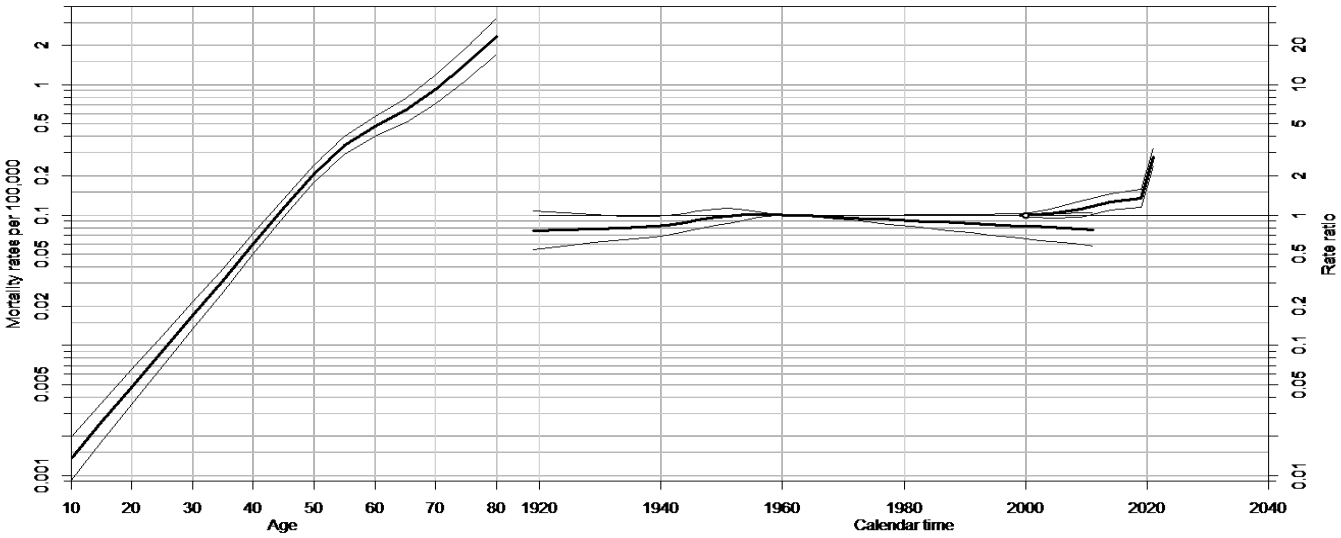

Figure 5. Summary of key findings.

DISCUSSION

Sex disparities

Sex-related disparities in breast cancer are notable, with MBC demonstrating distinct clinicopathological features and prognostic outcomes when compared to FBC[10-17]. MBC is a rare condition, accounting for approximately 0.5% to 1.0% of all breast cancer cases[10].

Men are typically diagnosed at a later age, ranging between 60–70 years median, as opposed to 48–61 years in women[10,11,13]. This delayed diagnosis in men is often associated with more advanced disease stages and higher tumor grades at presentation, contributing to treatment challenges[10,11,13].

The histological landscape of MBC also differs from that of FBC[11,14]. While invasive ductal carcinoma is the most prevalent histological subtype in both sexes, MBC presents with fewer instances of lobular carcinoma due to the lack of lobular tissue in the male breast[11,12,14]. Men are also more likely to present with hormone receptor-positive tumors, particularly estrogen receptor (ER)-positive, with higher rates than those observed in women[11-14]. This receptor positivity underpins the widespread use of endocrine therapies in MBC, yet, despite these interventions, outcomes remain less favorable than in FBC[11-14]. Cytokine-mediated inflammation, driven by tumor-associated macrophages and IL-6 (interleukin-6), may exacerbate tumor progression in both sexes but manifests distinct immunological signatures in men, likely influenced by androgen suppression of immune surveillance mechanisms[14].

Prognostically, MBC generally exhibits poorer outcomes[12,15,16]. Studies indicate that men experience lower overall survival (OS) and breast cancer-specific survival (BCSS) rates as compared to women[12,13,15,16]. For example, one study revealed a 5-year OS of 73.9% in men, compared to 86% in women, with a 5-year BCSS of 78.9% in men versus 94.7% in women[13]. This gap in survival is partially attributed to the higher burden of comorbidities in older male patients, such as diabetes mellitus, atrial fibrillation, and end-stage renal disease, all of which exacerbate mortality risks[13,16]. Additionally, male patients tend to present with larger tumors, higher tumor tissue invasion, greater lymph node involvement, and higher tumor grades at diagnosis, further complicating their prognosis[13,16].

The social and historical dimensions of breast cancer research have long skewed toward FBC, resulting in delayed recognition and underfunding of MBC studies[15,16]. Sociocultural stigmas surrounding MBC, compounded by limited public awareness, contribute to diagnostic delays and poorer outcomes[15,16]. Addressing these disparities requires not only equitable resource allocation but also public health initiatives to deconstruct gendered misconceptions and promote early detection[15,16].

Treatment modalities also differ significantly between the sexes[10-13,17]. Men are more frequently subjected to total mastectomy, whereas women often undergo breast-conserving surgery[12,17]. The higher prevalence of hormone receptor-positive tumors in men drives the increased use of endocrine therapy, particularly tamoxifen[10,17]. Despite these therapeutic approaches, men continue to experience poorer survival rates, a disparity that may stem from late-stage diagnoses, the aggressive nature of their tumors, and the underutilization of systemic therapies[17].

MBC particularities

MBC arises from a multifaceted interplay of genetic predispositions, lifestyle factors, and therapeutic disparities, each contributing to its unique pathogenesis and outcomes[14]. Genetic mutations, most notably in BRCA2 and less frequently in BRCA1, are central to the etiology of MBC, conferring significantly elevated lifetime risks[14,15]. Additional genomic alterations, such as TP53 (tumor

protein) mutations in Li-Fraumeni syndrome and PTEN (phosphatase and TENsin homolog deleted on chromosome 10) mutations associated with Cowden syndrome, underscore the hereditary predispositions inherent to this malignancy[14]. The androgen receptor pathway, distinct from the estrogen-driven mechanisms predominant in FBC, also plays a pivotal role, influencing tumor proliferation and therapeutic responsiveness[15]. Finally, epigenetic modifications, such as hypermethylation of tumor suppressor genes, have also been implicated, revealing a complex interplay between inherited and acquired genetic factors[14].

Lifestyle factors exacerbate these genetic susceptibilities[10-17]. Obesity, linked to higher aromatase activity and subsequent estrogen production, stands as a significant modifiable risk factor for MBC[15]. Similarly, alcohol consumption, implicated in epigenetic modifications of DNA (deoxyribonucleic acid) repair pathways, and smoking, associated with oxidative DNA damage, have been identified as contributors to tumorigenesis[16]. Chronic comorbidities, such as liver cirrhosis, which disrupts sexual hormone metabolism, further complicate the landscape of risk[15,16].

Treatment paradigms for MBC often reflect those established for FBC, despite evidence suggesting differential responses[17]. For example, tamoxifen—a cornerstone of hormone therapy—elicits higher rates of adverse effects in men, including thromboembolism and weight gain, potentially impacting adherence, possibly driven by its overinteraction with androgen receptors[17]. Furthermore, limited data on the efficacy of targeted therapies like CDK4/6 (cyclin-dependent kinase) inhibitors or immune checkpoint inhibitors in MBC underscore the critical need for sex-specific clinical trials to refine treatment algorithms and optimize outcomes[17].

Age

Age is a significant prognostic factor in MBC[1,10-17]. Sogunro et al. observed that older age at diagnosis, particularly ≥76.1 years, was linked to higher mortality, with an HR of 1.13 (p=0.004)[1]. Similarly, it was found that younger men (≤40 years) have better survival outcomes than those >40 years, with 5-year overall survival rates of 97.4% versus 86.4%, respectively[1]. The authors suggest that this survival difference may stem from biological changes associated with aging, such as decreased immune function and increased comorbidities, which negatively impact outcomes[1]. These findings align with other literature, noting that the age of onset plays a critical role in determining the prognosis of MBC, and younger men tend to present with less aggressive disease compared to their older counterparts[10-17].

Conversely, better survival in younger men may also result from earlier-stage diagnoses and potentially more aggressive treatment strategies[1]. The authors suggest that older patients might experience delays in diagnosis, contributing to the poorer outcomes observed[1,17]. This highlights the importance of age-specific screening and tailored treatment strategies to improve survival in older men diagnosed with MBC[1,17].

Period

The impact of distinct time periods on MBC incidence has been increasingly recognized[5,14,16]. Peng et al. identified a period effect contributing to rising MBC incidence between 2010 and 2019 in Taiwan and the USA[5]. The authors noted that societal changes, such as dietary shifts and greater exposure to environmental estrogens, might explain this trend[5]. The rise in incidence over these years possibly results from increased industrialization and the accompanying exposure to chemicals, such as xenoestrogens, which are known to interfere with hormone regulation and are potential carcinogens[6,10,13,18]. This is consistent with similar trends observed in FBC, suggesting shared environmental risk factors across the sexes[5,10,13,18].

Additionally, the authors highlight the role of improved diagnostic techniques and heightened awareness, which may have contributed to the apparent increase in MBC cases over recent decades[5,13-15,19]. Period effects, therefore, reflect not only actual rises in incidence but also enhanced detection rates[5,13-1518,19]. While these findings underline the importance of monitoring environmental changes over time, they also suggest that public health efforts should focus on mitigating these modifiable risks to reduce future incidence rates[11,19].

Birth cohort

The authors of a Taiwanese study identified a cohort effect, suggesting that men born after the 1960s exhibited higher MBC rates, likely due to increased exposure to Westernized lifestyles, including high-fat diets and obesity[5,12,15,16]. This cohort effect aligns with global trends showing that men from industrialized nations are more susceptible to MBC due to higher exposure to risk factors such as environmental estrogens and poor dietary habits[5,15,16]. These findings suggest that lifestyle changes over generations may partly explain the rising MBC incidence among younger birth cohorts[13,16,20].

Additionally, the authors discuss that earlier birth cohorts were less exposed to industrial chemicals like alkylphenols and bisphenol A, commonly found in household products and industrial waste, which have been linked to breast cancer risk[5,12,13,21]. The increased prevalence of obesity and Western dietary patterns among younger cohorts has further contributed to the cohort effect observed in MBC incidence, particularly in industrialized countries[5,15,16,20,21]. This underscores the necessity of addressing modifiable lifestyle factors across generations to mitigate future increases in MBC cases[5,15,16,20,21].

Men breast cancer global trends

Integrating the findings of this study within the context of global trends in MBC reveals both shared challenges and unique opportunities for public health interventions in Brazil[16,20]. MBC incidence, while consistently low worldwide, has exhibited slight upward trends in certain regions, likely attributable to improved diagnostic capabilities, heightened awareness, and changing environmental

exposures[16,20]. These global shifts underscore the need for proactive surveillance systems in Brazil, particularly as its demographic and epidemiological transition brings an aging male population at higher risk for malignancies, including breast cancer[16].

Men breast cancer impact on Brazilian public health:

Public health strategies in Brazil must also contend with socioeconomic and geographic disparities that influence access to care[16]. While high-income nations have embraced routine genetic screening for BRCA mutations among high-risk individuals, such practices remain limited in Brazil due to resource constraints[14,16,21]. Additionally, delayed diagnosis, frequently observed in low-resource settings, exacerbates the already poor prognosis associated with MBC[14,16,21]. To address these gaps, tailored strategies such as awareness campaigns targeting primary care providers, integration of genetic counseling services, and prioritization of early-stage treatment in national oncology guidelines are imperative[14,16,21].

Furthermore, the intersection of MBC with Brazil's epidemiological landscape—characterized by increasing rates of obesity, alcohol consumption, and metabolic syndromes—necessitates a multi-pronged approach[13,16]. Leveraging insights from global health initiatives, including lifestyle intervention programs and enhanced hormonal therapy accessibility, can serve as a framework for national policy adaptations[13,16]. Such strategies, bolstered by robust data collection and cross-regional collaborations, would not only align Brazil with global best practices but also ensure equitable and effective management of this rare but impactful malignancy[13,16].

Data lack on individual's level and its potential biases

The absence of individual-level data introduces significant potential biases, necessitating a sensitivity analysis to assess the robustness of the study's findings. Missing data often result in selection bias, particularly if the absence of records correlates with unobserved variables such as socio-economic status, comorbidities, or healthcare access[16]. For instance, in the context of MBC, underreporting may disproportionately affect rural or underserved populations where diagnostic infrastructure is limited, skewing mortality trends toward urbanized, better-resourced areas[16].

Sensitivity analyses employing multiple imputation techniques or inverse probability weighting could elucidate the extent to which these biases influence the results[15]. For example, imputing missing covariates such as tumor grade, genetic mutation status, or treatment regimens might reveal hidden associations or mitigate the overestimation of certain risk factors[15]. Additionally, employing stratified analyses by geographic region or income quintile could uncover systematic disparities masked in aggregate data, offering a more granular understanding of the biases introduced[15].

Moreover, the lack of granular data on individual-level treatment responses complicates the interpretation of survival outcomes[16]. Differential access to therapies such as tamoxifen or trastuzumab, coupled with variability in adherence rates, may distort apparent survival disparities[14]. Incorporating probabilistic sensitivity analyses to simulate scenarios of treatment allocation could provide a clearer picture of the extent to which these factors confound the results[14,16]. Addressing these gaps is not merely a statistical necessity but a scientific imperative, as it ensures that the conclusions drawn are not only statistically valid but also reflective of the lived realities of MBC patients across diverse contexts[14].

Reliance on death certificate data

The use of death certificate data as a primary source for studying MBC mortality is associated with inherent biases that may compromise the accuracy and interpretability of findings[16,22]. Death certificates, often completed under time constraints and with limited clinical insight, are prone to misclassification and/or underreporting the cause of death, particularly in less prevalent conditions like MBC[16,22]. This is exacerbated by the overlap of symptoms and complications with other prevalent conditions, such as cardiovascular disease or secondary malignancies, which can obscure the attribution of mortality to breast cancer itself[16,22].

Such inaccuracies carry profound implications for epidemiological analyses. Misclassified data may underestimate the true burden of MBC, skewing mortality rates and obscuring trends[16,22]. For instance, cases where metastatic breast cancer contributes to death might be recorded under related organ failures, such as hepatic or pulmonary causes, thereby diminishing the visibility of breast cancer as an underlying or contributory cause[16,22]. Moreover, differences in the thoroughness of death certification between urban and rural settings, or across socioeconomic strata, could introduce disparities that are falsely attributed to demographic or biological factors rather than systemic inconsistencies[16,22].

A nuanced discussion on the ramifications of these biases is essential to contextualize findings and guide future research. Incorporating data from cancer registries, autopsy reports, or hospital records could mitigate these limitations[16,22]. Additionally, leveraging molecular autopsy techniques, which identify specific oncogenic markers like BRCA mutations or HER2 (human epidermal growth factor receptor-type 2) amplification in deceased patients, could refine the classification of deaths and ensure a more accurate representation of MBC's impact on mortality statistics[16,22].

CONCLUSIONS

This study highlights a significant increase in male breast cancer mortality in Brazil over the past decade, particularly in men aged over 80. Cohorts from the late 20th century exhibited lower mortality risks. These findings underscore the importance of increased awareness and targeted interventions for this rare but impactful disease.

REFERENCES

1. Sogunro OA, Maini M, Deldar R, Maini AS, Greige N, Greenwalt I, et al. Prognostic predictors of mortality in male breast cancer: Outcomes in an urban population. J Surg Res. 2023;281:192-9. https://doi.org/10.1016/j.jss.2022.08.035
2. Li N, Wang X, Zhang H, Wang H. Young male breast cancer, a small crowd, the survival, and prognosis?: A population-based study. Medicine (Baltimore). 2018;97(40):e12686. https://doi.org/10.1097/MD.0000000000012686
3. Cronin PA, Romanoff A, Zabor EC, Stempel M, Eaton A, Smyth LM, et al. Influence of age on the clinical outcome of breast cancer for men and the development of second primary cancers. Ann Surg Oncol. 2018;25(13):3858-66. https://doi.org/10.1245/s10434-018-6767-0
4. Tural D, Selçukbiricik F, Aydoğan F, Beğe N, Yetmen O, Ilvan S, et al. Male breast cancers behave differently in elderly patients. Jpn J Clin Oncol. 2013;43(1):22-27. https://doi.org/10.1093/jjco/hys193
5. Peng JY, Lee YK, Pham RQ, Shen XH, Chen IH, Chen YC, et al. Trends and age-period-cohort effect on incidence of male breast cancer from 1980 to 2019 in Taiwan and the USA. Cancers (Basel). 2024;16(2):444. https://doi.org/10.3390/cancers16020444
6. Instituto Nacional de Câncer. Estimativa 2023: Incidência de Câncer no Brasil. Rio de Janeiro: INCA; 2023.
7. Holford TR. The estimation of age, period and cohort effects for vital rates. Biometrics. 1983;39(2):311-24.
8. Clayton D, Schifflers E. Models for temporal variation in cancer rates. I: age–period and age–cohort models. Stat Med. 1987;6(4):449-67. https://doi.org/10.1002/sim.4780060405
9. Carstensen B. Age-period-cohort models for the Lexis diagram. Stat Med. 2007;26(15):3018-45. https://doi.org/10.1002/sim.2764
10. Fentiman IS. The endocrinology of male breast cancer. Endocr Relat Cancer. 2018;25(6): R365-R373. https://doi.org/10.1530/ERC-18-0117
11. Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. Ann Oncol. 2013;24(6):1434-43. https://doi.org/10.1093/annonc/mdt025
12. Fox S, Speirs V, Shaaban AM. Male breast cancer: an update. Virchows Arch. 2022;480(1):85-93. https://doi.org/10.1007/s00428-021-03190-7
13. Gucalp A, Traina TA, Eisner JR, Parker JS, Selitsky SR, Park BH, et al. Male breast cancer: a disease distinct from female breast cancer. Breast Cancer Res Treat. 2019;173(1):37-48. https://doi.org/10.1007/s10549-018-4921-9
14. Khan NAJ, Tirona M. An updated review of epidemiology, risk factors, and management of male breast cancer. Med Oncol. 2021;38(4):39. https://doi.org/10.1007/s12032-021-01486-x
15. Chidambaram A, Prabhakaran R, Sivasamy S, Kanagasabai T, Thekkumalai M, Singh A, et al. Male breast cancer: current scenario and future perspectives. Technol Cancer Res Treat. 2024;23:15330338241261836. https://doi.org/10.1177/15330338241261836
16. Antonini M, Mattar A, Pannain GD, Buttenbender SF, Pinheiro DJPC, Teixeira MD, et al. Male and female disparities in breast cancer epidemiology: A comparative cross-sectional analysis of a Brazilian cohort (2017-2021). Heliyon. 2024;10(18):e38183. https://doi.org/10.1016/j.heliyon.2024.e38183
17. Hassett MJ, Somerfield MR, Baker ER, Cardoso F, Kansal KJ, Kwait DC, et al. Management of Male Breast Cancer: ASCO Guideline. J Clin Oncol. 2020;38(16):1849-63. https://doi.org/10.1200/JCO.19.03120
18. Cardoso F, Bartlett JMS, Slaets L, van Deurzen CHM, van Leeuwen-Stok E, Porter P, et al. Characterization of male breast cancer: Results of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Ann Oncol. 2018;29(2):405-17. https://doi.org/10.1093/annonc/mdx651
19. Piscuoglio S, Ng CKY, Murray MP, Guerini-Rocco E, Martelotto LG, Geyer FC, et al. The genomic landscape of male breast cancers. Clin Cancer Res. 2016;22(16):4045-56. https://doi.org/10.1158/1078-0432.CCR-15-2840
20. Avila J, Herrick B, Attai DJ, Leone JP. Treatments for breast cancer in men: late effects and impact on quality of life. Breast Cancer Res Treat. 2023;201(3):489-98. https://doi.org/10.1007/s10549-023-07027-6
21. Abboah-Offei M, Bayuo J, Salifu Y, Afolabi O, Akudjedu TN. Experiences and perceptions of men following breast cancer diagnosis: a mixed method systematic review. BMC Cancer. 2024;24(179). https://doi.org/10.1186/s12885-024-11911-9
22. Marinho MF, França EB, Teixeira RA, Ishitani LH, Cunha CC, Santos MR, et al. Dados para a saúde: impacto na melhoria da qualidade da informação sobre causas de óbito no Brasil. Rev Bras Epidemiol. 2019;22(Suppl 3):e19005. https://doi.org/10.1590/1980-549720190005.supl.3