



RESEARCH ARTICLE

Temporal Trend of Breast Cancer Diagnoses in Young Women in Different Regions of Brazil from 2014 to 2022

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ABSTRACT

Introduction: Breast cancer is the leading cause of female mortality in Brazil, and in young women, it generally presents more aggressively, with unfavorable characteristics, advanced stages, and a higher risk of recurrence.

Objective: To analyze the temporal trend of diagnosed breast cancer cases in young women in different regions of Brazil from 2014 to 2022.

Methods: An ecological time-series study using data from the Cancer Information System (SISCAN) of the Department of Informatics of the Unified Health System from 2014 to 2022. Reported cases of breast cancer according to ICD-10 C50 were included. For statistical analysis, standardized coefficients and simple linear regression were used.

Results: An increasing trend in the overall diagnosis rate of breast cancer in young women ($\beta=0.719$; $p<0.001$). Increase in diagnoses in all regions, especially in the North region ($\beta=0.888$; $p<0.001$). Increment in all age groups, particularly among those aged 25 to 29 years, with the age group 40 to 44 years ($\beta=1.817$; $p<0.001$) having the highest rates. A major increase in cases of Carcinoma In Situ ($\beta=0.047$; $p<0.001$), with Ductal Carcinoma ($\beta=0.394$; $p<0.001$) being the most incident during the period.

Conclusion: The data show an increase in the rate of breast cancer in young women in Brazil, across all regions, age groups, and histological types. This highlights the need for a better epidemiological understanding of the disease to develop strategies that reduce the associated morbidity and mortality.

Keywords: Cancer. Breast cancer. Young women. Epidemiology.

Introduction

Breast cancer is a disease that currently has a significant psychological, functional and social impact on women¹. It is a disease that develops from the uncontrolled proliferation of abnormal breast cells and is caused by, family history, medical history, advanced age, prolonged exposure to female hormones and numerous environmental factors². Moreover, genetic changes are also related to the development of this pathology, such as mutations in the BRCA1 and BRCA2 genes, which are responsible for repairing the genetic material of cells and preventing the emergence of neoplasms^{1,3}.

It is the most common malignant tumor in women in Brazil and worldwide, with the exception of non-melanoma skin cancer⁴⁻⁵. With 2.3 million new cases in 2022, it becomes the most commonly diagnosed cancer worldwide, surpassing lung cancer⁴. In Brazil, 94,728 new cases of breast cancer were estimated for 2022, corresponding to an adjusted incidence rate of 43.74 cases per 100,000 women⁵⁻⁶. The estimated diagnosis for the triennium 2023-2025 corresponds to an estimated risk of 66.54 new cases per 100,000 women⁷. In terms of mortality, according to the National Cancer Institute José Alencar Gomes da Silva (INCA), breast cancer is the leading cause of death among Brazilian women⁸. When analyzing the trends in the country's macro-regions, the data show significant regional differences, with the South and Southeast regions having the highest rates⁹.

The age group with the highest incidence of breast cancer is concentrated between 50 and 65 years old¹⁰⁻¹¹. In this group of women, the disease tends to present more favorable molecular characteristics, which contributes to a better prognosis and a higher chance of treatment success¹⁰⁻¹⁴. Additionally, women in this age group are covered by the mammographic screening program, which enables the detection of the disease in its early stages^{10,15-16}. On the other hand, the occurrence of this neoplasm in younger women is less common, representing about 7 to 10% of cases in women under 40 years old¹⁷⁻¹⁹. In this population, the condition tends to be more aggressive, with unfavorable clinicopathological characteristics, diagnosis at advanced stages, and a higher risk of recurrence when compared to older women²⁰⁻²².

An important factor that contributes to the poorer prognosis in young women is the difficulty in early diagnosis. Several studies show that mammography (MMG), the main method of population screening, has low sensitivity in younger women due to the high density of breast tissue, which makes it difficult to detect suspicious changes. Furthermore, this age group is not included in public health system screening programs, which further exacerbates the situation²³⁻²⁷.

In summary, recent studies have shown that due to the continental expansion and significant regional inequalities, the number of MMGs performed and the breast cancer mortality rate in Brazil are disproportionately high in the macro-regions^{5-6,9,28-31}. However, there is a lack of studies that comprehensively describe the epidemiologic profile of young women with malignant neoplasms of the breast in Brazil, comparing the five regions (South, Southeast, North, Northeast and

Central-West). Therefore, the analysis of trends over time will help to collect epidemiological data that can serve as a basis for research and intervention programs for early cancer detection³².

In this context, this study aims to analyze the temporal evolution of breast cancer cases diagnosed in young women in the different regions of Brazil between 2014 and 2022, in order to contribute to the planning of actions and prevention strategies.

Methods

Ecological time series study of the temporal evolution of breast cancer cases diagnosed in young women in different regions of Brazil, based on data from the Cancer Information System database (SISCAN) provided by the Department of Informatics of the Unified Health System (DATASUS), a publicly available resource.

The study analyzed breast cancer cases diagnosed in young Brazilian women between the ages of 20 and 44. All cases of malignant neoplasms of the breast registered according to the international classification code C50 (ICD-10) were included.

To determine the rate of diagnosed cases, the publicly available DATASUS database was used. Population size information for the calculation of breast cancer notification rates was obtained from the Brazilian Institute of Geography and Statistics (IBGE) based on population estimates by state, age and sex for the years 2000 to 2030.

The analysis of the temporal evolution of diagnosed cases was performed using records of breast cancer cases reported from 2014 to 2022 in Brazil and its regions. The dependent variables were the rates of total and specific cases by sex (female), age group (20 to 44 years), type of lesion and regions of the country, each expressed per 100,000 women. The independent variable was the year in which the data were collected. The period from 2014 to 2022 was selected because it represents the most recent and available data at the time of the research, ensuring an up-to-date analysis of the temporal trend.

Data organization and primary processing were performed using the TABWIN software available at DATASUS, and the data were then exported to Microsoft Excel. Data analysis was performed using the *Statistical Package for the Social Sciences (SPSS)*, version 18.0. [Computer program]. Chicago: SPSS Inc; 2009.

For each year of the study period, the coefficients for breast cancer cases, both crude and specific, were calculated for Brazil as well as for its regions, according to the dependent variables. The temporal evolution of breast cancer cases was analyzed using standardized coefficients with the simple linear regression method. The average rate for the period was calculated, along with the percentage deviation (PV) between the rates of the first (2014) and last year (2022), the β -value by the average annual change (AAC), with a 95% confidence interval (CI) and statistical significance for $p < 0.05$.

In this method, the standardized coefficients for breast

cancer cases were considered as the dependent variable and the calendar years of the study as the independent variable. The estimated model was determined using the formula $Y = b_0 + b_1X$, where Y = standardized coefficient, b_0 = average coefficient for the period, b_1 = average annual change, and X = year.

The study adhered to National Health Council Resolutions 466/12 and 510/16. As the study used publicly available data, it was not submitted to the Research Ethics Committee for review. The authors declare that they have no conflict of interest.

Results

A total of 19,506 new diagnoses of breast cancer in young women aged 20 to 44 years in Brazil between 2014 and 2022 were analyzed. A trend towards an increase in the overall diagnosis rate was observed (β 0.719; $p < 0.001$), with an average rate of 5.15 cases per 100,000 women and an increase of 272.76% when comparing the rates of the first and last year (Table 1, Figure 1).

The same trend of increase was observed in all regions of Brazil. The North (β 0.888; $p < 0.001$), Northeast (β 1.082; $p < 0.001$), Central-West (β 0.382; $p < 0.001$), Southeast (β 0.454; $p < 0.001$) and South (β 0.862; $p < 0.001$) regions had average rates of 3.30 to 9.45

diagnoses per 100,000 women, with increases between the first and last year of 1,393.11% to 117.48%. The highest rates were observed in the South and Northeast regions, while the largest increase was seen in the North (Table 1, Figure 2).

An increase was observed in all female age groups analyzed ($p < 0.05$) from 20 to 44 years, with average rates varying from 0.27 to 13.60 diagnoses per 100,000 women and increases ranging from 210.53% to 274.27% when rates were compared between 2014 and 2022. An increasing trend in the average annual change (AAC) was observed with increasing age. The highest percentage change (PV) was observed in the 25-29 age group (274.27%), while the highest rate and increase were seen in the 40-44 age group (Table 1, Figure 3).

Regarding lesion types, an increase were observed in lesions classified as Carcinoma In Situ (β 0.047; $p < 0.001$), Ductal Carcinoma (β 0.394; $p < 0.001$), Invasive Lobular Carcinoma (β 0.026; p 0.007) and other classifications (β 0.243; $p < 0.001$), with average rates of 0.31, 3.32, 0.20 and 1.19 per 100,000 women and increases of 499.38%, 215.01%, 282.11% and 481.50%, respectively, between the first and last year analyzed. The "special" classifications remained stable during the period (Table 1, Figure 4).

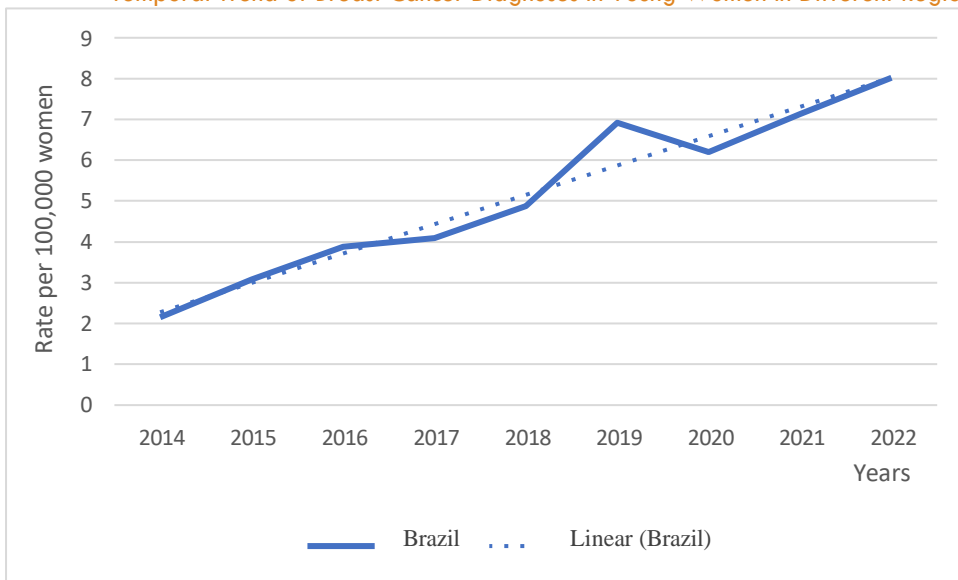
Table 1. Temporal trend of breast cancer diagnoses in young women, according to female age groups and regions in Brazil, from 2014 to 2022

Variables	Average Rate *	PV (%)†	AAR ‡(β)	95% CI of AAR§	P-value	Trends
Brazil	5.15	272.76	0.719	0.577 to 0.860	<0.001	Increase
Regions of Brazil						
North Region	3.93	1393.11	0.888	0.658 to 1.118	<0.001	Increase
Northeast Region	6.40	338.05	1.082	0.715 to 1.448	<0.001	Increase
Central-West Region	4.28	117.48	0.382	0.217 to 0.546	0.001	Increase
Southeast Region	3.30	335.43	0.454	0.331 to 0.576	<0.001	Increase
South Region	9.45	144.92	0.862	0.557 to 1.168	<0.001	Increase
Female Age Groups						
20 to 24 years	0.27	210.53	0.041	0,021 to 0.060	0.002	Increase
25 to 29 years	1.26	274.27	0.184	0.145 to 0.222	<0.001	Increase
30 to 34 years	3.64	218.99	0.454	0.339 to 0.569	<0.001	Increase
35 to 39 years	7.69	266.74	0.991	0.751 a 1.230	<0.001	Increase
40 to 44 years	13.60	241.64	1.817	1.387 a 2.246	<0.001	Increase
Type of injury						
Carcinoma In Situ	0.31	499.38	0.047	0.033 to 0.062	<0.001	Increase
Ductal Carcinoma	3.32	215.01	0.394	0.252 to 0.536	<0.001	Increase
Invasive Lobular Carcinoma	0.20	382.11	0.026	0.010 to 0.042	0.007	Increase
Specials	0.08	41.80	0.005	-0.002 to 0.011	0.139	Stability
Others	1.19	481.50	0.243	0.169 to 0.317	<0.001	Increase

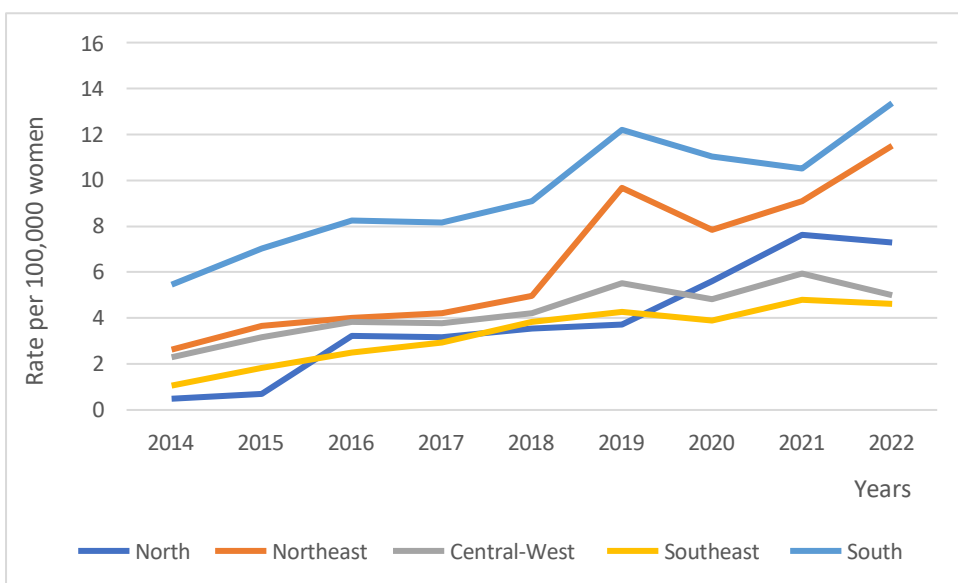
* Average Rate – the average of the rates over the period; † PV – percentage variation between the rates of the first year (2014) and the last year (2022); ‡ AAR (β) – Average Annual Rate (AAR) - Calculated by Linear Regression; § 95% CI of AAR – 95% Confidence Interval of the Average Annual Rate; || p-value <0.05 considered statistically significant.

Source: Prepared by the authors, 2024.

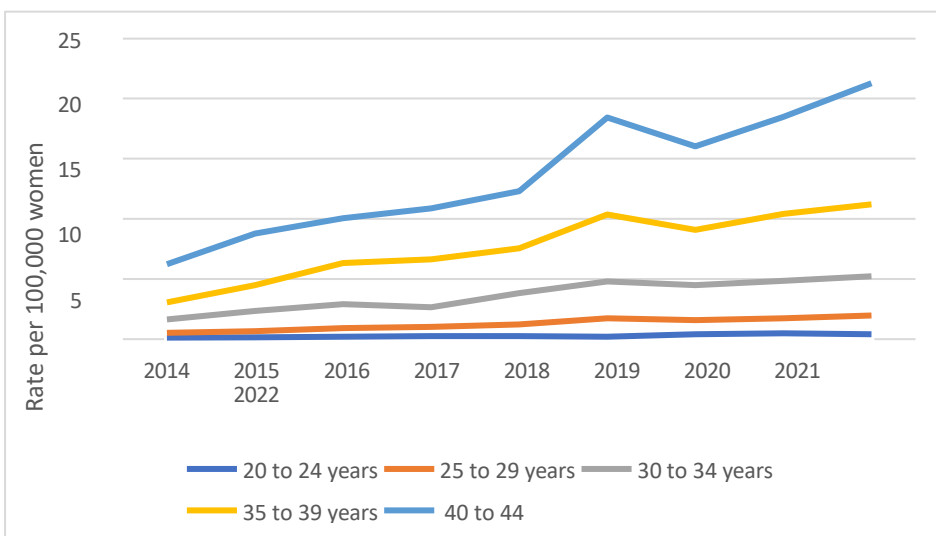
Temporal Trend of Breast Cancer Diagnoses in Young Women in Different Regions of Brazil from 2014 to 2022



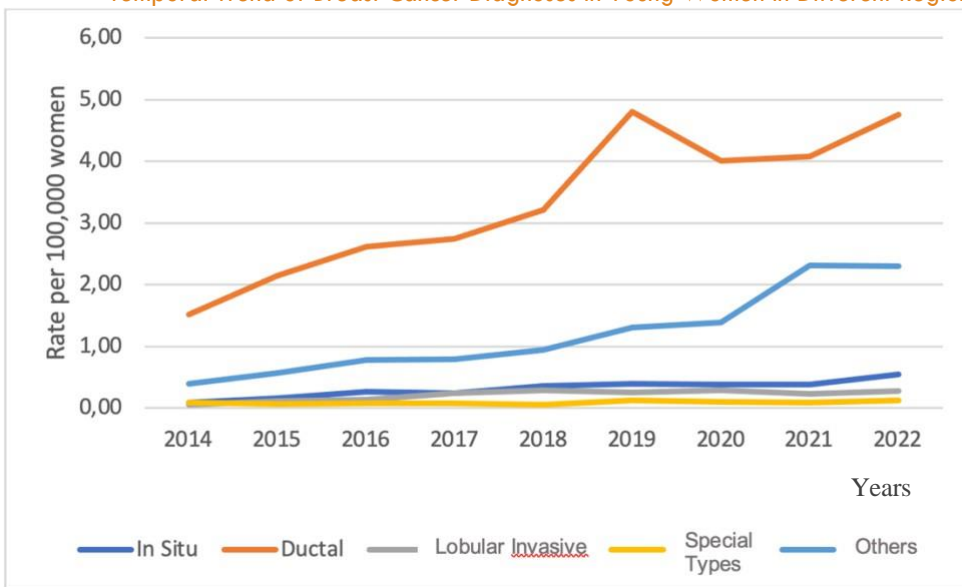
Graph 1. Overall Trend of Breast Cancer Diagnoses in Young Women in Brazil, from 2014 to 2022. ($\beta = 0.719$; $p < 0.001$).
Source: Prepared by the authors, 2024.



Graph 2. Temporal Trend of Breast Cancer Diagnoses in Young Women, According to Regions of Brazil, from 2014 to 2022. Regions: North ($\beta = 0.888$; $p < 0.001$), Northeast ($\beta = 1.082$; $p < 0.001$), Central-West ($\beta = 0.382$; $p = 0.001$), Southeast ($\beta = 0.454$; $p < 0.001$), and South ($\beta = 0.862$; $p < 0.001$).
Source: Prepared by the authors, 2024.



Graph 3. Temporal Trend of Breast Cancer Diagnoses in Young Women, According to Female Age Groups in Brazil, from 2014 to 2022. Age Groups: 20 to 24 years ($\beta = 0.041$; $p = 0.002$), 25 to 29 years ($\beta = 0.184$; $p < 0.001$), 30 to 34 years ($\beta = 0.454$; $p < 0.001$), 35 to 39 years ($\beta = 0.991$; $p < 0.001$), and 40 to 44 years ($\beta = 1.817$; $p < 0.001$).
Source: Prepared by the authors, 2024.



Graph 4. Temporal Trend of Breast Cancer Diagnoses in Young Women, According to Type of Lesion, from 2014 to 2022. Lesion Types: Carcinoma In Situ ($\beta = 0.047$; $p < 0.001$), Ductal Carcinoma ($\beta = 0.394$; $p < 0.001$), Lobular Invasive Carcinoma ($\beta = 0.026$; $p = 0.007$), Special Types ($\beta = 0.005$; $p < 0.001$), and Others ($\beta = 0.243$; $p < 0.001$).

Source: Prepared by the authors, 2024.

Discussion

Breast cancer stands out as the most common type of cancer, both in Brazil and worldwide. According to GLOBOCAN data, in 2022, 94,728 new cases were diagnosed in Brazil and 2,296,840 cases worldwide³³. Furthermore, in the same year, breast cancer was identified as the most prevalent in 158 countries, with Brazil ranking as the leader in Latin America regarding the incidence of this disease³³. These figures highlight the importance of an in-depth analysis of the factors contributing to this high incidence and the measures required to address it.

The results of this study reveal a concerning upward trend in the number of breast cancer diagnoses in young women in Brazil and across all regions of the country from 2014 to 2022. Specifically, it was found that the North region exhibited the largest percentage change in cases over this period, while the South region recorded the highest average incidence rate of this malignancy. These findings underscore the urgent need for a more detailed analysis of the factors contributing to this alarming increase, along with the implementation of effective strategies for the prevention and control of breast cancer in young women across the country.

Research has focused on understanding the factors contributing to this alarming trend, with key findings highlighting the influence of exposure to risk factors such as high-dose ionizing radiation, pesticides, organochlorines, long-term oral contraceptive use, alcohol consumption, and smoking^{2,8,34}. Genetic and hormonal factors, such as age at menarche, genetic mutations like BRCA1 and BRCA2, and family history of breast cancer, should also be considered due to their impact on the risk of breast cancer in young women^{2,8,34}.

A study involving 1,663 Brazilian patients, conducted between 2015 and 2017, demonstrated a high prevalence of pathogenic/possibly pathogenic mutations in genes such as BRCA1, BRCA2, and TP53 in young women. This reinforces the need for differentiated

guidelines for monitoring and risk reduction strategies for women with hereditary breast cancer (BC) in Brazil and their family members carrying the same genetic variants³⁵.

It is also crucial to reflect on the impact of changes in lifestyle patterns, such as long working hours influencing the preference for fast food and promoting sedentary habits, which contribute to the development of obesity, a known risk factor for breast cancer. Furthermore, advances in the early detection and diagnosis of breast cancer, driven by campaigns such as Pink October, promoted by the Primary Health Care Network, may have an impact by encouraging more women to seek early information about the disease, resulting in an apparent increase in cases, with more young women being diagnosed at earlier stages.

Given Brazil's vast regional diversity, including socio-economic, social, cultural, and healthcare access factors, significant differences in the epidemiological landscape of diseases are expected³⁶. Disparities between the South and North regions result in divergences in the incidence of diagnosed breast cancer cases, influenced by a variety of epidemiological and socio-economic factors. While the South region stands out for its more favorable socioeconomic indicators, directly impacting disease identification, such as access to preventive exams and more effective screening programs, the North faces challenges such as inadequate healthcare infrastructure, vast geographic distances, and a lack of information on prevention and healthcare, leading to later diagnoses^{34,37-38}.

One possible explanation for the sharp increase in the percentage change in case numbers in the North region may be attributed to the lack of access to adequate diagnoses for many women in previous years. Thus, with improved access to healthcare, these women gained better access to diagnoses, resulting in a higher incidence of this type of cancer. Furthermore, the highest rate of cases is found in the South region, which may be

explained by its greater healthcare infrastructure and higher socioeconomic indicators. Consequently, the population in this region has better access to exams and medical consultations, both through the public system and private or health insurance providers.

When analyzing different age groups, a worrying increase in the incidence of breast cancer was observed across all examined female age groups. Specifically, in the 40 to 44-year-old group, there was a significant increase in both the rate of new cases and the percentage variation between 2014 and 2022. Additionally, it was found that the 25 to 29-year-old age group showed the largest percentage variation in the incidence of breast cancer during the study period. These findings align with the concerning trend

identified in the AMAZONA III/GBECAM 0115 study, a prospective cohort study conducted in Brazil involving 2,950 women from 22 health centers distributed across nine states, diagnosed with tumors between January 2016 and March 2018. Of the participants, 43% were under 50 years old at the time of diagnosis, and 36.9% of these were at stage 3 of the disease, considered locally advanced³⁹.

The findings mentioned may be related to several factors, including late pregnancies, reduced breastfeeding, prolonged use of oral contraceptives, exposure to carcinogens, and greater reporting of diagnosed cases. It is also important to highlight that the observation of a significant proportion of women under 50 years of age diagnosed with advanced-stage breast cancer suggests the need for a review of early detection strategies and education on breast health for younger women^{8,40}.

Regarding histologic type, the current investigation revealed a relevant increase in the percentage change in the number of diagnosed cases of Carcinoma In Situ and identified that Ductal Carcinoma had the highest incidence rate during the study period. This phenomenon may be linked to the increasing performance of mammograms in younger women and greater access to information through technology and prevention campaigns. Additionally, the diagnosis of cancer in a woman triggers a chain reaction, motivating family members and women close to them to undergo preventive exams earlier, which may contribute to overdiagnosis of Ductal Carcinoma In Situ.

The finding that Ductal Carcinoma is the most common histologic type across different Brazilian regions corroborates previous research, which shows it as the most common pattern worldwide, both in young women and older women, with prevalence rates varying between 78% and 95.6% depending on the study^{23,41}.

It is important to note that the overdiagnosis rates of in situ carcinomas in screening exams vary across different studies, ranging from 10% to 52%⁴²⁻⁴⁴. Some studies concluded that, for every 2,000 women screened over 10 years, only one would have her life saved by early screening, while 10 would experience overdiagnosis and overtreatment, and 200 would face psychological stress due to false positives⁴⁴⁻⁴⁶. Consequently, the effects may encompass not only a false familial risk, generating a psychosocial impact that extends to subsequent

generations, as daughters and sisters of women with breast cancer believe they are at greater risk of developing the disease, but it is also estimated that half of overdiagnosed women will suffer chronic pain due to overtreatment⁴⁶⁻⁴⁷.

In light of this scenario, the Ministry of Health (MS) maintains the recommendation for mammography screening only for women aged 50 to 69, with the possibility of screening at younger ages in cases of high risk, such as a family history of early breast cancer or genetic mutations. This guidance is based on concerns about potential harms of the procedure in younger women, including an increase in false positive results and the harms associated with screening^{8,48}.

On the other hand, Brazilian medical organizations such as the Brazilian Federation of Associations of Gynecology and Obstetrics (FEBRASGO), the Brazilian Society of Mastology (SBM), and the Brazilian College of Radiology and Diagnostic Imaging (CBR) present a counterpoint to this guideline, advocating for annual mammograms for asymptomatic women aged 40 to 74, provided there are no comorbidities that reduce life expectancy by at least seven years⁴⁹. This recommendation is based on literature reviews that show an increase in breast cancer incidence in young women, as well as a reduction in mortality associated with mammography screening, especially among women aged 39 to 49. Moreover, Brazil, like other developing countries, has a higher proportion of breast cancer patients in this age group compared to developed countries⁵⁰⁻⁵².

Several factors limit the analysis of the results of this study. One of the issues relates to the high underreporting of diseases in Brazil, which, although significantly improved in recent years, is still influenced by demographic and socio-economic infrastructure factors in various regions^{34,36-37}. An additional challenge in the reporting and registration of breast cancer in young women lies in several factors, such as social and cultural barriers, limited access to healthcare services, socio-economic inequalities, lack of awareness and education about the disease, and the fear and stigma associated with cancer. Another factor to consider is the lack of recent scientific research on the trends in rates across different regions of Brazil, which could enable more in-depth comparative studies of the results.

In conclusion, considering the epidemiological and etiological aspects of breast cancer in young women, it is clear that it is a complex disease with various manifestations and unfavorable clinical evolutions. Despite its incidence rate showing variations across regions, it increases gradually in all of them, especially due to challenges in early diagnosis. This is exacerbated by barriers to healthcare access, such as mammograms and specialized medical consultations, and the scarcity of effective screening programs targeting younger age groups. Therefore, a better regionalized and epidemiological understanding of the disease's progression over time becomes an essential tool for defining health promotion strategies and the appropriate allocation of resources, as well as raising awareness about the clinical picture, prognostics, and mitigation of

modifiable risk factors to reduce the morbidity and mortality associated with breast neoplasms in young women.

Conclusion

A significant upward trend in the overall breast cancer diagnosis rate among young women in Brazil is observed. Regarding the regions of Brazil, the trend of increasing average rates was consistent across all regions, with the highest rates in the South and Northeast regions, and the greatest increase in the North region. Regarding the analyzed female age groups, all showed an increase in diagnosis rates, with the highest percentage variations observed in the 25 to 29-year-old age group and the highest incidence in the 40 to 44-year-old age group.

In terms of lesion types, there was a trend towards higher

diagnosis rates for carcinoma in situ, ductal carcinoma, invasive lobular carcinoma and other classifications, while cases classified as special remained stable throughout the period analyzed, with ductal carcinoma having the highest incidence.

Conflicts of interest statement

The authors have no conflicts of interest to declare.

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