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Evaluation of clinical, pathological and epidemiological profile of patients with breast cancer in the microregion of Lavras – MG

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ABSTRACT

Introduction: Breast cancer is associated with high frequency and mortality in Brazilian women. There have been limited studies portraying the characteristics of breast cancer cases in the countryside of the state of Minas Gerais for a long period of time, a fact that will allow us to better understand the epidemiology of these tumors. This descriptive study aims to analyze the epidemiology and clinical features of patients with breast cancer treated at a public health service facility in Lavras, MG. **Methods:** This is a transversal study with 299 women diagnosed with breast cancer between 2002 and 2022, based on data collection from medical records and subsequent descriptive analysis. **Results:** There were a total of 317 cases, and 299 were eligible for the study. The mean age at diagnosis was 54.2 years, and 36.1% of the patients were under 50 years old at diagnosis. Positive family history was found in 17.0% of the patients. The diagnosis was made by clinical alteration detected on physical examination in 71.5% of cases, and lump was the most frequent type of lesion (89.0%). Invasive carcinoma was 93.1% of the cases, and the mean tumor size was 28.6 mm. The average time between first medical appointment and diagnosis was 63.2 days, and between diagnosis and beginning of treatment was 39.6 days. **Conclusions:** This study showed that a significant number of cases occurred in women outside the recommended age for screening in Brazil. Diagnosis was predominantly performed by clinical examination, with delays in obtaining the histological diagnosis, and the stage at diagnosis was high, and these facts were associated with the health system limitations.

KEYWORDS: breast neoplasm; age groups; cancer screening.

INTRODUCTION

Breast cancer (BC) is the most common malignant neoplasm among women in Brazil and in the rest of the globe, accounting for 23% of all cancer cases worldwide[1,2]. Several risk factors have already been established, including endogenous and environmental factors. It is the leading cause of death from cancer in the Brazilian female population[3].

In the United States, BC mortality rates showed a 40% decline from 1989 to 2017, meaning over 375,000 fewer deaths[4]. In contrast, as is the case in most low- and middle-income countries, Brazilian estimates indicate stable or increasing mortality rates, with more than 16,000 deaths in 2017[5].

Early diagnosis is closely related to imaging diagnosis and clinical recognition of small tumors, strongly influencing the prognosis of the disease. According to Records from the Cancer Hospital, in Brazil there were 40% of BC diagnoses in stage 3 and 4 in 2010[6], Advanced stage at diagnosis is difficult and costly to treat, and is associated with increased morbidity and poor survival[7,8].

Among the prognostic factors, besides the intrinsic tumor characteristics, such as the hormonal receptors status and the human epidermal growth factor receptor-type 2 (HER2) overexpression, associated with the tumor size, axillary status, and staging, the time between the clinical manifestation of the disease and its diagnosis and initiation of treatment may be included[9,10].

The state of Minas Gerais has few and short isolated studies that portray the profile of patients with BC, as well as stage at diagnosis, time to obtain the diagnosis and to start treatment. Faced with such an incident pathology that causes significant morbidity and mortality among the female population in Brazil, studies must be conducted to better elucidate epidemiology, disease presentation and behavior, and the best methods involved in the screening and diagnosis of this disease[9,10].

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The justification for carrying out the present study is based on the proposal to present the unprecedented results of a series of patients with BC in the microregion of Lavras, Minas Gerais.

The purpose of this article is to verify clinical and pathological characteristics, age distribution, as well as the time interval for the diagnosis and the beginning of treatment, of patients with breast cancer attended in the public service at a secondary reference center in the countryside of Minas Gerais (MG). Such knowledge may, thus, subsidize the planning, implementation, and evaluation of policies and actions of the Unified Health System (SUS) at the regional level, especially regarding the availability of methods that enable early detection and adequate treatment by the SUS.

METHODS

A descriptive, retrospective study was carried out based on the analysis of medical records of patients attended at the Mastology Service of the *Centro Estadual de Atenção Especializada* (CEAE) in the city of Lavras, in the south of the state of Minas Gerais, Brazil. The CEAE is a secondary care center, a reference in mastology care in the microregion of Lavras. It offers mastology appointments, imaging tests (mammography and ultrasound) and breast biopsies. Breast cancer surgeries are performed at *Santa Casa de Misericórdia de Lavras* – MG, and adjuvant treatments (chemo and radiotherapy) are provided in a reference center for the microregion in another city (Varginha, Minas Gerais).

People included in the study came from Lavras and its microregion, which comprises 10 other municipalities. Data were collected in a standardized form and, subsequently, tabulated and analyzed exposing quantitative variables and absolute and relative frequencies.

This study was approved by the Ethics Committee in Research with Human Beings of *Universidade Federal de Lavras* – MG (UFLA) – CAAE: 36285320.2.0000.5148.

All cases of breast carcinoma diagnosis between January 2002 and April 2022 were selected. The inclusion criterion was the histologic diagnosis of breast carcinoma in patients over 18 years of age. There were a total of 317 cases during the established period, 18 of which were excluded because there was no information in their records to obtain the necessary data and/or because they had undergone treatment at another health facility soon after diagnosis. Thus, the final sample of the study consisted of 299 patients.

Only cases of first-degree relatives with the disease, i.e., mother, sister and/or daughter, were considered as a positive family history. For the classification of the menopausal status, the definition of post-menopause was used, involving the classification of the patient into one of these four groups: women aged 60 years or older, women who underwent bilateral oophorectomy, women without their uterus and with laboratory tests showing increased follicle-stimulating hormone (FSH) levels, and women younger than 60 years of age, with uterus, non-users of hormonal therapy, in amenorrhea for at least 12 months before the diagnosis of breast cancer. Other than the situations described, the classification was premenopausal.

To obtain data for staging, classification of Tumor, Node, Metastasis (TNM), the 8th edition of the American Joint Committee on Cancer (AJCC) was used.

Molecular classification was based on luminal A (ER+/PR+/HER2-/low Ki-67: <20%), luminal B Her2-negative (ER+/PR+/HER2-/high Ki-67: ≥20%), luminal B Her2-positive (ER +/PR+/HER2+), Her 2 (ER-/PR-/ HER2+), and triple negative (ER-/PR-/HER2-) BC subtypes[11]. Positive ER or PR was considered when ≥1% of invasive malignant cells exhibited nuclear staining or immunoreactivity. The HER2 test was scored from 0 to 3+, where: score 0 or 1 was negative; 2+ was undefined; and 3+ was positive. When there was any undefined result, FISH (Fluorescence in situ hybridization) was performed for definition.

Database, analysis of variance and mean tests, as well as procedures for frequency analysis, were performed by the software Sisvar 5.3 Build 77.

RESULTS

In the final sample of the study, 299 patients with breast carcinoma were included; 204 of them were from the city of Lavras and the other 95 were from cities in the microregion.

The average age of the patients was 54.2 years (±12.3). The division into groups by age is shown in Figure 1.

The evaluation of the menopausal status showed that 40.5% of the patients were premenopausal at diagnosis. As for parity, 14.4% of the patients were nulliparous at the time of diagnosis. Positive family history was found in 17.0% of the cases. Clinical characteristics are listed in Table 1.

The diagnosis of breast cancer was given based on alterations in the clinical examination in 71.5% of the cases. Lump was the most common type of lesion found: 89.0% of the cases (Figure 2).

In this study, 93.1% of the patients had invasive breast carcinoma, and 6.9% were diagnosed with ductal carcinoma *in situ*. In cases of invasive carcinoma, the analysis of the histological type revealed the high prevalence of the ductal type: 84.5% of the cases (Figure 3).

The mean tumor size of invasive carcinomas was 28.6 mm (±19.5; 0.3–13.3 cm) and median of 25 mm. At the time of diagnosis, 56.9% of the patients had clinically negative axilla, and 43.1% had clinically positive axilla. Regarding the histologic grade, most patients had a lesion with histologic grade 2 (59.4%). Histopathological characteristics are listed in Table 2. The most common stages at the time of diagnosis were IIA and IA: 28.9 and 24.4%, respectively (Table 3).

The average time between the medical appointment that motivated the investigative process and the histologic diagnosis was

66.2 days (±48.0). The average time between the histologic diagnosis and the beginning of the treatment was 39.6 days (±29.8).

DISCUSSION

Breast cancer is a disease of global impact, high incidence, prevalence, and mortality. In Brazil, 66.280 new cases were estimated for 2022, which represents an adjusted incidence rate of 43.74 cases per 100,000 women[5]. For the same period, 8,250 new cases were estimated in Minas Gerais[5].

In this study, the mean age at diagnosis was 54.2 years. The highest frequency of cases occurred in women of the 50–59 age group (30.4%; n=91), but the high prevalence of cases among women aged 40–49 years stands out (25.4%; n=76). Combined with the cases of the 30-39 age group, they represent 34.8% of the total figure, a rather significant number of cases. The data evidenced

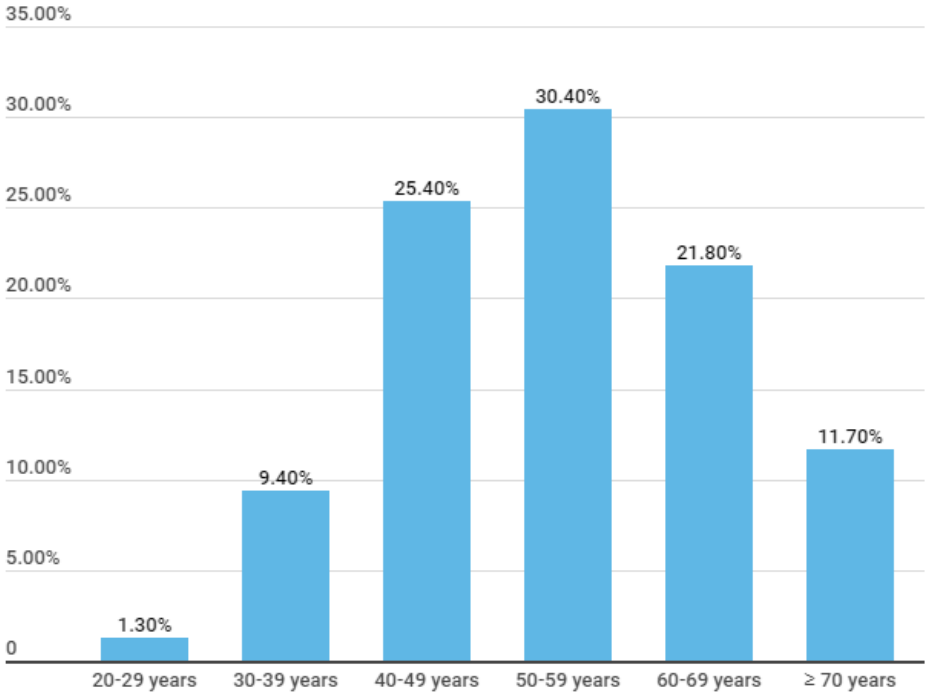

Figure 1. Distribution of breast cancer cases by age.

Table 1. Clinical characteristics of patients diagnosed with breast carcinoma.

	Category	Absolute frequency (n)	Percentage (%)
Parity	Nulliparous	43	14.4
	Primiparous	42	14.0
	Multiparous	214	71.6
Breastfeeding	Yes	231	77.3
	No	68	22.7
Menopausal status	Pre-menopause	121	40.5
	Post-menopause	178	59.5
Smoking	Yes	75	25.0
	No	224	75.0
Family History	Positive	51	17.0
	Negative	248	83.0
Type of Diagnosis	Clinical	214	71.5
	Imaging	77	28.5

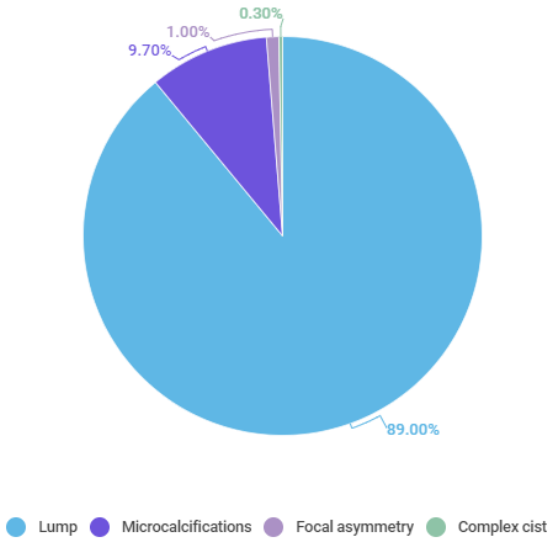

Figure 2. Type of lesion at disease presentation.

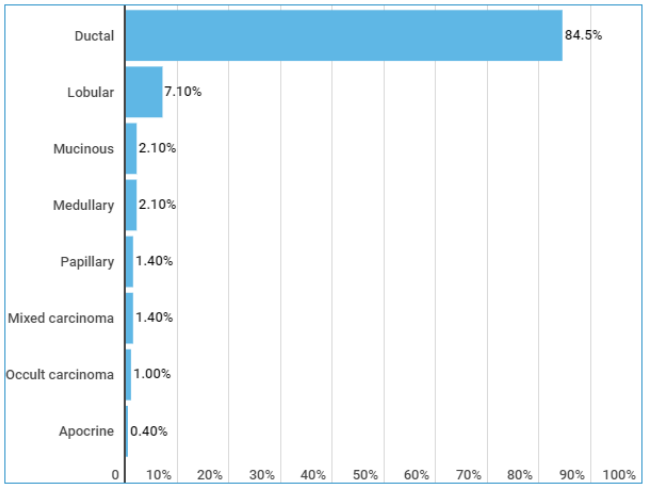

Figure 3. Distribution according to the invasive breast carcinoma histological type.

here are in agreement with other studies in the literature[12-14] Vale *et al.* found a prevalence of 34.4% in women under 50 years of age when surveying the number of breast cancer diagnoses given in the city of São Paulo between 2000 and 2015[15]. In the largest retrospective study on the breast cancer profile in the Brazilian population, called AMAZONA study, 41.1% of the patients were younger than 50 years old at the time of their diagnosis[16]. Such evidence raises the discussion regarding the need to expand the current screening program for breast cancer as adopted by the Ministry of Health in Brazil, which does not contemplate women between 40–49 years of age when they are at the usual risk. The high number of cases in women in this age group calls for greater attention for this public.

As for the histological type, it is known that the invasive ductal breast carcinoma, now called invasive carcinoma of no special type, is the most frequent subgroup, and the findings of this study are in line with the literature data[17]. The rate of ductal carcinoma *in situ* (DCIS) found was 6.9%. In Brazil, little information has been published on the epidemiology of carcinomas *in situ*. Its incidence is estimated to vary between 6.6 and 8.9%[12,18,19].

Table 3. Stage at diagnosis.

Stage	Absolute Frequency (n)	Percentage (%)
0	20	6.9
IA	71	24.4
IB	3	1.0
IIA	84	28.9
IIB	50	17.2
IIIA	33	11.3
IIIB	18	6.2
IIIC	5	1.7
IV	7	2.4

Table 2. Histopathological characteristics of the tumor.

Variable	Category	Absolute Frequency (n)	Percentage (%)
Estrogen receptor	Positive	234	81.5
	Negative	53	18.5
Progesterone receptor	Positive	215	74.9
	Negative	72	25.0
HER-2 Receptor	Positive	49	17.1
	Negative	237	82.9
Molecular Subtype	Luminal A	90	31.6
	Luminal B	114	40.0
	Luminal B-Her2	30	10.5
	HER-2	19	6.7
	Triple-negative	32	11.2

These numbers reflect the failure to establish an efficient mammography screening system. For the sake of comparison, internationally, DCIS now represents about 20% of all breast cancers diagnosed by screening[20,21].

Other data obtained in this study reveal that most patients (71.5%) had their diagnosis established when they already had palpable clinical lesions, which may have a direct relation to prognosis, type of treatment performed, and costs to the health system. The type of lesion most often found was lump (89.0%), which corroborates other studies that showed that the most associated sign of breast cancer is the breast nodule[12,22]. The presence of a nodule larger than or equal to 2 cm is related with increased risk of breast cancer[23]. In the present study, the average tumor size at diagnosis was 28.6 mm, which is not in line with a good early diagnosis strategy. The clinical examination of the breasts performed by trained health professionals associated with mammography remains the best strategy for diagnosis in women at usual risk. However, the low number of screening mammograms in Brazil reflects on the rates of diagnosis already with clinically identified lesions. It is also known that breast self-examination is not recommended as a cancer screening method and has not shown effectiveness in reducing mortality from BC, which further reinforces the need for organized screening programs in Brazil[24]. Recently, a large study carried out in Mumbai, India, has found that clinical breast examination conducted every two years by primary health workers significantly downstaged breast cancer at diagnosis, but with a non-significant 15% overall reduction in breast cancer mortality[25].

Nulliparity is recognized as a risk factor for the development of the disease. Nevertheless, in our study, only 14.4% of diagnosed patients had this condition. Pregnancy and lactation are considered important protective factors for breast cancer. In our analysis, most patients had such conditions: 71.6% of patients were multiparous and 77.2% had a history of breastfeeding. This information highlights the diversity of factors involved and their real weight in the development of a breast cancer.

A family history of breast cancer is also a crucial factor associated with an increased risk of BC. Approximately 16% of patients diagnosed with breast cancer report a first-degree relative affected by the same condition[17]. The data from our study showed a positive family history of breast cancer in 17.0% of the cases, numbers that are in agreement with other studies, such as Barboza ***et al***, in which 1,176 Brazilian patients were analyzed, and most had no cases of breast cancer in the family[26]. The positive family history of breast cancer in a minority of cases does not justify screening based on this circumstance by itself, requiring more careful risk assessment.

Data from the present study show that 25.0% of patients were smokers. It is noteworthy that carcinogens found in tobacco are transported to the breast tissue, increasing the likelihood of mutations in oncogenes and suppressor genes (p53 in particular). Moreover, a long smoking history and smoking before the first full-term pregnancy are additional risk factors, more pronounced in women with a family history of breast cancer[17]. Although it is controversial, the association between smoking and breast cancer is evidenced in several studies[3].

Axillary lymph node involvement is a prognostic marker in the management of BC, and sentinel lymph node biopsy is an important part of tumor staging[27]. Axillary lymph node clinical involvement was observed in 43.1% of cases (n=121), whereas 56.9% (n=160) of patients had no suspicious axillary lymph node at diagnosis. The National Surgical Adjuvant Breast and Bowel Project (NSABP) in B-32 trial reported 29% of sentinel lymph node positivity, while in specialized centers, and with effective screening, the positivity rate is dropping below 20%[28,29]. Such data reinforce the importance of the cyto/histological diagnosis of the axillary status, due to the considerable false positive and false negative results of the axilla clinical examination. In cases of histological lymph node involvement, late diagnosis negatively impacts survival, in addition to worsening quality of life when lymphadenectomy is performed.

The histological classification known as the Nottingham Classification System is a recommended grading system to help determine the prognosis of BC[30]. Several studies have shown that patients with histological grade 1 have the best prognosis, while grade 3 tumors have the worst prognosis[31]. In the present study, it was found that 13.0% (n=37) of the tumors diagnosed were histological grade 1, whereas most of the cases, 59.4% (n=170), were grade 2 and the other 27.6% (n=79) were classified as grade 3.

We observed that a smaller proportion of cases were diagnosed in early stages (stage 0 and I): 32,3%. Stage IIA was the most found, with 28.9% of cases (n=84), followed by IA with 24.4% (n=71), and IIB with 17.2% of diagnoses (n=50). These data are aligned with a previous descriptive study conducted in this same health center in the countryside of Minas Gerais, through the analysis of 112 cases of BC diagnosed between 2008 and 2013, which revealed stage II as the most common at diagnosis[12]. Dugno *et al.*, in a cross-sectional study with 273 patients in a hospital in southern Brazil, found that most patients had the disease diagnosed in stages I and II (70.8% of cases; 36.6%, and 34.2%, respectively)[32]. Similarly, Simon ***et al.*** observed in a retrospective cohort of 2,296 women with histologically proven breast cancer that more than half (53.5%) of cases were stage II at diagnosis[16]. On the other hand, such data also reflect the heterogeneity of BC in Brazil, given that another cohort of patients with BC treated surgically at *Hospital das Clínicas* in Belo Horizonte showed that the stage at diagnosis was higher among patients in the public health system compared with diagnoses made in the private system (58% of cases in the public health services were diagnosed in the initial stages and 42% in stage III, while in the private system 86.4% were detected in the initial stages and only 17.6% in stage III)[33]. We found a small number of cases in stages IIIB (6.2%), IIIC (1.7%) and IV (2.4%). These data

may reflect a possible bias related to the search or direct referral to a specialized oncology center, without the primary assessment in our service, in advanced cases. Possibly, the low rate of stage IV tumors is due to the fact that patients did not pass through our service. Our microregion has a reference center in oncology, located in another city, that offers surgeries, systemic treatment and radiotherapy, and some patients are referred directly to this center by their cities.

In Brazil, laws define the maximum period of 30 days between the diagnostic hypothesis of BC and the confirmation through exams necessary for elucidation, and of 60 days between diagnosis and the beginning of treatment[34]. In our study, it was found that the mean time between the first visit to the mastologist and the histological diagnosis of BC was 63.2 days, and the mean time between histological diagnosis and the beginning of treatment was 39.6 days. In a recent study conducted by Gioia *et al.* in Rio de Janeiro, Brazil, the mean time to start treatment was 39 days[35]. It can be perceived in our study that the beginning of the treatment is within what is recommended by law; however, as observed in other studies, a delay is identified concerning the time of diagnosis of BC, with reports of the average delay reaching 142.5 days in other Brazilian surveys[36]. We think that our delay in obtaining the diagnosis can be, in part, reduced with the adoption of a patient navigation process.

According to the World Health Organization, there are three main steps to early diagnosis: awareness of the cancer symptoms and getting medical care (access interval); clinical evaluation, diagnosis and staging (diagnostic interval); and transition to treatment (treatment interval)[37]. Strategies focused on reducing delays between the detection of the first sign or symptom and treatment initiation should address the delays in all these steps. Implementing a BC patient navigation program has great potential to alleviate the barriers faced by patients in the public sector, and improve the outcomes of patients with BC in Brazil.

It is important to note that the data found in the present study are limited by their retrospective methodology and the restricted number of participants. However, such data contribute to the discussion about the strategy of mammographic screening in a younger age range in comparison with the current recommendation of the Ministry of Health, considering the significant prevalence of cases in the 40–49-year-old age group, in addition to improving the coverage of mammography screening across the target population. Additionally, it was observed that there is still a delay between the first visit to a specialist and the histological diagnosis of the lesion, suggesting that the diagnostic strategy is not ideal, since a considerable portion of BC cases could have been diagnosed even earlier and faster.

CONCLUSION

This study showed an important number of cases of BC in women who have not reached the age range recommended for the beginning of screening. Although they do not correspond to the majority of cases, they deserve attention because of their significant observance in the total number of women affected in our microregion. There was a high number of diagnoses with palpable tumors, a considerable rate of disease with lymph node involvement and a longer time interval for obtaining the histological diagnosis, contributing to the rates of disease in advanced stages. The need for improvements in the performance of mammographic screening was demonstrated, aiming at early diagnosis, in addition to mechanisms that optimize patient navigation.

AUTHORS' CONTRIBUTION

CFH: Conceptualization, Investigation, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. CMR: Investigation, Methodology, Project Administration, Supervision, Validation, Visualization, Writing – original draft. ACOP: Investigation, Methodology, Validation, Visualization, Data curation. CACS: Data curation, Formal Analysis, Investigation, Validation, Writing – original draft. PHL: Data curation, Investigation, Visualization, Writing – review & editing. AOP: Data curation, Investigation, Visualization, Writing – review & editing. SMCR: Data curation, Investigation, Visualization, Writing – review & editing.

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