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BREAST CANCER IN RIO GRANDE DO NORTE, A RETROSPECTIVE STUDY: EPIDEMIOLOGICAL, CLINICAL AND THERAPEUTIC PROFILE

O câncer de mama no Rio Grande do Norte, um estudo retrospectivo: perfil epidemiológico, clínico e terapêutico

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ABSTRACT

Objective: To analyze the epidemiological, clinical, therapeutic profile of patients with breast cancer assisted at Liga Norte Riograndense Contra o Câncer, in Rio Grande do Norte, between 2011 and 2012. **Method:** This is a descriptive, retrospective, cross-sectional study. Physical records were analyzed to detect sociodemographic, clinical, and therapeutic characteristics of patients. **Results:** 1,176 records related to breast cancer from 2011 and 2012 were assessed. Female gender was predominant, with 99.6% of cases, followed by males, with 0.4% (five cases). The mean age was 55 years, brown ethnicity (63%), married women (51%), with incomplete primary education (27%), living in Natal and Great Natal (57%) with family history in 42% of cases. 64% of patients were coming from the Brazilian Public Health System (SUS). Therapeutic approach comprising surgery, radiotherapy, chemotherapy, and hormone therapy was the most performed (24%), with no evidence of disease after treatment (63%). The level of education did not affect diagnosis in early stages of the disease, and young patients had worse prognosis. **Conclusion:** Determining epidemiological, clinical, and therapeutic profile is a different vision for patients aging less than 40 years, so new breast cancer prevention and screening policies and campaigns are needed for this age group.

KEYWORDS: Epidemiology; breast neoplasms; therapy; diagnosis; medical records.

RESUMO

Objetivo: Analisar o perfil epidemiológico, clínico e terapêutico dos pacientes com neoplasia mamária no Rio Grande do Norte, assistidos na Liga Norte Riograndense Contra o Câncer entre 2011 e 2012. **Métodos:** Trata-se de um estudo transversal retrospectivo descritivo. Realizou-se análise de prontuários físicos para detectar as características sociodemográficas, clínicas e terapêuticas. **Resultados:** Foram analisados 1.176 prontuários com casos de câncer de mama entre 2011 e 2012. Houve predominância do sexo feminino (99,6%), seguido de 0,4% (5 casos) do sexo masculino. A média de idade foi de 55 anos, de etnia parda (63%), mulheres casadas (51%), com ensino fundamental incompleto (27%), residentes em Natal e na Grande Natal (57%), com histórico familiar presente em 42%. Observou-se que 64% eram procedentes do Sistema Único de Saúde (SUS). A conduta terapêutica de cirurgia, radioterapia, quimioterapia e hormonioterapia foi a mais realizada (24%), sem evidência da doença após o tratamento (63%). O grau de escolaridade não interferiu no diagnóstico em estágios iniciais da doença, e pacientes jovens apresentaram pior prognóstico. **Conclusão:** A determinação do perfil epidemiológico, clínico e terapêutico indica uma visão diferenciada para pacientes menores de 40 anos, gerando necessidade de novas políticas e campanhas de prevenção e rastreamento para o câncer de mama nessa faixa etária.

PALAVRAS-CHAVE: Epidemiologia; neoplasias da mama; tratamento; diagnóstico; prontuários.

Study carried out at Hospital Liga Norte Riograndense Contra o Câncer – Natal (RN), Brazil.
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INTRODUCTION

Cancer is a major public health problem in developed and developing countries which accounts for more than 6 million deaths per year and about 12% of all causes of death worldwide[1]. Breast cancer is the second most common type of cancer in the world, Brazil included, the most common among women — following skin cancer —, and the leading cause of death by cancer[2-4]. The distribution of new cases and deaths related to neoplasm have wide regional differences, with higher rates of incidence and mortality in the South and Southeast regions and lower rates in the North and Northeast regions[5]. Lower level of industrialization in the North and Northeast regions as compared to the South and Southeast regions explain that[6].

Breast neoplasms affect mainly women in perimenopause[7]. The main risk factors are related to hormonal and reproductive features, age, gender, and family history. They are not common in young women, constituting 5 to 7% of all cases[8]. Among women who develop the disease before the age of 50, the prognosis is worse, since diagnosis is usually made when the patient is symptomatic and, therefore, has already progressed to a more advanced stage[3,8]. Early diagnosis is related to awareness of the population and health professionals for the signs and symptoms of cancer, thus leading symptomatic people to consultation in health services. Screening means subjecting symptom-free individuals to screening tests to detect cancer or precursor lesions of cancer and to organize referrals for diagnosis confirmation and treatment[5].

The main strategies for controlling this type of cancer are: primary prevention, with identification and correction of avoidable risk factors; secondary prevention, with early detection and treatment; and tertiary prevention, with rehabilitation and palliative care. Secondary prevention strategies are the only ones able to reduce mortality rates and, for this reason, have been given greater attention at national health services[9]. The level of knowledge of patients increases proportionally to their educational level. Breast self-examination is very important for early diagnosis, which highlights the need for informative and educational projects that respect users' limitations as to schooling[6].

The guarantee of access to diagnosis method of mammography as a preventive measure for breast cancer to all women from the age of 40 on is given by Federal Law 11,664/2008. It is the method of choice for screening this condition, since it allows early detection of lesions smaller than or equal to one centimeter, which represents a better therapeutic response and healing capacity[10,11]. Ultrasound has great application in differentiation between cystic and solid tumors. This test brings better results when performed on dense breasts with exuberant glandular tissue, such as the breasts of young women under 35 years of age[12]. Tumor markers are another important test that consists of several substances such as proteins, carbohydrates, lipids, glycoproteins, tumor-specific or associated enzymes when secreted in high concentrations. These markers have contributed greatly with breast cancer predictive diagnosis and prognosis evaluation[13].

Currently, the therapy for breast neoplasm is performed by a multidisciplinary team, aiming at an integral treatment of the patient. Conducts to be instituted are combinations of conservative or radical surgeries, radiotherapy, chemotherapy or hormone therapy. Thus, the costs of this approach are subordinated to the disease staging upon diagnosis, that is, the more advanced the stage, the more expensive and difficult the treatment[14].

The objective of this study was to describe the epidemiological and clinical features of breast neoplasm in Rio Grande do Norte starting from the analysis of data record from the archive of Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

METHODS

This is a cross-sectional, retrospective, descriptive, hospital-based study. The target population was composed of patients diagnosed with breast cancer, whose data were available in the archive of Liga Norte Riograndense Contra o Câncer. Physical records were analyzed to detect sociodemographic features: gender, age, ethnicity (white, black, yellow, brown), schooling, origin (Natal, Grande Natal — Extremoz, Parnamirim, São Gonçalo do Amarante and Macaíba — and countryside), marital status (single, married, widowed, divorced/separated), family history of breast cancer, alcoholism, smoking, origin of referral. Description of clinical and pathological characteristics was based on previous diagnosis and treatment (without diagnosis and without treatment, with diagnosis and without treatment, with diagnosis and with treatment, and other variations); most important basis for diagnosis, most relevant exams (clinical examination, imaging, exploratory surgery, pathological anatomy, and tumor markers); histology (infiltrating ductal carcinoma, infiltrating lobular carcinoma, mucoid carcinoma, ductal carcinoma in situ, and others); laterality (right, left and bilateral); presence of more than one tumor (yes or no); distant metastases and their locations; clinical stage (0, IIA, IIB, IIIA, IIIB, IIIC, IV); types of treatments received (surgery, chemotherapy, radiotherapy, hormone therapy, bone marrow transplantation, immunotherapy, iodine therapy, and others); correlation with educational level and clinical staging, in order to verify the degree of influence of school level in early or late diagnosis; and total number of deaths and identification of

clinical staging upon obit in patients younger than 50 years, to verify the prognosis in young women.

Initially, 1,176 medical records were selected. The inclusion criteria were patients diagnosed with breast cancer and assisted at participating hospital units, in the mastology service of Liga Norte Riograndense Contra o Câncer, from 2011 to 2012. The analysis of medical records consisted of reading to collect sociodemographic and clinical data between January and April 2016. After that, the variables collected were accounted for in Microsoft Excel. Then, tables and graphs were generated to represent the information.

This study is in compliance with the current principles of the National Health Council (CNS/MS) Resolution 466/12, which addresses research involving human beings, and was approved by the Ethics Committee of Hospital Liga Norte Riograndense Contra o Câncer (CEP/LIGA), protocol 1,184,381.

RESULTS

In total, 1,176 medical records of patients with breast cancer diagnosed between 2011 and 2012 in the mastology service of the Liga Norte Riograndense Contra o Câncer were analyzed, with 569 cases in 2011 and 607 cases in 2012. Predominance of the female gender (99.6%) was found, but 0.4% (5 cases) in males was accounted for. Mean age was 55 years, and the prevalent age range was 41 to 59 years. The most prevailing race/ethnic group was brown (63%), and 40% (464 patients) were patients under 50 years of age with advanced staging (IIIA, IIIB, IIIC or IV, VAT). In 40% of these cases, elementary schooling was incomplete (27%), and 57% were residents of Natal and Grande Natal, being 51% married women. Family history was present in 42% of individuals. As to alcohol consumption and smoking, 52% of patients did not consume alcohol, and 43% were not smokers. Also, 64% of cases were referrals from SUS, with diagnosis and treatment being mostly funded by SUS (53 and 71%, respectively), as shown in Table 1.

As to previous diagnosis and treatment, most patients arrived at the hospital without diagnosis or previous treatment (68%). Considering the laterality of the tumor, there was prevalence of left breast (52%). In addition to the data already shown in Table 1, the occurrence of more than one tumor and metastasis was not prevalent, and the most prevalent site of metastasis was bone (48%). Cancer was predominantly diagnosed in clinical stage I and IIA (18% each). Among the most important bases for the diagnosis — such as clinical research, imaging, cytology, tumor markers, metastasis histology, and histology of primary tumor —,100% of the cases had diagnosis confirmed by histology of primary tumor. Clinical examination, imaging, and

Table 1. Sociodemographic features of patients with breast cancer assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

Variables	N	%
Age (years)		
>40	138	12
<40 e >60	625	53
>60	413	35
Gender		
Female	1,172	99.6
Male	5	0.4
Ethnicity/Skin color		
White	333	28.00
Black	90	8.00
Yellow	1	0.08
Brown	735	63
Educational level		
None	107	9.0
Incomplete elementary	313	27.0
Complete elementary	160	14.0
High school	281	24.0
Incomplete higher education	3	0.3
Complete higher education	205	17.0
Marital status		
Married	620	51
Single	305	30
Widowed	166	14
Separated	84	7
Origin		
Natal and Grande Natal	673	57
Rio Grande do Norte countryside	490	42
Other States	13	1
Family history of cancer		
Yes	495	42
No	294	25
Alcohol consumption		
Yes	102	9
No	606	52
Formerly	35	3
Smoking habit		
Yes	117	10
No	505	43
Formerly	198	17
Referred from		
SUS	757	64
Others	419	36
Diagnosis funded by		
SUS	619	53
Health insurance	208	18
Privately	66	6
Treatment funded by		
SUS	839	71.0
Health insurance	272	23.0
Privately	9	0.8

SUS: Brazilian Public Health System; *Differences in values result from lack of information.

exploratory surgery were the most relevant examinations in 100% of cases. Between 2011 and 2012, 160 deaths occurred, 38% (60) of cases in women younger than 50 years. In 88% of cases, the disease stages were III and IV. Mean age of death occurrences was 38 years, the lowest being 17 years, as shown in Table 2.

The histological types of tumors found are described in Table 3, the most frequent being infiltrating ductal carcinoma (81%).

As for types of treatment, the therapeutic approach comprising surgery, radiotherapy, chemotherapy, and hormone therapy was the most common (24%). After the first treatment, 63% of the patients did not show evidence of the disease. When the option was not to perform the treatment, the reasons were advanced staging (1%) and other reasons not clarified (3%), according to Table 4.

Correlation between educational level and clinical staging was also assessed and the results are shown in Figure 1.

DISCUSSION

The present study showed majority of female patients (99.6%), without losing sight of the five cases in male patients (0.4%). According to Nogueira et al.[15], male breast cancer is uncommon, accounting for about 1% of all breast neoplasms, which corresponds to less than 1% of neoplasms occurring in men, therefore being responsible for less than 0.1% of deaths among them. These data corroborate the results of several studies in the literature[6,15-17]. Mean age was 55 years, with a prevalent age range from 41 to 59 years (51%). Of the total, 40% were females aged less than 50 years with worse prognosis. This finding is in line with data reported by the National Cancer Institute (INCA) and scientific literature, both having reported rare incidence and worse prognosis in <35-year-old females, becoming progressive in women up to 50 year old[6,15-18]. Patients were predominantly married (51%). The literature[6] does not describe this data as a risk factor, but it is worth mentioning for a complete social profile assessment.

As to race/ethnicity, brown skin color was predominant (63%), which corroborates findings by Pinheiro et al.[16], according to which black and brown races are related to higher incidence of breast cancer compared to white-skin people. However, the proportion of cases in white people (28%) was higher than that in black people (8%), making the literature controversial at this point. It is worth noting that the Brazilian population is quite mixed, which makes this variable a limiting factor for the study. The most relevant educational level was incomplete elementary school (27%). The literature[16] describes that the lower the educational level, the lower the chances of diagnosis in early stages, which limits

Table 2. Clinical features of breast cancer cases assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

Variables	N	%
Previous diagnosis and treatment		
No previous diagnosis or treatment	798	68
Previous diagnosis without treatment	135	11
Previous diagnosis and treatment	243	21
Laterality		
Left	612	52
Right	545	46
More than one tumor		
Yes	30	3
No	1,146	97
Distant metastasis		
Yes	115	10
No	1,061	90
Metastasis location		
Liver	17	11.0
Bone	75	48.0
Lung	32	20.0
Colorectal	1	0.6
Brain	31	20.0
Pleura	1	0.6
Clinical staging		
0	63	5.00
I	206	18.00
IA	1	0.08
II	2	0.20
IIA	215	18.00
IIB	163	14.00
IIIA	177	15.00
IIIB	122	10.00
IIIC	38	3.00
IV	88	8.00
IVA	1	0.08
Deaths		
Breast cancer	158	99.0
Myocardial infarction	1	0.5
Others	1	0.5
Disease staging upon death of patients aged less than 50 years	60 deaths	
II	7	12
III	31	52
IV	22	36

*Differences in values result from lack of information.

Table 3. Histology of breast cancer patients assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

Histological type	N	%
Infiltrating ductal carcinoma	955	81.00
Leiomyosarcoma	1	0.08
Infiltrating lobular and ductal carcinoma	2	0.20
Apocrine adenocarcinoma	23	2.00
Papillary cystadenocarcinoma	5	0.40
Infiltrating lobular carcinoma	35	3.00
Mucinous carcinoma	24	2.00
Ductal carcinoma *in situ*	92	8.00
Small-cell carcinoma	2	0.20
Unclassified malignant tumor	3	0.30
Mixed infiltrating ductal carcinoma	3	0.30
Infiltrating papillary adenocarcinoma	7	0.60
Neuroendocrine carcinoma	1	0.08
Metaplastic carcinoma	5	0.40
Diffuse large-cell lymphoma	2	0.20
Apocrine metaplastic adenocarcinoma	1	0.08
Fibroadenoma-originated tumor	1	0.08
Malignant epithelial carcinoma of unknown origin	4	0.30
Mammary Paget's disease	2	0.20
Undifferentiated carcinoma	1	0.08
Microinvasive squamous-cell carcinoma	1	0.08
Papillary carcinoma	1	0.08
Medullary carcinoma	1	0.08
Lobular carcinoma *in situ*	3	0.30
Hodgkin's lymphoma	1	0.08
Tubular adenocarcinoma	1	0.08

*Differences in values result from lack of information.

Table 4. Types of treatment received by patients with breast cancer assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

Variable	N	%
Type of treatment		
Radiotherapy and hormone therapy	16	1.00
None	59	5.00
Surgery, radiotherapy, and hormone therapy	37	3.00
Surgery	107	9.00
Radiotherapy	159	13.00
Chemotherapy	48	4.00
Hormone therapy	19	2.00
Surgery, radiotherapy, and chemotherapy	166	14.00
Chemotherapy and hormone therapy	5	0.40
Surgery, radiotherapy, chemotherapy, and hormone therapy	277	24.00
Surgery and radiotherapy	111	9.00
Surgery and chemotherapy	54	5.00
Chemotherapy, hormone therapy and radiotherapy	13	1.00
Surgery, chemotherapy, and hormone therapy	37	3.00
Surgery and hormone therapy	35	2.00
Radiotherapy and chemotherapy	32	1.70
Surgery, chemotherapy, hormone therapy, and iodine therapy	1	0.08
Staging after treatment		
No evidence	740	63
Partial remission	13	1
Stable disease	156	13
Progressing disease	114	10
Non-treatment reasons		
Performed elsewhere	1	0.08
Advanced disease	17	1
Others	33	3

*Differences in values result from lack of information.

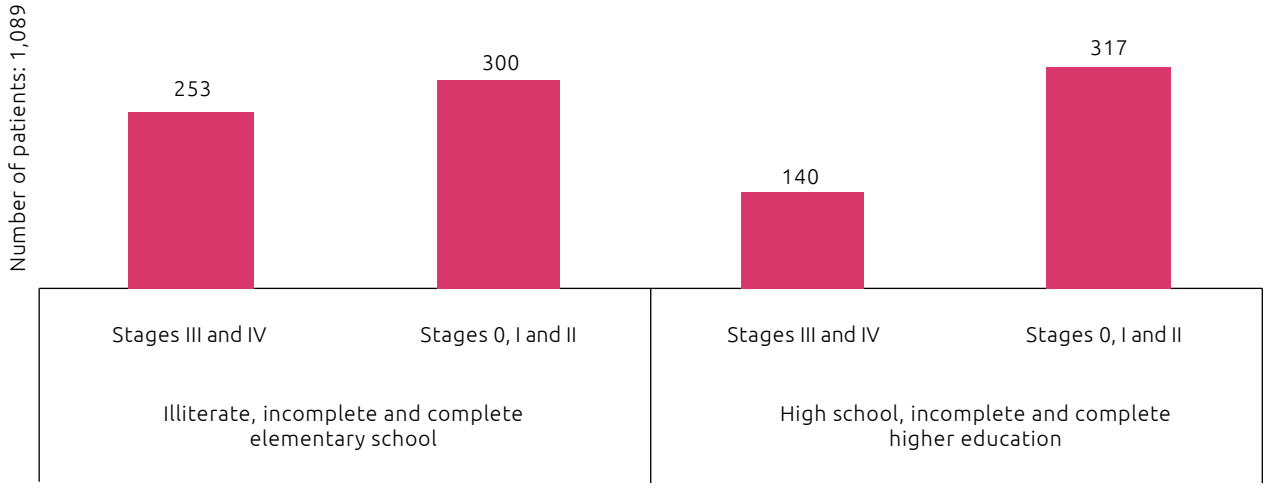

Figure 1. Comparison between educational level and clinical staging in breast cancer patients assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

the implementation of preventive measures. However, in our study, we found a higher proportion of early-stage neoplasia diagnosis in patients with low educational level — 30% of which were diagnosed in initial stages 0, I (including IA) or II (including IIA, IIB) —, and in those with higher schooling level, 31% of which were diagnosed in initial stages 0, I (including IA) or II (including IIA, IIB). These findings differ from those reported in the literature[6,16,19].

Family history is an important risk factor for breast cancer, due to mutations of the BCRA1 and BCRA2 genes, passed on from one generation to the next. Our study showed that 42% of patients had family history of breast cancer, which agrees with findings by Pinheiro et al.[16]. About 52% of patients reported not drinking alcohol. The consumption of alcoholic beverages is an important risk factor for breast cancer development, that is, the greater the consumption, the greater the chance of having it[20]. A total of 43% of patients reported not smoking. Most researchers agree that there is no consistent evidence to determine the influence of smoking habit on breast cancer[20]. Our study found the majority of medical records from Natal and Grande Natal (Extremoz, Parnamirim, São Gonçalo do Amarante, Macaíba) (57%) followed by patients from Rio Grande do Norte countryside (42%), an important finding for demographic characterization.

The number of patients referred by SUS for breast cancer diagnosis and treatment (53 and 71%, respectively) was higher compared to cases referred from private networks or people seeking care by their own (18% for diagnosis and 23% for treatment). In most cases, patients arrived at the hospital undiagnosed or without previous treatment, which is compatible with studies performed by Dugno et al.[6] and Pinheiro et al.[16]. As to tumor characteristics, infiltrating ductal carcinoma was the most frequent histological type, followed by ductal carcinoma *in situ*. Other histological types are less frequent and some are even rare, including mammary Paget's disease, results that agree with those of previous studies[4,16,21,22].

Regarding the laterality of the tumor, left breast was prevalent, which reinforces data described in previous studies[16,21,23]. Analysis data from this study showed that, in most cases, there was not more than one tumor or distant metastasis, finding that meets the scientific literature[4,16]. Bone was the most common location of distant metastasis (48%), a result that also coincides with previous findings. Previous studies have reported that bone, liver, and lung metastases are the most common ones, as observed in this study[24]. Clinical staging is established through the TNM system, which groups the size of the tumor (T), the number of lymph nodes involved (N), and presence or absence of metastases (M). In our study, most females had I, IIA and IIIA staging, which is compatible with data described in the literature[15]. Advanced staging (≥III) was found in younger women and less advanced staging in women aged 50 years or older, results also found by Gnerlich et al.[25].

Histology of primary tumor was the most important basis for diagnosis closure in all cases, a result that agrees with reports from the scientific literature[26]. In most cases, clinical examination, imaging and exploratory surgery were the most relevant search approaches, which is also in agreement with data described by previous studies[16,27].

According to our results, there was predominance of surgery associated with radiotherapy, chemotherapy and hormone therapy, followed by combination of surgery, radiotherapy and chemotherapy, with no evidence of disease after treatment. Results of combination therapy differ from data described in the literature, according to which the most common treatment is surgery plus chemotherapy, as mentioned by Pinheiro et al.[16] and Torres et al.[28]. Such findings corroborate the results obtained by Barros et al.[14]. Reasons for absence of treatment included advanced disease, once the approach in such cases is only palliative, as recommended by INCA[29].

Identification of staging in cases of death, bringing both years together, showed 38% (60 deaths out of 160 cases) of patients younger than 50 years of age with advanced staging, with prevalence of stages III and IV (88%), and therefore with worse prognosis. These results are similar to data from several studies in the literature[1,16,21,30]. The greater vulnerability of young women to diagnosis in advanced stages may be explained by the lack of screening actions and difficulty in reading and interpreting mammographic results due to high breast density[7]. Therefore, higher mortality rate and lower disease-free survival in young women are detected when compared to patients aged above 50 years, who have a better prognosis[12,16].

Conclusion is that determining epidemiological, clinical, and therapeutic profile in the present study constituted a different view for patients younger than 40 years old, causing the need for new breast cancer prevention and screening policies and campaigns that include this age group. In the population studied, most patients were from Natal and Grande Natal, mean age being 55 years, most of them married, with incomplete elementary school, brown ethnicity, non-alcoholic, non-smokers, and with treatment and diagnosis predominantly funded by SUS. Educational level did not influence early diagnosis. Both low-grade and high-grade patients had prevalence of 0, I (including AI) and II (including IIA, IIB) stages at diagnosis. The largest number of cases was in the left breast, there being no prevalence of more than one tumor or distant metastasis. When metastasis was confirmed, the bone type was more

common. In most cases, clinical staging was I, IIA, and IIIA, approached with surgery, radiotherapy, chemotherapy, and hormone therapy, the latter being the most used treatment. After treatment, there was no evidence of recurrence during follow-up in most patients. As to death occurrences, 38% of cases involved patients aged less than 50 years and with worse prognosis.

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