

EPIDEMIOLOGICAL PROFILE OF BREAST CANCER IN A REFERENCE HOSPITAL IN THE NORTH REGION

Perfil epidemiológico do câncer de mama em hospital de referência da Região Norte

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ABSTRACT

Introduction: Breast cancer is a public health issue, not only in underdeveloped countries, as is the case of Brazil, but also in developed ones, such as the United States and some Western European countries. The frequency of distribution of different types of cancer varies according to the characteristics of each region, which emphasizes the need to study geographical variations, risk factors, and disease patterns that pervade regional particularities. **Objective:** The present study describes the epidemiological profile of patients treated at a reference cancer hospital in the North Region of the country and determines the variables of clinical and epidemiological interest related to risk factors for breast cancer. **Methods:** This is a cross-sectional descriptive study conducted through interviews and analysis of medical records of 114 patients treated at Hospital Ophir Loyola between 2016 and 2017 in the city of Belém, Pará. Data were presented as absolute and relative frequencies. **Results:** Most women who participated in the study were multiracial, overweight, with a mean age of 51 years, and had low schooling. A little over half of them were born in the inland of the state; the majority lived in the metropolitan area of Belém, 42% in the inland, and only 11% in the countryside. The mean interval between clinical suspicion and diagnostic confirmation was almost 13 months. The most frequent histopathological classification was invasive ductal carcinoma, and the immunohistochemical profile with the higher incidence was luminal B, followed by luminal A. **Conclusions:** Overweight, considered a risk factor for breast cancer, is modifiable, which underlines the importance of awareness actions for early diagnosis, knowledge of the disease, and encouragement to physical activity and healthy eating habits, in order to reduce morbidity and mortality, and improve the prognosis of women affected by this pathology.

KEYWORDS: Breast cancer; epidemiological profile; risk factors.

RESUMO

Introdução: O câncer de mama é um problema de saúde pública não só em países subdesenvolvidos, como é o caso do Brasil, mas também nos desenvolvidos, como Estados Unidos e alguns países da Europa Ocidental. A frequência de distribuição dos diferentes tipos de câncer é variável em função das características de cada região, o que enfatiza a necessidade do estudo das variações geográficas, dos fatores de risco e dos padrões dessa doença que perpassam pelas particularidades regionais. **Objetivo:** O presente estudo descreve o perfil epidemiológico das pacientes atendidas no hospital de referência em oncologia da região Norte do país e determina as variáveis de interesse clínico e epidemiológico que se relacionam aos fatores de risco na ocorrência do câncer de mama. **Métodos:** O estudo é transversal e descritivo, realizado por meio de entrevista e análise de prontuários clínicos de 114 pacientes atendidas no Hospital Ophir Loyola entre os anos de 2016 e 2017, no município de Belém, no estado do Pará. Os dados foram apresentados em forma de frequências absoluta e relativa. **Resultados:** A maioria das mulheres pesquisadas era parda, com média de idade de 51 anos, encontrava-se acima do peso e apresentava baixa escolaridade. Um pouco mais da metade era natural do interior do estado, e a maioria era procedente da região metropolitana de Belém, 42% delas vinham do interior e apenas 11% residiam em zona rural. A média de tempo entre a suspeita clínica e a confirmação diagnóstica foi de quase 13 meses. A classificação histopatológica de maior frequência foi carcinoma ductal invasivo e o perfil imunohistoquímico de maior ocorrência foi o luminal B, seguido de luminal A. **Conclusões:** O sobrepeso, considerado fator de risco para o câncer de mama, é passível de modificação, o que evidencia a importância de ações de esclarecimento sobre detecção precoce, conhecimento da doença e incentivo à prática de exercício físico e alimentação saudável, a fim de reduzir a morbidade e mortalidade, melhorando o prognóstico das mulheres acometidas por essa patologia.

PALAVRAS-CHAVE: Câncer de mama; perfil epidemiológico; fatores de risco.

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INTRODUCTION

Currently, breast cancer is a public health issue in developed and underdeveloped countries. This situation is the result of difficulties found in the practice of primary care, such as eliminating risk factors or diagnosing and treating cancer precursor lesions¹.

Breast neoplasm is the most frequent type of cancer among women, with a slightly higher number of cases in underdeveloped regions (883 thousand cases) than in more developed ones (794 thousand). It is the fifth cause of death by cancer in the world, despite being the most common in less developed areas and the second in the more developed ones, after lung cancer.

According to the 2018 estimates of the National Cancer Institute José Alencar Gomes da Silva (*Instituto Nacional do Câncer* – INCA)², breast cancer in Brazil might reach 59,700 cases in each year of the biennium 2018-2019, with a risk of approximately 56 cases per 100 thousand women.

In the North Region, breast cancer is the second more incident tumor, with about 19 cases per 100 thousand women. Estimates indicate that the state of Pará could have 740 new cases of breast cancer in 2018, around 21 cases per 100 thousand women; in Belém, this number rises to about 33 cases per 100 thousand women².

The present study aimed to describe the clinical and epidemiological profile of patients treated at a reference cancer hospital in the North Region of the country and correlate it with the profile found in the literature. A better knowledge of physical (weight, height), demographic, age, histological type, and immunohistochemical cancer profile characteristics in the population assessed justifies the research on their epidemiological profile, as this information can aid in creating a priority care plan for women with these profiles affected by breast cancer and improve their prognosis.

METHODS

This is a cross-sectional, retrospective, and descriptive study submitted to and approved by the Committee for Ethics in Scientific Research of the Hospital Ophir Loyola (HOL), conducted in 2016 and 2017 in the city of Belém, Pará, Brazil. It comprised a sample of 114 breast cancer patients monitored by the mastology center of the hospital.

The information was obtained through interviews and analysis of medical records, and data were filled into a questionnaire previously elaborated. The participants signed the Informed Consent Form.

We divided the data collected into two categories: general characteristics (age, origin, ethnicity, weight, height, body mass index (BMI), habits, parity, menarche, menopausal status, date of diagnosis, and start of treatment) and clinical characteristics

(treatment option used – radiotherapy, chemotherapy, or surgery – interval between clinical suspicion and diagnostic confirmation, tumor size, histological grade, and immunohistochemical profile of the lesions).

Data were recorded in Microsoft Office Excel[®] 2010 spreadsheets in order to build a database for descriptive analysis using the distribution of absolute and relative frequencies and subsequent presentation of results in tables and charts.

RESULTS

Regarding general aspects, the mean age of the women under study was 51 years (ranging from 26 to 80 years), and most of them (75%) were overweight (Table 1). Alcohol consumption was more prevalent than smoking (28.07% versus 16.67%), as shown in Table 2.

Most patients did not reach or failed to finish high school – only 40% of them completed this education level; 64.91% were Catholic; 32% were married; and 71.05% were multiracial (Table 3).

Table 1. Clinical characteristics of the patients assessed.

Characteristics	Total	
	n	%
Patients	114	100
Age		
Mean	51	-
Range	26–80	-
Body mass index		
Underweight	0	0
Normal weight	28	24.56
Overweight	49	42.98
Obesity – grade I	25	21.93
Severe obesity – grade II	9	7.89
Morbid obesity – grade III	3	2.63

Table 2. Lifestyle habits: alcohol consumption and tobacco use

Habits	n	%
Alcohol consumption		
Ex-drinker	16	14.03
Yes	32	28.07
No	66	57.89
Tobacco use		
Ex-smoker	14	12.28
Yes (mean of 10 cigarettes/day)	19	16.67
No	81	71.05

With respect to personal history, the mean age at menarche was 13 years; at coitarche, 18 years; and at the start of menopause, 47.3 years. The interviewees reported using contraceptive in 43.86% of cases, and most (87.72%) did not use hormone replacement therapy (HRT). Among the patients with children (102), 99% breastfed, with 85% of them doing so for more than six months. The mean age at their first pregnancy was 21 years, and the average number of children per women was almost 3. Patients with a family history of breast cancer represented 27.19% of cases, with maternal aunts having the highest frequency.

Most patients lived in the metropolitan area of Belém (Marituba, Ananindeua, Castanhal, Benevides, and Belém), 42% in the inland, and only 11% in the countryside.

Concerning disease-related data, the mean interval between clinical suspicion and confirmation of diagnosis by biopsy was almost 13 months, ranging from 17 days to 120 months. The average tumor size was 4.11 cm. The most common histological type was invasive ductal carcinoma (IDC), corresponding to 83.33% of cases (Figure 1).

Table 3. Sociodemographic characteristics of patients.

Characteristics	Total	
	n	%
Patients	114	100
Schooling		
Illiterate	4	3.50
Literate	4	3.50
Incomplete elementary school	27	23.68
Complete elementary school	17	14.91
Incomplete high school	7	6.14
Complete high school	45	39.47
Higher education	10	8.77
Religion		
Catholic	74	64.91
Evangelical	38	33.33
Other	2	1.75
Marital status		
Married	37	32.46
Domestic partnership	12	10.52
Single	39	34.21
Divorced	8	7.02
Widow	18	15.79
Ethnicity		
White	19	16.66
Multiracial	81	71.05
Black	13	11.40
Indigenous	1	0.80

As to immunohistochemistry (IHC), the classification with the highest incidence was luminal B, followed by luminal A (Figure 2).

Most patients (63.16%) underwent chemotherapy, radiotherapy, and surgery. Chemotherapy was administered to 102 women (89.5%) – neoadjuvant had the greatest occurrence, around 55%. The most adopted chemotherapy regimen was doxorubicin + cyclophosphamide + docetaxel (TAC), given to approximately 74% of patients.

Among the participants, 12.28% had metastases, with 71% corresponding to bone metastasis, and only 5 out of the total number of women had locoregional metastasis.

Regarding performance status, 63% of medical records had no related information; followed by 28% reporting ECOG 0; 8%, ECOG 1; and 1%, ECOG 2.

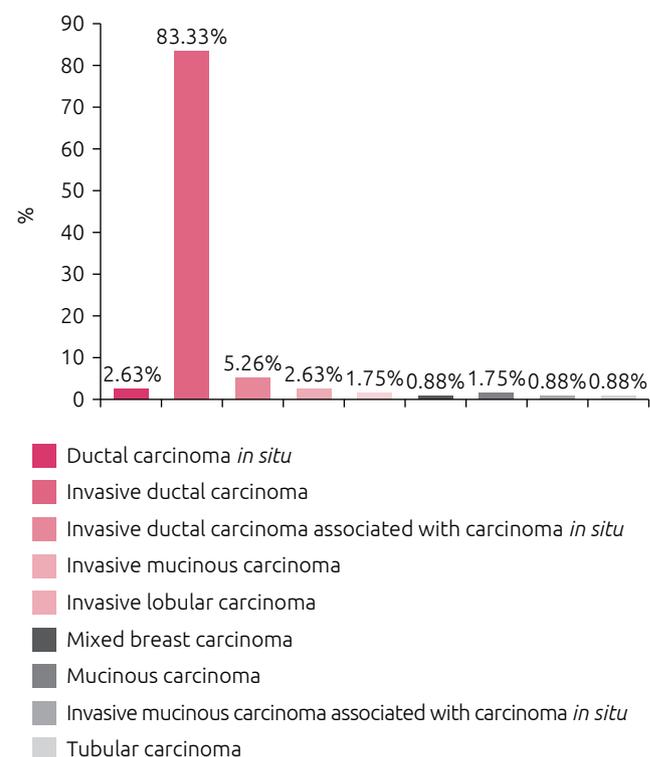


Figure 1. Histopathological classification of the patients' breast cancer.

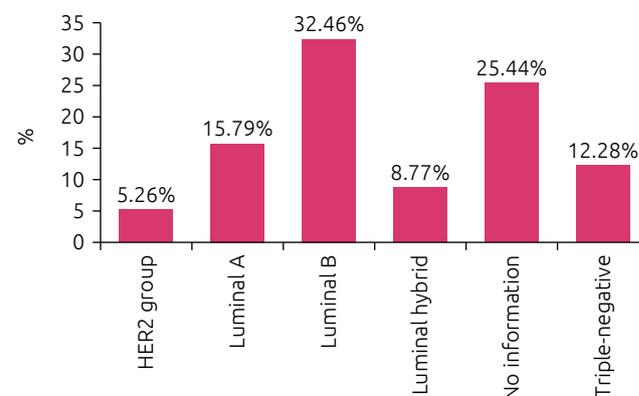


Figure 2. Immunohistochemical classification

DISCUSSION

This study showed that the mean age of women from the state of Pará affected by breast cancer was 51 years, about 75% of them were overweight, most (83.3%) were non-smokers, and 71.93% were non-drinkers. These findings are similar to other studies, such as the one conducted by Matos et al.³ in Maringá, Paraná, in which the mean age of the patients was superior to 50 years, most were non-drinkers, non-smokers, and overweight.

The literature indicates that age is one of the most important risk factors for the development of breast cancer. In consonance with other works, this study inferred that breast cancer is more prevalent around the fourth and fifth decades of life⁴⁻⁶.

The participants who consume alcohol reported drinking only socially (low ingestion of alcoholic beverages), which confirms women's concern for their health, especially as they grow older. These findings are similar to other studies^{3,5}.

The relationship between obesity and breast cancer has been studied for over 30 years. Although not recognized by half of patients⁸, obesity is considered one of the most important risk factors for breast cancer^{6,7} and is associated with an unfavorable prognosis for those affected by the disease⁹. Studies reveal that obesity is an important risk factor for the incidence of breast cancer in post-menopause, and a risk factor for recurrence and morbidity of the disease in pre- and post-menopausal women¹⁰.

According to a work by Neuhouser et al.¹¹ with 67,142 post-menopausal women, aged 50 to 79 years, obesity is associated with increased risk of invasive breast cancer in this population when compared to normal weight, with the risk being higher when the BMI is greater than or equal to 35 kg/m². This study showed that most women were in post-menopause and overweight – only 24.56% had normal weight. This information correlates with other studies described in the literature^{5,6,12}.

Weight is a risk factor modifiable by healthy eating habits and physical activity. Studies show that a diet rich in fruits and vegetables is related to the prevention of breast cancer, as these foods have antioxidant properties and low fat, which reduce the levels of circulating estrogen^{5,13}. Knowing that overweight has a negative impact on patient management, it is important to integrate these women in weight loss programs in the follow-up protocol of breast cancer⁹.

More than 50% of the patients under study did not finish elementary and high school⁸. This information is relevant in terms of the patients' knowledge level of prevention, diagnosis, and the disease itself, as this level increases the higher the education. A work by Lago et al.⁶ revealed that only a small number of the women interviewed – less than 5% – performed breast self-examination.

In studies by Reis et al.¹⁴ and the NCI¹⁵, 71.05% of the interviewees were multiracial, similarly to a research by Sousa et al.¹⁶, held in Tocantins. However, this result contradicts other studies

conducted in Brazil, such as those by Matos et al.³, carried out in the city of Maringá, Paraná, and Jung et al.⁵, performed in the metropolitan area of Porto Alegre, Rio Grande do Sul, in which there was a prevalence of white women among breast cancer patients. Nonetheless, these differences in findings are expected due to the wide miscegenation that resulted from the colonization process in Brazil¹⁶.

Concerning gynecological history, the mean age at menarche was 13 years – ranging from 10 to 17 years, similarly to the studies by Matos et al.³ and Jung et al.⁵. Women who had their first menstrual period before the age of 12 years have an increased risk of developing breast cancer¹⁵.

Late menopause – over the age of 55 years – is also associated with a higher risk of disease due to the prolonged period of estrogen and progesterone stimulation in the breasts^{3,15}. This study found that 63.15% of patients were menopausal, and 36.85% were premenopausal. The mean age of onset of menopause was 47 years, equivalent to the study by Matos et al.³.

Among the interviewees, 43.86% used oral contraceptives (OCs) with an average use time of 6.8 years. A work by Jung et al.⁵, which aimed to identify risk factors associated with breast cancer in Porto Alegre, Rio Grande do Sul, showed that 60% of women who participated in the study did not use this contraceptive, a result comparable to the present study.

The literature is divergent regarding the relationship between the use of OCs and the risk of breast cancer, mainly due to the emergence of contraceptives with low hormone doses. On the other hand, when the use is associated with other factors, such as smoking and obesity, the potential for developing the disease increases^{3,5}.

This work showed that 87.72% of the women involved did not use HRT. Out of the patients who used HRT, most did not know which hormone they used, evidencing the low schooling observed in this study. Estrogen is one of the most used hormones for this purpose and is related to breast tissue stimulation for the development of cancer^{3,17,18}.

Lactation is considered a protective factor for breast cancer¹⁹. This study revealed that among patients with children (102), only one reported not having breastfed. Thus, 99.02% of them breastfed, of which 85% did so for more than six months. This result is similar to other studies performed in different regions of Brazil due to ethnic-cultural factors^{3,5} and not knowledge related to reducing the risk of breast cancer, which can be corroborated by the findings of a work by Batiston et al.⁸.

The mean age at first pregnancy was 21 years, ranging from 13 to 35 years, equivalent to other studies conducted in Brazil^{3,5}. When the first pregnancy happens at early reproductive age, it becomes a protective factor against changes in breast cells, since late pregnancy and nulliparity make women more vulnerable to cancer, as they have a number of lobules with a higher amount of undifferentiated cells^{5,20}.

Among the population studied, 27.19% reported a history of breast cancer in the family in the following decreasing order of frequency: maternal aunt, maternal and paternal cousins, and sister, with a mean age around 45 years. This result shows that the incidence in first-degree relatives (mother and siblings) was low in this study but consistent with other works, such as those by Matos et al.³ and Jung et al.⁵, which also found a small percentage in first-degree relatives. About nine out of every ten cases of breast cancer occur in women with no family history²¹.

A study by Reis et al.¹⁴, carried out in Bahia with 32 women diagnosed with breast cancer, showed a low prevalence of metastasis, similarly to this study, which found around 12.28% of metastasis, with the bone as the most affected organ (71.42%), followed by lung (35.72%), liver (14.29%), and brain (7.1%), and locoregional recurrence (breast and chest wall) in 3.85% of cases. In consonance with Peres et al.²⁰, the data obtained could be the result of considering only a period no longer than two years after diagnosis.

This study showed that IDC was the most frequent type – 83.33% of cases – followed by IDC associated with ductal carcinoma *in situ* (DCIS) – 5.26% –, and DCIS – 2.63%. Comparing these results with the study by Raffo et al.²², we found similar data related to frequency, since, in their work, IDC was the most common type, followed by the mixed one. The difference between the two studies was that, in the first, DCIS held the third position, and in the second, this position belonged to mucinous carcinoma, with 11.5%.

Such data are in accordance with INCA, which declares that 80 to 90% of the total number of breast neoplasm cases correspond to IDC. Other studies performed in Brazil also showed a predominance of the histological type IDC, which presented a rate of 83.9% among women.

In this study, the luminal B type (32.46%) was more prevalent than luminal A (15.79%), followed by triple-negative (12.28%). Corroborating the findings of Cintra et al.²³, luminal B, HER2 negative (41.8%) had the highest frequencies. On the other hand, the study above identified triple-negative (24.2%) as the second most frequent type, followed by luminal A (17.1%), thus, differing from the present research.

A study by Peruzzi and Andrade²⁴ indicated that, among the cases analyzed, the luminal B molecular subtype was the most common, corresponding to 43.6% of cases, followed by luminal A, with 23.4%.

A Brazilian multicenter study by Carvalho et al.²⁵ analyzed profile distribution in the five regions of Brazil, resulting in prevalence variation for each subtype: first, luminal B, ranging from 30.8 to 39.5%; followed by luminal A, from 24.1 to 30.8%; and triple-negative, from 14.0 to 20.3%.

According to Barreto-Neto et al.²⁶, such results contradict international studies, which declare that the luminal A subtype is the most prevalent among all molecular types, corresponding to almost 60% of cases. Luminal B varies from 10 to 20% of cases, and triple-negative presents the same proportion.

The interval between diagnosis and start of treatment is essential for the good prognosis of the disease. In this study, the mean time between clinical suspicion and diagnosis was 12.56 months. A study by Barros et al.²⁷ showed that the mean time for women to start treatment after symptom onset was approximately seven months in the Federal District.

Concerning treatment, the 2018 Diagnostic and Therapeutic Guidelines for Breast Carcinoma include primary tumor surgery, radiotherapy, chemotherapy (neoadjuvant and adjuvant), and hormone therapy. The therapeutic modalities combined can be curative or palliative, and all of them in isolation can have a palliative purpose.

In this study, 63.16% of patients underwent a treatment that combined chemotherapy, radiotherapy, and surgery; chemotherapy was administered to 89.5% of them, with neoadjuvant having the highest occurrence, around 55% of cases. In comparison with the study by Haddad, Carvalho, and Novaes²⁸, 24.2% of women received neoadjuvant treatment.

As to the therapeutic regimen used, the same decree indicates that four cycles of AC associated with taxane are more beneficial, representing an additional reduction in mortality of 15 to 20%. The most adopted chemotherapy regimen in the present study was also TAC, administered to approximately 74% of patients. Another regimen used was four cycles of docetaxel associated with cyclophosphamide (TC) – 9% of patients received this regimen, demonstrating that the protocol adopted in the region agrees with the recommendation of the Ministry of Health.

CONCLUSIONS

In this study, most women were multiracial, lived in the metropolitan area of Belém, and their mean age was 51 years. The majority reported not consuming alcohol and/or cigarettes and were overweight; the mean age at menopause was 47 years, and menarche, 13 years. A large part did not use OCs or HRT. Only 11% of the women did not have children, and the period of breastfeeding among those who had was over six months. The degree of kinship most affected by cancer was paternal and maternal aunts, and bone metastasis had the highest incidence. The most common histological type was IDC, and the IHC with greater prevalence was luminal B.

This study identified age and overweight as risk factors for breast cancer. Thus, actions for early detection of cancer must be an integral part of health care, including clinical breast examination, quick access to mammography, and guidance for a lifestyle with healthy habits and weight control.

We consider alarming the delay in diagnosis and treatment. The mean time of 13 months to start the actual therapy is unacceptable. The implementation of secondary prevention programs that can perform mammographies and biopsies more promptly is urgent in this state.

REFERENCES

1. Gebrim LH, Quadros LGA. Rastreamento do câncer de mama no Brasil. *Rev Bras Ginecol Obstet*. 2006;28(6). <http://dx.doi.org/10.1590/S0100-72032006000600001>
2. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Diretrizes Diagnósticas e Terapêuticas do Carcinoma de Mama. Portaria conjunta nº 4 [Internet]. Brasil: Ministério da Saúde; 2018 [acessado em 28 mar. 2018]. Disponível em: <http://portal.arquivos2.saude.gov.br/images/pdf/2018/fevereiro/07/PORTARIA-no-04-PCDT.carcinoma.mama.2018.pdf>
3. Matos JC, Pelloso SM, Carvalho MDB. Prevalência de fatores de risco para o câncer de mama no município de Maringá, Paraná. *Rev Latino-Am Enfermagem* [Internet]. 2010 [acessado em 20 mar. 2018];18(3). Disponível em: <http://rlae.eerp.usp.br/DOI:http://dx.doi.org/10.1590/S0104-11692010000300009>
4. Pinho VFS, Coutinho ESF. Variáveis associadas ao câncer de mama em usuárias de unidades básicas de saúde. *Cad Saúde Pública* [Internet]. 2007 [20 mar. 2018];23(5):1061-69. Disponível em: http://www.scielo.br/scielo.php?pid=s0102-311x2007000500008&script=sci_abstract&tlng=pt <http://dx.doi.org/10.1590/S0102-311X2007000500008>
5. Jung W, Kieling EF, Kunzler IM, Lazzari DD, Nascimento ERP, Alves DLF. Fatores de risco para câncer de mama no setor calçadista. *Rev Baiana Enfermagem* [Internet]. 2014 [acessado em 20 mar. 2018];28(2):145-55. Disponível em: <https://portalseer.ufba.br/index.php/enfermagem/article/view/10083/8866>
6. Lloga TG, Iglesia YF, Garbey MN, Bornot YI, Ordúñez DF. Incidência de câncer de mama en mujeres de la provincia Guantánamo en el período 2015-2016. *Rev Inf Científica* [Internet]. 2017 [acessado em 20 mar. 2018];96(5):866-74. Disponível em: <http://www.medigraphic.com/pdfs/revinficie/ric-2017/ric175h.pdf>
7. Brasil. Ministério da Saúde. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa | 2016 Incidência de Câncer no Brasil [Internet]. Rio de Janeiro: Instituto Nacional de Câncer José Alencar Gomes da Silva; 2015 [acessado em 20 mar. 2018]. Disponível em: http://www.inca.gov.br/bvscontrolecancer/publicacoes/edicao/Estimativa_2016.pdf
8. Batiston AP, Tamaki EM, Souza LA, Santos MLM. Conhecimento e prática sobre os fatores de risco para o câncer de mama entre mulheres de 40 a 69 anos. *Rev Bras Saúde Matern Infant* [Internet]. 2011 [acessado em 20 mar. 2018];11(2):163-71. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1519-38292011000200007. <http://dx.doi.org/10.1590/S1519-38292011000200007>
9. Papa AM, Pirfo CBL, Murad AM, Ribeiro GMQ, Fagundes TC. Impacto da obesidade no prognóstico do câncer de mama. *Rev Bras Oncol Clin* [Internet]. 2013 [acessado em 21 mar. 2018];9(31):25-30. Disponível em <https://www.sbec.org.br/sbec-site/revista-sbec/pdfs/31/artigo3.pdf>
10. Picon-Ruiz M, Morata-Tarifa C, Valle-Goffin JJ, Friedman ER, Slingerland JM. Obesity and adverse breast cancer risk and outcome: mechanistic insights and strategies for intervention. *CA Cancer J Clin* [Internet]. 2017 [acessado em 21 mar. 2018];67(5):378-97. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5591063/>. <http://doi.org/10.3322/caac.21405>
11. Neuhauser ML, Aragaki AK, Prentice RL, Manson JE, Chiebowksi R, Carty CL, et al. Overweight, Obesity and Postmenopausal Invasive Breast Cancer Risk. *JAMA Oncol* [Internet]. 2015 [acessado em 21 mar. 2018];1(5):611-21. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5070941>. <https://dx.doi.org/10.1001%2Fjamaoncol.2015.1546>
12. Daling JR, Malone KE, Doody DR, Johnson LG, Gralow JR, Porter PL. Relation of body mass index to tumor markers and survival among young women with invasive ductal breast carcinoma. *Cancer* [Internet]. 2001 [acessado em 21 mar. 2018];92(4):720-9. Disponível em: <https://www.ncbi.nlm.nih.gov/pubmed/11550140>
13. Sedó KS, Lima CA, Carneiro PCPD, Albuquerque LS, Araújo CO, Castro AS, et al. Conhecimento nutricional de mulheres com câncer de mama e sua relação com o estado nutricional. *Rev Bras Promoç Saúde* [Internet]. 2013 [acessado em 21 mar. 2018];26(1):71-8. Disponível em: http://periodicos.unifor.br/RBPS/article/view/2626/pdf_1
14. Reis FP, Santos MEG, Sena WR, Santana R, Freitas TS, Silveira HF, et al. Perfil epidemiológico das pacientes com câncer de mama atendidas em uma unidade de saúde em São Francisco do Conde, Ba. *Rev Ciências Médicas Biológicas* [Internet]. 2016 [acessado em 21 mar. 2018];15(2):144-50. Disponível em: <https://portalseer.ufba.br/index.php/cmbio/article/view/1519>. <http://dx.doi.org/10.9771/cmbio.v15i2.15194>
15. National Cancer Institute. Breast Cancer Risk in American Women [Internet]. Bethesda: National Cancer Institute; 2012 [acessado em 23 mar. 2018]. Disponível em: <https://www.cancer.gov/types/breast/risk-fact-sheet>
16. Sousa MM, Figueredo SB, Fernandes RM. Perfil clínico-epidemiológico de mulheres com neoplasia de mama atendidas no hospital regional de referência no município de Araguaína-TO no período de 2000 a 2015. *Rev Interdisciplinar da Universidade Federal do Tocantins* [Internet]. 2016 [acessado 23 mar. 2018];2(2):283-306. Disponível em: <https://sistemas.uft.edu.br/periodicos/index.php/desafios/article/view/2124/8738>. <http://dx.doi.org/10.20873/uft.2359-3652.2016v2n2p283>
17. Russo J, Russo IH. Toward a physiological approach to breast cancer prevention. *Cancer Epidemiol Biomarkers Prev* [Internet]. 1994 [acessado em 27 mar. 2018];3(4):353-64. Disponível em: <https://www.ncbi.nlm.nih.gov/pubmed/8061586>
18. Ursin G, Bernstein L, Lord SJ, Karim R, Deapen D, Press MF, et al. Reproductive Factors and Subtypes of Breast Cancer Defined by Hormone Receptor and Histology. *Brit J Cancer* [Internet]. 2005 [acessado em 27 mar. 2018];93(3):364-71. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2361558>. <https://dx.doi.org/10.1038%2Fsj.bjc.6602712>
19. Dugno MLG, Soldatelli JS, Daltoé T, Rosado JO, Spada P, Formolo F. Perfil do câncer de mama e relação entre fatores de risco e estadiamento clínico em hospital do Sul do Brasil. *Rev Bras Oncol Clin* [Internet]. 2013 [acessado em 27 mar. 2018];60-6. Disponível em: <https://www.sbec.org.br/sbec-site/revista-sbec/pdfs/36/artigo3.pdf>
20. Peres VC, Veloso DLC, Xavier RM, Salge AKM, Guimarães JV. Câncer de mama em mulheres: recidiva e sobrevida em cinco anos. *Texto Contexto Enferm* [Internet]. 2015 [acessado em 28 mar. 2018];24(3):740-47. Disponível em: http://www.scielo.br/pdf/tce/v24n3/pt_0104-0707-tce-24-03-00740.pdf. <http://dx.doi.org/10.1590/0104-07072015000600014>

21. Martins LCM, Rezende RMD, Cordeiro JABL, Paula HSC, Bastos DR, Vilanova-Costa CAST, et al. Padrão de metástase no câncer de mama triplo negativo. *Rev Bras Mastologia* [Internet]. 2017 [acessado em 21 mar. 2018];27(1):8-14. Disponível em: https://www.researchgate.net/profile/Cesar_Vilanova-Costa2/publication/312600397_Metastatic_pattern_of_triple_negative_breast_cancer/links/5885fc03aca272b7b44ca4ab/Metastatic-pattern-of-triple-negative-breast-cancer.pdf. <http://dx.doi.org/10.5327/Z201700010003RBM>
22. Raffo CC, Hubie DP, Zanini GL, Abdul-Hak LP, Botogoski SR. Perfil histológico e imuno-histoquímico das pacientes com câncer de mama operadas no Hospital Santa Casa de Curitiba no período de 2014 e 2015. *Arq Med Hosp Fac Cienc Med Santa Casa São Paulo* [Internet]. 2017 [acessado em 20 mar. 2018]. Disponível em: http://www.fcmscsp.edu.br/images/Arquivos_medicos/Prelo/2017/AO-120_perfil_histologico_imuno_histoquimico_pacientes%20cancer_mama_operadas_hospital.pdf
23. Cintra JRD, Teixeira MTB, Diniz RW, Gonçalves Junior H, Florentino TM, Freitas GF, et al. Perfil imuno-histoquímico e variáveis clínico patológicas no câncer de mama. *Rev Assoc Med Bras* [Internet]. 2012 [acessado em 27 mar. 2018];58(2):178-87. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-42302012000200013&lng=en&nrm=iso. <http://dx.doi.org/10.1590/S0104-42302012000200013>
24. Peruzzi CP, Andrade VRM. Análise dos marcadores imuno-histoquímicos associados com câncer de mama em mulheres na Região das Missões, Rio Grande do Sul, Brasil. *Rev Bras Mastologia* [Internet]. 2016 [acessado em 27 mar. 2018];26(4):181-5. Disponível em: https://www.researchgate.net/publication/311244667_Analise_dos_marcadores_imuno-histoquimicos_associados_com_cancer_de_mama_em_mulheres_na_Regiao_das_Missoes_Rio_Grande_do_Sul_Brasil. <http://dx.doi.org/10.5327/Z201600040008RBM>
25. Carvalho FM, Bacchi LM, Pincerato KM, Rijn MV, Bacchi CE. Geographic differences in the distribution of molecular subtypes of breast cancer in Brazil. *BMC Women's Health* [Internet]. 2014 [acessado em 27 mar. 2018];14:102. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4153008/>. <https://dx.doi.org/10.1186%2F1472-6874-14-102>
26. Barreto-Neto NJS, Pinheiro AB, Oliveira JF, Crusoé NSDR, Bertrand SAB, Machado MCM, et al. Perfil epidemiológico dos subtipos moleculares de carcinoma ductal da mama em população de pacientes em Salvador, Bahia. *Rev Bras Mastologia* [Internet]. 2014 [acessado em 27 mar. 2018];24(4):98-102. Disponível em: <http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&src=google&base=LILACS&lang=p&nextAction=lnk&exprSearch=782263&indexSearch=ID>. <https://dx.doi.org/10.5327/Z201400040002RBM>
27. BARROS, A. F., UEMURA, G., MACEDO, J.L.S. Tempo para acesso ao tratamento do câncer de mama no Distrito Federal, Brasil Central. *Rev Bras Ginecol Obstet* [Internet]. 2013 [acessado em 27 mar. 2018];35(10):458-63. Disponível em <<http://www.scielo.br/pdf/rbgo/v35n10/06.pdf>>.
28. Haddad NC, Carvalho ACA, Novaes CO. Perfil sociodemográfico e de saúde de mulheres submetidas à cirurgia para câncer de mama. *Rev Hosp Univers Pedro Ernesto* [Internet]. 2015 [acessado em 28 mar. 2018];14(Supl. 1):28-35. Disponível em: http://revista.hupe.uerj.br/detalhe_artigo.asp?id=534. <https://dx.doi.org/10.12957/rhupe.2015.17923>