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Nutritional status and cardiovascular risk in women with breast cancer

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ABSTRACT

Objective: To evaluate the nutritional status and the cardiovascular risk in women with breast cancer and identify factors associated with excessive body weight. **Methods:** A descriptive, cross-sectional, quantitative study was carried out in an oncology outpatient clinic and, gynecology/oncology wards at the Hospital das Clínicas da Universidade Federal de Pernambuco, from March to August 2019. The data analyzed was related to sociodemographic, gynecologic, clinic, anthropometric and lifestyle factors. Nutritional status was assessed using Body Mass Index, considering excessive body weight when > 25 kg/m^2 for adults and > 27 kg/m^2 for elderly. Obesity was considered > 30 kg/m^2. Cardiovascular risk was defined by waist circumference (≥ 80 cm), neck circumference (≥ 34 cm) and waist-to-height ratio (> 0.5). **Results:** A total of 46 patients were included, with a mean age of 51.9 years, and the majority in outpatient follow-up. The population was mostly Caucasian women, who were married or in a civil union, who had had at least one pregnancy, were in menopause, and were sedentary. High frequencies of excessive body weight (76.1%) and obesity (43.5%) were observed, and anthropometric parameters revealed an elevated frequency of cardiovascular risk in this population, waist circumference (97.8%), neck circumference (84.8%), and waist-to-height ratio (95.7%). Unemployment ($p = 0.020$), and waist ($p = 0.001$) and neck ($p = 0.001$) circumferences were statistically associated factors to excessive body weight. **Conclusions:** The anthropometric profile of women with breast cancer indicated excess body weight and elevated cardiovascular risk, which suggests to the need for nutrition intervention and follow-up after the diagnosis.

KEYWORDS: breast neoplasms; nutritional status; obesity; lifestyle; cardiovascular diseases.

INTRODUCTION

Breast cancer originates from the uncontrolled and disordered growth of abnormal cells. There is a high incidence among females, with estimates that exceed two million new cases diagnosed in 2018 worldwide, and 66,280 new cases for the year 2020, in Brazil. Not considering non-melanoma skin tumors, breast cancer is the most common type of cancer in the Northeast Region of Brazil. It is estimated that, for every 100 thousand women, 47.86 new cases have been diagnosed in the state of Pernambuco in 2020. In Recife, this incidence rises to 61.44 new cases per 100 thousand women. It is also the major cause of cancer mortality in this population[1,2].

A large proportion of cancer cases in the world are related to exposure to environmental and behavioral risk factors throughout life. In the case of breast cancer, there are several factors related to increased risk, such as: reproductive factors (early menarche, nulliparity, menopause after 55 years, age at first pregnancy over 30 years old), alcoholism, physical inactivity, excess body weight, among others[3,4].

With the growing global obesity epidemic, an increase in the number of cancer cases related to excess weight has been observed concomitantly. In Brazil, 3.8% of cancer cases diagnosed in 2012 were related to a high body mass index (BMI), with a higher incidence in women (5.2%). Furthermore, breast cancer was most related to being overweight[5].

World-class evidence indicates that both high BMI throughout life and weight gain during menopause are risk factors for the development of post-menopausal breast cancer[6]. Excess weight has been associated not only with the development of the disease, but also with a worse prognosis, higher mortality, recurrences, larger tumors and clinical complications such as lymphedema, peripheral neuropathies, chemotherapy-related cardiotoxicity, chronic fatigue and worsening quality of life. After diagnosis, about half of this population tends to gain weight, especially those undergoing chemotherapy[7].

Cardiovascular disease (CVD) is an important cause of morbidity and mortality in breast cancer, and its development may

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be related or aggravated by antineoplastic treatment[8]. In the nutritional assessment, some anthropometric parameters can show the increased risk of developing CVD. Waist circumference (WC) is a measure used to identify this risk, as it reflects the individual's body composition, mainly showing visceral fat[9]. The 2016 Brazilian Obesity Guidelines portray the superiority of the WC compared to hip circumference and waist-to-hip ratio. However, they say that the waist-height ratio (WHR) is the best parameter when compared to WC and BMI, as it is a predictor of increased mortality[10]. Another recommended measure is neck circumference (NC), which is associated with adiposity, central obesity and other cardiovascular risk factors, such as arterial hypertension, dyslipidemia and insulin resistance[11,12].

Considering this, the objective of this study was to assess the nutritional status and cardiovascular risk in women with breast cancer, identifying factors associated with being overweight.

METHODS

This was a cross-sectional analytical observational study of a quantitative nature, which involved women with breast cancer, and was carried out from March to August 2019. It was carried out in the oncology and gynecology wards and the oncology outpatient clinic of the Hospital das Clínicas of the Universidade Federal de Pernambuco (HC/UFPE). The research was carried out in accordance with resolutions 466/2012 and 510/2016, of the National Health Council, having been approved by the Research Ethics Committee Involving Human Beings of HC/UFPE, under Certificate of Presentation for Ethical Appreciation (*Certificado de Apresentação para Apreciação Ética* - CAAE) number 06498919.4.0000.8807.

The sample was non-probabilistic, selected for convenience, and included women with a diagnosis of breast cancer established by histopathological examination, aged ≥ 19 years old. Those who were unable to answer the survey questionnaire and/or who had physical restrictions limiting the collection of anthropometric data were excluded.

The studied variables were comprised of sociodemographic data, such as age group, skin color (self-reported), marital status, education, origin, occupation, family income, number of people per household and access to basic sanitation; gynecological variables, such as age at menarche, history of breastfeeding, duration of breastfeeding, use of oral contraceptives and menopause; obstetric variables, such as number of pregnancies, parity, number of miscarriages, age at first pregnancy.

Nutritional status was assessed using BMI, while cardiometabolic risk was identified using WC, NC and waist-height ratio. To measure weight, an electronic scale with a capacity of 150 kg was used. For height, a stadiometer coupled to the scale was used to aid measurement. BMI was classified according to the World Health Organization (WHO) cutoff points[9] for adults, and according to Lipschitz[13] for elderly patients (> 60 years).

WC and NC were measured with the aid of a non-extensible measuring tape. The first was measured at the midpoint between the iliac crest and the outer face of the last rib. The second was measured with the tape measure positioned at the midpoint of the cervical spine to the middle-anterior part of the neck. For classification of WC, the values recommended by the WHO[9] were adopted. Those considered high risk were those with WC ≥ 80 cm, and very high risk were those with WC ≥ 88 cm. In the NC classification, the value ≥ 34 cm was considered as metabolic risk[14]. The WHR was obtained by dividing the waist (cm) by height (cm), and the values were at risk when above 0.5[10].

Clinical variables were collected from medical records. The time of diagnosis, age at diagnosis, presence of metastasis, treatment and relapse were investigated. As for lifestyle, the practice of physical activity, smoking and alcohol use were evaluated. In assessing the practice of physical activity, women who practiced physical exercise for at least 30 min/day five to seven days a week on a continuous or accumulated basis, were considered active and those considered inactive did not regularly practice physical activity[15]. Regarding alcohol consumption, women who drank alcoholic beverages above a dose (14g of ethanol) per day[15] were classified as alcoholics. Smokers were those who consumed one or more cigarettes a day[16].

The data were analyzed descriptively by means of absolute and percentage frequencies for categorical variables, and average, standard deviation and median for numerical variables. To assess the difference between the percentages relative to the categories of a variable, Pearson's χ^2 test was used for equality of proportions in a sample. In the numerical variables, the confidence intervals for the average were obtained and, to assess the association between two categorical variables, Pearson's χ^2 test or Fisher's Exact test was used when the condition for using the χ^2 test was not verified. The margin of error used in deciding the statistical tests was 5% and the intervals were obtained with 95% confidence. The data were entered into an Excel spreadsheet and the program used to obtain the statistical calculations was the Statistical Package for the Social Sciences (SPSS), version 23.

RESULTS

The sample consisted of 46 patients, 73.9% from the oncology outpatient clinic and the others were hospitalized. The mean age was 51.9 ± 10.91 years, with the adult age group prevailing. The other sociodemographic characteristics are described in Table 1.

Tables 2 and 3 show the gynecological and obstetric data of the population, in which the most common were: menarche was above 12 years old, no pregnancies older than 30 years old, parity ≥ 2, breastfeeding and currently menopausal.

Regarding anthropometric data (Table 4), the average BMI was 29.12 ± 5.53 kg/m^2, showing excess weight, while obesity, with a BMI ≥ 30 kg/m^2, was present in 43.5% of women. Regarding WC, the average was 99.16 cm (± 11.94), while 97.8% had measurements ≥ 80 cm, of which 84.4% had WC ≥ 88 cm, indicating a high frequency of abdominal obesity, with very high cardiovascular risk. The NC showed an average of 37.14± 3.14 cm, with a predominant metabolic risk classification. Table 5 shows the association between BMI and sociodemographic, gynecological and

Table 1. Sociodemographic characteristics of breast cancer patients. Hospital das Clínicas, Universidade Federal de Pernambuco. Recife, PE, Brazil, 2019.

Variable	n	%	p
Age group			
Elderly	15	32.6	p* = 0.018 **
Adults	31	67.4	
Race			
Caucasians	24	52.2	p* = 0.768
Non- Caucasians	22	47.8	
Marital status			
Married/Common-law married	25	54.3	p* = 0.555
Single/Divorced/Widowed	21	45.7	
Education level			
<9 years	21	45.7	p* = 0.555
≥ 9 years	25	54.3	
Place of birth			
Inhabitant of the Metropolitan Region of Recife	25	54.3	p* = 0.555
Inhabitant of other regions	21	45.7	
Occupation			
Part of the labor market	14	30.4	p* = 0.008**
Unemployed	32	69.6	
Family income (MW)			
Less than 1	5	10.9	p* < 0.001**
1 to 2	31	67.4	
More than 2	10	21.7	
People per household			
Up to 2	19	41.3	p* = 0.238
3 or more	27	58.7	
Basic sanitation			
Yes	37	80.4	p* < 0.001**
No	9	19.6	

*Significant difference at 5%; **using the χ^2 test to compare proportions in a sample; MW: minimum wage of R $998.00 (2019.1).

Table 2. Gynecological characteristics of breast cancer patients. Hospital das Clínicas, Universidade Federal de Pernambuco. Recife, PE, Brazil, 2019.

Variable	n	%	p
Age at menarche			
Up to 12 years old	16	34.8	p* < 0.001**
Older than 12 years old	30	65.2	
Breastfeeding history			
Yes	33	71.7	p* = 0.003**
No	13	28.3	
Breastfeeding time (months)			
< 6	11	23.9	p* = 0.913
6 to 12	12	26.1	
> 12	10	21.7	
Not applicable (did not breastfeed/was not pregnant)	13	28.3	
Use of oral contraceptives			
Yes	24	52.2	p* = 0.768
No	22	47.8	
Menopause			
Yes	35	76.1	p* < 0.001**
No	11	23.9	

*Significant difference at 5%; **using the χ^2 test to compare proportions in a sample.

Table 3. Obstetric characteristics of breast cancer patients. Hospital das Clínicas, Universidade Federal de Pernambuco. Recife, PE, Brazil, 2019.

Variable	n	%	p
Number of pregnancies			
0	3	6.5	p* = 0.043**
1	7	15.2	
2	14	30.4	
3	14	30.4	
4 or more	8	17.4	
Parity			
0	4	8.7	p* = 0.035**
1	10	21.7	
2	16	34.8	
3 or more	16	34.8	
Miscarriages			
0	32	69.6	p* = 0.008**
1 or more	14	30.4	
Age at first pregnancy			
12 to 19	13	28.3	p* = 0.850
20 to 24	16	34.8	
25 to 29	14	30.4	
No pregnancies	3	6.5	

*Significant difference at 5%; ** using the χ^2 test to compare proportions in a sample.

Table 4. Anthropometric characteristics of breast cancer patients. Hospital das Clínicas of the Universidade Federal de Pernambuco. Recife, PE, Brazil, 2019.

Variable	n	%	p
BMI			
Malnourished	3	6.5	p* < 0.001**
Eutrophic	8	17.4	
Overweight	35	76.1	
WC			
No risk (<80 cm)	1	2.2	p* < 0.001**
High risk (≥ 80 cm)	7	15.2	
Very high risk (≥ 88 cm)	38	82.6	
NC			
No risk	7	15.2	p* < 0.001**
Metabolic risk (≥ 34 cm)	39	84.8	
WHR			
No risk	2	4.3	p* < 0.001**
Metabolic risk (> 0.5)	44	95.7	

*Significant difference at 5%; ** using the χ^2 test to compare proportions in a sample; BMI: body mass index; WC: waist circumference; NC: neck circumference; WHR: waist-to-height ratio.

anthropometric variables. Significant associations were found with WC, NC and unemployment.

With regard to clinical variables, 73.9% reported a family history of cancer, 71.8% had a diagnosis time ≤ one year, while 26.1% were identified with distant metastasis. As for treatment, 60.9% had undergone breast surgery, 84.8% were undergoing chemotherapy, 26.1% had undergone radiotherapy and 17.4% had undergone hormone therapy. More than half of the group did not have other comorbidities associated with cancer, however, 21.7% were hypertensive, 6.5% were diabetic and 8.7% had these associated pathologies. Regarding lifestyle, 80.4% were sedentary and the majority (97.8%) were non-drinkers and non-smokers.

DISCUSSION

The results of this study corroborate the profile of breast cancer patients described in the literature, of women predominantly in the age group of 50 years old, married/in a civil union, who had at least one pregnancy, were in menopause, with a family history of cancer, and had a low adherence to physical activity.

Table 5. Association between body mass index (BMI) and sociodemographic, gynecological and anthropometric variables in patients with breast cancer. Hospital das Clínicas, Universidade Federal de Pernambuco. Recife, PE, Brazil, 2019.

Variable	Total		BMI				p-value*
	n	%	Malnourished and Eutrophic		Overweight		
			n	%	n	%	
Age group							
Elderly	15	32.6	6	54.5	9	25.7	p* = 0.137
Adults	31	67.4	5	45.5	26	74.3	
Race							
Caucasian	24	52.2	6	54.5	18	51.4	p** = 0.857
Non-Caucasian	22	47.8	5	45.5	17	48.6	
Age of menarche							
Less than 12 years old	16	34.8	3	27.3	13	37.1	p* = 0.722
≥ 12 years old	30	65.2	8	72.7	22	62.9	
Use of OAC							
Yes	24	52.2	3	27.3	21	60.0	p* = 0.058
No	22	47.8	8	72.7	14	40.0	
Occupation							
Part of the labor market	14	30.4	-	-	14	40.0	p * = 0.020 ***
Unemployed	32	69.6	11	100.0	21	60.0	
Education level							
< 9 years	21	45.7	5	45.5	16	45.7	p** = 0.988
≥ 9 years	25	54.3	6	54.5	19	54.3	
WC							
High (≥ 80 cm)	7	15.5	7	70	-	-	p* < 0.001***
Very high (≥ 88 cm)	38	84.5	3	30	35	100	
CP							
No risk (<34 cm)	7	15.2	7	89.7	-	-	p* < 0.001***
Risk (≥ 34 cm)	39	84.8	4	10.3	35	100	

*Fisher's exact test; **using Pearson's χ^2 test; ***significant difference at 5%; OAC: oral contraceptive; WC: waist circumference; NC: neck circumference.

The data are similar to those of other studies because they are derived from populations served by the Public Health System (*Sistema Único de Saúde* – SUS), even though they represent different regions of Brazil, However, a similar profile can also be found in international surveys[4,6,17-20].

As for the sanitary housing location, only 19.6% did not have access to adequate basic sanitation, an aspect that has been little explored in surveys involving this public. However, Queiroz et al.[18], in Rio Grande do Norte, identified that almost half of their sample had poor basic sanitation, which stood out as one of the risk factors associated with breast cancer. This factor may also be associated with the most vulnerable social class and low education levels, which converge to make accessing health services difficult, especially in the northeast of Brazil.

Cabral et al.[21] identified five profiles of patients with breast cancer, showing that women of greater social vulnerability were non-Caucasians, who had <8 years of schooling, and were SUS users. At the same time, they showed a social profile of Caucasian SUS users with 11 years of schooling, which would be a profile that is compatible with the present study, since more than half of this research sample had ≥ 9 years of schooling and was Caucasian. Nevertheless, in the study by Cabral et al., he observed that 39.6% of his sample had more advanced stages (III or IV) at the time of diagnosis, and the interval between diagnosis and the start of treatment exceeded 60 days in 45.8% of cases. Therefore, the evidence indicates that social characteristics and inequalities in access to health services have a relevant impact on early detection and treatment of breast cancer.

At the national level, the José Alencar Gomes da Silva National Cancer Institute (INCA)[22] points out that less than 10% of women diagnosed with breast cancer have the stage *in situ*, the initial stage of the disease, however, in the Northeast Region, the proportion of advanced cases represents about 40% of diagnoses. Such data are relevant when it is observed that 26.1% of the participants in the present study had metastasis in the diagnosis, which suggests a delay in the early identification of the disease.

The pathogenesis of breast cancer involves tissue response to environmental as well as hormonal stimuli. Risk factors are related to gynecological and reproductive history, such as early menarche (<12 years), nulliparity, age at first pregnancy (> 30 years) and use of oral contraceptives (OAC). Researching the clinical-epidemiological profile and related risk factors in the state of Ceará, Souza et al.[20] observed a predominance (greater than 70%) of women with early menarche, use of OAC and age at first pregnancy <25 years. Regarding this last factor, Sofi et al.[4], in India, found compatible results. Similar data were detected in this study only in relation to the age of the first pregnancy and the use of OAC. On the other hand, there were different results regarding young age at menarche, since only one third of the population studied had it at ≤ 12 years old. Such factors increase the risk of developing breast cancer by increasing exposure to estrogen and progesterone hormones throughout life[1,23].

Alcoholism and smoking are important behavioral factors related to this pathology. Souza et al.[20] reported that more than half of the group was formed by alcohol users and a third were smokers, data that differ from those found in this study, in which 97.8% reported being non-drinkers and non-smokers. Macacu et al.[24], in their meta-analysis, showed that active, as well as passive, exposure to tobacco is a moderate risk factor for the development of breast cancer. By the same token, alcohol consumption is related to endogenous hormonal changes, increased oxidative stress and changes in metabolic pathways, in addition to producing a known carcinogenic compound, acetaldehyde, through the metabolism of ethanol. In large quantities, alcohol can predispose women to folate deficiency, among other nutrients, making the breast more susceptible to carcinogenesis. In addition, alcohol facilitates the cellular penetration of environmental carcinogens, for example, what is present in tobacco[1].

As for breastfeeding, the Indian study[4] stands out. A total of 90% of the group performed breastfeeding for around 12 months. In Ceará[20], the number was 74%. These values agree with our findings, which may be related to public breastfeeding policies in Brazil in recent years[4]. The INCA points out that there is a reduction in the risk of breast cancer due to hormonal mechanisms and tissue exfoliation, in addition to the apoptosis of breast cells in the breastfeeding process[1].

Sofi et al.[4] report that miscarriages suffered throughout life have a positive association with breast cancer, a factor that is rarely present in the study population, in which only one third of women had one or more miscarriages. One of the changes that occur in women's' bodies during full term pregnancy is the differentiation of epithelial cells from breast tissue, which is the factor responsible for reducing the risk of breast cancer. As such, miscarriage is equivalent to an interruption of the differentiation process, increasing the risk of cellular changes that could culminate in breast cancer[25]. However, despite the evidence cited, there is still controversy in the literature, and there is no consensus that miscarriage is a risk factor[23].

In the analysis of the incidence of being overweight, which was determined based on BMI, there is a consensus in the literature that the frequency of this factor is extremely high. This was observed by Brazilian authors[17-19,26] who detected excess weight in the range of 53.4–85.5% of women and by international studies[6,27], which has data similar to that found in this study.

Similarly, Mota et al.[19], in the state of Goiás, showed 85.5% of excess weight by BMI in the studied sample. However, when assessing body composition using dual X-ray densitometry (DEXA), they observed that 100% of the group were overweight and had adiposity. Thus, they confirmed that BMI, in isolation, is not a good parameter for the nutritional assessment of this population. In this regard, it is worth highlighting the review published by Sheng et al.[7], with suggestions for practical interventions for weight loss, such as awareness about the impact of obesity and the implications of chemotherapy and hormone treatments in relation to weight gain.

With regard to cardiovascular risk, it was observed that 84.5% of women had a very high risk, identified by WC ≥ 88 cm, which corroborates most breast cancer studies[18,19,26]. These findings show the need for health care in preventing the development of morbidities related to excess weight, especially in those patients who have a greater deposition for abdominal fat.

NC is an anthropometric parameter that has been associated with increased blood glucose, total cholesterol and fractions, and is therefore a good predictor for identifying cardiometabolic risk factors. This measure is considered to be an efficient marker for insulin resistance and cardiovascular risk in the general population, however, there are still few studies that address this measure in women affected by breast cancer[12]. Santos et al.[28] found a prevalence of 90% in women with NC ≥ 34 cm. These data agree with those of the present study, which identified a high cardiometabolic risk for NC. A total of 84.8% of patients presented NC ≥ 34 cm and demonstrated a risk for the development of diabetes *mellitus* and dyslipidemias, among other pathologies. Cardiometabolic risk was significant, with NC ≥ 34.88 cm. In comparison to healthy women, breast cancer patients had an android obesity profile with a higher concentration of body fat in the upper body, a profile associated with higher cardiovascular risk[29].

As for the factors associated with excess weight, there was a statistical association with the anthropometric data of WC and NC, showing that women with excess weight have, concomitantly, a higher cardiovascular risk. In addition, unemployment had a statistically significant relationship, which may indicate the social vulnerability in which they are inserted. This factor influences access to healthy foods, mainly due to price and local availability, leading to a higher consumption of unhealthy foods with high energy density, which can cause predisposition to the development of excess weight, in addition to metabolic disorders[30].

A study by Custódio et al.[26], in Minas Gerais, found a relationship between low diet quality and nutritional status, showing that women with the worst scores were obese and had a higher cardiometabolic risk, assessed by WC, WHR, and waist-hip ratio. The authors also identified a reduction in the quality of the diet after chemotherapy, with consequently inadequate anthropometric parameters. Ribeiro-Sousa et al.[31] identified a reduction in the level of physical activity and an increase in food consumption in women who progressed with weight gain during neoplastic treatment. Such evidence points to the importance of lifestyle factors in being overweight.

The aforementioned study finds high WHR in most of the evaluated patients, which is in agreement with the results of the present study, in which 95.7% presented metabolic risk based on the WHR. According to the Brazilian Association for the Study of Obesity and Metabolic Syndrome (*Associação Brasileira para o Estudo da Obesidade e da Síndrome Metabólica* - ABESO)[10], the metabolic risk assessment is shown to be higher than the BMI and WC, demonstrating a relationship with the increase in mortality in the general population. Nutritional monitoring at the time of diagnosis, in addition to actions that promote a healthy lifestyle, are necessary interventions throughout the treatment of this public. Further studies are fundamental in order to confirm this data in populations with a greater number of women treated in outpatient or hospital settings.

A limitation of the present study was the reduced number of patients, in addition to the absence of biochemical tests such as lipid profile, which is related to increased cardiovascular risk.

CONCLUSION

The women with breast cancer studied had a high risk of cardiovascular disease, which was indicated by the anthropometric profile. WC, NC and lack of participation in the job market were factors associated with being overweight.

AUTHORS' CONTRIBUTIONS

M.G.P.B.: Design, methodology, investigation, project administration, supervision, visualization, writing — original draft, reviewing & editing.

T.R.S.C.: Methodology, data analysis, investigation, writing — reviewing & editing.

T.B.M.: Design, investigation, methodology, data collection, data analysis, writing — original draft, reviewing & editing.

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