







# Prevalence of obesity in patients with breast cancer followed-up at an oncology service in Goiânia

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## ABSTRACT

**Objective:** To verify the prevalence of obesity in patients undergoing cancer follow-up at Hospital das Clínicas in Universidade Federal de Goiás, analyzing the epidemiological and laboratory profile. **Methods:** Retrospective, analytical and observational study. The final sample consisted of 498 medical records of patients under regular follow-up with indication for chemotherapy between June 2018 and 2020. Anthropometric data, gestational history, personal and family history, menopausal status, comorbidities, staging, and laboratory tests were observed. **Results:** A mean body mass index of 28.3 kg/m<sup>2</sup> was found among the patients, and 26.51% were obese. Mean age at diagnosis was 52.79 years, and 51.81% were in menopause. Also, 26.23% had a personal history of breast cancer, and 44.76% had family history. Regarding comorbidities, 51.15% had them, being the most frequent one systemic arterial hypertension, more prevalent in the obese group compared to the normal body mass index. Also, 11.96% of the patients were nulliparous. Regarding staging, most were in T2N0M0 at diagnosis. In laboratory tests, it was found that among patients with breast cancer who had information on lipid profile, low-density lipoprotein and total cholesterol were above the reference limit. **Conclusion:** 57.63% were obese or overweight, demonstrating body mass index as a risk factor for breast cancer. It was observed that the group of patients with obesity had a statistically significant relationship with the presence of concomitant comorbidities; however, no statistically significant results were found regarding the relationship between body mass index and menopausal status.

**KEYWORDS:** breast cancer; obesity; body mass index; menopause; comorbidities.

## INTRODUCTION

Breast cancer is the most prevalent type of cancer among women around the world, being responsible for the highest number of deaths by cancer in this population. According to the International Agency for Research on Cancer, in 2020 there were 2.3 million new cases, representing 24.5% of new cases among women. In the same year in Brazil, new cases of breast cancer represented 30.3% in the female population<sup>1</sup>. Regarding the epidemiological profile of patients undergoing breast cancer treatment, there was high prevalence in the age group of 51 to 60 years, with no previous and family history of breast cancer, stage IIa according to the TNM classification<sup>2</sup>.

Likewise, the incidence of obesity in Brazil has also been increasing, following a global tendency<sup>3</sup>. In 2016, the prevalence

of this disease among people aged more than 18 years was 18.9%<sup>4</sup>. The map made by the Brazilian Society of Obesity for the Study of Obesity and Metabolic Syndrome shows that, in Goiânia (GO), 17% of the women present with obesity. According to the World Health Organization (WHO), the estimation is that in 2025 2.5 billion adults will be overweight around the world, and, of these, 700 million will be obese<sup>5</sup>.

Obesity is a known risk factor for several noncommunicable chronic diseases, such as cancer, and lifestyle plays a determinant role in this condition. The body mass index (BMI) is the main anthropometric indicator of generalized adiposity, whose ratio higher than 30 kg/m<sup>2</sup> characterizes obesity<sup>6,7</sup>.

There seems to be an association between obesity, risk of breast cancer and its prognosis. Among the possible variables

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related to worse outcome for obese patients, some are: more advanced stage at diagnosis, other associated comorbidities, faster tumor growth and hormonal influence<sup>8</sup>.

In postmenopausal women, obesity influences the risk for the onset of this type of cancer, because for these patients the conversion of androstenedione to estrone in the fat tissue is higher; this leads to higher concentration of free estrogen, besides lower levels of sex hormone-binding globulin, which also leads to higher availability of estrone. Besides, hyperinsulinemia can be generated and IGH-I can increase; the latter is responsible for stimulating cell proliferation, for regulating anabolic processes and for apoptosis<sup>9</sup>.

The presence of comorbidities, considering the most common ones such as obesity, systemic arterial hypertension (SAH) and diabetes mellitus, is considered as a prognostic and determinant factor in the choice of cancer treatment, since this treatment may compromise the health of these patients even more<sup>10</sup>.

Besides the fact that obesity is a risk factor for cancer, it can also interfere in the action of chemotherapy, once this condition can affect the metabolism of cytotoxic drugs, considering that its distribution in the fat and muscular tissue may interfere in its pharmacokinetics<sup>11</sup>.

Regarding lipid profile, it was observed that some chemotherapy drugs used to treat breast cancer may increase plasma lipoproteins, such as LDL-cholesterol and hypertriglyceridemia, or reduce HDL-cholesterol, thus worsening the patient's condition<sup>10,11</sup>. Besides, there seems to be a relationship between a worsen prognosis related to the increase of LDL-cholesterol and a reduction of HDL-cholesterol in the diagnosis<sup>12,13</sup>.

In this sense, there is a mutual relationship between weight and breast cancer; on the one hand, weight gain during the treatment of breast cancer is justified by several factors, such as chemotherapy, radiotherapy and decreased general status, leading to sedentary lifestyle, fatigue and indisposition; on the other hand, obesity is a risk factor for the onset of this type of cancer<sup>6</sup>.

Therefore, the knowledge of anthropometric parameters, comorbidities and nutritional profile of oncologic patients at different stages is a way to characterize the metabolic profile, to estimate the survival rate and the impact of obesity on cancer treatment, to predict the chances of aggravation, besides allowing the early intervention in the treatment of obesity, which would result in better chemotherapy and clinical response among patients with breast cancer. Facing the exposed, the objective of this study was to verify the prevalence of obesity in patients undergoing cancer treatment at Hospital das Clínicas of Universidade Federal de Goiás, analyzing their epidemiological and laboratory profile.

## METHODS

This is an observational, analytic, retrospective study. The data were collected between January and April 2021. The initial sample

was constituted of 606 charts; however, 108 were excluded for not being available for study at the time of analysis. The final sample was constituted of 498 charts of patients who were regularly assisted at the oncology service of Hospital das Clínicas in Universidade Federal de Goiás, with indication for chemotherapy between June 2018 and June 2020. The patients were found through authorizations of outpatient procedures and analyzed based on anthropometric data of weight and height, gestational history, recurrence, presence of another tumor, family history of breast cancer, menopausal status, comorbidities, cancer staging and laboratory exams.

Concerning menopausal status, we considered the fact that patients were in menopause (post-menopause) or not (pre-menopause) when receiving the diagnosis of neoplasm. In gestational history, the number of pregnancies was assessed, and nulliparous women were those who had never been pregnant. The positive personal history for breast cancer includes the presence of diagnosis of previous biopsy for this type of tumor; family history of breast cancer was collected through the first appointment file. Weight and height were collected from the charts in kilograms and meters, respectively, and based on that BMI was calculated per square meter. The history of comorbidities was collected in the first appointment chart regarding its absence or presence at the time of diagnosis.

Breast cancer staging was collected from the charts, and the classification used was the one defined by the Union for International Cancer Control<sup>14</sup>, which uses three definition criteria: breast tumor size (T), presence of damaged lymph nodes (N) and presence or absence of distant metastasis (M).

The laboratory data we used were not present in all sample charts. Therefore, the calculations were made according to the availability of data in each variable, forming an independent sample. Total cholesterol was found in 102 charts and classified as higher or lower than 190 mg/dL. HDL-cholesterol was present in 89 charts and classified as higher or lower than 40 mg/dL. LDL-cholesterol was found in 87 charts and categorized as higher or lower than 100 mg/dL. The values of triglycerides was present in 90 charts and were grouped as higher or lower than 150 mg/dL; fasting blood glucose was present in 282 cases and divided in higher or lower than 126 mg/dL<sup>15</sup>.

The project was approved by the Research Ethics Committee of Universidade Federal de Goiás (number 4.431.837). The research did not cause the participants any risk, and the data were handled in secrecy. The collected data were tabled and analyzed using Microsoft Excel, version 2016, GraphPd prism, version 7, and Epi info 7.2.4.0. For quantitative variables, we determined measurements of central tendency, such as mean, median, absolute and percentage frequency, standard deviation, minimum and maximum values. Qualitative variables were presented in absolute numbers and percentage. To verify the statistic relation between menopausal status and BMI, we used the chi-square

test, considering a 5% significance level. The chi-square test was also used to verify the statistic relation between BMI and the presence of comorbidities, positive family history for cancer and lymph node damage. Both analyses of statistical association were made by excluding the patients who did not present one of the parameters available for analysis in the chart.

## RESULTS

The study sample was comprised of a total of 498 participants, being 496 (99.60%) female and two (0.40%) male. Regarding the quantitative characterization of the population, we identified that the mean height of the individuals in the sample was 1.57 m, with minimum of 1.36 m and maximum of 1.76 m, median of 1.60 and mode of 1.60 m; standard deviation was 0.06 m. About weight, the mean was 68.66 kg, with minimum of 35 kg, maximum of 121.05 kg, median of 67 kg, mode of 70 kg; standard deviation was 14.57%. The mean BMI was 28.3 kg/m<sup>2</sup>, and numbers ranged between 16.67 and 50.22 kg/m<sup>2</sup>, with median and mode of 26 kg/m<sup>2</sup> and standard deviation of 6.88 kg/m<sup>2</sup>. By classifying the BMI of the studied population in groups, 132 (26.51%) patients presented with BMI ≥ 30 kg/m<sup>2</sup>; 155 (31.12%) between 25 and 29.9 kg/m<sup>2</sup>; 107 (21.49%) between 18.5 and 24.9 kg/m<sup>2</sup>, and 6 (1.20%) lower than 18,5 kg/m<sup>2</sup>.

The mean age at the diagnosis of cancer in the group was 52.79 years, being the youngest age of 25 years, and the oldest age of 92 years; median was 52 years of age, mode of 48 years of age, and standard deviation of 13.31. It was observed that, of the 496 women, 257 (51.81%) were in menopause at the time of diagnosis, and the mean age of the beginning of menopause was 45.6 years, ranging between 26 and 71 years; median was 44 years, mode was 42 years, and standard deviation, 8.08 years (Table 1).

As to the qualitative characterization of the population, it was found that 117 (26.23%) participants reported the recurrence of a cancer in the past at the time, or being with a second tumor

at the time of analysis; 201 (44.76%) had family history of breast cancer. Regarding comorbidities, 245 (51.15%) patients had some at the time when cancer was diagnosed. The most frequent ones were diabetes and SAH. About gestational history, 56 (11.95%) women were nulliparous (Table 1).

The study about breast cancer staging was conducted using the Union for International Cancer Control (UICC) classification (14), TNM. However, 55 (11.04%) participants did not have this information in their charts. By analyzing the tumor size at the time of diagnosis, it was observed that primary tumor could not be evaluated (Tx) in only one case (0.20%), whereas 94 (18.88%) participants were classified as T1; 179 (35.94%) were T2; 74 (14.86%) were T3; 95 (19.08%), T4. The presence of lymph node damage was observed in 213 cases, being 151 (30.32%) classified in N1; 57 (11.45%), N2; 5 (1%), N3. However, lymph node damage was not assessed at diagnoses for three (0.60%) patients, and 227 (45.58%) did not present with any lymph node damage. The presence of distant metastasis was also analyzed, and 337 (67.67%) did not present with it, classified as M0; 25 (5.02%) were at M1; 1 (0.20%), at M2; and 80 (16.06%) did not have this type of evaluation or it was not clear in the chart (Mx) (Figure 1).

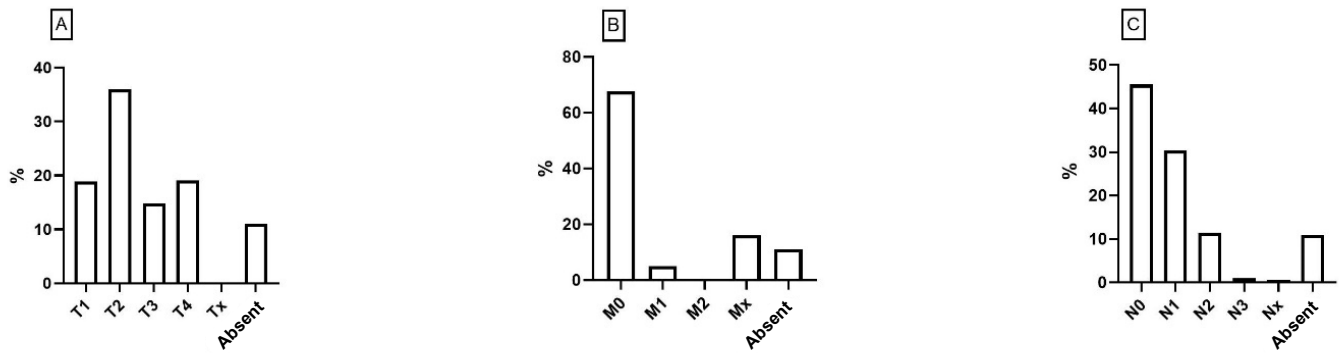
We analyzed laboratory examinations, observing that in most charts with this information total cholesterol was higher than 190 mg/dL (58.86%); o LDL was higher than 100 mg/dL (72.41%); HDL was higher than 40 mg/dL (74.16%); triglycerides were lower than 150 mg/dL (56.67%); and fasting glucose, in most charts, was lower than 126 mg/dL (88.30%) (Table 2).

The analysis of the association between BMI and menopausal status showed that, among postmenopausal women, the BMI of 48 of them was normal; 74 were overweight; and 75 were obese. Among pre-menopausal women, the BMI of 57 of them was normal; 74 were overweight; and 57 were obese (Table 3). In this study, we did not find a statistically significant result about the relationship between BMI and menopausal status in the sample (p=0.220).

**Table 1.** Characterization of patients with breast cancer undergoing na oncology service in Goiania-GO.

	Minimum	Maximum	Mean	Median	Mode	Standard deviation
Height (m)	1.36	1.76	1.57	1.60	1.60	0.063
Weight (kg)	35	121.05	68.66	67	70	14.59
BMI (kg/m <sup>2</sup> )	16.67	50.22	28.3	26	26	6.88
Age at diagnosis (years)	25	92	52.79	52	48	13.31
Age at menopause (years)	26	71	45.68	44	42	8.08
				<b>Present</b>		<b>Absent</b>
Recurrence or other tumors (%)				117 (26.23)		329 (73.76)
Family history of breast cancer (%)				201 (44.76)		248 (55.23)
History of comorbidities (%)				245 (51.15)		234 (48.85)
Nulliparity (%)				56 (11.96)		412 (88.03)

BMI: body mass index; m: meters; kg: kilograms; kg/m<sup>2</sup>: kilograms per square meter. Amounts expressed in absolute numbers and percentage rates (%).



Quantification of breast cancer staging based on the TNM classification. (A) Tumor size; (B) distant metastasis; (C) regional lymph node damage. Being T: tumor size; N: lymph node damage; M: distant metastasis. Amounts expressed as percentage rates.

**Figure 1.** Quantification of breast cancer staging at the diagnosis of patients being followed-up at an oncology service in Goiania.

**Table 2.** Laboratory examinations of patients undergoing cancer treatment (except patients whose information was not in the medical chart)

Laboratory examinations	Absolute frequency	Percentage (%)
Total Cholesterol		
>190 mg/dL	58	56.86
<190 mg/dL	44	43.14
HDL-c		
>40 mg/dL	66	74.16
<40 mg/dL	23	25.84
LDL-c		
>100 mg/dL	63	72.41
<100 mg/dL	24	27.58
Triglycerides		
>150 mg/dL	39	43.33
<150 mg/dL	51	56.67
Fasting glucose		
≥126 mg/dL	33	11.70
<126 mg/dL	249	88.30

HDL-c: high density lipoprotein; LDL: low density lipoprotein; mg: milligrams; dL: deciliters.

**Table 3.** Association between body mass index and menopausal status of patients with breast cancer being followed-up at an oncology service in Goiania.

BMI	Post-menopause	Pre-menopause	p-value
Normal	48	57	
Overweight	74	74	0.22
Obesity	75	57	

BMI: body mass index. Amounts expressed in absolute numbers.

Finally, we analyzed the relationship between BMI and the presence of comorbidities, positive family history for cancer and the presence of lymph node damage. We found that comorbidities were present in 36.27% of the patients with normal BMI; in 45.70% of those overweight; and 64.62% of those with obesity. As to family history of cancer, it was observed in 44.33% of patients with normal weight; 46.48% for those overweight; and 49.56% for those with obesity. About lymph node damage, 48.95% of the patients with normal weight were N0; 34.37%, N1; 13.54%, N2; and 3.12%, N3. Among overweight patients, 48.96% were N0; 36.55%, N1; 13.10%, N2; none in N3, and 1.37% were not assessed (Nx). Among those with obesity, 43.69% were N0; 38.65%, N1; 15.96%, N2; 0.84%, N3; and 0.84% did not have this parameter analyzed (Nx). The analysis of such data showed a statistically significant association ( $p < 0.001$ ) only between the presence or absence of comorbidities and BMI (Table 4).

## DISCUSSION

BMI is a good anthropometric indicator, and it is the most used on in the world. It is simple, practical and has no cost. However, there are some limitations for not considering differences in body composition due to gender, age, ethnicity, not distinguishing fat and lean body mass, and not reflecting the distribution of body fat. Therefore, the ideal is that BMI be used together with other methods to determine body fat, such as the association with the abdominal circumference measurement. This combined way to assess the risk helps to reduce the limitations of each one of the evaluations alone; but, in the initial screening, BMI can be used alone in a satisfactory manner<sup>14</sup>. This study found the fact that the abdominal circumference measurement was not present in the charts as a limitation.

Nowadays, the incidence of obesity has been increasing in Brazil, and 20.7% of the women present with  $BMI \geq 30 \text{ kg/m}^2$ . Evidence suggests that high BMI is associated with increased risk of breast cancer, which can be explained by physical and

**Table 4.** Relation between the body mass index and the presence of comorbidities, family history of breast cancer and lymph node damage.

	Normal (%)	Overweight (%)	Obesity (%)	p-value
Comorbidity	37 (36.27)	69 (45.70)	84 (64.62)	
No comorbidity	65 (63.73)	82 (54.30)	46 (35.38)	p<0.0001
FH +	43 (44.33)	66 (46.48)	59 (49.58)	p=0.74
FH -	54 (55.67)	76 (53.52)	60 (50.42)	
Lymph node damage				
Nx	0 (0)	02 (1.37)	01 (0.84)	
N0	47 (48.95)	71 (48.96)	52 (43.69)	p=0.46
N1	33 (34.37)	53 (36.55)	46 (38.65)	
N2	13 (13.54)	19 (13.10)	19 (15.96)	
N3	03 (3.12)	0 (0)	01 (0.84)	

FH+: Family history positive for cancer; FH-: Family history negative for cancer. Amounts expressed in absolute numbers and percentage rate (%).

pathological changes in the insulin IGF-1 axis, sexual hormones and adipokines, leading to the poor adjustment of endocrine and paracrine functions, which can promote metabolic changes and contribute with the increased risk of cancer and worse outcomes<sup>15,16</sup>. Besides, studies showed that obesity is related to the increased prevalence of triple negative breast cancer, the most aggressive subtype; when associated with the menopausal status, it is a predictor for sensitivity to neoadjuvant chemotherapy<sup>17</sup>. In this study, we observed that 132 women (26.51%) were obese (BMI higher than 30 kg/m<sup>2</sup>) during chemotherapy, and 155 (31.12%) were in pre-obesity (BMI between 25 and 29.9 kg/m<sup>2</sup>). There was a large number of obese patients, but there was no comparison with a second cohort of cancer-free patients to define if the BMI in fact increased the risk in this group of women. In other studies, obesity was present in 34.4% of the patients undergoing breast cancer treatment<sup>18</sup>, and pre-obesity affected 35.3%<sup>19</sup> of them; besides, obese patients had twice as many chances of being diagnosed with breast cancer at advanced stages when compared to patients with normal weight<sup>20</sup>.

Obesity seems to influence the development of breast cancer, especially after menopause, and that is justified by the fact that circulating estrogen deriving from the fat tissue is associated with the increased risk and progression of estrogen receptor positive breast cancer. This study did not find a statistically significant association between the presence or absence of obesity and menopausal status in patients with breast cancer. However, past studies showed that 75% of the patients who had breast cancer after menopause presented worse outcomes when they were obese in comparison to women with normal BMI. Obesity is associated with worse prognosis, leading to higher levels of lymph node and distant metastasis, increasing tumor load and risk of recurrence<sup>15,21</sup>. In this study, 197 women were menopausal; 74 were overweight and 75 were obese. A similar result

was found in another research, which showed an increasing risk of breast cancer together with an increase in BMI after 25 kg/m<sup>22</sup>. This study did not assess the use of hormone blockers in patients with a history of cancer because this information was not in the chart, which would be an important additional data.

Concerning the epidemiological profile of the study population, we observed that most did not present with recurrence or family history of breast cancer and had history of comorbidity, being SAH the most frequent one; the minority was nulliparous. Such data are in accordance with the study carried out with women undergoing breast cancer treatment in other states, such as Minas Gerais and Paraná, demonstrating a similar profile<sup>23,24</sup>. Regarding the age at diagnosis, the mean age was 52 years, similar to other studies that point out that the mean age of women diagnosed with breast cancer was between 50 and 69 years, thus leading to the need for programs of prevention and early diagnosis of breast cancer<sup>24-26</sup>.

Regarding the analysis of staging at the time of diagnosis, based on the TNM system, most presented with a tumor classified as T2 (35.94%), lymph node damage classified as N0 (45.56%), metastatic involvement as M0 (67.67%); and 55 (11.04%) participants of the studied population did not present the TNM classification in the chart, showing a flaw in the follow-up of these patients, considering that this parameter is important to monitor the disease. However, it was not possible to clinically classify the population and correlate it with the presence of obesity, since other information, such as the type of receptor and protein of the tumor and histological level, was not analyzed. However, a direct relationship between the presence of obesity and more advanced stage and the presence of higher lymph node damage at diagnosis has been observed in another study<sup>20</sup>.

About the laboratory profile of the patients, we observed that, in most charts, TC and LDL-c were above the reference value,



whereas fasting glucose, HDL-c e triglycerides were within normal limits<sup>26,27</sup>. In the literature, studies show that no direct associations were found between the lipid profile and the occurrence of breast cancer. On the other hand, the increasing lipoproteins can be a result of the disease itself, drugs used during chemotherapy and the lifestyle of the patients<sup>12</sup>.

We found that, in the group of patients with normal BMI, 36.27% had some comorbidity, whereas in the group of overweight and obese patients, 45.70% and 64.62%, respectively, presented with associated comorbidities, leading to a statistically significant relationship between the increase of BMI and the prevalence of other comorbidities together with breast cancer in the sample ( $p < 0.001$ ). This information is verified by studies that show that the higher the BMI of a patient, the higher the risk of developing diseases, such as SAH and diabetes. This can be explained by physical and pathological changes that occur in obesity, leading to a pro-inflammatory state and reducing the quality of life of patients. According to the WHO, in 2010 obesity and excess weight caused 3.4 million deaths in the world, reinforcing the severity of the problem, the impact on the follow-up of patients and the need for attention addressed to weight control, since the incidence of obesity has been increasing around the world<sup>28,29</sup>.

Observing the family history of cancer in obese and non-obese patients, we can notice that 49.58% of the group with obesity and 46.48% of the group with excess weight were positive, and 44.43% of the group with normal BMI was also positive. In this study, there was no statistically significant relationship ( $p = 0.74$ ) between family history of cancer and obesity; however, the literature reports that women with family history of breast cancer (first-degree relatives) present higher influence of BMI on the risk of developing cancer, which can be 2.9 times higher than when BMI is higher than 30 kg/m<sup>230</sup>; however, this study did not analyze the level of kinship, only the presence or absence of cases of cancer in the Family. By analyzing the relationship between obesity and lymph node damage in breast cancer, it is possible to notice that the level of damage increases in the group in which patients were overweight or obese, when compared to

the group with normal weight; however, there was no statistically significant difference ( $p = 0.46$ ).

## CONCLUSIONS

The results of the study in women undergoing regular breast cancer treatment at Hospital das Clínicas of Universidade Federal de Goiás characterized the percentage of participants who were overweight or with obesity as 57.63%, showing BMI as a relevant factor for the physician to assess. Besides, we found that the group with obesity presented a higher percentage of concomitant comorbidities when compared to the normal BMI group, pointing to a direct influence on the prognosis and quality of life of the patients. There was no statistically significant association between the presence or absence of obesity and menopausal status in patients with cancer; however, there may be a correlation between cancer and obesity based on the percentage found.

Therefore, due to the impact of breast cancer on the quality of life of the patients, we observed that the association with obesity or other comorbidities may worsen the status and lead to worse outcomes. So, it is possible to notice the importance of the analyses about implicated factors in the etiology and progression of breast cancer, thus leading to new possibilities of prevention and better prognosis. Thus, it is necessary to establish public health measures for the female population, in order to reduce the incidence of obesity/overweight and stimulate the early diagnosis of breast cancer.

## AUTHORS' CONTRIBUTION

ACJFS: Conceptualization, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. VBS: Conceptualization, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. LLB: Data curation, Formal Analysis, Writing – review & editing. DGSTS: Writing – review & editing. EJFT: Writing – review & editing. CMG: Formal Analysis, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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