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RESEARCH **Open Access**

Metabolic syndrome as independent risk factor among sample of Egyptian women with breast cancer

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Abstract

Background: Metabolic syndrome (MetS) and breast cancer (BC) are closely related and need more clarification. In clinical practice, the early diagnosis of BC is the most crucial issue. The current study aimed to investigate the incidence of metabolic syndrome among Egyptian women with breast cancer as independent risk factor, and the relationships between anthropometric indices (BMI, waist, hip, middle upper arm circumferences) and breast cancer risk.

Results: MetS rate was significantly higher among women with breast cancer ($n=89$, 65%) women; compared to CG: 43.5%, (37) women therefore metabolic syndrome was strongly associated with breast cancer. More than half of BC cases ($n=85$, 62%) were obese (BMI > 29.9), and 37 women (27%) were overweight (BMI 25–29.9). Additionally, the BC group had greater levels of fasting blood sugar than the control group (109.72 ± 51.31, 78.49 ± 22.79 mg/dL, respectively). Waist circumference, hip circumference, and WHtR values in BC women showed highly significant difference (p value = 0.000) compared to control group.

Conclusion: In our study, the metabolic syndrome and its elements were significantly correlated among Egyptian women with breast cancer. Anthropometric indices were linked to an increased risk of breast cancer.

Keywords: Breast cancer, Metabolic syndrome, Anthropometric indices

Background

One of the most common types of cancer diagnosed is breast cancer and comes secondly in the leading causes of death among women (Rajib 2022). The highest incidence of women malignant tumors is breast cancer, it affects all ages in the world, and it is caused not only by hormonal factors, reproductive factors but also due to environmental factors (Dong et al. 2021). Siegel et al. (2020) reported that it is the commonest female malignancy in the USA, with 276,480 new cases and 42,170 deaths expected. Moreover, Shohdy et al. (2021) stated that the Egyptian females' knowledge about breast cancer is low, although it represents 33% of female cancer cases and more than 22,000 new cases diagnosed annually. This is anticipated to increase enormously over the coming years as a result of bad lifestyle choices, population growth, and changes in the population pyramid. Despite significant increases in survival rates in many developed regions, research have shown that Egypt's 5-year survival rate, which ranges from 28 to 68%, has stayed lower. Numerous variables, including the fact that most patients receive diagnoses at advanced stages, are thought to have contributed to the poorer survival rates (Abdelaziz et al. 2021). MetS, including obesity, diabetes, and hypertension, is associated with increased BC risk. On the other

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hand, MetS is gradually being evaluated as a significant predictor of BC prevalence. Many studies have correlated different aspects of breast cancer with MetS and its associated derangements (Akinyemiju et al. 2022). According to Palmiero et al. (2021), MetS plays a critical role in defining BC because of its effects on hormonal pathways involving insulin, estrogen, cytokines, and growth factors among postmenopausal women in particular, Additionally, MetS is linked to a higher chance of death from breast cancer (Buono 2020). In people with MetS, chronic inflammation and oxidative stress contribute to the development of cancer (Zhang et al. 2021). Unfavorable treatment outcomes and increased side effects are caused by metabolic abnormalities, which also raise the likelihood of developing the disease and hasten tumor growth. Furthermore, due to the imbalance of these metabolic components, biochemical processes influence both the host's overall health and the tumor microenvironment unique to a particular organ, leading to higher rates of recurrence and mortality (Dong et al. 2021). While many studies assessed the relationship between BC risk and each individual MetS factor, such as abdominal visceral adiposity, serum lipid levels, and insulin and glucose levels, only a small number of studies attempted to consider multiple items of the cluster of MetS that are associated with BC risk. Early BC diagnosis is a tough issue in clinical practice today. As a result, it is helpful for BC prevention to have proof indicating that postmenopausal women with MetS have a significant risk of developing BC (Palmiero et al. 2021). Obesity, along with increased tumor burden and higher histopathological grade, is all linked to a higher risk of postmenopausal breast cancer (Dong et al. 2021). Given that adipose tissue is the primary source of estrogen in postmenopausal women and that excessive estrogen is known to drive the growth of breast tissue, one of the risk factors for breast cancer is an increase in the body's estrogen levels brought on by obesity (Dong et al. 2021).

Obese women have up to twice as much estrogen as normal weight women because after menopause, estrogen is primarily produced in body fat instead of a woman's ovaries. Additionally, obese women have lower levels of the protein "sex hormone binding globulin," which binds to and removes estrogen from the body. Women who are overweight and obese typically have higher insulin levels than lean women. Any potential relationship between insulin levels and breast cancer risk in premenopausal women is less evident (Mili et al. 2021). Changes in body size as measured by height, weight, body mass index (BMI), waist–hip ratio (WHR), waist circumference, and waist-to-height ratio (WHTR) are substantially related to breast cancer (WC). All of these metrics are discovered to be associated with menopausal status, and their significance is connected to levels of androgen and estrogen (Choi et al. 2021). Results from many studies continue to be contradictory, nevertheless. Surprisingly, women's sex steroid hormone synthesis depends heavily on peripheral fat tissue. Because estrogen and androgens are mitogenic mediators for breast cells, obesity after menopause increases their levels. Additionally, obesity is a reflection of poor eating habits and inactivity, both of which are linked to the development of breast cancer (Buono 2020).

In Western Europe, breast cancer affects more than 30% of patients, and obesity and physical inactivity are associated to it. Recently, anthropometric factors (high BMI and obesity, poor physical activity), smoking, unhealthy eating practices (low consumption of fruits and vegetables), and different treatments (injections, hormonal replacement therapy) have been identified as BC risk factors (Stankeviča et al. 2021). Obesity is thought to be a substantial risk factor for breast cancer and increases the mortality rate in postmenopausal women. The distinct stage of cancer, its size, angiolymphatic invasion, and lymph node involvement in the metastatic stage are all negatively impacted by adiposity. Breast cancer with obesity has aggressive tumor characteristics and a high death rate. The computation of body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and the skin fold thickness measuring test are the most widely used and efficient methods of evaluating adiposity (Stankeviča et al. 2021). The current study aimed to investigate the incidence of metabolic syndrome among Egyptian women with breast cancer as independent risk factor, and the relationships between anthropometric indices (BMI, waist, hip, middle upper arm circumferences) and breast cancer risk.

Methods

The study was a case–control, where the sample size ($n = 164$) was determined using PASS 11 Power Analysis and Sample Size System. Group sample sizes of 82 in group one (breast cancer women) and 82 (control women) in group two achieve 85% power to detect a difference between the group proportions of 0.2000. The proportion in group one (breast cancer women) is assumed to be 0.1500 under the null hypothesis and 0.3500 under the alternative hypothesis. The proportion in group two (control women) is 0.1500. The test statistic used is the two-sided Z test with pooled variance. The significance level of the test was targeted at 0.0500. The significance level actually achieved by this design is 0.0487 (Bujang et al. 2016). The total recruited number was ($N = 222$ Egyptian women), and they shared as volunteers in the periods from year 2019 until the end of 2021. The study was done at Baheya breast cancer hospital and organization in collaboration with National research Centre.

Patients were selected based on systematic randomized method; the mammogram screening was done for women attended the early screening clinic at Baheya hospital; then, patients with suspicious lesion were listed for surgery (Breast tissue core biopsy sampling), and every third patient on the surgery list was selected (average daily list includes 50 patients/day) to be selected and the inclusion and exclusion criteria were applied. Our visits to the screening clinic were scheduled as follows: every Sunday and Wednesday per week (2 days/ week) for 6 months. Women who had free mammogram were included in the study as control group.

Inclusion and exclusion criteria are: 222 women (age range was 25–75 years) were included in the present study, where 137 with breast mass by mammogram screening and diagnosis were confirmed by breast tissue core biopsy. Eighty-five women had free mammogram reports and participated as control group. All women were subjected to thorough clinical examination with detailed medical history of the complaints, present history (e.g., age of onset of diagnoses, symptoms present with the breast mass), past history (e.g., the history of pregnancy, lactation), family history of relatives with breast lesions, anthropometric assessments, and metabolic syndrome diagnosis. Women who had breast mass and confirmed as malignant tumor by breast tissue core biopsy were included as patient group (Breast Cancer group), and any patient with previous history of bleeding tendency was excluded for possible risk of bleeding during biopsy sample. Control group (CG) included women with free mammogram upon the screening. Any women were pregnant, or lactating women at the time of our study were excluded. Also, any women with disease or condition might interfere her with the study assessments or previously diagnosed and on treatment diabetic women, and women with high-risk condition that negates surgery were excluded from our study.

Anthropometric measurements

In accordance with the International Biological Program's recommendations, height and weight were measured. Using a Seca Scale Balance, the participant's body weight (Wt) was calculated to the nearest 0.01 kg, while they were not wearing any shoes or much clothing. Using a Holtain portable stadiometer, body height (Ht) was calculated to the nearest 0.1 cm. The trained research staff also took waist circumference, height, and weight measurements with a flexible tap, and the circumferences of the waist, hips, and middle upper arms were measured in cm. Waist-to-hip and waist-to-height ratios (WHR, WHTR, respectively) were calculated. Body mass index (BMI) was computed by dividing the user's weight in kilograms by their height in square meters (kg/m^2).

Metabolic syndrome diagnosis

MetS was defined as women having any three of the following: high blood pressure (≥ 130/85 mm Hg), low HDL (≤ 50 mg/d), elevated triglycerides (≥ 150 mg/d), high waist circumference (≥ 80 cm), and prior diagnosis of diabetes or an elevated fasting glucose level (≥ 100 mg/dL) based on the joint harmonized criteria. At the time of enrollment, systolic and diastolic blood pressures were measured three times and an average value was recorded. Immunoassay was done for measuring HDL and triglycerides levels using a Beckman DxC600 clinical analyzer and standard Beckman reagents (Brea, CA) (Dong et al. 2021; Akinyemiju et al. 2022).

Statistical analysis

Data were collected, revised, coded, and entered into the IBM SPSS version 23 Statistical Package for Social Science. Kolmogorov–Smirnov test was used to assess the distribution of numerical parameters, and quantitative data with parametric distribution were presented as mean, standard deviations, and ranges, while nonparametric data were presented as median with inter-quartile range (IQR). Qualitative variables were also presented numerically and as percentages. The chi-square test and/or Fisher exact test was used to compare groups regarding qualitative data. The independent t test was used to compare two independent groups with quantitative data and parametric distribution, while the Mann–Whitney test was used for nonparametric distribution. The confidence interval was set to 95%, and the acceptable margin of error was set to 5%. As a result, the p value was considered significant at the level of < 0.05.

Results

A total number of 222 women were included in this study, divided into breast cancer (BC) and control groups (CG); BC group ($n = 137$ women) and control group ($n = 85$ women) participated in the study. There was no statistically significant difference in number and age of participants between the both groups, and the age range was between 25 and 75 years. MetS rate was significantly higher (p value = 0.002) among women affected by breast cancer: 65% (89) women; compared to CG: 35% (48) women, therefore metabolic syndrome was strongly associated with breast cancer (Fig. 1).

MetS parameters were significantly higher among women affected by breast cancer except TG which was higher in BC group with no significant difference; metabolic syndrome was strongly associated with breast cancer, compared to the control group (Table 1), where MetS

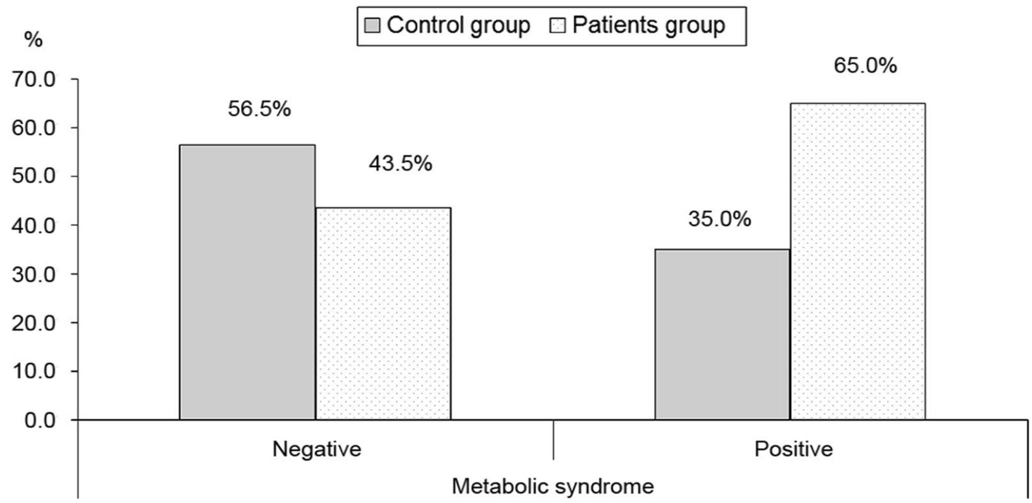

Fig. 1 Metabolic syndrome in the two groups

Table 1 MetS parameters in the two study groups

MetS parameters	Breast cancer group BC (mean ± SD)	Control group CG (mean ± SD)	Test value	*P* value
BMI (kg/m²)	33.84 ± 12.94	27.51 ± 7.10	−4.133•	0.000**
Waist circumference (cm)	100.30 ± 14.44	84.33 ± 13.78	−8.150•	0.000**
TG (mg/dL)	130.95 ± 58.57	119.29 ± 51.60	−1.507•	0.133
HDL cholesterol (mg/dL)	48.97 ± 12.53	41.7 ± 97.97	−4.723•	0.000**
Systolic BP (mm Hg)	132.30 ± 12.62	123.55 ± 2.59	−6.305•	0.000**
diastolic BP (mmHg)	85.82 ± 5.98	75.58 ± 3.81	−14.105•	0.000**
Fasting plasma glucose (mg/dL)	109.72 ± 51.31	78.49 ± 22.79	−5.292•	0.000**
Insulin (mIU/L)	13.6 (10 – 24.9)	6.8 (5.8—7.5)	−10.084‡	0.000**

BMI body mass index, *TG* triglyceride, *HDL* high-density lipoprotein, *BP* blood pressure

P value > 0.05: non-significant; *P* value < 0.05: Significant (*); and *P* value < 0.01: highly significant (**)

•Independent t test

‡ Mann–Whitney test

≠ All data were presented as mean ± SD except insulin level presented as median (IQR) due to nonparametric distribution

parameters are illustrated in Figs. 2, 3, 4, and 5 as follows; Fig. 2 shows that the weight and BMI among the study two groups (breast cancer women and control group) with highly significant differences (*P* value < 0.001), where 62.0% (85) of women with breast cancer were obese (BMI > 29.9 kg/m^2), while 18 women (21.2%) control group had their BMI > 29.9 kg/m^2. On the other hand, when blood pressure measurements were studied as one of the metabolic syndrome parameters, systolic SBP and diastolic DBP measurements showed higher values with highly significant difference (*P* value = 0.000) in breast cancer women groups in comparison with control group healthy women, as shown in Fig. 3. Waist and hip circumference among both groups is illustrated in Fig. 4 and showed with highly significant difference (*P* value = 0.000) between both groups. Cholesterol, HDL, TG, and LDL levels in (mg/dl) were studied among the both groups (breast cancer patients and control women), and their results showed that the highest values were among the women with breast cancer lesions with highly significant difference (*p* value = 0.000); lipid profile is illustrated in Fig. 5.

Anthropometric characteristics were collected for all women, where anthropometric indices were compared between BC cases and control women, and BC cases had higher weight, BMI, waist circumference, hip circumference, and WHtR with highly significant difference (*p* value = 0.000) (Table 2).

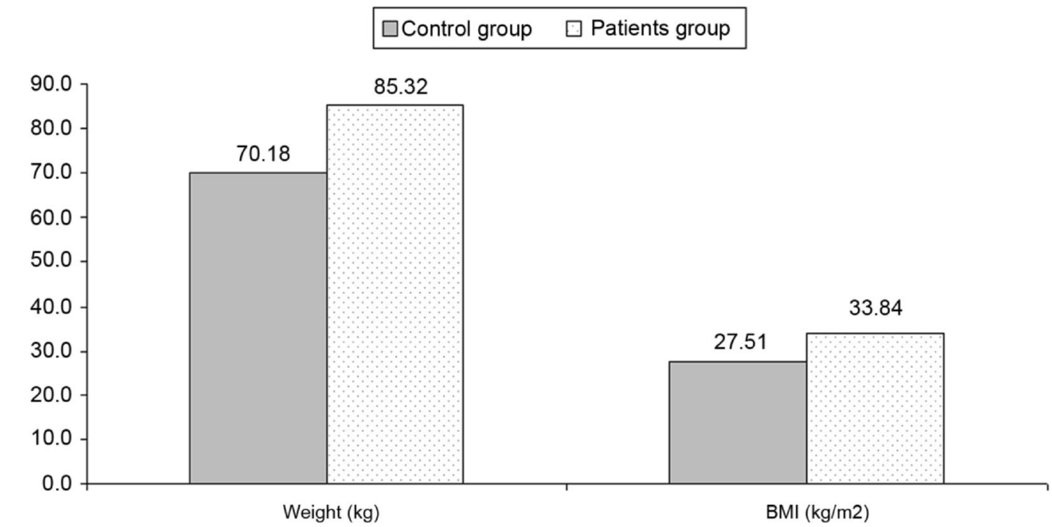

Fig. 2 Weight and BMI in the two groups

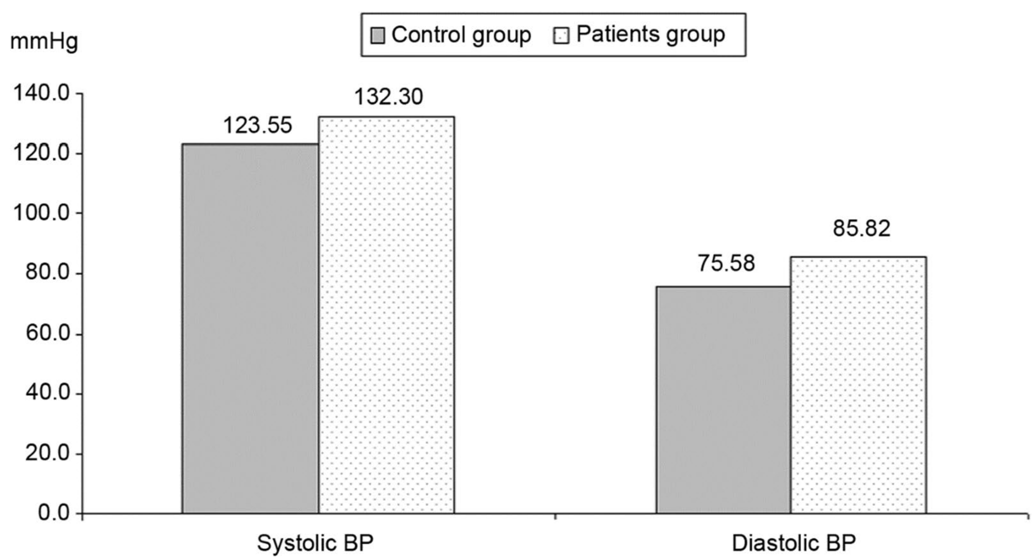

Fig. 3 Blood pressure in the two groups

The univariate logistic regression analysis showed that metabolic syndrome parameters (HDL, fasting plasma glucose, insulin, weight, BMI, HC, WC, and WHTR) were found associated with breast cancer; also, the multivariate logistic regression showed that fasting plasma glucose > 75 mg/dL was found the most important factor associated with breast cancer with p value = 0.016 and OR (95% CI) of 6.503 (1.418–29.819) (Table 3).

Discussion

In this study, we looked into the relationship between an Egyptian woman's risk for breast cancer and her metabolic syndrome (MetS). By identifying MetS as a significant risk factor that implies a significant role in the development of cancer in general and BC in particular, prior studies evaluating the role of MetS in the development of BC provided significant proof indicating an

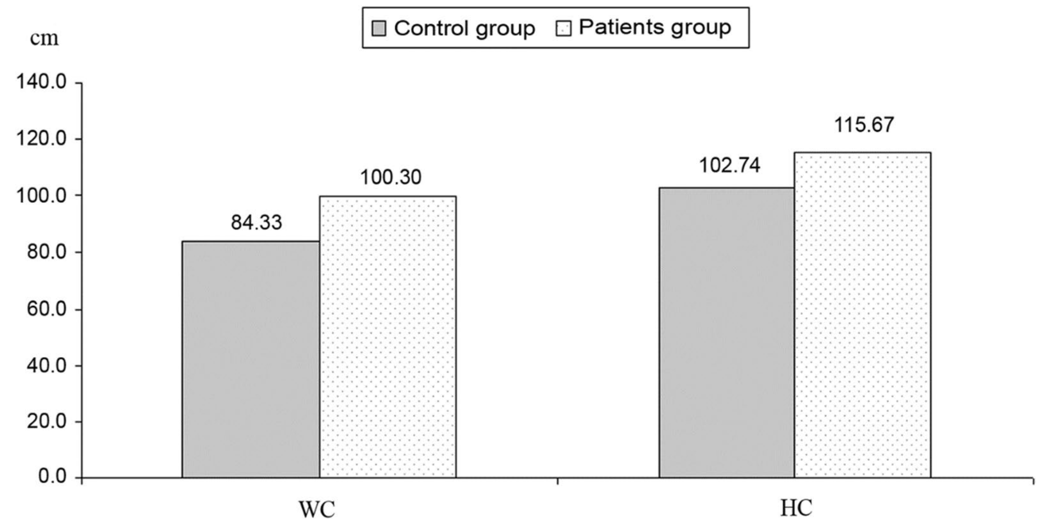

Fig. 4 Waist and hip circumference in the two groups

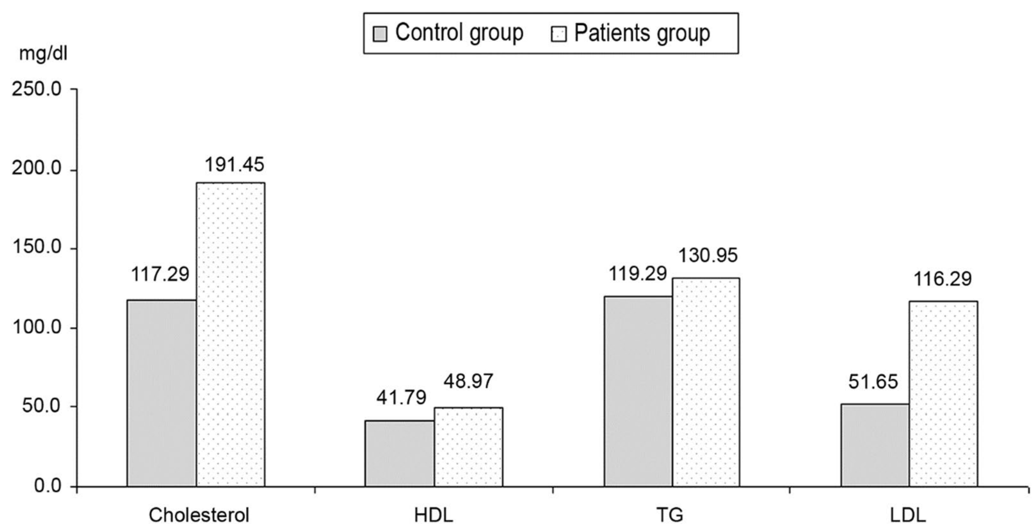

Fig. 5 Lipid profile in the two groups

Table 2 Anthropometric indices in the two groups

Anthropometric indices	Breast cancer group (BC)	Control group (CG)	Test value	*P* value
Weight (kg)	85.32 ± 20.35	70.18 ± 17.49	−5.680•	0.000**
Height (cm)	157.18 ± 19.90	158.99 ± 7.42	0.804•	0.422
HC (cm)	115.67 ± 22.02	102.74 ± 20.11	−4.389•	0.000**
WHR	0.84 ± 0.10	0.84 ± 0.55	−0.122•	0.903
WHTR	0.63 (0.58 – 0.69)	0.42 (0.35 – 0.47)	−9.666‡	0.000**
MUAC (cm)	36.34 ± 18.10	36.09 ± 4.80	−0.122•	0.903

HC hip circumference, *WHR* waist-to-hip ratio, *WHTR* waist-to-height ratio, *MUAC* mid-upper arm circumference

P value > 0.05: Non-significant; *P* value < 0.05: Significant (*); and *P* value < 0.01: highly significant (**). •Independent *t* test; ‡Mann–Whitney test

≠All data were presented as mean ± SD except WHTR presented as median (IQR) due to nonparametric distribution

Table 3 Univariate and multivariate logistic regression analysis for factors associated with breast cancer (BC)

Factors associated with BC	Univariate				Multivariate			
	P value	Odds ratio (OR)	95% CI for OR		*P* value	Odds ratio (OR)	95% CI for OR	
			Lower	Upper			Lower	Upper
HDL > 52 mg/dL	0.000	12.468	4.752	32.708	0.159	4.240	0.567	31.673
Fasting plasma glucose > 75 mg/dL	0.000	9.106	4.826	17.180	0.016	6.503	1.418	29.819
Insulin > 8 mIU/L	0.000	206.708	58.366	732.082	–	–	–	–
Weight > 71.9 kg	0.000	8.010	4.337	14.794	–	–	–	–
BMI > 29.9 kg/m2	0.000	6.084	3.259	11.360	–	–	–	–
HC > 107 cm	0.000	11.967	6.273	22.828	–	–	–	–
Waist circumference > 89 cm	0.000	15.106	7.760	29.404	0.673	1.427	0.274	7.446
WHTR > 0.47	0.000	178.667	50.599	630.879	–	–	–	–

HDL high-density lipoprotein, *BC* breast cancer, *BMI* body mass index, *HC* hip circumference, *WHTR* waist-to-height ratio

P value > 0.05: Non-significant; *P* value < 0.05: significant; and *P* value < 0.01: highly significant

increased risk of BC in women before or during menopause (Ademi-Islami et al. 2022). Our findings revealed a higher prevalence of MetS in women with BC compared to women without cancer. Metabolic syndrome is a type of multifactorial metabolic disease characterized by the presence of at least one of the following risk factors: obesity, diabetes, low/high-density lipoprotein, hypertriglyceridemia, and hypertension (Dong et al. 2021). In the current study, the BC group had greater fasting serum insulin and blood glucose levels than the control group (CG). Our finding is in agreement with Dong et al. (2021) who said that insulin resistance and hyperinsulinemia are both linked to an increased incidence of breast cancer and that diabetes is a risk factor for the disease. However, Palmiero et al. (2021) showed that abdominal fat is a significant source of both androgens and estrogens, and that the correlation between obesity and the risk of BC is supported by high estrogen levels. Estrogens and insulin work together to promote the growth of breast epithelial cells (Palmiero et al. 2021). Insulin has a gonadotropic effect, increasing the production of androgens by the ovaries, which are the main source of estrogens after menopause. Insulin also increases the activity of the aromatase enzyme (Palmiero et al. 2021).The current study showed that for higher levels of systolic and diastolic pressure (hypertension), low levels of HDL, high levels of triglycerides cholesterol, and low-density lipoprotein LDL in the BC group than CG with highly significant difference, these findings are in agreement with Choi et al. (2021); they discovered that increased risk of breast cancer was associated with greater systolic and diastolic blood pressure levels. Also, our results are in agreement with Palmiero et al. (2021) who revealed that due to a common condition of subclinical inflammation, hypertension is frequently present in the metabolic syndrome cluster and is connected to breast cancer. However, the precise underlying mechanism of MetS is still unknown. The same holds true for high triglyceride levels and low HDL cholesterol levels. But it is necessary to clarify these observations in their true context. MetS is a risk factor for BC as a whole in addition to the role that can have all of its components separately. MetS risk variables, such as body mass index (BMI), were more commonly linked to tumors that expressed hormone receptors (Ademi-Islami et al. 2022). Adiposity has been linked to an increased risk of breast cancer. The discrepancy may be due to variations in how body fat is distributed. For instance, premenopausal women with significant abdominal adiposity as measured by dual-energy X-ray absorptiometry (DEXA) had an elevated risk of breast cancer (Ramírez-Marrero et al. 2022). Abdelaziz et al., (2021) stated that according to the WHO, Egypt is among the top countries in the world for overweight and obesity, with female prevalence ranging from 74 to 86%. Similarly, current study showed that obesity was widespread among BC patients using anthropometric indices including weight, height, BMI, HC, WC, and WHtR. BMI finding is in agreement with numerous studies, which linked increased body mass index (BMI) with BC (Ramírez-Marrero et al. 2022). Numerous researches have examined the relationship between BC risk and each individual MetS factor—abdominal visceral adiposity, serum lipid levels, insulin levels, and glucose levels—but few have attempted to look at the cluster as a whole. The fact that a well-defined group of postmenopausal women who are affected by MetS show a significant risk of incidence is beneficial, for BC prevention, as early diagnosis of BC has until now been a confounding issue in clinical practice. (Palmiero et al. 2021; Ademi-Islami et al. 2022).

Conclusions

MetS and BC were found to be significantly correlated in our population over the entire sample. Metabolic syndrome and its components are also thought to be associated with the development and progression of breast cancer, abnormal systolic and diastolic pressure (hypertension), serum lipids and lipoproteins, low levels of HDL, high levels of triglycerides cholesterol, and LDL linked to an increased risk of breast cancer. Anthropometric measures were linked to an increased risk of breast cancer. To better understand the predictive significance of anthropometric parameters in the assessment of breast cancer risk in Egyptian women, future research should include direct measurements of body fat and the distribution of lean mass.

Abbreviations

MetS: Metabolic syndrome; BC: Breast cancer; BMI: Body mass index; Wt: Bodyweight; Ht: Body height; HC: Hip circumference; WC: Waist circumference; WHtR: Waist-to-height ratio; WHR: Waist-to-hip ratio; IGFs: Insulin-like growth factors; DEXA: Dual-energy X-ray absorptiometry; MUAC: Mid-upper arm circumference; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TG: Triglyceride; DBP: Diastolic blood pressure; SBP: Systolic blood pressure.

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Author contributions

WSM was responsible for conceptualization, data curation, methodology, project administration, supervision, and review and editing in addition to the manuscript submission to the journal. OMA was responsible for data curation, visualization, investigation, software, reviewing, and editing. MA-E aided in data curation, formal analysis, software, validation, and visualization. MMMG was the responsible of breast tissue biopsy sample and reporting the results. IEE was taking a part of laboratory investigations. DYH was in charge of investigation and anthropometric measurements. MMK was responsible for chemical and laboratory and investigations. EMA was responsible of data collection, preparation, and statistical analysis. WY was responsible for visualization, investigation, supervision, and project administration. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

A written informed consent was obtained from all participants after being informed about the purpose of the study, and the approval was obtained from Ethics Committee of NRC. (Registration Number is 19/202.)

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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