IJMS
Vol 48, No 5, September 2023

Original Article

Association between Metabolic Syndrome Risk Factors and Immunohistochemical Profile in Women with Breast Cancer

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Received: 07 May 2022
Revised: 25 August 2022
Accepted: 24 September 2022

Abstract

Background: The association between metabolic syndrome (MetS) and breast cancer may significantly impact the mortality and incidence of breast cancer. This study aimed to assess the association between MetS risk factors and immunohistochemical (IHC) profiles in women with breast cancer.

Methods: This cross-sectional study used the medical records of 300 breast cancer patients with an average age of 53.11±12.97 years in the Chemotherapy and Radiation Therapy Clinic of Dr. Anbiai, Tehran, Iran (2020-2021). The cases were divided into five subgroups including luminal A, luminal B (HER-2$^-$), luminal B (HER-2$^+$), HER-2 overexpressing, and triple negative.

Results: There was no difference in the prognostic indicators between the presence and absence of MetS in women with breast cancer. A higher proportion of luminal A tumors (39.3%), luminal B (HER-2$^+$) (25%), triple-negative (17%), luminal B (HER-2$^-$) (10.7%), HER-2 overexpression (8%) was observed in women with MetS than those without MetS. Multivariate logistic regression analysis showed that patients with MetS had a 41% higher chance of developing luminal A than those without MetS, and patients with a BMI≥30 Kg/m^2 had an 80% higher chance of developing luminal B (HER-2$^+$) than those with a BMI<30 Kg/m^2. Moreover, women with a waist circumference higher than 88 cm had a 14 % lower chance of developing Luminal B (HER-2$^+$) than those with a waist circumference less than 88 cm.

Conclusion: There was no difference in prognostic indicators and IHC profile in patients with and without MetS.

Please cite this article as: Danesh H, Anbiaei R, Ziamajidi N, Farhadian M, Barartabar Z, Abbasalipourkabir R. Association between Metabolic Syndrome Risk Factors and Immunohistochemical Profile in Women with Breast Cancer. Iran J Med Sci. 2023;48(5):456-464. doi: 10.30476/IJMS.2022.95039.2673.

Keywords ● Breast neoplasms ● Immunohistochemistry ● Metabolic syndrome

What's Known

- Metabolic syndrome increases the risk of cancer development and may have a significant impact on its incidence and mortality.
- Few studies have investigated the relationship between metabolic syndrome and the immunohistochemical profile of menopausal women with breast cancer.

What's New

- It was shown that the presence of metabolic syndrome is not related to the prognostic indicators of breast cancer, such as hormone receptor status and tumor size.
- There was no difference between breast cancer patients with and without metabolic syndrome in terms of standard clinicopathological risk and prognostic factors.

Introduction

Breast cancer is one of the most common neoplasms in women and is defined as the uncontrolled growth of breast tissue cells, including lobules or ducts.[1] The incidence of this disease has shown an increase in some studies, particularly in the Middle East.[2] Currently, the total number of breast cancer patients in Iran is approximately 40,000, and more than 7,000 new patients are diagnosed annually.[3] Several risk factors play essential roles in breast cancer development, including age, sex, race, previous benign breast disease, history of cancer, body mass index (BMI),

pregnancy-related factors, hormones, family history of breast cancer, exposure to ionizing radiation, and environmental factors.[4] The risk of breast cancer varies in different countries, possibly due to lifestyle differences such as reduced physical activity, poor eating habits, and environmental factors.[5] Studies showed that Metabolic Syndrome (MetS) is associated with a 52% increase in breast cancer risk, pathophysiology, and progression.[6, 7]

According to the World Health Organization (WHO) and the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP-III), MetS is defined as the presence of three or more of the following factors, including elevated fasting blood glucose (FBG) levels, elevated triglycerides (TG), decreased high-density lipoprotein (HDL) cholesterol levels, increased blood pressure (BP), and abdominal obesity.[8] MetS can affect the risk of breast cancer through changes in several hormonal pathways, including insulin, estrogen, cytokines, and growth factors.[9] Several studies have demonstrated that obesity increases glucose, fatty acid, and insulin secretion, subsequently reducing AMP-activated protein kinase (AMPK) activity through mitochondrial over-activation. As a result, AMPK reduction suppresses the tumor suppressor protein p53 gene and activates the mammalian target of rapamycin (mTOR) pathway. It was finally found that insulin resistance directly affects carcinogenesis.[10] Cholesterol is also an essential component of breast cell membranes. Studies have reported that extra cholesterol induces breast cancer proliferation, and endocrine tissues use cholesterol to produce steroid hormones involved in cell proliferation, differentiation, and cancer.[10, 11]

Some studies have linked MetS and related disorders to various aspects of breast cancer, such as pathological status. They found that MetS may predispose patients to breast cancer and might also worsen prognosis compared to patients without MetS.[12, 13] Recently, in the 8th edition of the TNM system of the American Joint Committee on Cancer, the IHC profile was considered an important tool to evaluate breast cancer diagnosis.[14] The relationship between MetS risk factors and IHC profile in breast cancer has not been studied extensively. Can and others explored the effect of MetS on prognostic factors in breast cancer women and found no differences in prognostic indicators (ER, PR, and HER-2, tumor size, axillary lymph node involvement, distant metastases, and tumor stage) between patients with and without MetS.[15] On the other hand, Motoki and colleagues conducted a study only on postmenopausal women with newly diagnosed BC. They observed the presence of MetS was associated with smaller tumor size, PR^+ and $HER\text{-}2^-$ status, and the luminal B tumor subtype.[12] The researchers concluded that further studies are necessary to reveal the metabolic effect on breast cancer prognosis. Based on these data, the present study was conducted to assess the association between MetS risk factors and the IHC profile in women with breast cancer.

Patients and Methods

Study Design and Data Collection Procedure

In this cross-sectional study, the medical records of 300 patients with breast cancer who were referred to the Chemotherapy and Radiation Therapy Clinic of Dr. Anbiai (Tehran, Iran) from 2020 to 2021 were investigated. All study procedures were approved by the Ethics Committee of the Hamadan University of Medical Sciences, Iran (IR.UMSHA.REC.1400.512). The inclusion criterion was female patients with breast cancer who provided written informed consent to participate in the study. Women aged 25-85 years who were diagnosed with breast cancer at any clinical stage were included. Exclusion criteria included a history of tumors in other tissues and organs and the unwillingness of the patient or her family to answer the questionnaire.

The information obtained from the patients included age, family history, marital status, breastfeeding status, first menstrual age, history of contraceptive use, waist circumference, height, weight, systolic blood pressure (BP), and diastolic BP.

Anthropometric Measurements

Anthropometric measurements, including height and weight, were performed in accordance with a standard program. The weights of the patients with and without shoes were measured using a Seca digital scale (accuracy 100 g, Germany) and recorded in Kg. The height was measured with a tape measure (accuracy of 1 cm) in a standing position without shoes, while the shoulders were in normal condition and recorded in cm. Waist circumference (WC) in the narrowest area was measured using a tape measure with an accuracy of 0.1 and inelasticity, without imposing any pressure on the patient's body, and was expressed in cm. It should be noted that to eliminate individual error, one person performed all measurements. The BMI was then calculated using the formula of weight in Kg divided by height squared in m. To measure BP, the cuff of the sphygmomanometer (ALPK2

model V300, Japan) was wrapped around the middle of the upper arm, while her arm was in the direction of the heart, and the average of the two BP was recorded. MetS indices were collected based on NCEP ATP III definitions. Based on these records, the patients with three or more of the following criteria were considered to have MetS, WC>88 cm in women, FBG greater than 100 mg/dL, TG>150 mg/dL, HDL less than 50 mg/dL, systolic BP>130 mm Hg, and diastolic BP>85 mm Hg.[8] Based on this definition, the patients were classified into two groups including those with MetS and those without MetS.

Biochemical Analysis

Fasting blood samples were collected upon consent from patients after 12-hour fasting. Then, plasma/serum was separated. The lipid and glucose profiles of the women were evaluated by measuring total cholesterol, HDL-c, LDL-c, TG, and glucose levels. TG, total cholesterol, HDL-c, and glucose were assayed in an RAXT automated biochemical analyzer (Techni-con, USA) using a colorimetric method with specific commercial reagents (Sera-Pak, Bayer, USA). Low-density lipoprotein cholesterol (LDL-c) level was calculated using the Friedewald formula when TG levels exceeded 400 mg/dL. LDL-c was calculated by subtracting the total cholesterol value from the sum of HDL-c and TG, divided by five.

Pathological Report Analysis

The patient anatomopathological and IHC reports included tumor location, tumor size, lymphovascular invasion, histological grade based on the observation of cancer cells under a microscope grade 1 (low-grade cancer), grade 2 (moderate cancer), grade 3 (High-grade cancer), hormone receptor status (ER, PR, HER-2), and epithelial proliferative activity (Ki-67). According to the IHC profile, Breast cancer was classified into five subtypes: luminal A, luminal B (HER-2$^-$), luminal B (HER-2$^+$), HER-2 overexpression, and triple-negative (TNBC) (table 1).[16]

Statistical Analysis

All statistical analyses were performed using SPSS version 24 (IBM Corp, Armonk, NY, USA). Data were expressed using the mean±SD for quantitative variables and the ratio and percentage for qualitative variables. The Student's *t* test was used to compare normally distributed data. The Chi square test was used to evaluate the association between the frequencies of categorical variables. Multivariate analysis by binary logistic regression was performed considering the breast cancer subtype as the dependent variable and the presence of MetS as the independent variable. A significance level of 95% and a P value of less than 0.05 were considered. There were no missing data for any of the variables in this study.

Results

A total of 300 patients with breast cancer were screened. The overall mean age was 53.11±12.97 years with a minimum and maximum age of 25 and 85 years, respectively. Among 300 patients, 224 (74.7%) had MetS, and 76 (25.3%) did not. The mean of FBG was 115.19±44.17 mg/dL, the TG was 193.71±103.63 mg/dL, the mean of HDL cholesterol was 49.33±17.75 mg/dL, the BMI mean was 29.14±4.33 Kg/m^2, the WC mean was 83.27±2.94 cm, the mean of systolic BP was 119.95±16.23 mm Hg, and diastolic BP mean was 81.62±13.14 mm Hg.

The distribution of diagnostic parameters of MetS in our study population was as follows: in breast cancer patients with MetS versus those without MetS, FBG: 117(39%) vs. 183 (61%); TG: 181 (60.3%) vs. 119 (39.7%); HDL: 186 (62%) vs. 114 (38%); systolic BP: 112 (37.3%) vs. 188 (62.7%); diastolic BP: 128 (42.7%) vs. 172 (57.3%); BMI: 216 (72%) vs. 84 (28%); and WC: 160 (53.3%) vs. 140 (46.7%). All diagnostic parameters, except FBG and BP, were higher in the MetS group than in the non-MetS group.

The distribution of risk factors associated with breast cancer in the two groups is shown in table 2. All breast cancer patients were evaluated for marital status, breastfeeding, menstrual age, menopause, and other individual factors. In this study, the patients with MetS were older than those without MetS. The marital status of the two

Table 1: Molecular subtypes of breast cancer based on IHC characterization

Molecular subtype	ER		PR	HER-2
Luminal A	+	And/or	+	-
Luminal B	+	And/or	+ (or negative <20% and ki67>14%)	-
Luminal B	+	And/or	+/-	+
HER-2 overexpression	-	And	-	+
TNBC	-	And	-	-

TNBC: Triple-negative breast cancer

Table 2: Distribution of risk factors associated with breast cancer in the studied groups

Risk factors		Total	With MetS (n=224)	Without MetS (n=76)	P value
Age (year)		53.11±12.97	55.41±12.68	46.32±11.43	<0.001[a]
Marital	Single	20 (6.7)	14 (6.3%)	6 (7.9%)	0.619[b]
	Married	280 (93.3)	210 (93.8%)	70 (92.1%)	
Breastfeeding	Yes	273 (91%)	208 (92.9%)	65 (85.5%)	0.054
	No	27 (9%)	16 (7.1%)	11 (14.5%)	
Menarche	<13 years	166 (55.3%)	125 (55.8%)	41 (53.9%)	0.779[b]
	>13 years	134 (44.7%)	99 (44.2%)	35 (46.1%)	
Menopause	Pre-menopausal	138 (46%)	88 (39.3%)	50 (65.8%)	<0.001[b*]
	Postmenopausal	162 (54%)	136 (60.7%)	26 (34.2%)	
Family history	Yes	132 (44%)	93 (41.5%)	39 (51.3%)	0.137[b]
	No	168 (56%)	131 (58.5%)	37 (48.7%)	
Drug use	Yes	4 (1.3%)	2 (0.9%)	2 (2.6%)	0.253[b]
	No	296 (98.7%)	222 (99.1%)	74 (97.4%)	
Contraceptive	Yes	153 (51%)	126 (56.3%)	27 (35.5%)	0.002[b*]
	No	147 (49%)	98 (43.8%)	49 (64.5%)	

Values are expressed as mean±SD or frequency (percentage). MetS: Metabolic syndrome; P<0.05 was considered statistically significant. [a]Student's *t* test; [b]Chi square test

groups was examined. Most of the patients in both groups were married and breastfeeding. Based on these data, patients with a low menstrual age (less than 13 years) did not show a significant difference in the chance of developing MetS compared to the second group. Examination of menstrual conditions revealed that 46% of the participants were pre-menopausal, and 54% were menopausal. Furthermore, there was a significant difference in the contraceptive use history between the two groups.

Table 3 shows the comparisons of anatomopathological and IHC reports between patients with breast cancer with and without MetS. In the samples of breast cancer patients with MetS, 88.8% had ductal carcinoma, 25% had lobular carcinoma, and most patients had tumors located in the right breast (68.3%). There were no differences in tumor size, tumor grade, lymph node involvement, metastasis, and IHC results (ER, PR, HER-2). Table 4 shows breast cancer subtypes according to the presence or absence of MetS. According to this table, it can be said that there was no significant relationship between subtype levels and MetS status. According to the IHC profile, 37% of the

Table 3: Comparison of anatomopathological and IHC characteristics in women with breast cancer between the two groups with and without MetS

Risk factors		Total	With MetS (n=224)	Without MetS (n=76)	P value
Tumor size (mm)	>20	99 (33%)	74 (33%)	25(32.9%)	0.925
	≤20	201 (67%)	150 (67%)	51 (67.1%)	
Tumor location	Right breast	205 (68.3%)	152 (67.9%)	53 (69.7%)	0.761
	Left breast	95 (31.7%)	72 (32.1%)	23 (30.3%)	
Histology	Lobular	31 (10.3%)	25 (11.2%)	6 (7.9%)	0.419
	Ductal	269 (89.7%)	199 (88.8%)	70 (92.1%)	
Histological grade	I-Low	30 (10%)	21 (9.4%)	9 (11.8%)	0.810
	II-Intermediate	199 (66.3%)	149 (66.5%)	50 (65.8%)	
	III-High	71 (23.7%)	54 (24.1%)	17 (22.4%)	
Lymph nodes	Positive	180 (60%)	139 (62.1%)	41 (53.9%)	0.213
	Negative	120 (40%)	85 (37.9%)	35 (46.1%)	
Estrogen receptor	Positive	226 (75.3%)	169 (75.4%)	57 (75%)	0.938
	Negative	74 (24.7%)	55 (24.6%)	19 (25%)	
Progesterone receptor	Positive	226 (75.3%)	169 (75.4%)	57 (75%)	0.938
	Negative	74 (24.7%)	55 (24.6%)	19 (25%)	
HER-2	Positive	107 (35.7%)	76 (33.9%)	31 (40.8%)	0.281
	Negative	193 (64.3%)	148 (66.1%)	45 (59.2%)	
Ki-67	<14%	63 (21%)	44 (19.6%)	19 (25%)	0.322
	≥14%	237 (79%)	180 (80.4%)	57 (75%)	

Values are expressed as frequency (percentage). HER-2: Human epidermal growth factor receptor 2; Ki-67: Epithelial proliferative activity; MetS: Metabolic syndrome; P<0.05 was considered statistically significant. Chi square test was used to analyze the data.

Table 4: Comparison of breast cancer subtypes in women with breast cancer with and without MetS

Variable	Total	With MetS (n=224)	Without MetS (n=76)	Pearson Chi Square	P value
Luminal A	111 (37%)	88 (39.3%)	23 (30.3%)	3.205	0.524
Luminal B, HER-2$^-$	31 (10.3%)	24 (10.7%)	7 (9.2%)		
Luminal B, HER-2$^+$	82 (27.3%)	56 (25%)	26 (34.2%)		
HER-2 overexpression	24 (8%)	18 (8%)	6 (7.9%)		
Triple-negative	52 (17.3%)	38 (17%)	14 (18.4%)		

Values are expressed as frequency (percentage). HER-2: Human epidermal growth factor receptor 2; MetS: Metabolic syndrome; P<0.05 was considered statistically significant. Chi square test was used to analyze the data.

Table 5: Multivariate analysis of breast cancer subtypes according to the presence of MetS

Variable		Luminal A	Luminal B (HER-2$^+$)	Luminal B (HER-2$^-$)	HER-2 overexpression	Triple-negative
		OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%C)	OR (95%CI)
MetS	NO	1	1	1	1	1
	YES	1.41 (1.656-3.031)	0.794 (0.368-1.713)	1.263 (0.446-3.578)	1.105 (0.365-3.349)	1.241 (0.214-2.441)
HDL (mg/dL)	≥50	1	1	1	1	1
	<50	0.562 (0.280-1.130)	0.694 (0.332-1.452)	0.933 (0.359-2.428)	0.525 (0.194-1.422)	0.213 (0.124-3.542)
Triglycerides (mg/dL)	<150	1	1	1	1	1
	≥150	0.497 (0.253-0.977)	0.845 (0.421-1.697)	0.594 (0.238-1.483)	1.080 (0.410-2.842)	0.865 (0.36-3.258)
Glucose (mg/dL)	<100	1	1	1	1	1
	≥100	0.444 (0.227-0.872)	0.690 (0.343-1.386)	0.441 (0.174-1.116)	0.556 (0.207-1.494)	0.751 (0.845-2.54)
BP (mg/dL)	<130/85	1	1	1	1	1
	≥130/85	0.847 (0.359-1.994)	1.017 (0.405-2.552)	0.440 (0.155-1.245)	0.795 (0.235-2.692)	0.587 (0.456-2.584)
WC (mg/dL)	<88	1	1	1	1	1
	≥88	0.850 (0.440-1.644)	0.864 (1.431-1.732)	0.824 (0.337-2.010)	0.714 (0.269-1.897)	0.254 (0.403-1.241)
BMI (Kg/m^2)	<30	1	1	1	1	1
	≥30	1.671 (0.805-3.470)	1.857 (1.845-4.083)	2.526 (0.825-7.732)	2.429 (0.717-8.225)	1.586 (0.241-5.246)

Logistic regression with the calculation of odds ratio (OR) and 95% confidence interval (CI), adjusted for age. BMI: Body mass index; BP: Blood pressure; HDL: High-density lipoprotein; MetS: Metabolic syndrome; WC: Waist circumference

tumors were luminal A, 10.3% were luminal B (HER-2$^-$), 27.3% were luminal B (HER-2$^+$), 8% were HER-2 overexpression, and 17.3% were TNBC. Multivariate analysis using binary logistic regression was performed for each breast cancer subtype [luminal A, luminal B (HER-2$^-$), luminal B (HER-2$^+$), HER-2 overexpression, and TNBC] with the response as (dependent) variable and the presence of MetS as the explanatory (independent) variable. Odds ratios (OR) and 95% confidence intervals (CI) were calculated after adjusting for age (confounders). The multivariate analysis adjusted for age and BMI (table 5) showed that people with MetS had a 41% (OR 1.41, 95% CI 1.656-3.031) higher chance of developing luminal A than those without MetS, and also those with a BMI greater than 30 had an 80% (OR 0.864, 95% CI 1.431-1.732) higher chance of developing luminal B (HER-2$^+$) than people with a BMI less than 30. Moreover, people with a WC of higher than 88 cm (OR 1.857, 95% CI 1.845-4.083) had a 14% lower chance of developing luminal B (HER-2$^+$) than those with a WC of less than 88 cm.

Discussion

In the present study, MetS was present in 74.7% of the breast cancer patients at the time of breast cancer diagnosis. The presence of MetS was not associated with prognostic indicators of breast cancer, such as tumor size or PR$^-$, ER$^-$, and (HER-2$^-$) status. MetS is predictably defined by the presence of at least three of the five dysmetabolic traits (hypertension, low plasma HDL-cholesterol, abdominal obesity, high FBG, and high TG) and has been associated with type 2 diabetes, cardiovascular diseases, and cancer.[17, 18] In India, a study conducted by Wani and colleagues found that MetS was strongly associated with a higher risk of breast cancer.[9] This study aimed to determine the association between MetS and IHC profiles in women with breast cancer.

According to the NCEP ATP III criteria, the results of this investigation showed that 74.7% of breast cancer patients had MetS. A study from the United Kingdom estimated the incidence of MetS to be approximately 94%,[19] which was higher than the frequency of MetS in our study. In addition, a study conducted by Wu and others in China reported a 32.6% prevalence of MetS in patients with breast cancer, which was lower than the frequency of MetS in our results.[20] The alteration in age, nutrition, and race of the study group could be the reason for this difference. We found a few significant differences in the risk factors of breast cancer between those with MetS and those without MetS. Patients with MetS were older and had higher TG levels, BMI, and WC than those in the second group. These results reflect those of Saadatian and others, who also found a significant relationship between age and MetS.[21] However, according to a study by Amiri and colleagues, there was no significant relationship between the prevalence of MetS and age.[22] This difference can be attributed to the variations in the study population; the present study was performed on patients with breast cancer and not on the general population.

The researchers conducted a study in Boston and reported that the highest prevalence of metabolic risk factors among individuals was associated with low serum HDL levels.[23] In this study, the most important factor after BMI in the prevalence of MetS was low serum HDL levels in patients with MetS, with 62% of the patients having lower HDL levels. In a study by Al-Lawati and colleagues in 1,419 adults aged ≥20 years in Oman, low serum HDL (75%) was found the most common cause of MetS, which is in line with our study.[24]

In the present study, after a decrease in HDL, an increase in TG levels played a significant role in the prevalence of MetS, which is comparable to the result of the Deurenbey-rap study.[25] In a study on 5,610 U.S. urban volunteers aged ≥20 years between 1999 and 2004, the overall prevalence of serum TG was 33%,[26] which is comparable with 60.3% in our study. In line with our study, some studies have identified high TG as the second most common cause of MetS.[27, 28]

The third most common factor in MetS in the present study was a high waist circumference. A study by AL-Lawati and others on Omani adults reported a frequency of 53% in women.[24] According to studies on the causes of abdominal obesity, the high prevalence of this risk factor in women can be attributed to their level of education, physical activity, lifestyle, dietary, amount of consumed fat, etc.[23, 29]

Some studies suggested that hypertension is the second most common cause of MetS.[30, 31] In the present study, hypertension was found to be a poor predictor due to the multifactorial nature of BP and the fact that the patients in the present study were taking antihypertensive and hyperlipidemic drugs.

Hyperglycemia was also a poor predictor of MetS in this study. This may be due to the variability in FBG levels and its low prevalence of FBG levels. This finding was observed in other studies, including those by Palaniappan and colleagues,[32] Goldhirsch and others, [16] and Cheung and others.[33]

Among all components of MetS, abdominal obesity associated with insulin resistance contributes to an increase in mammary estrogen synthesis, promoting the growth of hormone receptor –ER^- and PR^-, and positive breast cancer tumors.[12] The assessment of IHC results (ER, PR, HER-2, and Ki-67) has become crucial for the management of each diagnosed breast cancer. Breast cancer subtypes defined by ER, PR, HER-2, and Ki-67 statuses vary in prognosis and response to treatment.[16]

In this study, there were no differences in prognostic indicators, such as tumor size, histological grade, axillary lymph node metastasis, percentages of ER, PR, HER-2, and Ki67; and consequently, a higher proportion of tumors were of the luminal A subtype. In line with our study, Can and colleagues explored the impact of MetS on prognostic factors in 71 women with breast cancer, and found no differences in prognosis between patients with and without MetS.[34] Healy and others found no differences in the frequency of hormone receptors or triple-negative tumors between women with and without MetS in Ireland.[34] In contrast, Capasso and others reported a higher proportion of $Ki\text{-}67^+$, ER^-, and triple-negative tumors in women with MetS.[35] Andre and colleagues conducted a study in Brazil and reported a higher proportion of $HER\text{-}2^+$ and PR^+.[12] One reason for this discrepancy might be the study population. Their study populations included postmenopausal women with breast cancer. However, our study included postmenopausal and premenopausal women.

Breast cancer subtypes differ in their response to treatment and prognosis.[16] Grybach and colleagues demonstrated that survival rates were significantly lower in patients with MetS than those without MetS, particularly the elderly patients.[36] Therapeutic strategies designed to monitor and treat obesity represent novel approaches to the prevention and treatment of breast.[34] The results of this investigation showed

that there was a higher number of breast cancer patients with MetS than those without MetS, which suggests an increased risk of MetS in patients with breast cancer. The presence of MetS at breast cancer diagnosis may be a key factor in evaluating the metastatic potential of breast cancer. The present study had some limitations. First, the sample size was small. Second, there was a decline and distortion due to the unavailability of individuals during follow-up; and third, there was a lack of genomic testing due to the lack of funds. However, a strong relationship exists between the results of IHC and genomic testing, and the latter is, therefore, the most widely used method for subtype classification, assisting, and directing target therapies.

Conclusion

In women with breast cancer diagnosis, the presence of MetS was not associated with prognostic indicators such as tumor size, tumor grade, lymph node involvement, and IHC results (ER, PR, HER-2). MetS was associated with a higher frequency of luminal A tumors. In addition, patients with BMI≥30 (Kg/m^2) were also more likely to develop luminal B ($HER\text{-}2^+$) than patients with BMI<30 (Kg/m^2). According to the findings of this study, it can be concluded that we were unable to prove our hypothesis that breast cancer in patients with MetS differs from that in patients without MetS in terms of standard clinicopathological risk and prognostic factors.

Authors' Contribution

H.D: conceptualization and methodology, collection and analysis of the data, drafting and revising the manuscript; R.An: conceptualization, providing and collection of data; N.Z: monitoring the project and revising the manuscript; M.F: collection and analysis of the data; Z.B: Methodology; R.Ab: monitoring the project and revising the manuscript. All authors contributed in writing the manuscript. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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