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Frequency of Metabolic Syndrome and its Associated Factors in Patients with Breast Carcinoma at Tertiary Care University Hospitals of Pakistan

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Authors' contributions

This work was carried out in collaboration among all authors. Authors RBK, SA and SSQN were involved in conception of idea and study design. Authors RBK, SA and MI did data collection and performed bench work. Authors RBK and MAO performed the statistical analysis. Authors AGA and MI managed the literature searches. All authors read and approved the final manuscript.

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Opinion Article

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ABSTRACT

Objective: To determine the frequency of metabolic syndrome and its associated factors in patients with biopsy proven breast cancer at tertiary care university hospitals of Karachi, Pakistan.
Methods: This cross sectional study was conducted at the hospitals affiliated with Dow university of health sciences & Baqai medical university from January 2018 to September 2019.A total of 114women between 30 to 50 years of age presented to the out patients clinics and underwent triple assessment including detailed history &examination, radiological assessment and fine needle aspiration cytology for confirmation of breast cancer were included in the study after taking written informed consent. Along with the routine baseline investigations blood sugar for hyperglycemia&blood sample for lipid profile was taken in fasting from Dow Lab. Blood pressure of

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the patients was also checked along with the weight, height and waist measurements. The SPSS version 19 was applied to the data for description and analysis.
Results: Mean age of the patients was 42.57 ±4.90 years. Stages of cancer showed that stage III was found in majority (n=50, 43.9%). Frequency of metabolic syndrome was observed in 44 (38.6%) of the patients. A significant association of metabolic syndrome with educational status (p-value <0.001), Hypertension (p-value <0.001), Central obesity (p-value <0.001), Fasting blood sugar levels (p-value <0.001), Triglyceride levels (p-value <0.001), High density lipoprotein levels (p-value <0.001), and different Stages of breast cancer (p-value 0.003) was observed.
Conclusion: This study show that a significant number of patients with breast cancer are suffering from metabolic syndrome which is also correlates with the educational status of the patients.

Keywords: Metabolic syndrome; Breast carcinoma; hypertension; diabetes; obesity; educational status.

1. INTRODUCTION

Breast cancer is the most common cancer in women and has recently surpassed lung cancer as the most commonly diagnosed cancer worldwide, accounted for 2.3million new cases in [1]. The common risk factors for breast cancer are age, family history of cancers, nulliparity, early menarche and late menopause etc. however studies also recognizes overweight, lack of physical activity, and consumption of alcohol as relative risk factors [2].

Several of these risk factors are associated with metabolic syndrome. Metabolic syndrome is an emerging medical catastrophe attributed to modern life style [3]. It is defined as a group of disorders comprising of central obesity, insulin resistance, high blood pressure, and dyslipidemia. It is defined if three or more of the following five criteria are met: waist circumference over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl. It is estimated to be prevalent in at least a quarter of the adults in the Americas, in Europe, and in Asia etc [3].

The emerging role of metabolic syndrome in the oncogenesis is a matter of debate and has been extensively investigated for several cancers i.e. breast, pancreatic, colorectal, prostate cancers etc [4-5]. Individual components of metabolic syndrome, for example, abdominal obesity, high blood glucose, high BP, high triglycerides, and low HDL, are positively associated with the development of certain cancers, most notably breast cancer [6,7]. While studies show a positive association of breast cancer with diabetes [8,9] and obesity show a negative association with obesity in premenopausal women. Mixed results also specify hypertension [10] and dyslipidemia [11] as risk factors for breast cancer. In addition, although individual components of metabolic syndrome may not be strongly associated with the development of breast cancer, their combination may elevate the risk [12-13].

Metabolic syndrome may activate different molecular pathways through endocrine, metabolic, and immune cell changes, which in turn influence breast tumor genesis. Such pathways that enhance breast cancer cell proliferation and inhibit apoptosis include increased levels of circulating estrogen, higher levels of insulin, decreased level of circulating adiponectin, increased plasma leptin concentration, and increased production of pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor alpha [14].

Previous epidemiologic studies on metabolic syndrome and breast cancer risk show divergent results. The purpose of this study is to determine the frequency of metabolic syndrome in women with breast cancer in our population so that breast cancer screening protocols will be recommended for this high risk group of population.

2. MATERIALS AND METHODS

This cross sectional study was conducted at the hospitals affiliated with Dow University of Health Sciences & Baqai medical university, Karachi from January 2018 to September 2019. A total of 114 women between 30 to 50 years of age presented to the out patients clinics with a breast lump and underwent triple assessment including detailed history & examination, radiological

assessment and fine needle aspiration cytology for confirmation of breast cancer were included in the study. Patients with known history of diabetes mellitus, hypertension and steroid intake were excluded from the study. To control for effect modifiers patients who have started chemotherapy or hormonal therapy were also excluded from the study, as they would lead to deranged metabolic profile.

Written informed consent was taken from each patient regarding the assessment and laboratory investigations for participation in the study. For the confirmation of metabolic syndrome and its component factors blood sugar for hyperglycemia & blood sample for lipid profile and serum insulin levels was taken in fasting from Dow Lab along with the routine baseline investigations. Blood pressure of the patients was also checked along with the weight, height, waist and other anthropometric measures.

A detailed proforma was used to document findings. It included patient's age, gender, duration and stage of breast cancer, parameters of metabolic syndrome including fasting insulin, fasting blood sugar, triglycerides, HDL-cholesterol and blood pressure, personal information related to marital, educational and socioeconomic status etc. All proforma were filled by the principal investigator.After collection of data the analysis was conducted by using statistical package for social science (SPSS) software, version 19. Mean ± standard deviation was used for quantitative variables like age, blood pressure, fasting blood sugar TG and HDL-c. Simple frequency and percentage was computed for the tumor stages. Stratification with respect to age, tumor stages was done. Chi squire test was applied and a P value of ≤0.05 was considered significant.

3. RESULTS

The study consists of 114 patients with the diagnosis of breast cancer between 30 to 50 years of age. Mean age of the patients was 42.57 ±4.90 years. Mean duration of symptoms was 1.41 ±0.45 year.

Majority of the patients 73 (64%) were presented with >25 mg/dl of fasting insulin level with 88 (77.2%) were presented with >100 mg/dl of fasting blood sugar level. The mean calculated values of the variables are shown in Table 1.

Mean central obesity level was found to be 32.03 ± 3.57 inches. Majority of the patients 71 (62.3%) were presented with >35 inches of central obesity. Socioeconomic status of the patients is shown in Fig. 1.

Multiparty was found in 54 (44.7%), grand multiparty in 41 (36%) and nulliparity in 19 (16.7%) patients. There were 54 (47.4%) patients with one to two number of children followed by more than two children (n=41, 36%) while 19 (16.7%) were presented with no children. Stages of cancer showed that stage III was found in majority (n=50, 43.9%), stage II in 29 (25.4%), stage IV in 25 (21.9%) while stage I in 10 (8.8%) of the patients. (Fig. 2).

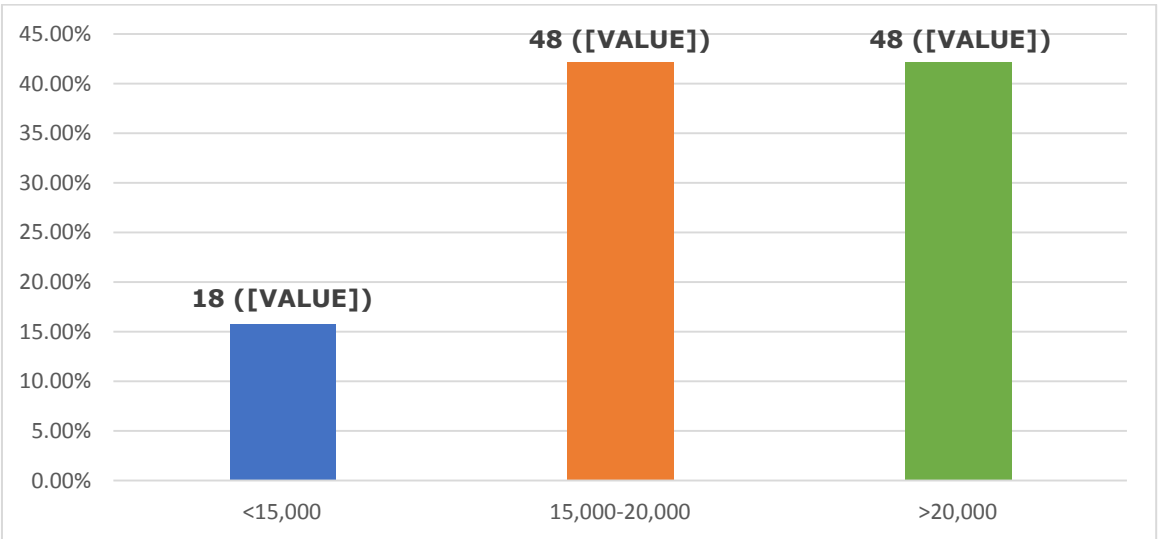

Fig. 1. Socioeconomic status of the patients

Frequency of metabolic syndrome was observed in 44 (38.6%) of the patients. Comparison of metabolic syndrome with baseline characteristics showed insignificant association of metabolic syndrome with age (p-value 0.813), duration of breast cancer (p-value 0.594), fasting insulin level (p-value 0.465), parity (p-value 0.905), number of children (p-value 0.526), socioeconomic status (p-value 0.820), while significant association with educational status (p-value <0.001) (Table 2), hypertension(p-value <0.001), central obesity (p-value <0.001), fasting blood sugar (p-value <0.001), triglycerides (p-value <0.001), high density lipoproteins (p-value <0.001), and stages of breast cancer (p-value 0.003) (Table 3).

Table 1. Calculated values of the variables

Variable	Mean ±SD	Minimum	Maximum
Fasting insulin level (in mlU/L)	24.26 ±4.14	12.44	27.06
Fasting blood Sugar (in mg/dl)	109.69 ±14.37	89	146
Triglyceride level (in mg/dl)	146.62 ±12.24	127	178
High Density Lipoprotein level (in mg/dl)	87.04 ± 12.89	44	139
Systolic blood pressure (in mmhg)	159.6 ±8.31	148	177
Diastolic blood pressure (in mmhg)	95.59 ± 4.73	87	104

Table 2. Comparison of metabolic syndrome with educational status of the women

Educational status	Metabolic Syndrome		Total	p-value
	Yes	No		
Uneducated	25 (67.6)	12 (32.4)	37 (100)	<0.001
Matric	10 (23.8)	32 (76.2)	42 (100)	
Intermediate	9 (25.7)	26 (74.3)	35 (100)	
Total	44 (38.6)	70 (61.4)	114 (100)	

Table 3. Comparison of metabolic syndrome with stages of cancer

Stages of cancer	Metabolic Syndrome		Total	p-value
	Yes	No		
I	0 (0)	10 (100)	10 (100)	0.003
II	7 (24.1)	22 (75.9)	29 (100)	
III	22 (44)	28 (56)	50 (100)	
IV	15 (60)	10 (40)	25 (100)	
Total	44 (38.6)	70 (61.4)	114 (100)	

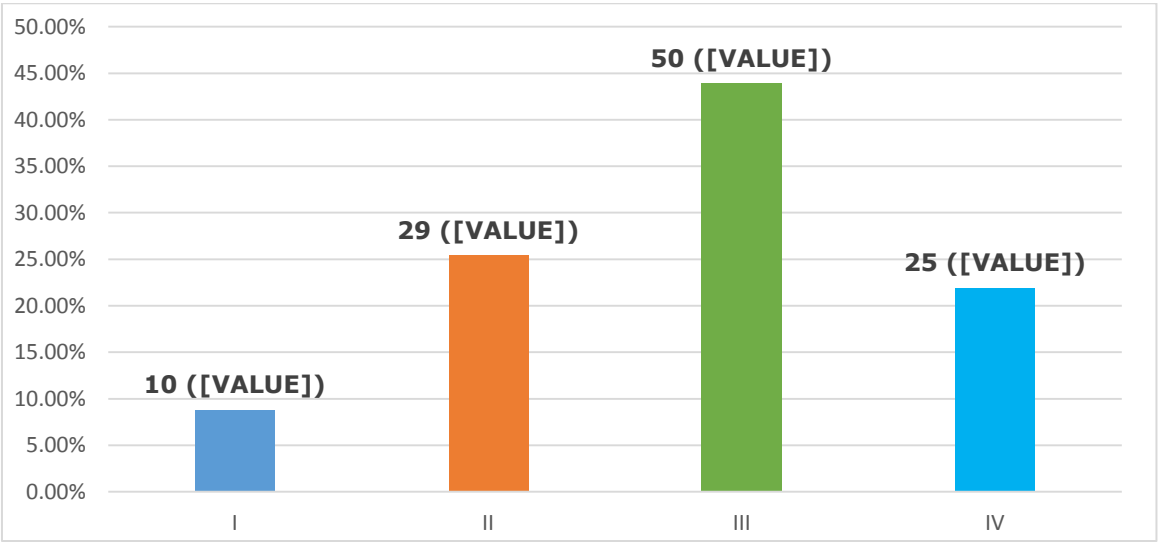

Fig. 2. Different stages of breast cancer

4. DISCUSSION

Our study has shown a significant association of metabolic syndrome and its individual components with breast cancer. More recent studies have shown it to be an independent risk factor for breast cancer [15]. It has also been associated with poorer prognosis [16] increased incidence [17] a more aggressive tumor phenotype [18].

A systematic review and meta-analysis showing association between diabetes mellitus and breast cancer has identified that patients with breast cancer and diabetes had a significantly higher all-cause mortality risk (pooled HR 1.49; 95% CI 1.35-1.65) compared with their non-diabetic counterparts. The finding was shown to be consistent across different populations, generally independent of possible confounding variables, and robust even after accounting for possible publication bias [19]. Also, diabetes has been shown to influence the breast cancer stage, modify treatment regimens, increase risk of being hospitalized for any chemotherapy toxicity and have an adverse effect on disease-free survival [20-23].

Our study highlighted significant association of hypertension, fasting blood sugar, central obesity and hyperlipidemia with breast cancer. In a similar study, the ORs of postmenopausal breast cancer were 1.33 (95% CI 1.09-1.62) for diabetes, 1.19 (95% CI 1.07-1.33) for hypertension, 1.08 (95% CI 0.95-1.22) for hyperlipidemia, 1.26 (95% CI 1.11-1.44) for BMI ≥30 kg/m2, and 1.22 (95% CI 1.09-1.36) for waist circumference ≥88 cm. The risk of postmenopausal breast cancer was significantly increased in women with metabolic syndrome as a single entity (OR 1.75, 95% CI 1.37-2.22) and the risk was higher in older age (OR 3.04, 95% CI 1.75-5.29, at age ≥70 years) [24].

Metabolic syndrome causes a myriad of alterations in the body metabolism. Some changes, which are attributable to the sum of all of the effects metabolic syndrome exerts on the body, are searched to better understand the overall mechanism through which the risk of breast cancer is increased. Plasminogen activator inhibitor-1 (PAI-1) is one of the molecules which is hypothesized to be altered by metabolic syndrome. This protein is a physiological inhibitor of urokinase (uPA), a serine protease known to promote cell migration and invasion. However, increased levels of PAI-1 are paradoxically associated with poor prognosis in breast cancer. A recently published study has put forth the hypothesis that, sustained by metabolic syndrome, adipocytokines alter PAI-1 expression to promote angiogenesis, tumor cell migration and procoagulantmicroparticle formation from endothelial cells, which generate thrombin and further propagates PAI-1 synthesis ultimately forming a vicious circle [25].

Though the relationship between breast cancer and metabolic syndrome with its components has been well established in multiple studies, the complete understanding at the molecular level of the complex interactions between various associated factors of metabolic syndrome that lead to oncogenesis is a challenging task. Metabolic syndrome is not an inherited disease with most of its associated risk factors are modifiable. This led to the belief that knowledge, awareness and establishment of preventive measures to lessen the ratio of patients with metabolic syndrome is imperative to improve the prevalence and outcome of breast cancer. This also explains the negative association of metabolic syndrome with the educational status of the patients. This is of great concern in a developing country like Pakistan, where a number of factors i.e. social, financial, cultural etc. are responsible for poor education and physical activities for women. The dietary recommendations include a reduction of alcohol, red meat and total dietary fat, and increase in vegetable and fruit consumption [26].

5. CONCLUSION

The frequency of metabolic syndrome in 38.6% patients with breast carcinoma. Further research that can links each of its components to one another is warranted in order to form a comprehensive understanding of the complex interplay of the multiple aspects of metabolic syndrome in breast cancer. The association of metabolic syndrome with the educational status of patients needs to be addressed.

CONSENT

Written informed consent was taken from each patient regarding the assessment and laboratory investigations for participation in the study.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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