Metabolic Syndrome in Breast Cancer Patients: An Observational Study

Breast Cancer: Basic and Clinical Research
Volume 15: 1–7

DOI: 10.1177/11782234211026788

Siddhant Khare[1], Santhosh Irrinki[1], Yashwant Raj Sakaray[1], Amanjit Bal[2], Tulika Singh[3] and Gurpreet Singh[1]

[1]Department of General Surgery, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh, India. [2]Department of Pathology, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh, India. [3]Department of Radiodiagnosis, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh, India.

ABSTRACT

BACKGROUND: The reported association between metabolic syndrome (MetS) and breast cancer may have a significant impact on the incidence and mortality related to breast cancer. We undertook this study to find if the disease is different in patients with MetS.

MATERIALS AND METHODS: Patients with biopsy-proven breast cancer were divided into groups based on the presence or absence of MetS (according to the IDF definition of 2006) and also based on menopausal status. The presence of known risk and prognostic factors were also recorded, and the groups were compared.

RESULTS: A total of 305 patients were recruited, of which 191 (62.6%) had MetS. Patients with MetS were older than those without (52.1 versus 48.3 years, $P = .014$) and had a lower incidence of nulliparity (4.1% vs 12.8%, $P = .005$) and dense breasts (2.9% in MetS vs 10.8% in no MetS, $P = .009$). On further dividing into premenopausal and postmenopausal, these differences persisted only in premenopausal patients. MetS group had a lower number of HER2-positive tumours (14.3% for MetS, 23.9% for no MetS; $P = .036$). After dividing into premenopausal and postmenopausal, significant differences were observed in distant metastases (5.4% in MetS vs 16.1% in no MetS, $P = .045$) and in grade (higher grade in MetS, $P = .05$) in premenopausal patients. In postmenopausal patients, difference was observed in HER2 positivity (12.3% in MetS vs 28.8% in no MetS, $P = .008$).

CONCLUSIONS: Breast cancer in patients with MetS may not be significantly different from breast cancer in patients without MetS.

KEYWORDS: Breast cancer, metabolic syndrome, risk factors, clinicopathological parameters

RECEIVED: September 20, 2020. **ACCEPTED:** May 27, 2021.

TYPE: Original Research

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Siddhant Khare, Department of General Surgery, Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh, 160012, India.
Email: khare.siddhant@gmail.com

Introduction

Breast cancer is the commonest cancer in India, constituting 14% of all new cancers and 27.7% of all new cancers occurring in women in 2018.[1] The incidence of breast cancer in Chandigarh is 37.5 per 100 000, being among the highest in the country.[2] The prevalence of metabolic syndrome (MetS) in Chandigarh is 59.6% in females and 40.4% in males.[3] Moreover, in women, this prevalence increases with age, being 52.4% in age group of 45 to 48 years and 73.1% in age group of 53 to 55 years.[4]

Many studies have correlated MetS and its associated derangements with different aspects of breast cancer, viz. pathological status, adverse factors like advanced stage at presentation, higher grade, triple negativity, HER2Neu positivity, types of tumours, and mammographic density and found that MetS may predispose to breast cancer especially in postmenopausal patients and may also lead to worse prognosis than in patients without MetS (No MetS).[5–17] In India, there has been only one study that has looked into the correlation between breast cancer and MetS,[18] and in this study, the analysis was done on patients who have already been treated and were under follow-up.

There is also significant evidence which suggest a poorer prognosis in patients who gain weight after the diagnosis of breast cancer. In a study done in Columbia University, women who gained weight more than 10% after diagnosis had worse survival (hazard ratio [HR] = 2.67; 95% confidence interval [CI] = [1.37, 5.05]) than women who maintained their prediagnosis weight.[19] This effect was more pronounced during the first 2 years after diagnosis (>5% gain, all-cause mortality in the first 2 years, HR = 5.87 [0.89, 47.8] when compared with after 2 years (1.49 [0.85, 2.57]). This was further confirmed in a meta-analysis which included 12 studies, and the results confirmed that a weight gain of ⩾5.0% compared with maintenance was associated with increased all-cause mortality with a significant HR of 1.12.[20]

We propose that the patients with MetS and breast cancer have tumours with poor prognosis in terms of the standard clinicopathological prognostic factors. This observational study was undertaken to prove/disprove this hypothesis.

Materials and Methods

This study prospectively recruited 305 consecutive patients, who attended the outpatient of the Department of General

Surgery, PGIMER, Chandigarh and whose biopsy results came out between August 1, 2016 and June 30, 2017. Female patients with biopsy-proven, treatment-naïve invasive breast cancer, willing to participate in the study, were included.

All patients underwent complete clinical examination, relevant investigations, and treatment as per stage of the disease. The treatment plan was not changed because of the study.

Patients underwent assessment of central obesity (body mass index [BMI] and waist circumference [WC]) and blood pressure (BP) measurement, and fasting bloods were drawn for blood sugar (FBS), high-density lipoprotein (HDL) cholesterol, and triglycerides (TG). International Diabetes Federation consensus statement 2006 criteria to define MetS in south Asian females is WC $\geq$ 80 cm with any 2 of raised TG ($\geq$150 mg/dL or any specific treatment for this lipid abnormality), low HDL($<$40 mg/dL or any specific treatment for this lipid abnormality), raised BP (systolic $\geq$ 130 mm Hg, diastolic $\geq$ 85 mm Hg or treatment of previously diagnosed hypertension), raised fasting plasma blood glucose (fasting plasma glucose $\geq$ 100 mg/dL or previously diagnosed type-2 diabetes).[21] Based on this definition, patients were classified into 2 groups:

- Those with MetS.
- Those without MetS (No MetS).

All patients were assessed for the presence of risk factors associated with breast cancer – age at menarche, age at first childbirth (FCB), breastfeeding, and the presence of family history of breast cancer. Menopause was defined as amenorrhea for more than 1 year or history of prior bilateral oophorectomy. Early menarche was defined as onset of menses before the age of 12 years. Late FCB was defined as FCB after the age of 30 years. Late menopause was defined as menopause after the age of 55 years.

All patients underwent a mammogram as part of diagnostic work up. Breast density was defined according to ACR's BI-RADS density classes A to D. Fully automated analysis of breast density was done using Volpra Software (v1.4.5, Matakina Technology Ltd, Wellington, New Zealand).[22]

Clinical stage, type and grade of tumour, hormone receptor status, HER2 status, and Ki67 index were recorded. Estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki67 results were reported as assessed by immunohistochemistry (IHC). All patients with HER2 result of 2+ on IHC were subjected to fluorescence in situ hybridization (FISH) for confirmation and final classification. Based on the IMPAKT working group statement, the patients were then classified into Luminal-A (LA), Luminal-B (LB), HER2-enriched (HE), and Basal-like (BL) subtypes.[23]

Written informed consent was obtained from all patients at enrolment. The trial was done in accordance with the Good Clinical Practice guidelines and the Declaration of Helsinki. The study protocol was approved by the Institutional Ethics Committee.

Statistical analysis

Statistical analysis was done using SPSS version 13. K-S test was used to check the normality of the data. Student's *t*-test was used for comparison between normally distributed data, whereas for skewed data, Mann-Whitney *U*-test was used. For nominal data chi-square test or Fisher exact test (whichever was applicable) was used.

Results

A total of 305 patients were recruited in the study. The overall mean age was 50.7 $\pm$ 12.4 (range: 20-84) years. Out of these 305, 196 (64.3%) patients had MetS, whereas 109 (35.7%) did not. There were 131 (42.9%) premenopausal and 174 (57.1%) postmenopausal women. Seventy-four (56.5%) premenopausal and 122 (70.1%) postmenopausal women had MetS (P = .014).

The mean BMI in the study was 27.2 $\pm$ 5.4 kg/m^2, mean WC was 91.2 $\pm$ 11.2 cm, mean TG was 140.1 $\pm$ 66.7 mg/dL, mean of HDL cholesterol was 48.7 $\pm$ 11.1 mg/dL, mean systolic BP was 132.2 $\pm$ 21.7 mm Hg, mean diastolic BP was 81.6 $\pm$ 11.9 mm Hg, and mean FBS was 104 $\pm$ 22.1 mg/dL. There were 26.2%, 80.9%, 39.7%, 63.3%, 57.4%, and 50.2% subjects in the study in whom BMI, WC, TG, HDL cholesterol, Systolic BP, Diastolic BP, and FBS were deranged, respectively. The distribution of diagnostic parameters of MetS in the 2 groups is shown in Table 1. Although the patients in Group II did not meet the diagnostic criteria for MetS, the individual parameters were deranged in a variable number of patients. In group-II, there were only 11 patients (11.9%) who had no abnormal parameter. All diagnostic parameters except WC and hypertension were evenly distributed in both premenopausal and postmenopausal women. Waist circumference higher than cutoff limit of 80 cm was found more commonly in postmenopausal patients (77.8% vs 92.5%, $P < .001$), as was the presence of hypertension (45.8% vs 66.1%, $P < .001$).

Correlation between MetS and risk factors

Patients with MetS were significantly older than those without MetS (52.1 vs 48.3 years, P = .014). There was a significantly lower incidence of nulliparity in patients with MetS (4.1% vs 12.8%, P = .005). The groups were also not equal in terms of parity (P = .032). The rest of the risk factors were evenly distributed in both groups (Table 2). The distribution of the risk factors associated with breast cancer according to the menstrual status is shown in Table 3. On dividing the populations into premenopausal and postmenopausal, the age difference was noted only in premenopausal populations (42.6 $\pm$ 7.9 in MetS vs 38.8 $\pm$ 7.1 years in no MetS, P = .004). There was also a statistically significant difference in premenopausal population in terms of positive family history (6.8% in MetS vs 17.8% in no MetS, P = .049).

The no MetS group had a statistically significant higher incidence of dense breasts when compared to MetS group

Table 1. Distribution of diagnostic parameters of MetS in study population.

DIAGNOSTIC PARAMETER	METS (N = 196)	NO METS[a] (N = 109)
BMI > 30 kg/m²	70 (35.7%)	10 (9.2%)
Waist circumference ⩾ 80 cm	196 (100%)	67 (61.5%)
Triglycerides ⩾ 150 mg/dL	112 (57.1%)	9 (8.3%)
HDL cholesterol < 50 mg/dL	154 (78.6%)	39 (35.8%)
Systolic BP ⩾ 130 mm Hg or diastolic BP ⩾ 85 mm Hg	154 (78.6%)	21 (19.3%)
Fasting plasma glucose (⩾100 mg/dL)	129 (65.8%)	24 (22%)

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; MetS, metabolic syndrome.
[a]Thirteen patients (11.9%) of no MetS group had no abnormality in any parameter.

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

	METS (N = 196)	NO METS (N = 109)	*P* VALUE
Age	52.1 ± 11.3	48.3 ± 13.8	**.014**
Age at menarche	14.6 ± 1.5	14.5 ± 1.4	.158
Early menarche (<13 years)	1 (0.5%)	0	1.000
Late menopause (>50 years)	1 (0.5%)	1 (0.9%)	1.000
Age at FCB	23.0 ± 3.8	23.4 ± 3.4	.313
Late FCB (>30 years)	6 (3.1%)	3 (2.7%)	1.000
Parity			**.032**
0	8 (4.1%)	14 (12.8%)	
1	16 (8.2%)	11 (10.1%)	
2	87 (44.4%)	44 (40.4%)	
>2	85 (43.3%)	40 (36.7%)	
Nulliparous	8 (4.1%)	14 (12.8%)	**.005**
No breastfeeding	2 (1.0%)	1 (0.9%)	1.000
Positive family history	14 (7.1%)	12 (11.0%)	.247

Abbreviations: FCB, first childbirth; MetS, metabolic syndrome.
Bold value indicate the parameters with significant *p* values.

(10.8% in no MetS vs 2.9% in MetS group, *P* = .009). When divided according to menopausal status, this difference remained significant only in premenopausal patients (17% in no MetS in premenopausal vs 4.3% in MetS in premenopausal, *P* = .022; Tables 4 and 5).

Correlation between MetS and prognostic factors

Patients with MetS were found to be less likely to have HER2-positive tumours (14.3% for MetS, 23.9% for no MetS; *P* = .036). Apart from HER2 positivity, no difference was observed between the 2 groups in terms of other prognostic factors. However, when the patients were divided into premenopausal and postmenopausal, significant differences were observed in distant metastases (5.4% in MetS vs 16.1% in no MetS, *P* = .045) and in grade (higher grade in MetS, *P* = .05) in premenopausal patients. In postmenopausal patients, significant difference was observed in HER2 positivity (12.3% in MetS vs 28.8% in no MetS, *P* = .008) and molecular subtype (lower HE in MetS, *P* = .034; Tables 6 and 7).

Distribution of diagnostic parameters of MetS according to molecular subtype of breast cancer

There was no diagnostic parameter of MetS that was significantly different among the molecular subtypes.

Table 3. Distribution of risk factors associated with breast cancer in the 2 groups according to menstrual status.

	PREMENOPAUSAL (N = 131)			POSTMENOPAUSAL (N = 174)		
	METS (N = 74)	NO METS (N = 57)	*P* VALUE	METS (N = 122)	NO METS (N = 52)	*P* VALUE
Age	42.6 ± 7.9	38.8 ± 7.1	**.004**	57.9 ± 9.0	58.5 ± 11.9	.703
Age at menarche	14.2 ± 1.3	14.2 ± 1.3	.989	14.8 ± 1.5	14.5 ± 1.4	.201
Early menarche	0	0		1 (0.8%)	0	1.000
Age at FCB	23.6 ± 3.6	23.9 ± 3.9	.429	22.8 ± 4.1	22.8 ± 2.7	.557
Parity			.209			.407
0	5 (6.8%)	10 (17.5%)		3 (2.5%)	4 (7.7%)	
1	10 (13.5%)	9 (15.8%)		6 (4.9%)	2 (3.8%)	
2	38 (51.4%)	22 (38.6%)		49 (40.2%)	22 (42.3%)	
>2	21 (28.3%)	16 (28.1%)		64 (52.4%)	24 (46.2%)	
Nulliparous	5 (6.8%)	10 (17.5%)	.055	3 (2.5%)	4 (7.7%)	.108
Late FCB	2 (2.7%)	2 (3.5%)	1.000	4 (3.3%)	1 (1.9%)	1.000
No breastfeeding	1 (1.4%)	0	1.000	1 (0.8%)	1 (1.9%)	.496
Late menopause	1 (1.4%)	1 (1.8%)	1.000	–	–	–
Positive family history	5 (6.8%)	10 (17.5%)	.049	10 (8.2%)	3 (5.8%)	.757

Abbreviations: FCB, first childbirth, MetS, metabolic syndrome.

Table 4. Distribution of breast density in the 2 groups.*

	METS (N = 196)	NO METS (N = 109)	*P* VALUE
Breast density			.125
ACR A	27 (15.8%)	12 (12.9%)	
ACR B	101 (59.1%)	51 (54.8%)	
ACR C	38 (22.2%)	20 (21.5%)	
ACR D	5 (2.9%)	10 (10.8%)	
Dense breasts (ACR D)	5 (2.9%)	10 (10.8%)	.009

Abbreviations: ACR, American College of Radiology; MetS, metabolic syndrome. *Some data were missing as some of the mammograms were done outside of PGI. Percentage in brackets is derived as percentage from available data.

Discussion

Both breast cancer and MetS are a common occurrence in the increasingly urbanizing populations. It is also well accepted that MetS and increase in body weight after diagnosis leads to a poorer outcome in breast cancer patients. Whether it happens because the disease in patients with MetS is inherently different from those without MetS is unclear. This study was undertaken to find whether there was any difference in the patients having breast cancer and co-existing MetS when compared to patients having breast cancer but no co-existing MetS, in terms of the known risk and prognostic factors of breast cancer.

We found a few significant differences in the risk factors of breast cancer in the MetS versus the no MetS group. The patients with MetS were older, had higher parities with lesser incidence of nulliparity and had lesser incidence of dense breasts on mammography (ACR D). The higher parity and lower incidence of nulliparity in MetS may reflect one of the mechanisms that contribute towards the increased risk of breast cancer in MetS patients. However, the lesser incidence of dense breasts may just be because of the younger population in no MetS group and may not reflect the decreased risk attributable to denser breasts. This finding also goes in concordance to the findings in the studies by Conray et al[8] and Tehranifar et al[9] of a lower breast density in patients with MetS when compared to patients without MetS.

When we further subdivided our groups into premenopausal and postmenopausal, we found that all the differences were lost

Table 5. Distribution of breast density in the 2 groups according to menstrual status.*

	PREMENOPAUSAL (N = 131)			POSTMENOPAUSAL (N = 174)		
	METS (N = 74)	NO METS (N = 57)	*P* VALUE	METS (N = 122)	NO METS (N = 52)	*P* VALUE
Breast density			.057			.756
ACR A	6 (8.7%)	5 (10.6%)		21 (20.6%)	7 (15.2%)	
ACR B	41 (59.4%)	23 (48.9%)		60 (58.8%)	28 (60.9%)	
ACR C	19 (27.5%)	11 (23.4%)		19 (18.6%)	9 (19.6%)	
ACR D	3 (4.3%)	8 (17.0%)		2 (1.9%)	2 (4.3%)	
Dense breasts (ACR D)	3 (4.3%)	8 (17.0%)	**.022**	2 (1.9%)	2 (4.3%)	.407

Abbreviations: ACR, American College of Radiology; MetS, metabolic syndrome. *Some data were missing as some of the mammograms were done outside of PGI.
Percentage in brackets is derived as percentage from available data.
Bold value indicate the parameters with significant *p* values.

Table 6. Distribution of the prognostic factors of breast cancer in the 2 groups.

	METS (N = 196)	NO METS (N = 109)	*P* VALUE
Staging			.250
I	21 (10.7%)	11 (10.1%)	
II	109 (55.6%)	63 (57.8%)	
III	52 (26.6%)	21 (19.3%)	
IV	14 (7.1%)	14 (12.8%)	
Type of tumour			.960
IDC	173 (88.3%)	96 (88.1%)	
Non-IDC	23 (11.7%)	13 (11.9%)	
Grade			.445
I	39 (19.9%)	19 (17.4%)	
II	77 (39.3%)	51 (46.8%)	
III	80 (40.8%)	39 (35.8%)	
Hormone receptor positive	130 (66.3%)	65 (59.6%)	.243
HER2Neu positive	28 (14.3%)	26 (23.9%)	**.036**
Low Ki67 (<14%)	62 (31.6%)	27 (24.8%)	.206
Ki67 (mean ± SD)	26.5 ± 19.8	26.7 ± 17.5	.923
Molecular subtype			.057
LA	38 (19.4%)	15 (13.8%)	
LB	92 (46.9%)	50 (45.9%)	
HE	6 (3.1%)	11 (10.1%)	
BL	60 (30.6%)	33 (30.2%)	
Presence of distant metastases	14 (7.1%)	14 (12.8%)	.096
Visceral metastases	10 (71.4%)	8 (57.1%)	.430

Abbreviations: BL, Basal like; HE, HER2 enriched; LA, Luminal A; LB, Luminal B; SD, standard deviation; MetS, metabolic syndrome.
Bold value indicate the parameters with significant *p* values.

in postmenopausal patients, and even in premenopausal patients, significant differences between MetS and no MetS were found only in age (older in MetS) and family history (higher incidence of positive family history in no MetS group). This finding again suggests that if the disease between MetS and no MetS is different, it is probably not related to the difference in risk factors.

Table 7. Distribution of prognostic factors of breast cancer in the 2 groups according to menstrual status.

	PREMENOPAUSAL (N = 131)			POSTMENOPAUSAL (N = 174)		
	METS (N = 74)	NO METS (N = 57)	*P* VALUE	METS (N = 122)	NO METS (N = 52)	*P* VALUE
Staging			.203			.744
I	5 (6.8%)	5 (8.8%)		16 (13.1%)	6 (11.5%)	
II	45 (60.8%)	32 (56.1%)		64 (52.5%)	31 (59.6%)	
III	20 (27.0%)	11 (19.3%)		32 (26.2%)	10 (19.2%)	
IV	4 (5.4%)	9 (15.8%)		10 (8.2%)	5 (9.6%)	
Type			.273			.305
IDC	67 (90.5%)	48 (84.2%)		106 (86.9%)	48 (92.3%)	
Non-IDC	7 (9.5%)	9 (15.8%)		16 (13.1%)	4 (7.7%)	
Grade			**.05**			.298
I	11 (14.9%)	12 (21.1%)		28 (23.0%)	7 (13.5%)	
II	28 (37.8%)	30 (52.6%)		49 (40.2%)	21 (40.4%)	
III	35 (47.3%)	15 (26.3%)		45 (36.9%)	24 (46.2%)	
Hormone receptor positive	55 (74.3%)	38 (66.7%)	.338	75 (61.5%)	27 (51.9%)	.242
HER2Neu positive	13 (17.6%)	11 (19.3%)	.800	15 (12.3%)	15 (28.8%)	**.008**
Low Ki67	23 (31.1%)	13 (22.8%)	.293	39 (32.0%)	14 (26.9%)	.508
Ki67 (mean ± SD)	26 ± 20.0	27.4 ± 18.2	.687	26.7 ± 19.8	25.9 ± 16.8	.795
Molecular subtype			.613			**.034**
LA	12 (16.2%)	10 (17.5%)		26 (21.3%)	5 (9.6%)	
LB	43 (58.1%)	28 (49.1%)		49 (40.2%)	22 (42.3%)	
HE	3 (4.1%)	5 (8.8%)		3 (2.5%)	6 (11.5%)	
BL	16 (21.6%)	14 (24.6%)		44 (36.1%)	19 (36.5%)	
Distant metastases	4 (5.4%)	9 (16.1%)	**.045**	10 (8.3%)	5 (9.6%)	.773
Visceral MetS	3 (75%)	5 (55.6%)	.506	7 (70%)	3 (60%)	.699

Abbreviations: BL, basal like; HE, HER2 enriched; LA, luminal A; LB, luminal B; SD, standard deviation; MetS, metabolic syndrome.
Bold value indicate the parameters with significant *p* values.

There were also very few differences in the known prognostic factors of breast cancer. Apart from the HER2 positivity (lower in MetS), there were no significant differences between the MetS and no MetS groups. This result was almost identical to the results shown by Can et al[15] where they found no statistically significant difference in patients with MetS or no MetS in terms of size of tumour, axillary lymph node (LN) MetS, distant MetS, grade, ER, PR, and HER2 status.

After subdivision into premenopausal and postmenopausal, no difference was noted in the hormone receptor positivity in the 2 groups. Premenopausal patients having MetS had a higher number of Grade-3 tumours (despite a higher mean age in MetS group) but a lesser incidence of distant metastases. The higher grade of tumours was in concordance to the prevailing wisdom of poorer outcomes in MetS patients. On the contrary, postmenopausal patients with MetS had less chances of having HER2-positive tumours and HE molecular subtype and higher chances of having a luminal A type of disease. These observations lead us to believe that the mechanism involved in poorer prognosis of breast cancer in premenopausal MetS patients may be related to higher incidence of Grade-3 tumours but is different from the known prognostic factors in postmenopausal women.

If we look at Table 1, we can find that even in patients with no MetS, there were significant numbers of patients in whom one or more diagnostic parameters for defining MetS was deranged. In fact, there were only 13 (11.9%) patients in no MetS group that had no abnormality in these parameters. We usually assume that the difference in risk and prognosis in MetS versus No MetS is cumulative of all the individual

parameters. This may be one of the reasons that we could not identify significant difference between the MetS and No MetS group. A larger study especially that compares patients with no abnormality in any parameters to patients with MetS might be able to give a better perspective on this problem.

It is now well accepted that there is a positive correlation between MetS and the development of breast cancer. A meta-analysis published in 2014[24] had shown that women with MetS had a relative risk of 1.47 of developing breast cancer when compared to women without MetS, although, in this meta-analysis, little stress was given on the individual parameters defining the MetS. And although, our study was not designed to give us any information with regard to the increased risk of breast cancer conferred by MetS, there were a higher number of breast cancer patients who had MetS than those who did not. This may suggest an increased risk conferred by MetS to breast cancer or may just indicate the overall prevalence of MetS in the populations these patients come from.

It can be concluded from the findings of this study that we were not able prove our hypothesis that the breast cancer in patients with MetS is different from breast cancer in patients without MetS in terms of standard clinico-pathologic risk and prognostic factors.

Conclusions

Breast cancer in patients with MetS may not be significantly different from breast cancer in patients without MetS.

Author's Note

This work was presented at the ESMO Congress, 2018, Munich, Germany.

Author Contributions

The roles of the authors are as follows: conceptualization, supervision, and methodology: G.S.; formal analysis and investigation and writing – original draft preparation: S.K.; writing – review and editing: S.I., Y.R.S., A.B., T.S., and G.S.

Ethical Approval

The study was carried after approval from the institutional (PGIMER, Chandigarh) ethics committee. The study was performed in accordance with the ethical standards of the institution and national research committee (Indian Council of Medical Research Guidelines 2017) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

ORCID iD

Siddhant Khare https://orcid.org/0000-0001-9142-1115

REFERENCES

1. Globocan 2018: India factsheet. India Against Cancer. http://cancerindia.org.in/globocan-2018-india-factsheet/. Updated 2020. Accessed 15 March 2020.
2. Thakur JS, Budukh A, Kapoor R, et al. Urban–rural differences in cancer incidence and pattern in Punjab and Chandigarh: findings from four new population-based cancer registries in North India. *Int J Non-Commun Dis*. 2017;2:49-55. doi:10.4103/jncd.jncd_11_17.
3. Mangat C, Goel NK, Walia DK, et al. Metabolic syndrome: a challenging health Issue in highly urbanized Union Territory of north India. *Diabetol Metab Syndr*. 2010;2:19-27. doi:10.1186/1758-5996.
4. Sharma S, Aggarwal N, Joshi B, Suri V, Badada S. Prevalence of metabolic syndrome in pre- and post-menopausal women: a prospective study from apex institute of North India. *J Midlife Health*. 2016;7:169-174. doi:10.4103/0976-7800.195695.
5. Sinagra D, Amato C, Scarpilta AM, et al. Metabolic syndrome and breast cancer risk. *Eur Rev Med Pharmacol Sci*. 2002;6:55-59.
6. Iversen A, Thune I, McTiernan A, et al. Ovarian hormones and reproductive risk factors for breast cancer in premenopausal women: the Norwegian EBBA-I study. *Hum Reprod*. 2011;26:1519-1529. doi:10.1093/humrep/der081.
7. Agnoli C, Berrino F, Abagnato CA, et al. Metabolic syndrome and postmenopausal breast cancer in the ORDET cohort: a nested case control study. *Nutr Met Cardiovasc Dis*. 2010;20:41-48. doi:10.1016/j.numecd.2009.02.006.
8. Conroy S, Butler L, Harvey D, et al. Metabolic syndrome and mammographic density: the study of women's health across the nation. *Int J Cancer*. 2011;129:1699-1707. doi:10.1158/1940-6207.
9. Tehranifar P, Reynolds D, Fan X, et al. Multiple metabolic risk factors and mammographic breast density. *Ann Epidemiol*. 2014;24:479-483. doi:10.1016/j.annepidem.2014.02.011.
10. Kim B, Chang Y, Ahn J, et al. Metabolic syndrome, insulin resistance, and mammographic density in pre- and postmenopausal women. *Breast Cancer Res Treat*. 2015;153:425-434. doi:10.1007/s10549-015.
11. Tehranifar P, Protacio A, Schmitt K, et al. The metabolic syndrome and mammographic breast density in a racially diverse and predominantly immigrant sample of women. *Cancer Causes Control*. 2015;26:1393-1403. doi:10.1007/s10552-015.
12. Healy L, Ryan A, Carroll P, et al. Metabolic syndrome, central obesity and insulin resistance are associated with adverse pathological features in postmenopausal breast cancer. *Clin Oncol*. 2010;22:281-288. doi:10.1016/j.clon.2010.02.001.
13. Maiti B, Kundranda M, Spiro T, Daw H. The association of metabolic syndrome with triple-negative breast cancer. *Breast Cancer Res Treat*. 2009;121:479-483. doi:10.1007/s10549-009.
14. Agresti R, Meneghini E, Baili P, et al. Association of adiposity, dysmetabolisms, and inflammation with aggressive breast cancer subtypes: a cross-sectional study. *Breast Cancer Res Treat*. 2016;157:179-189. doi:10.1007/s10549-016.
15. Can A, Alacacioglu A, Kucukzeybek Y, et al. The relationship of insulin resistance and metabolic breast cancer prognostic factors in postmenopausal breast cancer patients. *J Buon*. 2013;18:845-850.
16. Calip G, Malone K, Gralow J, Stergachis A, Hubbard R, Boudreau D. Metabolic syndrome and outcomes following early-stage breast cancer. *Breast Cancer Res Treat*. 2014;148:363-377. doi:10.1007/s10549-014.
17. Fan Y, Ding X, Wang J, et al. Decreased serum HDL at initial diagnosis correlates with worse outcomes for triple-negative breast cancer but not non-TNBCs. *Int J Biol Markers*. 2015;30:e200-e207. doi:10.5301/jbm.5000143.
18. Kate A, Kadambari D. Incidence of metabolic syndrome in breast cancer survivors on adjuvant hormonal therapy. *J Pharmacol Pharmacother*. 2016;7:28-30. doi:10.4103/0976-500X.179362.
19. Bradshaw P, Ibrahim J, Stevens J, et al. Postdiagnosis change in bodyweight and survival after breast cancer diagnosis. *Epidemiology*. 2012;23:320-327. doi:10.1097/EDE.0b013e31824596a1.
20. Playdon M, Bracken M, Sanft T, Ligibel J, Harrigan M, Irwin M. Weight gain after breast cancer diagnosis and all-cause mortality: systematic review and meta-analysis. *J Natl Cancer Inst*. 2015;107:djv275. doi:10.1093/jnci/djv275.
21. Alberti Zimmet P, Shaw J. Metabolic syndrome – a new world-wide definition. *Diabet Med*. 2006;23:469-480. doi:10.1111/j.1464-5491.2006.01858.x.
22. Jeffers A, Sieh W, Lipson J, et al. Breast cancer risk and mammographic density assessed with semiautomated and fully automated methods and BI-RADS. *Radiology*. 2017;282:348-355. doi:10.1148/radiol.2016152062.
23. Guiu S, Michiels S, Andre F, et al. Molecular subclasses of breast cancer: how do we define them? The IMPAKT 2012 Working Group Statement. *Ann Oncol*. 2012;23:2997-3006. doi:10.1093/annonc/mds586.
24. Bhandari R, Kelley G, Hartley T, Rockett I. Metabolic syndrome is associated with increased breast cancer risk: a systematic review with meta-analysis. *Int J Breast Cancer*. 2014;2014:189384. doi:10.1155/2014/189384.