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Original Article

Correlation between Tumor Size and Stage of Tumor among Different Body Mass Index Categories in Females with Breast Cancer

Aveen Yousuf, Ghulam Haider, Neelma Bukhari, Maryum Nouman

Department of Medical Oncology, Jinnah Postgraduate Medical Centre, Karachi Pakistan

ABSTRACT

Objective: To assess the correlation between tumor size and stage of tumor among BMI categories in females presenting with breast cancer at a tertiary care hospital of Karachi.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Medical Oncology, Jinnah Postgraduate Medical Center, Karachi Pakistan, from Nov 2018 to Dec 2019.

Methodology: One eighty-seven women presenting with histologically proven breast carcinoma of age more than 20 years were included. Body Mass Index was estimated by dividing weight in kilogram with height in meter square (BMI= Weight/Height kg/m^2). The data regarding histological type and grade, stage of tumor, tumor size, lymph node status, hormone receptor status and menopausal status were also collected.

Results: On comparing body mass index categories with clinic-pathological factors; menopausal status, ER status, PR status, HER 2/Neu status and lymph node status showed statistically significant difference between groups (p<0.05). Underweight patients showed very strong correlation between stage and tumor size (r=0.894), whereas obese (r=0.678) and normal weight (r=0.676) females showed strong correlation between stage and tumor size.

Conclusion: In conclusion, the present study reveals that body mass index is significantly associated with menopausal status, ER status, PR status, HER 2/Neu status and lymph node status. Though obesity is a modifiable factor which carries risk of developing fatal diseases, data relevant to obesity and breast cancer outcomes is still erratic. We further recommend more in-depth study in this context.

Keywords: Body mass index, Breast cancer, Menopausal status, Obese, Overweight.

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INTRODUCTION

Obesity has been tripled since 1975 and has become the major health concern worldwide.[1,2] More than 1.9 billion people were overweight and, among them, more than 650 million were obese, according to estimates from the WHO for 2016.[2] Pakistan ranks 19th out of 188 countries for raising the prevalence of obesity, accounting for 26% of females, and is higher in urban areas than in rural areas.[3-5] Obesity is recognized as an increase in BMI >28kg/m^2. Raised BMI is one of the risk factors for certain cancers, one of which is breast cancer.[2] Breast cancer remains common in female malignancy, and being obese and overweight increases the risk of breast cancer among females. In addition to its proven position as a risk factor, the significance of being overweight or obese as a harmful prognostic factor for BC is now widely recognized.[6]

The high BMI also moderately increases the odds of postmenopausal breast cancer. Overweight postmenopausal women have a 10-20% higher risk of breast cancer comparative to thin females, while obese postmenopausal women have a 30% higher risk. Females with a BMI of <22.5kg/m^2 have a risk reduction of 15% compared to women with a BMI of 22.5-24.9 kg/m^2. Whereas obese premenopausal mothers, on the other side, reduce the risk of cancer by 20%.[7] Pakistan has the largest breast cancer incidence in Asia. Breast cancer impacts Pakistani young women more than Western nations. According to recent research, in 2017 there were 34,038-90,000 new cases of breast cancer and 16,232 breast cancer related deaths in Pakistan occurred.[8] Wide variety of epidemiological studies have confirmed the association between breast cancer and body weight. Though, discrepancies in the statistics propose that association between obesity and breast cancer remains inadequately understood. The discrepancies exist at population level for incident disease risk, clinical manifestations of the disease at diagnosis and on disease prognosis and outcomes. In breast cancer, there is increased number of tumor necrosis factor–alpha that is linked to increase in tumor size and stage.[9]

Correspondence: Dr Aveen Yousuf, House No. B-20, Sector-Y1, Ghulshan-e-Maymar, Karachi, Pakistan

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Breast cancer is highly prevalent in overweight and obese women and is related to increase tumor grading and staging. The obese women are more likely to have aggressive tumor with large tumor size in contrast to normal to underweight women. Moreover, menopausal status has also proven to increase body mass index but it's still controversial.[10] However, correlation between them still needs evidence. A very limited work has been conducted in Pakistan to assess the correlation between tumor grading and staging and body mass index among females presenting with breast cancer at a tertiary care hospital of Karachi. Majority of females are overweight in Pakistan especially married women. It is very crucial to find out correlation which would help in better management and prognosis of the disease by spreading awareness and reducing obesity in Pakistan.

METHODOLOGY

The cross-sectional study was conducted at the Department of Medical Oncology, Jinnah Postgraduate Medical Center, Karachi Pakistank, from November 2018-December 2019. Sample size was estimated using frequency of BMI 25-30 kg/m^2 as 38%,[11] of females with BC, absolute precision as 7% and 95% confidence level, the calculated sample size came out as 185≈187.

Inclusion Criteria: All women presenting with histologically proven breast carcinoma of age >20 years were included.

Exclusion Criteria: Women who underwent hysterectomy or artificial menopause, bilateral BC and females reporting menopause induced by chemot-herapy (as aggressive multiple sclerosis and can also result in menopause) were excluded from the study.

The ethical approval (No.F.2-81/2018-GENL/6883/JPMC was sought from ethical review committee before initiation of data collection. The written informed consent was obtained from all the eligible females after explaining the purpose of study. Pathological characteristics of the tumor was assessed using the WHO classification,[12] whereas staging of the tumor was assessed using AJCC TNM staging system.[13] The BMI was estimated by dividing weight in Kg with height in m^2 (BMI=Weight/Height kg/m^2). The estimated BMI was classified into four categories according to WHO criteria i.e. ≤18.5kg/m^2 as underweight, 18.5-25 kg/m^2 as normal, 25-30 kg/m^2 as overweight and ≥30kg/m^2 as obese.[14] The data regarding histological type and grade, stage of tumor, tumor size, lymph node status, hormone receptor (ER, PR, HER2/neu) status and menopausal status were also collected along with demographic data on pre-designed proforma by researcher herself.

SPSS 23 was used to analyze data. Mean and SD were computed for numeric data whereas frequency and percentage were computed for catego-rical and nominal data. Chi-square/Fisher exact test was used to see association of BMI categories with other factors. *p*-value≤0.05 will be taken as statistically significant.

RESULTS

In table-I, the mean age of the females was estimated as 44.29±11.50 years. Majority of the females

Table-I: Study Characteristic (n=187)

	Mean±SD
Age (years)	**44.29±11.50**
	n(%)
Ethnicity	
Sindh	62(33.2)
Punjabi	36(19.3)
Balochi	16(8.6)
Pakhtoon	5(2.7)
Urdu speaking	68(36.4)
Histological Subtype	
Invasive Ductal Carcinoma (IDC)	174 (93)
Invasive Lobular Carcinoma (ILC)	11(5.9)
Mucinous Carcinoma	1(0.5)
Leiomyosarcoma	1(0.5)
Grade	
I	12(6.4)
II	107(57.2)
III	68(36.4)
Stage	
I	34(18.2)
II	89(47.6)
III	44(23.5)
IV	20(10.7)

	Mean±SD
Tumor size	
T1	45(24.1)
T2	105(56.1)
T3	34(18.2)
T4	3(1.6)
Lymph Node Status	
No	17(9.1)
N1	70(37.4)
N2	86(46)
N3	14(7.5)
Estrogen Receptors Status	
+ve	128 (68.4)
-ve	59(31.6)
Progesterone Receptors Status	
+ve	136(72.7)
-ve	51(27.3)
HER 2-NEU	
+ve	102(54.5)
-ve	85(45.5)
Menopausal Status	
Premenopausal	112(59.9)
Postmenopausal	75(40.1)

were Urdu speaking 68(36.4%) followed by Sindhi 62(33.2%). Out of 187, 174 patients had IDC histological subtype (93%), 107 patients had grade 2 of tumor (57.2%), 89 had stage 2 of tumor (47.6%), 105 had T2 tumor size (56.1%) and 170 patients had lymph node positive (N1-N3) (90.9%). Of all patients, 128(68.4%), 136(72.7%), and 102(54.5%) were ER +ve, PR +ve, and HER2/Neu +ve, respectively. Out of 187 females about 59.9% were premenopausal.

The mean BMI was noted as 27.17±5.97 kg/m^2. Most of the females 82(44%) were obese. About 52 (28%) females had normal body mass index, 47 were overweight (25%) and 6 were underweight (3%).

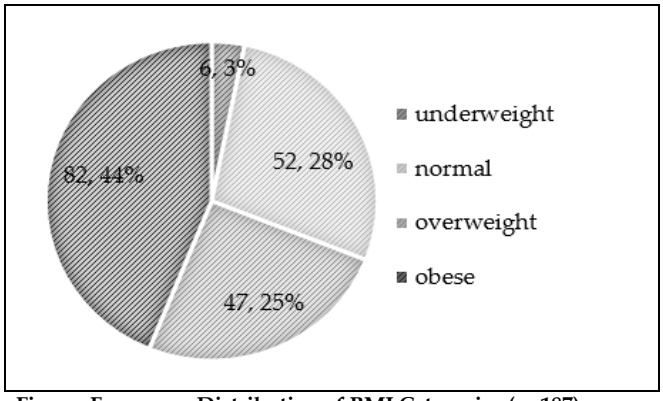

Figure: Frequency Distribution of BMI Categories (n=187)

In table-II, on comparing BMI categories with clinicopatho-logical factors; menopausal status (p= 0.04), ER status (p=0.011), PR status (p=0.004), HER 2/Neu status (p=0.002) and lymph node status (p= 0.001) showed statistically significant difference between groups.

In table-III, underweight patients showed very strong correlation between stage and tumor size (r= 0.894), whereas obese (r=0.678) and normal weight (r= 0.676) females showed strong correlation between stage and tumor size. In overweight females, weak correlation was found between stage and tumor size (r=0.303).

DISCUSSION

The present study results revealed that weight of women have great impact upon different clinico-pathological features of breast cancer. Most of the women in the present study were fond obese which validates the increase obesity in Pakistan.[3-5] The present study reveals that body mass index has significant impact on menopausal status of women. However, literature have revealed inconsistent results. Most of the literature favors that obese and post-menopausal women having breast cancer has significant association.[15-18] Cecchini RS *et al*. found that majority of the breast cancer women were found overweight and

Table-II: Association of BMI (Kg/m^2) with Menopausal Status and Clinicopathological Characteristics among Females with Breast Cancer (n=187)

	Under-weight (%)	Normal weight (%)	Over-weight (%)	Obese (%)	*p*-value
Menopausal Status					
Premenopausal	1(16.7)	37(71.2)	25(53.2)	49(59.8)	0.04
Postmenopausal	5(83.3)	15(28.8)	22(46.8)	33(40.2)	
Histological Grade					
I	0	1(1.9)	1(2.1)	10(12.2)	0.093
II	3(50)	33(63.5)	32(68.1)	39(47.6)	
III	3(50)	18(34.6)	14(29.8)	33(40.2)	
Histological Subtype					
Invasive ductal carcinoma (IDC)	6(100)	48(92.3)	45(95.7)	75(91.5)	0.673
Invasive lobular carcinoma (ILC)	0	4(7.7)	1(2.1)	6(7.3)	
Mucinous carcinoma	0	0	0	1(1.2)	
Leiomyosarcoma	0	0	1(2.1)	0	
Estrogen Receptors Status					
+ve	3(50)	27(51.9)	37(78.7)	61(74.4)	0.01
-ve	3(50)	25(48.1)	10(21.3)	21(25.6)	
Progesterone Receptors Status					
+ve	3(50)	29(55.8)	38(80.9)	66(80.5)	0.004
-ve	3(50)	23(44.2)	9(19.1)	16(19.5)	
HER 2/NEU					
+ve	4(66.7)	38(73.1)	27(57.4)	33(40.2)	0.002
-ve	2(33.3)	14(26.9)	20(42.6)	49(59.8)	
Stage of Tumor					
I	2(33.3)	9(17.3)	7(14.9)	16(18.2)	0.737
II	3(50)	29(55.8)	20(42.6)	37(45.1)	
III	1(16.7)	9(17.3)	12(25.5)	22(26.8)	
IV	0	5(9.6)	8(17)	7(8.5)	
Tumor Size					
T1	2(33.3)	13(25)	8(17)	22(26.8)	0.695
T2	4(66.7)	28(53.8)	31(66)	42(51.2)	
T3	0	9(17.3)	8(17)	17(20.7)	
T4	0	2(3.8)	0	1(1.2)	
Lymph Node Status					
No	0	4(7.7)	2(4.3)	11(13.4)	0.001
N1	2(33.3)	12(23.1)	29(61.7)	27(32.9)	
N2	4(66.7)	34(65.4)	15(31.9)	33(40.2)	
N3	0	2(3.8)	1(2.1)	11(13.4)	

Table-III: Correlation between Tumor Size and Stage of Tumor among BMI Categories (n=187)

BMI categories			Tumor size
Underweight	Stage	r	0.894*
		p-value	0.001
Normal	Stage	r	0.676*
		p-value	0.001
Overweight	Stage	r	0.303*
		p-value	0.019
Obese	Stage	r	0.678*
		p-value	0.001

obese with hazards ratio 1.07 (95% CI, 0.88–1.30) and 1.14 (95% CI, 0.94–1.38) respectively in comparision with women having normal body mass index.[19] In Pakistan, it was found that among 3998 breast cancer patients, 30% patients had BMI ranging between 25-29.9 kg/m^2 and 54.3% had were having BMI >30 kg/m^2.[20] In a study that emphasizes ascertaining potential factors of increasing risk of breast cancer also claimed that BMI >25kg/m^2 increase the risk of developing breast cancer by 1.6 times in individuals who are >50 years old.[21]

In a study, breast cancer patterns were observed and it was found that around quarter percent of the females who had breast cancer were obese.[22] In contrast to a study conducted by Qureshi SA, the mean BMI was noted as 25.87±5.29 kg/m^2. Most of the females (44.27%) were between the range of 23.1-30 kg/m^2. About 24.37% females had >30kg/m^2 BMI, 8.4% were underweight and 22.38% were normal.[23] Apart from obesity being the risk for breast cancer, one study found that females with raised body mass index were more likely to be associated with survival from breast cancer as compare to underweight females.[24] This might be due to the fact that underweight females had weak immune system and could be lacking some important mineral and vitamins required for proper functioning of the body.

According to the present study findings, ER/PR status is also a significant factor among different BMI categories. Munsell MF *et al*. also found similar results.[25]

CONCLUSION

The present study reveals that body mass index is significantly associated menopausal status, ER status, PR status, HER 2/Neu status and lymph node status (p=0.001). The underweight women had very strong correlation with stage and tumor size whereas obese and normal weight women had strong correlation with stage and tumor size. Though obesity carries risk of developing fatal diseases, data relevant to obesity and breast cancer outcomes is still erratic. We further recommend more in depth study in this context.

Conflict of Interest: None.

Author's Contribution:

Following authors have made substantial contributions to the manuscript as under:

AY & GH: Conception, study design, drafting the manuscript, approval of the final version to be published.

NB & MN: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

Authors 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.

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