SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 6.
Issue: 4.
Page N. 31-35
Year: 2022

Original Article www.wjahr.com

IMPACT OF BMI ON CLINICOPATHOLOGICAL PARAMETERS AMONG THE PATIENT WITH BREAST CANCER

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Received date: 02 February 2022 **Revised date:** 22 February 2022 **Accepted date:** 14 March 2022

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ABSTRACT

Background: Breast cancer is the second most common cancer in the world and by far the most frequent cancer among women with an estimated 1.67 million new cancer cases diagnosed in 2012 (25% of all cancers). Breast cancer allocated into Luminal, HER2 augmented and basal subtype according to immunohistochemically indicators like ER, PR and HER2/neu. High body mass index (BMI) associated with more aggressive tumor behavior and a poor prognosis. **Objective:** The goal of this study is to determine the impact of BMI on molecular subtypes defined by (ER), (PR), and (HER2/neu) expression, histopathological types, grade and stage of breast carcinoma in pre- and postmenopausal patients. **Method:** This study carried out on (70) cases of breast cancer. **Results:** no significant differences between BMI means according to immunohistochemistry of breast Cancer in perimenopause and postmenopausal. No significant association between histopathological subtypes, grade and stage of breast cancer and BMI among study sample. **Conclusions:** The obese patients constitute the largest percentage of women with breast carcinoma. Occurrence of large Percentage of invasive ductal carcinoma of (NOS) among the obese women.

KEYWORDS: body mass index (BMI), carcinoma of breast, ER, PR, HER2/neu.

INTRODUCTION

Breast cancer is the 2nd utmost communal malignancy wild world and most recurrent malignancy among women an assessed 1.7 million current patients diagnosed in 2012 (25% of all malignancies). It is the peak communal malignancy in females together in high and low developed republics with considerably high patients in fewer developed countries (883) thousand patients than in high developed countries (794) thousand.[1] Obesity has been found to increase risk of breast cancer in postmenopausal patients.[2]

The fact that the involvement of hormone receptors (estrogen and progesterone) in tumor tissues correlates well with the response to hormone therapy and chemotherapy has been a key advancement in the treatment of breast carcinoma.[3] Breast cancer allocated into Luminal, HER2 augmented and basal subtype according to immunohistochemically indicators like ER, PR and HER2/neu. High body mass index (BMI) associated with more aggressive tumor behavior and a poor prognosis. Therefore, there are little studies in relation of BMI and increase proliferation guide, histological status, and big size of malignancy and increase phase of diagnosis time.[4] The aim of study is to determine the impact of BMI on molecular subtypes defined by (ER), (PR), and (HER2/neu) expression, histopathological types, grade and stage of breast carcinoma in pre- and postmenopausal patients.

METHODS

This cross sectional study includes (70) cases of breast cancer collected from patients referred to the Marjan medical city hospital department of medical oncology in Babylon during the period from February to August 2019, 2020. The age of the patients ranged between (25-78) years. relevant data (demographic and clinical) were obtained by direct communication with the patients and from the file sheet questionnaire records. The studied parameters include age, stage of the disease, histological type, grade of breast cancer besides IHC description of ER, PR, HER2, those cases were randomly selected.

breast cancers were classified into five subtypes as follows: luminal A (ER+, PR+ or PR-, HER2-, and low Ki-67 index), luminal B (HER2 -) (ER+, PR+ or PR-, HER2-, and high Ki-67 index), Luminal B (HER2+) (ER+, PR+ or PR-, and HER2+), HER2 (ER-, PR-, and HER2+), and basal-like (ER-, PR-, And HER2-). BMI (Kg/m2) according to WHO; Underweight (<18.5), Normal (18.5-24.9), Overweight (25-29.9), Obese (≥ 30). Statistical analysis done by SPSS 22 frequency and percentage used for categorical data, mean and SD for continuous data. Chi-square used for assessed association between variables, ROC curve also used to show more specific and sensitive cutoff point. P-value less or equal to 0.05 is consider significant.

RESULTS

Mean age was (51.03 ± 13.38) and range was (25-78), mean BMI was (30.83 ± 5.86) and range was (18.0-46.0). (52.9%) of patients at age 40-60 years old. (61%) of females postmenopausal. (58.6%) of female are obese. (92.9%) of females are invasive lobular cell carcinoma. (58%) of females are in grade 2. And (64.3%) of females are in stage II. As in table (1).

In table 2; no significant difference in BMI of patients according to immunohistochemistry of breast cancer. In table 3; no significant difference in BMI of patients according to immunohistochemistry of breast cancer among premenopausal patients. In table 4; no significant difference in BMI of patients according to immunohistochemistry among premenopausal patients. In table 5; no significant difference in BMI of patients according to immunohistochemistry of breast cancer among premenopausal patients.

In table 5; no significant association between histopathological subtypes, grade and body mass index. In table 6; no significant association between stage of breast cancer and body mass index.

DISCUSSION

Breast cancer is the second most common cancer in the world and by far the most frequent .cancer among women (1)**.** In this study, the peak age frequency of breast cancer was displayed in middle. age women with mean age (51.03+13.38). These findings are in accordance with the Iraqi Cancer Registry (14) an and other studies performed in Iraq (5, 6, 7, 8). In current study bulky of patients (93%) associated with invasive ductal cancer of breast and (7.1%) was invasive lobular cancer this close to what was observed in the results of published research in Iraq and China (9,10). Mean BMI was (30.83+5.86) and range was (18.0-46.0) and the obese patients comprised 58.6% this agree. With results of Iraqi study at Erbil (11), and disagree with Indian that revealed .the mean BMI of 476 patients was 24.1 kg/m2 and the obese patients constituted 10% (12), which could be due to difference in .sample size, different life style and body activities. We find the Majority of patients presented with grade 2 (58.6%) and in stage II (64.28%),. which were In agreement. With the results of Iraqi (11, 13), current results were not agree with Indian study (14) that stated 68% in stage 1, 22% in stage 2 and 10% in stage 3. Regarding immunohistochemically profile of the molecular subtypes of breast cancer including (ER +and/or PR+ 22/70 (31%), ER +and/or PR+\Her2+ 29/70 (41%), human epidermal growth factor receptor-2 (HER2enriched) 7/70 (10%) and Triple negative 12/70 (17%). While *P*. Urmila Devi et al (2015).[14] In India, ER/PR that revealed the. Followings ER+/PR+/HER2 –ve: 9/31 (29%), ER-/PR-/HER2/neu +ve: 5/31 (16%), ER- /PR-/HER2-ve (Three-way negative): 17/31 (55%), and reported results by Sahar A Ahmed et al 2019[11] have. shown the most frequent type was. ER+/PR+/Her2- 35/74 followed by ER+/PR+/Her2+ 21/74, ER-/PR-/ Her2+ 5/74, triple negative 13/74. After the evaluation of the results of the menopausal status of the patients in recent study, they were in accordance with study on Iranian women, which revealed 3 fold increase of occurrence of breast carcinoma in postmenopausal obese women due to high level of estrogen in blood (15). Aromatase enzyme that play important role in conversion androstenedione to estrogen and testosterone to estradiol, this enzyme activate by interleukin-6 and tumor necrosis. factor-a, which are frequently abundant inside the adipose tissue.[16,17] High androgen level (estrogen and progesterone) contain mutagenic and morph genic effects on breast tissue 4, 18. In premenopausal females, these effects become very little because of increase baseline level. Despite The non-significant differences between means of BMI and molecular subtypes of breast cancer p value (>0.05%) in our. study, we detected increasing frequencies of luminal like (hormone receptors positive /Her2 –ve or +ve) tumours with increasing average of BMI to reach its peak in the obese and largest percentage of triple negative (ER-/PR-/Her2-) tumours (8 cases out of total 12 cases) was among the obese patients, this in agree with Iranian study in which differences between. three subtypes of breast cancers (luminal like, HER2enriched and Triple negative were not statistically significant. In contrast to our study the proportion of obese Iranian. Women was higher in triple-negative. group which comprised (35.3%) of total 374 patients[15], so the sample size difference might explain the. variety in these results. In our study there was no significant association between immunohistochemically profile (molecular subtypes) and BMI in postmenopausal women and in premenopausal p value (>0.05%). this was in agree with results of Iraqi study and Turkish in Ankrah[11,18] While other study in India[12] detected a significant. correlation between mean BMI and molecular. subtypes of breast cancer, this difference could be attributed to difference in the size of sample. In this study, we also observed no significant association between histopathological subtypes and body mass index this in agree with study in US that stated the absence of significant association between BMI and danger of cancer according to subtype[19], in current study detected

large percentage of invasive ductal carcinoma of (NOS) among the obese women. BMI was further powerfully relate with ductal cancer when compared with lobular cancer[8], an inverse relationship between BMI and mixed cancer of ductal-lobular with no significant relations for the other subtypes.[7] There was no significant association between, grade and body mass index among studied sample. These finding are consistent with study in western china[10], they recorded no significant correlation of mean BMI with the tumor grade in both premenopausal and postmenopausal patients and disagree with Nihad et al study in Jordan, which showed Grade of carcinoma was. Significantly correlated with BMI in the whole population examined (P=0.003).[20] Regarding the stage, our study disclose an independent relationship between BMI and stage of breast carcinoma P=0.778, which agree with study in Morroco that had been included 481 patients and., reported no influence of BMI on the tumor stage.[21] In addition, disagree. With study in Mexico which showed that obesity is associated with the more advanced. stages of breast cancer, (P= 0.02).[22]

Table (1): Socio-Demographic features of patients.

variables	frequency	percentage
Age (years)		
20-40 years	15	21.4%
40-60 years	37	52.9%
≥ 60 years	18	25.7%
Total	70	100.0%
menopausal status		
postmenopausal	43	61.4%
premenopausal	27	38.6%
Total	70	100.0%
BMI (kg/m2)		
Underweight	1	1.4%
Normal	10	14.3%
Overweight	18	25.7%
Obese	41	58.6%
Total	70	100.0%
histopathological subtypes		
Invasive ductal cell carcinoma	5	7.1%
Invasive lobular cell carcinoma	65	92.9%
Grade of breast cancer		
Grade 1	0	0.0%
Grade 2	41	58.6%
Grade 3	29	41.4%
Total	70	100.0%
Stage of breast cancer		
I	6	8.6%
II	45	64.3%
III	17	24.2%
IV	2	2.9%
Total	70	100.0%

Table (2): The mean differences of BMI according to immunohistochemistry of breast cancer.

BMI	ER+and/orPR+ Luminal	ER+and/orPRHer2+ Luminal	Her2 enriched	Triple negative	Total	P value
Under weight	0	0	0	1(100%)	1(1.42%)	>0.05
Normal	4(40%)	5(50%)	0	1(10%)	10(14.29%)	
Over weight	4(24%)	8(47%)	3(17%)	2(12%)	17(24.29%)	
Obese	14(33.3%)	16(38.1%)	4(9.5%)	8(19.1)	42(60%)	
Total	22(31.4%)	29(41.4%)	7(10%)	12(17.1%)	70(100%)	

P ≤ 0.05 was significant

Table (3): The differences of BMI means according to immunohistochemistry of breast cancer among premenopausal patients.

BMI	ER+and/orPR+ Luminal	ER+and/orPR+Her2+ Luminal	Her 2 enriched	TN (Triple negativ)	Total	P value
Under weight	0	0	1(100%)	0	1(3%)	>0.05
Normal	2(40%)	3(60%)	0	0	5(19%)	
Over weight	2(25%)	4(50%)	1(12.5)	1(12.5%)	8(30%)	
Obese	3(23.1%)	4(30.7%)	3(23.1%)	3(23.1%)	13(48%)	
Total	7(26%)	11(40.7%)	5(18.5%)	4(14.8%)	27(100%)	

P ≤ 0.05 was significant

Table (4): The mean differences of BMI according to immunohistochemistry among postmenopausal patients.

BMI	ER+\PR+ (luminal)	ER+\PR+\Her2+ (luminal)	Her2+ enriched	TN	Total	P value
Under weight	0	0	0	0	0	>0.05
Normal	2(40%)	2(40%)	1(20%)	0	5(11.63%)	
Over weight	2(22.22%)	4(44.44%)	1(11.11%)	2(22.22%)	9(20.93%)	
Obese	11(38%)	12(41.3%)	5(17.2%)	1(3.5%)	29(67.44%)	
Total	15(34.88%)	18(41.86%)	7(16.27%)	3(7%)	43(100%)	

P ≤ 0.05 was significant

Table (5): Association between histopathological subtypes, grade and body mass index (n=70)

Study variables	Histopathological subtypes		Total	P-value
	Ductal	Lobular		
BMI				0.452
Underweight	1 (1.5)	0 (0.0)	1 (1.4)	
Normal	9 (13.8)	1 (20.0)	10 (14.3)	
Overweight	18 (27.7)	0 (0.0)	18 (25.7)	
Obese	37 (56.9)	4 (80.0)	41 (58.6)	
Total	65 (100.0)	5 (100.0)	70 (100.0)	
Study variables	**Grade**		**Total**	**P-value**
	Grade 2	**Grade 3**		
BMI				0.369
Underweight	0 (0.0)	1 (3.4)	1 (1.4)	
Normal	6 (14.6)	4 (13.8)	10 (14.3)	
Overweight	13 (31.7)	5 (17.2)	18 (25.7)	
Obese	22 (53.7)	19 (65.5)	41 (58.6)	
Total	41 (100.0)	29 (100.0)	70 (100.0)	

P ≤ 0.05 was significant

Table (6): Association between stage of breast cancer and body mass index (n=70)

Study variables	Stage				Total	P-value
	Stage I	Stage II	Stage III	Stage IV		
BMI						0.778
Underweight	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	1 (1.4)	
Normal	1 (16.7)	7 (15.6)	2 (11.8)	0 (0.0)	10 (14.3)	
Overweight	0 (0.0)	11 (24.4)	6 (35.3)	1 (50.0)	18 (25.7)	
Obese	5 (83.3)	26 (57.8)	9 (52.9)	1 (50.0)	41 (58.6)	
Total	6 (100.0)	45 (100.0)	17 (100.0)	2 (100.0)	70 (100.0)	

P ≤ 0.05 was significant

CONCLUSION

The obese patients constitute the largest percentage of women with breast carcinoma. Occurrence of large percentage of invasive ductal. carcinoma of (NOS) among the obese women.

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