Relationship between BMI and Risk Factor of Breast Cancer

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ABSTRACT

Breast cancer is the commonest cancer affecting women worldwide. Different studies have dealt with the etiological factors of that cancer aiming to find a way for early diagnosis.

This investigation was carried out on 74 patients (all were females) who received satisfactory therapy. The present study investigated the relationship between BMI and evaluation of some etiological risk factors among breast cancer patients in Iraq.

They were confirmed for breast cancer by histopathological examinations at Nanakali Hospital in Erbil. All women were between 20-72 years. Ages, Weight, height, stage (II, III), hormone receptors ER, PR and Her2 were taken into account as risk factors.

Among the breast cancer patients, 45% were pre-menopausal and 28% were menopausal and 27% were post-menopausal. Body mass index (BMI) is widely used as a measure of obesity. We investigated the relationship between obesity (BMI >= 30 kg/m^2) and outcomes in women with ER-positive early stage breast cancer.

Women with high BMI presented with more aggressive stage at the time of diagnosis. Their tumor usually show positive hormonal status (ER/PR), HR+/Her2- being the most Predominant molecular subtypes. most of obese women have tumor hormonal status positive with favorable molecular subtype (ER+/Her2-), thus Decreasing weight will mainly contribute to decrease tumor exposure to high endogenous estrogen especially in postmenopausal age dramatically effect response to treatment in return.

Keywords: *BMI, Breast cancer, Risk factor*

Introduction

Breast cancer is the commonest malignancy found in women in Europe and the United States, and the incidence continues to rise slowly [(1)]. Breast cancer is the most common cancer among women in Arab countries with a younger age of around 50 years at presentation. Locally advanced disease is very common and total mastectomy is the most commonly performed surgery [(2)]. In Iraq, breast cancer is the commonest type of female malignancy, accounting for approximately one-third of the registered female cancers according to the latest Iraqi Cancer Registry. This shows that the breast is the leading cancer site among the Iraqi population in general, surpassing even bronchogenic cancer[(3)]

Worldwide, at least 2.8 million people die each year as a result of being overweight or obese, and an estimated 35. 8 million (2.3%) of global Disability –Adjusted Life Years (DALYs) are caused by overweight or obesity. Overweight and obesity lead to adverse metabolic effects on blood pressure, cholesterol, triglycerides and insulin resistance. Risks of coronary heart disease, ischemic stroke and type 2 diabetes mellitus increase steadily with increasing body mass index (BMI), a measure of weight relative to height. Raised body mass index also increases the risk of cancer of the breast, colon, prostate, endometrium, kidney and gall bladder [(4)]

It was shown from studies that obesity is associated with the incidence of breast cancer [(5-7)]. Overweight patients with breast cancer often have higher mortality rate than patients with normal weight. Obesity is a factor leading to poor prognosis in breast cancer [(8-10)]. At present, body mass index (BMI) is applied to measure whether a person is obese or not. Both the weight and the height of the body are considered in BMI, which reflect the relationship between body mass and height. BMI is

easy to measure, and it is currently the standard index used internationally to measure the extent of obesity and to evaluate the overall fitness.

Materials and Method

Patients: This study was a retrospective-prospective study, carried out at Nanakali hematology/oncology hospital of Erbil on a sample of 74 cases, who were diagnosed with breast cancer (stage II and stage III).

Collected data included full questionnaire regarding (age, weight, height, body mass index) and clinic-pathological assessment (such as TNM staging, histology grade, ER/PR and HER2 status).

Body Mass Index (BMI): BMI was calculated as weight in kilograms divided by height in meters squared and rounded to the nearest tenth, according to the following equation [11].

Following current recommendations, normal weight was defined as a BMI of 18. 5-24.9, overweight as BMI of 25.0 to 29.9, and obesity as a BMI of 30. 0 or higher[12].

$$\text{Body Mass Index (BMI)} = \frac{\text{Wight (kg)}}{(\text{Height m}^2)} \quad \text{Kg/m}^2$$

Data Analysis: The relationship of BMI to the stage of breast cancer at diagnosis was evaluated using the x^2 test for frequency tables of BMI by stage of breast cancer. The Pearson correlation test was used to determine any association between BMI and age.

Results and Discussions

A total of 74 breast cancer patients (age range = 20–72 years) were included in the present study (Table 1).

Table 1: Menopausal Distribution of Breast Cancer Patients

VARIABLE	No.	%
Premenopausal	33	45
Menopausal	21	28
Postmenopausal	20	27
Total	74	100

We classified them into three age groups:

1. Premenopausal. women less than 45 years of age (45% of patients)
2. Menopausal women between 45 - 50 years of age (28% of the patients)
3. Postmenopausal those greater than 50 years of age (27% of the patients).

(81%) of our breast cancer patients had positive ER, (82%) of breast cancer patients had positive PR. About one third (38%) of our breast cancer patients had positive HER2 and 62% of them had negative HER2. These findings are shown in Table 2. This was similar to studies done in Iraq and Turkey[13, 14].

Table 2: Hormone Receptors, HER2 Receptors Status and TNM Staging of Breast Cancer Patients

Variable	No.	%
ER		
Positive	60	81
Negative	14	19
Total	74	100
PR		
Positive	61	. 82
Negative	13	. 18
Total	74	. 100
Her2/neu		
Positive	28	. 38
Negative	46	. 62
Total	74	. 100
TNM Staging		
II	49	66. 2
III	25	33. 8
Total	74	100

As regards the staging of breast cancer, according to AJCC staging, stage II and III breast cancer were found in 66. 2% and 33. 8% of the patients (Table 2).

They were classified according to BMI into three groups Normal (9.4% of the patients), Overweight (36.4% of the patients) and Obese (54.2% of the patients). Mean BMI of the studied breast cancer patients was 32. 9 Kg/m² (Table3).

Table 3: BMI Distribution of Breast Cancer Patients

Variable	No.	%
BMI mean ± SD (32. 9 ± 3. 8 Kg/m²)		
Normal	7	9. 4
Overweight	27	36. 4
Obese	40	54. 2
Total	74	100

There was a significant association between obesity and breast cancer patients with positive ER (p≤0. 05) by using chi square test. A significant association was observed between obesity among breast cancer patients and positive PR (p<0. 05). Data are shown in Table 4.

Table 4: Distribution of Hormone Receptors, HER2 Receptor, and Stage According to BMI Categories

Variable	Normal		Overweight		Obese		X^2	P-value
	No.	%	No.	%	No.	%		
ER								
Positive	3	43	24	89	33	82	60. 08	**0. 001**
Negative	4	57	3	11	7	18		
PR								
Positive	5	71	23	85	33	82	6. 628	**0. 030**
Negative	2	29	4	15	7	18		
Her2/neu								
Positive	3	43	10	37	17	42	0. 57	**0. 650**
Negative	4	57	17	63	23	58		
Nottingham Grading System								
II	4	57	20	74	23	57	8. 234	**0. 010**
III	3	43	7	26	17	43		

There was a significant association between breast cancer patients with positive ER and obesity (p≤0. 05), as showed in Table 4 and a significant association was also observed between Breast cancer women with positive PR and obesity. These findings are consistent with results of Peng Xing, *et al*. study [15]

There was significant association between BMI categories and breast cancer patients regarding stage of tumor (Nottingham Grading System) (p <0. 05). Data are shown in Table 4. Breast cancer patients in our study with TNM stage II and III were associated significantly with obesity (p≤0. 05), see Table4. This finding agreed with results of study done by Eichholzer M. *et al*. study and Cui y. *et al* study which suggested that higher body mass index was associated with advanced stages of breast cancer [16, 17]. There may be several reasons for the observed association between body mass and stage of breast cancer at diagnosis. First, this association could be due to a delay in diagnosis among obese women. Overweight/obese women have larger breasts, and thus tumor detection may be more difficult in these women simply because tumors are more difficult to palpate in larger breasts. This hypothesis is supported by several studies that show a positive relationship between breast size and stage of breast cancer. [18] Second, obesity is associated with advanced breast cancer at diagnosis, high tumor proliferation rates, and more triple-negative phenotypes, indicating that it may adversely contribute to prognosis. [19] Some studies suggest that locally increased estrogen levels promote tumor growth. [20] Obesity causes an increased production of the estrogen known as estrone via the aromatization of androstenedione in peripheral adipose tissue. In addition, obesity is associated with low levels of sex hormone-binding globulin, which results in a significantly higher level of the biologically active, unbound form of estrogen known as estradiol. [15] Therefore, it is possible that obesity leads to an overall increase in the active levels of estrone and estradiol and that the high levels of these hormones promote the growth of breast tumors in obese women.

There is significant association between obesity and hormonal receptor subtype ER+/PR+ (P≤0. 001), as shown in Table 5.

Table 5: ER/PR Receptor Distribution According to BMI in Breast Cancer Patients

BMI ER & PR	ER &PR +ve		ER+ve/PR-ve ER-ve/PR+v		ER & PR. -ve		X^2	P value
	No.	%	No.	%	No.	%		
Normal	3	0. 5	7	46. 6	2	3. 0	**96. 1**	**<0. 001**
Overweight	23	42. 0	3	20. 0	27	39. 1		
Obese	29	57. 5	5	33. 4	40	57. 9		
Total	55	100	15	100	69	100		

There is strong association between high BMI and ER+/PR + hormone receptor subtype in our study (p ≤0. 001), as shown in Table5. These results are somewhat similar to results of 9 cohort and 22 case-control studies comparing the highest versus the reference categories of relative body weight showed that the risk for ER+PR+ tumors was 20% lower (95% CI = −30% to −8%) among premenopausal (2, 643 cases) and 82% higher (95% CI = 55–114%) among postmenopausal (5, 469 cases) women [21]. Current study found a significant association between obese postmenopausal breast cancer patients and HR+/Her- subtype (p≤0. 001) and this finding was more significant in postmenopausal obese women (p=0. 001) as data show in Table 6. This finding agrees with results of study carried in Iraq [22].

Table 6: Distribution of BMI According Molecular Subtypes for Menopausal and Postmenopausal Breast Cancer Patients

Molecular Subtypes	Premenopausal BMI						Menopausal BMI						Postmenopausal BMI					
	Normal		Overweight		Obese		Normal		Overweight		Obese		Normal		Overweight		Obese	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
HR+/ Her2-	3	100	7	50	7	53. 8	0	0	2	28. 5	5	71. 5	0	0	5	62. 5	6	54. 5
HR+/ Her2+	0	0	3	21. 5	4	30. 7	0	0	3	37. 5	5	62. 5	0	0	2	25	4	36. 3
HR-/ Her2+	0	0	3	21. 5	0	0	0	0	0	0	1	100	0	0	0	0	0	0
HR-/ Her2-	0	0	1	7	2	15. 5	0	0	0	0	1	100	0	0	1	12. 5	1	9. 2
Statistical test	χ^2=6. 123						χ^2=3. 651						χ^2=3. 715					
P Value	0. 295						0. 06						0. 08					

Obesity has been recognized as a significant risk factor of breast cancer among postmenopausal women and is associated with poor prognosis. This result was in agreement with the results of another study that showed patients with high BMI are most clearly associated with hormone receptor–positive tumors and suggest that triple-negative tumors may have distinct etiology [23, 24]

This result disagrees with Lesley A. Stead study that triple negative tumors were equally common in black wo men diagnosed before and after age 50 (31% vs 29%), and who were obese and non-obese (29% vs 31%). Considering all patients, as BMI increased, the proportion of triple negative tumors decreased (p=0. 08) [25]. Body mass index (BMI) is widely used as a measure of obesity. Dignam *et al.* investigated the relationship between obesity (BMI ≥30.0 kg/m²) and outcomes in women with lymph node-negative, ER-positive early stage breast cancer. They found that obese women as compared with normal weight women had greater all-cause mortality [26] Obesity also has an adverse prognostic effect in women with lymph node-negative and ER-

negative breast cancer. However, this prognostic effect has not been consistent and may be influenced by several factors such as menopausal status, extent of disease, and receptor status [27, 28]

Conclusions

1. Most of Iraqi women with breast cancer were either obese or overweigh at the time of diagnosis.
2. Women with high BMI presented with more aggressive stage at the time of diagnosis. Their tumor usually show positive hormonal status (ER/PR), HR+/Her2- being the most Predominant molecular subtypes.
3. Increase awareness for not only breast cancer paticnts but also thcir physician about thc importance of weight control during management of breast cancer patient and also breast cancer survivors.
4. Hence most of obese women have tumor hormonal status positive with favorable molecular subtype (ER+/Her2-), thus decreasing weight will mainly contribute to decrease tumor exposure to high endogenous estrogen especially in postmenopausal age, dramatically effect response to treatment in return.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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