Assessment of the Relationship between Obesity and Female Breast Carcinoma in Imamein Kadhumein Medical City

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Abstract

Background: Obesity, measured by body mass index (BMI), is a well-known danger feature for a widespread variation of illnesses. Yet, in breast carcinoma (B.Ca.) the link is a little discussed and differs according to different entities.

Aims: This study aimed to assess the relationship between obesity and breast cancer in premenopausal women.

Subjects and Method: This is a prospective study in which 800 women who were attending breast clinic in Al-Imamain Al-Kadhumain Medical City/Baghdad during the period from January 2016 to December 2017 were followed up for the occurrence of BCa. of these, 50 women who developed BCa during this period were selected to represent cases group. Other 50 age-matched women who did not have BCa were selected to represent control group. General obesity (BMI) and central obesity (waist circumference (WC), hip circumference (HC) and waist/hip ratio (WHR)) were measured obtained from each patients either by direct interview or from patient's record.

Results: Demographic, reproductive and laboratory data were comparable between the two groups. Stratification of BMI revealed significantly less cases having BMI < 25 and more having BMI>30 than controls. Moreover, cases showed significantly higher mean of WC (84.12±6.22 cm) than controls (77.6±7.18 cm), Regarding hormonal receptor statuses, mean BMI (30.18± 9.21 kg/m2) was significantly higher in hormonal receptor negative cases compared to 26.31±9.1 kg/m^2 in estrogen and progesterone receptors positive with significant difference. **Conclusions:** These data shows that obesity is a possible risk factor for breast carcinoma in premenopausal women.

Keywords: *Relationship, Obesity, Female Breast Carcinoma, Imamian Khdymian Medical City.*

Introduction

Worldwide, breast cancer (BCa) is the most frequently occurring malignancy among women, accounting for about 18% of all female cancers [1]. In 2012, the number of new cases among women was 1.7 million (about quarter of all cancer cases), with more cases observed in the developed countries (883,000 cases in developed versus 794,000 in developing countries)[2]. In Iraq, BCa comprises for about one-third of female cancers[3]. So far, the exact causes of BCa are not fully clarified; however, many risk factors such as family history[4], life style[5], adipoprotein levels[6] and age at menarche [7] were well illustrated. On the other hand, genetic factors were subjected to massive investigations and many genetic loci have been found to strongly associate with this malignancy[8]. However, the role of many other factors, such as obesity and oral contraceptive pills remained controversial issues [9,10]. The association of obesity with the incidence of BCa is a very complicated. For better understanding of this

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effect, the impact of obesity on BCa is firstly illustrated in general term and then the BCa is overlooked in premenopausal period, then each category is further specified according to estrogen and progesterone receptors [11]. Several mechanisms have been proposed for the effect of excess adipose tissue on tumorigenesis. Recently, Divella et al. proposed that the extra adipose tissue connected to the variations of the lipids focuses in the blood stream,stages of class responsive oxygen as well as to excretion of adipokines and blood stream hormones [12]. Inflammation become chronic in the adipose tissue and occur due to hypertrophy and hypoxia so cytokines secretion occur as a result of inflammation of adipose tissue, angiogenic factors excretion, macrophages M1 infiltration and resistance of insulin related to obesity and stimulus of a favorable microenvironment for tumorigenesis. Blucher and Stadler (2017) state that molecular mechanism that describes the communication between fat and BCa.Increase the fat, adipose become enlarge and increase triglycerides (TAGs) levelwith increase secretion adipokines and pro-inflammatory cytokines. These particles are chemoattractant for macrophages lead to lipolysis and release raised quantities of free fatty acids (FFAs). High mount of fatty acids could be a straight instrument through which adiposity may stimulate cancer development[13]. Despite the importance of BMI as an indicator for obesity, other body size indices, particularly waist circumference (WC), hip circumference (HC) and waist-to-hip ration (WHR), were profoundly found to have a role in BCa. A term of "central obesity" was used to express the ratio between WC and HC. Central obesity, or abdominal obesity,well-defined as extreme abdominal fat cover the stomach and abdomen [14] and is designated by WHR and WC. of special importance regarding the BCa is the presence or absence of estrogen receptor and, to less extension, the progesterone receptors. This study aimed to assess the relationship between obesity and breast cancer in premenopausal women.

Method

Approximately 800 women (age range 21-48 years, mean 37.43±8.9) who were attending breast clinic in Al-Imamain Al-Kadhumain Medical City/Baghdad (for early detection) during the period from January 2016 to December 2017 were followed up for the occurrence of BCa. of these, 50 women who developed BCa during this period were selected to represent cases group. Other 50 age-matched women who did not have BCa were selected to represent control group. The inclusion criteria for case were being between 20 and 48 years old with BCa was investigated by fine needle aspiration (FNA). The controls were apparently healthy women who had normal ultrasound and mammogram findings and having no evidence for cancer. The exclusion criteria are those: with genetic breast ca. and post-menopausal women. Data were collected from both cases and controls through direct interview or patients records whenever possible. Four kinds of data were collected.

1. Demographic data: age, height, weight, educational level (high, intermediate, low), smoking status (never, ex/current), dwelling (rural, urban), waist circumference and hip circumference.
2. Physiological and reproductive features: age at menarche, number of births and breast feeding.
3. Family history of BCa: first or second degree relative with BCa
4. Laboratory investigations: only for cases and included status of hormonal receptor (estrogen receptor and progesterone receptor). Cases who were not having such investigation were excluded from the study.

Statistical package for Social Sciences (SPSS version 20) was used for data analysis. Continuous variables were expressed as a mean± standard deviation (SD), while categorical variables were expressed as percentages. a $P \leq 0.05$ was considered statistically significant.

Results

Demographic and Reproductive Characteristics of the Study Population: The baseline characteristics of BCa patients and controls are shown in table 1.

Table 1: Baseline characteristics of the study population

Variable	Cases (n=50)	Controls (n=50)	P-value
Age (years)	36.81±5.12	34.23±6.4	0.324
Overall BMI	29.48±3.12	26.52±6.09	0.068
BMI<25	7(7.14%)	16(16.32%)	0.031
BMI 25-30	31(30.62%)	30(28.88%)	0.83
BMI 30-50	12(12.24%)	4(4.8%)	0.026
Age at menarche	12.22±1.14	13.2±1.67	0.081
Number of birth			
Nulliparous	22(44%)	16(32%)	0.486
1-2	19(38%)	23(46%)	0.259
≥3	9(18%)	11(22%)	0.351
Duration of breastfeeding			
No	19(38%)	16(24%)	0.294
≤ 6 months	18(36%)	17(34%)	0.18
> 6 months	13(26%)	17(34%)	0.233
Diabetes mellitus			
No	46(92%)	46(92%)	1.0
Yes	4(8%)	4(8%)	
Family history			
No	43(86%)	48(96%)	0.073
Yes	7(14%)	2(4%)	
Educational level			
Low	9(22.6%)	14(27.7%)	0.498
Intermediate	24(45.2%)	21(40%)	0.270
High	17(38.7%)	15(32.3%)	0.307
Smoking			
Never	48(96%)	49(98%)	0.554
Ex/current smoker	2(141.3%)	1(2%)	
Using of contraceptive			
Never	39(78%)	43(866%)	0.296
Yes	11(22%)	7(14%)	
Residence			
Rural	13(26%)	21(42%)	0.093
Urban	37(74%)	29(58%)	

Interestingly, cancer occur more in obese women and those taking contraceptives than control, although the differences did not rise to a significant level (P= 0.068 and 0.296 respectively).others have no significant differences.

Distribution of Body Mass Index: Stratification of this index did. Women with BMI below 25 kg/m^2 were more frequent among controls (16, 32%) than case (7, 14%%) with significant difference (P=0.03). In contrast, women with BMI over 30 kg/m^2 were far more frequent among cases (12, 24%) than controls (4, 8%) with significant difference (0.026) as shown in figure 1.

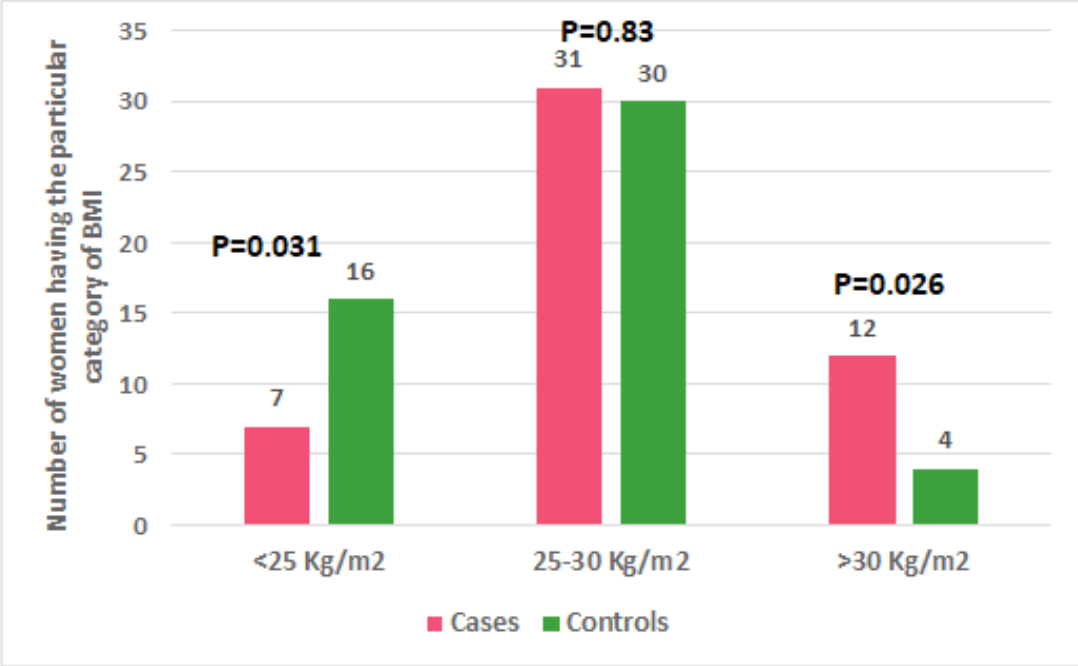

Figure 1: Body mass index stratification in cases and controls

Waist and Hip Circumferences: Figure 2 shows waist and hip circumferences in BCa patients and controls. For waist the circumferences were 84.12±6.22 cm and 77.6±7.18 cm respectively with significant difference (P=0.028). Likewise, BCa shows higher mean hip circumference (98.74±12.71 cm) than controls (92.17±9.14 cm); however, the difference was not significant (P=0.069).

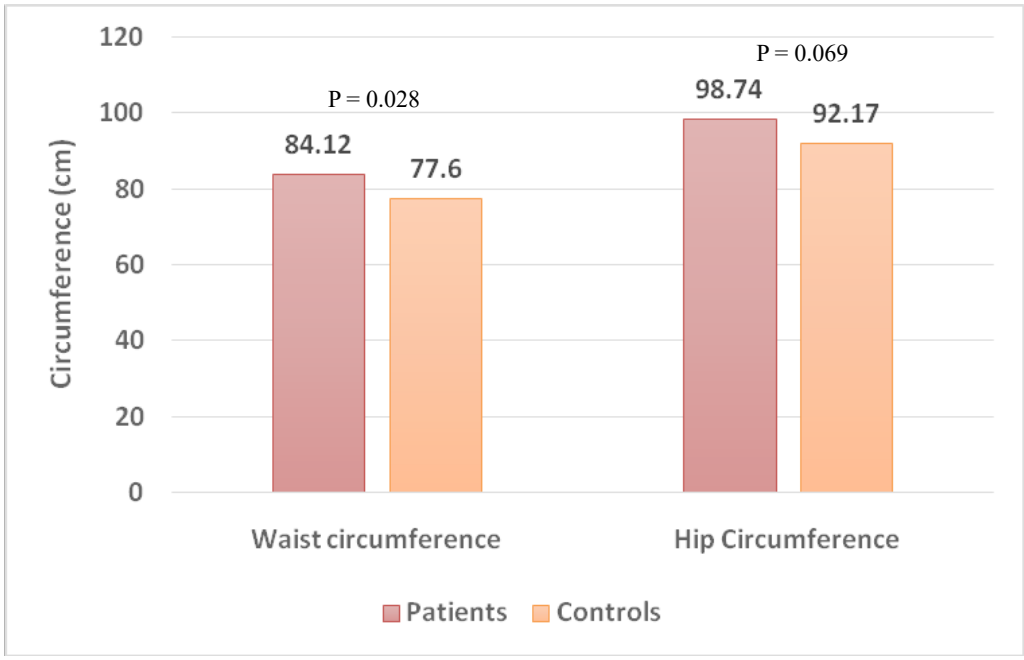

Figure 2: Waist and hip circumferences in breast cancer cases and controls

Discussion

This study aimed to assess the role of obesity as a risk factor for BCa. Apart from obesity, there was no significant differences in all studied risk factors between the two groups and this will highly assist to evaluate the role of obesity in BCa. The study revealed interesting results. Below 25 kg/m^2, BMI showed a significant negative association with BCa, while this association was positive with BMI greater than 30 kg/m^2. A recent study performed by Wang et al. involving 2800 Chinese women revealed that BMI greater than 32 kg/m^2 was positively influence the occurrence of BCa especially in premenopausal women[11]. In another study including 183940 Japanese women, Wada et al. reported a significant positive association between BMI and premenopausal BCa[15]. Obesity considered as a danger factor for BCa[16]. Yu et al. stated that increase BMI was meaningfully connected with BCa among Asian women[17]. Renehan et al. stated that there is a relation between increase BMI and both before and after menopausal BCa in Asian-Pacific women[18] obtained almost similar result. Other studies, although have shed a light on obesity as a risk factor for BCa, but they neglected other very important factors which influence this association such as the body size indices (waist and hip circumferences), hormone receptor status and the period at which BCa occurs whether pre- or postmenopausal. Reduction in weight as Amandu et al noticed have different percentages of BCa reduction among races. These differences in results may be attributed to many factors, the most important of which is the ethnicity, dietary life style. Furthermore, these data indicate that there are no standard values of BMI, which could be considered as risk for or protect from BCa. [19]

One of the most prominent results in the current study was that WC but not HC nor WHR is significantly associated with increased risk of BCa in premenopausal women. Compared with the other international studies, this results are in accord with that reported by Wang et al. who found that WC was positively associated with BCa among premenopausal Chinese women [10].

Stratification of BMI according to hormonal receptor statuses in the current study showed a significant difference in mean BMI between HR-negative group and ER/PR positive group. This implies two facts. The first one is that even in peremenopause woman negative for both receptors, BMI≥30 kg/m^2 can predispose for BCa and women positive for both receptors are at increased risk of BCa even with slight obesity. The second fact is that the effect of obesity is more prominent in hormonal receptor negative women. These results are in agreement with that obtained by Munsell et al. who analyzed 16 case/control studies and reported a significant decreased in premenopausal BCa risk in obese women positive for hormonal receptors (OR=0.78, 95% CI=0.67-0.92) but not for those negative for hormonal receptors[20]. Another large study included 1149 BCa women, obesity was found to decrease risk of the disease in premenopausal women positive for hormonal receptors [21]. There is no clear explanation for this negative association between BMI and hormonal receptor statuses as risk factors for BCa in premenopausal women[22]. Renehan et al. analysed 20 cohort and case/control studies including more than 2.5 million women and 7930 premenopausal BCa and reported a 8% decreases in the incidence of this malignancy for every 5-point increase in BMI [18]. Interestingly, the reduced risk was seen in hormone receptor-positive but not hormone receptor negative. Supporting these reports are two large meta-analyses involved 6106 and 2468 premenopausal women with ER+ BCa. of note, this inverse association was restricted to white women, while null association was found in African American women[23,24]. However, this reduction in BCa with obesity was not seen in all studies. A meta-analysis of 12 population based studies[25] showed different results. i.e. increased BMI in premenopausal women was connected with an increased danger of ER+ or PR+ BCa. Furthermore, the BCa Inhibition trial, which included 5864 females, stated that obesity was significantly related with advanced premenopausal BCa. Thus, it seemed that other factors, particularly ethics, have a crucial role in formulation the association of obesity with premenopausal BCa.On the other hand, studies regarding the effect of obesity on HR- BC are vealed either positive association or no association at all. Two meta-analysis of 620 females and 1358 females with HR- BCastated 80% and 43% advanced danger for BCa in premenopausal females correspondingly[24,25], while an Indian case/control study on HR- menopausal women failed find any significant association between obesity and BCa[26].

Conclusions

These data shows that obesity is a possible risk factor for breast carcinoma and possibly has poor prognosis because of negative hormone receptor status in obese women with breast carcinoma.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq.

Conflict of Interest: Non

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