Overweight and Obesity in Pre- and Postmenopausal Women of Northeastern Iran: Protecting Against or Risk Factors for Breast Cancer?

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ABSTRACT

Breast cancer is the most common type of cancer among women worldwide and affects Iranian women at least one decade earlier than their counterparts in the developed countries. The aim of this study was to determine whether northeastern Iranian breast cancer patients, who were either pre- or postmenopausal, had differences pertaining to their body mass index (BMI) and obesity incidence in comparison with controls. A case-controlled, cross-sectional study was performed to assess the BMI of 214 patients, who were either pre- or postmenopausal and had been diagnosed with breast cancer via excisional biopsy. Patients were compared to 463 healthy women. Regardless of their menstrual status, patients and controls exhibited a significant difference in the mean BMI (P-value = 0.04). When the menstrual status and BMI were analyzed, the obesity rate was higher among both premenopausal (P-value = 0.03) and postmenopausal women. Our results showed that there was an increased risk of breast cancer among obese, premenopausal women in northeastern Iran.

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Introduction

Breast cancer is the most frequently occurring cancer among women worldwide [1]. It was the most common type of cancer (32% of cases) and the second-largest cause of cancer mortality (19%) among Iranian women in 2004 [2]. Research shows that there is an increased risk of endometrial, ovarian, and breast cancers among obese women [3,4]. A number of studies indicate that a higher body mass index (BMI) value is a major risk factor for breast cancer among postmenopausal women in western countries [5,6]. On the other hand, slight overweightness may be a protective factor against breast cancer in premenopausal women [7-9]. Also, weight at certain periods of life is more important than just the current weight [10-12]. Obesity is associated with an increased breast cancer mortality [13]. The greatest risk for the postmenopausal development of breast cancer seems to be associated with gaining postmenopausal and not premenopausal period weight [13].

The association between higher BMI and the risk of breast cancer is well-established in western populations. A few studies have also been conducted among Asian women to identify associations between BMI and the risk of breast cancer [10-14]. In Iran, breast cancer affects women at an average of one decade earlier than their counterparts in the developed countries [2]. This study was conducted to determine whether northeastern Iranian pre- and postmenopausal breast cancer patients had a higher incidence of obesity in comparison with controls.

Materials & Methods

Selection and Description of Participants

This was a case-control study comprising a group of patients diagnosed with breast cancer at the departments of radiation oncology of Omid and Ghaem Educational Hospitals at the Razavi Khorasan province, Iran, between June 2007 and June 2008. Local ethics committee approval was obtained from the Mashhad University Research Ethics Committee. Inclusion criteria were women diagnosed with breast cancer before starting the treatment and that they consented to measurements of their height and weight. The exclusion criterion was the presence of metastatic breast cancer. Diagnosis of breast cancer in patients was confirmed by a histological

assessment using excisional biopsy. Weight and height were measured by a physician. Questionnaires related to age and menstrual status were also completed. Healthy women from the community of Razavi-Khorasan province who were attending Omid and Ghaem Educational Hospitals for clinical breast examinations during the same period were also recruited as controls. The presence of breast cancer in controls was ruled out by physical examination and a clinical oncology expert's judgment. All patients and controls gave written informed consent.

Technical Information

Height was measured by stadiometer to the nearest 0.5 cm in patients and healthy controls. All patients and healthy controls were weighed using a digital scale with a measurement accuracy of 0.1 kg. BMI is a definition of the degree of adiposity or a mathematical formula that correlate with body fat [15]. It was calculated for patients and controls using the following equation: Weight (kg) / Height^2 (m) [15]. Subgroup distributions were used to categorize BMI to facilitate comparisons; BMI below 25 kg/m^2 (normal and underweight), 25–30 kg/m^2 (overweight) and above 30 kg/m^2 (obese and severely obese).

Postmenopause was defined in women as the presence of at least 6 months amenorrhea, and all other women were considered pre-menopausal. The worldwide mean age at menopause is 51 years, so this age was defined as the cut-off point for menopause at the time of diagnosis.

Statistics

SPSS 13.5 for Windows was used for statistical analysis. To test the statistical normality, the Kolmogorov–Smirnov test was used. Descriptive methods were used to show characteristics of cases and controls. Pearson's chi-square and Student's t-tests were used to compare all categorical and continuous variables, respectively. In all cases, $P < 0.05$ was considered to be statistically significant.

Results

Participants comprised 214 patients with infiltrative invasive breast carcinomas and 463 healthy controls (Table 1). There was a significant difference in BMI between patients and controls (Table 2).

When menstrual status was considered along with BMI, the mean BMI was found to be higher among

both pre- and postmenopausal patients, but the difference was only significant for premenopausal women (P-value = 0.03) (Table 2).

The numbers and percentages of patients and healthy women, classified according to different categories of BMI and menopausal status, are shown in figures 1–3. Without considering menses status, the mean BMI for patients and healthy women was significantly different for all three BMI categories, but mean BMI did not differ significantly when participants were further divided into pre- and postmenopausal groups (Figures 1–3). Mean BMI values by age for patients and healthy women is shown in figure 4.

Table 1. Characteristics of study participants

Group	Premenopause	Postmenopause	Mean age ± SD (years)	Mean BMI ± SD (kg/m^2)
Patient	124	90	49.70 ± 10.03 (range: 32-75)	27.53 ± 5.05
Healthy (control group)	301	162	48.37 ±9.71 (range: 32-75)	26.70 ± 4.38

Table 2. Differences in body mass index between patients with breast cancer and controls

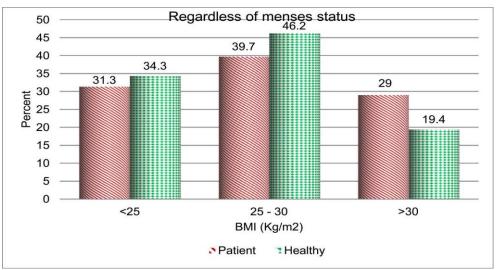| Group	Patients (kg/m^2)	Healthy women (kg/m^2)	P value
Premenopause	27.53 ± 5.02	26.53 ± 4.28	0.03
Postmenopause	27.54 ± 5.11	27.02 ± 4.55	0.43
All	27.53 ± 5.05	26.70 ± 4.38	0.04

Figure 1. Difference of BMI between patients and healthy women in three BMI categories without considering menses status. P value of Pearson Chi-Square test was 0.02
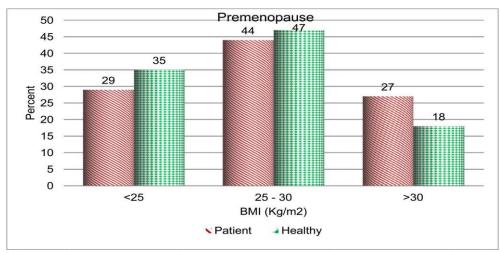
Figure 2. Difference of BMI between patients and healthy women in three BMI categories of premenopause women. P value of Pearson Chi-Square test was 0.09
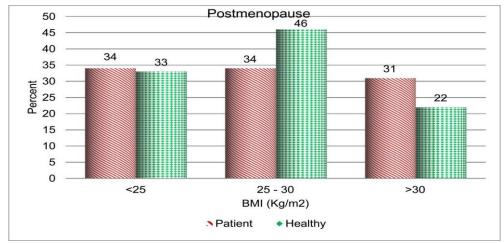

Figure 3. Difference of BMI between patients and healthy women in three BMI categories of postmenopause women. P value of Pearson Chi-Square test was 0.14
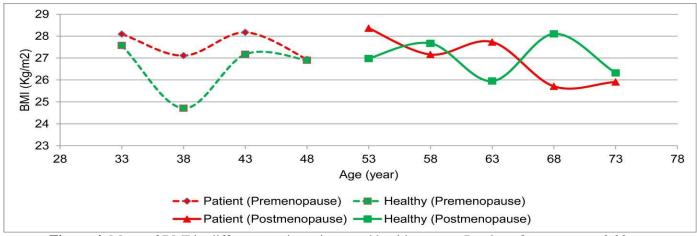

Figure 4. Mean of BMI in different age in patients and healthy group. P value of anova test = 0.02

Discussion

The main finding of this study was that there was an increased risk of breast cancer in premenopausal women with higher BMI. The BMI of premenopausal patients at the time of diagnosis was significantly higher than premenopausal healthy women, suggesting that obesity may be a risk factor for breast cancer in premenopausal Iranian women. This study is one of the few that have reported a direct relationship between elevated BMI and risk for premenopausal breast cancer [16,17]. In other studies, the difference in BMI between premenopausal patients and healthy women was not significant [18-21]. However, most the studies reported an inverse relation between obesity and premenopausal breast cancer existed [7-9,22-27]. Some studies showed that this inverse relationship is limited to estrogen–progesterone receptor positive tumors [24,25,28-32]. In one review article in 2010 [33], the premenopausal protective effect was suggested to be limited to women under 35 years of age. Also, Weiss' study [34] showed that the inverse relationship was present for in situ and local tumors, but not for regional or distant cancers.

The discrepancy between the results of this study and these other studies may be due to the following reasons, which require further study in the Iranian population:

- ✓ Most of the premenopausal breast cancer cases in Iranian women may involve estrogen–progesterone receptor positive or inflammatory breast cancer [16].
- ✓ The results may be related to the younger average age of onset for breast cancer in Iranian women [3;35]
- ✓ Because of low breast cancer screening rates among Iranian women, most patients in this study were diagnosed at advanced stages, so the result of Weiss' study may hold true for Iranian women.

In postmenopausal women, the BMI of breast cancer patients was higher than that of controls, but this difference was not significant. The lack of significance may be the result of small sample size of postmenopausal women in our study. In almost all other studies about postmenopausal breast cancer, obesity was reported to be a risk factor for developing breast cancer, [5,6;13,18,23,33,36-38] and in one study [39] the elevated risk associated with increased BMI appeared to be most pronounced among younger postmenopausal women. A previous study showed that women with a BMI of 31.1 or higher had a 2.5-fold greater risk of developing breast cancer than those with a BMI of 22.6 or lower [13]. In Berstad's study [9], the association of postmenopausal breast cancer with BMI at diagnosis was found to vary by race and hormone receptor status. Those data were obtained from white and African-American patients and controls. Among postmenopausal white women, but not African-American women, there was an inverse relationship between recent BMI and cancer risk. Elevated recent BMI was associated with an increased risk of estrogen–progesterone receptor positive tumors among postmenopausal African-American women [9].

Limitations

This study had some limitations:

- The data were obtained from one region in Iran. However, the pattern of breast cancer and obesity may differ in other parts of Iran.

- The time limit of the study did not allow the investigators to evaluate other factors related to breast cancer such as family history of breast cancer, parity, use of oral contraceptives, and use of hormone replacement therapy.

- Dietary patterns of participants were not assessed in this study.

Conclusions

According to most previous studies, obesity was found to protect against developing premenopausal breast cancer. However, the results of this study showed that obesity may predict a higher risk of breast cancer in both pre- and postmenopausal Iranian women. Further studies with larger sample sizes of Iranian women would be useful in resolving these discrepancies.

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