

Body Mass Index and Breast Cancer Risk: A Retrospective Multi-Institutional Analysis in Saudi Arabia

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Received December 4, 2012; revised January 6, 2013; accepted January 14, 2013

ABSTRACT

Background: The purpose of this study was to evaluate the association between the body mass index (BMI) of breast cancer patients and non-cancer females of the Eastern Province of Saudi Arabia. **Methods:** The weight, height and age was obtained from the patient records of 706 newly diagnosed breast cancer patients and of 20,872 non-cancer female patients who consulted the two largest hospitals in the Eastern Province of Saudi Arabia between 2006 and 2012. Factorial analysis of variance (ANOVA) was used to assess the association between the BMI, age and breast cancer status. **Results:** The mean BMI of the non-cancer females was 29.4 and the percentage of obese patients of the different age groups ranged from 23.9% to 66.5%. The BMI increased significantly with age. The ANOVA revealed that breast cancer patients older than 50 years had a significantly lower BMI compared to their non-cancer counterparts ($p = 0.01$). **Conclusion:** Our data confirm the high BMI of the Saudi Arabian female population. The reason for our finding of a lower BMI of postmenopausal breast cancer patients compared to their non-cancer counterparts is unclear. Future studies are warranted to assess the impact of possible confounding factors on the association between obesity and breast cancer risk. An interesting factor to investigate in future studies would particularly be the use of the anti-diabetic and cancer-protective drug metformin considering that diabetes mellitus is endemic in Saudi Arabia with a prevalence of 30%.

Keywords: Breast Cancer; Body Mass Index; Adolescent; Female; Saudi Arabia

1. Introduction

The prevalence of obesity has been rapidly increasing in many middle-income and low-income countries. At present more than 1.3 billion people globally are estimated to be overweight or obese [1].

Obesity is a generally recognized risk factor for metabolic syndrome, type II diabetes mellitus, cardiovascular disease and several cancers including breast cancer [2]. The risk of developing postmenopausal breast cancer is increased by 30% - 50% in obese women [2]. Furthermore, obesity has been shown to be associated with a poorer prognosis in breast cancer patients regardless of the menopausal status [3]. A recent systematic review showed an increased risk of 33% for both breast cancer-specific death and death from all causes in obese women compared to lean women [4].

Breast cancer is the most common malignancy in Saudi Arabia. It amounts to 26% of all newly diagnosed

cancers in women and to 13.8% in the combined genders. With an age-standardized rate of 21.6/100,000 for female population, the incidence of breast cancer in Saudi Arabia is lower than that in the United States (124/100,000) [5,6]. About 25% of the breast cancer patients in Saudi Arabia are younger than 40 years of age and the mean age at diagnosis is 47 years [6-8]. The high percentage of young breast cancer patients in Saudi Arabia may at least in part be explained by the young age structure of the Saudi Arabian population where approximately 50% of the females are younger than 20 years of age [6]. In contrast, in the United States about 7% of breast cancer patients are younger than 40 years [9], and the median age at diagnosis is 61 years.

While the prevalence of obesity in Saudi Arabia has been thoroughly investigated, no data of the BMI of Saudi Arabian breast cancer patients are available according to a MEDLINE (PubMed) search.

The goal of this study was to evaluate the BMI of breast cancer patients and non-cancer females in Saudi Arabia, and to compare the BMI with published corre-

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sponding data from the United States.

2. Methods

Patient records were reviewed of patients who consulted Saad Specialist Hospital and King Fahad Specialist Hospital in Dammam between 2006 and 2012. The Saad Specialist Hospital and King Fahad Specialist Hospital in Dammam are the two largest tertiary hospitals in the Eastern province of Saudi Arabia. Eligible for the study were non-pregnant female patients of Saudi Arabian nationality with a minimum age of 20 years, a tissue biopsy-proven new diagnosis of invasive breast cancer ("breast cancer patients"), or any other diagnosis apart from cancer or other malignant tumors ("non-cancer females"). The height, weight and age at the time of diagnosis of invasive breast cancer, or at the first consultation in the hospital of non-cancer patients, respectively, were anonymously transferred into a database. The weight and height were routinely assessed and documented in the patient records in both hospitals. The BMI was calculated as $\text{weight} \cdot \text{kg} / \text{height} \cdot \text{m}^2$.

Data of 706 newly diagnosed female breast cancer patients and of 20,872 female non-cancer patients were collected and analyzed. Of the non-cancer patients, the data were obtained from the Departments of Gynecology (29.4%), Dermatology (10.1%), Primary Care (6.5%), and in smaller percentages from other departments.

The study was approved by the Institutional Review Boards of both hospitals.

Statistical Analysis

Descriptive statistics of the BMI of breast cancer and non-cancer female patients of different age groups were calculated. The difference between the BMI of breast cancer patients and non-cancer females of different age groups was assessed for statistical significance using the two-tailed student t-test. For the student t-tests, no correction for multiple testing was used, and the corresponding p-values have to be considered descriptive.

The association between BMI, age and breast cancer status was assessed using factorial analysis of variance (ANOVA). For the ANOVA, the log-transformed BMI was used as continuous dependent variable and the age and breast cancer status (breast cancer versus non-cancer) as categorical variables.

3. Results

Our data show that the BMI significantly increases with age, and that the percentage of obese women is high in all examined age groups (range, 23.9% to 66.5%; **Figure 1, Tables 1 and 2**). Compared with recent data from the United States [10], the prevalence of different grades of obesity among Saudi Arabian women was markedly

higher in the age groups older than 40 years (factor 1.4 - 1.7) and comparable in the younger age group of 20 - 39 years (**Table 3**).

The ANOVA and the student t-test showed that Saudi Arabian breast cancer patients older than 50 years had a significantly lower BMI than their non-cancer counterparts. No difference of the BMI was found for women younger than 50 years (**Figure 1, Tables 1 and 2**).

4. Discussion

Our data confirm the high prevalence of obesity in the Saudi Arabian female population. Compared to the United States, the prevalence of obesity was higher in Saudi Arabian women older than 40 years and comparable in women younger than 40 years.

A surprising finding of our analysis was the statistically significant lower BMI of postmenopausal breast cancer patients compared to their non-cancer counterparts. It is generally recognized that the risk of postmenopausal breast cancer increases with increasing BMI [11,12] and therefore the opposite result was expected.

The reason for this unexpected finding is unclear. Due to limitations of a retrospective study and the relatively low number of breast cancer patients investigated in our study ($n = 706$; non-cancer females, $n = 20,872$) a statistical artifact or bias cannot be fully excluded. However, the BMI of non-cancer females in our study was in full agreement with recently published reports evaluating the BMI of the Saudi Arabian population, suggesting that our data are representative [13,14]. On the other hand, there are several factors that may mask or alter the expected relation between high BMI and increased postmenopausal breast cancer risk. In studies where the use of

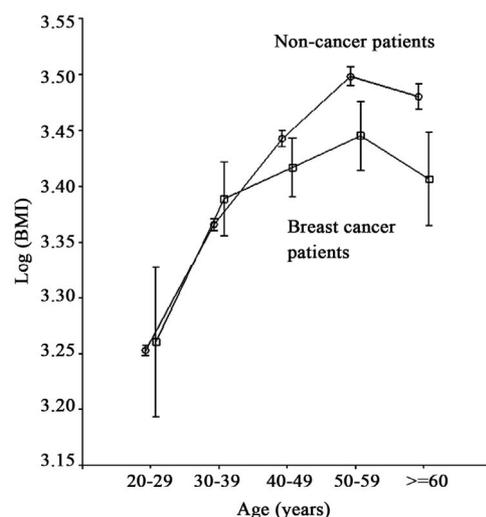


Figure 1. Association between BMI and age of newly diagnosed female breast cancer patients and female non-cancer patients. The squares and vertical lines represent the mean and standard deviation of the log-transformed BMI.

Table 1. Body Mass Index of breast cancer patients at time of diagnosis and of non-cancer patients stratified by age.

Breast cancer patients					Non-cancer patients				
BMI					BMI				
Age	n	Mean	SD	>30 (%)	n	Mean	SD	>30 (%)	p-value*
20 - 29	37	26.6	5.6	27.0	8491	26.5	6.1	23.9	0.91
30 - 39	153	30.3	6.1	48.4	5441	29.6	6.4	40.8	0.22
40 - 49	241	31.2	7.0	55.2	3284	31.9	6.2	58.7	0.15
50 - 59	179	32.1	6.7	61.5	2385	33.7	6.6	69.3	<0.01
≥60	96	30.9	6.9	50.0	1271	33.1	6.4	66.5	<0.01
Total	706	31.0	6.8	53.1	20872	29.4	6.8	41.6	<0.01

Abbreviations: BMI: Body mass index; SD: Standard deviation; *Student t-test.

Table 2. Association between the body mass index, age, and breast cancer status. Results of the Analysis of Variance (ANOVA).

Source of variation	Degree of freedom	Sums of squares	Mean squares	F	p
Intercept	1	20766.66	20766.66	478982.3	<0.001
Age	4	7.09	1.77	40.9	<0.001
Breast cancer status	1	0.27	0.27	6.1	0.01
Age* Breast cancer status interaction	4	0.73	0.18	4.2	<0.01
Error	21568	935.10	0.04	478982.3	

Table 3. Comparison of different grades of obesity of American women (Flegal et al. 2012, n = 6074, [10]) and non-cancer patients of this study (n = 20,872).

Age (years)	BMI ≥ 30 (%)		BMI ≥ 35 (%)		BMI ≥ 40 (%)	
	Flegal et al.	This study	Flegal et al.	This study	Flegal et al.	This study
≥20	36.3	41.6	18.3	19.1	8.2	7.4
20 - 39	31.9	30.8	17.2	12.4	7.5	4.8
40 - 59	36.0	62.4	17.6	30.7	8.4	11.8
≥60	42.3	66.8	20.6	35.0	8.8	13.9

hormone replacement therapy (HRT) was considered as predictive factor in the statistical analysis the risk of developing breast cancer was only increased in the subgroup of postmenopausal women who have never received HRT [15-18]. Type II diabetes mellitus has been shown to be associated with an increased risk of postmenopausal breast cancer [19,20] and a worse prognosis [21], and insulin use with an increased breast cancer incidence [22,23] and recurrence [21,24]. Another interesting factor currently in the scientific focus is the drug "metformin". Metformin is the drug of first choice in the management of type 2 diabetes, in particular in overweight and obese patients [25]. Recent studies have shown

that metformin significantly reduces breast cancer incidence [26-28]. With a prevalence of 30%, diabetes mellitus type 2 is "endemic" in Saudi Arabia [29]. It can be speculated that our observation of a significantly lower BMI of Saudi Arabian postmenopausal breast cancer patients may be due to the anti-cancer effect of metformin.

In conclusion, future studies are warranted to assess the impact of possible confounding factors on the association between obesity and breast cancer risk. Relevant factors like comorbidities (e.g. diabetes), medication use (e.g. metformin, insulin, HRT), race and ethnicity, and other factors should be carefully assessed in a time-dependent and exposure-related manner.

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