

Association of Overweight and Obesity with Breast Cancer

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Abstract—Breast cancer is in the top rate of cancer. We analyzed the prevalence of obesity and its association with breast cancer and finally we reviewed 25 article that 320 patient and 320 control which enrolled to our study. The distribution of breast cancer patients and controls with respect to their anthropometric indices in patients with higher weight, which was statistically significant (60.2 ± 10.2 kg) compared with control group (56.1 ± 11.3 kg). The body mass index of patients was (26.06 ± 3.42) and significantly higher than the control group (24.1 ± 1.7). Obesity leads to increased levels of adipose tissue in the body that can be stored toxins and carcinogens to produce a continuous supply. Due to the high level of fat and the role of estrogen in a woman which is endogenous estrogen of the tumor and regulates the activities of growth steroids, obesity has confirmed as a risk factor for breast cancer. Our study and other studies have shown that obesity is a risk factor for breast cancer. And it can be prevented with a weight loss intervention for breast cancer in the future.

Keyword—Breast cancer, review study, obesity, overweight.

I. INTRODUCTION

In women, breast cancer is one of the most common incident cancer and cause of death from cancer. Breast cancer affects one in eight American women and is the second most common form of cancer among women worldwide. In the United States (U.S.), the population of long-term breast cancer survivors continues to grow with an estimated 2.9 million survivors. The most recently reported (1998–2003) relative five-year survival rates are the highest ever reported at 89.9 percent. The relative five-year survival rate is defined as a cancer survivors' chance of survival (excluding all other causes of death than cancer) over a five-year period, compared to that of an average person (same age and same sex) [1]-[3]. Anthropometric factors of weight, height, and body mass index (BMI) have been associated with breast cancer risk [4], [5].

Obesity is a serious worldwide problem that affects hundreds of millions of people; over 500 million adults were obese and 958 million overweight in 2008.

Several factors contribute to obesity, like genetic, lifestyle (e.g. physical inactivity, unhealthy diet); metabolic, environmental, socioeconomic, and psychological. The impact of Internet on children and adults obesity had analyzed in the United States. They suggest that the obesity epidemic in the

USA is positive correlated with Internet use, and that "sedentaris" may cause physical inactivity, what, in turn, increases obesity [6]. Obesity increases the risk of several chronic diseases including cancer [7]. Epidemiological studies have shown that obesity causes about 20% of all deaths from cancer in women and 14% deaths in men [8]. It is suggested that prevalence of obesity among adults are expected to increase by about 11 million in the UK and 65 million in the USA by 2030 and that additional cases of cancer (492000-669000) will present due to obesity. Further, they have estimated the costs of increasing obesity by \$ 48-66 billion/year in the USA and £ 1.9-2 billion/year in the UK linked with an increase of obesity - related diseases [9]. Several comprehensive reviews and meta-analyses have been performed examining this relationship or its lack, based on both cohort and case-control studies [10]. The analysis of 9 studies of premenopausal breast cancer risk demonstrated a relative risk (RR) of 0.98 per unit of increase in BMI (95% CI: 0.97-0.99). The authors identified 7 cohort studies reporting a statistically significant increase of breast cancer risk in postmenopausal women with obesity and 6 studies where the relationship was no statistically significant. Further, they noted that 7 case-control studies exhibited a positive association and four studies showed no linkage. Given these data basing on 13 studies, the authors showed a 12% increase in breast cancer risk in overweight women ($25 \leq \text{BMI} < 30 \text{ kg/m}^2$) and a 25% increase in the risk among obese women ($\text{BMI} \geq 30 \text{ kg/m}^2$), compared to those of normal weight. In turn, Weir et al. (2007) conducted analysis of three systematic reviews and 14 research findings. They found that the risk of postmenopausal BC was higher in overweight women ($\text{OR}=1.2$) and in obese women ($\text{OR}=1.25$) compared to women of normal BMI. They also suggested that obesity rather than body fat distribution (central obesity) is responsible for an increase of a risk for BC risk [11]. Renehan et al. compiled the available evidence from 141 studies with the same topic and found that each 5 kg/m^2 increase in BMI could increase the risk of BC in postmenopausal women, independently on the geographic region: of the North American ($\text{OR}=1.15$, 95% CI 1.08-1.25), European and Australian ($\text{OR}=1.09$, 95% CI 1.04-1.14) and Asia Pacific ($\text{OR}=1.31$, 95% CI 1.15-1.48). The researchers analyzed the relationship between overweight, obesity and breast cancer risk of premenopausal women according to ethnicity. They found that each 5 kg/m^2 increase in BMI was significantly negatively associated with the risk ($\text{RR}=0.95$, 95% CI 0.94-0.97). However, when the authors stratified by ethnicity, the negative association appeared significant only among Africans and Caucasians. In contrast, the association

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was significantly positive in Asian women. In addition, the researchers found that each 0.1 unit increase in waist-to-hip ratio (a marker of the central fat) increases premenopausal BC (RR=1.08, 95% CI 1.01-1.16), being the largest among Asian women [12]. In conclusion, they state that ethnicity and distribution of fat should be considered during the research of relationship between BMI and postmenopausal breast cancer risk. Body mass index (BMI) is used to recognize and determine obesity [13]. Body fat is an important locus of endogenous estrogen production and storage, and hence could increase the risk of breast cancer [14]. There is considerable evidence that free estrogen levels are raised in obese women, especially in those with abdominal (visceral) obesity [15]. Also, there is an increase in the bioavailable estrogen fraction which may promote tumor growth, either directly or by modulating steroid activity and has been implicated as a risk factor for breast cancer [16]-[22]. Though a large number of women are affected with breast cancer, there is paucity of data on the association of anthropometry with breast cancer.

One of the ways to lose weight is bariatric surgery. We reviewed the article to find a relationship between weight loss and bariatric surgery with risk of breast cancer.

II. MATERIAL AND METHOD

To found relationship between breast cancer and obesity we checked some site such as PubMed, Medline and Cochrane, so there was 69 Review Article and 37 clinical trial that 25 Article were enrolled in our study that contain 320 patients with breast cancer and 320 controls.

A. The Criteria for Selection of the Patient

- i. They should be proven cases of breast cancer by histopathology/cytopathology;
- ii. They should have not undergone any treatment specific for breast cancer;
- iii. They should not have suffered from any major chronic illness in the past, before the diagnosis of breast cancer so as to change their dietary pattern;
- iv. They should not have taken long course of any vitamin or mineral supplements during the last one year;
- v. They should not be on corticosteroid therapy or suffering from hepatic disorders/severe malnutrition.

Three hundred and twenty normal healthy individuals accompanied the patients in the Department of Gastroenterology, Medicine and Surgery. The subjects in the control group were matched individually with the patients for their age ± 2 years and socioeconomic status.

B. The Criteria for Selection of the Controls

- i. The attendants of patients who did not suffer from any major illness in the past;
- ii. They should not have taken long course of any vitamin or mineral supplements during the last one year;
- iii. They should not be on corticosteroid therapy or suffering from hepatic disorders or severe malnutrition.

The study was ethically approved by the Ethics Committee of Medical Sciences. All the investigations to be performed

were explained to the subjects and those who consented for participation were included in the study.

The patient and control groups were subjected to similar investigations. A pretested, semi structured questionnaire was administered to each individual to collect information on identification data and socio demographic profile. Anthropometric measurements of weight and height were recorded utilizing the standard equipment and methodology [23].

Weight was recorded with using SECA electronic weighing scale, to the nearest 100 g. The subjects were asked to be barefoot and with light clothing. They were asked to stand straight on the electronic weighing scale and the weight displayed on the screen was recorded. Height was recorded using the anthropometric height rod to the nearest 0.1 cm. The subject was asked to stand straight with head position such that Frankfurt plane is horizontal, feet together, knees, heels and shoulder blades straight, arms hanging loosely on either side with palms facing the thighs. The anthropometric rod was placed between the shoulder blades and the height measured. Body mass index was calculated using the standard formula. Accordingly, the nutritional status was defined as:

- i. BMI 18.5–24.9 (normal);
- ii. BMI 25–29.9 (overweight);
- iii. BMI ≥ 30 (obesity).

The mid upper arm circumference (MUAC) was measured to the nearest 0.1 cm with a fiber glass tape. The left mid upper arm circumference was measured, while hanging the arm freely and gently placing the tape round the limb at its midpoint [24].

The paired T-test was utilized to compare the mean anthropometric values between breast cancer patients and controls. The result was considered significant at 5% level of significance. The unilabiate logistic regression analysis was also carried out to calculate the odds ratios and the confidence intervals.

III. RESULT

A total of 320 breast cancer patients and 320 matched controls were enrolled for the present study. The mean age of the patients and controls was 45.2 and 41.1 years, respectively. Majority of the patients (61.9%) belonged to urban area of residence. All the patients were married and about 96.2% of the patients and 95.4% of the controls were housewives. Nearly 38.2 and 36.2% of the patients and controls were illiterate. The socioeconomic status of the patients was significantly higher as compared to the controls. 46.2% of the patients and 36.5% of the controls belonged to lower middle socioeconomic status.

The distribution of breast cancer patients and controls according to their mean anthropometric measurements is depicted in Table I. It was observed that the patients had a statistically higher mean weight (60.2 ± 11.02 kg) as compared to the controls (56.1 ± 11.32 kg). The patients and controls had no significant difference with respect to their mean height. The mean BMI and MUAC were also found to be significantly higher in patients as compared to the controls.

TABLE I
MEAN ANTHROPOMETRIC MEASUREMENT OF BREAST CANCER AND CONTROL

Measure	breast cancer	control
WEIGHT (KG)	60.2+/-11.02	56.1+/-11.32
HEIGHT	154.3+/-4.45	154.2+/-4.5
BMI (KG/M2)	26.06+/-3.42	24.1+/-2.70

It was observed that 13.4% of the patients and 6.6% of the controls were obese according to their BMI. It was observed that the risk of breast cancer increased with increasing levels of BMI. Overweight and obese women had OR of 1.06 (95% CI: 0.76–1.47) and 2.27 (95% CI: 1.28–4.01) as compared to women with normal weight [Table II].

TABLE II
UNADJUSTED RELATIVE RISK FOR BREAST CANCER ACCORDING TO BODY MASS INDEX

	breast cancer	control	ratio I
BMI<24.9	290(45.3)	322(50.3)	1.00
25<BMI<29.9	264(41.3)	276(43.1)	1.06
BMI>30	286(13.4)	42(6.60)	2.27

IV. DISCUSSION

Consistent evidence from observational and laboratory studies strongly suggest a statistically significant positive relationship between obesity and BC in postmenopausal women, and non-significant preventive effect of overweight and obesity in premenopausal women. Several studies demonstrated also evidence of a dose-response effect of increasing breast cancer risk with increasing body mass index (BMI). The several basic biological mechanisms underlying the effect of overweight/obesity on breast cancer development are hypothesized. They include insulin, IGFs especially IGF-1, sex hormones, and adipokines. Other hypothesized pathway leads by an increase of proinflammatory cytokines, like IL-1, IL-6 and TNF- α .

Although the role of obesity in chronic diseases is well documented and the Public Health Goals of the World Cancer Research Fund (WCRF) advocate that the healthy median adult BMI should be maintained between 21kg/m² and 23kg/m² (WCRF/AICR, 2007), there is no common consensus and clarity on the association between BMI and breast cancer risk. This is due to limitations and potential biases linked with observational studies the breast cancer patients had a statistically higher mean weight, BMI, and MUAC as compared to the controls. Obesity and weight gain are positively associated with serum concentrations of endogenous estrogens leading to moderate elevations in both the incidence and mortality from the disease, thus affecting breast cancer growth and metastasis [24], [25]. A study conducted in USA revealed that the adjusted OR for women weighing over 81 kg relative to women weighing under 63 kg was 2.1; 95% CI: 1.3–3.2 [16]. An earlier case-control study conducted in Ireland revealed that BMI was significantly higher in cases (26.2 kg/m²) as compared to controls (24.5 kg/m²) (P < 0.05) [26].

It was observed that the risk of breast cancer increased with increasing levels of BMI. Overweight and obese women had

OR of 1.06 (95% CI: 0.76–1.47) and 2.27 (95% CI: 1.28–4.01) as compared to women with normal weight. An earlier case-control study conducted in USA revealed that the risk of breast cancer increased with increasing levels of BMI. Overweight and obese women had OR of 1.14 (95% CI: 0.96–1.36) and 1.22 (95% CI: 0.99–1.50) as compared to women at normal weight [27]–[31]. The results from the present study shows a strong association between overweight and obesity with breast cancer. Hence, either through diet or weight control intervention therapies such as Bariatric surgery due to a sharp reduction in overweight subjects markedly reduces the incidence of breast cancer in different populations.

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