

Obesity, Body Mass Index and Risk of Breast Cancer: A Case-Control Study

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ABSTRACT

Aim: To investigate the relationship between obesity, body mass index (BMI) and the incidence of breast cancer, so as to making contribution to breast cancer screening in high-risk groups and better treatment modalities.

Methodology: BMI status of 146 breast cancer patients and 40 healthy individuals at different ages were assessed and compared.

Results: The mean BMI was significantly greater in patients than in controls 28.77±3.07 vs. 22.50±1.43kg/m², p<0.001. When stratified by age, BMI was significantly greater in ≥60 age for breast cancer patients as compared to healthy controls (67.5% vs. 32.5%, p <0.001)

Conclusion: BMI and obesity have a liaison with the incidence of breast cancer, particularly for females ≥60 yrs.

Keywords: Body mass index, Obesity, breast cancer

INTRODUCTION

It has been demonstrated from different research studies that obesity is linked to the risk of developing breast carcinoma¹. Breast cancer patients who are overweight as well have greater mortality rate as compared to breast cancer patients who have normal weight. Obesity is an established risk factor which is also associated to poor prognosis in the patients of breast cancer². Currently, body mass index (BMI) is the criteria to assess the obesity status of an individual. Both height as well as weight of the body are considered when calculating BMI. Considerably easy to measure, BMI is the internationally used current standard index to assess the degree of obesity. In this research study, we studied the BMIs of 146 breast cancer patients and 40 age matched healthy controls to compare and correlate between the BMI and the risk of developing breast carcinoma.

METHODOLOGY

This study was performed on BRCA patients who were divided into four subgroups on the basis of BMI according to WHO criteria of Working Group on Obesity in China⁽³⁾. They were diagnosed both on the basis of mammography and then confirmed histologically. Keeping this in view, only biopsy proven patients were included in this study. A total number of 186 study subjects were taken, of which 146 females were taken as cases and 40 age matched females were included in the control group.

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The criteria for inclusion were histologically diagnosed cases of any stage of BRCA falling in the age range of 20-84 years with the median age of 53 years. Exclusion criteria was patients with benign breast lesions, any malignancy other than breast cancer. These patients were selected from the oncology department of INMOL Hospital, Lahore. Besides, the clinical physical examination, the age, gender, height and weight upon admission, along with the pathological diagnosis of each patient was surveyed. The control group consisted of healthy individuals that came to the breast clinic at INMOL hospital, Lahore and participated in the cancer screening program and met the criteria of no breast lumps or any other benign breast diseases as evidenced by screening with a BIRADS category of 1 or 2, or breast ultrasonography, females at least 20-year old, not pregnant and not having any other kind of malignancy. 40 healthy individuals were selected across age groups that roughly corresponded with the age groups of patients.

For anthropometric analysis, a standard height measuring scale was used to assess the height (cm), weight was taken in kilograms (kg) on the Camry weight scale. The Body Mass Index (BMI) in kg / m² was calculated to assess the extent of obesity and calculated for each individual by the formula:

$$BMI = \frac{Weight(kg)}{Height(m^2)}$$

In both groups, the individuals were further divided into four groups based on the standards on obesity and overweight published by the Working Group on Obesity in China³. The four categorized groups were: underweight females group, with aBMI of <18.5 kg/m²; females with normal BMI range

group, in the range of 18.5-23.9 kg/m²; and females who were overweight, with a BMI falling in the range of 24-27.9kg/m²; and obese females, with a BMI of ≥28.0 kg/m² (Table 1).

All data was analyzed by using SPSS 20.0. Data following normal distribution were presented in mean±SD. T-test was performed to evaluate the difference in BMI between case group and control group. P<0.05 was considered statistically significant.

RESULTS

No statistically significant difference was found between the mean age and height of the BRCA patients and control groups (Table 2). The mean weight and BMI showed significant difference between the two groups. The mean weight in patients was found to be 69.80±9.37 kg which was highly significant (p < 0.001) as compared to controls which was 52.90±5.74kg. Similarly, the mean BMI in patients was 28.77±3.07 which was highly significantly higher (p<0.001) as compared to controls which was 22.50±1.43 (Table 2).

Table 1: Distribution of BRCA Cases and Controls according to BMI

Groups	Cases	%	Control	%
Under weight<18.5kg/m ²	27	18.4	5	12.5
Normal 18.5-23.9kg/m ²	37	25.3	13	32.5
Over weight24-27.9 kg/m ²	38	26	9	22.5
Obese>28 kg/m ²	44	30.1	13	32.5
Total	146	100	40	100

Table 2: Comparison of age, weight, height and BMI in controls and BRCA patients. Mean±SD is given. Figures in parentheses indicate number of cases in each group.

Group	Controls (40)	BRCA patients(146)
Age (yr)	40.40 ± 3.28	38.94 ± 5.51
Weight (Kg)	52.90 ± 5.74	69.80 ± 9.37***
Height (m)	1.52 ± 7.08	1.55 ± 6.69
BMI (kg/m ²)	22.50 ± 1.43	28.77 ± 3.07***

***p< 0.001 significantly higher as compared to control

All individuals were grouped according to BMI and divided into subgroups by age. The results showed that, among the individuals in case group, 56 patients (38.35% of the cases) were less than 60-years old. 90 cases (64%) were more than 60 years old. The mean BMI of these patients was higher than that of the corresponding subgroup in control group (27 females). The difference was statistically significant (P<0.001). Furthermore, the obese population proportion in females > 60 yrs in cases was significantly higher than that in controls (67.5% vs 32.5%) (Table 3).

Table 3: Comparison of BMI between cases and controls after grouping by age

BMI(kg/m ²)	Cases	Controls	P value
< 60 years			
< 18.5	11	3	0.637
< 18.5-23.9	20	4	
24-27.9	13	2	
>28.0	12	4	
Total	56	13	
≥60 years			
< 18.5	16	2	0.001***
< 18.5-23.9	17	9	
24-27.9	25	7	
>28.0	32	9	
Total	90	27	

*** p< 0.001 significantly higher as compared to control

DISCUSSION

Presently, obesity is one of the major health concerns worldwide⁴. It is associated with hypertension, cardiovascular disorders; type II diabetes mellitus, metabolic syndrome, dyslipidemia and various malignancies including endometrial cancer, ovarian carcinoma, malignancies of head and neck region and colorectal carcinoma⁵. It has been reported in various research studies that obese females have a predisposition to develop breast carcinoma⁶. Consequently, a BMI on the higher side could present with an enhanced risk factor of developing carcinoma of the breast in these females.

The division of cases and controls into subgroups on the bases of BMI was to diminish any influence on the results that could arise from incongruous grouping of study subjects. The mean BMI was 28.77±3.07kg/m² in patients and higher than in controls (22.5±1.43kg/m²) (p<0.001). Additionally the mean BMI of the patients in the age group more than 60 years and above was also significantly greater than that of the analogous subgroup in controls (p <0.001). This suggests that obesity is an independent risk factor linked with the development of breast cancer, especially for elderly females. This might be due to the fact that in postmenopausal females the levels of endogenous sex hormones are changed significantly as compared to their premenopausal levels. This influences greatly on the woman's health in this age group. Unambiguously, an increased estrogen levels has been confirmed to be an established risk factor for oncogenesis especially breast malignancy and that too in post-menopausal females⁷. After menopause, the body converts testosterone to estrogen via aromatase, as the hypo function of ovary. Estrogen enhances the proliferation of mammary gland cells via estrogen receptors and

downstream intracellular cell signaling pathways⁸. It has been found that obese post-menopausal female express higher aromatase levels in their adipocytes as compared to post-menopausal females with normal BMI. This could lead to raised endogenous estrogen levels in obese women thus leading to mammary gland cellular hyperproliferation. Furthermore, subcutaneous adipose tissue thickening might lead to enhanced levels of 17 β -hydroxysteroid dehydro-genase, thus promoting the conversion of androstenedione to testosterone. This will indirectly increase the estrogen levels in the body⁹. Hence it can be elucidated that in post-menopausal females obesity plays a pivotal role in the development of breast cancer¹⁰. These results are congruent with the literature cited. Nonetheless some studies have reported a reverse relationship between increasing BMI and decreasing breast carcinoma severity in premenopausal females¹¹. According to another study the weight gain was significantly higher ($p < 0.01$) in breast cancer patients as compared to controls¹². Many studies report an increasing risk of postmenopausal breast carcinoma with weight gain and increasing BMI¹³, whereas a majority of studies report an inverse relationship of weight gain and increasing BMI with BRCA in premenopausal females¹⁴. The difference of results may be due to the differences between socioeconomic factors, diet, geographical variations, ethnical differences and environmental factors.

CONCLUSION

According to some studies the effect of BMI on the incidence of breast cancer could be race and ethnic dependent as well¹⁵. Thus, explicating the exact correlation and underlying mechanism between BMI and the incidence of breast cancer amongst Pakistani females will greatly contribute to the discovery and characterization of the risk factors of breast malignancy. Furthermore, it would facilitate public education to raise the mindfulness of cancer prevention. In conclusion, it could improve the formulating of beneficial therapeutic regime against breast carcinoma.

REFERENCES

1. Emaus A, Veierød MB, Tretli S, Finstad SE, Selmer R, Furberg A-S, et al. Metabolic profile, physical activity, and mortality in breast cancer patients. *Breast Cancer Res Treat.* 2010 Jun;121(3):651–60.

2. Santillán-Benítez JG, Mendieta-Zerón H, Gómez-Oliván LM, Torres-Juárez JJ, González-Bañales JM, Hernández-Peña L V, et al. The Tetrad BMI, Leptin, Leptin/Adiponectin (L/A) Ratio and CA 15-3 are Reliable Biomarkers of Breast Cancer. *J Clin Lab Anal.* 2013;27(1):12–20.
3. Zhou B, Cooperative Meta-Analysis Group Of China Obesity Task Force. [Predictive values of body mass index and waist circumference to risk factors of related diseases in Chinese adult population]. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2002 Feb;23(1):5–10.
4. Fontaine KR. Years of Life Lost Due to Obesity. *JAMA.* 2003;289(2):187.
5. Tan X, Nelson HH, Langevin SM, McClean M, Marsit CJ, Waterboer T, et al. Obesity and head and neck cancer risk and survival by human papillomavirus serology. *Cancer Causes Control.* 2014;26(1):111–9.
6. Montazeri A, Sadighi J, Farzadi F, Maftoon F, Vahdaninia M, Ansari M, et al. Weight, height, body mass index and risk of breast cancer in postmenopausal women: a case-control study. *BMC Cancer.* 2008;8(1).
7. Yager JD, Davidson NE. Estrogen Carcinogenesis in Breast Cancer. *N Engl J Med.* 2006;354(3):270–82.
8. Lorincz AM. Molecular links between obesity and breast cancer. *Endocr Relat Cancer.* 2006;13(2):279–92.
9. Boonyaratanakornkit V, Pateetin P. The Role of Ovarian Sex Steroids in Metabolic Homeostasis, Obesity, and Postmenopausal Breast Cancer: Molecular Mechanisms and Therapeutic Implications. *Biomed Res Int.* 2015;2015:1–13.
10. McKenzie F, Ferrari P, Freisling H, Chajès V, Rinaldi S, de Batlle J, et al. Healthy lifestyle and risk of breast cancer among postmenopausal women in the European Prospective Investigation into Cancer and Nutrition cohort study. *Int J Cancer.* 2014;136(11):2640–8.
11. Huang Z, Hankinson SE, Colditz GA, Stampfer MJ, Hunter DJ, Manson JE, et al. Dual Effects of Weight and Weight Gain on Breast Cancer Risk. *JAMA.* 1997;278(17):1407.
12. Kumar NB, Lyman GH, Allen K, Cox CE, Schapira D V. Timing of weight gain and breast cancer risk. *Cancer.* 1995 Jul 15;76(2):243–9.
13. Cleary MP, Maihle NJ. The role of body mass index in the relative risk of developing premenopausal versus postmenopausal breast cancer. *Proc Soc Exp Biol Med.* 1997 Oct;216(1):28–43.
14. Ligibel J. Obesity and breast cancer. *Oncology.* 2011;25(11):994.
15. Zhonghua Liu Xing Bing Xue Za Zhi. Body mass index reference norm for screening overweight and obesity in Chinese children and adolescents. *Gr China Obes Task Force.* 2004 Feb;25(2):97–102.