

## Correlation between stages of breast cancer and BMI in females: a multi-centre study

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### Abstract

**Objective:** To determine the link between breast cancer and obesity in women by using body mass index at the time of diagnosis.

**Method:** The cross-sectional study was conducted from October 2019 to April 2020 at Pakistan Ordnance Factories Hospital, Wah Cantt, and Islamabad Medical Complex National Engineering and Scientific Commission Hospital, Islamabad, Pakistan. The sample comprised women aged 40-70 years with a recent diagnosis of breast cancer. Patients' body mass index values were calculated after they were diagnosed and additional staging examinations were carried out. Data was analysed using SPSS 21.

**Results:** There were 100 cases with a mean age of 52.24±7.47 years. There was a significant link between obesity and breast cancer ( $p=0.002$ ), with higher body mass index carrying a higher risk of advanced breast cancer.

**Conclusion:** Obesity may contribute to postmenopausal breast cancer in women.

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### Introduction

Over two million new cases of breast cancer (BC) are detected each year,<sup>1,2</sup> making it the second most common malignancy worldwide after lung cancer. Additionally, it is the top cause of death from cancer in women globally.<sup>3</sup> BC is the most common form of female cancer in the United States, and the second greatest cause of cancer death among women. Premenopausal BC is more common<sup>4</sup> in Asian countries.

BC is the most common kind of cancer among Pakistanis.<sup>3</sup> It affects one in every nine Pakistani women.<sup>5</sup> Although obesity is a risk factor for postmenopausal BC, it is not the only one. In both developed and developing countries, obesity and overweight are major public health issues. Overweight and obesity affected an estimated 1.9 billion adults globally in 2018, with 650 million people classified as morbidly obese.<sup>6</sup>

About 2.8 million people around the world have died as a result of obesity and obesity-related conditions. Pakistan is the 10th most obese country in the world.<sup>7</sup> Obesity and overweight are on the rise in Pakistan, and there is a correlation between obesity and BC, but it is less obvious in patients with early symptoms.<sup>6,8,7</sup> BC is more common in obese postmenopausal women, although the majority

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of studies show that both pre- and postmenopausal women have poor disease outcomes, even though some studies yield inconclusive data.<sup>3</sup>

There appears to be a correlation between sex hormones, insulin and several adipokines associated with obesity.<sup>3</sup> Recent studies have strongly linked obesity to an increased BC risk. A total of 268,600 new instances of invasive BC in women were expected in 2019-20, according to the American Cancer Society.<sup>6</sup> Over 3.8 million American women with a BC history were still alive in early 2019.<sup>1</sup> In the US, more than 150,000 women who have battled BC have been diagnosed with metastatic disease.<sup>9</sup> As of 2015, 28.3% of adults in the US and 22.9% of adults in Europe were overweight or obese, representing increases of 2.22 and 1.66 times, respectively, since 1980.<sup>10</sup>

Despite high prevalence of obesity and BC in Pakistan, there have been very few important local studies. The current study was planned to determine the link between BC and obesity in women by using body mass index (BMI) at the time of diagnosis.

### Patients and Methods

The cross-sectional study was conducted from October 2019 to April 2020 at Pakistan Ordnance Factories (POF) Hospital, Wah Cantt, and Islamabad Medical Complex (IMC) National Engineering and Scientific Commission (NESCOM) Hospital, Islamabad, Pakistan. After approval from IMC-NESCOM ethics review committee, the sample size was calculated using the World Health Organisation

(WHO) calculator<sup>11,12</sup> with projected population 23%,<sup>13</sup> confidence range 95% and absolute precision 8%. The sample was raised using non-probability consecutive sampling technique from among patients who either presented to the surgical outpatient department (OPD) or were admitted to the surgical ward. Those included were women aged 40-70 years who had just been diagnosed with BC. Patients with a history of BC or any other cancer were excluded, and so were those who fell outside the defined age range and those who were already getting treatment for BC.

Data was collected after taking informed consent from all the participants. Initial data on age, parity, marital status and family history was collected on a predesigned Performa before the patients were subjected to a thorough history and examination.

BMI was computed by multiplying an individual's weight in kilograms by the square of individual's height in meters, or  $BMI = \text{weight (in kg)}/\text{height}^2 \text{ (in m}^2\text{)}$ .<sup>14</sup> Diagnosis of BC was determined via triple assessment.<sup>15</sup>

Additional staging examinations were also done. The radiologist reported mammography results using Breast Imaging Reporting and Data System (BIRADS) scoring system.<sup>16,17</sup> These categories determine the likelihood of a normal, benign or malignant diagnosis. If a mammography is classified as category 0, further investigation and characterisation is necessary. This may involve obtaining multiple mammographic images, an ultrasound, and in certain cases a magnetic resonance imaging (MRI) scan.

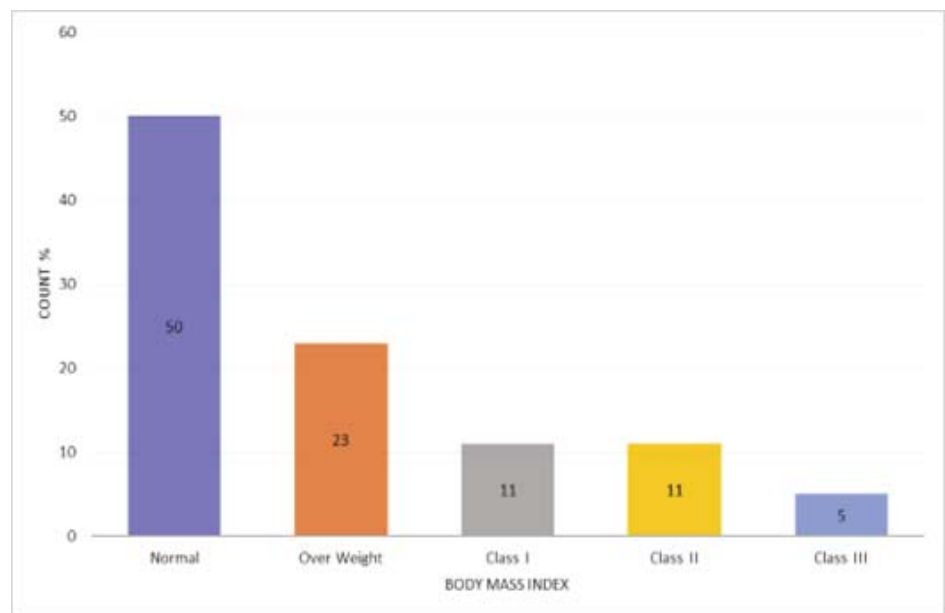
Several mammographic screening procedures were used at various angles and magnifications, including spot compression. In the event of any abnormalities, breast ultrasonography was employed to identify cystic and solid tumours. Additionally, an axillary ultrasound was conducted to check for axillary lymph node (LN) metastases. Finally, breast MRI and biopsy were conducted to confirm the diagnosis. Following the diagnosis, staging investigations were undertaken, using the Tumor, Nodes and Metastases (TNM) categorisation

systems<sup>18</sup> developed by the American Joint Committee on Cancer and the International Union for Cancer Control. Clinical examination and/or imaging were utilised to identify the clinical tumour (T) stage (Table 2).

Data was analysed using SPSS 21. Frequencies and percentages were calculated for qualitative variables, while mean value and standard deviations (SDs) were used for quantitative variables. To account for effect modifiers, such as age, marital status, family history, parity and menopausal status, stratification was applied. Chi-square test was used following the stratification.  $P < 0.05$  was considered statistically significant.

## Results

There were 100 cases with a mean age of  $52.24 \pm 7.47$  years, with 46(46%) being in their 20s. Of the total, 91(91%) subjects were married, and 36(36%) having a family history of BC. As per the Asian classification of BMI (Table 1), of the total 100 patients, 25(25%) women had normal BMI, 25(25%) were overweight, 23(23%) were



**Figure-1:** Body mass index (BMI) of newly-diagnosed breast cancer cases (n=100)

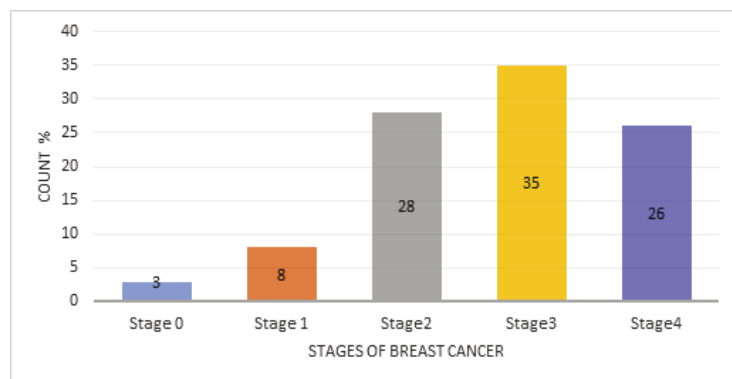
**Table-1:** Asian Body mass index (BMI) categories of WHO<sup>30,31</sup>

Underweight	< 18.5
Normal Weight	18.5 – 22.9
Overweight	23.0 – 24.9
Obese I	25.0 – 29.9
Obese II	≥ 30

**Table-2:** Staging of breast cancer as measured on histopathology.

Stage 0	T N M
	Tis N0 M0
Stage I	T1 N0 M0
	T0 N1mi M0
	T1 N1mi M0
Stage II A	T0 N1 M0
	T1 N1 M0
	T2 N0 M0
Stage II B	T2 N1 M0
	T3 N0 M0
Stage III A	T0 N2 M0
	T1 N2 M0
	T2 N2 M0
	T2 N2 M0
Stage III B	T3 N2 M0
	T4 N0 M0
Stage III C	Any T N3 M0
Stage IV	Any T Any N M1

T: Tumour, N: Node, M: Metastasis-



**Figure-2:** Frequency of different stages of breast cancer in females at the time of diagnosis (n=100)

**Table-3:** Demographic characteristics and frequency of different stages of carcinoma of breast based on body mass index (BMI) in female patients (n=100).

Variables	Mean ± SD	95% Confidence Interval for Mean	
		Lower Bound	Upper Bound
Age (years)	52.24±7.47	50.76	53.72
Weight (Kg)	68.27±16.93	64.91	71.63
Height (cm)	159.41±8.07	157.81	161.01
BMI (Kg/m <sup>2</sup> )	26.77±5.91	25.59	27.94

Stage	Body Mass Index			P-Value
	Normal (n=50)	Overweight (n=23)	Obese I-III (n=27)	
Stage 0	3 (6%)	0%	0%	0.002
Stage 1	8(16%)	0%	0%	
Stage 2	19(38%)	5 (21.7%)	4 (14.8%)	
Stage 3	14(28%)	9 (39.1%)	12 (44.4%)	
Stage 4	6(12%)	9 (39.1%)	11 (40.7%)	

SD: Standard deviation.

Obese I and 27(27%) were obese II (Figure 1).<sup>30,31</sup>

Further, 8(8%) of the women had stage I carcinoma, 28(28%) stage 2, 35(35%) stage 3, and 26(26%) stage 4. There were 54(54%) postmenopausal women with BC, compared to 46(46%) premenopausal subjects.

There was a significant link between obesity and breast cancer (p=0.002), with higher BMI carrying a higher risk of advanced breast cancer (Table 3).

### Discussion

Among Pakistani women, BC is the most often diagnosed cancer. Among Asian countries, Pakistan's population has grown significantly.<sup>19</sup> Preventive measures are needed in the light of rising number of BC patients.<sup>20</sup> There is a global epidemic of obesity, and it is just getting worse. An increased risk of certain diseases, such as cancer, and an increase in mortality are both linked to a higher BMI.<sup>21</sup>

Overweight and obese patients have a considerably shorter overall survival rate.<sup>22</sup>

In the current study, 25(25%) women had normal BMI, 25(25%) were overweight, 23(23%) were Obese I and 27(27%) were obese II.<sup>30,31</sup> Women with high BMI are more likely to develop BC if their peripheral adipose tissue is overactive in the aromatase enzyme.<sup>23</sup> High BMI and obesity are associated with an increased risk of developing triple-negative BC in premenopausal women<sup>24</sup> and in BC patients regardless of their menopausal state.<sup>25</sup> The current findings in line with such research.

BC incidence in the current study was higher in postmenopausal women than in premenopausal women. Stage I carcinoma affected 8% of females, stage 2 affected 28%, stage 3 affected 35%, and stage 4 affected 26% females at the time of diagnosis. When compared to patients with a normal BMI, women with stage 3 and stage 4 BC had considerably higher rates of obesity and overweight (p=0.002).

Yadong Cui et al. discovered that obesity was strongly linked to a higher BC stage at the time of diagnosis.<sup>26</sup> Another study showed that 23% invasive BC was more likely to strike women with a higher BMI, and, in addition, obesity grades 2 and 3 were linked to more advanced disease.<sup>27</sup> The risk of recurrence and death in obese women was significantly higher than that of lean women, with hazard ratio of 1.3 to

>2 in a study.<sup>28</sup>

According to the American Cancer Society, being overweight or obese increases one's chances of developing postmenopausal BC and reduces one's overall chances of survival.<sup>29</sup>

## Conclusion

Obesity and BC were found to have a significant association. Postmenopausal BC may develop more slowly if a woman is obese. The impact of BMI on the incidence and prognosis of BC must be regularly monitored. BC screening and prevention measures should run parallel to weight management.

**Disclaimer:** The text is based on a dissertation approved by the College of Physician and surgeons of Pakistan (CPSP).

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