

The Relations Between High Body Mass Index and Breast Cancer Characteristics

Shwan Salam Marouf ¹

¹ College of Dentistry, Hawler Medical University, Erbil, Iraq

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Correspondence: Shwan Salam Marouf

Email: shwan.marouf@gmail.com

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Abstract

Background: In the context of rising obesity rates globally, understanding the effect of high body mass index (BMI) on breast cancer characteristics is crucial. Previous research has hinted at associations between obesity and some specific features, such as tumor receptor status and axillary lymph node involvement. However, a comprehensive investigation into these relationships is essential for informing targeted interventions and advancing our understanding of breast cancer in the context of obesity.

Objective: To investigate the relationship between high BMI and some key tumor characteristics such as hormone receptor status, HER2 receptor status, tumor grade, tumor size and axillary lymph node status.

Patients and Methods: A retrospective analysis of the medical records of 186 female breast cancer patients treated at Rizgary Teaching Hospital's Oncology Department in Erbil City during the year 2021.

Results: The study revealed a statistically significant association between elevated BMI and certain pivotal breast tumor characteristics, particularly HER2 receptor status. Additionally, obese individuals exhibited a significantly greater probability of having axillary lymph node-positive disease compared to their non-obese counterparts.

Conclusion: This study establishes a noteworthy association between high BMI and some critical breast cancer characteristics, which may underscore the clinical relevance of body mass index in shaping breast cancer profiles.

Keywords: Body mass index (BMI), breast cancer, tumor characteristics.

Introduction

Nowadays, a high body mass index (BMI), encompassing both overweight and obesity, is a prevalent health issue with a rising occurrence on a global scale. The United Nation's World Health Organization (WHO) considers the global obesity as an epidemic; for instance, in 2016 more than 1.9 billion adults worldwide were overweight, and 650 million adults (13 percent of the world's adult population) were obese [1,2]. Contemporary research conducted worldwide

has indicated a correlation between global obesity and heightened susceptibility to various chronic health conditions, including cardiovascular diseases, diabetes mellitus, and cancer. It is noteworthy that these associations may exhibit variations among diverse ethnic and racial groups [3,4].

The complexity of relationships between obesity and cancer is multifactorial that involves a numerous combination of many factors such as genetics, environmental and

lifestyle influences, some of which are very intricate and not fully understood. Some explanations explicate that obesity induces a state of persistent low-grade inflammation, especially in white adipose tissue, resulting in immune dysfunction characterized by heightened production of pro-inflammatory cytokines, alternative macrophage activation, and impaired T-cell function. Given that the breast by itself consists predominantly of white adipose tissue, the development of breast cancer involves direct interactions with cells and signals from the adipose tissues, which are influenced by the state of obesity [5,6,7,8,9].

Importantly, variations in breast cancer subtypes and tumor characteristics could contribute to prognosis in obese individuals. According to several studies, obesity is linked to an elevated risk of hormone receptor-positive breast cancer, which may be influenced by an increase in circulating estrogen levels [10,11,12,13,14]. The higher adiposity in obese patients can lead to elevation in aromatase production and subsequently increase the circulating estrogen. Additionally, obese patients may experience a decrease in sex hormone-binding globulin (SHBG), a liver-produced glycoprotein that restricts estrogen biological activity.

Consequently, a reduction in SHBG levels in obese women could elevate the risk of hormone receptor-positive breast cancer [15,16,17]. Also, there is a complex and incompletely-understood relationship between obesity and human epidermal growth factor receptor (HER2) status in breast cancer. Based on some studies, obesity consistently correlates with poorer overall

survival in early HER2-positive breast cancer [18,19,20].

Additionally, some studies have shown that obesity has linked to a higher disease stage, increased tumor size, elevated lymph node ratio, and the presence of more aggressive tumors at the time of diagnosis [10,21]. Notably, individuals with breast cancer and obesity face a up to 46% higher likelihood of developing distant metastases a decade after diagnosis of the disease [22]. Besides, obesity in breast cancer patients might also be related to increased frequencies of disease recurrence, diminished quality of life, second primary tumors, and heightened risk of disease-related complications such as lymphedema and other comorbidities like diabetes mellitus, hypertension, and cardiovascular diseases [23].

The aim of this study was to investigate the relationship between high body mass index (BMI) and key breast cancer tumor characteristics, including hormone receptor status, HER2 receptor status, tumor grade, primary tumor size and axillary lymph node status. Through this exploration, we sought to identify potential associations that could enhance our understanding of the impact of BMI on breast cancer presentation and progression.

Patients and Methods

Data source and study design

In this retrospective study, data were extracted from the medical records of patients diagnosed and treated for breast cancer at Rizgary Teaching Hospitals Oncology Center in Erbil, Iraq, covering the period from the beginning to the end of 2021. The aim was to comprehensively investigate the relationship between high body mass

index (BMI) and breast cancer characteristics. The study exclusively included the records of 186 female patients aged 23 to 84 with histologically confirmed breast cancer. Cases with incomplete data in their records were excluded to ensure a focused and relevant dataset for analysis.

To systematically collect relevant data from patient records, a structured data collection form was designed. This form included fields for essential variables such as patient demographics, high BMI indicators, and breast cancer characteristics (e.g., hormone receptor status, HER2 receptor status, tumor grade, and disease stage). The form was meticulously crafted to ensure comprehensive data extraction aligned with the study objectives.

The body mass index (BMI) was calculated based on the recorded weight and height of the patients, using the following equation: $BMI = \text{weight (kg)} \div \text{squared height (meters)}$. It placed patients into four distinct categories: underweight ($BMI < 18.5$), healthy (normal) weight ($BMI = 18.5 - 24.9$), overweight ($BMI = 25.0 - 29.9$) and obese ($BMI \geq 30.0$) [24].

The variables of interest in breast cancer characteristics, including hormone receptor status, HER2 receptor status, tumor grade, tumor size, and axillary lymph node status, were precisely extracted from the patients' pathology and immunohistochemistry reports. In addition to histopathology reports, medical imaging reports such as CT scans and MRI scans were employed for the tumor

staging based on the TNM Staging System of Union for International Cancer Control (UICC), 8th edition [25]. This comprehensive approach, combining histopathological assessment and imaging data, aimed to provide a thorough and accurate representation of the breast cancer cases under scrutiny in this study.

Statistical Analysis

The statistical analysis was conducted utilizing the Statistical Package for the Social Sciences (SPSS) software, version 25. Descriptive statistics were employed to summarize the demographic characteristics of the study population. Cross tabulation and the Chi-Square test in SPSS were utilized to assess significant associations between body mass index and other studied variables. In instances where tables exhibited small frequencies, Fisher's Exact test was employed for a more robust analysis. The significance level was set at a threshold of 0.05 ($p < 0.05$), indicating statistical significance.

Results

This retrospective study included 186 patients' records with confirmed breast cancer diagnosis. Table (1) shows the frequency distribution of body mass index (BMI) amongst the studied cases. Of note, there were no any underweight patients; only minority (around 11%) had a normal (healthy) weight; while the rest of the studied patients were either overweight or obese, at 58.1 percent and 30.6 percent respectively.

Table (1): Distribution of patients with breast cancer according to BMI. (no=186).

Body Mass Index	Frequency	Percentage (%)
Underweight	0	0.0%
Healthy weight	21	11.3%
Overweight	108	58.1%
Obese	57	30.6%
Total	186	100.0%

The frequency distribution of various breast cancer tumor characteristics, including hormone receptor status, HER2 receptor status, tumor grade, tumor size, and axillary lymph node status were examined. This is in addition to identifying their relations with the patients' body mass index.

Regarding the associations between body mass index and the hormone receptor status

in the studied patients' records, as seen in Table (2), generally just under three quarters of the patients were hormone receptor negative. There were no statistically significant differences in hormone receptor status expression among different BMI categories. The Pearson Chi-Squared p-value was 0.734.

Table (2): Association between BMI and hormone receptor status. (no=186).

BMI Category	Hormone Receptor Status			p-value
	Negative	Positive	Total	
Healthy, n (%)	6 (28.6%)	15 (71.4%)	21 (100%)	0.734
Overweight, n (%)	23 (21.3%)	85 (78.7%)	108 (100%)	
Obese, n (%)	14 (24.6%)	43 (75.4%)	57 (100%)	
Total	43 (23.1%)	143 (76.9%)	186 (100%)	

On the other hand, in regard to the distribution of HER2 receptor status among the breast cancer patients, as depicted in Table (3), around 80 percent of the patients had negative HER2 receptor status. This distribution was statistically different between various BMI subgroups. For

instance, comparing to the obese patients, the non-obese (healthy and overweight) patients were significantly more likely to have HER2 negative disease at the time of presentation. The Fisher's Exact two-tailed p-value was 0.007.

Table (3): Correlation between BMI and HER2 receptor status. (no=186).

BMI Category	HER2 Receptor Status			p-value
	Negative	Positive	Total	
Healthy, n (%)	17 (81.0%)	4 (19.0%)	21 (100%)	0.007
Overweight, n (%)	93 (86.1%)	15 (13.9%)	108 (100%)	
Obese, n (%)	37 (64.9%)	20 (35.1%)	57 (100%)	
Total	147 (79.0%)	39 (21.0%)	186 (100%)	

Another important studied variable was tumor grade. Table (4) shows the distributions of the three tumor grades amongst the studied patients' records. Referring to data in Table (4), only seven percent of the patients had grade I (low grade) disease, around half of them had grade

II (intermediate grade) disease, and more than a third of them had grade III (high grade) breast cancer. This distribution of the tumor grades was almost similar between the different BMI categories without any significant difference between them. The p-value was very close to one.

Table (4): Relations between tumor grade and BMI. (no=186).

BMI Category	Tumor Grade				p-value
	Grade I	Grade II	Grade III	Total	
Healthy, n (%)	2 (9.5%)	10 (47.6%)	9 (42.9%)	21 (100%)	0.914
Overweight, n (%)	8 (7.4%)	59 (54.6%)	41 (38.0%)	108 (100%)	
Obese, n (%)	3 (5.3%)	32 (56.1%)	22 (38.6%)	57 (100%)	
Total	13 (7.0%)	101 (54.3%)	72 (38.7%)	186 (100%)	

Similarly, there were no statistically meaningful association between the primary tumor size and body mass index of the studied patients. Table (5) illustrates that about three quarters of the patients, regardless of their BMI groups, had small tumor sizes (T1 and T2), and about 10

percent of the patients, whether healthy, overweight or obese, have advanced (T4) disease. Obviously, there was no any statistically significant difference between the BMI categories related to the primary breast tumor size at the time of presentation. The Fisher's Exact p-value was 0.599.

Table (5): Exploring the connection between tumor size and BMI. (no=186).

BMI Category	Tumor Size						p-value
	Tis	T1	T2	T3	T4	Total	
Healthy, n (%)	0 (0.0%)	5 (23.8%)	11 (52.4%)	3 (14.3%)	2 (9.5%)	21 (100%)	0.599
Overweight, n (%)	4 (3.7%)	25 (23.1%)	58 (53.7%)	10 (9.3%)	11 (10.2%)	108 (100%)	
Obese, n (%)	0 (0.0%)	7 (12.3%)	37 (64.9%)	7 (12.3%)	6 (10.5%)	57 (100%)	
Total	4 (2.2%)	37 (19.9%)	106 (57.0%)	20 (10.8%)	19 (10.2%)	186 (100%)	

Another crucial tumor characteristic in breast cancer patients is the status of axillary lymph nodes, indicating whether they are affected by the malignancy. Examining Table (6) indicates that, in general, just under 60% of patients had axillary node-positive disease at the time of breast cancer diagnosis. Notably,

obese patients were significantly more susceptible to axillary node-positive disease, surpassing 70%, compared to approximately half of the healthy and overweight patients. The Pearson Chi-Square analysis yielded a p-value of 0.039.

Table (6): Association between BMI and axillary lymph node status. (no=186).

BMI Category	Axillary Nodal Status			p-value
	Node Negative	Node Positive	Total	
Healthy, n (%)	10 (47.6%)	11 (52.4%)	21 (100%)	0.039
Overweight, n (%)	52 (48.1%)	56 (51.9%)	108 (100%)	
Obese, n (%)	16 (28.1%)	41 (71.9%)	57 (100%)	
Total	78 (41.9%)	108 (58.1%)	186 (100%)	

Discussion

Because many studies link the associations between excess body weight and cancer, many health establishments such as the World Health Organization (WHO), have recently advocated for ongoing monitoring of body mass index to assess obesity trends in populations over time [26].

Regarding the relationship between body mass index and the hormone receptor status expression in breast cancer, the current study showed that there was no statistically significant effect of overweight or obesity on the types of hormone receptor characteristics (positive vs. negative). Based on previous studies, there are contradicting results about that. For instance, akin to the findings of the present study, research conducted in Indonesia demonstrated a lack of a substantial association between obesity and the hormone receptor status of primary breast cancer [27]. On the other hand, some other studies are opposing the results of our study. For example, a study found that obese women, with body mass index of 35 or higher, have a strong likelihood to develop estrogen receptor-positive/progesterone receptor-positive breast cancer, but not estrogen-negative breast cancer [28]. This could be primarily attributed to elevated levels of free estradiol circulating in the blood stream of obese individuals.

Discrepancies in population characteristics and other factors influencing hormone receptor expression in primary breast cancer may contribute to variations in this outcome [11,29].

On the contrary, our study revealed a strong relationship between obesity and human epidermal growth factor receptor (HER2) expression status in the studied women with breast cancer. Based on the current study, the chance of being obese were about three times higher in those with HER2-positive disease, compared with those with HER2-negative disease. The connection between obesity and HER2-positive breast cancer remains not fully comprehended. According to certain studies on this matter, obesity consistently correlates with poorer overall survival in early-stage HER2-positive breast cancer patients. However, the evidence regarding the association between obesity and advanced HER2-positive breast cancer is still diverse [18].

Concerning the relationship between excessive body weight and breast cancer staging characteristics, while the present study did not identify a significant link between excess body weight and the grade and size of the primary tumor, it did establish a statistically significant association between obesity and axillary lymph node status. These

findings, to some extent, align with other studies investigating the impact of excess body weight on breast cancer staging. For instance, research conducted at the Geneva Cancer Registry in Switzerland compared diagnostic features among obese and non-obese breast cancer patients. The results indicated that obese patients more frequently presented with advanced disease stages, experiencing higher rates of surgical delays and extended hospital stays post-surgery. The authors suggested that weight-related embarrassment might contribute to reluctance among obese women for physical examinations. They propose that educating obese women about breast self-examination and clinical breast examination may be less effective, highlighting the need to develop strategies to prevent advanced disease upon diagnosis in this expanding patient demographics [26,30].

To end with, more studies in this field are necessary to elucidate the link between elevated body mass index and the occurrence of breast cancer, and to gain deeper insights into how obesity influences breast cancer behavior. Revealing the mechanisms associated with obesity could help identify at-risk populations, and interventions targeting these mechanisms may mitigate breast cancer-related morbidities and fatalities [31,32].

Conclusions

In conclusion, this study underscores a significant association between high body mass index (BMI) and some important breast cancer prognostic characteristics, particularly impacting tumor receptor status and axillary lymph node involvement. Compared to non-obese individuals, obese patients exhibited a

significantly higher prevalence of HER2-receptor positive disease, and a higher rate of axillary lymph node positivity, emphasizing the clinical relevance of BMI in breast cancer staging and prognosis.

Moving forward, further investigations should explore the underlying mechanisms of this relationship, providing a more nuanced understanding. This study contributes valuable insights into the complex interplay between obesity and breast cancer, paving the way for targeted interventions and personalized treatment strategies.

Recommendations

Further studies in this field are necessary to better clarify the mechanisms of links between elevated body mass index and the breast cancer tumor characteristics; and to further understand how obesity affects breast cancer behavior and aggressiveness.

Source of funding: The current study was funded by our charges with no any other funding sources elsewhere.

Ethical clearance: The study was approved by the Research Ethics Committee in Hawler Medical University/College of Dentistry in May 2022. There were minimal ethical implications since the study was retrospective; and the participants' identities were protected by assigning each single patient with a specific serial number.

This study was conducted according to the approval of College of Medicine/ University of Diyala and in accordance with the ethical guidelines of the Declaration of ethical committee of the College (Document no.2023SSM797).

Conflict of interest: Nil

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العلاقات بين ارتفاع مؤشر كتلة الجسم وخصائص سرطان الثدي

شوان سلام معروف^١

الملخص

خلفية الدراسة: في سياق ارتفاع معدلات السمنة على مستوى العالم، فإن فهم تأثير ارتفاع مؤشر كتلة الجسم (BMI) على خصائص سرطان الثدي أمر بالغ الأهمية. وقد أشارت الأبحاث السابقة إلى وجود ارتباطات بين السمنة وخصائص محددة للورم، مثل حالة مستقبلات الورم وتورط العقدة الليمفاوية الإبطية. ومع ذلك، فإن إجراء تحقيق شامل في هذه العلاقات أمر ضروري لإبلاغ التدخلات المستهدفة وتعزيز فهمنا لسرطان الثدي في سياق السمنة.

اهداف الدراسة: لدراسة العلاقة بين مؤشر كتلة الجسم المرتفع وبعض خصائص الورم الرئيسية مثل حالة مستقبل الهرمون، وحالة مستقبل (HER2)، ودرجة الورم، وحجم الورم، وحالة العقدة الليمفاوية الإبطية.

المرضى والطرائق: تحليل بأثر رجعي للسجلات الطبية لـ ١٨٦ مريضة بسرطان الثدي تم علاجهن في قسم الأورام في مستشفى زركاري التعليمي في مدينة أربيل خلال عام ٢٠٢١.

النتائج: كشفت الدراسة عن وجود علاقة ذات دلالة إحصائية بين ارتفاع مؤشر كتلة الجسم وبعض خصائص أورام الثدي المحورية، وخاصة حالة مستقبل (HER2). بالإضافة إلى ذلك، أظهر المرضى الذين يعانون من السمنة المفرطة احتمالية أكبر بكثير للإصابة بمرض العقدة الليمفاوية الإبطية الإيجابية مقارنة بنظرائهم غير المصابين بالسمنة.

الاستنتاجات: هذه الدراسة تثبت وجود علاقة جديرة بالملاحظة بين ارتفاع مؤشر كتلة الجسم وبعض خصائص سرطان الثدي الحرجة، والتي قد تؤكد الأهمية السريرية لمؤشر كتلة الجسم في تشكيل ملامح سرطان الثدي.

الكلمات المفتاحية: مؤشر كتلة الجسم (BMI)، سرطان الثدي، خصائص الورم

البريد الإلكتروني: shwan.marouf@gmail.com

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^١ كلية طب الاسنان - جامعة هولير الطبية - أربيل - العراق