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The Impact of Obesity on Breast Cancer Development in Women: A Study from Kirkuk Governorate, Iraq

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Abstract

Objective: Breast cancer (BC) is a malignant tumor arising in breast tissue due to abnormal cell growth and has the ability to spread to other body parts. It is the second most prevalent cancer, and its incidence rate among women has significantly increased, prompting research into contributing factors. Obesity is recognized as a critical factor linked to the development and dissemination of this disease. This research aims to understand the potential impact of obesity on BC development in women.

Methods: A statistical analysis was conducted with 130 women diagnosed with breast cancer to evaluate the relationship between obesity levels and the development and dissemination of BC among obese women in Iraq (Kirkuk governorate). Data were collected via a specifically designed questionnaire, which classified obesity levels as moderate or high. SPSS Statistics software was used for data processing and analysis. Relationships and differences among the variables were assessed via the chi-square test, t test, and standard deviation.

Results: The analyses revealed a significant increase in obesity prevalence among women with BC. These findings indicate that obese women are at increased risk of developing BC, highlighting obesity as a potential risk factor for this disease.

Conclusion: The findings of this study underscore that obesity is a considerable risk factor linked to an increased probability of BC development in women. Statistical analysis confirmed that obesity rates were significantly higher among women diagnosed with BC. These findings support the notion that excess weight may significantly contribute to the onset and progression of the disease. Evidence suggests that obesity influences various biological processes contributing to cancer, including chronic inflammation, hormonal changes, and elevated insulin levels. Emphasizing obesity as a risk factor for BC is crucial for developing effective prevention and treatment strategies.

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Introduction

Epidemiological data have demonstrated a consistent increase in the number of cancer diagnoses. In the Globocan 2018 report, the International Agency for Research on Cancer (IARC), which is a component of the World Health Organization (WHO), estimated that over 8 million individuals were diagnosed with cancer and that cancer may have been the cause of mortality in approximately 9.6 million cases. Over 40 million individuals worldwide have been diagnosed with cancer within the past five years. According to the IARC, approximately one in six women and one in five men will develop cancer during their lifetime. The maturation of societies worldwide is responsible for the consistent increase in the number of individuals contracting cancer. According to a previous report, 20.3% of cancer-related fatalities will occur, and 23.4% of Europeans will develop cancer. Cancer is the second most prevalent cause of mortality worldwide, according to the WHO. Nevertheless, cancers have already supplanted cardiovascular disease as the primary cause of premature mortality in 28 European countries of the western region. In 2018, the most frequently diagnosed cancer types were breast cancer (BC), lung cancer, and colorectal cancer, the latter two categories of which are caused by obesity [1]. Concurrently, there is a consistent increase in the prevalence of obesity and overweight among both adults and adolescents. In 2016, the WHO reported that among more than 1.9 billion adults, approximately 39% of individuals were overweight, with a total of more than 650 million individuals, thirteen percent of whom were obese. The number of obese individuals aged 5--19 years has increased by a factor of ten over the past four decades. Currently, 430 million children are overweight [2].

Materials and methods

A statistical analysis was conducted on 130 women with BC and 130 women without cancer (control group) to evaluate the associations between obesity levels and the progression and development of BC in obese women. The data were gathered through a questionnaire designed explicitly for this purpose.

Statistical analysis

SPSS statistical software was used to statistically process and analyze the data that were collected. To evaluate the relationships and differences among the variables, the chi-square test, t test, and standard deviation were used for analysis. A P value ≤ 0.05 was regarded as statistically significant.

Results

The body mass index (BMI) was determined for both the patient group and the control group according to the WHO classification, and we utilized the following ranges for classification: less than 20, normal range 20.5--25.85, medium obesity 25--30, and high obesity > 32. As described in Table 1, upon reviewing the patient data according to the study's designated form, the prevalence of obesity (both moderate and severe) among the examined samples (n=130) was 104 samples, equating to 80%. The chi-square test revealed that the proportion of obese individuals who also had BC was 67.5%, whereas the percentage of obese individuals who were healthy was 20%. These findings indicate a statistically significant increase in obesity factor among BC patients compared with healthy individuals.

Table 1 shows that 86 (66.2%) of the BMI groups were above 32 kg/m2, whereas the smallest number of age groups were less than 20 kg/m2, accounting for 9 (6.9%) of the total. There was also a significant difference (P < 0.05) between BMI groups.

Table 1: BC risk based on body mass index (BMI).

BMI (kg/m^2)	BC patients (n=130)
Less than 20	9 (6.9%) *
Normal range 20.5-25.85	35 (26.9%) *
High range > 32	86(66.2%) *
Total	130(100%) **
P value	0.001

* = Not significant
** = Significant

Discussion

Obesity Risk Factors:

Obesity is a significant risk factor that increases the chance of developing cancer, second only to smoking. An elevated body mass index (BMI) is responsible for nearly half a million cancer cases annually, according to the International Agency for Research on Cancer (IARC) [1]. According to research conducted by the IARC, obesity was responsible for approximately 3.6% of all cancer cases that were diagnosed in 2012. Obesity is responsible for 39% of uterine cancer cases, 37% of esophageal cancer cases, 25% of kidney carcinoma cases, 11% of colorec-

tal cancer cases, and 9% of postmenopausal breast cancer cases in Europe [2]. The American Cancer Society (ACS) has obtained data indicating that overweight and obesity are correlated with an elevated mortality rate from specific forms of carcinoma, such as BC, Hodgkin lymphoma, and pancreatic cancer [3]. Obesity has a determinable impact on the efficacy of treatment and patient outcomes, in addition to increasing the risk of malignancy. The precise determination of whether chemotherapy regimens are complicated by excess weight may reduce the impact of cancer therapies. This can result in a greater probability of metastasis, less effective treatment, and an increased risk of adverse side effects [4].

Adipose tissue:

Adipose tissue is not only an energy reservoir but also functions as an endocrine organ that secretes bioactive substances. The secretion of adipokines is determined by the location of the tissue, which is distinguished by its structure and functional diversity [5]. Adipose tissue, which is composed of fat cells, macrophages, lymphocytes, preadipocytes, fibers, and endothelial cells, is distributed throughout the body and can be categorized into subcutaneous fat in the thighs, buttocks, and visceral fat. Obesity increases adipocyte hypertrophy, insulin resistance, and inflammatory cytokine secretion, affects the immune response, lipid metabolism, and angiogenesis, and plays a significant hormonal role [6]. Leptin is a primary adipokine that regulates energy homeostasis and food intake. Leptin levels are inversely linked to the quantity of adipose tissue and increase in conjunction with visceral fat. It has anti-inflammatory properties; however, it can also accelerate the progression of cancer by augmenting the expression of vascular endothelial growth factor (VEGF), which supports the angiogenesis required for tumor growth [7]. Researchers have reported that the hormone visfatin affects some carcinomas, including gastrointestinal and prostate cancer. It induces oxidative stress and proinflammatory cytokines and promotes angiogenesis. Its increased expression is observed in cells resistant to chemotherapy, and it stimulates the production of inflammatory cytokines, weakening the anti-inflammatory effect of adiponectin [8].

Chronic inflammation:

Chronic inflammation arises from the overgrowth of visceral fat, which results in the improper activation of signals that promote inflammation and the production of cytokines. Excitation of the defense system, particularly macrophages, and eviction of free fatty acids in the bloodstream increase this condition. In obesity, macrophages in adipose tissue expand and transform into proinflammatory macrophages. These macrophages release cytokines, such as α-TNF [9].

The NF-kB transcription factor, which is associated with insulin resistance and plays a significant role in epithelial carcinogenesis, is activated by free fatty acids. This transcription factor indirectly stimulates cancer cell proliferation, apoptosis and inflammation. Its activation is linked to metastasis and angiogenesis. Growth factors and proinflammatory cytokines are the only stimuli that activate NF-kB transcription. The development of gastric, lung, colonic, breast, or head and neck squamous cell carcinoma may be affected by elevated levels of NF-kB activity [9], [10].

Fat tissue secretes proinflammatory interleukins, TNK-alpha, MCP-1, and CRP, causing local inflammation in adipose tissue and systemic effects on organs, increasing cancer risk [11].

Chronic inflammation, primarily caused by C-reactive protein (CRP), is a significant risk factor for cancer development and progression. High levels of CRP increase the risk of developing ovarian cancer in women with excessive body mass. TNF-α, a proinflammatory cytokine secreted by adipocytes, plays a role in oncogenesis, including cell transformation, survival, invasion, angiogenesis, and metastasis. IL-6, a key modulator in carcinogenesis associated with inflammation, is also elevated in obese individuals [12]. Interleukin-1, another proinflammatory mediator, indirectly influences the expression of angiogenic VEGF, which is necessary for tumor growth and metastasis. Chronic inflammation in obesity creates a tissue environment that produces oxidative stress, stimulates DNA damage, increases cell proliferation, and inhibits apoptosis. Infections and chronic inflammatory reactions are estimated to cause 15–25% of cancer-related deaths worldwide [13].

Sex hormone:

BMI significantly influences sex hormone concentrations, which are responsible for cancer development. Visceral fat affects hormone synthesis and bioavailability, leading to estrogen and progesterone deficiency, which can lead to breast and endometrial cancer. Excess androgens and progesterone deficiency in women with polycystic ovarian syndrome increase cancer risk before menopause [5]. Obese women are at a greater risk of developing postmenopausal breast cancer due to high levels of sex hormones and a smaller synthesis of sex hormone-binding globulin. This combination may lead to endometrial and BC [10].

Hyperinsulinemia and hyperglycinemia:

Chronic inflammation and excessive body weight, particularly visceral obesity, are the most significant factors affecting insulin resistance. Hyperinsulinemia is the most prevalent side effect of this condition. An explanation for the increased risk of numerous types of carcinomas is the role of insulin and insulin-like growth factor (IGF)-1, which are two important factors that are associated with abdominal obesity. Insulin is a hormone that induces cell division by activating MAP-kinase, and elevated levels in the bloodstream promote cell proliferation, which can result in bladder or colon cancer in women and non-Hodg-

kin's lymphoma or liver cancer in men. Insulin has the capacity to bind to IGF-1 and mitogenic hybrid receptors. It has the potential to promote tumorigenesis by inhibiting apoptosis and stimulating the synthesis of IGF-1 [14]. The synthesis of IGFBPI and IGFBP2-binding proteins, which are associated with decreased IGF-1 levels, is increased. This affects the development of tumors and affects cell surface receptors. The control of the ras gene is facilitated by IGF. In the initial phases of cancer development, mutations in this gene have been identified. This mechanism is particularly important in the development of colorectal and breast cancer, as nearly 90% of cells exhibit increased expression of IGF. The levels of insulin and IGF in breast cancer cells are tenfold greater than those in healthy cells [15], [16]. Hyperinsulinemia leads to rapid cancer development in postmenopausal women, causing DNA damage and mutagenesis. High insulin concentrations cause mitochondrial ROS production, causing DNA rupture and tumor growth [14], [17]. Cancer cells constantly divide and use glucose for mass increase, requiring greater glucose uptake through aerobic glycolysis. This leads to a higher incidence of cancer in people with diabetes. Studies have shown a link between tumors and fasting glucose levels, with the risk of cancer and death increasing with increasing fasting blood glucose levels [4], [9].

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Conflict of interest

The authors declare that they have no competing interests.

Ethical approval

The study was conducted using a simple questionnaire at the lab where I work, involving patients who voluntarily participated after giving verbal consent. The study did not involve any medical interventions or sensitive information requiring formal ethics committee approval. The study was conducted in accordance with established ethical principles, with full respect for the privacy and confidentiality of participants.

Authors' contributions:

All authors participated in the design of the review strategy, the analytical strategy for this study, the quality assessment, the interpretation of the data, and the final approval of the research was provided by all authors.

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