RESEARCH ARTICLE

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Assessing the Role of Lifestyle in Modulating Serum IGF-1 and Association with Breast Cancer Risk among Palestinian Women in the Gaza Strip: A Case-Control Study

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Abstract

Background: Breast cancer (BC) continues to be one of the most commonly diagnosed cancers worldwide, predominantly affecting women. Insulin-like growth factor-1 (IGF-1) is vital for cellular growth and metabolism. Dysregulation of IGF-1 has been linked to an increased risk of cancer. We hypothesized that unhealthy lifestyle factors (e.g., poor diet, low physical activity) are associated with higher serum IGF-1 levels and an increased risk of BC. This research examines the relationship between lifestyle factors, IGF-1, and BC risk in Palestinian women in the Gaza Strip. **Methods:** A case-control study was conducted with 112 newly diagnosed BC women and 222 healthy controls. Data were collected using the International Physical Activity Questionnaire and the Food Frequency Questionnaire. IGF-1 levels were measured. Data were analyzed using SPSS version 28. **Results:** BC patients had significantly lower physical activity than controls (58.9% vs. 44.6%, p = 0.014). Eight of the 14 food groups studied were linked to reduced BC risk, with reductions of 3.4% for fruit, 3.7% for meat, 5.6% for grains, 3.0% for low-fat dairy, 16.5% for nuts, 3.3% for snacks and sweets, and 5.5% for soups and sauces, while eggs increased risk by 12.5%. Drinks and beverages were positively correlated with IGF-1 levels (rp = 0.121, p = 0.027), suggesting that these factors may influence BC risk. **Conclusion:** Lifestyle factors, including diet and physical activity, influence IGF-1 levels and BC risk. Public health interventions promoting healthier lifestyles may help reduce BC risk.

Keywords: Breast cancer- Lifestyle- Physical activity- IGF-1- Palestinian women

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Introduction

Globally, breast cancer (BC) is the most common cause of cancer-related deaths and the most common cancer diagnosed in women. In 2020, over 2.3 million women were diagnosed, leading to 685,000 deaths globally [1]. The incidence of BC is still rising despite improvements in early detection and treatment, especially in low- and middle-income nations with inadequate access to healthcare [2]. In Palestine, BC poses a significant public health burden, especially in the Gaza Strip, where unique socio-economic and environmental challenges exist. These challenges include food insecurity, limited access to healthcare due to political instability, and restrictions on movement resulting from ongoing conflict. The blockade and political situation result in restricted access to fresh, nutrient-dense foods, which can affect the overall diet quality of the population [3-5]. For example, a high reliance on processed foods, grains, and imported food items, coupled with limited access to fresh fruits, vegetables, and high-protein foods, creates a distinctive dietary pattern that may influence cancer risk factors such as IGF-1 levels [6, 7].

Additionally, limited mobility and economic hardship affect physical activity levels, with many women unable to engage in regular exercise, further contributing to obesity and associated risks for BC [8]. Studies have shown that restricted mobility and lack of recreational facilities are linked to lower physical activity levels in conflict zones, leading to higher rates of obesity and other metabolic

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disorders [9, 10]. In addition, BC accounts for 36.9% of female cancers in Gaza, with many cases diagnosed at advanced stages, which complicates treatment outcomes [5]. These factors make the Gaza Strip an important region for exploring how lifestyle and environmental factors contribute to cancer risk, especially when healthcare resources and preventive programs are scarce.

BC development is influenced by both non-modifiable risk factors (family history, age, genetic mutations) and modifiable risk factors (physical inactivity, obesity, poor diet, alcohol consumption, smoking) [11]. One biological pathway linking lifestyle factors to BC risk is through the hormone insulin-like growth factor 1 (IGF-1), which plays a crucial role in cellular growth, survival, and metabolism. It is a peptide hormone with effects similar to insulin, influencing cell division, differentiation, and apoptosis [12]. The action of IGF-1 is primarily mediated through its receptor, IGF-1R, which activates downstream signaling pathways, most notably the PI3K/Akt and MAPK pathways. These signaling cascades promote cell survival, proliferation, and resistance to cell death, all of which are key processes in cancer development [13, 14]. In BC, elevated IGF-1 levels have been shown to enhance tumor cell proliferation and inhibit apoptosis, contributing to tumorigenesis. IGF-1 can also influence the tumor microenvironment by promoting angiogenesis and metastasis, which are critical for cancer progression [15].

Additionally, IGF-1R signaling can interact with other oncogenic pathways, such as ER and PR, which are involved in the development of hormone receptor-positive BC [16]. Increased levels of IGF-1 are associated with obesity and other lifestyle conditions and have been linked to increased BC risk [17]. However, lifestyle interventions like weight loss and increased physical activity have been shown to reduce serum IGF-1 levels, potentially lowering cancer risk [18].

We hypothesize that unhealthy lifestyle factors, such as low physical activity and poor dietary patterns, are associated with elevated serum IGF-1 levels and increased BC risk among Palestinian women. To test this hypothesis, we conducted a case-control study assessing IGF-1 levels, physical activity, and dietary intake in newly diagnosed BC cases and age-matched controls in the Gaza Strip.

The purpose of this study is to evaluate how dietary and lifestyle choices affect serum IGF-1 levels and BC risk among women in the Gaza Strip. It seeks to illuminate modifiable risk factors that could inform public health initiatives aimed at reducing BC incidence through tailored lifestyle interventions for this high-risk population.

Materials and Methods

Study Design and Setting

A case-control study was conducted in the Gaza Strip from January 1, 2021, to January 7, 2023, to investigate the relationship between various factors and serum IGF-1 levels in newly diagnosed BC women and healthy controls. The required sample size was calculated using G*Power version 3.1.9.6, applying the Correlation: Bivariate Normal model to assess the relationship between participants' profiles (including socio-demographic, anthropometric, reproductive, medical, and lifestyle factors) and serum level of IGF-1 among cases and controls. The minimum sample size is 306 participants. After accounting for a 10% non-response rate, the final sample size was set at n = 336, including 112 newly diagnosed BC women from Al-Shifa and Turkish Palestinian Friendship Hospitals, and 222 age-matched healthy controls from Al-Remal Clinic. Participants were matched by age, both BMI (categorized as normal weight, overweight, and obese) and menopausal status (pre-menopausal vs. post-menopausal) to control for potential confounders known to influence both BC risk and IGF-1 levels. This design aimed to accurately assess the associations between IGF-1 and BC risk, accounting for these critical factors.

Ethical Approval

The Helsinki Committee provided its ethical permission (approved number PHRC/HC/699/20) for the study project in the Gaza Strip during its meeting on February 3, 2020. Further ethical approval was received on January 13, 2022, from the Universiti Sains Malaysia (USM) Human Research Ethics Committee with the JEPeM USM Code: USM/JEPeM/20020122.

Informed Consent and Patient Details

Informed consent was obtained from all participants before their recruitment into the study. To ensure participant privacy and confidentiality, interviews were conducted in a private room, separate from clinical areas, by trained research staff. Participants were informed that their participation was voluntary and their responses would be kept strictly confidential. All data collected were anonymized by assigning a unique study ID to each participant, and all identifying information was removed before data analysis. Data were stored securely on password-protected computers and accessed only by authorized research personnel.

Data Collection and Study Tools

Face-to-face validated interview questionnaires included socio-demographic data, anthropometric measurements such as height, weight, and waist circumference, and lifestyle factors such as physical activity, smoking, and diet were conducted among participants.

Physical Activity

The International Physical Activity Questionnaire (IPAQ) is a well-established and widely used instrument for measuring physical activity, evaluating both recreational and household activities during the previous week. To ensure cultural relevance and accuracy, we used a previously validated version of the IPAQ, specifically the Arabic short-format version, to assess the physical activity patterns of participants [19]. This version had been validated through comparisons with accelerometer data. The questionnaire inquired about the time spent on various activities over the last 7 days, including those performed at work, as part of household chores, for transportation, recreation, exercise, and sports. Vigorous

physical activities were defined as those requiring high physical effort, making participants breathe much harder than normal. In contrast, moderate activities required moderate physical effort, resulting in a more moderate increase in breath rate.

Data collected with the IPAQ were reported as continuous scores, with an average metabolic equivalent of task (MET) score derived for each activity. Activities were classified into three categories: light (1.1–2.9 METs), moderate (3.0–5.9 METs), and vigorous (6 or more METs). The frequency (days per week), duration (minutes per day), and intensity (light, moderate, vigorous) of physical activities were recorded to calculate total physical activity [20]. Additionally, sitting time was used as an independent measure of sedentary behaviour, including time spent sitting (in days and minutes per day) at work, at home, during coursework, and leisure activities such as reading, watching TV, or visiting friends [19].

Dietary Assessment

A comprehensive dataset regarding dietary patterns was collected using a validated semi-quantitative food frequency questionnaire (FFQ). The FFQ is relatively easy and inexpensive to administer and can be used to measure dietary intake over a prolonged time period [21]. In this study, the FFQ gathered data on the frequency of consumption of food types divided into 14 categories: ((1) fresh vegetables/salad; (2) fresh fruits and their juices; (3) meat and meat products; (4) poultry; (5) fish and seafood; (6) grains; (7) dry beans; (8) milk and dairy products; (9) eggs and derivatives; (10) nuts; (11) drinks and beverages; (12) snacks and sweets; (13) soups and sauces; and (14) candies). These food groups contain a total of ninety-eight types of food, and the FFQ permits estimation of the consumption of twenty-two nutrients, including energy. The FFQ was developed and validated among the Palestinian population in 2014. FFQ was tailored to reflect the typical Palestinian diet, including foods commonly consumed in the Gaza Strip [22]. In this study, data were gathered on the consumption or non-consumption of an item and the number of times it was consumed per day, week, or month during the previous year. The amounts of food consumed were expressed in grams or millilitres, or other common measures, such as a slice, tablespoon, or cup, or as a standard serving size. The daily intake of each nutrient was calculated by multiplying the amount reported in the questionnaire by the corresponding value in the food composition tables [23]. The data collected were analysed to explore correlations between dietary intake, IGF-1 levels, and their potential impact on BC susceptibility.

Biochemical Analyses

Fasting blood samples were collected from all participants, and serum IGF-1 levels were analyzed using the MAGLUMI 800 auto-chemiluminescence immunoassay analyzer (Snibe, China). This assay system is widely used for determining IGF-1 concentrations and has been validated for sensitivity and reproducibility.

To ensure the reliability of the IGF-1 measurements, several quality control procedures were implemented. These included the use of external control samples with known IGF-1 concentrations to monitor assay performance daily. The inter-assay coefficient of variation (CV) was calculated by measuring the same sample across different runs, while the intra-assay CV was assessed by measuring the same sample within a single run. Regular calibration and maintenance of the auto-chemiluminescence analyzer were performed to ensure consistent assay performance. These quality control measures ensure that the IGF-1 measurements are accurate and reliable, which is essential for the validity of the study's findings.

Statistical Analyses

The IBM SPSS version 28 was used for all statistical analyses. In the computation of descriptive statistics, categorical variables were represented by frequencies (n) and percentages (%), whereas continuous variables were represented by means and standard deviations (SD). Univariate and multivariate logistic regression and Pearson correlation were performed to assess the relationship between lifestyle factors, serum levels of IGF-1, and BC risk. A p-value of ≤ 0.05 is considered statistically significant.

To account for potential confounders, such as BMI and menopausal status, covariate adjustment was applied, and multivariable logistic regression models were utilized to adjust for these confounders and other relevant variables. The univariate analysis table in the supplementary material provides additional details on these factors before adjustment.

Results

Risk factors of BC among Palestinian females in the Gaza Strip

The multivariable analyses revealed that women under 40 had a significantly decreased BC risk by 57.3% compared to older women (OR = 0.427, p = 0.042). Additionally, women who engaged in lower-intensity physical activity were 9.6 times more likely to have BC than those with more vigorous or moderate exercise (OR = 9.609, p = 0.049). Serum IGF-1 levels were also significantly associated with increased BC risk (OR = 1.013, $p \leq 0.001$). However, while the association between serum IGF-1 levels and BC risk is statistically significant, it represents a small effect size. The odds ratio indicates a statistically significant relationship, but the clinical relevance of a 1.013 increase per unit rise in IGF-1 may be limited. This small effect suggests that while elevated IGF-1 levels may contribute to BC risk, other factors are likely more significant in influencing the risk. Therefore, it is crucial to interpret this finding with caution, acknowledging that other lifestyle and biological factors may have a stronger impact on BC risk (Table 1).

Comparison of Mean IGF-1 Levels, Age, Waist Circumference, and BMI Between BC Cases and Controls

BC cases had significantly increased levels of serum IGF-1 compared to controls (121.69 ± 59.15 ng/mL vs. 92.33 ± 48.81 ng/mL, $p \leq 0.001$). The mean age of BC cases was higher than that of controls, and the two groups'

Table 1. The Risk Factors Associated with BC among Palestinian Females in the Gaza Strip Using the Multiple Logistic Regression

Multivariable model with variable selection		Cases N = 112	Control N = 222	B	Adj. OR (95%CI)	P-value
Age of participant n (%)	<35	24 (21.4)	47 (21.2)		0	
	35-40	18 (16.1)	66 (29.7)	-0.851	0.427 (0.188, 0.971)	0.042
	41-45	18 (16.1)	32 (14.4)	0.021	1.021 (0.391, 2.667)	0.966
	46-50	14 (12.5)	31 (14.0)	-0.404	0.668 (0.232, 1.918)	0.453
	>50	38 (33.9)	46 (20.7)	-0.367	0.693 (0.205, 2.341)	0.555
Physical activity n (%)	High	1 (0.9)	12 (5.4)		0	
	Moderate	45 (40.2)	111 (50.0)	1.91	6.753 (0.706, 64.581)	0.097
	Low	66 (58.9)	99 (44.6)	2.263	9.609 (1.009, 91.471)	0.049
IGF-1 (ng/mL)		121.69 ± 59.15	92.33 ± 48.81	0.013	1.013 (1.007, 1.019)	≤ 0.001
Mean ± SD						
*Significant at the level of 0.05.						

Note. BC, Breast cancer; IGF-1, Insulin-like growth factor-1; n, Frequency; SD, Standard deviation; Wald, Wald statistics; Adj. OR, Adjusted Odds ratio; CI, Confidence interval.

differences were statistically significant (45.45 vs. 41.84 years, p = 0.002). Additionally, waist circumference was significantly greater in BC cases (91.12 cm) than in controls (88.79 cm, p = 0.029). BC women had a higher BMI (29.89 kg/m^2) than healthy controls (29.08 kg/m^2) without a statistically significant difference (p = 0.221) as shown in Table 2.

Food patterns and their association with BC

Table 3 highlights the associations between dietary factors and BC risk. Eight food items were associated with a reduced BC risk, while one food group was associated with increased risk. Notably, fresh fruits and their juices were associated with a 3.4% reduction in BC risk (OR = 0.966, p ≤ 0.001), and meat products reduced the risk by 3.7% (OR = 0.963, p = 0.016). Higher intake of grains and low-fat dairy also decreased the risk by 5.6% (OR = 0.944, p ≤ 0.001) and 3.0% (OR = 0.970, p = 0.021), respectively. Additionally, consumption of nuts, snacks and sweets, and soups and sauces were associated with reductions in BC risk of 16.5%, 3.3%, and 5.5%, respectively, with p-values < 0.05. In contrast, eggs and their derivatives were associated with a 12.5% increase in BC risk (OR = 1.125, p = 0.020).

The correlation between food intake and the serum levels of IGF-1 among study participants

A Pearson correlation analysis was conducted to assess the relationship between food intake and serum levels of IGF-1. The results revealed a weak positive correlation between the consumption of drinks and beverages and serum IGF-1 levels (r_p = 0.121, p = 0.027). This suggests that increased beverage consumption may elevate serum IGF-1 levels, potentially contributing to a higher risk of developing BC. No other significant correlations were observed in this analysis (Table 4).

Discussion

The findings of this study support the hypothesis that modifiable lifestyle factors particularly diet and physical activity are significantly associated with serum IGF-1 levels and BC risk among women in the Gaza Strip. The hypothesis was accepted, as evidence demonstrated that higher IGF-1 levels were significantly associated with increased BC risk, and that several dietary components (such as fruits, grains, low-fat dairy, and nuts) were inversely associated with both IGF-1 and BC. Additionally, women with low physical activity were nearly 10 times more likely to have BC than those with moderate or vigorous activity (p = 0.049). These results not only reinforce IGF-1 as a potential mechanistic link between lifestyle and cancer but also highlight actionable dietary and behavioral targets for cancer prevention. This study advances the field by providing context-specific evidence from an underrepresented Middle Eastern population and emphasizes the relevance of lifestyle-based interventions in reducing BC risk through hormonal modulation.

Table 2. Comparison of Mean IGF-1 Levels, Age, Waist Circumference, and BMI Between BC Cases and Controls

Variables	Mean ± SD		Mean differences (95%CI)	P- value
	Cases N = 112	Controls N = 222		
IGF-1 (ng/mL)	121.69 ± 59.15	92.33 ± 48.81	-29.36 (-42.14, -16.58)	£ 0.001
Age of participant	45.45 ± 10.53	41.84 ± 8.94	-3.61 (-5.90, -1.31)	0.002
Waist circumference (cm)	91.12 ± 7.61	88.79 ± 11.61	-2.33 (-4.42, -0.24)	0.029
BMI (kg/m^2)	29.89 ± 5.64	29.08 ± 5.65	-0.80 (-2.09, 0.48)	0.221

*Significant at the level of 0.05; Normality assumption is fulfilled; Note. SD, Standard deviation; BMI, Body mass index; IGF-1, Insulin-like growth Factor-1; df, Degree of freedom.

Table 3. The Association between Dietary Pattern and BC among Women in the Gaza Strip Using the Univariate Logistic Regression

Univariate models	Mean ± SD		B	Crude OR (95%CI)	P-value
	Cases N = 112	Control N = 222			
Fresh vegetables/salad	89.56 ± 19.66	92.89 ± 19.96	-0.008	0.992 (0.980, 1.003)	0.15
Fresh fruits and their juices	42.07 ± 11.62	47.12 ± 12.59	-0.034	0.966 (0.947, 0.985)	≤ 0.001
Meat and meat products	17.16 ± 6.68	19.30 ± 7.94	-0.038	0.963 (0.934, 0.993)	0.016
Poultry	10.91 ± 2.82	10.90 ± 3.16	0.001	1.001 (0.929, 1.079)	0.978
Fish and seafood	7.21 ± 4.75	6.34 ± 4.13	0.045	1.046 (0.994, 1.102)	0.086
Grain	17.31 ± 6.63	20.00 ± 6.95	-0.058	0.944 (0.912, 0.977)	≤ 0.001
Dry beans	19.43 ± 7.34	19.24 ± 6.43	0.004	1.004 (0.971, 1.039)	0.803
Milk and dairy products	19.90 ± 7.76	22.34 ± 9.56	-0.03	0.970 (0.945, 0.995)	0.021
Eggs and derivatives	6.45 ± 2.48	5.78 ± 2.40	0.118	1.125 (1.019,1.243)	0.02
Nuts	4.66 ± 2.28	5.41 ± 1.89	-0.18	0.835 (0.745, 0.936)	0.002
Drinks and beverages	23.62 ± 9.02	23.28 ± 8.37	0.005	1.005 (0.978, 1.032)	0.735
Snacks and sweets	19.54 ± 8.37	21.38 ± 6.99	-0.033	0.967 (0.937, 0.998)	0.036
Soups and sauces	13.14 ± 5.87	15.61 ± 7.07	-0.057	0.945 (0.911, 0.979)	0.002
Candies	12.88 ± 6.45	14.64 ± 8.33	-0.03	0.970 (0.941, 1.000)	0.052

*Significant of P-value less than 0.05; Note. BC, Breast cancer; Wald, Wald statistics; OR, Odds ratio; CI, Confidence interval.

Table 4. The Correlation between Food Items and the Serum Levels of IGF-1 among Study Participants

Food Items	Serum IGF-1	
	Corr. Coeff.	P- value
Fresh vegetables/salad	-0.049	0.367
Fresh fruits and their juices	-0.043	0.432
Meat and meat products	0.006	0.913
Poultry	0.033	0.55
Fish and seafood	0.084	0.124
Grain	0.033	0.545
Dry beans	-0.076	0.164
Milk and dairy products	-0.014	0.803
Eggs and derivatives	0.051	0.349
Nuts	-0.063	0.249
Drinks and beverages	0.121*	0.027
Snacks and sweets	0.039	0.48
Soups and sauces	-0.036	0.513
Candies	0.043	0.438

Note. IGF-1, Insulin-like growth factor-1; SD, Standard deviation; Corr. Coeff., Correlation coefficient; r_p, Pearson correlation.

Our study revealed an inverse relationship between BC risk and participant age (35-40 years) (p = 0.042). This finding could be interpreted as a potentially protective factor against BC within this particular age range. Similar to our results, a study done by Shuvo et al. discovered that women aged 31-45 had a decreased chance of developing BC than those aged 46-60 years [24]. Compared to more vigorous physical activity, BC women who had low-intensity exercise were ~ 10 times more likely to have a higher chance of developing BC (p = 0.049). Hassen et al.'s study supports our findings, showing that women who engaged in physically demanding sports such as swimming and jogging for fewer than five hours a week had probabilities of BC that were 0.343 times lower [25]. It is postulated that physical activity may exert its preventive effects on cancer development by altering immune system response, lowering exposure to endogenous sex hormones, or affecting IGF-1 levels [26]. Many theories have been proposed to elucidate the protective role of physical activity in relation to the incidence of BC. It is postulated that physical activity may exert its preventive effects on cancer development by reducing exposure to endogenous sex hormones, modifying immune system responses, or influencing the levels of IGF-1 [26]. Physical activity has been shown to lower circulating IGF-1 levels through multiple mechanisms. Regular exercise, particularly moderate to vigorous intensity activities, reduces adiposity and improves insulin sensitivity. Adipose tissue, a major source of oestrogen and other growth factors, can release these factors. However, reducing body fat through exercise may lower IGF-1 levels by decreasing the release of such growth factors [27]. Additionally, exercise-induced changes in muscle and liver metabolism can lead to alterations in the IGF axis, promoting a shift toward lower IGF-1 levels, which is thought to be protective against cancer [28]. Physical activity also enhances the immune system's ability to detect and eliminate abnormal cells, potentially reducing BC risk [29].

Our study has found a link between higher serum levels of IGF-1 and an increased BC risk, which is consistent with a previous study [30, 31]. Our study revealed that the levels of serum IGF-1 in BC patients were considerably higher than those in the control group (cases: 121.69 ng/mL, controls: 92.33 ng/mL; p ≤ 0.001). In line, a study done in China explored that women with BC had higher IGF-1 concentrations than the control group (p = 0.032) [12].

Concerning participant age and BC risk, cases and controls in the study had a mean age of 45 years and 42 years, respectively (p ≤ 0.05). Our findings are in line with

research done by Marzbani et al., who found that the mean ages of the case and control groups were 41.5 and 39.5 years, respectively [32]. Additionally, waist circumference was significantly greater in BC cases (91.12 cm) than in controls (88.79 cm, $p = 0.029$), while BMI did not show a significant difference ($p = 0.221$). This suggests that central obesity, as indicated by waist circumference, may be a more relevant factor for BC risk in this population than general obesity (BMI). Consistent with our results, a study revealed a significant disparity in mean waist circumference between cases (112.32 cm) and controls (96.45 cm), solidifying the pivotal role of abdominal adiposity in the development of BC [33]. This finding should be highlighted as a key result, as it suggests that interventions focusing on reducing central obesity may be more effective in mitigating BC risk than those focused on general weight reduction.

The consumption of fresh fruit and juice was linked to decreased BC risk by 3.4%. Our findings are consistent with case-control research demonstrated that a significant number of fruits consumed overall was inversely associated with BC risk ($p < 0.001$) [34]. El-Hissi et al.'s research demonstrated that the antioxidants, fiber, and other nutrients in fruit had a preventive impact and reduced the incidence of BC [33].

Surprisingly, we discovered that a higher red meat intake was substantially linked with decreased BC risk by 3.7%. This finding aligns with the outcomes observed by Nguyen et al. that revealed an inverse association between BC and red meat intake ($p = 0.04$) [34]. Alternatively, Kim et al. discovered that all women had a noticeably increased chance of BC when they ate grilled meat [35]. This variation in results can be explained by factors such as the degree of doneness, cooking method, and type of meat ingested. Specifically, red meat cooked at high temperatures, particularly by grilling or frying, may pose a higher BC risk due to the production of carcinogenic by-products like polycyclic aromatic hydrocarbons and heterocyclic amines, which are formed from animal fat, heme iron, and N-glycolinic acid. These compounds have a strong affinity for oestrogen and androgen receptors and may cause inflammation, oxidative stress, and tumor formation [36].

However, in Gaza, the consumption of red meat is often limited to small portions, and the method of preparation may differ from the typical high-risk cooking methods observed in other regions. Additionally, the nutritional composition of meat consumed in Gaza might differ from the processed or fatty meats that are commonly linked to higher BC risk. For instance, local meats may be leaner or cooked with fewer unhealthy fats, potentially reducing their cancer-promoting effects. Another important factor to consider is the socio-economic context in Gaza, where limited purchasing power may influence dietary choices. The lower economic status in the region, with unemployment at 45% in 2022 and over half the population living below the national poverty line [37, 38], may restrict meat consumption and mitigate the potential risk.

Women who consumed a large number of grains had a 5.6% decrease in developing BC ($p \leq 0.001$). A systematic review showed an 8% decrease in the chance of acquiring BC among those who consumed fiber overall [39].

Our study found that consuming low-fat milk and dairy products was associated with reduced BC risk ($p = 0.021$). Our results are consistent with earlier studies done by Bao et al. and Shuvo et al. that reported a lower BC risk with the consumption of milk [40, 24]. On the other hand, we observed that higher intake of eggs is associated with an increased chance of developing BC ($p = 0.020$), with meta-analyses supporting the association between consuming five or more eggs per week and elevated BC risk [41]. The nutritional components of eggs may be the most likely mechanism linking egg consumption to an increased risk of BC. According to reports, eggs have a very high cholesterol content (425 mg per 100 g), exceeding the 300 mg daily recommended intake [42]. This high cholesterol content may contribute to BC development by influencing hormone-related signaling pathways, such as steroid hormone receptors, potentially leading to cancer formation.

Additionally, malignant cells often exhibit disrupted cholesterol homeostasis, resulting in cholesterol accumulation, which may promote cancer progression. Cholesterol can also be converted into estrogen-like molecules in the body, possibly contributing to cancer development in hormone-sensitive tissues [43]. Another plausible explanation is that certain cooking techniques, such as frying eggs at high temperatures, can alter their composition, producing carcinogenic substances like heterocyclic amines. These substances have been shown to increase the likelihood of cancer occurrence [43, 44]. Thus, the combination of the nutritional profile of eggs and how they are prepared may influence the increased risk of BC.

The results of this investigation showed a significant inverse link between nut consumption and BC risk, reducing it by 16.5%. This protective association is in line with a case-control study conducted by Sharif et al., which discovered a similar protective association between BC risk and nuts [45]. The consumption of snacks and sweets was found to have a protective effect against BC risk, and decreased the risk by 3.3%. Our findings, however, go counter to a recent epidemiological study that showed the increasing frequency of sweet consumption was associated with elevating the opportunity of getting BC [32]. The inconsistencies in findings regarding the relationship between sweet consumption and BC risk could stem from several sources. Differences in how studies define and measure sweet consumption play a crucial role in generating varied outcomes. Studies often use diverse methods to quantify sweet consumption, including assessing overall sugar intake, consumption of specific sweets or desserts, or broader categories like sweetened beverages. These variations in definitions and measurements across studies can lead to discrepancies in the observed associations with BC risk. Additionally, factors such as lifestyle and dietary habits, socioeconomic status, demographics of the studied population, and cultural preferences for specific sweets or desserts can influence results. In the current study, BC patients reported consuming a diet significantly lower in sweets

and desserts compared to controls (cases: 19.54 vs. controls: 21.38, p = 0.034), with a preference for sweets containing ingredients like dark chocolate and nut-based snacks (almonds, hazelnuts, and peanuts) that are rich in antioxidants, which may have a protective effect on BC occurrence. This finding suggests that in populations where sweet consumption is generally low, the impact of sweets on BC risk may differ, or other dietary or lifestyle factors may play a more prominent role in influencing the outcome. These observations highlight the importance of considering population-specific dietary habits and cultural contexts when evaluating the relationship between sweet consumption and BC risk.

The Mediterranean nutritional pattern is reflected in the Palestinian diet [46]. It is abundant in fruit and vegetables, nuts, legumes, unrefined cereal grains, and olive oil, but fish and dairy intake are modest, and red meat consumption is minimal. Numerous potential health benefits have been associated with this dietary pattern [47, 48]. Interestingly, the incidence of BC has shown a decline, attributed to the preventive effects of the Mediterranean diet against the development of the disease [49-51]. Overall, the Palestinian diet, resembling the Mediterranean pattern, showcases numerous health benefits, potentially including a decreased risk of BC. However, while diet plays a role, other lifestyle and genetic factors could also influence disease incidence, making it crucial to consider a holistic approach to health and disease prevention.

Concerning food intake and the serum levels of IGF-1, we found a weak positive correlation with the consumption of drinks and beverages. This suggests that consuming beverages could potentially elevate the IGF-1 serum levels, thereby possibly contributing to an increased risk of developing BC. The types of drinks and beverages examined vary among studies. Some studies might focus on beverages with a high glycaemic index, like sugary sodas and alcoholic drinks [52, 53], and others explore the effects of coffee or tea, each of which contains different compounds that could potentially affect IGF-1 levels in distinct ways. According to Hang et al., individuals who consumed ≥3 cups of coffee overall per day had higher serum IGF-1 concentrations than non-drinkers (p = 0.03) [54]. The role of high sugar intake in BC development has been suggested, particularly through its influence on the IGF-1 axis [55]. Diets high in glycaemic content generally correlate with increased blood insulin levels. Increased insulin levels may affect the risk of BC directly by activating insulin receptors in breast tissue or indirectly by increasing IGF-1 bioactivity. This improvement is partially brought about by lowering IGFBP levels, which in turn encourages cell division and prevents apoptosis. In addition, data indicate that IGF-1 and insulin both lower the level of globulin that binds to sex hormones while increasing the production of oestrogens and androgens. The surge in bioavailable androgens may play a major role in the higher tissue concentrations of oestrogens produced via androgen conversion locally. Oestrogens, along with insulin/IGF-1, exert potent stimulatory effects on the proliferation of mammary epithelial cells and oestrogen-dependent BC cells [56-58].

In conclusion, this study highlights the significant role of lifestyle factors particularly diet and physical activity in influencing BC risk among Palestinian women in the Gaza Strip. Several key findings were identified, including the association between elevated IGF-1 levels and increased BC risk, as well as the potential protective effects of certain dietary components like fresh fruits, meat, grains, low-fat dairy, nuts, sweets, and soups, which were linked to a reduced BC risk. Conversely, the consumption of eggs was associated with an increased risk of BC. The study also emphasizes the importance of central obesity, as indicated by waist circumference, suggesting that abdominal adiposity may be more relevant than general obesity in BC risk.

Furthermore, beverage consumption was found to influence IGF-1 levels, with a weak positive correlation observed, suggesting that further research is needed to fully understand the specific role of beverage intake in BC risk. These results underscore the necessity of preventative measures and further studies to comprehensively explore the intricate relationships among hormone regulation, diet, and BC risk. The findings highlight the need for a deeper understanding of how dietary patterns and lifestyle factors influence hormonal mechanisms, like IGF-1, in shaping BC risk.

Limitations of the Study

This study had several limitations that must be considered when interpreting the findings. One of the primary limitations is the reliance on self-reported data for physical activity and dietary intake, which is subject to recall bias, potentially affecting the accuracy of the associations between lifestyle factors and IGF-1 levels or BC risk. Additionally, the case-control design limits the ability to establish causality between high IGF-1 levels and BC risk, as it is unclear whether high IGF-1 is a cause or consequence of BC. Although some confounders were controlled for, other unmeasured factors such as genetic background, environmental exposures, or psychological stress could influence both IGF-1 levels and BC risk and may have introduced residual confounding. Lastly, the generalizability of the findings was also limited to Palestinian women in the Gaza Strip, and further research in other populations is necessary to assess broader applicability.

Author Contribution Statement

Conceptualization, H.M.A., and O.M.SH.; Methodology, H.M.A., and O.M.SH.; Validation, H.M.A.; Data curation, H.M.A., T.A.D.A., I.A.N., and N.S.; Writing-original draft preparation, H.M.A.; Writing-review and editing, H.M.A., I.A.N., O.M.SH., N.A.L., N.S., R.B.M., and T.A.D.A. All authors revised the manuscript and approved the final version to be submitted.

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Ethical Declaration

The Helsinki Committee provided its ethical permission (approved number PHRC/HC/699/20) for the study project in the Gaza Strip during its meeting on February 3, 2020. Further ethical approval was received on January 13, 2022, from the Universiti Sains Malaysia (USM) Human Research Ethics Committee with the JEPeM USM Code: USM/JEPeM/20020122.

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