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

Heba Mohammed Arafat[1]*, Tengku Ahmad Damitri Al-Astani[1], Noorazliyana Shafii[1], Rosediani Muhamad[2], Ihab Naser[3], Nahed Al Laham[4], and Ohood Mohamed Shamallakh[5]

[1]Department of Chemical Pathology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Kelantan, Malaysia.

[2]Department of Family Medicine, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Kelantan, Malaysia.

[3]Department of Clinical Nutrition, Faculty of Applied Medical Sciences, Al-Azhar University-Gaza, Gaza City, Palestine.

[4]Department of Laboratory Medicine, Al Azhar University-Gaza, Gaza City, Palestine.

[5]Department of Medical Laboratory Sciences, Faculty of Health Sciences, Islamic University of Gaza, Gaza City, Palestine.

*E-mail: hebaarafat4@student.usm.my

ABSTRACT

Background: Breast cancer continues to be one of the most diagnosed cancers worldwide, predominantly affecting women. Insulin-like growth factor-1 is vital for cellular growth and metabolism. Dysregulation of IGF-1 has been linked to an increased risk of cancer. This research explores the relationship between lifestyle factors, IGF-1, and BC risk in Palestinian women in the Gaza Strip.

Methods: Case-control study included 112 newly diagnosed BC women and 222 healthy controls. Data were collected using the International Physical Activity Questionnaire and 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 fruits, 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 egg increased risk by 12.5%. Drinks and beverages were positively correlated with IGF-1 levels (r_p=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.*

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 (World Health Organization, 2023). 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 (Bhagat et al., 2024). In Palestine, BC poses a significant public health burden, especially in the Gaza Strip, where unique socio-economic and environmental challenges—such as restricted healthcare access due to political conflict and resource constraints—exacerbate the problem. BC accounts for 36.9% of female cancers in Gaza, with many cases diagnosed at advanced stages, which complicates treatment outcomes (Abu-El-Noor et al., 2023; Ministry of Health, 2023; Moawad et al., 2024).

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) (Cohen et al., 2023). One biological pathway linking lifestyle factors to BC risk is through the hormone-insulin-like growth factor 1 (IGF-1), which plays a role in cell growth and development (Zhu et al., 2020). Increased levels of IGF-1 are associated with obesity and other lifestyle conditions and have been linked to increased BC risk (Ajabnoor, 2023). However, lifestyle interventions like weight loss and increased physical activity have been shown to reduce serum IGF-1 levels, potentially lowering cancer risk (Swain et al., 2022).

In the Gaza Strip, where economic hardship, food insecurity, and restricted mobility limit lifestyle choices (Abu Hamad et al., 2021), these factors likely contribute to the rising BC incidence (El Sharif & Khatib, 2021). However, the specific role of lifestyle factors in modulating serum IGF-1 levels and their association with BC risk among Palestinian women remains poorly understood.

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.

METHODS

STUDY DESIGN AND SETTING

A case-control study was conducted in the Gaza Strip from January 1, 2021, to January 7, 2023, including 112 newly diagnosed BC women from Al-Shifa and Turkish Palestinian Friendship Hospitals, and 222 age-matched healthy controls from Al-Remal Clinic. Written informed consent was obtained before recruiting histopathologically confirmed cases and healthy controls with negative mammograms or ultrasounds. The ethical approval was awarded by the Helsinki Committee (PHRC/HC/699/20), and the USM Human Research Ethics Committee (JEPeM USM Code: USM/JEPeM/20020122).

DATA COLLECTION AND STUDY TOOLS

Face-to-face validated interview questionnaires include 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.

A. PHYSICAL ACTIVITY

The International Physical Activity Questionnaire (IPAQ), which evaluated recreational and household activities during the previous week, was used to measure physical activity. Based on metabolic equivalents (METs), activities were categorized into 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 (Blasco-Peris et al., 2024).

B. DIETARY ASSESSMENT

A Food Frequency Questionnaire (FFQ), which collected information on the frequency of consumption of 103 food items during the previous year, covering 103 food kinds classified into 14 categories, was used to assess dietary intake. The amount of food consumed was determined by taking the amounts consumed every day, every week, or every month.

C. BIOCHEMICAL ANALYSIS

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).

STATISTICAL ANALYSIS

The IBM SPSS version 28 was used for all statistical analysis. 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 considered statistically significant.

RESULTS

Risk factors of BC among Palestinian females in the Gaza Strip

The multivariable analysis revealed that women under 40 had a significantly decreased BC risk by 57.3% compared to older women (OR = 0.427, p = 0.042), as shown in Table 1. 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), as shown in Table 1. Serum IGF-1 levels were also significantly associated with increased BC risk (OR = 1.013, p ≤ 0.001), as shown in Table 1.

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	32 (14.4)	0.021	1.021 (0.391, 2.667)	0.966

		(16.1)				
	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)	1.910	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) Mean ± SD		121.69 ± 59.15	92.33 ± 48.81	0.013	1.013 (1.007, 1.019)	≤ 0.001

*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.

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 controls, and the two groups' 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) compared to controls (88.79 cm, $p = 0.029$). BC women had higher BMI (29.89 kg/m^2) than healthy control (29.08 kg/m^2) without statistically significant difference with ($p = 0.221$) as shown in Table 2.

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

Variables	**Mean ± SD** **Cases** ***N* = 112**	**Controls** ***N* = 222**	**Mean differences (95%CI)**	***p*-value**
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.

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, $p \leq 0.001$), 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, $p \leq 0.001$) 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, $p = 0.020$)

Table 3: The association between dietary pattern and BC among women in the Gaza Strip using the univariate logistic regression

Univariate models	Mean ± SD Cases *N* = 112	 Control *N* = 222	B	Crude OR (95%CI)	*p*-value
Fresh vegetables/salad	89.56 ± 19.66	92.89 ± 19.96	-0.008	0.992 (0.980, 1.003)	0.150
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	-0.030	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)	0.020
Nuts	4.66 ± 2.28	5.41 ± 1.89	-0.180	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	-0.030	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.

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: 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	0.550
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	0.480
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.

DISCUSSION

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 (Shuvo et al., 2017).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. 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 (Hassen et al., 2022). 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 (Lukasiewicz et al., 2021). Our study has found a link between higher serum levels of IGF-1 and an increased BC risk, which is consistent with previous study (Baglietto et al., 2007; Vatten et al., 2008).

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; $p \leq 0.001$). In line, a study done in China explored that women with BC had higher IGF-1 concentrations than the control group ($p = 0.032$) (Zhu et al., 2020).

Concerning participant age and BC risk, cases and controls in the study had a mean age of 45 years and 42 years, respectively ($p \leq 0.05$). Our findings are in line with research done by Marzbani et al. who found that the mean ages of case and control groups were 41.5 and 39.5 years, respectively (Marzbani et al., 2019). Additionally, waist circumference was significantly greater in BC cases (91.12 cm) compared to controls (88.79 cm, $p = 0.029$). 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 (El-Hissi et al., 2016).

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 ($p < 0.001$) (Nguyen et al., 2022). 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 (El-Hissi et al., 2016). 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) (Nguyen et al., 2022). Alternatively, Kim et al. discovered that all women had a noticeably increased chance of BC when they ate grilled meat (Kim et al., 2017). The degree of doneness, cooking method, and type of meat ingested are thought to be the possible causes of this variation in the results. 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 (Farvid et al., 2020).

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 (Bao et al., 2012; Shuvo et al., 2017).

Our data showed that the intake of eggs is associated with an increased chance of developing BC (p = 0.020). Meta-analysis supported the association which revealed that eating five eggs or more per week significantly elevated the opportunity of having BC compared to no consumption of eggs (Keum et al., 2015). 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 (Zhang et al., 2020). 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 (Sharif et al., 2021). The consumption of snacks and sweets was found to have a protective effect against BC risk and decreased 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 (Marzbani et al., 2019). The inconsistencies in findings may result from variations in how studies define and measure sweet consumption, which significantly influences the outcomes.

The Mediterranean nutritional pattern is reflected in the Palestinian diet (Hamdan et al., 2020). It is abundant in vegetables and fruit, legumes, nuts, unrefined cereal grains, and olive oil, but fish and dairy intake is modest, and red meat consumption is minimal. Interestingly, the Mediterranean diet has been linked to a decrease in the incidence of BC, preventing the disease from developing (Guasch-Ferre & Willett, 2021; Mentella et al., 2019).

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 (Hoppe et al., 2009; Key et al., 2010), 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) (Hang et al., 2019).

CONCLUSION

This study highlights the significant associations between dietary patterns, lifestyle factors, and BC risk. Consuming fresh fruits, meat, grains, low-fat dairy, nuts, sweets, and soups was linked to a reduced BC risk, while eggs were associated with increased risk. The study also highlights potential hormonal mechanisms, with beverage consumption influencing IGF-1 levels and BC development. These results highlight the necessity of preventative measures and additional studies to fully comprehend the intricate relationships among hormone regulation, diet, and BC risk.

LIMITATION OF STUDY

As a case-control study, there is potential for recall bias, despite controlling for some confounders, other unmeasured factors such as environmental or genetic factors may influence both IGF-1 levels and BC risk. These factors were not fully accounted for in the analysis and may have introduced some residual confounding, potentially affecting the study's findings.

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