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Healthy Lifestyle and Breast Cancer Risk in Palestinian Women: A Case-Control Study

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ABSTRACT

The aim of this study was to investigate the association between a combined healthy lifestyle score and the risk of breast cancer (BC) in Palestinian women. A hospital-based case-control study compared 237 BC cases with confirmed diagnoses to 237 healthy controls. Women's lifestyle components were assessed using a validated questionnaire. A healthy lifestyle index (HLI) has been developed. We used logistic regression models to investigate the relationship between combined lifestyle scores and BC odds. The results revealed that HLI was significantly higher in the control group than in the study group. A higher HLI score was associated with a lower risk of BC in the multivariate analysis. The adjusted odds ratios (AOR) were 0.19 for all women, 0.15 for postmenopausal women, and 0.23 for premenopausal women when the HLI highest and lowest tertiles were compared. HLI score increases of one point resulted in a 41% reduction in the risk of BC for all women, a 42% reduction for postmenopausal and premenopausal women, and a 39% reduction for postmenopausal women. Women who live a healthy lifestyle, according to our findings, have a lower risk of breast cancer. BC prevention programs must promote long-term healthy food and lifestyle choices.

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Background

Breast cancer (BC) is the most common cancer to be diagnosed and the leading cause of cancer death among females worldwide. The World Health Organization estimates that 2.3 million women had been diagnosed with BC in 2020; 7.8 million women who have been diagnosed in the previous five years are still alive; and 68,500 people died globally (1). According to the Palestinian Ministry of Health (MoH), BC had an incidence rate of 19.1 per 100,000 people in Palestine in 2020, making it the third leading cause of cancer mortality (12.9%) behind lung cancer (18.7%) and colon cancer (13.9%) (2).

There are several recognized BC risk factors that have each been independently linked to an increased risk of developing BC (3). These risk factors, which are typically linked to lifestyle choices including being overweight or obese, being sedentary or inactive, drinking alcohol, and having bad eating habits, have been shown to increase the risk of BC (4–7). Other risk factors include sex, age, genetic traits, such as a family or personal history of BC, ethnicity, and early menarche or menopause, which are non-modifiable risk factors (8–10). The association between behavioral factors and lifestyle factors linked to BC has been investigated in a number of studies (11–13). Therefore, it is necessary to consider these lifestyle factors simultaneously and consider their combined effects.

A healthy lifestyle was associated with a lower risk of BC in studies that investigated the link between multiple lifestyle characteristics and the likelihood of developing BC (5, 14, 15). Healthy living, according to Mexican researchers, can lower premenopausal women's risk of BC by 50% and postmenopausal women's risk by 80% (16). Similar findings were found in Morocco by Khalis et al. who found that for all women, premenopausal women, and postmenopausal women, a one-point increase in the healthy living score was associated with 56%, 49%, and 59% lower risks of BC, respectively (17). According to the Iranian study, BC risk was 44% lower in women with the highest HLS scores compared to those with the lowest scores. But these results were not evident in premenopausal women (5). The healthcare system in Palestine

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faces a substantial challenge as a result of rising cancer rates. The issue is exacerbated by infrastructure and financial constraints, as well as political uncertainty (18). The relationship between many lifestyle factors and the risk of BC in Palestine is less well understood. We previously showed that several reproductive risk factors, parental consanguinity marriage, and positive family history were significant risk factors for BC in Palestine (19).

This study aimed to investigate the association between a healthy lifestyle score and the risk of breast cancer in Palestinian women. A "healthy lifestyle index" was established in which study participants were assessed based on their lifestyle behaviors, i.e., diet, physical activity, body mass index (BMI), smoking, alcohol consumption, breastfeeding, and the risk of developing BC in Palestinian women.

Materials and Methods

Study Context and Settings

In the West Bank, four hospitals provide cancer care, including diagnosis and treatment. Since isotope scans are unavailable in Palestine, all cases are referred to Israeli hospitals. The study was carried out at the major government institution Beit-Jala Hospital. Cancer patients can receive oncology services in the daycare clinic of Beit-Jala Hospital in the central and southern West Bank. Hospital databases were utilized for the selection of study subjects. The controls were recruited from primary care clinics in the southern West Bank that offers mammography as part of a national screening program administered by the Palestinian Ministry of health.

Study Design

This case-control study was conducted between 2016 and 2017 at the Beit-Jala Governmental Hospital in the West Bank of Palestine.

Cases and Controls Selection

At the time of the interview, 237 patients aged 40 or older were selected at random. Using a type I error of 5% and a study power of 80%, the sample size was determined. We hypothesized that an unhealthy lifestyle may increase the risk of developing breast cancer by a factor of three, with a correlation coefficient of 0.2 between case and control exposures. We randomly selected cases from the Beit-Jalal hospital database based on the file numbers of patients who visited the daycare oncology department or the chemotherapy unit.

In order to be included in the study, women had to be diagnosed with BC as a primary malignancy rather than a secondary disease. To serve as comparable and representative controls, we randomly selected 237 women of the same age range and geographic area from the BC screening program. The medical records of potential control participants were reviewed for the presence of normal mammograms (BIRADS 1). Excluded from the study were participants referred by physicians for suspected breast problems or who had a history of cancer or neoplastic disease.

This study was approved by the Al Quds University Ethical Review Committee. Written approval was obtained from the Ministry of Health to access the patient's records from the oncology department and cancer registry. All women provided written informed consent.

Data Collection and Measurements

We retrieved information from cancer patients' medical records regarding the date of diagnosis, stage, type, and treatment strategy.

During the patient's visit to the oncology department, two trained and standard female interviewers administered an in-depth structured questionnaire. A nurse from the mammography department invited participants to represent as controls. If a control subject declined to attend the clinic, a telephone interview was conducted.

The General Study Questionnaire

The questionnaire includes questions on sociodemographic factors, lifestyle factors (diet, smoking, physical activity, alcohol consumption), parental consanguinity marriage, reproductive history (age at menarche, age at first full-term pregnancy, parity, menopausal status, age at menopause, contraceptive history; use of hormone therapy; menstrual history; pregnancy and breastfeeding history), medical history (including cancer and mammogram history), and family history of breast cancer. Postmenopausal status was defined as the self-reported absence of menstruation within the previous year. Moreover, anthropometric characteristics of women were also reported. The participants' last recorded weight and height at the clinic were obtained from their patient records. BMI was calculated by dividing weight (kg) by height^2 (m^2). In addition, women were asked if they had

undergone partial or total removal of one or both ovaries through surgery. They were also asked if they had a hysterectomy or tubal sterilization, as well as the month and year of the procedure (s).

The Dietary Intake Questionnaire

The study dietary questionnaire was based on a previously validated questionnaire, i.e., the British Cancer Cohort Study (Cancer Research UK, 2014). Dairy products (milk and yogurt), vegetables, fruits, legumes, cereals, potatoes, white bread, whole grain bread, butter, eggs, peas and beans, biscuits, cakes, fish, meat, processed meat, soft drinks, nuts and peanuts, pizza, and pastries are among the foods reported in the food frequency questionnaire (FFQ). The frequency of FFQ was estimated by selecting one of nine categories: never, once to three times per month, once a week, twice to four times per week, five to six times per week, once per day, twice to three times, more than four times, and more than six times daily. An expert translated the questionnaire into Arabic and then back into English (see Supplement S1). The internal consistency coefficient (Cronbach's alpha) of the dietary intake questionnaire was 0.60.

Assessment of Physical Activity

Using the Global Physical Activity Questionnaire (GPAQ), the current level of physical activity was determined (20). Women were asked to recall the number of days in the previous week in which they engaged in vigorous-intensity and/or moderate-intensity physical activity in three major settings (activities at work/home, travel to and from places, and recreational activities), as well as the number of hours and minutes per day, respectively. The weekly metabolic equivalent (MET) hours were multiplied by the relevant total hours of physical exercise. The corresponding combination of moderate- and vigorous-intensity physical activity attained at least 600 MET-minutes; hence, the data were classified as low physical activity (<600 MET-minutes) and moderate- and vigorous-intensity physical activity (≥600 MET-minutes).

Assessment of Smoking and Alcohol Consumption

A self-administered questionnaire was used to assess smoking. The STEPwise instrument was used to determine the smoking status (21). Our study scale was developed using the following questions: current, former, and never smokers. Those who answered, "Yes" to the question "Do you currently smoke any tobacco products, such as cigarettes, cigars or pipes" were categorized as current smokers, and those who answered "No" to the question "In the past, did you ever smoke any tobacco products," were considered "never" smokers, and those who answered "Yes" to this question were identified as "former" smokers.

Lifestyle Index Score

The lifestyle index (HLI) score utilized in this study was derived in accordance with public health and cancer prevention guidelines (14, 22). It was based on eleven parameters, as described elsewhere: consumption of red and processed meat, white meat, cream, cheese, seafood, fruit, and vegetables (except potatoes), physical activity, BMI, smoking, alcohol consumption, and breastfeeding (15).

We assigned 0, 0.5, or one point to categories of each element when calculating the HLI score for each participant. As presented in Table 1, the healthy lifestyle behaviors were defined as limiting the intake of red meat and avoiding processed meat (<once per week), consuming more white meat (≥2 times per week), consuming more fish (≥2 times per week), high fruit and vegetable consumption (at least five servings per day), no cream or cheese consumption, no alcohol consumption, never having smoked, having a high physical activity level (at least 60 min of moderate or 30 min of vigorous physical activity daily), a healthy BMI (<25 kg/m^2), and longer cumulative duration of breastfeeding (≥24 mo). None of the participants were underweight.

Participants received 0.5 points for each intermediate category of each health behavior and 0 points for the least healthy category. For analysis, the index score was divided into tertiles. Using the sum of the individual scores for each of the lifestyle variables, a lifestyle index score ranging from 0 (least healthy) to 11 points was calculated for each participant (most healthy).

Since obesity is one of the most common modifiable lifestyle-related risk factors for postmenopausal BC, we ran sensitivity analyses to see if any observed association between HLI and BC was due mainly to BMI. As a result, the HLI index without BMI ranges from 0 (least healthy) to 10 points (most healthy).

Statistical Analysis

For data analysis, the Statistical Package for the Social Sciences (IBM SPSS) version 23 (IBM Corp., Chicago,

Table 1. Univariate analysis for the individual components of the healthy lifestyle index score and their distribution among cases and controls.

			Controls $N=237$	Cases $N=237$	Chi square	Univariate analysis	
Characteristic			Freq. (%)	Freq. (%)	P-value	Sig.	OR (95% CI
Recommendation: Limit intake of red meat							
Marker: Red meat weekly	0	≥2 times	14 (5.9)	69 (29.1)	<0.001		Ref.
	0.5	one time	92 (38.8)	71 (30.0)		<0.001	0.16 (0.08–0.30)
	1.0	<1 time	131 (55.3)	97 (40.9)		1.000	0.15 (0.08–0.28)
Recommendation: Choose a variety of protein foods							
Marker: White meat Weekly	0	<1 time	5 (2.1)	26 (11.0)	<0.001		Ref.
	0.5	1 time	22 (9.3)	32 (13.5)		0.020	0.28 (0.09–0.84)
	1.0	≥2 times	210 (88.6)	179 (75.5)		<0.001	0.16 (0.06–0.43)
Recommendation: Increase the amount and variety of seafood							
Marker: fish Weekly	0	<1 time	162 (68.4)	109 (46)	<0.001		Ref.
	0.5	1 time	67 (28.3)	83 (35)		0.003	1.84 (1.23–2.75)
	1.0	≥2 times	8 (3.4)	45 (19)		<0.001	8.36 (3.79–18.4)
Recommendation: Reduce the intake of calories from solid fats							
Marker: Cheese weekly	0	≥2 times	118 (49.8)	125 (52.7)	0.012		Ref.
	0.5	1 time	78 (32.9)	51 (21.5)		0.029	0.61 (0.40–0.95)
	1.0	<1 time	41 (17.3)	61 (25.7)		0.156	1.40 (0.87–2.24)
Recommendation: Limit consumption of energy-dense foods							
Marker: Butter weekly	0	≥2 times	7 (3.0)	27 (11.4)	0.001		Ref.
	0.5	1 time	17 (7.2)	22 (9.3)		0.040	0.33 (0.11–0.95)
	1.0	<1 time	213 (89.9)	188 (79.3)		0.001	0.22 (0.09–0.53)
Recommendation: Eat mostly foods of plant origin							
Vegetables and fruits	0	≤once weekly	85 (35.9)	125 (52.7)	<0.001		Ref.
	0.5	2-6 weekly	103 (43.5)	68 (28.7)		0.049	1.64 (1.002–2.68)
	1.0	≥once daily	49 (20.7)	44 (18.6)		0.240	0.74 (0.44–1.22)
Smoking	0	current	8 (3.4)	12 (5.1)	0.140		Ref.
	0.5	former	0 (0.00)	3 (1.3)		—	—
	1.0	never	229 (96.6)	222 (93.7)		0.350	0.65 (0.26–1.61)
Physical Activity MET-Min/Week)†	0	≤600	48 (20.3)	50 (21.1)	0.820		Ref.
	1.0	>600	189 (79.7)	187 (78.9)		0.820	0.95 (0.61–1.48)
Recommendation: Be as lean as possible without becoming underweight							
BMI (kg/m^2)†	0	<25	29 (12.2)	44 (18.6)	<0.001		Ref.
	0.5	25–<30	112 (47.3)	56 (23.6)		<0.001	0.33 (0.19–0.58)
	1.0	30+	96 (40.5)	137 (57.8)		0.820	0.94 (0.55–1.61)
Recommendation: Breastfeed infants							
Breastfeeding total number of years	0	never	20 (8.4)	50 (21.1)	<0.001		Ref.
	0.5	>0 to <6 years	29 (12.2)	64 (27.0)		0.720	0.88 (0.45–1.74)
	1.0	≥6 years	188 (79.3)	123 (51.9)		<0.001	0.26 (0.15–0.46)
Healthy Lifestyle index score (range = 1–11)‡	0	Unhealthy	68 (28.7)	131 (55.3)	<0.001		Ref.
	0.5	Middle	112 (46.3)	69 (29.1)		<0.001	0.30 (0.21–0.49)
	1.0	Healthy	57 (24.1)	37 (15.6)		<0.001	0.34 (0.20–0.56)
Healthy lifestyle index‡		Mean (SD)	7.22 (0.98)	6.66 (1.15)	<0.001**	<0.001	0.61 (0.50–0.73)

*Student T-test significance, **Kruskal Wallis test.

†Physical Activity: low is <600 MET and Moderate is 600–1500, body mass index (BMI): calculated by dividing weight in kilogram by the square of height in meters and was categorized into three groups: less than 25 kg/m^2, 25–29.9 kg/m^2 (overweight), and 30 kg/m^2 or higher (obese). kg/m^2: kilogram divided by meter square height.

‡Healthy Lifestyle score was calculated for each participant based on the average week last year: how many times a week a participant ate red meat, white meat, fish, cream, and cheese; servings of vegetables and fruits (excluding potatoes), and drinks containing alcohol. In addition, exercise intensity, duration of breastfeeding, smoking status, and body mass index (BMI) categories were included in the score. The tertile of this index was categorized into the unhealthy score (low tertile ≤6.5), middle score (tertile 6.6–7.5), and healthy score (tertile >7.5).

IL, USA) was used. Initially, descriptive analyses were performed to investigate the variable values and summarize the data. Chi-squared tests for categorical variables and Kruskal-Wallis tests for continuous variables were used to compare exposure distributions between cases and controls. To investigate the relationship between BC and independent variables, univariate logistic regression models were used. To determine the precision of the estimates, crude odds ratio (OR) and adjusted odds ratio (AOR) and their 95% confidence intervals (CIs) were calculated. The p-values were two-sided, with 0.05 indicating significance.

A healthy lifestyle score was calculated for each participant based on their average week from the previous year: the number of times they had red meat, white meat, seafood, cream, and cheese; vegetable and fruit servings (excluding potatoes); and alcoholic beverages. The score also includes factors for exercise intensity, breastfeeding length, smoking status, and body mass index (BMI) categories. This index's tertiles

were classified as follows: unhealthy score (low tertile ≤7.0), middle score (tertile 7.0–7.5), and healthy score (tertile >7.5). The tertile of this index was categorized as unhealthy (low tertile ≤6.5), middle (tertile 6.6–7.0), and healthy (tertile >7.0) when the BMI was excluded from its calculations.

Using conditional logistic regression models, the association between BC and the lifestyle index (HLI) by menopausal state and diabetes was estimated. All confounding variables were selected based on prior publications. The HLI was assessed as a categorical variable and modeled as a continuous (1-point increment) variable, adjusting for all other covariates as categorical variables: educational level, home type, family size, income level, parity, work status, consanguinity level, marital status, menopause status or diabetes status, body mass index, family history of breast cancer, use of hormonal replacement therapy (yes/no), and use of oral contraceptives (yes/no). Based on the score distribution of controls, the HLI score was divided into tertiles, with the lowest tertile (0 to 6.5 points) serving as the reference group.

Results

Distribution of Healthy Lifestyle Index among Cases and Controls

There were 237 cases and 237 age-matched controls in this study. Table 1 shows the proportions of cases and controls for each component of the lifestyle index score. The controls had a significantly higher mean healthy lifestyle index. Cases consumed significantly more red and processed meat (≥2 times per week: 29.1% vs. 5.9%), cheese (≥2 times per week: 52.7% vs. 49.8%), and butter, and significantly less white meat, vegetables, and fruits, and had fewer total breastfeeding years. However, cases consumed more fish on a weekly basis. The cases were also significantly heavier than the controls (body mass index, BMI > 30: 57.8% and 40.5%, respectively), but the level of physical activity was not significantly different. Significant inverse associations were found in the univariate analysis of BC risk with the recommended limited intake of various diets, the healthy lifestyle index (HLI), BMI, and breastfeeding, but not with fish intake or physical activity.

General Characteristics of Study Participants

Eighty-two percent of study cases were diagnosed within five years of the survey and all patients received at least one treatment.

The distribution of selected case and control characteristics is presented in Table 2. The cases had lower monthly family incomes than the controls while having significantly higher levels of education and living in separate dwellings ($p < 0.05$). The cases had a lower number of live births, a higher reported family history of BC, a higher identified rate of diabetes, and a higher reported level of consanguinity of first relative degree (cousin) ($p < 0.05$).

According to a comparison of participant characteristics across HLI categories, the participants with the highest HLI scores were significantly younger, had higher incomes, were married, had children, and had larger families. Individuals with the highest HLI scores had a normal BMI, were more physically active, had never smoked, had breastfed for more than six years, were from families with no history of BC, did not have diabetes, and did not have consanguineous parents (Table 2).

Association between Healthy Lifestyle Index and Odds of Breast Cancer

Table 3 shows the multivariate-adjusted odds ratios (ORs) and 95 percent confidence intervals (CIs) for the association between the HLI score and BC risk for all women and by menopausal status. After potential confounders were eliminated, a higher HLI score was associated with a lower risk of BC. When comparing the highest and lowest tertiles of the HLI, the adjusted odds ratio was 0.19 (95% CI: 0.09 to 0.44) for all women, 0.15 (95% CI: 0.04 to 0.48) for postmenopausal women, and 0.23 (95% CI: 0.07 to 0.72) for premenopausal women.

As a continuous variable, the model shows that for every one-point increase in the HLI score, there is a 41%, 42%, and 39% lower risk of BC in all, postmenopausal, and premenopausal women, respectively. Furthermore, even after the BMI component was removed from the HLI score index, the HLI score remained strongly associated with lower BC risk among all women, including pre-and postmenopausal women.

Table 3 also shows the adjusted OR for diabetic women comparing the highest and lowest tertiles, which were 0.02 (95% CI: 0.002 to 0.29), and 0.32 (95% CI: 0.13 to 0.76) for non-diabetic women. A one-point increase in the HLI score as a continuous variable was associated with a 33% and 50% lower risk of BC in diabetics and non-diabetics, respectively. Even after removing the BMI component, the HLI score was still significantly associated with lower BC risk.

Table 2. Characteristics of study participants and their association with the healthy lifestyle index.

		Groups			Healthy lifestyle index			
		Controls	Cases	Chi-square	Unhealthy	Moderate	Healthy	
		N = 237	*N* = 237		*N* = 199	*N* = 181	*N* = 94	
		Freq.(%)	Freq.(%)	Sig.	Freq.(%)	Freq.(%)	Freq.(%)	Sig.
Age groups (years)	39–44	50 (21.1)	50 (21.1)	—	44 (22.1)	25 (13.8)	31 (33.0)	0.026
	45–49	40 (16.9)	40 (16.9)		36 (18.1)	26 (14.4)	18 (19.1)	
	50–54	37 (15.6)	37 (15.6)		30 (15.1)	29 (16.0)	15 (16.0)	
	55–59	40 (16.9)	40 (16.9)		34 (17.1)	35 (19.3)	11 (11.7)	
	60–64	19 (8.0)	19 (8.0)		13 (6.5)	18 (9.9)	7 (7.4)	
	65–69	27 (11.4)	27 (11.4)		25 (12.6)	22 (12.2)	7 (7.4)	
	70–100	24 (10.1)	24 (10.1)		17 (8.5)	26 (14.4)	5 (5.3)	
Educational level (years)	1-6	117 (49.3)	81 (34.2)	0.001	75 (37.7)	90 (49.7)	33 (35.1)	0.150
	7-9	62 (26.2)	59 (24.9)		55 (27.6)	40 (22.1)	26 (27.7)	
	10–12	44 (18.6)	49 (20.7)		39 (19.6)	30 (16.6)	24 (25.5)	
	>12	14 (5.9)	48 (20.2)		30 (15.1)	21 (11.6)	11 (11.7)	
Home type	Separate house	147 (62)	198 (83.5)	0.001	154 (77.4)	123 (68)	68 (72.3)	0.120
	Apartment	90 (38)	39 (16.5)		45 (22.6)	58 (32)	26 (27.7)	
Family monthly income**	<1000 NIS	55 (23.2)	78 (32.9)	0.012	69 (34.7)	49 (27.1)	15 (16.0)	0.004
	≥1000 NIS	182 (76.8)	159 (67.1)		130 (65.3)	132 (72.9)	79 (84.0)	
Family size (persons)	1–5	93 (39.2)	108 45.6)	0.160	86 (43.2)	88 (48.6)	27 (28.7)	0.006
	6 or more	144 60.8)	129 54.4)		113 (56.8)	93 (51.4)	67 (71.3)	
Working status	Yes (now or then)	23 (9.7)	35 (14.8)	0.090	30 (15.1)	17 (9.4)	11 (11.7)	0.240
	No	214 (90.3)	202 (85.2)		169 (84.9)	164 (90.6)	83 (88.3)	
Marital status	Single	10 (4.2)	19 (8.0)	0.200	22 (11.1)	4 (2.2)	3(3.2)	0.004
	Married	189 (79.7)	185 (78.1)		146 (73.4)	151 (83.4)	77 (81.9)	
	Divorced or widowed	38 (16.1)	33 (13.9)		31 (15.6)	26 (14.4)	14 (14.9)	
Parity	No	12 (5.1)	36 (15.2)	<0.001	34 (17.1)	9 (5.0)	5 (5.3)	<0.001
	Yes	225 (94.9)	201 (84.8)		165 (82.9)	172 (95.0)	89 (94.7)	
Parental consanguinity relation	No Relation	123 (51.9)	100 (42.2)	0.001	84 (42.2)	88 (48.6)	51 (54.3)	0.001
	1st degree	52 (21.9)	102 (43.0)		84 (42.2)	44 (24.3)	26 (27.7)	
	2nd degree	62 (26.2)	35 (14.8)		31 (15.6)	49 (27.1)	17 (18.1)	
Menopausal status	Premenopausal	110 (46.4)	105 (44.3)	0.360	94 (47.2)	66 (36.5)	55 (58.5)	0.002
	Postmenopausal	127 (53.6)	132 (55.7)		105 (52.8)	115 (63.5)	39 (41.5)	
Have Diabetes	No	202 (85.2)	180 (75.9)	0.010	149 (74.9)	152 (84.0)	81 (86.2)	0.025
	Yes	35 (14.8)	57 (24.1)		50 (25.1)	29 (16.0)	13 (13.8)	
Family history of Breast ca	No	214) 90.3(	16 4)69.2(	<0.001	134 (72.4)	130 (83.9)	114 (85.1)	0.006
	Yes	23)9.7(	73)30.8(		51 (27.6)	25 (16.1)	20 (14.9)	
Body Mass Index	obese ≥30	96 (40.5)	137 (57.8)	<0.001	139 (69.8)	78(43.1)	16(17.0)	<0.001
	25–<30	111 (46.8)	56 (23.6)		57(28.6)	88(48.6)	22(23.4)	
	<25	30 (12.7)	44 (18.6)		3(1.5)	15(8.3)	56(59.6)	
Physical Activity MET-Min/Week)	≤600	48(20.3)	50 (21.1)	0.820	25 (16.8)	40 (26.3)	10 (12.3)	0.020
	>600	189(79.7)	187(78.9)		124 (83.2)	112 (73.7)	71 (87.7)	
Smoking	current	8(3.4)	12(5.1)	0.140	13 (8.7)	2 (1.3)	0 (0.0)	0.0012
	former	0(0.00)	3(1.3)		2 (1.3)	1 (0.7)	0 (0.0)	
	never	229(96.6)	222(93.7)		134 (89.9)	149 (98.0)	81 (100)	
Breastfeeding total number of years	never	20 (8.4)	50 (21.1)	<0.001	39 (26.2)	12 (7.9)	4 (4.9)	<0.001
	>0 to <6 years	29 (12.2)	64(27.0)		42 (28.2)	24 (15.8)	15 (18.5)	
	≥6 years	188 (79.3)	123 (51.9)		68 (45.6)	116 (76.3)	62 (76.5)	

*p-value was calculated by using Pearson's chi-square test, **NIS: new Israeli Shekels: 1000 NIS is about 300 dollars, Freq.: frequency, %: percentage.

Table 3. Healthy lifestyle and its association with breast cancer risk between post- and premenopausal women, and between diabetic and non-diabetic women.

	All women*		Post-Menopause**		Pre-Menopause**		Diabetics†		Non-diabetics‡	
	273/273		132/127		105/110		35/57		202/180	
Frequency (Control/cases)	Co/Ca Freq.	AOR (95% C.I.)*	Co/Ca Freq.	AOR (95% C.I.)*	Co/Ca Freq.	AOR (95% C.I.)*	Co/Ca Freq.	AOR (95% C.I.)*	Co/Ca Freq.	AOR (95% C.I.)*
Healthy lifestyle score Range (1–11)										
Unhealthy score	134/178	Ref.	73/106	Ref.	61/72		23/52		111/126	
Middle score	46/22	0.48 (0.24–0.94)	29/12	0.34 (0.14–0.84)	17/10	0.62 (0.20–1.87)	3/1	0.21 (0.02–2.37)	43/21	0.58 (0.28–1.20)
Healthy score	57/37	0.19 (0.09–0.44)	25/14	0.15 (0.04–0.48)	32/23	0.23 (0.07–0.72)	9/4	0.02 (0.002–0.29)	48/33	0.32 (0.13–0.76)
P trend		<0.001		0.001		0.041		0.007		0.024
1-point increase in score		0.41 (0.31–0.54)		0.42 (0.29–0.51)		0.39 (0.26–0.59)		0.33 (0.18–0.63)		0.50 (0.36–0.69)
P value		0.001		<0.001		<0.001		0.001		<0.001
Healthy lifestyle score, Range (1–10) excluding BMI										
Unhealthy score	107/156	Ref.	54/83	Ref.	53/73	Ref.	15/42		92/114	
Middle score	57/51	0.94 (0.54–1.65)	36/39	0.81 (0.41–1.58)	21/12	0.86 (0.29–2.55)	9/11	.374 (0.13–1.10)	48/40	1.12 (0.62–2.2)
Healthy score	73/30	0.14 (0.07–0.29)	37/10	0.08 (0.03–0.24)	36/20	0.28 (0.10–0.75)	11/4	.016 (0.001–0.22)	62/26	0.21 (0.10–0.45)
P trend		<0.001		<0.001		0.038		<0.001		<0.001
1-point increase in score		0.44 (0.33–0.58)		0.38 (0.26–0.56)		0.48 (0.31–0.73)		0.33 (0.18–0.63)		0.50 (0.36–0.69)
P value		<0.001		<0.001		<0.001		0.001		<0.001

AOR: adjusted odds ratio, 95%CI: 95% Confidence interval, Ref.: reference category, Co/Ca: Controls/cases.

*Multivariate analysis includes all variables presented in Table 1. It was adjusted for having diabetes, educational level, home type, family size, income level, parity, work status, consanguinity level, marital status, menopause status, body mass index, family history of breast ca, in addition, using hormonal replacement therapy (yes/no), and using oral contraceptives (yes/no) were added.

**Menopause status was not included in the model.

†Multivariate analysis includes all variables presented in Table 1. It was adjusted for having diabetes, educational level, home type, family size, income level, parity, work status, consanguinity level, marital status, menopause status, body mass index, family history of breast ca, in addition, using hormonal replacement therapy (yes/no), and using oral contraceptives (yes/no) were added.

‡Having diabetes was not included in the model.

Discussion

Our case-control study found a significant inverse relationship between healthy lifestyle index adherence and BC risk. After adjusting for several confounding variables, this association remained significant. When stratified by menopausal status, the association remained significant among premenopausal women but not among postmenopausal women. Furthermore, stratifying by diabetes status revealed a significantly stronger association among women with diabetes and a significantly weaker association among women without diabetes. This is the first study to look into the association between BC risk and the healthy lifestyle index in Palestinian women.

The most common healthy habits, according to the healthy lifestyle index score, were breastfeeding and eating white meat, while fruit and vegetable consumption, exercising, and cheese consumption received the lowest scores. The findings of this study revealed that higher HLI scores were associated with a lower risk of BC. Our findings are consistent with previous studies in other groups that found an inverse relationship between BC risk and HLIs. Using the same HLI definition, Khalis et al. found that higher HLI scores were associated with a lower risk of BC in Morocco; the adjusted OR comparing the highest to the lowest tertile was 0.15 (95% CI: 0.07–0.32) (17). In a similar study, Ghosn et al. found that Iranian women who scored high on the HLS were 0.38 times less likely to develop BC than those who scored low (OR: 0.62; 95% CI: 0.40–0.93) (5). Furthermore, the Canadian Study of Diet case-cohort found that those with high HLI scores had a 30% lower risk of BC (hazards ratio 0.70; 95% CI 0.53–0.93) (23). Furthermore, breastfeeding was found to be an important component of these Palestinian women's healthy lifestyle index. Breastfeeding is widely practiced in Palestine. Although 96% of women exclusively breastfeed their newborns at birth, only 40% continue to do so until their child is six months old (24).

A high HLI score was inversely associated with the risk of BC in pre-and postmenopausal women when comparing premenopausal to postmenopausal risk. Our findings are strikingly similar to those of the Moroccan women; the adjusted OR between the highest and lowest tertiles for premenopausal women was 0.22 (95% CI: 0.10–0.49) and 0.11 (95% CI: 0.04–0.30) for postmenopausal women (17). Furthermore, in a case-control study conducted in Mexico, women who lived healthier lifestyles and scored in the top quintile of the HLI had a significantly lower risk of BC than those who scored in the bottom quintile (premenopausal OR 0.50, 95% CI 0.29 to 0.84; postmenopausal OR 0.20, 95% CI 0.11 to 0.37) (16). In contrast, postmenopausal women who adhered to the highest Healthy Eating Index score had 61% lower odds of BC compared to those who adhered to the lowest Healthy Eating Index score (OR: 0.39; 95% CI: 0.26, 0.56) in Iranian women, but there was no association between Healthy Eating Index score and odds of BC in premenopausal women (5). This finding was confirmed in a study of postmenopausal women in New Zealand, who had more evidence of BC than premenopausal women (14). A nine-year follow-up study had similar findings. In postmenopausal women, there was a strong inverse relationship between dietary pattern and risk of BC, but not in premenopausal women (25).

It was found that women with a high body mass index have an increased risk for breast cancer. In our study, height and weight were obtained from the records of women. We cannot therefore verify if these measurements are biased. Adiposity has been identified as a BC risk factor (26, 27). To exclude the BMI effect from this study, we eliminated it from the healthy lifestyle index in a separate analysis. Comparing the HLI index with and without the BMI component did not significantly alter the risk for BC risk, according to our results. This conclusion was equivalent to those of several studies with populations of a similar size (5, 15). It has been found, however, that postmenopausal women with abdominal fat tissue have a higher risk of developing BC. In addition, the incidence of postmenopausal breast cancer is 1.5 to 2.0 times greater in overweight or obese women with estrogen receptor-positive (ER+) and progesterone receptor-positive (PR+) breasts (28). Although having a high BMI is a sign of a poor lifestyle, it did not affect the results of our study

In our study, a one-point rise in the HLI score was linked with a 33% lower risk of BC in diabetic women compared to non-diabetic women. Several studies have shown a relationship between diabetes and an increased risk of BC. In a meta-analysis of studies conducted in Palestine, diabetes mellitus was identified as one of the risk factors associated with the development of BC. The likelihood of developing BC was approximately fivefold greater in diabetes patients than in non-diabetic patients. (OR: 4.97, 95% CI 3.00–8.25) (29). According to another meta-analysis of studies, women with type 2 diabetes have a 20% higher likelihood of developing BC, however, several cohort studies revealed no association (30). In addition, adherence to a diabetes risk-reduction diet was found to reduce the occurrence of breast cancer

(31–33). Ebrahim Mousavi et al. found a substantial opposite relation between DRRD and the likelihood of BC (33). In the prospective Nurses' Health Study in the United States of America (1980–2016), being in the highest diabetes risk reduction diet adherence (DRRD) quintile compared to the lowest was associated with a modestly lower risk of BC (Multivariable-adjusted hazard ratio 0.89, 95% confidence interval [CI]: 0.84 to 0.95, $p = 0.0002$]). This association was explained by the lower weight gain observed with DRRD, whereas among postmenopausal women, strong adherence was moderately associated with a lower risk of BC independent of weight change (31). Postmenopausal women with the highest adherence to the DRRD exhibited a significant inverse relationship with BC risk compared to those with the lowest adherence (OR: 0.57; 95% CI: 0.36–0.90), but not premenopausal women (OR: 0.76; 95% CI: 0.19–2.96) (33). There are a number of possible biological mechanisms that could explain how obesity, high-fat diets, and smoking may affect the risk of BC. Chronic inflammation, dysregulation of hormone metabolism, and dysregulation of gene expression are all potential triggers of carcinogenesis (13, 34, 35). Also, another possible explanation might be attributed to the fact that the body fat percentage of postmenopausal women rises with age, as well as estrogen, insulin, and IGF-1 concentrations, leading to an increase in mammary gland mass (36–38). Therefore, lowering insulin resistance and hyperinsulinemia through dietary and lifestyle changes may reduce the risk of breast cancer, particularly in postmenopausal women, and may be a potential BC primary prevention strategy (30). In contrast, it is believed that certain dietary components, such as fruits and vegetables, and physical activity prevent processes, such as oxidative stress, inflammation, and DNA damage, that promote the development and progression of BC (38, 39). Despite the relatively small size of our sample of diabetic women, the HLI score was associated with lower BC by 33% in diabetic women compared to 50% in non-diabetic women. We were unable to stratify based on menopausal status.

Strength and Limitations

In Palestine, a country with a low-to-middle income, this is the first epidemiological study to examine the association between HLI scores and breast cancer risk. It examines dietary patterns and reproductive factors associated with breast cancer risk (18). Case-control studies are commonly used as one of the first studies to provide evidence of a relationship between exposure and an occurrence or disease. The case-control methodology of this study strengthens its conclusions and ushers in a new age of research on lifestyle factors and cancer in Palestine. However, it may have some limitations that should be taken into account while evaluating its results. For instance, case-control studies based on interviews may be susceptible to selection and recall bias. In addition, the level of detail available for some exposures was limited, especially with regard to dietary information. This study's healthy lifestyle score was dependent on a subset of food items that were relevant to this type of cancer research, but not on the complete food frequency questionnaire. Other forms of seafood, processed meat, and other foods were not included in this index, but they can still be applied to represent the HLI based on previous studies in similar contexts (5, 14). Also, the study focused on particular patterns of behavior rather than specific exposures and sought to capture the combined effect of multiple food choices and health behaviors. Therefore, each component of the index was given equal weight as they were viewed as markers of healthy living or habitual exposures rather than specific BC risk factors. In addition, due to the lack of Palestinian-specific dietary guidelines, our HLI score was based on international standards for public health and cancer prevention. Consequently, Palestinian dietary recommendations are required.

In our study, the inverse association between a healthy lifestyle and the risk of developing breast cancer is more pronounced than in other populations. This may be due to a bias in the evaluation of exposure in our study. After a BC diagnosis or symptoms, our participants may have altered their lifestyles, such as becoming more physically active and smoking less, which could affect the HLI index calculation and the interpretations of the study findings. Lastly, this study included a relatively small number of participants, which may have affected data stratification based on menopausal and diabetes status in some strata. Despite the fact that the low number of individuals in this stratification may affect the accuracy of the healthy lifestyle index estimates, this stratification still shows a number of key characteristics related to the risk of BC.

In conclusion, healthy lifestyles (such as a healthy diet, moderate and vigorous-intensity exercise, avoiding tobacco and alcohol consumption, and a low body mass index) have been associated with a decreased risk of BC. The combined healthy lifestyle score was associated with breast cancer risk more strongly than the individual components. In light of these findings,

it is recommended that breast cancer prevention policies include strategies to engage all women in long-term healthy lifestyles and eating habits. This research may have significance for the development of cancer preventive programs in Palestine; hence, larger cohort studies are required.

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Author Contributions

Nuha El Sharif: Conceptualization, Methodology, validation supervising of data management and analysis. Nuha El Sharif was responsible for original draft writing, editing, and reviewing. Imtithal khatib: Fieldwork, software development, data analysis, and data interpretation, and MS review. All authors read and approved the final manuscript

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Consent for Publication

NA.

Disclosure Statement

No potential conflict of interest was reported by the author(s).

Ethics Approval and Consent to Participate

This study was approved by Al Quds University Ethical Research Committee, which is based on the Helsinki declarations. Therefore, all study methods were performed following the Helsinki guidelines and regulations. Al Quds University's ethical research regulations adhere to Helsinki regulations

Written approval was obtained from the Ministry of Health to access patient records from the oncology department and cancer registry. All participants provided written informed consent.

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