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The Intake of some Nutrients is Associated with the Risk of Breast Cancer: Results from Jordanian Case-Control Study

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Abstract

Breast cancer (BC) is the most commonly diagnosed cancer and is considered the leading cause of cancer deaths in women globally. The aim of this study is to evaluate the relationship between macro- and micronutrient intake and BC risk among Jordanian women. A case-control design was used in this study, and BC patients were recruited from the main two hospitals provide cancer therapy in Jordan. Four hundred women aged 20-65 years of age were enrolled in the study. For the cases, 200 recently diagnosed BC women were selected from the two hospitals and matched in age and marital status to 200 BC-free women. Dietary data were collected through face-to-face interview using a validated food frequency questionnaire between October 2016 and September 2017. To calculate odds ratio (OR), logistic regression was used; while for p-*trend* the linear regression was performed. The study results demonstrated that increasing the intake of total energy and percentage of fat was significantly and positively associated with BC (p-= 0.001). The risk of BC increased significantly and positively as carbohydrate, sugar, fat, saturated fat and polyunsaturated and monounsaturated fatty acids intake increased. A significant trend in BC risk was found for cholesterol (p-= 0.005). The ORs for higher intakes of vitamins E, B_1, B_2, and B_3, folate and phosphorus showed a significant association with the risk of BC (p-*trend* =0.001). A significant inverse effect was detected between iron intake and BC risk (p-=0.001). The study findings resulted in insight of the associations between the total energy intake and some macro/micronutrients intake can be an increasing risk of BC.

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Introduction

Cancer is a primary cause of death in both developed and developing countries. The implication of all types of cancer is expected to grow globally owing to the growth and aging of the population.[1] About 18.1 million new cancer cases and 9.6 million deaths occurred in 2018 worldwide.[2] Breast cancer (BC) is the leading cause of cancer deaths in women globally.[1,2] Breast cancer alone is responsible for 24.5% of all cancer deaths among Jordanian women.[3] In the year 2014 there, were 1187 newly diagnosed cases of BC in both sexes accounting for 20.8% of all newly diagnosed cancer cases.[3]

Several factors for preventing or developing BC have been reported in studies, including age, lactation, hormone levels, family history of BC, use of hormones or hormone replacement therapy and breast density,[4] dietary patterns,[5,6] physical activity (PA)[7], tobacco smoking,[8] reproductive history, weight status[9,10] and macro- and micronutrients intake.[11]

Preventing cancer is more important than treating or inhibiting its progression. Prevention of such health problem means reducing the suffering and the pain of patients with cancer and their families. Scientific evidence showed that prevention of cancer could be achieved by reducing intake of alcohol, protein and fat and increasing intake of fiber and vitamin D from different food sources.[10,11] The mechanisms of dietary risk factors are not clearly stated.[10,11] Although, large body of scientific researches admitted the association between BC and diet,[5,6,11] cultural differences between countries showed a main role in BC risk attenuation or enhancement in spite of the world globalization.[11]

In Jordan, there is a gap in the scientific knowledge that shows the dietary risk factors for developing BC. Only one study by Al-Qadire *et al.,* (2018) was conducted to identify lifestyle-related risk factors for breast cancer among Jordanian women.[12] The authors revealed that physical activity and fruit and vegetable intake were found to be associated with reduced breast cancer risk. However, calcium intake (>3 times a week) was associated with increased risk of breast cancer.[12] From all the nutrients only association between calcium intake and risk of BC was investigated. Therefore, this study aimed to explore the association between energy and macro- and micronutrients intake and the BC risk among Jordanian women.

Materials and Methods

Study Design and Sample Recruitment

A case-control design was used to determine macro- and micronutrient intake as a risk factor linked to BC among Jordanian women. Two hundred women who were lately (last three months) diagnosed with BC were recruited in the study. All BC patients were taken from King Hussein Cancer Center (KHCC) and Al-Basheer Hospital. These two hospitals are the main facilities in Jordan that offer cancer therapy. The control group was included from the community (the employees and visitors of KHCC and Al-Basheer Hospital, patients' accompanying persons as well as women who visited KHCC to perform mammogram). To become eligible, the women in the control group underwent either a clinical examination or mammogram to ensure that they were BC free. The researcher asked all the participants in controls group if they had undergone a prior clinical examination or mammography during the last year before participating in the study. The ratio was 1:1 cases to control and they were matched by age and marital status.

For cases, the inclusion criteria were recent diagnosed with BC (last three 3 months), age 20-65 years, being Jordanian and able to communicate verbally. For both of cases and controls who were critically or terminally ill, hospitalized, unable to talk verbally, complaining from any other cancer and chronic disease that requires following specialized diet and being pregnant or lactating were excluded from the study.

Data were collected in the outpatient departments in both hospitals. Each hospital provided a private room where the interviews took place. The study was conducted according to the ethical standards of the responsible committee on human experimentation and in compliance to the Helsinki declaration of 1975, as revised in 1983. The proposal was approved by the Institutional Review Board of both hospitals. Written consent form was completed and obtained before starting data collection. Patients' information was kept confidential. Only the investigator knew patients' names and gave them number (ID). All used questionnaires were labeled with patient ID.

Data Collection

In-person interview was conducted to collect the requested data and the questionnaires were completed and finalized by a trained researcher. Measurement of weight and height was taken and body mass index (BMI) was calculated by dividing weight in kilograms on height in meters square.

Personal Information Sheet

This sheet contained questions related to some socioeconomic status including age, family income/ month, marital status, education, employment, smoking status, and family members diagnosed with cancer.

Dietary Assessment

Nutrients intake was assessed using Arabic validated food frequency questionnaire (FFQ).[13] This FFQ included 109 questions on food and beverages. Response categories provided in the FFQ were "<1/month, 2-3/month, 1-2/week, 3-4/week, 5-6/week, 1/day, 2-3/day, 4-5/day, or 6/day". Food lists in the modified FFQ questions were classified based on types of foods: 21 items of vegetables; 16 items meat such as red meat (lamb and beef), chicken, fish, cold meat and others; 21 items of fruits and juices; 9 items of milk and dairy products; 8 items of cereals; 4 items beans; 4 items of soups and sauces; 5 items drinks; 9 items of snacks and sweets; 14 items of herbs and spices. After completing the FFQ, the selected frequency category was converted to a weekly intake. For calculating the nutrient intake, software (ESHA Food Processor SQL version 10.1.1; ESHA, Salem, OR, USA) that calculates macro- and micronutrients intake based on the foods intake was used. Standardized food prototypes (*Nasco* Company, USA) and standard cups and spoons were used to help participants in estimating the portion size of the main foods (cereals, fruits and vegetable, oils, meats and dairy products) included in the FFQ precisely.

Physical Activity Levels Assessment

The physical activity recall (PAR) questionnaire was completed to determine the physical activity level (PAL) among participants on weekly basis as described by Sallis *et al.,* (1985).[14] Physical activity recall was measured using a metabolic equivalent (MET) score and the total METs was estimated. In PAR calculations, it is necessary to take into consideration the frequency, intensity, time, and type of the physical activity. The 7-day PAR is a structured interview that depends on participant's recall of time spent engaging in physical activity (PA) over a seven day period. Different levels of PA such as aerobic exercise, gardening, work-related activities, recreation, walking, and leisure-time activities were covered in PAR.[14] We measured PA using a metabolic equivalent (MET) score.[14] The number of hours spent in sleep and different activity levels are obtained and converted into Kilocalories. Time spent in sleeping (1 MET), light (1.5 METs), moderate (4 METs), hard (6 METs), and very hard (10 METs) activities for the past 7 days are multiplied by their respective MET values and then summed. An estimate of total kilocalories of energy expenditure per day was calculated.[14]

Statistical Analysis

To find the differences between continuous variables of cases and controls, T-test was used. Data are presented as Mean±SD for the continuous variables and percentages for categorical ones. To calculate odds ratio OR and CI, logistic regression was used, while for p-*trend* linear regression was performed. Age (continuous), marital status (categorical), total energy intake (continuous), BMI (continuous), physical activity level (continuous), education level (categorical), occupation (categorical), lactation (categorical) health problem (categorical), number of pregnancy (categorical), hormonal replacement therapy (categorical) and family history (categorical) for all participants were considered as possible confounding factors.[5] The significance level was set at $p \leq 0.05$. All statistical analyses were done using SPSS version 22.0 (IBM SPSS Statistics for Windows, IBM Corporation).

Results and Discussion

This study aimed to evaluate the association between energy and macro- and micronutrients intake and the risk of BC. Table 1 shows participants' socio-demographic, anthropometric measurements, health and lifestyle characteristics.[15] Average age for cases was 48.9±0.63 years and 47.5±0.59 years for control. BMI, education level, employment status, smoking and family history of BC, were all significantly different as BC cases compared to the controls.[15]

Table 1: Characteristics of the Study Participants[15]

Variables	Treatments		p-value
	Cases (n=200)	Controls (n=200)	
	Mean ± SEM		
Age (y)	48.9 ± 0.63	47.5±0.59	0.106
Height (cm)	159.3±0.42	161.7±0.41	0.001
Weight (Kg)	75.7±1.05	73.2±0.95	0.080
BMI (kg/m^2)	29.8±0.39	27.9±0.36	0.001
Number of pregnancy	4.6±0.23	3.40.20	0.001
Number of miss carriage	1.1±0.11	0.90±0.09	0.226
Duration of lactation (months)	8.2±0.54	7.7±0.55	0.599
Physical activity (METs)	1425.4±133.3	3464.7±1205.6	0.019
	N (%)		
Marital Status			
Married	154 (77.0)	156(78.0)	0.789
Single	26 (13.0)	29(14.5)	
Divorce	8 (4.0)	5(2.50)	
Widow	12 (6.0)	10(5.0)	
Education Level			
Illiterate	12(6.0)	5(2.5)	0.001
School	52(26.0)	12(6.0)	
High school	65(32.5)	46(23.0)	
Diploma	47(23.5)	65(32.5)	
Bachelor	14(7.0)	55(27.5)	
Master degree	7(3.5)	12(6.0)	
Doctorate degree	3(1.5)	5(2.5)	
Work Status			
Yes	53(26.5)	89(44.5)	0.001
No	147(73.5)	111(55.5)	
BMI categories			
Under weight	0(0.0)	1(0.5)	0.013
Normal weight	33(16.5)	58(29.0)	
Overweight	91(45.5)	70(35.0)	
Obese	76(38.0)	71(35.0)	
Smoking			
Yes	40(20.0)	14(7.0)	0.001
No	160(80.0)	186(93.0)	
Family members diagnosed with cancer			
Yes	109(54.5)	73(36.5)	0.001
No	91(45.5)	127(63.5)	

Significance is at $p \leq 0.05$.

Table 2: Macronutrients Intake Per Day for the Study Participants

Nutrients	Cases (n=200) Mean ± SEM	Controls (n=200) Mean ± SEM	p-Value
Energy (kcal)	2410.6 ± 52.9	2015.7 ± 49.5	0.001
Energy from Fat (kcal)	901.0 ± 25.2	704.3 ± 21.3	0.001
Energy from saturated fat (kcal)	245.3±8.6	207.1±7.1	0.001
Energy from trans-fat (kcal)	6.2±0.86	2.4±0.41	0.001
% Carbohydrate	56.9±1.4	62.2±2.2	0.045
% Protein	14.8±0.38	14.1±0.32	0.001
% Fat	36.9±0.46	34.5±0.51	0.001
% Saturated Fat	9.9±0.21	10.1±0.21	0.509
% Trans-fat	0.24±0.03	0.11±0.02	0.001
Protein (g)	80.7±1.1	71.5±14.9	0.540
Carbohydrate (g)	311.8±3.2	269.5±2.9	0.001
Starch (g)	3.4±0.20	2.6±0.20	0.031
Fiber (g)	22.5±0.5	22.2±0.50	0.720
Soluble Fiber (g)	3.4±0.12	3.5±0.13	0.750
Insoluble Fiber (g)	7.3±0.21	7.9±0.26	0.710
Sugar (g)	110.9±2.5	89.9±2.49	0.001
Fat (g)	100.5±1.23	78.5±1.16	0.001
Saturated Fat (g)	27.2±0.59	23.1±0.46	0.001
Monounsaturated Fat (g)	32.0±0.56	23.4±0.55	0.001
Polyunsaturated Fat (g)	16.7±0.38	12.08±0.29	0.001
Trans-Fat (g)	0.65±0.08	0.27±0.05	0.001
Cholesterol (mg)	245.8±9.9	198.1±8.56	0.001

Significance is at $p \leq 0.05$.

The mean daily intakes of total energy, macronutrients, and micronutrients are illustrated in Table 2 and 3. The BC group reported significant higher intakes of total energy, energy from fat, saturated fat and trans-fats, percentage of protein, fat, trans-fats and carbohydrate (CHO), amount of total CHO, sugars, saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), trans-fat and cholesterol ($p<0.05$) compared to the control group. In addition, the BC group in table 3 showed significant higher intakes of vitamins B_1, B_2 and B_3 folate, vitamin E and phosphorus ($p<0.05$) when compared to the control group while the control group had higher iron intakes when compared to the BC group ($p<0.05$). Similar to our study finding of the association between energy intake and BC risk, García-Arenzana *et al.,* (2014) demonstrated that high energy intake can increase the risk of having BC.[16] Nevertheless, mechanisms in which energy intake can promote the development of BC may include different theories; alterations in the production of ovarian steroid hormones,[17] changes in the availability of insulin growth factor-1 (IGF-1) and increasing cell proliferation[18] and increasing tissue susceptibility to damaging carcinogens by an increasing DNA replication that reduces the rate of apoptosis.[19]

In the current study, CHO and sugar intake is significantly associated with the risk of BC. Similarly, Romieu *et al.,* (2011) revealed that CHO intake was positively associated with an increased risk of developing some types of classified BC among postmenopausal women.[20] CHO may affect BC risk by elevated circulating insulin concentrations either directly, by stimulating insulin receptors in breast tissue, or indirectly, through the mitogenic effects of insulin-like growth factor-I (IGF-I).[21] However, a

case-control study performed by Sulaiman *et al.,* (2014) showed that dietary CHO intake has no association with BC risk, but a significant increased risk of BC among premenopausal and postmenopausal women was observed with increased sugar intake.[22] Similar findings were also documented by Wong, (2015) who stated that high sugar intake precisely sugar comes from sweetened beverages may increase the risk of BC.[23]

Table 3: Micronutrients Intakes per Day of the Study Participants

Nutrients	Cases (n=200) Mean ± SEM	Controls (n=200) Mean ± SEM	p-Value
Retinol (RE)	302.2 ± 18.4	298.1±34.1	0.920
β-carotene (µg)	5443.4±256.5	5810.7±603.2	0.570
Vitamin B_1 (mg)	1.9±0.04	1.6±0.04	0.001
Vitamin B_2 (mg)	2.2±0.04	1.9±0.04	0.001
Vitamin B_3 (mg)	20.8±0.31	18.5±0.26	0.001
Vitamin B_6 (mg)	1.3±0.04	1.3±0.07	0.690
Vitamin B_{12} (µg)	2.3±0.13	2.4±0.18	0.580
Vitamin C (mg)	121.9±4.04	153.7±28.7	0.270
Vitamin D (µg)	1.9±0.16	1.5±0.1	0.090
Vitamin E (mg)‡	9.3±0.20	7.4±0.26	0.001
Folate (µg)§	197.1±5.4	159.9±5.8	0.001
Vitamin K (µg)	254.7±12.2	290.4±46.9	0.460
Calcium (mg)	662.1±21.01	638.7±15.8	0.370
Copper (mg)	1.4±0.04	1.3±0.03	0.180
Iodine (µg)	68.98±3.78	60.1±2.45	0.051
Iron (mg)	11.17±0.18	14.27±0.34	0.001
Phosphorus (mg)	972.5±15.5	862.9±12.3	0.001
Potassium (mg)	2920.5±44.6	2777.1±83.8	0.130
Sodium (mg)	2715.5±80.9	3609.3±994.1	0.370

Significance is at $p \leq 0.05$.
‡ Vitamin E as α-Tocopherol
§ Folate as dietary folate equivalents

The present study cases reported a consumption of protein in grams higher than the controls but the difference was insignificant. High protein intake may influence the risk of BC by elevating IGF-1 level which plays important roles in tissue growth and tumor progression. However, foods that are major sources of protein differ widely in their nutrient profiles and may have different effects on BC risk.[24] Farvid *et al.,* (2016) documented that higher intake of total red meat was associated with an increased risk of BC.[24] However, higher consumption of other protein sources such as legumes, fish, poultry, eggs and nuts were not related to BC overall. The authors also suggested that substituting red meat with a combination of legumes, fish, poultry and nuts may lessen the risk of BC, but according to hormonal status.[24]

Table 4 shows the OR and 95%CI for energy and energy sources, after adjusting for potential confounders. The study results revealed that increasing the intake of total energy and percentage of fat in third quartiles and forth quartiles were significantly associated with BC with a p-*trend* = 0.001. A significant direct *trend* (p-*trend*= 0.001) in BC risk was detected in our study for energy

from fat (especially in forth quartiles with OR 5.91 (95%CI: 2.56-13.64)) and energy from trans-fat (especially in forth quartiles with OR 2.63 (95% CI: 1.18-5.84)). Additionally, percentage of trans-fats showed a significant *trend*s ($p<0.05$) in BC risk.

Table 4: Association between energy and energy sources and BC risk among participants

Nutrients	†Q1	Q2	Q3	Q4
Energy (kcal)				
Number of case	31	54	49	66
Number of control	69	46	50	34
*OR (95%CI)	1	1.91 (0.86-4.21)	2.46 (1.11-5.45)	4.86 (2.13-11.12)
P-trend			0.001	
Energy from fat				
Number of case	35	45	53	67
Number of control	65	55	46	33
*OR (95%CI)	1	1.21 (0.55-2.68)	1.83 (0.81-4.13)	5.91 (2.56-13.64)
P-trend			0.001	
Energy from Saturated fat				
Number of case	48	42	50	60
Number of control	52	58	49	40
*OR (95%CI)	1	0.67 (0.30-1.49)	1.22 (0.58-2.59)	2.19 (1.01-4.76)
P-trend	0.220			
Energy from trans fat				
Number of case	47	55	26	72
Number of control	53	59	59	28
*OR (95%CI)	1	0.89 (0.43-1.84)	0.43 (0.19-0.97)	2.63 (1.18-5.84)
P-trend			0.001	
% of Carbohydrates				
Number of case	50	52	54	44
Number of control	50	47	46	56
*OR (95%CI)	1	0.78 (0.37-1.65)	0.88 (0.41-1.89)	0.69 (0.32-1.49)
P-trend			0.384	
% of Fat				
Number of case	38	46	54	62
Number of control	62	53	46	38
*OR (95%CI)	1	1.92 (0.90-4.11)	3.13 (1.45-6.77)	2.39 (1.08-5.26)
P-trend			0.004	
% of Trans-Fat				
Number of case	48	43	39	70
Number of control	52	55	62	30
*OR (95%CI)	1	0.70 (0.33-1.49)	0.57 (0.27-1.20)	2.01 (0.92-4.37)
P-trend			0.001	

* Adjusted for Energy, Age, Martial statues, education, work, income, physical activity, smoking, family history, health problem, number of pregnancy, lactation, hormonal replacement therapy.
Significant at $p \leq 0.05$

Table 5: Association of macronutrients with BC risk among participants

Nutrients	†Q1	Q2	Q3	Q4
Carbohydrate (g)				
Number of case	22	40	53	85
Number of control	78	59	47	15
*OR (95%CI)	1	3.18 (1.31-7.76)	5.43 (2.30-12.80)	34.28 (13.06-89.95)
P-trend			0.001	
Starch (g)				
Number of case	41	49	52	58
Number of control	58	52	48	41
*OR (95%CI)	1	1.94 (0.92-4.11)	2.09 (0.97-4.52)	2.07 (0.98-4.36)
P-trend			0.033	
Sugar (g)				
Number of case	29	38	66	67
Number of control	71	61	34	33
*OR (95%CI)	1	3.35 (1.44-7.78)	8.03 (3.51-18.36)	6.80 (2.92-15.80)
P-trend			0.001	
Fat (g)				
Number of case	19	31	60	90
Number of control	81	68	40	10
*OR (95%CI)	1	1.99 (0.85-4.67)	8.13 (3.62-18.24)	34.11 (12.18-95.53)
P-trend			0.001	
Saturated Fat (g)				
Number of case	30	50	52	68
Number of control	69	50	48	32
*OR (95%CI)	1	2.67 (1.35-5.27)	3.39 (1.66-6.92)	5.32 (2.61-10.85)
P-trend			0.001	
Monounsaturated Fat (g)				
Number of case	17	34	65	84
Number of control	83	66	34	16
*OR (95%CI)	1	2.18 (1.00-4.75)	10.28 (4.71-22.46)	28.93 (11.78-71.05)
P-trend			0.001	
Polyunsaturated Fat (g)				
Number of case	22	37	56	85
Number of control	78	62	44	15
*OR (95%CI)	1	2.05 (0.99-4.25)	4.10 (1.98-8.49)	20.85 (9.03-48.16)
P-trend			0.001	
Cholesterol (mg)				
Number of case	41	41	52	66
Number of control	58	59	48	34
*OR (95%CI)	1	0.89 (0.46-1.73)	1.39 (0.71-2.71)	1.76 (0.88-3.51)
P-trend			0.005	

Significant at $p<0.05$

* Adjusted for Energy, Age, Martial statues, education, work, income, physical activity, smoking, family history, health problem, number of pregnancy, lactation, hormonal replacement therapy.

Additionally, table 5 represents ORs for the intake quartile of macronutrients, after adjusting for confounders, and the risk of BC. The ORs of the quartiles of carbohydrate, sugar, fat, saturated fat, PUFA and MUFA intake as g/day were significantly associated with the risk of BC in at least two quartiles (p-*trend*= 0.001). As noted in table 5, a significant direct *trend* in BC risk was found for cholesterol (p-*trend*= 0.005) but none of the quartiles are statistically significant. Comparable results were highlighted by Thiébaut *et al.,* (2007) who reported the presence of direct association between fat intake and the risk of postmenopausal invasive BC.[25] Moreover, a positive association of SFA intake with BC has been documented in several case-control studies.[26-28] Regarding the intake of MUFA and its association with the risk of BC, Khodarahmi and Azadbakht (2014) has shown a positive role of MUFA in the pathogenesis of BC.[28] In addition, Saadatian-Elahi *et al.,* (2004) reported a significant increase of BC risk with increasing MUFA intake.[29] While several cohort studies showed an inverse association of MUFA intake and BC risk,[30,31] others reported no association MUFAs intake and BC risk.[32] Also, Michels *et al.,* (2018) illustrated that MUFA intake was unrelated to BC risk in cis-form, however, they found that high serum level of trans-MUFA.[33] With regards to PUFA intake and BC risk, a similar result was obtained by Chajès *et al.,* (2011).[34] The authors documented that PUFA intake increased the risk of BC significantly. However, Anna *et al.,* (2012) found that the total PUFA was not associated with BC.[35]

Regarding cholesterol results, similar direct association between cholesterol and BC risk has been reported by Farvid *et al.,* (2014).[36] Farvid *et al.,* (2014) found that cholesterol intake was associated with higher risk of BC, but this association was attenuated after accounting for intake of red meat.[36]

The OR and 95% CI for micronutrient after adjusted confounders are shown in table 6. The ORs for higher intakes of vitamin B_3, folate and phosphorus showed a significant association the risk of developing BC with p-*trend*= 0.001. The study findings also showed that the intake of vitamins E, B_1 and B_2 had a significant *trend* for BC. On the other hand, iron intake showed significant protective effect against BC (p-*trend*= 0.001) and vitamin D showed its protective effect on the second quartile (OR 0.48 (95%CI: 0.24-0.94). These findings are on contrary to what has been documented by Kabat *et al.,* (2008) who found that folate intake reduce the risk of common cancers parallel with B vitamins.[37] However, Larsson *et al.,* (2007) found that adequate folate intake may reduce the increased risk of BC that has been associated with moderate or high alcohol consumption, but no clear support for an overall relationship between folate intake and the risk of BC was concluded.[38] However, thiamine is commonly supplemented in processed foods and readily consumed in over-the-counter vitamin and nutritional supplements in Western countries with generally high cancer incidences.[39] However, like so many other nutritional correlations with cancer incidence, the dietary intake of B vitamins and folate with BC risk has provided conflicting results.[40] Our data shows that vitamin E increased the risk of BC and this could be explained by the risk of food sources of vitamin E. The main sources of vitamin E are PUFA and MUFA which already have a significant association BC. Moreover, Nagel *et al.,* (2010) demonstrated that no associations between BC risk and vitamin E had been detected in their study.[41] On the other hand, no significant difference between the cases and controls in vitamin D intake has been detected, however, the risk of BC decreased significantly in the second quartile with insignificant p-*trend* (0.488). This is in agreement with Jamshidi-Naeini *et al.,* (2016) who concluded that dietary intake of vitamin D was associated with decreased risk of BC.[42] Kuhn *et al.,* (2013) indicated that vitamin D may block estrogen signaling by inhibiting estrogen synthesis and by down regulating estrogen receptor expression in BC cells.[43] On the other hand, higher phosphorus intake by our study cases increased the risk of BC which this could be attributed the higher intake of proteins. Proteins are considered the main sources for phosphorus. Our study showed that the dietary iron intake in controls was higher than BC cases. In addition, the risk of BC decreased by increasing the intake of dietary iron. Similar result was found by Bae *et al.,* (2009) in their case-control study and they documented that dietary iron intake was higher in the control than BC case group.[44] However, Kabat *et al.,* (2007) did not report any association between iron intakes and BC risk.[45]

Table 6: Association of micronutrients and BC risk among participants

Nutrients	†Q1	Q2	Q3	Q4
Vitamin B_1 (mg)				
Number of case	43	40	46	71
Number of control	57	59	54	29
*OR (95%CI)	1	0.72 (0.37-1.42)	1.05 (0.54-2.03)	3.01 (1.50-6.06)
P-trend			0.001	
Vitamin B_2 (mg)				
Number of case	39	27	54	80
Number of control	60	73	46	20
*OR (95%CI)	1	0.62 (0.30-1.26)	1.71 (0.88-3.32)	5.21 (2.47-10.95)
P-trend			0.001	
Vitamin B_3 (mg)				
Number of case	31	37	65	67
Number of control	69	63	34	33
*OR (95%CI)	1	2.30 (1.13-4.67)	4.82 (2.36-9.84)	4.97 (2.45-10.09)
P-trend			0.001	
Vitamin D (µg)				
Number of case	52	37	57	54
Number of control	47	63	43	46
*OR (95%CI)	1	0.48 (0.24-0.94)	1.13 (0.58-2.21)	0.82 (0.42-1.61)
P-trend			0.488	
Vitamin E (mg)‡				
Number of case	24	41	60	75
Number of control	76	59	39	25
*OR (95%CI)	1	1.56 (0.76-3.18)	4.20 (2.04-8.61)	8.20 (3.80-17.7)
P-trend			0.001	
Folate (µg)§				
Number of case	29	52	60	59
Number of control	71	47	40	41
*OR (95%CI)	1	2.55 (1.27-5.12)	4.01 (1.98-8.10)	2.66 (1.34-5.29)
P-trend			0.001	
Phosphorus (mg)				
Number of case	30	41	56	73
Number of control	70	58	44	27
*OR (95%CI)	1	2.08 (1.04-4.17)	3.18 (1.58-6.41)	5.50 (2.66-11.37)
P-trend			0.001	
Iron (mg)				
Number of case	87	61	34	18
Number of control	13	39	66	81
*OR (95%CI)	1	0.20 (0.09-0.46)	0.07 (0.03-0.17)	0.03 (0.01-0.07)
P-trend			0.001	

Significant at $p \leq 0.05$.

* Adjusted for energy, age, martial statues, education, work, income, physical activity, smoking, family history, health problem, number of pregnancy, lactation, hormonal replacement therapy.

‡ Vitamin E as a-Tocopherol

§ Folate as dietary folate equivalents

Although, no diet or lifestyle pattern can guarantee full protection against any disease; the potential health benefit represents a decreased likelihood that the disease will occur, not a guarantee of total protection.[46] However, weight control, physical activity, and healthy nutrition may contribute in the prevention of cancer especially those types related to diet and lifestyle.[46]

The main strength of this study is the use of a validated, detailed and culture-sensitive FFQ to collect dietary data from our study population. Although dietary data was collected at only one time, the FFQ has been reported to be a suitable tool for estimating nutrients intake. The major limitation is the using of FFQ to assess the possible association between nutrients intake and BC risk. Our study relied greatly on the ability participants to recall their memories to complete the questions of the FFQ. It is well-known that there are obvious differences in recall among participants, and consequently biases may exist. Like all other studies, it was difficult to take into consideration the possible effects of cooking on the bioavailability of the various nutrients. Although the sample size is small but it is representative as calculated by the statistician. In 2014, a total of 1187 of newly BC diagnosed cases in both sexes had been reported by Jordanian Cancer Registry.

Conclusions

The study revealed that the intake of carbohydrate, sugar, fat, SFA, trans fats, MUFA, PUFA and cholesterol from the macronutrients as well as phosphorus, vitamins B_1, B_2, B_3 and E, and folic acid from the micronutrients was al higher in cases as compared to controls. Clearly, the risk of BC may increase in women on higher dietary intake of energy, carbohydrate, sugar, fats, cholesterol and some minerals and vitamins. Only iron intake was found to be associated with lower risk of BC among our study participants.

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Conflict of Interest

The authors do not have any conflict of interest.

Author Contributions

RFT and RIM participated in conception and design of the study. RIM and LSM recruited participants. RIM collected data from hospitals. RFT, RIM and LSM interpreted the results and drafted the manuscript.

Ethical Standards

This study complies with Helsinki declaration of 1975, as revised in 1983.

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