Risk factors assessment of breast cancer among Iraqi Kurdish women: Case-control study

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ABSTRACT

Background: To our knowledge, there is no international publication on risk factors of breast cancer among Kurdish women. There are several risk factors of breast cancer may differ in different geographical cultures. The aims of this study are to assess the established and probable risk factors of breast cancer among Iraqi Kurdish women as well as to investigate the effect of some Mediterranean food items on this issue. **Materials and Methods:** This retrospective case-control study was constructed in Sulaimanyah governorate-Iraq. Data were collected regarding socio-demographic characters, established risk factors, and dietary habits of 338 cases that were registered in Sulaimanyah Breast Center during January 2015-February 2019 with collection of same items for 338 age-matched controls. **Results:** The marriage was appeared to be a protective factor with (OR = 0.596, CI: 0.364-0.974, P = 0.039). Age at menarche ≥14 years has a protective effect with (OR: 0.326, P = 0.027) and 152 cases (45.0%) had menarche at ≤12 years compared to 56 controls (16.6%) with (P = 0.000). Numbers of children ≥ 3, regular exercise, and breastfeeding for >48 months duration have protective role. Consumption of fast foods and some Mediterranean foods weekly >2 times are risk factors, while taking stewed meat weekly one time, fish weekly ≥1 time, fruit daily>1 time and vegetables daily≥1 time, and black tea daily >3 cups have preventative effect on breast cancer. **Conclusion:** Among Kurdish women, some items of Mediterranean food have the same causative effect as fast food items. Marriages, consumption of stewed meat, fish, fruit, vegetables, and black tea may have preventative effect.

Keywords: Breast cancer, Iraq, Kurdish women, risk factors

Introduction

Breast cancer is the most prevalent form of cancer affecting female population worldwide.[1-3] including developed and developing countries and the leading cause of cancer mortality among women.[4,5] Breast cancer incidence trends are different among countries, likely due to their ethnic and cultural background,[6] and there are several factors implicated to the etiology of breast cancer which may differ for different geographical locations.[7] A number of risk factors for breast cancer have been established including age, reproductive factors, such as early menarche, late menopause, age at first life

birth >30 year, nulliparity, family history, previous breast biopsy, genetics, and hormonal use.[8-15] There are other probable risk factors, such as high Body Mass Index (BMI),[16] low physical activities,[17] and dietary factors.[5,18-21] Ageing is one of the greatest risk factors for the development of breast cancer.[22] It was well established that the chance of breast cancer occurrence increase with the increase of age[7] with an estimated 64% of women over the age of 55 years at the time of breast cancer diagnosis, while about one-third of breast cancer cases in Middle-East countries were diagnosed among women aged 40-49 years.[23] Breast cancer risk increases with decreasing age at menarche, and a 1-year delay in the onset of menarche is associated with a 5% reduction in risk for developing breast cancer in later life, late menopause is another important risk factor for breast cancer. Each 1-year delay in the onset of menopause is associated with a 3% increase in risk.[22] It was strongly proven that women having their first birth before the age of 18 years old have only about one-third the breast cancer risk of those whose first birth after the age of 35 years.[7] Although, pregnancy has dual effects on the risk of breast cancer, the short-term risk of breast cancer may increase after pregnancy,[14] but having at least one child is associated with a decrease in the long-term risk of developing breast cancer and this protective effect increases with number of children.[22] Family history is one of the most well-established breast cancer risk factors.[15] The influence of family history on breast cancer risk is complex and depending on the numbers, age, and degree of involved relatives.[10,24] Benign breast disease and previous breast biopsy are strong breast cancer risk factors. An elevated risk of breast cancer is associated with a spectrum of histologic changes, specifically, proliferative disease without atypia and atypical hyperplasia.[7,25,26] Traditionally, hormonal factors and estrogen in particular, have been viewed as the main risk factors for breast cancer.[13] Many epidemiological studies have shown that there was a significant positive association of BMI with breast cancer in postmenopausal women[16,27] and premenopausal women.[4] Breastfeeding is associated with hormonal changes and alterations in molecular histology in the breast that may reduce on individual's breast cancer risk.[28] Regular and long-term moderate aerobic exercise enhances fat metabolism which results in the reduction in adipokine secretion, and has been shown to decrease estradiol levels, then may decrease risk of breast cancer.[9,17] The role of specific dietary factors in breast cancer causation is not completely determined and the studies on relation between breast cancer and diet have conflicting results.[22] Some studies have indicated an increase in breast cancer risk with the consumption of meat and other studies have found no association was observed.[22] Some studies have found a higher risk of breast cancer with fast foods and western diet,[5,7,22] whereas the effect of Mediterranean foods on breast cancer is conflicting, some studies were reported no association between them,[29,30] while others reported their protective effect.[31,32] Some cohort studies found no effect of self-reported fish intake on breast cancer risk,[33] while a case-control study in China was reported a preventative effect of fish intake on breast cancer.[34] Epidemiological studies were unsuccessful to establish a strong relationship between dairy products and breast cancer.[21] A study in Denmark has observed that high intake of fruit and vegetables can reduce breast cancer risk significantly.[33] Experimental studies have shown that black tea and tea polyphenols have anti-carcinogenic properties against breast cancer,[35] whereas in other studies conflicting results were observed.[36,37]

The main aims of this study are to estimate the established and probable risk factors of breast cancer among Iraqi Kurdish women, as well as, to investigate the impact of some traditional food items on breast cancer occurrence Kurdish society. Moreover, we intended to identify the strength effect of each risk factor on Kurdish women through estimation of their odds ratios, subsequently we can identify added and avoided food items to decrease breast cancer incidence in our region at future.

Materials and Methods

This retrospective case-control study was conducted on total 676 Iraqi Kurdish women, 338 women who diagnosed with breast cancer and registered in breast center of Sulaimanyah governorate, Kurdistan region/Iraq, between January 2015 and February 2019. The data were extracted from patient medical records in breast center of Sulaimanyah. The controls comprised 338 age-matched women who admitted in surgical ward for a wide range of elective surgical procedures without having history of breast cancer. The protocol of this study was approved by Ethics Committee of Sulaimani University (reference no. 7-5-10676 on 8/10/2018) and a necessary permission was obtained from breast center of Sulaimanyah.

Data collection

Data of incident breast cancer cases were extracted from the patient medical records in Sulaimanyah Breast Center. The basic inclusion criteria for the cases were Kurdish females diagnosed with breast cancer during the above period. The exclusion criteria were Arabic nation females and patients who had missed information in their medical records. The controls that had no history of breast cancer were selected through age-matched sampling among patients who were admitted for elective surgical procedures. The questionnaire questions were recorded about socio-demographic characteristics for both cases and controls, such as age, marital status, residency, level of education, occupation, economic status, and menopausal status. Women were regarded as post menopauses that have stopped menstruation for the last 12 months or more before their diagnosis. Self-reported educational level was categorized as: illiterate, primary, secondary, institute, and completed college. The questions also were covered both established and probable risk factors of breast cancer, including age at menarche, age at menopause, age at first life birth, family history of breast cancer, history of previous breast biopsies, use of oral contraceptives, use of hormone replacement therapy, BMI, number of life birth (parity), total breastfeeding duration, and regular exercise. The duration of breastfeeding was estimated by summation of breastfeeding duration of all children collectively. Physical activity was evaluated with specific questions regarding regular

exercise during their life before the diagnosis of breast cancer. In addition, our questionnaire included some items that covered dietary habits and lifestyle during the period before having breast cancer, including traditional Kurdish food and western food items which were popular during the last years. The food items were grouped into nine categories: (1) Red meat: stewed red meat; (2) White meat: stewed chicken meat; (3) Fast food items: Hamburgers, Doner, Pizza; (4) Mediterranean food items: Minced meat Kebab, beef meat skewers, chicken skewers; (5) Fish; (6) Dairy product: Yogurt, Cheese, Milk; (7) Fruits; (8) Vegetables; and (9) black Tea. On the other hand, we obtained data concerning the frequency for each food item. For stewed meat, stewed chicken, fast foods, and Mediterranean foods, we collected data to determine their frequency score intake on a fife groups ranging from intake weekly more than two times to never, for fish: weekly ≥1 time to never, for dairy product: daily ≥1 time to never, for fruit and vegetables: daily >1 time to monthly 1-3 times never, and for tea intake, we estimated the amount in cups per day. Regarding the controls, the same questionnaire was used to obtain data through face-to-face interviews that were conducted by one of the authors. Some missed data about the cases were obtained through telephone call.

Statistical analysis

The collected data were entered to excel sheet then into (SPSS version 22) statistical package for doing statistical analysis. The continuous variables were expressed by mean and standard deviation (SD), while the qualitative data were expressed by number and percentage. Chi-square test was used to estimate the associations between variables of socio-demographic characters. Multinomial logistic regression method was used to assess the Odds Ratios for both established and probable risk factors with 95% confidence intervals of variables. Probability value (*P*-value) of < 0.5 was considered as significant statistical value.

Results

A total of 676 Iraqi Kurdish women (338 cases and 338 age-matched controls) were enrolled in this study. The age range of incident breast cancer patients was 23-80 years with mean age 47 ± 11.0. The frequency of 10-year age groups were calculated, the highest frequency was reported for the age group 40-49 years [Figure 1]. There was a statistical significant association between marriage and breast cancer, about 86.4% of cases were married compared to controls 91.4% (*P* = 0.037). The marriage was appeared to be a protective factor with (OR = 0.596, CI: 0.364-0.974, *P* = 0.039). Out of 338 patients, 243 were premenopausal at the time of diagnosis which is account 71.9% of them compared to controls 68.0%, but there was no significant association. After further analysis of data, we could not find any association between breast cancer and other socio-demographic characteristics of patients [Table 1]. Concerning the analysis of established risk factors of breast cancer, age at menarche 14 years and more has a protective effect with (OR: 0.326, CI: 0.120-0.881, *P* = 0.027) and 152 cases (45.0%) had menarche
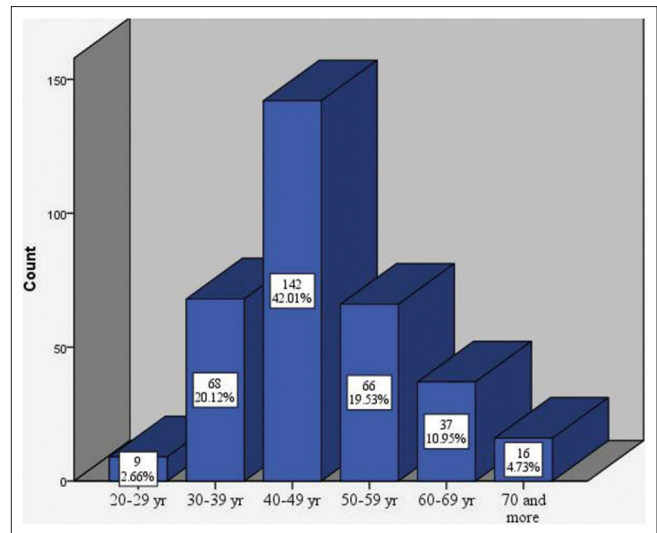

Figure 1: Distribution of age groups for patients with breast cancer

Table 1: Socio-demographic characteristics of breast cancer patients			
Variables	Cases, *n* (%) *n*=338	Controls, *n* (%) *n*=338	*P*
Age (Mean±SD)	47.52 years±11.0		
Marriage			0.037
Married/widow	292 (86.4)	309 (91.4)	
Never married	46 (13.6)	29 (8.6)	
Residency			
Urban	198 (58.6)	221 (65.4)	0.068
Rural	140 (41.4)	117 (34.6)	
Level of education			
Illiterate	151 (44.7)	130 (38.5)	0.167
Primary	68 (20.1)	71 (21.0)	
Secondary	39 (11.5)	35 (10.3)	
Institute	46 (13.6)	69 (20.4)	
University	34 (10.1)	33 (9.8)	
Occupation			
Employed	83 (24.6)	100 (29.6)	0.141
Unemployed	255 (75.4)	238 (70.4)	
Economic status			
Low	86 (25.4)	85 (25.2)	0.069
Moderate	221 (65.4)	237 (70.1)	
High	31 (9.2)	16 (4.7)	
Menopausal status			
Premenopause	243 (71.9)	230 (68.0)	0.157
Postmenopause	95 (28.1)	108 (32.0)	

at ≤12 years compared to 56 controls (16.6%) with (*P* = 0.000), age at menopause more than 51 years, age at first life birth 30 years or more, and positive family history have causative effect on breast cancer (high OR) with significant *P* value. The correlation between hormonal use and breast cancer was not significant without evaluation of their usage duration [Table 2]. Numbers of children ≥3, regular exercise, and breastfeeding for >48 months duration have protective effect. In relation to diet, we found that consumption of fast foods and Mediterranean foods weekly >2 times have high same Odds Ratio, while taking stewed meat weekly 1 time and fish weekly ≥1 time, fruit daily >1

Table 2: Odds ratios for the association between factors and breast cancer

Variables	Cases *n*=338	Controls *n*=338	OR	95% CI	*P*
Age at menarche					
<12 years	13	6	Ref.	0.217 - 1.570	0.287
12-13 years	205	162	0.584	0.120 - 0.881	0.027
≥14 years	120	170	0.326		
Age at menopause*					
≤45 years	6	15	Ref.	0.365 - 3.142	0.900
46-50 years	21	49	1.071	1.333 - 10.379	0.012
51-55 years	61	41	3.720	1.119 - 30.403	0.036
≥56 years	7	3	5.833		
Age at first life birth**					
≤20 years	81	80	Ref.	0.470 - 1.015	0.059
21-29 years	123	176	0.690	1.044 - 2.840	0.033
≥30 years	68	39	1.722		
Family History					
No	284	304	Ref.	1.075 - 2.689	0.023
Yes	54	34	1.7		
Previous Breast Biopsy					
No	314	328	Ref.	1.180 - 5.327	0.017
Yes	24	10	2.507		
Hormones (OCP)					
No	267	278	Ref.	0.840 - 1.806	0.285
Yes	71	60	1.23		
Hormones (HRT)					
No	324	323	Ref.	0.510 - 2.263	0.849
Yes	14	15	1.075		
Obesity (BMI)					
18.5 - 24.9	63	107	Ref.		
25-29.9	138	137	1.711	1.157 - 2.529	0.007
≥30	136	93	2.484	1.652 - 3.735	0.000
Parity (No. of children)					
Nulli para	66	43	Ref.	0.511 - 1.509	0.638
1-2 children	62	46	0.878	0.374 - 0.941	0.027
3-4 children	113	124	0.594	0.318 - 0.860	0.011
5-6 children	69	86	0.523	0.252 - 0.869	0.016
≥7 Children	28	39	0.468		
Exercise					
Never	243	216	Ref.		
Regular	95	122	0.692	0.500 - 0.958	0.026
Breastfeeding					
0-6 months	106	71	Ref.	0.417 - 1.042	0.075
6-12 months	64	65	0.660	0.437 - 1.054	0.084
13-24 months	75	74	0.679	0.293 - 1.081	0.085
25-48 months	21	25	0.563	0.315 - 0.933	0.027
49-72 months	34	42	0.542	0.252 - 0.691	0.001
>72 months	38	61	0.417		

OR=Odds ratio; CI=Confidence intervals. *Only included postmenopausal women. **Only included parous women

time and vegetables daily ≥ 1 time, and black tea daily >3 cups have preventative effect on breast cancer [Table 3].

Discussion

In analysis of the data, the mean age of patients was 47.52 years ± 11.0 and the highest frequency at 40-49 years age group. This result is nearly similar to results of some studies have been done on Middle-East nations.[7,9,23,38] During analysis of socio-demographic variables of patients, we have observed a significant association between marriage and breast cancer. The odd ratio of marriage was 0.596 (95% CI: 0.364-0.974, *P* = 0.039), which shows that marriage is likely to be considered

a preventative factor. In this society, because of religious beliefs, marriage is the only way to create the family and the women will become pregnant only through the religious marriage that increases the possibility of breastfeeding and multiparty. In this study, there was no significant association between breast cancer and other demographic characters. Although a study on Iraqi Kurdish women described that more than half of breast cancer cases were premenopausal,[23] we found the same result without statistical significant association compared to controls. This phenomenon may reflect the normal distribution of age groups over the Kurdish population including both cases and controls. Overall, 82.14% of Iraqi Kurdish females lie below the age of 50 years,[23] this indicates that the Kurdish society is composed

Table 3: Odds ratios for the association between food items and breast cancer.					
Variables	Cases *n*=338	Controls *n*=338	OR	95% CI	*P*
Stewed Meat					
Yearly or never	35	21	Ref.		
Monthly 1-3 times	113	112	0.605	0.332 - 1.104	0.102
Weekly 1 time	65	109	0.358	0.192 - 0.667	0.001
Weekly 2 times	25	13	1.154	0.488 - 2.730	0.745
Weekly >2 times	100	83	0.723	0.391 - 1.336	0.301
Stewed Chicken					
Yearly or never	11	10	Ref.		
Monthly 1-3 times	64	23	2.530	0.949 - 6.740	0.063
Weekly 1 time	139	163	0.775	0.320 - 1.880	0.573
Weekly 2 times	103	131	0.715	0.292 - 1.748	0.462
Weekly >2 times	21	11	1.736	0.563 - 5.346	0.337
Fast Foods					
Yearly or never	159	198	Ref.		
Monthly 1-3 times	63	53	1.480	0.972 - 2.255	0.068
Weekly 1 time	22	14	1.957	0.970 - 3.948	0.061
Weekly 2 times	13	10	1.619	0.692 - 3.789	0.267
Weekly >2 times	81	63	1.601	1.084 - 2.364	0.018
Mediterranean Foods					
Yearly or never	49	66	Ref.		
Monthly 1-3 times	98	93	1.419	0.891 - 2.262	0.141
Weekly 1 time	18	26	0.932	0.461 - 1.888	0.846
Weekly 2 times	10	16	0.842	0.352 - 2.014	0.699
Weekly >2 times	163	137	1.603	1.038 - 2.473	0.033
Fish					
Yearly or never	147	118	Ref.		
Monthly 1-3 times	74	81	0.733	0.493 - 1.091	0.126
Weekly ≥1 time	117	139	0.676	0.478 - 0.954	0.026
Dairy Products					
Rarely or never	11	10	Ref.		
Weekly 1-3 times	16	30	0.485	0.170 - 1.385	0.176
Weekly 4-6 times	24	37	0.590	0.217 - 1.601	0.300
Daily ≥1 time	287	261	1.000	0.418 - 2.392	0.999
Fruit					
Monthly 1-3 times	60	43	Ref.		
Weekly 1-3 times	93	80	0.833	0.509 - 1.364	0.468
Daily 1 time	166	178	0.668	0.428 - 1.043	0.076
Daily >1 time	19	37	0.368	0.187 - 0.725	0.004
Vegetables					
Monthly 1-3 times	91	61	Ref.		
Weekly 1-3 times	101	89	0.761	0.494 - 1.171	0.214
Daily 1 time	120	144	0.559	0.373 - 0.837	0.005
Daily >1 time	26	44	0.396	0.221 - 0.710	0.002
Black Tea					
Rarely	17	16	Ref.		
Daily 1-2 times	110	68	1.522	0.772 - 3.212	0.270
Daily 3 times	174	143	1.145	0.559 - 2.347	0.711
Daily >3 times	37	111	0.314	0.144 - 0.683	0.003

of a larger proportion of young women compared to elderly, this phenomenon increases the possibility of more premenopausal breast cancer cases. In addition, it may be explained partially by the fact that younger age groups have higher exposure to risk factors, such as westernization of lifestyle including marriage at older age, age of first life birth >30 years, fewer number of pregnancies, and less breastfeeding duration, and younger ages are more adapted to consumption of fast foods, while old women are adhere to traditional Kurdish foods. A portion of this study includes analysis of established risk factors of breast

cancer among Iraqi Kurdish women. According to our results, age at menarche ≥14 years has a protective effect on breast cancer, while age at menarche ≤12 years is a risk factor for breast cancer and age at menopause ≥51 years has a positive association with breast cancer. Our results are in agreement with a well-known knowledge that early menarche and late menopause are breast cancer risk factors due to increased lifetime exposure of breast tissues to endogenous estrogen.[7,9,25,39] Age at first life birth ≥30 years and positive family history have the same odds ratio, which was 1.7 with (*P* = 0.003, 0.023), respectively. In this

analysis, there was no association between hormonal use and breast cancer risk. This result is not accordance with findings of some studies,[13,38] while a study was done in USA could not find this relation,[40] because it can be affected by the duration of usage and composition of the formula, although we could not assess the duration of taking hormone by both cases and controls due to high rate of recall bias. In our analysis, BMI ≥ 25 kg/m^2 may regard as a risk factor for breast cancer. However, there were controversies about this issue in different geographical locations,[7,27] but this result is consistent with a study which was done in Iraq, they observed a positive association between BMI and breast cancer for both pre- and postmenopausal women.[16] In the result of the present study concerning the effect of diet on breast cancer, we found that consumption of stewed meat weekly one time has a protective effect. This finding is nearly similar with result of a study which was done in Spain that clarified the consumption of 16.29-25.3 g/day of red meat has protective effect on postmenopausal breast cancer,[20] while our result is inconsistent with other studies.[41,42] In fact, many studies couldn't find the association between red meat and breast cancer,[43-45] which may partially explain by the fact that this factor can be affected by the type of red meat, amount, frequency, and different cooking methods. In the present study, we observed that there was no association between stewed chicken and breast cancer, which is in line with result of a study that done on 2154 women.[20] In our result, consumption of fast food weekly more than two times is risk factor for breast cancer. It is well known that some fast food items may have carcinogenic character on breast tissues, because they have a higher amount of saturated fat with low fibers and vitamins.[46-49] Our result is showing that taking some Mediterranean food items weekly more than two times may increase risk of breast cancer. Published studies on Mediterranean foods and breast cancer are conflicting, some studies have reported no association,[29,30] some inverse associations,[31,32] but our study was only included the Mediterranean foods that contain red and white meat, such as minced meat kebab, beef meat skewers, and chicken meat skewers. Hence, the risk effect of Mediterranean foods may be limited to specific subgroups of Mediterranean food items that have a higher content of meat with low fibers or it may be related to the methods of cooking, amount of fibers content, and frequency of intake. Our result shows that intake of fish weekly one time has a protective effect. This result is accordance with finding of a case-control study which was done in China,[34] while a study in Denmark could not find any association.[33] This issue may be explained by the fact that the Kurdish people mainly are depending on taking a limited types of fish that are breeding in aquarium, because our region has no boundary with the sea. Furthermore, this relation might be affected by the type of the fish, frequency of intake, and methods of cooking in different cultures. In our study, there was no observed association between dairy products and breast cancer. Most of the epidemiological studies were unsuccessful to establish the effect of dairy products on breast cancer.[21] Our result can clarify that intake of fruit and vegetables daily more than one time has protective effect. Vegetables and fruit contain a list of vitamins, high dietary fibers

and antioxidants that may have cancer preventing effect.[33] Our data suggest that taking black tea daily more than three cups has inverse association with breast cancer occurrence. Although for black tea, conflicting results have observed among studies, but a number of case-control and cohort studies have shown that black tea has an anti-carcinogenic property against breast cancer.[35] These conflicting results may be due to different types of tea that contain different kinds and concentrations of polyphenols, or may be related to methods of tea leaves manufacture and varying methods of processing tea among different countries. The major limitation of this study is recall bias that most of the data were depending on self-reporting information by both cases and controls. In addition, it was difficult to assess the exact amount of food items by standard measures (e.g. g, kg), and obligatory we depended on the frequency of consumption for each food item.

Conclusion

Among Iraqi Kurdish women, all socio-demographic characters have no significant association with breast cancer apart from marriage that has a protective effect. All established risk factors are also risk factors in Kurdish women. High BMI more ≥ 25 kg/m^2 is regarded as a risk factor, while exercise, breastfeeding more than 48 months, and parity more than two children have protective effect. Although the role of diet on breast cancer is complex and can be influenced by some other factors, among Kurdish women, there were no association between stewed chicken and dairy product. We have observed that fast foods and some items of Mediterranean foods have the same risk factor effect on developing breast cancer, while consumption of stewed beef meat weekly 1 time, fish weekly 1 time and more, fruit daily >1 time and vegetables daily ≥ 1 time, and black tea daily more than 3 times have preventive effect on breast cancer.

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Conflicts of interest

There are no conflicts of interest.

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