Association between Nutrient Contents of Foods and Occurrence of Breast Cancer, A Case –Control Study

دراسة ارتباط ما بين مكونات الغذاء والاصابة بمرض سرطان الثدي مقارنة بالأشخاص الاصحاء

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الخلاصة:
هدف البحث:تهدف الدراسة إلى مقارنة محتوى الغذاء ما بين مرضى سرطان الثدي والاشخاص الاصحاء.
المنهجية :شملت هذه الدراسة 59 مريضة بسرطان الثدي و 65 حالة سالمة من جميع انواع الامراض السرطانية يترددون على المستشفى التعليمي الجمهوري ومستشفى رزكاري في اربيل/ العراق .تم جمع المعلومات الديموغرافية ، النسائية ، والمعلومات عن نمط الحياة والاغذية بواسطة استبيان مكون أربعة أجزاء، من 1 اذار الى 30 تموز سنة 2011.
النتائج: أظهرت الدراسة زيادة معنوية في الإصابة بسرطان الثدي نتيجة قلة الوعي والدخل، وتاريخ العائلة للإصابة بمرض السرطان، وزيادة اخذ الاغذية الغنية بالطاقة و كربوهيدرات بسيطة و شحوم مشبعة و كوليسترول و فيتامينات (ثايمينB_1 ، و الكوليسيفيرول ,D)، والمعادن (فوسفور، صوديوم، زنك، منغنيز، مع سلينيوم) تأثيرات وقائية من الاصابة بسرطان الثدي وجدت ضمن الاشخاص ذات مستويات التعليم المتوسطة، و اخذ الكميات المقررة من العناصر الصغرى و فيتامين ك .K و الياف غير الذائبة، والبقوليات و الشاي.
الاستنتاج: نستنتج بان الاطعمة الغنية بالطاقة والملح يؤدي الى الاكسدة الكامنة و عدم توازن الهورمونات وبالتالي زيادة الإصابة بسرطان الثدي. اخذ كميات محدودة من العناصر الصغرى و بالمستويات المتوازنة في الدم يحمي الانسجة من السرطان.
التوصيات: توصي الدراسة بتطبيق تقييم الحالة التغذويه وبرنامج التثقيف الغذائي من قبل ممرضين مختصين بالتغذية وأخصائيي التغذية

Abstract
Objective: The study conducted to identify association of nutrient contents of foods with occurrence of breast cancer compares to control group.
Design: It is descriptive (analytic case-control study). Interview questionnaire was used to collect data of; socio-demographic properties, reproductive history, familial cancer history, and life style factors included indices of obesity, and diet history data to calculate intake of; energy, macronutrient, vitamins and minerals by quantitative food frequency questionnaire.
Methodology: The study included (59) women with diagnosed breast cancer, and (65) controls women free from all types of cancer attending Rizgary and Hawler teaching hospital / Erbil / Iraq , from the period of 1st April to 30 July 2011. Statistical analysis included Descriptive statistic, and logistic regression analysis
Results: The results showed significant increase in the risk of breast cancer by; low income and low awareness, family history of cancer, and higher intake than controls of; energy, digestible and high glycemic load carbohydrates, saturated fats, cholesterol, vitamins; thiamin, and cholecalciferol and minerals; phosphors, sodium zinc, manganese, and selenium. While primary education level act as significant protective factor in addition to slight protective effect of; vitamins **K (**naphthoquinones), insoluble fiber and (beans and tea) as foods.
Conclusion: High dietary intake of rich energy nutrients, and salty foods could cause; oxidative stress, hormone disturbance and associate with breast cancer risk. Low and safe levels of dietary micro-nutrients and their blood homeostasis may decrease tissues damage and risk of breast cancer.
Recommendations: The study recommended implementation nutritional status assessment and nutritional educational program by nutritional specialized nurses, and nutritionists.
Keywords: Dietary habit, nutrient intakes, risks of breast cancer.

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Introduction

Breast cancer is a cancer of the glandular breast tissues. Incidence of female breast cancer in most Asian countries is much lower than that in western countries, and has been shown to be rising due to changes in lifestyle[1]. It is caused by heredity, environment pollution, biomechanics, dietary intake (which are mainly consisting of fats and starches) and the way of living. Recent Iraq wars affect the aggressiveness of disease and began to select its victims within young ages of women (thirties and twenties) [2].

In Erbil governorate breast cancer has been shown to be the most common cancer among women attending outpatients clinics of hospitals; Rizgary, Maternity and Hawler teaching hospitals and Nanakly according to statistical data from ministry of Health, 2006 [3,4]. Breast cancer is predominantly a disease of pre-menopausal Kurdish Iraqi women in Sulaimaniyah [5]. Almost all cancers (80 – 90%) are caused by environmental factors and of these (30-40%) of cancers are directly linked to the diet and there is significant relation between lifestyle (including food consumption) and cancer [6]. Much of the international variation is due to difference in established genetic risk factors but diet might also contribute to risk and provide a potentially modifiable target for prevention. Recent efforts have focused on identifying dietary risk modulators [2] .Comparison studies of food intake and its nutrient content association with breast cancer patients in Iraq and Erbil are rare. Therefore we compared nutrient content of foods consumed between breast cancer patients and controls and risks associated with demographic properties, reproductive history, and history of familial cancer, obesity, and physical activity

Methodology:

Case-control study was carried out in Rizgary and Hawler teaching hospital in Erbil governorate, Kurdistan region/Iraq. The patients (cases) included a purposive sample of (65 women and 6 dropped out because they didn't complete the interview questionnaire), they were diagnosed with breast cancer (after mastectomy), at different stage, attending outpatient unit of chemotherapy of Rizgary teaching hospital (2 days/ week) from the period of (1st April to 30 July 2011) and frequency age matched (± 5 years) controls included (65) available sample of women attending the same outpatient clinics of both Rizgary and Hawler teaching hospital of Erbil city from 1st September to 30 November 2011. They were free from all types of cancer. All patients and controls were interviewed by questionnaire. (After their consent had been taken) and composed of three parts of questions. The first part of questions included socio-demographic properties; age, educational level, residency, occupation and marital status. The second part of questions were about risk factors associated with reproductive property; age at menarche, age at menopause status, age at first pregnancy, number of children, type of breast feeding, oral contraceptive use, and hormonal therapy. The third part of questions included life style risks; family history of cancer with relationships to affected family members, physical activity, measurement of obesity by body mass index (BMI) and waist to hip ratio and dietary intake data by quantitative food frequency questionnaire to estimate (type and quantity) of food intake during the two years before the diagnosis for cases and before interview for controls.

Indexes of obesity were measured for controls and patients (whose weighs not changed after disease) and included recording the anthropometric measurements which were; weight and height to calculate body mass index (BMI), waist and hip circumferences measurement to calculate waist to hip ratio. BMI classified according to the world Health Organization (WHO), which defined abdominal obesity as a waist–hip ratio above 0.90 for males and above 0.85 for females, or a body mass index (BMI) above 30.0 [7]. Physical

activity levels (PAL) were calculated by asking the study population about their habitual activities as house work, office work, sleeping, watching TV, chatting, and walking per day then calculating energy costs and (PAL) using tables adapted from human energy requirement of FAO/ WHO/ UNU 2001 [8] .

The questionnaire of dietary intake data included (35) food items which were; Most frequency food item and Food items consumed in greatest amounts. Selected food items were categorized according to food groups and subdivided by source content and types. Food items in each category were cereals (cereal were differentiated to white bread, whole bread and whole grain), meats (red meats, chicken meats and fish), egg, legumes, milk and dairy products, vegetables and fruits most consumed by season, oils and fats, sweat snack, hot beverage (coffee and tea) and soft drinks (orange juice and cola). Subjects asked to state the average frequency of consumption of each food item according to the categories of frequency varying from; never or less than once per month, once per month, to 6 or more times per day. The food portion sizes were standard household measures and food models and photographs of the standard portion sizes of foods were commonly eaten. The subject was asked to refer to those portions when selecting the amounts of foods consumed. Once food intake data had been collected the quantities of foods reported in household measures were converted into quantities in grams for one day manually. Then data of foods intake in grams were analyzed for nutrient intake by a computer aided nutrient analysis program for Mosby's Nutitric Nutrition Analysis Software, version IV (CD-ROM). Daily macronutrients intakes were categorized to low, normal and high levels according to recommended amounts by the Institute of Medicine (IOM) National Academy Dietary Reference Intakes of 2002 Normal category of energy represents women's energy intake levels based on Estimated Energy Requirements (EER) which had taken in consideration age and activity of women. While the low and high categories represent women's with lower or higher intake of energy than (EER). The same principle was used for categories of macronutrient depending on the range of Acceptable Macronutrient Distribution Ranges (AMDRS) of; carbohydrates (45% - 65%), protein (10% - 35%), and fat (20% - 35%) of total energy and their energy value in one gram of food. The mid of total energy intake 2100) kilocalorie/day (Kcal/day) among the studied women was used in calculation [9]. Saturated, fat intake categorized to three levels comparing to normal recommended levels which ranges between (7 – 10% of total energy) for saturated (European Food Safety Authority (EFSA), 2010) [10].

A maximum healthy level of cholesterol was limited to (200-300) mg/day as recommended by Dietary guideline of American, while the healthy low levels were lower than 200 mg/day and higher levels were regarded as unhealthy level [11]. Dietary fiber intakes categorized into low, normal, and high intakes. Normal was 20-30 g/day depending on caloric intake (20g for 2000 calories) recommends by Academy of Nutrition and Dietetic previous (ADA) [12]. Daily caffeine intake categorized to low (< 0.2) g/day and moderate healthy levels which is equal to ≤ 0.3 g/day (Sata, 2005) and abnormal levels > 0.3 g /day [13]. Vitamins and minerals were categorized depending on recommended Dietary Allowance (RDA) and Tolerable Upper Intake Levels (UL) of Dietary Reference Intakes (DRIs) Food and Nutrition Board, Institute of Medicine, National Academies, and Upper Safe Levels of Intake for Adults: Vitamins and Minerals (Judy,2009) [14]. All data were analyzed by SPSS version 18.0. Include descriptive statistic independent samples t-test, Chi-square test Adjustment odds ratio (OR) value inclusion confounders; residency, occupation, and education levels were calculated to test risk of diseases or association between different risk factors and breast cancer. For binominal (yes and No) Cochran's and Mantel Haenszel descriptive test and binary logistic regression analysis for other

variables were used. The P- value was considered significant when P ≤ 0.05 and was considered as highly significant when P ≤ 0.01.

Results:

Table1: Socio-demographic characteristics for study population

Socio-demographic Data		Cases			Control			P-value	OR	(95% CI
		F.	%	Mean± SD	F.	%	Mean± SD			
Age Groups (years)	≤ 29	3	5.1	47.2± 10.3	7	10.7	46.5± 11.9	Ns.	First as reference	
	30-39	12	20.3		10	15.4			1.63	0.- 8.6
	40-49	14	23.7		16	24.6			0.64	0.2- 2.3
	50-59	23	**39.0**		22	**33.9**			0.90	0.3 - 2.9
	≥ 60	7	11.9		10	15.4			0.58	0.19 -1.8
Residency	Urban	32	54.2		46	70.8		Ns.	0.55	0.24- 1.25
	Rural	27	45.8		19	29.2				
Marital Status	Married	52	88.1		58	89.2		Ns	0.78	0.24 -2.5
	Single	7	11.9		7	10.8				
Occupation	Not working	49	83.1		32	49.2			**7.8****	**2.4 - 25.6**
	Working	10	16.9		33	50.8		**< .001****		
Educational Levels	Illiterate	32	54.2		30	46.2			First reference	
	Read& Write	10	16.9		4	6.2				
	Primary school	5	8.5		10	15.4				
	Intermediate school	1	1.7		5	7.7		Ns	0.28	0.07 - 1.1
		8	13.6		6	9.2			**0.12***	0.02- 0.7
	Secondary school	3	5.1		10	15.4			0.600	0.11 – 3.2
	College & above								1.500	0.1 – 18.4
									0.225	0.04 -1.2

** P **< 0.001**** High significant difference between cases and controls. F. Frequency, OR. Odds Ratio, CI. Confident interval

Table 1 shows the socio-demographic properties for cases and controls. Age means were 47.2± 10.3 year for cases and 46.5 ± 11.9 years for controls. Chi square analysis showed no significant difference between breast cancer and the control group in; residency, marital status and education levels. There was a high significant difference between cases and controls in occupation status, 50.8% of controls had official work, while 83.1% of breast cancer patients were housewife with no income. Not working was found to increase significantly the risk of breast cancer by more than seven fold (OR = 7.8, 95% CI 2.4 – 25.6). In spite of no significant difference in educational levels, primary school level significantly decrease breast cancer risk by 88% (OR= 0.12, 95% CI, 0.02- 0.7).

Table 2: Reproductive characteristic of study population

Reproductive factors		Cases			Control			P-value	OR	95% CI)
		F.	%	Means ±SD	F.	%	Means ± SD			
Age of Menarche	< 12 years	6	10.2		7	11.9			First reference	
	12 -14 years	39	66.1	13.5 ± 1.7	48	73.8	13.4 ± 1.34	Ns	1.6	0.4-6.4
	≥15 years	14	23.7		10	15.3			1.7	0.7-4.3
Age at first pregnancy	No pregnancy	13	22						First reference	
	< 20 years	16	27.1	17.3± 10.6	10	15.4	18.9± 9.97	Ns.	0.67	0.18- 2.5
	20-29 years	23	39		29	44.6			1.69	0.51- 5.6
	≥ 30 years	7	11.9		18	27.7			0.66	0.2- 2.15
					8	12.3				
Number of children	0 (No children)	13	21.3	3.9± 3.2	11	16.9	4 ± 2.9		First reference	
	1-4	23	37.7		26	40		Ns.	0.85	0.2- 3.7
	5-8	18	29.5		23	35.4			1.13	0.3 - 4.4
	≥ 9	5	8.2		5	7.7			1.28	0.3 –5.1
Menopause status	No menopause (No)	31	52.5	39.1 ± 6.1	36	55.4	38.8 ± 8.8	Ns.	1.1	0.6-2.3
	Menopause (yes)	28	47.5		29	44.6				
Ages at menopause	≤ 45 years	8	27.6	47.7 ± 6.2	8	27.6	48.9 ± 5.6		First reference	
	46-50 years	11	37.9		10	34.5			1.2	0.3 – 4.7
	> 50 years	10	34.5		11	37.9			0.83	0.3 – 2.8
Baby feeding status	No feeding	14	23.7		11	16.9			First reference	
	Breast feeding	22	37.3		34	52.3		Ns.	1.1	0.39 -3.1
	Formula feeding	2	3.4		5	7.7			2.2	0.92 -5.1
	Both	21	35.6		15	23.1			3.5	0.6– 20.5
Using oral contraceptive	No	43	72.9		44	67.7			1.24	0.53- 2.9
	Yes	16	27.1		21	32.3		Ns.		
Hormone intake	No	31	52.4		39	60			0.9	0.4-1.97
	Yes	28	47.5		26	40		Ns.		

Table 2 shows reproductive characteristic of study population associated with breast cancer risk. Majority 66.1% of cases and 73.8 % of controls had menarche age at (12-14) years, and there was no significant difference between categories of menarche age. According to age of first full term pregnancy; the high percentage 34% of cases had full term pregnancy at age (20-29) years, while high percentage 44.6% of controls ages at full term pregnancy were less than 20 years. There was no significant difference between categories of two groups. There was no significant difference between two groups in number of children, breast feeding status, oral contraceptive and hormone intake.

Regarding menopause status, 52.5 % of cases and 55.4% of controls were not at menopause stage. Highest percentage 37.9% of cases were menopause at age (46-50) year compared to (50) years of menopause age for majority of controls.

Table 3: Life style factors associated with breast cancer

Life style factors (A)	Cases		Controls		P-values of Chi square	OR	%95 CI
	F.	%	F.	%			
Family history					**< 0.001****	**0.14****	**0.04—0.49**
No relation (No)	35	**59.3**	61	**93.85**			
Family relation (Yes)	24	40.	4	6.15			
First degree relative							
Father	3	5.1	1	1.54			
Mother	3	5.1	1	1.54			
Brother	1	1.7	1	1.54			
Sister	0	0	1	1.54			
Second degree	17	28.8					
Physical activity levels					Ns.	First as reference	
Sedentary (1.4-1.69)	45	**76.3**	45	**69.2**			
Moderate (1.7-1.99)	14	23.7	20	30.8		0.49	0.07—3.34
Active (2.0-2.3) value	----	------	-----	------		0.77	0.34 – 1.73

	Case			Control					
	No	%	Mean ±SD	No	%	Mean ±SD	**P-value**	**OR**	**%95 CI**
Body Mass Index								First as reference	
< 25	6	10.2	31.6± 5.4	6	9.2	30.5± 4.9	Ns.		
25-29	18	30.5		22	33.8			0.6	0.3- 3.2
≥ 30	35	**59.3**		37	**56.9**			1.2	0.5 –2.5
Waist to hip ratio									
< 0.8	11	18.6		15	23.1			First as reference	
0.8-0.85	27	**45.8**	0.84± 0.1	24	36.9	0.84± 0.1	Ns.		
> 0.85	21	35.6		26	**40**			1.1	0.42-2.9
								0.7	0.3-1.6

** P **< 0.001**** High significant difference between cases and controls using Chi squared test

Table 3 represents categories of life style factors. There was no significant difference between cases and controls in; physical activity (most had sedentary life style with physical activity values less than 1.5), and obesity indexes. Majority of both groups were obese with body mass index more than 30 and waist to hip ratio between (0.8- 0.85) in cases and more than 0.85 in controls.

Family history with cancer showed high significant difference between breast cancer and controls. High percentage 93.8% of controls had no family history of cancer compared to cases 40.7% had family history of cancer which composed of 11.9% with first degree relatives and 28.8% with second degree relatives. No familial history caused 86% (95% CI 0.03-0.38) decrease in risk of breast cancer.

Table 4: Levels and categories of daily intake of energy and macronutrient

Levels and categories of Kcal & Macronutrients (g/d)	Cases			Controls			P- value	OR	%95 CI)
	F.	%	Means ± SD	F.	%	Means± SD			
Kcal/d							Ns.	Low as reference	
Low (< 2000)	**28**	**47.5**	4858.1± 8958.5	**42**	**64.6**	2828.9± 4402		**2.5***	1.1-5.9
Normal (2000- 2200)	8	13.6		10	15.4			2.5	0.8-8.2
High (> 2200)	23	38.9		13	20				
Carbohydrates (g/d)			**788.4± 472.7***			**522.5 ±1036***	Ns.	Low as reference	
Low (< 236)	22	**37.3**		36	**55.4**			**2.5***	1.1- 6.1
Normal (236-345)	17	28.8		16	24.6			1.45	
High (> 345)	20	33.9		13	20				0.6-3.9
Dietary fiber (g/d)								Low as reference	
Low (< 21)	18	30.5	70.6 ± 158.5	34	**52.3**	54.0±. 1	**≤0.05***		
Normal (21-27.5)	24	**40.7**		13	20				0.67-4.4
High (> 27.5)	17	28.8		18	27.7			1.7	
								0.45	0.16-1.2
Protein (g/d)			156.2± 396.4			67.8± 80.8	Ns	Low as reference	
Low (< 53)	**27**	**45.8**		**42**	**64.6**				
Normal (53-184)	24	40.7		17	26.2			0.33	0.05-2.29
High (> 184)	8	13.5		6	9.2				
								0.30	0.05-1.98
Total Fat (g/d)			139.6± 354.1			79.3± 95.6	**≤0.05***	Low as reference	
Low (< 46.7)	14	23.7		26	**40**				
Normal (46.7-81.7)	20	33.9		26	40				
High (> 81.7)	25	**42.4**		13	20			4.03	0.22-72.8
								4.86	0.46-51.4
Saturated Fats (g/d)			56.19± 230.3			17.2± 20.5	: **0.001***	Low as reference	
Low	19	32.2		39	**60**			**5.2***	**1.2-22.7**
Normal	11	18.6		15	23.1			2.9	).84-9.8
High	29	**49.2**		11	11.9				
Cholesterol (milligram/day)			386.9± 1392.4			124.1±126.	**< 0.01***	Low as reference	
Healthy (< 200)	37	**62.7**		57	**87.7**				
Limited (200- 300)	14	23.7		6	9.2			**5.96***	**1.2-30.3**
High (> 300)	8	13.6		2	3.1				
								1.99	0.3-12.8
Caffeine (gram/day)			**.095 ± 0.07**			**0.2 ± 0.67**	Ns.	Low as reference	
Low (< 0.2)	48	**81.4**		44	**67.7**			**0.52**	0.04- 6.5
Moderate (0.2- 0.3)	10	16.9		19	29.2				
High (> 0.3)	1	1.7		2	3.1			1.46	0.1-20.4
Insoluble Fiber (g/d)			**15.7 ± 59.2**			**22.8 ±60.9**	Ns.		

*significant difference by independent samples T- test between cases and controls in the mean levels of carbohydrates (P= 0.03) and the mean levels of poly unsaturated fats (P= 0.008) , (gram/day) = g/d

Table 4 shows daily dietary energy and macronutrient intake of cases and controls. There was no significant difference between cases and controls in categories of; energy, carbohydrates, proteins, insoluble fiber and caffeine intake. (High energy and carbohydrates caused significant increase risk of breast cancer by 2.5 times among cases with 95% CI 1.1-5.9 and 1.1- 6.1 respectively). While significant differences were found between categories of; dietary fiber, total fat, saturated fats, and cholesterol intake. Most breast cancer patients had high level intake of saturated fats (increased risk of cancer significantly by 5.2 times, 95% CI 1.2-22.7) and normal intake of, dietary fiber compare to controls which had low intake of energy and all macro-nutrients. Majority of controls (87.7%) had healthy level ((< 200) mg/d intake of dietary cholesterol while B-cancer patients had higher levels intake of dietary cholesterol which caused significant increase cancer risk (5.9 times (95%1.2-30.3).

Carbohydrates in cases had significant higher mean levels compare to controls. Also insoluble fibers and caffeine in controls showed higher mean levels of intake than cancer patients.

able 5: Levels and categories of daily water soluble vitamins intake

levels of water soluble Vitamins Categories	Cases F.	%	Means ± SD	Controls F.	%	Means ± SD	P- value	OR	95% CI
Vitamin B_1 (mg/d)			4.23 ± 8.13			3.3± 7.1	Ns.	Low as reference.	
Low (**<** 1.1)	8	13.6		18	27.7			**2.94***	**1.11- 7.8**
Safe (1.1-1.5)	17	28.8		21	32.3			1.62	0.71- 3.7
High (> 1.5)	34	**57.6**		26	**40.0**				
Vitamin B_2 (mg/d)						2.3±3.6	Ns	Low as reference.	
Low **(<** 1.1)	16	27.1		22	33.8			1.62	0.65- 4.0
Safe (1.1-1.7)	23	**39**		26	**40**				
Abnormal (> 1.7)	20	33.9	4.5 ±15.24	17	26.2			1.33	0.6 – 3.1
Vitamin B_3 (mg/d)			43.3 ± 85.34			22.7±29.9	Ns	Low as reference	
Low **(<** 14)	17	28.8		32	**49.2**				
Safe (14-35)	31	**52.5**		26	40.0			2.91	0.91- 9.3
High (> 35)	11	18.7		7	10.8			1.16	0.36 3.74
Vitamin B_6 (mg/d)			**3.65 ± 5.26**			**4.94±14.2**	**< 0.05***	Low used as ref	
Low **(<**1.3)	12	20.3		27	**41.5**				
Safe (1.3 - 2)	31	**52.6**		23	35.4			2.4	0.90 – 6.4
Upper safe (3 - 100)	16	27.1		15	23.1			0.79	0.3 – 1.9
Vitamin B_9 (mcg/d) (microgram/day)			1197.1±2604.			1069.3± 3293.1	Ns.	Low as reference	
	25	**42.4**		37	**56.9**				
Low **(<**400)	22	37.3		20	30.8			2.22	0.79 – 6.2
Safe (400- 1000)	12	20.3		8	12.3				
High (> 1000)								1.36	0.46 – 4.0
Vitamin B_{12} (mcg/d)	44	**74.6**	**7.86 ± 40. 6**	60	**92.3**	**1.6 ± 2.8**	**< 0 .05***	Low as reference	
Low (**<** 2.4)	12	20.3		4	6.2			4.1	0.41- 40.7
Safe (2.4-6)	3	5.1		1	1.5				
High (> 6)								1.0	0.1 -12.6
Vitamin C (mg/d)			589.5± 1123.3			749.9± 2733.6	Ns.	High used as ref.	
Low(**<** 75)	3	5.1		7	10.8			1.67	0.28 – 9.8
Safe (75-2000)	51	**86.4**		51	**78.4**				
High (> 2000)	5	8.5		7	10.8			**0.71**	0.21 -2.4

* P **< 0.05*** Significant difference between cases and controls using Chi squared test.

Table 5 shows daily intake of water soluble vitamins. There was significant difference between cases and controls in categories of vitamins; pyridoxine **(B_6)**, & cobalamin **(B_{12})**, intake. Most of cases 42.4% and 56.9% of controls had low intake of dietary vitamin folate (**B_9**).While intake of vitamin **B_{12}**, was low in more than half (74.6%) of cases compared to majority (92.3%) of controls. Cases had mean levels of **(B_{12})** 7.86 ± 40.6 mcg/d, higher than safe levels and mean level of controls 1.6±2.8 mcg/d. Vitamin **B_6** & **B_3 (Niacin**) intake were in safe levels by most of cancer patients but these vitamins were low in controls. Most of cases and controls had high intake of vitamin thiamine **(B_1)** particularly in cases which caused significant increase risk of breast cancer by (2.94) times with (95% CI 1.11- 7.8). Both cases and control were in safe level intake of vitamins; Riboflavin (**B_2**) and ascorbic acid (**C)**.

Table 6: Levels and categories of daily intake of fat soluble vitamins

Categories of fat soluble vitamins levels	Cases F.	%	Means ± SD	Controls F.	%	Means ± SD	P-value	OR	95% CI
Vitamin A (mcg/d) (microgram/day)			**3763.3± 15044**			**978.8 ± 1813.4**	Ns.	Low as reference	
Low(< 700)	**28**	**47.5**		**41**	**63.1**			1.95	0.4- 9.4
Safe (700-1500)	25	42.4		17	26.2			0.91	0.18- 4.6
Upper safe (1500-3000)	2	3.4		4	6.1			2.67	0.3- 25.6
Abnormal (> 3000)	4	6.7		3	4.6				
Vitamin D (mcg/d)			**0.8 ± 1.02**			**0.51 ± 0.9**	**< 0.05**	low level as reference	
Low (≤ 0.065)	14	23.7		18	27.7				
Low (≤ 0.26)	9	15.3		22	**33.8**			1.6	0.58- 4.2
Low (≤ 0.76)	19	**32.2**		11	16.9			**2.97***	**1.04- 8.5**
Safe (≤ 5)	17	28.8		14	21.5			0.70	0.3- 1.96
Vitamin E (mg /d)			16.34 ± 47.84			10. ± 23.4	Ns.	Low as reference	
Low (< 15)	48	**81.3**		57	**87.7**			2.7	0.3- 25.6
Safe (15-22)	6	10.2		3	4.6			1.2	0.32- 4.34
Upper safe (23-1000)	5	8.5		5	7.7				
Vitamin K (mcg/d)			**47.5 ± 103.6**			**126.8± 539.3**	Ns.	Low as reference	
Low (< 80)	55	**93.2**		55	**84.6**			0.25	0.05-1.23
Safe (80-90)	2	3.4		2	3.1			0.25	0.02-3.04
Abnormal (> 90)	2	3.4		8	12.3				

Table 6 shows the daily intake of fat soluble vitamin. Majority of both groups had low intake of fat soluble vitamin. There was significant difference between cases and controls in categories of vitamin **D (**cholecalciferol) intake that caused significant increase risk by 2.97 times with (95% (1.04 – 8.5). There was higher intake of vitamin **A** (retinol) than Tolerable Upper Intake levels, (UL). Lower mean level than RDA of vitamin **K** (naphthoquinones) in cases.

Table 7: Levels and categories of daily macro minerals intake

Levels of macro-mineral categories	Cases F.	%	Means ± SD	Control F.	%	Means ± SD	P-value	OR	95% CI
Calcium (mg/d)			2833.1± 13203.4			1110.9±2188.8	Ns	Low as reference	
Low (< 1000)	48	**81.4**		54	**83.1**			1.1	0.4- 3.1
Safe (1000- 2500)	5	8.5		6	9.2				
Abnormal (> 2500)	6	10.1		5	7.7			1.0	0.12- 8.7
Magnesium (mg/d)			792.53 ± 1550.9			579.95± 1181.9	Ns	Low as reference	
Low (310<)	36	**61.0**		45	**69.2**			1.4	0.62-3.2
Safe (310-350)	6	10.2		5	7.7			0.94	0.24-3.7
Abnormal (> 350)	17	28.8		15	23.1				
Phosphorus (mg/d)			3027.4± 10482.5			1320.7± 1990.9	Ns	Low as reference	
Low (< 700)	21	**35.6**		30	**46.2**				
Safe (700-1000)	17	28.8		23	35.4			**2.7***	**1.1 – 6.8**
Upper safe(1000- 4000)	21	**35.6**		12	18.4			**2.7***	**1.03-7.0**
Potassium(mg/d)			9719.7± 23374.5			8350.5±20818	Ns	Low as reference	
Low (< 3500)	32	**54.2**		45	**69.2**				
Safe (3500-4700)	15	25.4		9	13.8			1.3	0.5- 3.1
Abnormal (> 4700)	12	20.4		11	17.0			.49	0.15- 1.6
Sodium (mg/d)			**3541.4± 7172.9**			**11900.9± 3964.3**	**< 0.05***	Low as reference	
Low (< 1300)	16	27.1		28	43.1			**4.6****	**1.6-13.1**
Safe (1300-2300)	261	**44.1**		30	**46.2**				
Abnormal (> 2300)	7	**28.8**		7	10.7			**3.9****	**1.4- 11.0**

* P **< 0.05*** Significant difference between cases and controls using independent Chi squared test.

Table 7 shows daily of macro mineral intake. All study populations had low levels of macro mineral intake and there was no significant difference in categories of intake between cases and controls except sodium and phosphorus which were safe and low in controls while cases intake were safe, upper safe for phosphorus and safe and abnormal. Cases had higher level of mean than UL for sodium. Phosphorus and sodium intake caused significant increase in risk by 2.7 times, (95% CI, 1.1 – 6-8) and 4.6 times, (95% CI 1.62-13.1) respectively.

Table 8: Levels and categories of daily micro - mineral intake

Levels of micro mineral categories milligram /day	Cases F.	%	Means ± SD	Control F.	%	Means± SD	P-value of χ^2	OR	95% CI
Iron(mg/d)			33.2± 70.5			17.9±26.1	Ns.	2.96	0.79-11.1
Low (< 8)	9	15.3		20	33.8			1.3	.42- 4.24
Safe (8-18)	**35**	**59.3**		**35**	**53.8**			0.76	0.15 -3.9
Upper safe (18-45)	7	11.8		4	6.2			High as reference	
Abnormal (> 45)	8	13.6		6	9.2				
Zinc (mg/d)			25.4± 68.9			9.1±11.2	**< 0.001****	Low as reference	
Low (< 8)	**33**	**55.9**		**49**	**75.4**			**5.3***	1.04- 27.1
Safe (8- 45)	19	32.2		16	24.6			2.3	0.43- 13.4
Abnormal (> 45)	7	11.9		0	0				
Cupper (mg/d)			2.8 ± 5.5			2.3± 4.4	Ns.	Low as reference	
Low (< 0.9)	14	23.7		22	33.8			0.94	0.19- 4.6
Safe (0.9- 2)	34	**57.6**		34	**52.3**			0.6	0.13-2.7
Upper safe (2-10)	8	13.6		4	6.2			0.3	0.04-1.9
Abnormal (> 10)	3	5.1		5	7.7				
Manganese (mg/d)			11.3± 25.7			5.3± 7.13	**< 0.05***	Low as reference	
Low (< 1.8)	0	0		3	4.6			2.2	0.45 - 11.1
Safe (1.8- 2)	10	16.9		22	33.9			**4.8 ***	1.04-21.8
Upper safe (2-11)	**42**	**71.2**		**35**	**53.8**			1.2	0.34 – 4
Abnormal (> 11)	7	11.9		5	7.7				
Selenium (mcg/d)								Low as reference	
Low (< 55)	5	8.4	**100 ± 40.9***	13	20	**81.1± 30.4***	**< 0.05***	**3.4***	1.09- 10.4
Safe (55-70)	10	16.9		18	27.7			2.33	0.95- 5.7
Upper safe (70-400)	**44**	**67.7**		**34**	**52.3**				

*significant difference between breast cancer and controls in the mean level of selenium by independent T- test (P= 0.003). * P **< 0.05*** Significant difference between categories of cases and controls using Chi squared test.

Table 8 shows daily intake of micro-minerals. They had safe or upper safe intakes, except intake of zinc which was lower than RDA particularly in (75.4 %) of controls. There was significant difference in categories of zinc, manganese and selenium intake, between cases and controls. They increased risk significantly by 5.3 times 95% (1.04 – 27.1) for zinc, 4.76 times 95% CI (1.04- 21.8) for manganese, and 3.37 times 95% CI (1.09-10.4) for selenium.

Table 9: Means (g/d) of food item in cases (Breast cancer) and controls

Food items	Cases	No.	Mean ± Std. Deviation	P- values
Cereals	B- cancer	59	358.2 ± 200.8	**< 0.01****
	Controls	65	269.3 ± 128.6	
Animal meats	B- cancer	58	59.7 ±44.5	**< 0.001****
	Controls	65	33.2 ± 21.6	
Egg	B- cancer	59	15.9 ± 14.9	Ns
	Controls	65	11.6 ± 11.9	
Total Beans	B- cancer	59	36.9 ± 34.4	Ns.
	Controls	65	43.7 ± 34.5	
Dairy Product	B- cancer	59	205.4 ± 139.8	Ns.
	Controls	65	196.0 ± 160.2	
Fruit	B- cancer	58	572.9 ± 267.6	**< 0.05***
	Controls	65	458.1 ± 323.3	
Vegetables	B- cancer	59	275.4 ± 155.3	Ns.
	Controls	64	262.3 ± 178.2	
Fats	B- cancer	58	14.8 ± 27.4	**< 0.001****
	Control	65	0.8 ± 2.8	
Tea	B- cancer	59	321.2 ± 250.1	Ns.
	Controls	65	415.4 ± 328.7	
Orange Juice (soft drink)	B- cancer	59	110.6 ± 147	Ns.
	Controls	65	70.5 ± 89.8	
Cola (soft drink)	B- cancer	58	114.7 ± 120.6	**< 0.05***
	Controls	65	62.5 ± 133.9	
Sweat snack	B- cancer	59	43.6 ± 106.4	**< 0.05***
	Controls	65	11.4 ± 23.6	

Table 9 shows mean of daily food item intake in gram of cases and controls. The independent samples T-test showed that breast cancer patients consumed significantly at ($p \leq 0.001$) greater quantities of cereals, meats, fats, and at ($p \leq 0.05$) for fruit, soft drink

and sweat snack. While they consumed lower quantity of bean and tea compared to controls.

Discussion:

Most cancer patients were house wives compare to controls which had official work. This result may be attributed to low income and low awareness to; early detection, factors affecting cancer survivors and social and culture barriers, as stated by [15] especially in low- and middle-income countries [15] .This result in line with previous studies who observed that (81% and 72.57%) of cancer patients were house wives [16, 17]

Significant decrease in risk of breast cancer after six year education (primary school compare to secondary school) is in consistent that women with more than 16 years of education had a 36% increased risk compared to the lowest educated (7-9 years) and was slightly stronger among postmenopausal than among premenopausal women [18].

There was no significant difference between cases and control in life style factors (although they differ in occupation status) except family history. Decreasing risk among individual with no familial relation of cancer, support several studies had been done in Erbil city [19, 20] .Also with a study in Sulaimaniyah [5].

The results of foods intake in this study showed significant difference between categories of two groups in; total fat, especially saturated and cholesterol which significantly increased risk of breast cancer. These bad fats may relate to high significant intake of meats (animal protein) and fats as food item. This result supported with previous studies who found lower total fat intake in the controls compare to breast cancer patients and positive correlation between fat intake and mortality of breast cancer especially in postmenopausal [1, 21]. And cholesterol functions like the hormone estrogen to fuel the growth and spread of the most common types of breast cancer [22].

Significant difference between cases and controls in the mean level of carbohydrates and significant risk increase by carbohydrates and energy, reflect high significant intake of cereals (which composed mainly of refined grains), sweat snacks and beverages. These high glycemic index compound increase insulin activity and tumor growth and it is consistent with [23] who concluded that a high glycemic diet may increase breast cancer risk particularly among premenopausal women with body mass index > 25. High intake of animal protein, saturated fats and rapidly digestible carbohydrates is associated with increased risks of many cancers and attributed to increase the bio-activity of Insulin Growth Factor-1(IGF-1) that promote tumor development [24].

Most breast cancer patients had normal and higher intake than controls of dietary fiber (soluble and insoluble fiber), which reflects high significant fruit intake and does not appear protective against breast cancer. These results consistence with most prospective cohort studies have found no relation between dietary fiber intake and breast cancer [25] who found no relation of breast cancer with fiber from grains, fruit, vegetables, and beans. Fiber sources are more important than total fiber intake as indicated by the protective effect of insoluble fiber from whole grains among controls than from fruits and vegetables [26] and may be related to increase fecal excretion of estrogen and reduction in circulating estrogen level [27].

According to vitamins intake, it is still unclear whether more **B** vitamins will protect against cancer or increase cancer risk. Some scientists have proposed that inherited differences in the way a person's body uses **B** vitamins influence whether these supplements will harm or help a person [28].

Significant risk increase by vitamin $\mathbf{B_1}$ (thiamine) may demonstrate the significance of thiamine-dependent enzymes in cancer cell metabolism [29] and agrees with[30] who

found few significant association between individual B vitamins (**B_1, B_2, B_3**,and Vitamin **B_9**) with the breast cancer risk in women.

Significant difference between categories of cases and controls in vitamins **B_6** (Pyridoxine), and **B_{12}** (Cobalamin) intake may by be related to lower intake of these vitamins than RDA (especially vitamin B_{12}) by majority of controls compared to cases. These vitamins had modification effect on vitamin **B_9** (folate) and methylation of DNA [31].

Most of cases and controls had lower levels than (RDA) of dietary intake of fat soluble vitamins.This may indicate to no relation of dietary intake of most of fat soluble vitamins with risk of breast cancer. It reveals the same view that overall, dietary intake of β-carotene, and **E (**tocopherols**)** was not related to breast cancer risk in neither pre- nor postmenopausal women [32].

Significant difference between categories of cases and controls in vitamin **D** intake indicated to protective effect of low dietary vitamin **D** intake and maintenance of its blood threshold. This supported with [33] who observed positive association between circulation 25- hydroxyl cholecalciferol and risk of breast cancer among women who were overweight or obese, and reported that 25 (OH) cholecalciferol levels may inhibit aromatase, which in turn could lead to increased ovarian estrogens production in premenopausal women. Risk of breast cancer didn't decrease when the women have circulating vitamin **D** levels above 35 ng/ml[34].

Higher mean levels of dietary vitamin **A** intake than (UL) in cases is consistent with studies found positive association between high levels of retinol and RE+/RP+ breast cancer and could be due to animal source of retinol in contrast to caroteinoids and vitamin C [35].

Higher mean level of dietary vitamin **K** (naphthoquinones) intake in controls compare to case (which is lower than RDA) may indicate to anti-carcinogenic and antitumor activities of this vitamin for various cancer cell lines, including breast cancer, leukemia and hepatocellular liver carcinoma [36].

Macro-mineral dietary intake showed no significant differences except dietary phosphor and sodium intake and increased risk of cancer. This reveals that association between inorganic phosphate and cancer risks may be related to abnormal levels of hormonal and metabolic factors regulating inorganic phosphate, such as; vitamin D, growth factor (GF-23) and parathyroid hormones [37]. Increasing risk by sodium intake reflects the view that high salty food consumption may contribute to insulin resistance which cause hyperglycemia, oxidative stress, and increased risk of breast cancer [38].

Safe or upper safe (in the range of UL) levels of dietary zinc and antioxidant trace minerals (manganese and selenium) may increase risk of breast cancer among oxidative stress patients. Zinc is known to be essential for cell proliferation, and tumor growth [39]. Dietary manganese (Mn.) intake influence gene expression of Mn-dependent enzymes; manganese superoxide dismutase (MnSOD) and may be associated with increased risk of cancer [40].

Significant difference in categories of selenium intake between cases and controls indicated to safety of RDA levels of dietary selenium and avoiding over-supplementation due to an intriguing U-shaped dose–response relationship between selenium status and deoxy ribonucleic acid (DNA) damage [41].Among the food items, intake of beans and caffeine (especially as tea) were lower by cases compared to controls. This indicated that beans may reduce the risk of breast cancer by greater excretion of phyto-estrogen by urine [42].

Conclusions:

The results conclude that low education level decrease risk of breast cancer. In contrast to low income, awareness, and family history, increase dietary intake of; saturated fats, cholesterol, digestible high glycemic load carbohydrates, vitamins (**B_1**, and **D**) and minerals (sodium, phosphors, zinc, manganese and selenium) could increase the risk of breast cancer. While safe levels of micronutrients with considering their blood threshold can act as protective factors. Food items (beans, tea) and insoluble fiber fraction may decrease the risk of breast cancer.

Recommendations

The study recommended implementation nutritional status assessment and nutritional educational program as a means for nutritional health awareness and providing supervision on the quality of the food by nutritional specialized nurses, nutritionists.

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