

Role of Food Choice for Breast Cancer Prevention in Developing Societies: A Case Control Study in North Cyprus

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Abstract

Background: Breast cancer incidence is increasing in developing societies. The Mediterranean eating regimen has been suggested to play a preventive role in reducing breast cancer risk.

Objective: This study investigated the preventive role of fruits and vegetables, eggs, fish, olives and olive oil and fresh potatoes consumption similar to western Mediterranean diets on breast cancer development in the women of North Cyprus.

Methods: This case-control study was carried out in Dr. Burhan Nalbantoglu Devlet Hastanesi, Lefkosa, North Cyprus. The study group were 305 women with confirmed cases of breast cancer and control group were 302 women without breast cancer. Due consent to participate was obtained. Information on dietary intake was collected, which included age, menopausal status, breast density, age at menarche and dietary consumption of fresh potatoes, fruits and vegetables, olives and olive oil, fish and eggs. logistic regression model was used to analyze the link between the dietary intake and breast cancer risk.

Results: Consumption of fruits and vegetables, Olives and olive oil 5 or more servings per day and fish 2 servings per week showed an OR=0.09(0.04,0.18), 0.06(0.03,0.16) and 0.04(0.02,0.10) respectively, with the 3-6 eggs per week and 4 or more servings of fresh potatoes per week OR=0.10(0.54,0.20) and 0.15(0.08,0.28) respectively.

Conclusion: The consumption of olives and olive oil 5 or more times, and fish 2 or 1 times weekly played a more significant role in reducing the risk of breast cancer in women. Investigating at a larger scale in the study population is yet to be done.

Introduction

Breast cancer is the most predominant malignancy among the women of North Cyprus [2] as well as in similar developing societies. [36] Yearly, worldwide deaths from breast cancer is about 327,000. It is estimated that 1.35 million new cases will be observed each year and in 2020, 1.7 million cases are going to be diagnosed with more than 50% of the cases in developing regions [24].

The increase in breast cancer risk is suggested to be due to changes in lifestyle, reproductive factors, increased life expectancy [50], genetic factors, race, environmental conditions, physical activity, socioeconomic status, body mass index and nutrition [35].

Among all primary preventions for breast cancer in developing societies, the consumption of the right foods is the most cost-effective cancer preventive intervention [19].

Inter-societal differences in response to dietary consumption and breast cancer risk maybe linked to genetics. [38] There are polymorphisms in the interactions of diets intake and gene, that may influence epigenetics and further modify the expression of genes which influences the risk of breast cancer. [39]

A French cohort study reported, that there was an inverse relationship with breast cancer risk following the intake of “healthy/Mediterranean diet” consisting of fruits, raw or cooked vegetables, fish and crustaceans, olive oil and sunflower oil in post-menopausal women especially those with ER+/PR- tumors [13] and breast cancer was also observed to decrease in Latino and non-Latino Caucasian women in a study carried out in the United States to investigate the function of Mediterranean diets such as; alcoholic beverages, chicken, seafood, vegetables, green salads, olive oil and salad oil among this group.[14] ⌘ Though a study by Bessaoud et al reported no association between breast cancer risk and the intake of fruits, raw and cooked vegetables, fish and olive oil in France, [15] Another study observed an inverse/positive relationship between the consumption of the Mediterranean diet and breast cancer risk in women. [17] Further investigation on the Mediterranean dietary intake and breast cancer risk carried out among Greek-Cypriot women, reported that the adherence to a dietary pattern rich in vegetables, fish, legumes and olive oil may favorably influence the risk of breast cancer [16]. The foods consumed on the Mediterranean reduce breast cancer risk [1] and diets of a sort conventional in Mediterranean societies are portrayed by a high intake of vegetables, fruits, fish, olive oil and moderate consumption of protein, which are thought to present health advantages. [1]

The defensive role of the Mediterranean foods on breast cancer is biologically plausible with the Mediterranean diet rich in fiber, antioxidants such as flavonoids, vitamins, carotenoids and squalene, and the diets might modulate breast cancer risk by diminishing endogenous estrogens [4], increasing sex-hormone binding globulin levels [5], neutralizing free radicals and preventing DNA damage [6], lessening oxidative stress [7,8] and genetic modification [41].

Previous studies on Mediterranean foods and breast cancer have provided mixed results. North Cyprus has a typical western Mediterranean way of life with living conditions and diets that ought to be ideal for healthy wellbeing [12]. Culture may drive the consumption of certain types of foods in high amount base on local availability. [40] Limited evidence exists that support the probable causal role of western Mediterranean diets. Finding the specific foods that have significant impact on breast cancer risk will allow for a targeted consumption to achieve maximum benefits.

Also, the awareness on the pivotal role of Mediterranean foods should be encouraged, most especially among populations vulnerable to micronutrients deficiencies [20] such as developing societies.

The purpose of our study was to investigate the potential positive impact of western Mediterranean dietary life style through investigating the significance of the varying amount of intake of fruits and vegetables, fish, olives and olive oil, fresh potatoes (cooked) and eggs on breast cancer risk among the women of North Cyprus.

Methods

Subjects

This was a hospital-based case-control study that was carried out in Dr. Burhan Nalbantoglu Devlet Hastanesi, Lefkosa, North Cyprus. The investigation was carried out in accordance with the declaration of Helsinki, 2013. Ethical approvals were obtained from Near East University, North Cyprus ethical community and the ethical community of Dr. Burhan Nalbantoglu Devlet Hastanesi, Lefkosa, North Cyprus.

From convenient sampling the women enrolled were as follows:

- Case group = 305 women with confirmed cases of breast cancer.
- Hospital-based control groups = 302 women without breast cancer attending the cancer hospital for other reasons.

Data collection

Breast cancer cases were approached while waiting for their oncologist appointment or while receiving chemotherapy. Patients with breast cancer were selected as diagnosed pathologically based on international classification of diseases for oncology 3rd edition (C50.0 – C50.9)[9] and registered with the cancer center's database.

The hospital-based controls were women attending the hospital for other reasons and have no history of breast cancer. The goals of the study was explained clearly to them and due consent to participate was verbally obtained or by filling a consent form. The controls were asked questions about their dietary intake in the past 5-10 years, while the cases were also asked same questions about their dietary intake 5-10 years before diagnosis.

Data were collected with the use of a specially designed questionnaire through a standardized interview. The questionnaire included information on age, menopausal status, age at menarche and breast density. In addition, a diet interview was conducted on each subject using a food frequency questionnaire designed to capture the consumption of 5 food items selected from previously validated questionnaires, [49,25] and commonly consumed by the people of North Cyprus. The frequency of intake of the 5 food items were categorized as follows : Eggs intake: 3-6 per week, 1-3 per week and none; Fruits and vegetables intake: 5 or more servings per day, 3-4 servings per day, 2 servings per day and none; Olives and olive oil intake: 5 or more servings per day, 3-4 servings per day, 2 servings per day and none; Fish intake: 2 servings per week, 1 serving per week and never; Fresh potatoes : 4 or more servings per week, 2-3 servings per week and 1 serving or none per week. Only the completely answered questionnaires were analyzed (table 1).

Table 1. The standard serving of the studied foods

Foods	Amounts
1 serving of vegetables	1 cup of raw leafy vegetables, 1/2 a cup of raw or cooked vegetables
1 serving of potatoes	1 cup of diced, mashed or medium size boiled potato
1 serving of fruits	1 cup of chopped fruits, 125ml(1/2cup) of fruit juice (no added sugar) and ½ cup dried fruits
1 serving of fish	1 can of fish, 1 cup of sliced fish or 1 fish
1 serving of egg	1 egg
1 serving of olive oil	1 table spoon per meal
1 serving of olives	5 olives per meal

Table 1 shows the standard used for the servings of each studied Mediterranean food [10,11,34]. A serving is equal to the quantity per meal and this can be cooked, fresh or dried.

Statistical analysis

They women age, menopausal status, breast density, age at menarche and dietary intake between cases and controls were first analyzed by cross-tabulation and chi-square test. The significance was $P < 0.05$. To analyze the link between the frequency of dietary intake and breast cancer risk, A multivariable logistic regression model was used and only diets consumption frequency was analyzed. No cofounding variable were used in the analysis. The fit of the model was assessed on the basis of Pearson chi-square or Hosmer-Lemeshow goodness of fit. The Statistical analysis was carried out using IBM spss.

Results

A total of 305 breast cancer cases and 302 hospital-based controls were studied.

The age range of the participants studied was between 18-69 years, with a mean age of 45.60 years.

Table 2. The distribution of characteristics in the study population

Variables	Breast cancer patients	Hospital-based controls	Sig.
Age:			
0-29 years	6	109	
30-39 years	41	67	
40-49 years	54	52	
50-59 years	93	48	
60-69 years	111	26	<0.05
Breast density:			
Extremely dense	25	34	
Heterogenously dense	179	129	
Almost-entirely fatty	101	139	<0.05
Menopausal status:			
Premenopausal	117	221	
Postmenopausal	188	81	<0.05
Age at menarche			
=<12years	73	6	
13years	170	214	
>=14years	62	82	<0.05

The highest number of 221 women in menarche group were premenopausal women with 13 years age at menarche, while following is 163 postmenopausal women in the same category. The lowest, which is 29 premenopausal women had their menarche at age =<12 years. 50 postmenopausal women had their menarche at age =<12 years. The women with menarche at age =>14 were 88 pre and 56 postmenopausal women.

The highest number from 201 women, with heterogeneously dense breast were premenopausal, followed by 155 post menopausal women with almost entirely fatty breast and the lowest was 7 postmenopausal women with extremely dense breast. 52 premenopausal women had extremely dense breast.

Table 3. Table of the dietary consumption of the study population

Diets	Breast cancer patients	Hospital-based controls	Sig.
1. Eggs:			
3-6 per week	154	225	
1-3 per week	50	49	
None	101	28	<0.05
2. Fruits and Vegetables:			
5 or more servings per day	106	161	
3-4 servings per day	48	58	
2 servings per day	45	65	
None	106	18	<0.05
3. Olives and olive oil:			
5 or more servings per day	41	49	
3-4 servings per day	52	86	
2 servings per day	115	150	
None	97	17	<0.05
4. Fish:			
2 servings per week	83	160	
1 serving per week	119	132	
Never	103	10	<0.05
5. Fresh potatoes (cooked):			
4 or more servings per week	59	134	
2-3 servings per week	98	117	
1 or none per week	148	51	<0.05

From table 3, more women in the hospital-based control group consumed fruits and vegetables 5 or more servings per day (n=161) with less women in the breast cancer group consuming the same amount (n=106).

Olives and olive oil was highly consumed in the hospital-based controls group with 49 women consuming 5 or more servings per day and 41 women in the breast cancer cases group. The number of women not consuming olives and olive oil increased in the breast cancer cases group while the reverse was the case in the hospital-based control group.

83 breast cancer cases consumed 2 or more servings per week of fish while 160 hospital-based controls consumed the same amount. 119 breast cancer cases and 132 hospital-based controls consume fish once in a week.

The breast cancer cases that consumed 4 or more servings per week of fresh potatoes were 59 with 134 women observed in the hospital-based control group. 98 and 117 women consumed 2-3 servings per week of fresh potatoes (cooked) in the breast cancer cases and hospital-based control groups respectively.

3-6 eggs and 1-3 eggs were consumed per week by 154 and 50 breast cancer cases respectively, while 225 and 49 women with the same consumption rate were observed in the hospital-based control group.

Table 4. The logistic regression analysis of food intake frequency of the study group.

Diets	B	Sig.	OR	95% C.I		
				Lower	Upper	(P%)
1.Fruits and vegetables						
Never (Ref)		0.00	1.00			
5 or more servings/day	-2.4	0.00	0.09	0.04	0.18	7%
3-4 servings/day	-2.3	0.00	0.10	0.04	0.20	9%
2 times/day	-2.0	0.00	0.12	0.06	0.27	10%
2. Eggs						
Never (Ref)		0.00	1.00			
3-6 /wk	-2.2	0.00	0.10	0.05	0.20	9%
1-3/wk	-2.1	0.00	0.11	0.05	0.25	10%
3.Olives and olive oil						
Never (Ref)		0.00	1.00			
5 or more servings/day	-2.7	0.00	0.06	0.03	0.16	5%
3-4 servings/day	-2.3	0.00	0.10	0.04	0.21	8%
2 servings/day	-1.9	0.00	0.16	0.08	0.32	13%
4. Fish						
Never (Ref)		0.00	1.00			
2 servings /wk	-3.1	0.00	0.04	0.02	0.10	3%
1 serving/wk	-2.7	0.00	0.06	0.03	0.15	5%
5.Fresh potatoes (cooked)						
Never (Ref)		0.00	1.00			
4 or more servings/wk	-1.9	0.00	0.15	0.08	0.28	13%
2-3 servings/wk	-1.7	0.00	0.18	0.10	0.33	15%

A multivariable logistic regression model was used to analyze the food intake frequency, the least frequency of intake was used as the reference. table 4. The omnibus test's of models coefficients was significant ($p < 0.05$). Cox and Snell $R^2 = 0.442$ and Nagelkerke $R^2 = 0.590$. The Hosmer and Lemeshow test was also significant ($p < 0.05$). From the regression analysis the intake of fruits and vegetables 5 or more servings/week and 2 servings/week had an OR=0.09 and 0.12 respectively. The OR=0.10 and 0.11 was observed for the intake of 3-6 eggs/week and 1-3 eggs/week respectively. Olives and olive oil intake 5 or more servings/week was 0.06, while the OR of 1 serving of fish/week was 0.06, Intake of 2 servings/week of fish OR=0.04. Fresh potatoes 4 or more servings/week OR=0.15.

The percentage Probabilities (P) of breast cancer linked to each dietary category was calculated as $P = \text{Exp}(B) / (1 + \text{Exp}(B)) * 100$ and represented in the table 4.

Discussions

Nutrition has long been suggested to impact breast cancer etiology in about 35% of disease cases [3], the sufficient consumption of foods containing the essential nutrients is crucial to the modification of breast cancer risk in women.

The studied foods commonly consumed on the Mediterranean island of North Cyprus, which include, fresh potatoes, Olives and olive oil, fruits and vegetables, eggs, and fish reduced the probability of breast cancer in all the women, proving that they are among the healthiest diets [21]. Interestingly, the intake of fish 2 or 1 times per week followed by 5 or more times of olives and olive oil provided the highest protection in reducing the probability of breast cancer disease in the women.

An inverse relationship with fish intake is linked to the consumption of dietary marine n-3 polyunsaturated unsaturated fatty acids [28].

While an epidemiological and experimental proof recommended that olive oil may decrease the risk of specific tumors, specifically breast cancer [26], this may be due to the high monounsaturated fat content and concentration of poly-phenolic compounds in virgin and extra-virgin olive oil [27].

These are the main wellspring of lipids within the customary Mediterranean diet [49]. According to studies Mediterranean dietary lipids have been shown to impact breast cancer. [29] These Lipids play a significant role in the regulation of biological activity and are important components of the cell membrane [30]. But when the concentration of polyunsaturated lipids in membranes is too high it may lead to an upsurge in fluidity and peroxidation. [31] Thus moderate consumption of these lipids is effective in decreasing oxidation damage in the membranes. The protective effect of the intake of Mediterranean dietary lipids on breast cancer may be through the signaling pathways such as ErbB4-truncated protein, which plays a part in mammary development and breast cancer and Akt pathway linked to apoptosis. [33]

Mediterranean dietary lipids may decrease proliferation via the down surge of epidermal growth factor-2 signaling pathway as Ki-67 has been shown to decrease following the administration of lipids in malignant and benign breast neoplasm. [33,37] Dietary Lipids influence the decrease of factor-kB nuclear translocation and signaling on peroxisome proliferation-activated gamma receptor and through the interaction with the G-protein receptor GPR 120, which reduces apoptosis inhibitors and cytokines adhesion molecules. [42] Dietary lipids from Mediterranean foods are shown to partially and beneficially affect the expression of atherosclerosis-related genes, [32] Tumor suppressor gene p53 expression increased with the intake of fish sourced docosahexaenoic acid (DHA) [43]. Phenolic extracts from Brava extra virgin olive oil minimized cell viability and induced cell death in MCF-7 breast cancer cells [44]. BRCA1 and 2 genes also increased with exposure of breast cells lines to omega-3 polyunsaturated fatty acid (EPA and DHA) from fish [45]. An accompanied decrease in Her-2/neu an oncogene has been seen in BT-474 and SKBr-3 breast cancer cells treated with oleic acid supplements. [46] Dominguez et al observed a 30% lower risk of breast cancer linked to glutathione-S-transferase T1 null genotype in post-menopausal Chinese women living in Singapore after the intake of marine dietary lipids from fish. [47] The benefits were more in post-menopausal women with GST polymorphisms that led to low or no GSTT1, GSTP1 and GSTM1 activity. [47]

To be able to recommend the right nutrition for a given population, it is important to find the dietary intake that incorporates all the nutrients required [22] and when consumed in the right amounts will provide optimum benefits.

The ability of a diet to provide prevention and reduction to diseases that are linked to it determines its nutritional sufficiency [23] and genotype may be determining factor on how these nutrients are made available for body use and function. The frequency of polymorphism differ with ethnicity this interplay needs to be studied to find out how breast cancer can be modified by food intake in relation to genotype [48] in this population. Most societies especially the developing societies can explore the advantages of Mediterranean diets through research that look for diets that are affordable, effective and locally available source of sufficient micronutrients that can reduce the risk of breast cancer.

The long-term control of breast cancer can be achieved, when the association between culture and nutritional selections are considered when making policies because most societies consider food as an essential part of their cultures, religious and social experiences.

Policies and programs that advocate home farms and gardens can lead to the increase availability, affordability and consumption of healthy foods such as potatoes, vegetables, fruits, eggs, fish, and olives in developing societies.

Also encouraging with incentives people to set up neighborhood supermarkets and eateries that sell these foods will improve affordability and availability.

Agricultural subsidies in developing societies for producers of these foods will encourage others to start producing thus reducing cost and increasing availability.

Cultural festivals that promote and protect healthy foods are important in sustaining healthy eating.

Civil society organizations such as farming and fishing cooperatives, religious groups, charitable organizations, women groups, should play a part in public policies creation and implementation.

Transnational food trade with proper regulations will enable the availability of variety of healthy foods coming from across the borders.

Governments of developing societies that want to ensure that nutritional objectives are adhered to in order to improve the well being of their citizens need to carry out school and public education campaigns on diets and engage the food and agriculture sectors [19]. The awareness on the pivotal role of these diets in breast cancer prevention will go a long way in increasing implementation of policies and programs that target the right population.

Our study was carried out in a typical Mediterranean setting and reproducible. The cognitive impairment arising from illness and treatment may influence the answers provided by some breast cancer patients but to overcome this, patients were ensured to be in stable state by qualified medical practitioners before the interviews was conducted.

The case-control study method used has its limitations in the sense that the information collected is subject to recall bias. To minimize this a few food items were used in the food frequency questionnaire and the consumption categories were such that the participants could easily recall. However such bias may not affect the results because the true effect may not be far from what was observed. The completeness of answers to the food items was used as a conformity test. [18]

Despite the limitations considering that the dietary habits of the people of North Cyprus is similar to the traditional Mediterranean diets, an investigation of its effect on breast cancer risk is needed at the very moment because of the increase onset of the disease.

Conclusion

The Mediterranean diet has been shown to confer lots of health benefits and the intake of olives and olive oil 5 or more times daily, and fish 2 times weekly more significantly reduced the risk of breast cancer risk in the women of North Cyprus, the benefits of these foods can only be maximized when the appropriate policies that encourage the intake of healthy diet are established. The protection against breast cancer in comparison with other foods may be genotype related and calls for a need to study on a large scale the interplay between dietary intake in association with the genotype of this population.

Declarations

Conflict of Interest

There is no conflict of interest and no funding was received for the research.

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