RESEARCH ARTICLE

Family History Attributes and Risk Factors for Breast Cancer in Turkey

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Abstract

Background: When dealing with breast cancer, early detection is closely associated with determining and closely monitoring high risk groups. The aim of this study was to determine the preventable risk factors that are specific for our country, and to understand which risk factors were most predominant. Materials and Methods: The study was planned as a case-control design. Women diagnosed with breast cancer who visited the Surgery, Obstetrics and Gynaecology, and Radiation Oncology outpatient clinics of the Izmir Dokuz Eylul University (DEU) School of Medicine were accepted as the case group. Then a control group matched for age was established among females who visited the outpatient clinics on the same days. A questionnaire prepared by the researchers was implemented using a face-to-face interview technique. The Mann-Whitney U test was used in the comparisons of the group averages, and the Pearson chi-square test in the comparisons between groups. In order to determine the dominant risk factors, binary logistical regression test was implemented. Results: A total of 138 patients, 69 cases and 69 controls, were included in the study. A significant difference can be detected between the groups in terms of BMI, smoking, breast cancer prevalence among first degree family members, presence of breast cancer among distant family members, existence of other types of cancers among family members and the age of onset of menopause ($p<0.05$). Logistical regression analysis revealed that the presence of breast cancer among first degree relatives increased the risk of developing breast cancer 5.7 times. Conclusions: Although some results of this study are compatible with findings in the literature, some are not. In order to determine unique risk factors, there is a clear need for large-scale studies.

Keywords: Breast cancer - risk factors - preventive oncology - Turkey

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Introduction

Breast cancer is the most widespread female cancer observed in both developed and developing countries (Breast cancer: prevention and control). It accounts for 37% of the cancer related deaths in females between the ages of 25-64 (Siegel and Jemal, 2011). The lifelong possibility of a woman of medium risk to experience breast cancer is 13% (SEER Cancer Statistics Review). The International Agency for Research on Cancer (IARC) estimated that compared to the 1,150,000 newly diagnosed breast cancer incidents in 2002, there will be 2,500,000 diagnoses in 2020 (IARC Handbooks of Cancer Prevention, 2002; Parkin and Fernandez, 2006). The prevalence of breast cancer shows serious geographical differences. The developed countries have the highest prevalence of breast cancer while the underdeveloped countries in Asia and Africa have the lowest incidence (Porter, 2008).Even though the developing countries have a lower incidence than the developed ones, mortality and annual incidence rates are higher in those countries (Parkin et al., 2005).

When standardized according to age, the incidence ratio is 99.4/100.000 in North America, and 16.5/100.000 in Central Africa. In addition, there are significant increases in the frequency of breast cancer incidences in medium and lower income nations (Porter, 2008). On the other hand the increases in the frequency of breast cancer in other nations show the opposite inclination. The American Cancer Society predicts that 39,620 women will die of breast cancer in 2013. The decrease in the last 20 years as of 2002 can be attributed to the fact that the earlier hormone replacement therapy used as a treatment for menopausal women caused an increase in the risk of heart diseases and. breast cancer, and has since been terminated. Nevertheless, after lung cancer, breast cancer is still the second mortality reason in women (What are the key statistics about breast cancer?).

According to the Turkish Statistics Yearly of 2011, in 2006 and 2007, of the top ten cancer types, breast cancer was the most commonly observed cancer among Turkish women with a ratio of 38 and 36 out of 100,000 women

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respectively (TurkStat in Statistics, 2012).

While the five-year survival percentage for breast cancer victims in developed countries is 83%, it is 53% in developing countries. This significant difference can be due to early detection using mammography scans and the better health care treatments available in the developed countries (Houssami et al., 2012). Early detection is closely associated with determining and closely monitoring the risk groups. However, the risk groups have to be defined clearly in order to be sustainable and cost-effective.

Genetic tendencies, family history, previous incidence of breast cancer, increased Body Mass Index (BMI), diabetes, heavy alcohol consumption (exceeding 45g per day), smoking, thyroid illnesses, radiation effects, socioeconomic factors, education levels, metabolic syndrome, sex hormones are some of the risk factors of breast cancer (Hunter, 2000; Hamajima et al., 2002; Lee, 2003; McTiernan, 2003; Korde et al., 2004; Cannata et al., 2010; Muller et al., 2011; Wong et al., 2011; Gadeyne et al., 2012; Domchek et al., 2013; Esposito et al., 2013; Hartz and He, 2013; Kutanzi and Kovalchuk, 2013; Ogrondik et al., 2013; Pfeiffer et al., 2013; Szychta et al., 2013; Warner et al., 2013).

It is possible that several and various risk factors show differences at national and regional levels. Determining the risks can also enhance the focusing on preventable risk factors. However, a risk factor that may be critical for one nation may have less priority in Turkey (Harman, 2007). Knowledge of the specific risk factors is particularly important for early detection using screening practices in primary care.

The aim of this study was to determine the preventable risk factors that are specific for our country, and to understand which risk factor was more predominant.

Materials and Methods

The study was planned as the case-control design. The women diagnosed with breast cancer who visited the Surgery. Obstetrics and Gynaecology. and Radiation Oncology outpatient clinics of the Izmir Dokuz Eylul University (DEU) School of Medicine were accepted as the case group. The sample size was calculated considering p: 85%. OR: 3.5% standard error and 10% prevalence. The control/case ratio was estimated to be 1/1 with 67 in the case. and 67 in the control group. Since the sample was for women. the matching was made according to age. Using this framework. the breast cancer patients above the age of 18. and based on the voluntary principle. who visited the forementioned outpatient clinics on Mondays and Thursdays between February and April, 2013, were included in the group. Then a control group matched for age was established among the females who visited the outpatient clinics on the same days. A questionnaire prepared by the researchers was implemented using the face-to-face interview technique. In addition to demographic data. questions were asked to determine the risk factors of breast cancer.

Based on the World Health Organization, the Body Mass Index criteria is calculated according to the division of the measurements of the weight in kilograms with the height in square meters and classifies low weight as (<18.50), normal (18.50-24.99), overweight (25.00-29.99), and obese as (≥30.00). Since physical activity is a compound behavior, it also incorporates type, intensity, frequency and duration. Thus, it is necessary to reach a correct assumption because development corresponds directly to exercise intensity. This can be accomplished with metabolic equivalents (METs). In this study, the state of exercise was calculated as METs calculations and analyzed accordingly. Based on this, <40 METs was considered light, 40-90 METs moderate and >90 METs was considered heavy exercise.

Ethical commission approval was obtained from the Non-Interventional Scientific Research Ethical Committee of the Izmir Dokuz Eylul University School of Medicine.

The statistical evaluation of the data was done by using the Windows program: Statistical Package for Social Sciences (SPSS) Version 15.0. The Mann-Whitney U test was used in the comparisons of the group averages. and the Pearson chi-square test was used in the comparisons between the groups. In order to determine the dominant risk factor. the binary logistical regression test was implemented. In addition. while the existence of breast cancer was a dependent variable. other statistically significant variables indicated according to the chi-square test results were classified as independent variables. A p value of <0.05 was accepted as statistically significant.

In the model implemented for logistical regression, different variables such as breast cancer diagnoses in first degree family members, diabetes mellitus diagnoses, age of menopause onset, BMI, breast cancer diagnoses in distant family members, and the presence of cancers other than breast cancer among family members were used. These variables were chosen either due to their consideration as risk factors in the literature or due to p values that shows statistically significant difference between the groups (they were implemented first as "enter'', then "backward''). In the study group, the presence of breast cancer among first degree family members, the diagnoses of diabetes mellitus, and the presence of cancers other than breast cancer among family members were found to be statistically significant (Table 3).

Results

A total of 138 patients: 69 case and 69 controls, were included in the study. The median age of the patients was 55.0±11.3. The case and control groups' age averages were 55.8±11.5 and 54.1±11.1 respectively. No statistically significant difference was observed between the two groups (t=0.886, p=0.377). Various characteristics such as the ages, educational background, and presence of co-morbid diseases of both the case and control groups are presented in Table 1.

When the risk factors of the two groups are taken into consideration, a significant difference can be detected between the groups in terms of BMI, smoking, breast cancer prevalence among first degree family members, the presence of breast cancer among distant family members, the existence of other types of cancers among family

members and the age of onset of menopause (p<0.05). However, no significant differences were observed regarding alcohol consumption, age of first menstruation, age of first pregnancy, and the age of last pregnancy (p>0.05). These data are provided in Table 2. Moreover, no significant differences were detected in terms of the presence of other cancers among family members in terms of their types or the sex of the members.

Table 1. The Demographic Characteristics of the Participants

		Has breast cancer		Doesn't have breast cancer		p
		n	%	n	%	
Age	≤39	4	5.8	6	8.7	
	40-49	17	24.6	16	23.2	0.146
	50-59	23	33.3	32	46.4	
	60-69	18	26.1	7	10.1	
	≥70	7	10.1	8	11.6	
Education	Illiterate	10	14.5	6	8.7	
(At most)	Primary School	28	40.6	20	29.0	
	Middle School	6	8.7	8	11.6	0.261
	High School	14	20.3	15	21.7	
	Higher Education	11	15.9	20	29.0	
Chronic diseases	Prevalent	39	52.0	36	48.0	0.608
	Not prevalent	30	47.6	33	52.4	

The logistical regression analysis to evaluate the effectiveness degree of the risk factors which were found to be statistically significant indicated that the presence of breast cancer among first degree relatives increased the risk of developing breast cancer 5.7 times. A diagnosis of diabetes mellitus increased the risk by 3, and compared to those who did not indicate any prevalence among family members, the presence of other cancers increased the risk of getting breast cancer by 2 (Table 3).

Discussion

In this study, some risk factors were found to be compatible with the literature while different outcomes were observed for other factors.

Table3. Logistic Regression Results

	Exp(B)	%95EXP(B)GA		Sig
		Lower	Upper	
Breastcancerprevalenceinfirst-degreerelatives				
	5.742	1.517	21.741	0.010
DiabetesMellitusdiagnosis				
	3.136	1.280	7.684	0.012
Existenceofothercancersinfamilymembers				
	2.140	1.043	4.390	0.038

Table 2. Risk Factors

		Has breast cancer		Doesn't have breast cancer		p
		n	%	n	%	
BMI	Under 25	13	18.8	28	40.6	0.004*
	>25 or above	56	81.2	41	59.4	
Smoking	Never smoked	44	63.8	38	55.1	0.010*
	Quit smoking	20	29	13	18.8	
	Still smoke	5	7.2	18	26.1	
Alcohol	Doesn't drink	54	78.3	49	71	0.186
	Drinks on special occasions	15	21.7	17	24.6	
	Drink smore than glasses/week	3	0	0	3	4.3
First degree relatives with breast cancer	Prevalent	13	81.3	3	18.8	0.000*
	Not prevalent	56	29.3	135	70.7	
Breast cancer in distant relatives	Prevalent	15	21.7	2	2.9	0.000*
	Not prevalent	54	78.3	67	87.7	
Family members with cancers other than breast cancer	Prevalent	42	60.9	27	39.1	0.002*
	Not prevalent	27	39.1	39	56.5	
Age of first pregnancy	<19	13	18.8	25	36.2	0.061
	20-25	43	62.3	28	40.6	
	>25	9	13.0	12	17.4	
	No pregnancies	4	5.8	4	5.8	
Age of last pregnancy	<25	14	20.3	11	15.9	0.721
	25-35	44	63.8	42	60.9	
	≤35	7	10.1	10	14.5	
	Planning pregnancy	4	5.8	6	8.7	
Age of Menopause	<48	38	55.1	31	44.9	0.027*
	48-52	22	31.9	20	29.0	
	>52	4	5.8	1	1.4	
	Not in menopause	5	7.2	17	24.6	
Age of first menstruation	<11	4	5.8	1	1.4	0.304
	11-13	44	63.8	42	60.9	
	>13	21	30.4	26	37.7	
METs groups	Light exercise	14	20.3	10	14.5	0.047*
	Medium exercise	48	69.6	58	84.1	
	Heavy exercise	7	10.1	1	1.4	
Chronic Illness	Prevalent	39	56.5	36	52.5	0.608
	Not prevalent	30	43.5	33	47.5	
Useofhormonal treatments for birth control	Prevalent	16	53.3	14	46.7	0.680
	Not prevalent	53	49.1	55	50.9	

*A p value of <0.05 was accepted as statistically significant

Age; Unlike the literature, in this study age was not identified as a risk factor. The identification of age as a risk factor is critical in planning screening strategies. Various studies have shown that screening using a mammography is effective in women between the ages of 50 to 70 (Health, 2007; Hall et al., 2013; Tria, 2013).

In this study, the percentage of women 30-49 years old or above 70 who were diagnosed with breast cancer was 40.5%. Therefore, for this reason, research studying the development of different diagnostic methods unique to each age group has gained importance (Devolli-Disha et al., 2009; Health, 2010; Korpraphong et al., 2013).

Family history; The tendency of cancer to run in families has become a critical issue in research and there is ample evidence of familial influences on breast cancer in Turkey (Sezer et al., 2011; Ceber et al., 2013) and elswhere in Asia (Lin et al., 2013; Shamsi et al., 2013). Compatible to the literature, this study also found that the presence of breast cancer among first degree family members is a risk factor. However, the presence of breast cancer among distant family members and/or any other type of cancer in the family was also identified as a risk factor. The relationships between certain cancers prevalent in the family have been shown in some studies. Walsh and his colleagues have shown that the frequency of breast cancer has increased in families where all members have colon cancer (Walsh et al., 2010). In this study, the existence of any cancer in the family, regardless of type, was determined and found to be significantly higher in the case group. However, there was no significant difference between the two groups in terms of cancer types. Therefore, it appears to be crucial for anyone who has family members with any type of cancer to be screened for early detection of cancer and to be monitored closely. The work load involved in such a venture and the problems of labeling necessitate further extensive studies in this field.

General health status and behaviors BMI; An increased BMI has been shown to be a risk factor for breast cancer. Although there are various studies indicating the relationship between hormonal effects or the obesity gene and its direct effects, the mechanism has not yet been understood clearly (da Cunha et al., 2013). BMI was also found to be a risk factor in this study.

Exercise; There are various studies that show that despite the fact that exercise is known to have a protective effect, it is not known what amount of exercise is effective or whether it should be done before or after the onset of menopause (Thune et al., 1997; Lee, Coook et al., 2001; Orio et al., 2013). This study has shown that when comparing the two groups, moderate exercise may be beneficial (p=0.047).

Smoking; Smoking is generally considered to be a risk factor but research in this field has not provided conclusive evidence. For example, Luo et al. (2011) found that the highest risk rates for postmenopausal females with invasive breast cancer were for those who still smoked and those who had started smoking in puberty (Luo et al., 2011). On the other hand, Lynn Rosenberg et.al emphasized that among premenopausal females of African American heritage, active smoking or being exposed to second-hand smoke affected premenopausal estrogen receptor positive females and increased the risk of breast cancer in these women. However, there was no evidence in the same study to indicate whether active or passive smoking increased the risk of breast cancer in postmenopausal women (Rosenberg et al., 2013). In this study, although there seems to be a significant relationship between smoking and breast cancer, it appears to be a protective one. When the results are analyzed in-depth, it is apparent that this is due to the presence of the active smokers. It was observed that many women who were diagnosed with cancer consciously chose to quit while many of the healthy ones continued to smoke.

Alcohol; It is widely accepted that heavy alcohol intake is one of the risk factors in breast cancer (Scoccianti et al., 2013). Even among light drinkers, those who drink one glass of a standard drink every day, there is a slightly increased risk of breast cancer (RR=1.05; 95% CI 1.02-1.08) (Bagnardi et al., 2013). This study did not indicate a significant correlation between alcohol consumption and a diagnosis of breast cancer. This outcome may be due to the fact that the participants in this study consumed alcohol at amounts much lower than those which can be considered "light". Studies have shown that alcohol intake can lead particularly to the development of lobular carcinoma in postmenopausal women (Li et al., 2003; 2010). Since such a result was not observed in this study, it is not possible to explain the reason why alcohol intake was not determined as a risk factor.

Diabetes mellitus; Although there are several studies indicating that compared to hyperglycemia, hyperinsulinemia is more of a risk factor in breast cancer (Onitilo et al., 2014), it has been shown that in meta-analysis, diabetes mellitus is a risk factor (De et al., 2013). It has also been indicated as a factor that increases the risk of breast cancer by 2 among women who do not have other cancers present in their families (Table 3). Still diabetes mellitus is not identified as a risk factor in the Gail method used worldwide or in the American National Cancer Institute guidelines (National Cancer Institute. Breast cancer risk assessment tool). This situation is the basis for the need to evaluate different communities accordingly.

Reproductive functions; Endogenous and exogenous hormones are also cited as important risk factors in breast cancer. It is believed that hormones also have an effect on breast cancer, for example factors such as late menopause, early menstruation, use of oral contraceptives, and postmenopausal hormone replacement therapy etc.; dieting, exercise, alcohol intake, and obesity also affect hormones. Many epidemiological studies completed within this framework have indicated that estrogens have a significant impact on the development of breast cancer in females. In this study, being in menopause or entering menopause at a later age has been indicated to be a risk factor. On the other hand, age of first menstruation, age of first pregnancy, age of last pregnancy, use of oral contraceptives or other hormones were not determined to be risk factors. Nevertheless, even if the fact that reproductive function poses a risk is explained with hormonal mechanisms, neither the interaction nor its relation to age is clear. Thus, it is believed that different studies have varying results. For instance, Althius et.al

showed that while being nullipar ER(+) increases the risk of breast cancer, ER (-) doesn't increase the risk. On the other hand, early menarche is more closely related with tumors ER(+)/PR(+) compared to those with tumors ER(-)/PR(-) (Althuis et al., 2004; Kohut et al., 2012).

Strengths and weaknesses of the study; The incomes of the patients weren't questioned in the survey as it was believed they would reflect patients' perceptions rather than reality. The study was conducted only among patients who applied to the forementioned outpatient clinics of DEU School of Medicine. This fact that this was limited as it did not cover hospitals at other centers did not hinder the study as it is known that the DEU School of Medicine is one of the prominent regional hospitals and therefore the results of the study are found to be indicative and leading. It is interesting that although the outcomes are different from those in the literature, the results which were obtained in this study should be verified using larger sampling sizes.

In conclusion, although some results of this study are compatible with findings in the literature, some are not. In order to determine the unique risk factors, there is a clear need for large-scale studies.

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