Original Article

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The Relationship Between Breast Cancer and Risk Factors: A Single-Center Study

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ABSTRACT

Objective: To determine the relationship between breast cancer and known risk factors in patients who had mammography (MG) for breast cancer screening or ultrasonography and/or MG for diagnostic purposes.

Materials and Methods: In the period of January-December, 2011, a questionnaire composed of 17 questions was applied to 2862 female patients and MG and/or US examination was performed afterwards. Chi-square and Kruskal-Wallis tests were used for statistical analysis.

Results: The mean age was 51.05±8.98, age at menarche was 13.0±1.6 and age at menopause was 47±5.2. The first pregnancy was at 20±4.6. Out of 2862 cases, 242 had breast cancer diagnosis and 32 were newly diagnosed. There was no correlation between menarche age, age at menopause or first pregnancy and breast cancer. There was no relationship between breast cancer risk and hormone replacement therapy or oral contraceptive use. In patients with the diagnosis of breast cancer (242 cases), 61 had (25%) a positive family history. There was a significant correlation between the presence of a positive family history and having breast cancer (p=0.003).

Conclusion: The presence of breast cancer in the family has the strongest relationship among all risk factors. It is important to have regular follow-up of these patients and to raise the awareness of patients.

Keywords: Breast cancer, screening, risk factors

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Introduction

Breast cancer is the most frequently observed type of cancer among women (40.6/100,000) in Turkey (1). According to the national cancer statistics, it has had an increasingly rising incidence in the past decade (1). Today, mammography (MG) is the most effective screening method for the early diagnosis of breast cancer (2, 3).

Hereditary and non-hereditary factors are effective in the etiology of breast cancer. It is accepted that the majority of hereditary breast cancer cases are related to the BRCA1 and BRCA2 mutation (4). Among the non-hereditary factors, the most important factor that contributes to breast cancer is the female sex and age. Age-specific breast cancer incidence increases rapidly starting at the age of 40 (5, 6). The other risk factors include menarche, age at menopause, age at first birth, number of births, breastfeeding, smoking, radiation exposure, oral contraceptive and postmenopausal hormone use, fatty diet and obesity (4, 7, 8).

In our study, the risk factors in cases presenting to the breast screening unit were inquired by means of a survey. The aim of our study is to identify the relationship between cases diagnosed with breast cancer and risk factors.

Materials and Methods

In this retrospective study, 2878 cases that presented to the breast imaging unit for the purposes of breast cancer screening and diagnosis between January, 2011 and December, 2011. The patient information form of 17 questions referring to the risk factors for breast cancer

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Table 1. Breast screening - patient information form

Date:

Name Surname:

Age:

Citizenship ID No:

Educational background: O Primary school O Secondary school O High school O University

Employment status: O Employed O Housewife

Age at menarche: Date of the last menstrual period:

Age at first pregnancy: Age at menopause:

Number of live births: The longest breastfeeding duration:

Have you ever used contraceptive pills? (Trademark and duration):

Did you take hormones during the menopause period? (Trademark and duration):

If you have any disorders or a diagnosed disease, please specify:

If there is a medicine that you regularly, please specify its name and duration of use:

Please specify if you have diagnosed cancer involving an organ:

What is Your Reason to Present for Mammography?

O I have no complaints; I am here only for control purposes (for screening).

O I have a breast-related complaint (you can mark multiple options):

Palpable mass-gland: O Right O Left

Pain in breast: O Right O Left

Discharge from the nipple: O Right O Left

Nipple shrinkage: O Right O Left

Skin thickening-shrinkage: O Right O Left

Mass in the armpit: O Right O Left

Other:.....

Have you ever had mammography scans?: O Yes O No

Have you ever undergone breast ultrasonography?: O Yes O No

Have you ever had breast surgery or breast biopsy?: O Yes O No

X-ray therapy: O Yes O No

Chemotherapy: O Yes O No

Has Breast Cancer Been Detected in Any of Your Close Relatives?

O No

O Yes (please mark the relationship degree)

O Mother O Maternal Aunt O Sister O Father O Paternal Aunt O Grandmother

O Other:.....

RESULT: BI-RADS- (0) (1) (2) (3) (4) (5) (6)

was applied before the study upon consent by patients (Table 1). 16 cases were excluded from the study due to omissions in the survey form and the study was completed with 2862 cases.

All the cases that presented to the imaging unit for diagnosis and screening purposes were included in our study. The screening was opportunitic in type and included female cases that presented at their own will or were referred by the clinician. As for the diagnostic group, it was composed of patients who had breast-related symptoms or follow-up patients diagnosed with breast cancer. All the cases were included in the study towards the aim of creating a more homogeneous group.

The patient information form included the socio-demographic and personal information (age, educational level, civil state, number of children had, family and personal history of breast cancer, breastfeeding, menarche, menopause, etc.). The information requested the form was filled in by 2 members of staff at the department before the study in a 'question and answer' format. The cases that were not willing to answer the questions were excluded from the study. The patient information form was completed by the participants in approximately 5-10 minutes. The cases received mammography and/or ultrasonography imaging studies after the survey. The examination results were categorized according to the BI-RADS classification. The cases with known breast cancer and newly diagnosed cases were compared with cases not identified to have cancer in terms of risk factors.

For statistical analysis, the Chi-square and Kruskal-Wallis tests were used. The statistical significance was considered to be as p≤0.05. The study was approved by the Ethics Committee of the Ankara Numune Hospital. The study meets the standards of the Helsinki Declaration. All the participants were informed using an informed consent form.

Results

The average age of our cases was 51.05±8.98, average at menarche 13.0±1.6, average age at menopause 47±5.2 and average age at pregnancy 20±4.6 years (Table 2).

It was determined that 68.2% of the cases (n=1952) that presented to our clinic for diagnostic and screening previously received MG studies and 30.6% of the cases (n=861) were about to have their first MG study. The most frequent symptoms at diagnosis were mastalgia with %23.3 (n=655) and palpable mass with %16.5 (n= 464).

83.9% of the cases (n=2360) had previous breast-related biopsy procedure and 11% (n=311) had breast-related surgery.

Out of the 2862 cases, 242 were patients diagnosed with breast cancer. 210 of them were cases in the follow-up period for breast cancer and 32 patients were newly diagnosed bresat cancer cases. In the group that did not have breast cancer, the average age at menarche was found to be 13.0±1.6, average age at menopause 47±5.1 and the age at first pregnancy 20±4.5 (Table 2). Among the cases diagnosed with breast cancer, the average age at menarche was found to be 14±1.5, average at menopause 48.5±5.4 and average age at first pregnancy 21±4.8. As a result of the statistical analysis, no relationship was identified among the age at menarche, age at menopause, age at first pregnancy and breast cancer (p=0.67, p=0.61, p=0.70).

When the intervals between the age at menarche and age at menopause was examined, this period was measured at 32.9±5.9 years for the breast cancer cases and at 32.7±5.3 years for the non-patient group. No statistically significant relationship was identified (p=0.99).

Table 2. Distribution of patients with and without breast cancer according to demographic and reproductive factors

Variables	Breast cancer cases (%)	Non-breast cancer cases (%)	All patients
Age	51.1±6.7	49.5±7.8	51.05±8.98
Age at menarche	14±1.5	13.0 ±1.6	13.0±1.6
Age at menopause	48.5±5.4	47±5.1	47±5.2
Age at first pregnancy	21±4.8	20±4.5	20±4.6
Breastfeeding			
Yes	211	2356	2567
No	31	264	295
OCS use	50	503	553
HRT use	15	177	192

HRT: hormone replacement therapy; OCS: oral contraceptive

When examination was made regarding breastfeeding, it was identified that 295 (11.4%) cases never breastfed and 31 (1.1%) of those were cases diganosed with breast cancer. The breastfeeding periods of women that breastfed were assessed and it was determined that 45% breastfest for more than 12 years, 22.7% for 6-12 months and 20% for 0-6 months. Regarding the distribution of breastfeeding women diagnosed with breast cancer, it was found that 47.1% breastfed for more than 12 months, 24.7% for 6-12 months and 15.2% for 0-6 months. As a result of the statistical analysis, no relationship was identified between the presence and duration of breastfeeding and breast cancer. (p=0.39, p=0.6)

With respect to the use of oral contraceptives and hormone replacement therapies, it was seen that 553 (20.2%) of all the cases used OCS and 192 (7%) used hormone replacement therapy (HRT) in one period of their lives. The number of people diagnosed with breast cancer who took OCS was 50 (9%) and those who used HRT was 15 (7.8%). As a result of the statistical analysis, the use of OCS and HRT was not identified to be associated with breast cancer (p=0.39, p=0.6, respectively).

When the presence of breast cancer in family was assessed, it was seen that 575 (20%) of the cases had history of breast cancer in their family. Out of 242 cases diagnosed with breast cancer, 61 (25%) had family history. Family history was present most frequently in the sister (n=17) and the mother (n=12). A statistically signifcant relationship was identified between the presence of breast cancer in family and having breast cancer (p=0.003).

When the presence of endometrium, ovary and gastrointestinal system cancer genetically associated with breast cancer was assessed, it was identified that 2054 patients did not have the types of cancer specified in the family, 220 cases had tumors of gastrointestinal origin, 7 cases ovarian cancer and 43 cases endometrium cancer. In the cases diagnosed with breast cancer, n=25 cancers of GIS origin and n=3 cases associated with endometrium cancer were identified. A statistically significant relationship between the presence of non-breast cancer in family and breast cancer was identified (p=0.07).

Discussion

Family history of breast cancer is a very important factor. Approximately 3-10% of breast cancer cases are hereditary cancers. It is stated

that approximately 85% of them are associated with BRCA1 and BRCA2 mutations (9). In breast cancer, the relationship degree of the family member that has history of breast cancer and the start date of the disease are important (10, 11). A women who lives until the age of eighthy has a cancer incidence of 7.8% if she has no 1. degree relatives with breast cancer while the risk goes up to 13.3% if one 1. degree relative has breast cancer and to 21.1% if two 2. degree relatives have cancer (12). Similarly, our study also found a significant relationship between the presence of family history and breast cancer. In 20% of all the cases and in 25% of those with breast cancer had positive family history. Those who had family history of breast cancer, it was present most frequently in their sister (n=17) and mother (n=12).

An early age of first menarche and a late age of menopause increase the risk of developing breast and endometrium cancer. It is estimated that every year of delay after the age of 12 reduces the premanopausal breast cancer risk by 7% and postmenopausal cancer by 3% (13, 14). Women with a menopause age of 55 have 2 times higher risk for developing breast cancer as compared to those with a menopause age of 45 (15, 16). In our study, the average age at menarche of cases diagnosed with breast cancer was found to be 14±1.5, the average at menopause 48.5±5.4, the age at menarche of the non-breast cancer group 13.0±1.6 and the average age at menopause 47±5.1. There were no statistically significant differences between the two groups.

The relationship between breastfeeding and breast cancer is controversial. An analysis conducted on this subject spanning 30 countries, 47 epidemiological studies, 50302 breast cancer and 96973 non-breast cancer patients demonstrated that breastfeeding for 12 months decreased the risk for breast cancer by 4.3% (8). A study with meta-analysis and case control encompassing four cohort studies reported that every act of breastfeeding for 5 months reduced cancer risk by 2% (17). On the other hand, Stuebe et al. identified breast cancer in 608 out of 60.705 cases that they followed during the period of 1997-2005. They did not identify any significant relationship between premenopausal breast cancer and breastfeeding then they assessed the duration and intensity of breastfeeding (18). Similarly, in our study, no relationships were identified in terms of the presence and duration of breastfeeding when cancer cases were compared with the non-patient group.

The relationship between oral contraceptives and breast cancer is controversial. In the year 1996, a study that reviewed 53297 breast cancer patients and 100239 non-breast cancer patients reported that 40% of the patients took OCS at one period of their lives and the use of OCS resulted only in a small increase of risk (relative risk=1.24) for breast cancer (19). They demonstrated that there was no significant difference in the development of breast cancer during 10 years after the discontinuation of oral contraceptive use. Ban and Godellas conducted a recent study where they reported that women taking oral contraceptives had 24% higher risk of developing cancer compared to those who never took them in their lives and that this risk especially materialized during the use of oral contraceptives (11). Westhoff CL did not identify any relationship between oral contraceptives and breast cancer risk in a way similar to our study (12). Changes in the formulation of oral contraceptives overtime, the duration of their use and different oral contraceptive formulation may result in a differentiation of breast cancer risk. In our study, only 9% of cases with breast cancer (n=50) were using OCS. No relationship was identified between the use of OCS and breast cancer. We suggest that the difference may not have been significant since the use of OCS was low.

It is thought that hormone replacement therapy increases the levels of sex hormone in circulation and breast cancer risk (20, 21). However, the relationship between HRT and breast cancer development is complex and heterogeneous. HRT combination and types, age at menopause, age of starting HRT and other breast cancer risk factors are associated with the cancer risk. People of black race, obese women and those with breast tissue of mostly fatty content may benefit from HRT with only minimal breast cancer risk increase. According to the guidelines, the use of HRT for less than 5 years does not change the risk (20). In the study conducted by Bae et al., it was stated that the use of HRT did not change the cancer risk (21). In our study, no relationship was identified between HRT and breast cancer risk (p=0.6). We attribute this to the fact that HRT use rates in our series were low (7% in the entire series).

It is accepted that a great majority of reproductive cancers associated with breast, especially ovarian cancer, are related to genetic mutations. Breast cancer associated with these cancers is seen at a younger age (22). Claus et al. (22) conducted a case-controlled study on 4730 women with breast cancer aged 20-54 and stated that cases with family history of ovarian cancer developed breast cancer at an earlier age than the expected age. In our study, a statistically significant relationship between the presence of non-breast cancer in family and breast cancer was identified (p=0.07). We believe that the reason why this difference, which is very close to statistical significance, arose out of the fact that the number of cases in our series was not adequate. On the other hand, all the cancer types in the family were inquired jointly and no sub-group analyses were carried out. We believe that this association can be demonstrated through more detailed studies.

The fundamental limitation of our study is that the cases included in the study were not cases that participated in the general community screening, but were cases that presented to our hospital for opportunistic screening or diagnostic purpose mostly upon clinician's referral. There may be statistical differences between general community screening cases and cases that present to the hospital. The other limitation is the limited number of cases included in the study. Studies with larger series are needed to be able to more clearly identify the risk factors pertaining to the community in Turkey.

Conclusion

In our study, the presence of breast cancer in family was found to be the most important risk factor among the risk factors for breast cancer. Performing regular follow-ups on this group and raising the awareness of patients gain importance in early diagnosis and therapeutic efficacy for breast cancer.

Ethics Committee Approval: Ethics committee approval was received for this study from Ankara Numune Hospital.

Informed Consent: Informed consent was obtained from patients who participated in this study.

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