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Breast Cancer Risk Factors: A Case-Control Study in Iranian Women

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Abstract

Background: Breast cancer is the most frequent malignancy and the leading cause of cancer-related death among women all around the world. In Iran, the mean age of the patients is approximately 10 years younger than that in other countries. We conducted the present study to assess the risk factors of breast cancer among Iranian women in Mashhad.

Method: This case-control study was carried out between February 2016 and January 2018 on 460 women (230 cases and 230 controls) in the academic hospitals of Mashhad. The data from our cases and controls were collected and analyzed using SPSS version 18.0 software (SPSS Inc., Chicago, IL, USA). We employed logistic regression models and frequency tables to estimate odds ratio (OR) and to examine the predictive effect of each factor on breast cancer risk. $P < 0.05$ was considered to be significant.

Results: According to multivariate analysis, there was significant associations between breast cancer risk and body mass index (BMI) (Odds ratio (OR), 1.1; 95% Confidence interval (CI), 1.0-1.2), age at menarche (OR, 0.56; 95% CI, 0.47-0.68), menopausal age (OR, 1.1; 95% CI, 1.0-1.1), family history of non-breast malignancies (OR, 7.9; 95% CI, 2.2-21.1), and oral contraception pills (OR, 3.1; 95% CI, 8.34-1.16).

Conclusion: This study revealed that age at menarche, family history of non-breast cancer malignancies, BMI, menopausal age, and oral contraception pills were significantly associated with breast cancer.

Keywords: Breast neoplasm, Risk factors, Incidence

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Introduction

Breast cancer is the most prevalent malignancy and the leading cause of cancer-associated death among women in the world.[1, 2] Approximately 1.7 million new cases of breast cancer were diagnosed in 2012 and an estimated of 521,900 deaths occurred worldwide.[3] Since 2006, the incidence rate of breast cancer is on a rising trend, which might be a consequence of obesity and declining parity.[2,4,5] Among young women, aged 20 to 59 years, breast cancer is the main reason for cancer death.[4] Moreover, the higher rate of psychological distress in breast cancer patients could affect the quality of life.[6]

In Iran, breast malignancy is an important health issue in which the mean age of the patients is approximately 10 years younger than their western peers.[7,8] The factors causing this rapid rise among young Iranian women are not fully known; however, exploring breast cancer-associated risk factors may provide some clues.

Many breast cancer risk factors have been introduced to date, proven, controversial or even disproved.[9] Only less than 10% of breast cancers could be assigned to an inherited genetic mutation.[10,11] More commonly, breast cancer is related to environmental factors, some of which are potentially modifiable, including lifestyle, alcohol consumption, obesity, smoking, exogenous hormones, aging, nulliparity, breastfeeding, early age at menarche, late menopause, first full-term pregnancy, and insulin resistance.[12]

The recent remarkable decline in breast cancer mortality rate showed that effective and well-planed measures were taken in early detection and treatment of this malignancy.[13,14] However, the increasing incidence of breast cancer at an average rate of 0.4% per year may propose that not a significant progress has been achieved in the breast cancer prevention domain.[2] Therefore, conducting studies regarding the prevention of this malignancy, illustrating risk factors, and predicting the women who are at increased risk, particularly in areas with an increasing incidence trend, would be beneficial. In this context, the current study aimed to identify the risk factors of breast cancer among Iranian women in Khorasan province.

Methods and Materials

This case-control study was conducted between February 2016 and January 2018 on 460 women (230 cases and 230 controls), at Omid and Imam Reza Hospitals in Mashhad; these hospitals are the academic hospitals in east of Iran, which offer cancer screening and treatment services. Based on the data from a study by Montazeri and colleagues,[15] with a 95% confidence interval and 80% power, this trial sample size comprised 230 subjects in each group.

All the cases were women with pathologically confirmed breast cancer with the treatment record in Imam Reza or Omid Hospitals. All the controls were the patient's neighbors of equal age, sex, and socioeconomic status, who were free of any cancer, based on national cancer screening programs. The subjects with incomplete data on their records and those unwilling to participate in the study were excluded. All the participants provided oral and written informed consent. The ethical approval was obtained from the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.sm.rec.1394.299).

The data were collected directly interviewing with the cases and controls or making phone calls in order to complete the checklist. The checklist was developed based on the recent studies which have focused on well-known risk factors of breast cancer, including the following variables: age, residency, ethnicity, occupation, height and weight (body mass index(BMI), marital status, contraception method, number of children, number of pregnancies and abortions, breastfeeding duration, age at the first full term pregnancy, age at menarche, and menopause. In addition, history of previous diseases or radiation therapy, previous mammography, family history of cancer, alcohol consumption, tobacco usage or addiction, and drug history were also included.

Residency was categorized as urban and rural. Ethnicity was categorized as six major ethnic groups of the country. The women were defined

Table1. Sociodemographic characteristic of the participants

	Case Group (n=230)	Control Group (n=230)	*P*-Value	Total (n:460)
Age (years)				
(mean ± SD*)	49.4±10.2	48.3±10.6	0.16	
Residency n (%)			0.26	
Urban	187 (81.3)	196 (85.5)		383 (83.2)
Rural	43 (18.7)	34 (14.8)		68 (16.7)
Ethnic group n (%)			0.73	
Turkman	9 (3.9)	15 (6.5)		24 (5.2)
Fars	180 (78.3)	170 (73.9)		350 (76.0)
Turk	25 (10.9)	25 (10.9)		50 (10.8)
Sistani	6 (2.6)	8 (3.5)		14 (3.0)
Kurd	7 (3.0)	10 (4.3)		17 (3.6)
Baluch	3 (1.3)	2 (0.9)		5 (0.0)
Marital Status n (%)			0.001	
Married	195 (84.8)	192 (83.5)		387 (84.1)
Single	1 (0.4)	22 (9.6)		23 (5.0)
Divorced / widowed	34 (14.8)	16 (7.0)		50 (10.8)
Occupation n (%)			0.001	
Housewife	176 (76.5)	142 (61.7)		318 (69.1)
Employee	36 (15.7)	52 (22.6)		74 (16.0)
Labor Worker	14 (6.1)	12 (5.2)		26 (5.6)
Farmer	2 (0.4)	4 (0.3)		6 (1.3)
Other	2 (0.4)	20 (8.7)		24 (5.2)
Education n (%)			0.001	
Illiterate	60 (26.0)	26 (11.3)		86 (18.6)
< High school diploma	86 (37.3)	62 (27.0)		113 (24.5)
High school diploma	51 (22.1)	68 (29.8)		119 (25.8)
Associate Degree	15 (6.5)	34 (14.8)		49 (10.6)
≥ Bachelor Degree	16 (7.0)	40 (17.4)		56 (12.1)
Smoking n (%)			0.07	
Yes	36 (15.7)	23 (10)		59 (12.8)
No	194 (84.3)	207 (90)		401 (87.1)
Passive smoker n (%)			0.01	
Yes	87 (37.8)	63 (28.4)		150 (32.6)
No	143 (62.2)	167 (72.6)		310 (67.3)
Addiction n (%)			0.09	
Yes	20 (8.7)	11 (4.8)		31 (6.7)
No	210 (91.3)	219 (95.2)		429 (93.2)

*SD: Standard deviation

as postmenopausal if they did not have menstrual periods within the previous 12 months or had bilateral oophorectomy. Menarche was defined as the initial occurrence of menstrual period of the individual.

We collected and analyzed the data of the cases and controls using SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). Logistic regression analysis was also performed to eliminate the role of confounding factors.

Continuous and categorical data are reported as mean±standard deviation (SD) and percentages, respectively. In order to compare the frequency distribution of categorical variables between various groups of the cases and controls, we utilized Pearson chi-square tests and to compare the mean values for the continuous variables, we employed t-tests or its equivalent non-parametric test. Logistic regression models and frequency tables were used to estimate odds ratio (OR) and to examine the predictive effect of each factor on breast cancer risk. $P < 0.05$ was considered

Table 2. Non-reproductive variables distribution in the participants

Factor	Case Group	Control Group	*P*-Value
Weight (Mean±SD*)	69.3±13.2	64.4±9.2	0.001
Height (Mean±SD)	159.3±7.3	160.9±5.4	0.01
BMI (Mean±SD)	27.5±6.2	24.8±3.2	0.001
NSAID use n (%)			0.26
Yes	23 (10.1)	31 (13.5)	
No	205 (89.9)	199 (86.5)	
Hormonal medicine n (%)			0.001
Yes	119 (52.2)	49 (21.3)	
No	109 (47.8)	181 (78.8)	
1° family History of breast cancer n (%)			0.74
Yes	22 (9.6)	20 (8.7)	
No	208 (90.4)	210 (91.3)	
2° family History of breast cancer n (%)			0.1
Yes	16 (7)	26 (11.3)	
No	214 (93)	204 (88.7)	
Family History of other Cancers n (%)			0.001
Yes	84 (36.5)	35 (15.2)	
No	146 (63.5)	204 (84.8)	
Breast mass History n (%)			0.11
Yes	22 (9.6)	13 (5.7)	
No	208 (90.4)	217 (94.3)	
Breast biopsy\surgery n (%)			0.79
Yes	8 (3.5)	7 (3)	
No	222 (96.5)	223 (97)	
Head\Neck radiotherapy n (%)			0.41
Yes	2 (0.9)	4 (17)	
No	228 (99.1)	226 (98.3)	
Mammography n (%)			0.001
Yes	115 (50)	179 (78)	
No	115 (50)	61 (22)	

*SD: Standard deviation; BMI: Body mass index

to be significant.

Results

In general, the study population was 460 women, including 230 breast cancer cases and 230 controls. All of the cases and controls were female whose mean ages were 49.4 ± 10.2 years in the case group and 48.3 ± 10.6 years in the control group. Table 1 represents the socio-demographic characteristics of the cases and controls.

There were no significant differences between the cases and controls in terms of age, residency, ethnic group, smoking, and addiction, as is shown in table 1. However, marital status, occupation, education level, and passive smoking were statistically different between the two groups (P<0.05).

Between the smoker cases and the controls, there were no statistical differences in terms of the number of years they smoked (P= 0.18). Passive smoking found to be significantly different between the groups (P= 0.01) with 95% confidence interval (CI): 1.08-2.4, OR: 1.6, as indicated in table 1. Moreover, the duration of being a passive smoker was statistically different between the groups (P=0.001).

Addiction and duration of addiction were not significantly different between the groups (P= 0.09, P = 0.4, respectively). The addiction period was < 5 years in 5 cases (35%) and 5 controls (45.5%), between 6 to 10 years in 10 cases (5.5%) and 3 controls (27.3%), and over 10 years in 3 cases (11.1%) and 1 control (9.1%).

Table 2 illustrates the non-reproductive factors distribution and their association with breast

Table3. The reproductive variables distribution in the participants

Factor	Case Group	Control Group	*P*-Value
Gravidity (Mean±SD*)	3.7±2.3	2.7±1.7	0.001
Number of children (Mean±SD)	3.0±1.8	2.4±1.4	0.001
Number of abortions (Mean±SD)	0.4±0.6	0.2±0.5	0.001
Number of stillbirths (Mean±SD)	0.5±0.3	0.0±0.2	0.71
Age at first pregnancy (years) (Mean±SD)	21.2±5.7	22.3±4.1	0.02
Breastfeeding duration (mouths) (Mean±SD)	18.1±7.8	19.1±7.5	0.18
Menopausal status n (%)			0.001
Age at menopause (year) (Mean±SD)	46.5±5.8	45.5±4.7	0.09
Age at menarche (year) (Mean±SD)	13.4±1.9	15.9±2.9	0.001
Age at first Pregnancy (year) (Mean±SD)	21.2±5.7	22.3±4.1	0.02
Contraception method n (%)			0.001
Fertility awareness methods	91 (40.5)	105 (48.5)	
Contraceptive pills	75 (33.5)	30 (13.8)	
Intrauterine device	4 (1.8)	29 (13.3)	
Condom	10 (4.5)	17 (7.9)	
Tubal ligation	6 (2.7)	2 (0.9)	
Combination of these methods	38 (17)	34 (15.6)	

*SD: Standard Deviation

cancer using univariate analysis. There were no significant differences between the cases and controls in view of NSAID consumption (P = 0.26), personal history of benign breast mass (P = 0.11), breast surgery or biopsy (P = 0.79), and history of breast cancer in first-degree or second-degree family (P = 0.74 and 0.1, respectively).

There was a positive history of hormonal medicine use in 119 (52.2%) women in the case group and 49 (21.3%) women of the control group, which was statistically different (P = 0.001). In addition, weight, height, BMI, and mammography history were significantly different between the groups (P = 0.001, 0.01, 0.001, and 0.001, respectively). The non-breast cancers family history was positive in 84 women (36.5%) of the cases and 35 women (15.2%) of the controls, which reached statistical significance (P = 0.001, 95% CI: 2.04-5.02, OR: 3.2).

Table 3 introduces the reproductive factors distribution and their association with breast cancer using univariate analysis. No statistical differences were found in parity, number of stillbirths, breastfeeding duration, and age at menopause (P > 0.05).

However, gravidity (P = 0.001), number of children (P = 0.001), number of abortions (P = 0.001), age at first pregnancy (P = 0.02), menopausal status (P = 0.001), age at menarche (P = 0.001), and the contraception method (P = 0.001) were significantly different between the cases and controls.

The contraception method found to be statistically different between the case and control groups (P = 0.001). This methods included fertility awareness methods (n: 91, 40.5% vs. n: 105, 48.5%), oral contraceptive pills (n: 75, 33.5% vs. n: 30, 13.8%), physical barrier (n: 10, 4.5% vs. n: 17, 7.9%), intrauterine device (IUD) (n: 4, 1.8% vs. n: 29, 13.3%), tubal ligation (n: 6, 2.7% vs. n: 2, 0.9%), and a combination of contraceptive methods (n: 38, 17% vs. n: 34, 15.6%).

Table 4 shows that following multivariate logistic regression analysis, a significant association was observed between the risk of breast cancer and menarche age (OR: 0.56, 95% CI: 0.47-0.68), family history of non-breast cancers (OR: 7.9, 95% CI: 2.2-21.1), BMI (OR: 1.1, 95% CI: 1.0-1.2), age at menopause (OR: 1.1, 95% CI: 1.0-1.1), and the contraception method. Accordingly, for each one-year increase in menarche age, the breast cancer risk increased 0.5 times and for each one-unit (Kg/m2) increase in BMI, this risk augmented 1.1 times. Using oral contraceptives rather than fertility awareness methods, would increase the risk of breast cancer 3.1 times (OR: 3.1, 95% CI: 8.34-1.16).

Table 4. Logistic regression analysis model for breast cancer risk factors

Factor	*P*-value	OR	95% CI	
			Lower	Upper
Age at menarche	0.001	0.56	0.47	0.68
Family history of other Cancers	0.001	7.94	2.26	21.13
BMI*	0.02	1.14	1.02	1.27
Age at menopause	0.01	1.1	1.01	1.19
Contraception (fertility awareness)	0.01	-	-	-
Contraception (OCP)	0.02	3.10	1.16	8.34
Contraception (Condom)	0.63	0.65	0.11	3.86
Contraception (IUD)**	0.09	0.30	0.07	1.20

*Body Mass Index; ** Intrauterine Device; OR: Odds ratio; CI: Confidence interval

Discussion

The results obtained from regression analysis indicated a significant difference between the two groups regarding the age at menarche, family history of non- breast cancers, BMI, menopausal age, and the methods of contraception. According to this study, these factors should be considered as the risk factors for breast cancer.

Age is one of the best-known breast cancer risk factors as with the increase in it, the number of breast cancer cases increases.[16-18] However, in this study, we observed no significant differences between the two groups regarding the age. The mean age of the cases and controls were 49.4 ± 10.2 and 48.3 ± 10.6 years, respectively. This may be due to lower age of breast cancer patients in the current study compared with the previous studies. A recent research has indicated a 25% increase in breast cancer risk among overweight, obese individuals and those with a sedentary lifestyle.[19] The results of the present study are consistent with the above-mentioned research. Moreover, it appears that the risk of breast cancer varies according to the occupation, with the highest risk among military personnel, dentists, and physicians, and the lowest risk among gardeners and farmers.[20] Physical activity seems to have a decisive role in the impact of the occupation on the risk of breast cancer. In this study, we found a significant difference between the two groups in terms of occupation, yet no significant differences were observed between the two groups based on the results of regression analysis along with other variables.

The incidence rate of breast cancer varies widely throughout the world and also depends on geographical regions.[21,22] According to our findings, there were no significant differences between the two groups regarding the place of residence since most of the participants lived in the same urban conditions.

Certain studies have found that married people are more likely to be affected by this cancer; however, in another study single people were regarded as being more prone to develop breast cancer.[23] In this study, marital status was a factor of significant difference between the two groups; however, there were no significant differences on the regression analysis along with other variables.

The protective effects of breastfeeding against breast cancer were controversial in some studies.[24,25] In the present study, breastfeeding did not differ significantly between the two groups, which may be because of the small sample size of the current study. On the other side, regarding the contraceptive methods, there was a significant difference between the cases and controls. The results of the regression analysis showed that the oral contraceptive pill increased the risk of breast cancer about 3.1 times, compared to using condoms. This result is in accordance with the findings of a previous study.[26]

Pregnancy has a protective effect against breast cancer according to certain studies.[27,28] In this study, there were no significant differences between the two groups regarding the parity status and the age of mothers in their first pregnancy based on the results of the regression analysis.

Some studies revealed that breast cancer

correlated significantly with smoking (cigarettes, hookah) and passive smoking.[29] In the present study, there was a significant difference between the two groups regarding passive smoking and the duration of it. However, no significant differences were observed between the two groups in terms of direct smoking. On the other hand, there were no significant differences between the two groups in terms of addiction, smoking, and the duration of smoking based on the regression analysis. This difference might be due to the small number of smokers in the current study.

Early age full-term pregnancies seems to have a protective effect against breast cancer.[30,31] On the contrary, the young age of mothers at their first pregnancy was considered as a risk factor for breast cancer in the current study. However, there were no significant differences between the two groups based on the results from the regression analysis along with the other factors.

Moreover, the results of a study have revealed that early age at menarche and advanced age at menopause are risk factors for developing breast cancer due to boosting the reproductive period among females.[32] In the current study, early age at menarche was recognized as a risk factor for breast cancer, which is in conformity with the results obtained from the regression analysis.

This study had certain limitations, including some cases in the control group who did not have the results of the national breast cancer screening program to evaluate the presence of any lump or malignancies in the breast. Accordingly, they were excluded from the study. Therefore, it is suggested that future studies be designed in different geographical regions in Iran to reach further comprehensive assessments of the breast cancer-associated risk factors.

Conclusion

According to the results of this study, the regression model revealed that lower age at menarche, family history of non-breast cancer malignancies, BMI, higher menopausal age, and contraceptive methods were significantly different between the two groups and should be considered as breast cancer risk factors.

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Conflict of Interest

None declared.

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