RESEARCH COMMUNICATION

Risk Factors of Breast Cancer in North of Iran: A Case-Control in Mazandaran Province

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Abstract

Introduction: Breast cancer is the most common cancer among Iranian women. This study aimed to determine risk factors for breast cancer in the north of Iran. Method: A matched case-control study was conducted in Mazandaran province of Iran in 2004 of 250 biopsy proven cases of breast cancer and 500 neighbor controls that were matched by age within a 3 year period. Statistical analysis was carried out using conditional logistic regression with the backward elimination method and crude and adjusted odds ratios with related 95% CIs were estimated with Stata 8.0 software Results: Multivariate analysis showed that higher education (OR=4.70, 95%CI: 1.71-12.88), late menopause (OR=4.18, 95%CI: 2.54-6.88), history of induced abortion (OR=1.62, 95%CI: 1.13-2.31), positive first-degree family history of breast cancer (OR=3.14, 95%CI: 1.37-7.20), and BMI (OR=1.02, 95%CI: 1.01-1.03) were risk factors for breast cancer. Furthermore, having more episodes of full term pregnancy (OR=0.87, 95%CI: 0.80-0.95), longer duration of breast feeding (OR=0.993, 95%CI: 0.989-0.997) and parity more than 2 were shown to be protective factors. Conclusions: Our study revealed the role of some modifiable determinants of breast cancer that can be focused by public health intervention in the northern community of Iran. Accordingly, the women who have one or more of the following risk factors should take the special attention to risk of breast cancer: obesity, being menopause, positive family history of breast cancer and history of induced abortion. The protective effect of longer duration of breast feeding should be encouraged too.

Keywords: Malignancy - breast - risk factor - Iran

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Introduction

Breast cancer is the most common cause of cancer mortality among all women in the world (Harris et al., 2000) and also the most common cancer among Iranian women by 22.26 percent of women's cancer totally (Center for Disease Management, 2000) and incidence of 18.24 cases per 100,000 population (MOH and ME, 2004). Despite this fact, a few studies have investigated the risk factors of breast cancer in Iran (Ebrahimi et al.,2002;Yavari et al., 2005).

Breast cancer risk factors includes a wide spectrum of risk factors from molecular to social levels, which can be different among communities (Harris et al., 2000) indicating the role of environmental factors and lifestyle at least in some part of breast cancer causality network.

The present study was conducted to determine some risk factors of breast cancer in a northern province of Iran, Mazandaran, which is covered by the cancer registry of Babol Research Station (with ex-name of Caspian Cancer Registry founded by IARC). Mazandaran is located in south coast of Caspian Sea and has a population of about 1,350,000 with breast cancer incidence rate of 16.60 per 100,000 (MOH&ME, 2004).

Subjects and Methods

A matched case-control study was conducted on women living in Mazandaran province in spring and summer of 2004. According to the cancer registry in Babol Research Station (with ex-name of Caspian Cancer Registry) the last 250 biopsy proved cases of breast cancer, regarding the study time, were selected.

Two controls from the neighbors of the cases in the 5th and the 10th households on the right were studied for each case (totally 500 controls). Control group and cases were matched individually based on age within three years interval. Face-to-face interview were conducted by trained female interviewers. If a case was deceased, interview was conducted with one of the informed women of the same family.

Independent variables were education status, being menopause (yes/no), history of induced abortion (yes/no),

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Table 1. Distribution, Crude and Adjusted Odds Ratio and Related 95% Confidence Intervals of Studied Variables

		Cases Mean (SD) n (%)	Controls Mean (SD) n (%)	Crude OR† (95%CI‡)	P value	Adjusted OR (95%CI)	P value
Education level	Illiterate	78 (32.2)	189 (37.8)	1.00		1.00	
	Elementary	76 (30.4)	132 (26.4)	1.56 (0.92-10.1)	0.07	1.54 (0.93-2.57)	0.09
	Middle	24 (9.6)	58 (11.6)	1.25 (0.67-2.33)	0.48	1.19 (0.57-2.46)	0.63
	High school	52 (20.8)	106 (21.2)	1.59 (0.91-2.87)	1.00	1.41 (0.73-2.73)	0.29
	University	20 (8.0)	15 (3.0)	4.89 (2.04-11.7)	<0.001	4.70 (1.71-12.88)	0.003
Age at-menarche	Year	13.12 (1.27)	13.36 (1.25)	3.98 (2.96-6.91)	0.43	NI***	
Irregular-menstruation	Yes	65 (26.0)	112 (22.4)	1.22 (0.85-1.76)	0.27	NI	
	No	185 (74.0)	388 (77.6)				
Menopause	Yes	157 (62.8)	228 (45.6)	3.29 (2.14-5.08)	<0.001	4.18 (2.54-6.88)	<0.001
	No	93 (37.2)	272 (54.4)				
Parity	0	30 (12.0)	29 (5.8)	1		1	
	1	9 (3.6)	21 (4.2)	0.42 (0.16-1.10)	0.07	0.45 (0.15-1.33)	0.15
	2	30 (12.0)	47 (9.4)	0.55 (0.25-1.19)	0.13	0.48 (0.19-1.18)	0.11
	3	36 (14.4)	76 (15.2)	0.35 (0.17-0.73)	0.005	0.32 (0.14-0.74)	0.008
	4	44 (17.6)	72 (14.4)	0.43 (0.21-0.88)	0.02	0.30 (0.13-0.71)	0.006
	5 ≤	101 (40.4)	255 (51.0)	0.25 (0.13-0.51)	<0.001	0.19 (0.08-0.43)	<0.001
Number-of full-term pregnancies	No.	3.77 (2.66)	4.27 (2.56)	0.89 (0.82-0.96)	0.003	0.87 (0.80-0.95)	0.003
Age at first birth	Year	21.47 (4.63)	20.74 (4.27)	1.03 (0.99-1.07)	0.07	1.02 (0.98-1.07)	0.27
Spontaneous abortions	No.	0.25 (0.58)	0.29 (0.67)	0.91 (0.71-1.16)	0.46	NI	
Induced-abortions	No.	0.21 (0.59)	0.14 (0.50)	1.37 (1.00-1.86)	0.04	1.62 (1.13-2.31)	0.008
Duration-of breast feeding	Month	61.57 (56.9)	74.42 (53.6)	0.99 (0.99-0.99)	<0.001	0.99 (0.99-1.00)	0.002
Oral-contraception	Yes	150 (60.0)	289 (57.8)	1.10 (0.79-1.53)	0.54	NI	
	No	100 (40.0)	211 (42.2)				
Duration-of OCP	Month	38.50 (60.1)	62.63 (36.8)	1.00 (0.98-1.00)	0.71	NI	
History-of benign breast disease	Yes	25 (10.0)	40 (8.4)	1.21 (0.74-2.00)	0.43	NI	
	No	225 (90.0)	460 (91.6)				
First-degree relative history of breast cancer	Yes	19 (7.6)	13 (2.6)	2.96 (1.46-5.99)	0.003	3.14 (1.37-7.20)	0.007
	No	231 (92.4)	487 (97.4)				
Smoking	Pack/Year	0.49 (6.1)	0.26 (3.53)	1.01 (0.97-1.04)	0.53	NI	
Body Mass Index	Kg/m2	28.7 (5.2)	28.5 (4.9)	1.01 (0.99-1.02)	0.06	1.02 (1.01-1.03)	0.004
Monthly family income	100.000 Rls	1.17 (1.97)	10.5 (0.13)	1.00 (1.00-1.00)	0.31	NI	

**= Not included in the model

first-degree family history of breast cancer (yes/no), parity, number of full term pregnancies, duration of breast feeding (month), age at first birth (year), age at menarche (year), history of irregular menstruation (yes/no), spontaneous abortion (yes/no), history (yes/no) and duration (month) of using oral contraceptives, personal history of benign breast disease (yes/no), smoking cigarette (yes/no), body mass index (BMI) (kg/m2), and household income (Iranian Rial).

Data analysis was carried out using Stata 8.0. Bivariate and multivariate conditional logistic regression were used to assess the association of breast cancer with independent variables and crude and adjusted odds ratio (OR) and related 95% confidence intervals (CI) were calculated to determine the precision of the estimates. The backward elimination method was applied for multivariate analysis and Wald was the significance test applied for logistic model parameters. Age was included as a covariate in the

logistic model as well. Considering the ethical issues, verbal agreement for interview participation was obtained from all subjects and all personal information was considered confidential.

Results

We studied 250 cases of breast cancer and 500 matched controls. At the study time 14 cases (5.4%) were deceased. Cases were 48.7±11.3 years old ranged from 22 to 80 years and controls were 48.0±11.4 years old ranged from 19 to 77 years. Table 1 indicates the distribution of studied independent variables in case and control groups, crude and adjusted odds ratios and related 95% confidence intervals.

Bivaraite analysis revealed statistically significant risk factors effect of higher education, being in menopause, history of induced abortion and positive first-degree family history of breast cancer and protective effect of higher parity, more full term pregnancy, and longer duration of breast feeding ($P<0.05$). No statistically significant association were observed between breast cancer and the age at menarche, history of irregular menstruation, spontaneous abortion, age at first birth, history and duration of using oral contraceptives, history of benign breast disease, smoking cigarette, body mass index (BMI), and household income ($P>0.05$).

Multivariate analysis showed that higher educational (OR=4.70, 95%CI: 1.71-12.88), being in menopause (OR=4.18, 95%CI: 2.54-6.88), history of induced abortion (OR=1.62, 95%CI: 1.13-2.31), positive first-degree family history of breast cancer (OR=3.14, 95%CI: 1.37-7.20), and BMI (OR=1.02, 95%CI: 1.01-1.03) have been the risk factor of breast cancer. While having more full term pregnancy (OR=0.87, 95%CI: 0.80-0.95), and longer duration of breast feeding (OR=0.993, 95%CI: 0.989-0.997) have been shown to be the protective factors. In addition, women with more than 2 children showed the lower risk of breast cancer. The risk have been decreasing with increasing number of parity compared with no parity as odds ratio related to women with parity 3, 4 and ≥5 have been 0.19, 0.30 and 0.32, respectively ($P<0.05$).

Discussion

In this study higher educational, menopause, history of induced abortion, positive first-degree family history of breast cancer, and BMI have been the risk factor of breast cancer. While having more episodes of full term pregnancy, longer duration of breast feeding and higher parity were recognized as protective factors.

Breast cancer is usually considered as a disease of high socio-economic status (Krieger, 1990). This is concordant with our result regarding educational status; while the household income did show any significant association with breast cancer. We expect the under reporting of income, although it does not seem to have any reason for differences between cases and neighbor controls. More studies are needed to evaluate the effect of income and socio-economic status on breast cancer in Iran.

The controversial effects of oral contraceptives on breast cancer have been studied extensively. For instance, some (Tessaro et al., 2001) have found no significant association between history of oral contraceptives use and breast cancer but other studies have showed an effect (Brinton et al., 1982; Hankinson et al, 1997;Yavari et al., 2005). No association was observed in our study between history and duration of oral contraceptives use and breast cancer.

The relationship between history of benign breast disease and breast malignancy has been determined in different studies (Dongan et al., 2002). We did not observed the same result in our study. This difference can be arisen from the difference in diagnostic methods of benign breast diseases.

There is a dispute about the relationship between smoking cigarettes and breast cancer. For example, positive results were obtained in one study (Baron et al., 1996), but others could not confirm this (Hirayama, 1984; Lawlor et al., 2004). In the present study this relationship was not observed. However, the low frequency of smoking cigarette prevalence in Iranian females is worth noting in this context.

Increase of BMI is considered as an important breast cancer risk factor (Huang et al., 1997; Key et al., 2003) and such relationship was observed in this study too. The separate analysis of women with and without menopause showed the same result.

Family history of breast cancer in different studies shows the increase of breast cancer risk around 2-3 times (Colditz et al., 1993; Eby et al., 1994; Pharoah et al., 1997; Ebrahimi et al., 2002). This relationship was observed in the present study, although multivariate analysis led to wider standard error, still highly significant.

Association of reproductive factors and breast cancer is related to the effect of ovary hormones, which start at the age of puberty, continue with monthly cycles and finish at menopause occurrence (Willett et al., 2002). Several studies have shown that the risk of breast cancer among women had been decreased with increasing of parity (Rosner et al., 1996; Tavani et al., 1999; Russo et al., 2001;Yavari et al., 2002). Some studies have taken into consideration the role of full term delivery as well (Brinton et al., 1983). In the present study, the protective effect of parity and the number of full term delivery on the risk of breast malignancy were observed. We also observed about four times more odds of breast cancer risk in the menopause women, which is concordant with earlier studies (Hsieh et al., 1990; Talamini et al., 1996; Yavari et al, 2005).

Increasing the age at the first birth has been associated with increasing risk of breast cancer (Kelsay et al., 1993; Andrieu et al., 2000;Yavari et al., 2005). In the present study, the odds ratio confirms the previous studies, although it does not show a significant effect.

Breast-feeding can prevent from breast cancer (Romieu et al., 1996). This point was also observed in the present study and by increasing the cumulative breast-feeding duration; the breast cancer proportion has decreased.

Several studies have indicated the protective effect of older age of first menstruation in suffering from breast

cancer because of lower menstruation cycles and related harmonic changes (Apter et al., 1983; Titus-Ernstoff et al., 1998), this effect was not observed in this study.

Although the case-control designs are more feasible to study the etiology of cancers, however, they are subject to incomplete or biased recall. We tried to minimize this bias through assisting the memory of subjects, however it is expected that the breast cancer cases remember the events more precisely due to suffering from illness. The information bias due to non-comparable accuracy in assessing exposure for deceased cases is also expected, although the most informed relatives were selected for the interviews. Because of feasibility constraints, two groups of important variables have not been addressed by our study; genetic mutations and nutritional factors. These clearly need to be recommended for consideration in future studies.

In conclusion, our study revealed roles for some modifiable determinants of breast cancer that can be focused by public health intervention in the northern community of Iran. Accordingly, public awareness should be increased regarding the role of obesity, family history, higher education, menopause, and history of induced abortion and protective effect of more of full term pregnancy, longer duration of breast feeding and higher parity in developing breast cancer. More studies are recommended to explore the determinant of breast cancer in Iran.

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