RESEARCH ARTICLE

Breast Cancer Risk Factors in Women Participating in a Breast Screening Program: a Study on 11,850 Iranian Females

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Abstract

The incidence rate of breast cancer in developed countries is almost three-fold higher than in developing countries. Iran has had one of the lowest incidence rates for breast cancer in the world, but during the recent decades a marked increase has been seen. The purpose of this study was to investigate some established risk factors of breast cancer in Iranian women. A study of 11,850 women participating in abreast screening program was conducted. The 197 women diagnosed with breast cancer and 11,653 healthy women were compared. Logistic regression was performed to investigate associations of reproductive and anthropometric factors with breast cancer risk. Family history of breast cancer (OR=1.94 , 95%CI=1.35-2.78), occupation (OR= 1.65,95%CI=1.20-2.25), education level (OR=0.50,95%CI=0.28-0.91), parity (OR=0.27, 95%CI=0.12-0.59), menopausal status (OR=3.15, 95%CI=2.35-4.21), age at menarche (OR=0.33, 95%CI=0.15-0.70), and age at the first pregnancy (OR=4.10 , 95%CI=1.13-14.77) were related to the risk of breast cancer. Decrease in parity may to some extent explain the rising trend of incidence of breast cancer incidence in Iranian women.

Keywords: Breast neoplasms - risk factors - screening program - epidemiology - Iran

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Introduction

The number of breast cancer cases is growing in developing countries and breast cancer is the most common diagnosed cancer in women with a geographical variation in occurrence (Jemal et al., 2011). Middle East and Asian countries have lowest rates of breast cancer in the world, but the incidence rate has increased during the recent decades (Dey and Soliman, 2010). In Iran, even though the prevalence of breast cancer is lower compared to western countries, it is the most common malignancy among women (Rezaianzadeh et al., 2011). There is an increasing trend for breast cancer mortality in Iran during 1995 to 2004 from 1.40 to 3.52 per 100,000 (Taghavi et al., 2012). In the next decades, Iran will face an upsurge in the incidence of the disease (Dey and Soliman, 2010). The existing information about the etiology of breast cancer is typically derived from the investigations performed in developed countries, while, Iran is a country with different ethnic and cultural groups facing relatively rapid demographic and life style changes. For example, the average number of childbirths per woman dropped from over 7 in the early 1980s (after the Islamic Revolution) to 1.7 in 2007 (Jalal Abbasi-Shavazi and McDonald, 2006). Such demographic changes can affect the pattern of chronic diseases, including breast cancer and thus investigating on breast cancer in developing countries may provide unique information on breast cancer etiology, Nevertheless, due to lack of large epidemiological data, it is hard to recognize the causes of the lower incidence of breast cancer in Iran and Persian Gulf region (Dey and Soliman, 2010). Therefore, we undertook a large study based on the results of breast cancer screening program in 11850 women referring to Shahid Motahhari breast clinic affiliated to Shiraz University of Medical Sciences between 2004 and 2012 to assess some risk factors of breast cancer in Iran.

Materials and Methods

Clinical breast examination was initially performed for all the women participating in the screening program. Then, depending on the physician's decision, they underwent mammography or sonography, fine needle aspiration or biopsy, and surgery in case of indications. For all the women, face-to-face interviews were performed by trained staff using a structured questionnaire to collect information regarding age, height, weight,

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marital status, education level, family history of breast cancer, age at menarche, occupation, parity, past use of oral contraceptives (OC), age at the first pregnancy, and lifetime breastfeeding. Afterwards, the women with pathological confirmation of breast cancer were referred to Motahhari clinic for postoperative care and follow-up.

Statistical analysis

Bivariate analysis and multi-variate logistic regression models were used to estimate the crude and adjusted ORs, respectively. Statistical significance was set at 5% and all P-values were computed 2-sided. All the statistical analyses were performed using the SPSS statistical software (v. 16.0).

Results

This study was conducted on 11,850 women. The mean age of the 197 women diagnosed with breast cancer was 49.4 years (±8.7 standard deviation [SD], median=49, range: 26-68) and that of the 11653 healthy women was 40.9 years (±10.5 SD, median=41, range: 17-79). The results of bivariate analysis showed statistically significant differences between the cases and healthy women regarding education level, occupation, age at menarche, age at the first pregnancy, menopausal status, breastfeeding, and family history of breast cancer. However, no statistically significant differences were found between the two groups with respect to OC usage, marital status, parity, height, weight, and Body Mass Index (BMI) (Table 1). After adjustment in the logistic model, only occupation, parity, menopausal status, OC usage, family history of breast cancer, and breastfeeding revealed significant associations with the risk of breast cancer (Table 1). Level of education and occupation were used as a proxy of socioeconomic status. Healthy women were more educated compared to the cases (OR=0.50 (0.28-0.91). However, after adjustment for other variables, the effect of education declined and was not statistically significant. In terms of marital status, the proportion of married women was higher among the cases compared to the healthy women (92.2% *vs* 94.9%). The proportion of divorced/widowed and single individuals was also higher among the cases, but these differences were not statistically significant (Table 1). Moreover, employment rate was significantly higher among the cases in comparison to the healthy women (28.9% *vs* 19.8%, p<0.002). After adjustment for other variables, however, employment was not significant. Furthermore, earlier age at menarche (<12 years) was associated with an increased risk of breast cancer. After adjustment for other variables in multivariate analysis, the women who had menarche before the age of 12 years were at a significantly increased risk of breast cancer. Age at the first pregnancy also showed a relationship with the risk of breast cancer, and those who had experienced their first pregnancy at above 35 year ages were at a higher risk of breast cancer (OR: 4.10; 95%CI: 1.13-14.77). Postmenopausal women

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

		Cases (N =197) (%)	Healthy Women (N =11653) (%)	Unadjusted OR (95%CI)	Adjusted OR (95%CI)	P-Value
Marital status	Married	187 (94.9)	10745 (92.2)	1	1	0.15
	Never married	10 (5.1)	908 (7.8)	0.6 (0.3-1.2)	1.04 (0.42-2.56)	
Occupation	Housewife	140 (71.1)	9346 (80.2)	1	1	0.002
	Employed	57 (28.9)	2307 (19.8)	1.65 (1.20-2.25)	1.25(0.71-2.17)	
Education level	Illiterate	18 (9.1)	632 (5.4)	1	1	0.05
	Elementary &High school	148 (75.1)	8875 (76.2)	0.58 (0.35-0.96)	0.63 (0.33-1.19)	
	University	31 (15.7)	2144 (18.4)	0.50 (0.28-0.91)	0.75 (0.31-1.83)	
Age at menarche	<12	33 (16.8)	896 (7.7)	1	1	0.0001
	12-15	155 (78.7)	10028 (86.1)	0.42 (0.28-0.61)	0.34 (0.21-0.55)	
	>15	9 (4.6)	729 (6.3)	0.33 (0.15-0.70)	0.40 (0.16-0.95)	
Age at first pregnancy	<15	6 (3.3)	646 (6.5)	1	1	0.002
	15-24	129 (71.7)	7585 (76)	1.83 (0.80-4.16)	2.08 (0.81-5.31)	
	25-34	41 (22.8)	1645 (16.5)	2.68 (1.13-6.35)	3.07 (1.09-5.85)	
	>35	4 (2.2)	105 (1.1)	4.10 (1.13-14.77)	4.66 (1.09-19.93)	
Parity	Nulliparous	19 (9.6)	1765 (15.1)	0.64 (0.39-1.05)	1.05 (0.64-1.73)	0.02
	1 to 3	109 (55.3)	6541 (56.1)	1	1	
	4 to 6	62 (31.5)	2843 (24.4)	1.30 (0.95-1.79)	0.68 (0.48-0.94)	
	>6	7 (3.6)	504 (4.3)	0.83 (0.38-1.79)	0.27 (0.12-0.59)	
Menopause status	Pre-menopausal	77 (39.1)	1972 (16.2)	1	1	0.0001
	Post-menopausal	120 (60.9)	9681 (83.1)	3.15 (2.35-4.21)	1.14 (0.71-1.83)	
Breastfeeding (months)	<37	91 (46.2)	6501 (55.8)	1	1	0.007
	>37	106 (53.8)	5152 (44.2)	1.47 (1.10-1.95)	0.68 (0.45-1.02)	
OCP	Never	83 (42.1)	5145 (44.2)	1	1	0.57
	Ever	114 (57.9)	6508 (55.8)	1.08 (0.81-1.44)	1.09 (0.75-1.58)	
Family history of B.C.	No	160 (81.2)	10412 (89.4)	1	1	0.0001
	Yes	37 (18.8)	1241 (10.6)	1.94 (1.35-2.78)	1.54 (0.96-2.46)	
Height (cm)	<152	54 (31)	2196 (27)	1	1	0.37
	153-159	86 (59.3)	5057 (62.2)	0.83 (0.57-1.19)	1.05 (0.71-1.56)	
	>160	14 (9.7)	874 (10.8)	0.78 (0.42-1.42)	0.92 (0.46-1.84)	
BMI	<25	58 (29.6)	4005 (34.5)	1	1	0.07
	25-29.9	81 (41.3)	4820 (41.5)	1.16 (0.82-1.63)	1 (0.65-1.56)	
	>30	57 (29.1)	2796 (24.1)	1.40 (0.97-2.03)	1.24 (0.78-1.98)	

also tended to be at a higher risk of breast cancer, but this association was declined and was not significant in multivariate analysis (OR: 3.15; 95%CI: 2.35-4.21).

Considering parity, no significant association was found in bivariate analysis. Nevertheless, after adjustment for other variables, in comparison to parity 1-3, parity equal to or more than 4 had a strong protective effect on development of breast cancer. Yet, longer duration of breastfeeding (37 months or more *vs*. less than 37 months) showed no significant effects on the risk of breast cancer.

According to the results, the cases used OC more compared to the healthy women (57.9% *vs* 55.8%); however, this difference was not statistically significant (Table 1). Moreover, family history of breast cancer was significantly higher among the cases in comparison to the healthy women (18.9% *vs* 10.6%, p<0.001). Nonetheless, no significant association was observed between the risk of breast cancer and height, weight, and BMI (Table 1).

Discussion

This study on Iranian women demonstrated that family history of breast cancer, occupation, education level, parity, menopausal status, age at menarche, and age at the first pregnancy were related to the risk of breast cancer. Accordingly, employed women were at a higher risk of breast cancer compared to the housewives. This might be either due to socioeconomic status or exposure to stress or occupational carcinogens. In consistence with a Population-Based research conducted in Iran (Harirchi et al., 2012) literacy was a protective factor for breast cancer in our study. In consistence with other studies (Clemons and Goss, 2001; Naieni et al., 2007; Das et al., 2012) , the present study results showed early age at menarche to be associated with a higher risk of breast cancer. This association can be related to longer exposure to endogenous estrogens (Peeters et al., 1995). However, younger age at the first pregnancy has been revealed to be a protective factor for the risk of developing breast cancer. This might be due to the higher degree of terminal differentiation of mammary epithelial cells at the first birth, which makes the epithelium capable to metabolize carcinogens and repair DNA destructions more efficiently (Russo et al., 2005). Our results showed a strong relationship between age at the first pregnancy and risk of breast cancer, and the women who had experienced their first pregnancy after the age of 35 were at a higher risk of breast cancer compared to those experiencing pregnancy at below 15 year ages (OR: 4.10; 95%CI: 1.13-14.77). In the present study, age at first pregnancy was in a lower range than other studies. For instance, 82% of the healthy women had their first pregnancy before 25 years of age, while this value was obtained as 35% and 68% in the US and New Zealand, respectively (MacMahon et al., 1970; McCredie et al., 1998). In our study, compared to parity 1-3, parity equal to or more than 4 had a protective effect on development of breast cancer. Similarly, a population-based study in Finland (Hinkula et al., 2002) indicated that women with at least five births had a significantly decreased risk of breast cancer. A similar reduction in the risk of breast cancer was also reported for the women with at least seven childbirths in Nigeria (Huo et al., 2008). The protective effect of multiparty can be to some extent attributed to lifestyle factors, such as calorie intake and physical activity. In 1980, the total fertility rate was about seven in Iran, but it declined to 1.7 in 2007 (Abbasi-Shavazi et al., 2007). According to this decrease in the total fertility rate and life style changes, the number of new breast cancer cases is expected to double in 2030 (Mousavi et al., 2007). In line with the studies by Naini et al. in Mazandaran province, Iran (Naieni et al., 2007) and Yavari et al. in Tehran (Yavari et al., 2004), the results of bivariate analysis showed that postmenopausal status increased the risk of breast cancer, but this effect diminished in multivariate analysis after adjusting for age, which is also in agreement with the results of other studies conducted on the issue (Ghiasvand et al., 2011). Similar to other studies (Yavari et al., 2004; Ghiasvand et al., 2011; Ghiasvand et al., 2012; Ronco et al., 2012a), the present study revealed no significant association between breastfeeding and risk of breast cancer (Yavari et al., 2004; Naieni et al., 2007; Gajalakshmi et al., 2009). Although childbearing could reduce the risk of breast cancer, the role of breastfeeding is not clear yet (do Carmo Franca-Botelho et al., 2012). Our study results showed no significant association between OC usage and breast cancer. Up to now, contradictory results have been reported in this regard. Some studies (Naieni et al., 2007) have come to the same conclusions as the present study, while some others have reported a significant association (Ghiasvand et al., 2011). Consistent with other epidemiological researches (Naieni et al., 2007; Ghiasvand et al., 2011; Ghiasvand et al., 2012; Zare et al., 2013), the results of the current study in consistent with other studies (Ren, 2012; Ronco et al., 2012b; Toleutay et al., 2013) indicated a significant relationship between family history of breast cancer and increased risk of breast cancer. This finding suggests the existence of genetic and environmental factors that are common among families. However, no significant relationship was found between the risk of breast cancer and height, weight, and BMI, which is consistent with the results of other studies (Ghiasvand et al., 2011; Yadav et al., 2012; Sangrajrang et al., 2013). Although some studies have shown a direct association (Ghiasvand et al., 2012), others have revealed an inverse relationship between BMI and the risk of breast cancer (Tehard et al., 2004). To the best of our knowledge, this study with 11850 participants is one of the largest studies on breast cancer risk factors in Iran. However, our study had some limitations. Although Shahid Motahhari breast clinic is a referral center in Fars province and other southern provinces, because the screening program was not mandatory for all women, our study population might not be representative of the total population. In addition, we did not collect information about Hormone Replacement Therapy (HRT) which is a known risk factor for breast cancer. Nevertheless, it has been reported that less than 1% of Asian women used HRT (Lea et al., 2009). Reproductive factors are the main risk factors of breast cancer and Iranian population is one of the youngest populations in the world that will face aging in the following decades. Therefore, although the incidence rate of breast cancer is increasing in young

women, it will increase even more in future. Moreover, there is unfortunately no guarantee that the current breast cancer prevention measures which are based on results of the studies conducted in developed countries would be operative and conceivable in Iran with different religious beliefs and ethnic, cultural, and socioeconomic status. Yet, almost 50% of breast cancer risk is attributable to known factors (Sprague et al., 2008). Therefore, further studies are necessary to explore unknown risk factors. Furthermore, decrease in parity may relatively explain the rising trend of incidence of breast cancer. Hence, further studies are required to investigate the possible causes of such trend in Iran and other Middle Eastern countries.

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