

Parity and breastfeeding are preventive measures against breast cancer in Iranian women

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Abstract

Background Breast cancer (BC) is the most prevalent cancer in Iranian women and the fifth most common cause of cancer-related death in Iran. Among predicting factors and preventive measures for BC, the parity and breastfeeding (BF) are controversial issues. We therefore conducted this case–control study to find out the relation of parity and BF to incidence and risk of BC.

Method A structured questionnaire that covered demographic criteria and BC risk factors was completed for case (376 cases) and control (425 subjects) groups, both matched in terms of demographic variants, reproductive issues, and socioeconomic status. Odds ratio (OR) and 95% confidence intervals (CI) were computed as measures of association from the logistic models. All p values reported are two-sided.

Results Parity significantly reduces the risk of BC ($p < 0.001$, OR 2.05, CI 1.4–3.3), and BF is protective ($p = 0.0001$, OR 0.39, CI 0.27–0.56). The best result was gained with 1–3 parity and 24 months BF and mean duration of 18–24 months per child ($p = 0.037$, OR 0.7, CI 0.5–0.98).

Conclusion On the basis of breast anatomical and physiological changes during pregnancy, and parity and breastfeeding, full-term pregnancies and parities with efficient BF significantly reduced the risk of breast cancer

compared with nonpregnant and nulliparous women or those who never breastfed. The number of children should ideally be limited to 1–3, and the cumulative duration of BF not less than 25–36 months. We would recommend 1–3 pregnancies and a BF duration not less than 18 months, with best results being achieved with 24 months per child.

Keywords Parity · Breastfeeding · Breast cancer · Iran

Introduction

Breast cancer is the most prevalent cancer in Iranian women and, similar to the situation in many other countries all over the world, has experienced a steadily increasing incidence and relative stability in mortality over the years. In Iran, breast cancer is the fifth most common cause of death for women; age-specific rate for breast cancer in Iran is about 25 per 100,000 population with 7,500 new cases annually [1, 2].

Although the etiology of breast cancer has not been thoroughly clarified yet, multiple factors have been defined and diagnosed as determinants which include risk factors and predicting factors for it. Risk factors for in situ breast cancer are similar to those for invasive disease [3, 4]. Among them the parity and breastfeeding are controversial issues, particularly the number of parities and duration of breastfeeding [5–7].

One case–control study conducted in Brazil [8] showed that breastfeeding does not have a protective effect against breast cancer. The odds ratio (OR) for women who breastfed was 0.9 (95% CI 0.8–1.2), compared with women who had not breastfed. For women who breastfed for 6 months or less, the OR was 1.0 (95% CI 0.6–1.8). In

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premenopausal and postmenopausal women who breastfed for more than 25 months the odds ratio was 0.95 (95% CI 0.5–3.5) and 1.27 (95% CI 0.5–3.1), respectively [8]. The Brazilian investigators believe that the parity is reliable and protects mothers from breast cancer significantly, the odds ratio for one, two, three, and four or more parities are 0.5, 0.4, 0.5, and 0.3, respectively, with 95% CI.

A systematic review study performed by researchers at George Mason University (VA, USA) yielded 30 case–control studies, and showed that only 11 of 27 studies assessing the effect of ever breastfeeding compared with never breastfeeding found significant protection effect against breast cancer. Of 24 studies assessing the effect of breastfeeding duration, only 13 found a reduced risk of breast cancer with extended lactation. The researchers also found that gravidity and parity associated with extending an ovulation period during lifetime are effective against breast cancer [9]. Another study, which was conducted in Nigeria, showed that parity and breastfeeding are protective against breast cancer [10]. Investigators in cancer research from Seattle (WA, USA) confirmed that lactation may have a slight and perhaps long-lasting protective effect, not only in premenopausal, but in postmenopausal women [11]. Due to such controversies, the aim of our case–control study was to clarify the relationship of breastfeeding duration, gravidity, and number of children to incidence of breast cancer in Iranian women.

Materials and methods

This is a case–control study in which cases affected by breast cancer (376 patients) were under study at the Cancer Research Center, Shahid Beheshti University of Medical Sciences (Azar Sample), and were diagnosed between 2001 until 2006. There were 425 controls comprising (1) 172 people with benign breast disease or referral subjects for breast checkup selected from hospitals or health centers (Azar clinic), (2) 253 subjects selected from the community and who had no breast complaint; the latter subgroup was chosen to reduce the bias, because the hospital-based control group might not be representative of the normal population from which cases were recruited, particularly if severity of disease and/or adjuvant disease were not compared together.

A structured questionnaire that covered demographic criteria and breast cancer risk factors, such as marriage status, gravidity, parity, breastfeeding duration, family history of breast cancer, diet, tobacco consumption, hormone use, and menopausal status, was completed for every case and control group from documentation and telephone or face-to-face interviews conducted by general practitioners and trained nurses. The two groups comprised females

only and they were matched in terms of demographic variants and socioeconomic status. The collected data were analyzed by using SPSS-16 software; logistic regression models were used to examine the relationship between breast cancer risk and reproductive factors. Odds ratio (OR) and 95% confidence intervals (CI) were computed as measures of association from the logistic models. All *p* values reported are two-sided.

Results

There were 801 women in this study; 376 cases and 425 controls. Table 1 shows the demographic characteristics and some matched confounding variables; the age, age at menarche/menopause, and history of abortion were matched statistically (*p* = 0.18, 0.3, 0.9, 0.25 respectively); the number of singles, married, and postmenopausal subjects in the case and control group were not significant statistically (*p* = 0.06, 0.06, 0.07 respectively).

Table 2 presents the distribution of gravidity and parity with some effective confounding factors for cases and controls. Cases were more likely than controls to be non-pregnant (*p* < 0.001, OR 2.05, CI 1.4–3.3); also the mean number of pregnancies was higher (3.4 ± 2.3) in the control group rather than cases (2.9 ± 2.2) (*p* < 0.001). In terms of parity status, the parous women had a lower risk than nulliparous women (*p* < 0.001, OR 1.8, CI 1.3–2.7); the number of children reduced the risk of breast cancer, but it was statistically significant only for 1–3 parities (*p* = 0.009, OR 0.69, CI 0.52–0.91) and not for four or more deliveries (*p* = 0.7). The mean number of deliveries was different between case and control group (2.4 ± 1.8 and 2.8 ± 1.8 with *p* = 0.003).

Tobacco consumption and fatty diet, as we expected, increased the risk of breast cancer (*p* = 0.02 and 0.04, respectively), but use of hormones (estrogen, progesterone) did not increase the risk of disease. Positive family history for breast cancer was 22.8% in cases and 44.4% in the hospital sample and 16.9% in the community portion of

Table 1 Demographic and some matched confounding factors in the case and control group

Subject	Case (%)	Control (%)	<i>p</i> value	OR	CI
Age (mean)	45.9 ± 9.5	46.8 ± 9.2	0.18 (NS)		
Age at menopause	46.4 ± 5.7	46.3 ± 6.5	0.9 (NS)		
Age at menarche	13.4 ± 1.2	13.6 ± 2.9	0.3 (NS)		
Number of menopause	154 (45.4)	164 (38.9)	0.07 (NS)		
Abortion	115 (30.5)	146 (34.3)	0.25 (NS)	1.2	0.88–1.6
Single	13 (3.5)	27 (6.4)	0.06 (NS)	0.5	0.3–1.03
Married	363 (96.5)	398 (93.6)	0.06 (NS)	0.5	0.3–1.03

NS nonsignificant

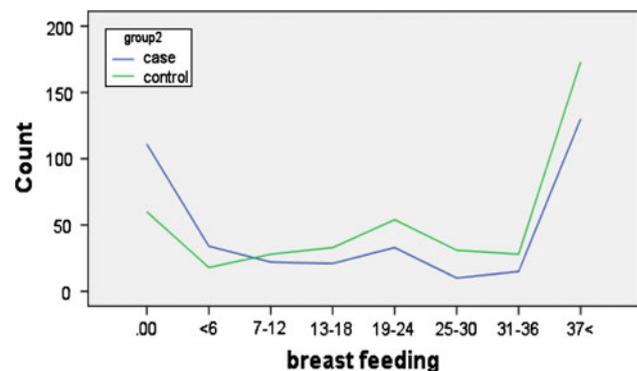
Table 2 Confounding factors in breast cancer in the case and control group

Subject	Case (%)	Control (%)	<i>p</i> value	OR	CI
Gravidity					
None	78 (20.7)	48 (11.3)	0.0001	2.05	1.4–3.03
1–3	172 (45.7)	220 (51.7)	0.089	0.7	0.59–1.04
4–6	102 (27.1)	123 (28.9)	0.6	0.9	0.67–1.25
≥7	24 (6.4)	34 (8)	0.4	0.78	0.45–1.35
Average of gravidity	2.9 ± 2.2	3.4 ± 2.3	0.001		
Parity					
None	81 (21.5)	55 (12.9)	0.001	1.8	1.3–2.7
1–3	202 (53.7)	267 (62.8)	0.009	0.69	0.52–0.91
4–6	83 (22.1)	90 (21.2)	0.7	1.05	0.75–1.48
≥7	10 (2.7)	13 (3.1)	0.7	0.87	0.38–1.99
Average of parity	2.4 ± 1.8	2.8 ± 1.8	0.003		
Smoking	36 (9.6)	23 (5.1)	0.02	1.8	1.1–3.2
Fatty diet	132 (35.1)	121 (28.5)	0.04	1.4	1.1–1.8
Hormone use	140 (37.2)	218 (51.3)	0.1	0.8	0.6–1.1
Family history	85 (22.8)	BBD 76 (44.4) NBD 55 (16.9)	0.05	1.4	

BBD benign breast disease, NBD non breast disease

controls, which shows that it is significant in cases and the community portion of controls. The high rate of positive family history in hospital samples is due to the nature of this sample, because many of these people are referred to hospitals or health centers following family involvement.

Comparing ever versus never breastfed showed that breastfeeding is significantly protective against breast cancer; 70% of cases and 86% of controls had ever breastfed, and 29.5% of cases and 14% of controls had never breastfed ($p < 0.001$, OR 0.39, CI 0.27–0.56). To assess the association between duration of breastfeeding and risk of breast cancer, we compared the two groups by dividing the breastfeeding duration into intervals of 6 months. This showed that breastfeeding for less than 6 months was not protective against breast cancer in either group ($p = 0.02$, OR 2.2, CI 0.27–0.56). Among the other durations, breastfeeding was only significantly protective in groups with 25–36 months duration ($p = 0.01$, OR 0.54, CI 0.33–0.89). In terms of trend, breastfeeding was significantly protective against breast cancer: more than 6 months breastfeeding consistently showed a trend towards decreasing breast cancer risk with increasing duration of breastfeeding (Fig. 1). This decreased risk appeared to be duration-related, as mothers who breastfed for more than 6 months were at lower risk than women who breastfed for shorter duration. This effect was essentially present in mothers who had breastfed until 48 months, but was not significantly protective for those who breastfed for more than 4 years. Table 3 presents this association without considering the number of pregnancies

**Fig. 1** Trend of breastfeeding in the case and control group

or children. Table 4 shows that the duration of breastfeeding per child is very important in relation to the protective effect; 12, 18, and 24 months per child are significantly effective and follow a rising trend until 24 months, but not thereafter ($p = 0.0001$, 0.014, 0.035, 0.83 respectively). The mean duration of breastfeeding per child for cases and controls was significant (12.4 ± 9.04 , 15.8 ± 15.78 , $p = 0.001$). Because of the high standard deviation (SD) for mean duration of breastfeeding and to determine a meaningful duration with an effective cutoff point, we calculated the effect of breastfeeding for a child by comparing two periods: the first, infant till 18 months; the second, more than 18 until 24 months, which statistically was significant ($p = 0.037$, OR 0.7, CI 0.5–0.98) for a duration of 18–24 months per child.

Table 3 Duration of breastfeeding in the case and control group, excluding number of children

Subject	Case (%)	Control (%)	<i>p</i> value	OR	CI
Breastfeeding duration (months)					
Ever	265 (70.5)	365 (85.9)	0.0001	0.39	0.27–0.56
Never	111 (29.5)	60 (14.1)			
Ever breastfed					
<6	20 (7.5)	13 (3.6)	0.027	0.45	0.22–0.93
≥6	245 (92.5)	352 (96.4)			
<12	154 (41)	92 (21.6)	0.0001	0.39	0.29–0.54
≥12	222 (59)	333 (78.4)			
<18	180 (47.9)	129 (30.4)	0.0001	0.48	0.35–0.63
≥18	196 (52.1)	296 (69.6)			
<24	195 (51.9)	160 (37.6)	0.0001	0.56	0.42–0.74
≥24	181 (48.1)	265 (62.4)			
<36	236 (62.8)	232 (54.6)	0.02	0.7	0.54–0.95
≥36	140 (37.2)	193 (45.4)			
<48	263 (69.9)	286 (67.3)	0.4	0.88	0.65–1.2
≥48	113 (30.2)	139 (32.7)			

Table 4 Duration (months) of breastfeeding per child

Subject	Case (%)	Control (%)	<i>p</i> value	OR	CI
<6	88 (29.9)	55 (15)	0.001	4.2	2.5–6.8
≥6	206 (70.1)	312 (85)			
<12	135 (45.9)	134 (36.5)	0.014	0.67	0.49–0.93
≥12	159 (54.1)	233 (63.5)			
<18	195 (66.3)	214 (58.3)	0.035	0.7	0.52–0.98
≥18	99 (33.7)	153 (41.7)			
<24	232 (78.9)	287 (78.2)	0.83	0.96	0.66–1.4
≥24	62 (21.1)	80 (21.8)			
Mean	12.4 ± 9.04	15.8 ± 15.78	0.001		
<18	195 (66.3)	214 (58.3)	0.037	0.7	0.5–0.98
18–24	85 (28.9)	133 (36.2)			

Discussion

Avicenna (980–1,037) gave the first scientific explanation of breast cancer and treatments, related to hormonal effect and reproductive factors [12]. Nowadays there are a lot of researchers who investigate the association between breast cancer risk and reproductive related factors with different results. Some researches believe that the number of children does not make sense for avoiding breast cancers [13], some find that the risk of breast cancer in mothers with parity equal or more than four is higher than nonparous women [14], but many other studies revealed that null parity is a great risk for breast cancer and the number of children is a protective factor against breast cancer [8–10].

Many investigators confirmed the efficacy of ever breastfeeding and duration of it against breast cancer [10, 15, 16], and some studies accept this with a definite cutoff point of breastfeeding from less than 6 months, 12 or 24 months, or even more [10, 13, 17–19]. Also some studies found that breastfeeding did not have a protective effect against breast cancer [8, 14].

In our study parity and ever breastfeeding and their trends were significantly effective against breast cancer. Theoretically there are well-known anatomical and physiological changes during pregnancy, parity, and breastfeeding which enable mothers to reduce the risk of breast cancer. For example parity and breastfeeding may lead to differentiation of mammary cells, and contribute to differentiation of breast tissue particularly during the first full-term pregnancy; also parity and lactation period reduce the lifetime number of ovulatory cycles, reducing the risk of breast cancer particularly in young mothers [20]. This also possibly reduces estrogen and increases prolactin production, which might decrease women's cumulative exposure to estrogen, thereby inhibiting the initiation or growth of breast cancer cells. It has also suggested that a protective effect of breastfeeding against breast cancer risk might be attributed to the excretion of carcinogenic agents from breast ductal tissue [15]. Such hypotheses form the basis for our study. In the cases and control group, full-term pregnancy and parity significantly reduce the risk of breast cancer compared with nonpregnant and nulliparous women. The best result was gained within 1–3 full-term pregnancies and parities; this relationship is complex, but it was epidemiologically confirmed that each birth reduces the relative risk of breast cancer to 7% in the absence of breastfeeding and each child breastfed corresponds 3.4% decreased risk, and each additional birth and breastfeeding will decrease the risk of breast cancer [10]. We and others [14] believe that there may be a physiological difference between a woman with one child breastfed for 24 months and a woman with four children, each breastfed for 6 months. We therefore divided the breastfeeding duration into 6-month intervals and showed that the best cumulative duration of breastfeeding for reducing the risk of breast cancer is 25–36 months, and never breastfeeding is a great risk compared with ever breastfeeding. Also it was confirmed that cumulative breastfeeding for 4 years or more is not statistically effective against breast cancer. Breastfeeding each child for less than 6 months and more than 24 months did not reduce the risk of breast cancer, and the duration of 18–24 months of breastfeeding was the best and most effective duration against breast cancer among Iranian women. Because some relation between parity and breast cancer with estrogen receptor (ER)-positivity has been reported [20, 21], we also evaluated our data which showed (Table 5) that there was no significant correlation

Table 5 ER and parity status in the breast cancer patient

Parity	ER+ (%)	ER- (%)	<i>p</i> value	OR (CI)
1 or more	106 (93)	44 (88)	0.29	1.8 (0.5–5.5)
Null parity	8 (7)	6 (12)		

among them ($p = 0.29$, OR 1.8, CI 0.5–5.5), and the parity was independent of estrogen receptor status.

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Conflict of interest statement The authors have no conflict of interests in this article.

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