

# BREAST CANCER RISK FACTORS IN AN URBAN AREA OF YAZD CITY- IRAN, 2006

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**Abstract-** Breast cancer is the most common malignancy in women in many parts of the world. The risk factors for breast cancer cover a broad range of conditions, from age to complex genetic alterations. Present data is showing an increase in the annual incidence rates of disease and it is ranked as the first recorded malignancies among Iranian women after 1999. To study the association of reproductive and non reproductive factors with breast cancer among women with age group 30-75 years residing in urban area of Yazd city, Iran, this community based case-control study was carried out. A total of 160 subjects including 80 cases and 80 community controls were studied. Age was matched for both the case and control groups. Association of various kinds of risk factors with breast cancer was studied using odds ratios with 95% confidence intervals through both the univariate and multivariate analysis. The findings based on multivariate analysis showed that being employment in outdoor jobs, positive familial history of breast cancer amongst the first grades, early onset of the first menstruation cycle ( $\leq 13$  ys.), delayed age of the first marriage ( $\geq 19$  ys.), less number of live children ( $\leq 3$ ) and less duration of breastfeeding ( $\leq 2$  ys.) were significantly associated with breast cancer. However, consumption of OCPs was found to be a protective factor for breast cancer. Our study showed that the role of reproductive factors in the causation of breast cancer was more important than in other factors like socio-economic, psychological, behavior and nutritional factors.

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**Key words:** Breast cancer, risk factors, women, case-control study

## INTRODUCTION

Breast cancer is the most common malignancies in women in many parts of the world including one-third of all cancers. It is the second cause of the death in females created by cancers followed by lung malignancy (1). The cancer has multi-factor etiology and is one of the most widely studied tumors in terms of its determinants. Epidemiological studies and basic research have identified a series of

conditions that can predispose women to breast cancer. Such research is crucial to knowledge of the tumor biology and to identify risk factors and especially habits that can be altered or controlled in the attempt to decrease the number of new cases or deaths from the disease (2, 3). The risk factors for breast cancer cover a broad range of conditions, from age to complex genetic alterations. In addition to age, first degree family history is probably the most widely acknowledged and scientifically proven risk factor. Nevertheless, aspects in the woman's hormonal and childbearing history show evidence of association between the disease and early menarche, late menopause, nulliparity, late first gestation, and consumption of oral contraceptive pills (2-6).

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Environmental characteristics such as diet, body weight, exposed to X-ray and being smoker (7) have also been extensively investigated in the etiology of breast cancer. Studies conducted in populations from countries in which the incidence is low and who immigrated to high-incidence countries have demonstrated that descendents begin to present an incidence similar to the country where they are residing, raising the hypothesis that hormonal, reproductive, and environmental factors are as important as genetic factors and probably account for the variation in rates between different locations (8, 9). 21.4% of all reported malignancies among Iranian women are attributed to breast cancer where the concurrent crude incidence rate of disease is 22.4 per 100,000 female.

Present data is showing an increase in the annual incidence rates of disease and it is ranked as the first recorded malignancies among Iranian women after 1999 (10). Since there was no evidence in relation to the different views of breast cancer in Yazd province, I.R. of Iran, the present study is an attempt to explore the disease risk factors among women with age group 30-75 years residing in urban area of Yazd city through a retrospective case-control strategy.

## MATERIALS AND METHODS

The present community based case-control study was carried out on the women age group 30-75 years residing in the urban areas of Yazd city from February 2006 to December 2006.

A total of 80 female cases with breast cancer were consecutively selected from different clinical centers involved in the diagnostic and treatment of disease. 80 healthy controls also were selected from community of Yazd city according to an initial analysis of cases as per their place of residence. Cases were defined as female subjects with age range 30 to 75 years, survivors of a new breast cancer confirmed by pathological evidences, residing in the urban area of Yazd city and referring to centers for the diagnostics or treatment of cancers. The same number of controls also were drawn from neighborhood place of cases. Using appropriate formula and considering a confidence level of 95%

and study power of 80%, a total of 160 Study subjects including 80 Cases and 80 community controls were studied. We obtained informed consent from all participants.

The tool of enquiry was a pretested-precoded questionnaire administered to both the case and control groups. Age was matched for both the case and control groups (with an interval of  $\pm 2$  years). Informed consent was obtained from cases and controls. Association of socio-economic factors, reproductive characteristics, psychological-behavior factors and nutritional habits with disease was studied using conditional and unconditional Logistic Regression to calculate Odds ratios (ORs) and 95% confidence intervals (CIs).

## RESULTS

Mean  $\pm$  SD age of cases and controls was  $48.9 \pm 9.7$  and  $49.1 \pm 9.8$  years respectively (range 31-74) and median of age variable in total subjects was 48 years. The obtained results of Univariate Logistic Regression analysis based on Odds ratios and 95% confidence interval for each of breast cancer factors have been shown in table 1. In this study, employed women had a chance of approximately three times more getting cancer than unemployed women (95% CI= 1.34-6.37). The similar risk times of disease was seen in women giving an overall positive familial history of breast cancer than that in women without the history (95% CI= 1.34 -6.37).

However, the risk reduced to nearly two and half times if there was the history in the individuals of first grade of family. In our study, consumption of oral contraceptive had a protective effect on breast cancer where women with history of OCP (oral contraceptive pills) using had approximately 40% reduction in the probability of getting cancer (OR= 0.41 (95% CI= 0.20– 0.85).

The risk of disease among female subjects who had an early onset of menstruation ( $\leq 12$  years) increased up to nearly seventeen times more than those with onset of after 15 y. Compared to individuals with menstruation age of 13 and 14 years, this significant higher risk also was shown among aforesaid females.



**Table 1.** Reproductive and non-Reproductive characteristics of case & control groups along with OR (CI 95%)

Variable	Cases vs. Controls			
	Case	Controls	OR (95% CI)	P value
<b>Marital status</b>				
Married	68(86)	72 (90)	1	
Single	11 (14)	8 (10)	1.46 (0.5- 4.26)	NS
<b>Education</b>				
Illiterate	20(25)	23(29)	1	
Primary	26 (32.5)	19 (24)	1.57 (0.62-3.99)	
middle	11 (13.5)	12 (15)	1.05 (0.34 -3.28)	NS
High and intermediate	15 (19)	16 (20.5)	1.08 (0.39 – 3.01)	
Graduate- post G.	8 (10)	9 (11.5)	1.02 (0.29 – 3.63)	
<b>Occupation</b>				
Housewife	47(59.5)	64 (81)	1	
employment	32(40.5)	15 (19)	2.90 (1.34 -6.37)	<. 01
<b>Positive family history of breast cancer</b>				
Yes	17 (21.5)	5 (6.5)	4.05 (1.30 – 13.37)	<. 001
No	63 (78.5)	75 (93..5)	1	
<b>Relative grade of Positive family history of breast cancer</b>				
First grade	20(25)	9(11.5)	2.40 (1.05 – 6.29)	<.05
Second grade	8(10)	15(18.5)	0.57 ( 0.20 – 1.60)	
None	52(65)	56(80)	1	
<b>Continuation of Menopause</b>				
Yes	53(66.3)	36(45)	2.40 (1.21 – 4.79)	<.01
No	27 (33.7)	44( 55)	1	
<b>History of OCP consumption</b>				
Yes	26 (32.9)	38 (47.5)	0.41 (0.20 – 0.85)	<.01
No	53 (67.1)	42 (52.5)	1	
<b>Age of menstruation onset</b>				
≤ 12	19 (23.8)	3 (3.8)	16.89 (3.71-88.42)	
13	31 (38.3)	25 (31.2)	3.31 (1.31-8.46)	<.01
14	18 (22.5)	20 (25)	2.90 (1.20-6.70)	
≥15	12 (15.4)	32 (40)	1	
<b>Age of first marriage</b>				
<16	20 (25)	22 (27.4)	1	
16-18	19 (23.7)	35 (43.8)	0.60 (0.24 – 1. 47)	< .05
19-22	28 (35)	12 (15)	2.57 (1.31 – 7.07)	
>22	13 (16.3)	11 (13.8)	3.24 (2.02 - 4.01)	
<b>Age of mother at first delivery</b>				
16 -18	22 (27.6)	41 (51.3)	1	
19-22	32 (40)	25 (31.3)	2.39 (1.07 – 5.34)	
>22	26 (32.5)	14 (17.5)	3.46 ( 1.40 – 8.69)	<.01
<b>Number of live birth</b>				
0-2	25 (31.6)	9 (11.3)	22.2 (2.19 – 122.1)	
3	31 (39.2)	16 (20)	15.50 (1.67 – 111.2)	
4	14 (17.7)	19 (23.7)	5.89 (0.60 – 22.45)	.000
5-6	8 (10.2)	28 (35)	2.29 (0.22-56.3)	
>6	1 (1.3)	8(10)	1	
<b>Duration of breastfeeding (month)</b>				
0-12	11 (13.8)	4 (5)	6.13 (1.55-26.02)	
13-24	19 (23.8)	3 (3.8)	14.11 ( 3.42 -67.39)	
25-36	17 (21.3)	9 (11.3)	4.21 (1.48-12.2)	.000
37-48	11 (13.8)	15 (18.8)	1.63 (0.59 – 4.55)	
>48	22 (27.5)	49 (61.3)	1	
<b>Body mass Index</b>				
<25	17 (22.4)	35 (45.5)	1	
25-29.9	22 (28.9)	26 (33.8)	1.74 (0.72 – 4.26)	<.01
≥30	37 (48.7)	16 (20.7)	4.76 ( 1.94 – 11.74)	
<b>History of Genital system surgery</b>				
Yes	43 (53.8)	30 (37.5)	1.98 (1.01 – 3.83)	<.05
No	37 (46.2)	50 (62.5)	1	
<b>History of physical activity</b>				
Yes	13 (16.3)	33 (41.3)	1	
No	67 (83.7)	47 (58.7)	3.62 (1.63 – 8.15)	<.001
<b>History of X-ray Exposure up to 30 years</b>				
Yes	15 (18.8)	5 (6.3)	3.46 ( 1.10 – 11.6)	<.05
No	65 (81.2)	75 (93.7)	1	

**Table 2.** Effect of multiple breast cancer risk factors, modeled with logistic regression

Variable	Cases vs. controls			
	Coefficient	SE	Adjusted OR (95% CI)	P value
<b>Occupation</b>				
Housewife (1)*	----	----	----	----
Employment	1.28	.64	3.61 (1.02-12.72)	<.05
<b>Positive Family history of breast cancer</b>				
No (1)	----	----	----	----
Yes	1.74	.78	5.71 (1.22-26.58)	<.05
<b>Age of first menstruation</b>				
>13 ys.(1)	----	----	----	----
≤13 ys	----	----	----	----
<b>OCP consumption</b>				
No (1)	2.1	.67	8.20 (2.18-30.78)	<.01
Yes	----	----	----	----
<b>Age of first marriage</b>				
<19 ys. (1)	-1.66	.58	.18 (.06-.59)	<.01
≥19 ys.	----	----	----	----
<b>Number of live birth</b>				
>3. (1)	1.48	.58	4.41(1.41-13.76)	<.01
≤3	----	----	----	----
<b>Duration of breastfeeding</b>				
≤24 months	2.03	.56	7.65(2.53-23.07)	.000
25-48 months	2.29	.79	9.95(2.08-47.49)	<.01
>48 months (1)	.89	.79	2.45(.51-11.72)	>.05
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\* = Reference category

In this study, delay in the age of the first marriage and of the first delivery were found to be significant risk factors for breast cancer where the odds of getting cancer amongst these women increased concomitant with increase in the age of the first marriage and of the first delivery ( $2.5 < OR < 3.5$ ). Other reproductive factors which were found to be significantly different in case and control groups were; number of live birth, duration of breastfeeding and history of surgery in genital system. Concomitant with increase in the duration of breastfeeding, there was nearly seen a significantly decrease in the chance of getting cancer. In the other word, the odds of disease amongst women with breastfeeding duration of  $\leq 36$  months were from more than 4 to 14 times higher than in women with breastfeeding duration of  $> 48$  months. Such a trend was seen in respect with number of live birth so that women with live birth number of  $> 3$  had significantly less chance of getting disease compared

with that one having live birth of  $\leq 3$ . No significant difference was observed between women with live birth number of 4 and 5-6 with women having  $> 6$  live birth. There was seen an odds of approximately two times more getting cancer amongst individuals giving history of surgery in their genital system compared to that one without this history ( $P < 0.05$ ,  $OR = 1.98$ ,  $95\% CI = 1.01 - 3.83$ ). History of not having regular leisure time physical activity and history of exposure to X-ray up to 30 years were other significant factors in our study where the chance of taking disease amongst women with on regular leisure time physical activity and women giving history of exposure to X-ray within the first three decades of live were nearly three and half times higher than that in women giving history of regular leisure time physical activity and women with no history of exposure to X-ray. The last significant risk factor observed in our study was body mass index of  $\geq 30$ , which the frequency of

women cases with this BMI score was significantly higher than that in control group, consequently the probability of taking breast cancer amongst women with BMI  $\geq 30$  was more than four and half times higher than in women with BMI  $< 25$  ( $P < 0.01$ , OR= 4.76, 95% CI = 1.94 – 11.74).

### Step-wise regression analysis

Stepwise logistic regression analysis was carried out for both continuous and categorical variables having p-value less than .05 on the univariate analysis (Table 3). Seventeen eligible variables were considered for the model out of which 7 could remain significant after adjusting with the other factors. Being employment in outdoor jobs and having a positive familial history of breast cancer were those non-reproductive variables which in this study could account for as predictors of breast cancer. Controlling with the other factors, the chance of getting disease among employed women was more than three and half times higher than that in households ( $P < 0.05$ ). Similar significant association was also seen between positive familial history of breast cancer in the first grads and disease on the model where women giving the history in their first grade relatives had approximately eight times more odds of getting cancer compared to those with negative such a history. The frequency of early onset of menstruation cycle ( $\leq 13$  ys.), delayed age of first marriage ( $\geq 19$  ys.), having less number of live children ( $\leq 3$ ) and less duration of breastfeeding ( $\leq 2$  ys.) among women cases was higher as compared to controls where these main reproductive variables were independently considered as breast cancer risk factors on the model. The last significant factor was related to OCP consumption where in spite of previous variables, it was found to be a protective factor for breast cancer on the multivariate model (Table 3).

## DISCUSSION

The Multivariate based findings of this community based case-control study have introduced some of the conditions as breast cancer risk factors among women residing in the urban area of Yazd city, I.R. of Iran. These factors were; to be employed, positive familial history of breast cancer, no history of OCP

consumption, early onset of menstruation ( $\leq 12$  years), delayed in the age of the first marriage, number of live birth  $\leq 3$ , and duration of breastfeeding  $\leq 36$  months.

In our study, the results of multivariate analysis showed that women involved in the outdoor jobs were more at risk of breast cancer compared to household women. This finding is accordance with result of study carried out by Fathinajafi *et al.* where they found that to be employing in outdoor occupations and also duration of employment could act as a significant predictor of breast cancer (11). Various studies have showed that factors like age and positive familial history of cancer play an important role in the causation of disease (2, 11, 12). In this study, marital status was not found to be statistically significant predictor factor of disease on the model, but other reproductive factors such as delayed age of the first marriage ( $> 19$  y), number of live births  $< 3$  and duration of breastfeeding  $\leq 36$  months were those variables that were found to be significantly associated with cancer on the logistic model. This can be explained by the fact that according to some documents there is a positive interaction between delayed marital age and less number of deliveries and of live births on the establishment of breast cancer. Age variable was matched for the both cases and controls but having a positive familial history of cancer especially amongst individuals of the first grade of family was found to be a strong independent predictor factor for disease on the model. It is said that compared to other reproductive characteristics, the role of familial history of cancer is a genius one in the causation of disease and the protective effect of high number of deliveries or live birth is not substantial in women who give familial history of cancer (13). In this study, early age of the first menstruation ( $\leq 13$  y) could act as an independent risk factor for cancer based on multivariate analysis. This is accordance to findings reported by other researchers (12, 14, 15). However, some of authors like Becher *et al.* have considered a protective role for age of the first menstruation  $> 15$  y against breast cancer in women giving positive familial history of cancer (16).

Although the role of breastfeeding in the causation of breast cancer is in an ambiguity condition, but there has been considered a protective

effect for the number of live birth in the reduction of cancer rates. In our study the both factors were found to be significantly associated with breast cancer where women with live birth number of  $\leq 3$  and breastfeeding duration of  $\leq 24$  months had high risk of getting disease compared to who with higher amounts of those factors. The similar findings were also reported by other studies (12, 17). Becher *et al.* believes that the higher number of pregnancies and prolonged duration of breastfeeding have significant effect on the reduction of breast cancer, however, it is not as much as of which can neutral the hazardous effect of genetic agents. The role of OCP consumption on the breast cancer based on present documents is controversial where some of the reports consider no significant risk for the consumption of these hormonal agents (18). On the other hand, a number of studies have proven that using of OCP before or after menopause can increase chance of getting cancer (12, 19). In this study, the use of oral contraceptive pills was found to be a significant protective factor for the breast cancer on the model. However, this protective effect may be explained by the fact that duration of OCP consumption has not been considered in this investigation or it can be due to recall bias occurred in this manner. Of course, in this study there was no the possibility of assessment of the various compounds of estrogen and progesterone separately, resulting in not reaching to more precise findings. In attention to beneficial effects of OCPs, however, it is needed to carry out the more studies including definite groups of patients to clear whether consumption of these hormonal compounds increase the risk of cancer or not. It has been examined that obese women and those who without regular physical activity have tendency to get breast cancer (20) especially after recovering from disease, it can influence long-term prognosis (21). In our study, such women showed significant higher chance of getting breast cancer as compared with those who had regular leisure time physical activity and those were in a normal body weight.

It is concluded that the role of reproductive factors in the causation of breast cancer was more important than in other factors like socio-economic, psychological, behavioral and nutritional factors. Therefore, it is suggested that the intervention

programs should be focused on the marital and reproductive status of Iranian women.

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### Conflict of interests

The authors declare that they have no competing interests.

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