

Article

A case-control study on risk factors of breast cancer in Damghan, Iran

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Abstract

Background: The available information denotes the increased annual occurrence of breast cancer in Iranian women and the decreased age of developing this disease.**Objectives:** The present study aimed to assess risk factors for breast cancer in Iranian women.**Methods:** The present research was conducted in a hospital-based case-control study on 46 cases and 43 controls from March 2019 to March 2020 in Damghan. The interview was conducted to collect data by a predesigned questionnaire consisting of socio-demographic variables, nutrition and physical activity, and a checklist for fertility, and care items. Descriptive and analytical statistics, including the chi-square and logistic regression models, were used to analyze data by SPSS- ver16.**Results:** The findings showed that out of 46 cases, only 6 (6.7%) were detected by self-examination and two cases by health workers. The average age of breast cancer in the case group was 53.28 ± 10.4 years. The results showed significant association in many terms of education level, employment status, physical activity, nutrition and fertility factors ($OR \leq 1$, $P\text{-value} \leq 0.05$). Based on the determination coefficient obtained considering the mentioned variables, at minimum, 68.2%, and at maximum, 91% of the changes in the likelihood of developing the risk of breast cancer can be explained.**Conclusion:** Consistent with most studies, the findings of the current research showed a significant association with the developing risk of breast cancer. Considering that most factors identified in the present study are preventable, there should be effective interventions to control the disease and its complications in society.

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Application of Study Results in Preventive Care in Nursing and Midwifery:

Because most of the breast cancer factors are preventable, Healthcare professionals should be able to offer counseling, and education for girls and women.

- - Also, Community-based breast cancer screening plans should be performed actively and passively

Introduction

Breast cancer is one of the most common cancers among women and is considered the leading cause of death in women. According to the World Health Organization (WHO) report, this cancer affects 2.1 million women annually, and it also causes the highest rate of deaths due to cancer among women [1,2].

Breast cancer is also the first common cancer among Iranian women [3]. A systematic review in Iran has estimated the prevalence of breast cancer in Iranian women at 23.6% (95% CI: 15.3–34.7%) [4]. According to the latest National Cancer Registry reports, the rate of breast cancer has increased from 25% to 26.47% of all cancers diagnosed in Iranian women in recent years [5].

A study based on cancer registration data reported an increase in the age standardized rate of breast cancer in Iranian women from 15.96 to 40.72 per 100,000 from 2003 to 2017 [6]. Another study showed that the number of new cases of breast cancer in Iranian women increased 8-fold from 1990 to 2016 [7].

The GLO-BOCAN project predicted the increasing trend of breast cancer incidence and deaths in Iran. The GLO-BOCAN predicted 14920 new cases of breast cancer and 5248 related deaths in Iran in 2025. Population growth, changes in the age pyramid and increasing age-specific rates support this upward trend [5].

Patients with breast cancer show a wide spectrum of physical, cognitive, psychological, and social symptoms due to the treatments applied, which

may have numerous long-term negative effects on the quality of life in this group of patients [8].

Research has shown that the incidence and survival of this cancer are associated with a family history of breast cancer, early menstruation, late menopause, age, race, gene, obesity, lack of breastfeeding, and the use of contraceptives. On the other hand, Lifestyle factors such as exercise, nutrition, mental well-being, the environment and substance use are known factors in the development of breast cancer [9,10]. Surveys show that socio-demographic differences are the main factor among the causes of death and health inequalities in general [11,12]. Individuals who live at lower socio-demographic levels behave differently in their way of coping with the disease and experience poorer health and shorter lives than those at higher levels [13,14]. Therefore, socio-demographic factors create different conditions regarding developing the disease, the quality of acceptance of the disease, the behavior in the state of the illness, the reaction to the disease, and the treatment quality.

Considering the huge psychological and socioeconomic impact of cancer on the lives of patients, their families and their health system, knowing the risk factors of cancer in each society and carrying out effective interventions according to the locality can be a factor in preventing and reducing the disease and its complications in the society.

Since no information is available regarding the relationship between different factors to breast cancer and taking into account that no study has been found in this regard in the city of Damghan, the research has been designed and conducted.

Methods

The present study was carried out as a hospital-based case-control study from March 2019 to March 2020 after obtaining the code of ethics (IR.SBMU.SME.REC.1399.066).

The case group included all individuals whose breast cancer had been confirmed according to pathology tests. The control group was also selected from the individuals were referred to the same hospitals and finally had no breast problems. Given that age is one of the risk factors, matching was performed in two groups. Also, residents of other cities were excluded from the study.

Before completing the information, obtain the participant's consent to participate in the study and assure them about the confidentiality of the information.

A questionnaire and checklist were used to collect data. The questionnaire consists of socio-demographic variables [14,15], nutrition and physical activity.

The food frequency questionnaire (FFQ) was used to investigate the nutritional habits of the research participants. Several studies in Iran have assessed the validation of FFQ. The result of a systematic review; generally, the cumulative estimate indicated good validity with the correlation coefficient with Dietary References in the range of 0.16- 0.65. Its reliability with the correlation coefficient of 0.28-0.85 indicated the appropriate reliability. For the content validity of the questionnaire in the research population, the advice of a nutritionist was used. The items related to alcohol consumption were removed due to the lack of common use among the research participants. The interview was used to get a deeper view of their nutrition and the high-quality filling of questionnaires. The amount of intake of a specific food item based on the scale mentioned in the questionnaire was completed daily, weekly, rarely and never used [16,17].

Also, a checklist of factors related to fertility, and care items were used [9,18,19]. Each part of the relevant studies was extracted, and its validity was then reviewed and confirmed by the opinions of experts (nutritionist, social medicine, general physician, midwife, and gynecologist) [14-19]. The content validity was assessed by the Lawshe method and confirmed totally with CVR=69%.

The fertility factors consisted of the age of menarche and menopause, the age of the first pregnancy, the number of childbirths and breastfeeding, and the history of taking hormonal contraception. The section on the care and treatment status consists of the first symptom of the disease at the time of diagnosis, detector, and breast routine monthly examinations, history in the family and first-degree relatives.

We used descriptive statistics of mean, standard deviation, frequency, percentage, chi-square test, and logistic regression test at a 95% confidence level to analyze the data. Analysis was performed using SPSS software, version 16.

Results

Socio-demographic information on cases and controls is presented in Table 1. There was no difference in the distribution of age, place of birth, or main place of residence between the groups ($P>0.05$).

The highest frequency regarding education level in the cases includes diploma and under diploma with 93.5%, while in the controls, 55.8% are post-diploma and above, and was significant (p -

value ≤ 0.05). The results showed significantly more cases were housewives (Table 1).

There was a significant difference between the cases and control group in terms of marital status, education level, father's education and spouse's education ($P<0.05$). However, the mother's education is not significantly different between the groups ($P>0.05$). The findings showed that the controls spent more leisure time travelling than the cases (Table 1).

Table 1: Frequency distribution of socio-demographic information in two groups

	Variables	Case		Control		Test statistic*	P-value
		Frequency	Percent	Frequency	Percent		
Age	Less than 40 years old	7	15.2	7	16.3	0.753	0.861
	41 to 50	10	21.7	11	25.6		
	51 to 60	19	41.3	14	32.6		
	Higher than 60	10	21.7	11	25.6		
Main place of residence	Urban	32	69.6	37	86	3.465	0.063
	Rural	14	30.4	6	14		
Marital status	Married	39	84.8	37	86	0.866	0.028
	Single	7	15.2	6	14		
employment status	Housewife	40	87	16	37.2	23.575	0.001
	Other	6	13	27	62.8		
Education level	Diploma and Lower	43	93.5	19	44.2	25.552	0.001
	Associate degree and higher	3	6.5	24	55.8		
Father's education	Secondary school and lower	39	84.8	19	44.2	16.136	0.008
	Diploma and higher	7	15.2	24	55.8		
Mother's education	Secondary school and lower	40	87	34	79.1	0.986	0.321
	Diploma and higher	6	13	9	20.9		
Spouse's education	Secondary school and lower	22	47.8	6	14	11.826	0.001
	Diploma and higher	24	52.2	37	86		
Household level of income	≤20 Million Rial	13	28.3	7	16.3	1.83	0.176
	≥ 20 Million Rial	33	71.7	36	83.7		
Spending leisure time	Travelling	11	23.90%	29	67.40%	17.018	0.0001
	Watching TV	38	82.60%	37	86.00%	0.198	0.656
	Religious places	26	56.50%	17	39.50%	2.568	0.109

*Chi-square (X^2) test

According to the results of current research, most individuals in the cases (63%) do not exercise, while in the controls, 81.4% do exercise (Table 2). The results showed the difference in exercise and minutes at each time is a significant

difference between the groups ($X^2=5.43$ P-value=0.020), but regular exercise and the exercise frequency per week are not significantly different between the groups ($X^2=.231$, P-value=0.631).

Table 2: The findings related to Exercise between the controls and cases

Exercise	Case (with breast cancer)		Control		χ^2		
	Frequency	Percent	Frequency	Percent	Test statistics	df	P-value
Yes	17	37	35	81.4	18	1	<0.001
No	29	63	8	18.6			
Regular Exercise							
Yes	13	28.3	23	53.5	0.231	1	0.631
No	5	10.9	12	27.9			
No Answer	28	60.9	8	18.6			
Several Times a Week							
3 Times And Less	5	10.9	9	20.9	0.579	1	0.447
More Than 3 Times	13	28.3	14	32.6			
No Answer	28	60.9	20	46.5			
A Few Minutes at a Time							
Minutes And Less 30	15	32.6	10	23.3	5.43	1	0.020
More Than 30 Minutes	4	8.7	13	30.2			
No Answer	27	58.7	20	46.5			
Total	46	100	43	100			

The results of questions related to nutrition in Table 3 show no significant difference in the type of oil consumed in both cases and controls respectively, and also a significant difference in the type of food (cooked and fried) Between the groups.

There was a significant difference in the consumption of vegetables, fresh cucurbits and salad, red meat, liver, offal, fish and shrimp, milk and dairy products, fast food and canned foods, and sugar in both cases and controls ($P < 0.05$).

Table 3: The findings related to nutrition between the controls and cases

How to use	Group s	Daily		Weekly		Seldom		Never		Fisher's exact test	
		Frequency	Per cent	Frequency	Per cent	Frequency	Per cent	Frequency	Per cent	Test statistics*	P-value
Fresh vegetables, cucurbits, and salad	Case	26	55.3	19	40.4	1	2.1	0	0	5.42	0.004
Fresh fruits	Control	34	75.6	9	20	0	0	0	0		
Red meat, liver, and offal	Case	39	83	7	14.9	0	0	0	0	0.028	0.866
Chicken and poultry	Control	37	82.2	6	13.3	0	0	0	0		
Fish and Shrimp	Case	9	19.1	35	74.5	2	4.3	0	0	6.73	0.034
High-fat food	Control	14	31.1	22	48.9	7	15.6	0	0		
Milk and dairy products	Case	17	36.2	28	59.6	1	2.1	0	0	3.32	0.199
Salty food and old foods	Control	12	26.7	26	57.8	5	11.1	0	0		
Fast food and canned foods	Case	0	0	2	4.3	37	78.7	7	14.9	13.5	0.004
Sugar	Control	2	4.4	12	26.7	21	46.7	8	17.8		
Unsaturated fats such as stew water, chicken broth, and butter	Case	1	2.1	19	40.4	24	51.1	2	4.3	3.65	0.474
Fresh vegetables, cucurbits, and salad	Control	2	4.4	24	53.3	16	35.6	1	2.2		
Fresh fruits	Case	21	44.7	24	51.1	1	2.1	0	0	8.17	0.010

Red meat, liver, and offal	Control	32	71.1	10	22.2	1	2.2	0	0		
Chicken and poultry	Case	1	2.1	9	19.1	25	53.2	11	23.4	4.25	0.236
Fish and Shrimp	Control	2	4.4	13	28.9	24	53.3	4	8.9		
High-fat food	Case	1	2.1	3	6.4	32	68.1	10	21.3		
Milk and dairy products	Control	2	4.4	13	28.9	19	42.2	9	20	9.86	0.020
Salty food and old foods	Case	28	59.6	11	23.4	7	14.9	0	0		
Fast food and canned foods	Control	28	62.2	15	33.3	0	0	0	0	7.82	0.019
Sugar	Case	4	8.5	24	51.1	16	34	2	4.3		
Unsaturated fats such as stew water, chicken broth, and butter	Control	4	8.9	29	64.4	9	20	1	2.2	2.77	0.458

The results showed that the age of getting breast cancer in the investigated sample with the mean (SD) was 53.28 (10.4). According to the results presented in Table 4, there was no statistically significant difference in terms of the age of menopause and the age of first pregnancy between cases and controls ($P < 0.05$), but there was a statistically significant association in terms of the number of childbirths and the history the hormonal use for contraception for more than six months, age of onset of menstruation and the

history of breastfeeding between two groups ($P < 0.05$).

Most people in both case and controls had no history of breast disease in family members or first-degree relatives. The first symptom of the disease at the time of diagnosis in most people, (32 people; 35.6% in the cases) included lumps and stiffness. The detector in most individuals was a doctor. The individuals with a frequency of 18 people (43.9%) mentioned breast routine monthly examinations once in a while.

Table 4: Presenting fertility and care factors in the controls and cases

Variables	Case(with breast cancer)		Control		Test statistics*	χ^2	P-value
	Frequency	Percent	Frequency	Percent			
Menstrual age							
13 years and lower	24	52.2	12	27.9	5.433	0.02	
14 years and higher	22	47.8	31	72.1			
Menopausal people							
Yes	33	71.7	24	55.8	2.44	0.118	
No	13	28.3	19	44.2			
Age of first pregnancy							
18 years and lower	18	39.13	12	27.27	1.643	0.20	
18 years and higher	25	54.35	30	68.18			
No pregnancy	3	6.52	2	4.55			
The number of childbirths and breastfeeding							
≤2	18	39.1	32	74.4	11.242	0.001	
≥3	28	60.9	11	25.6			
The hormonal use for contraception							
Lower than 6 month	2	4.3	10	23.3	18.2	0.001	
Higher than 6 month	25	54.3	6	14			
No use	19	41.3	27	62.8			
The history of breast disease in family members or first-degree relatives							
Yes	9	19.6	7	16.3	0.163	0.687	
No	37	80.4	36	83.7			

*chi-square (χ^2) test

According to the fitted regression model, consuming vegetables weekly or rarely increased

the risk of breast cancer ($OR > 1$) than individuals who consume vegetables daily; as well as the age

of onset of menstruation over 13 years (OR<1), an associate's degree and higher to diploma and lower (OR<1), women's employment status (employee, worker, retired, student) than being housewives (OR<1), and women who do exercise have a much lower risk of breast cancer (OR<1).

Based on the determination coefficient obtained considering the mentioned variables, at minimum, 68.2%, and at maximum, 91% of the changes in the likelihood of developing the risk of breast cancer can be explained (Table 5).

Table 5: Investigating factors influencing breast cancer using multiple conditional logistic regression model

Variables	Coefficient(β)	S.E.	Wald test	df	Sig.	OR* Exp(B)	95% CI *	
							Lower limit	Higher limit
The hormonal use for contraception	4.983	2.012	6.133	1	0.013	1<	2.827	7524.891
Fresh vegetables, cucurbits, and salad	3.594	1.824	3.881	1	0.049	1>	1.019	1298.05
The menstrual age(13 years old lower and higher)	-4.488	1.888	5.649	1	0.017	0.011	0	0.455
Education status (diploma,.)	-5.663	2.652	4.558	1	0.033	0.003	0	0.629
Occupation status (housewife and other)	-4.15	1.815	5.231	1	0.022	0.016	0	0.552
Exercise(yes, no)	-4.085	1.814	5.069	1	0.024	0.017	0	0.589
Constant	5.055	1.899	7.083	1	0.008	156.783		
Coefficients			Cox & Snell R Square		Nagelkerke R Square			
			0.682		0.91			

*Odds Ratio (OR)

Discussion

This study aimed to compare various factors such as physical activity, nutrition and fertility care between breast cancer patients and a control group. The findings in the current study indicated that the mean age of the patients with breast cancer was 53.28±10.4 years. Asgarian et al.'s study conducted in the city of Kashan [20] indicated that the incidence of cancer increased up to the age of 59 years. The findings of Nafisi's study on reducing the mean age of incidence of breast cancer in Iran [21] also confirm the necessity of designing and performing broad breast cancer screening programs for younger ages in the country [22].

The current research showed a significant difference in education levels between the groups. Even the education levels of the father and the spouse of the controls were higher than the cases. Consistent with the study, Josette Sin et al. showed in a study on 5393 affected patients that a higher education level was associated with the early stage of the disease at the time of diagnosis [23]. In an epidemiological study entitled Social Differences in Breast Cancer Survival in Sweden, Eaker et al. showed that after adjusting for age and stage at the time of diagnosis, the risk of death

due to breast cancer in individuals with high education levels was 35% less than individuals with low education levels [24].

In the present study, after controlling the influencing factors, women's employment status (employee, worker, retired, student) than being housewives and was statistically significant between the two groups. A large number of studies have suggested occupation as one of the factors influential in developing breast cancer [25,26]. Laden et al. indicated that the increased risk of developing breast cancer was associated with certain occupations such as teaching, management, and religious and medical occupations [27].

The findings of the present study showed that without considering the effects of other variables, the consumption of vegetables, fresh cucurbits, and salad was significantly associated with breast cancer, so individuals who consumed these groups of food rarely or weekly showed the odds ratio of developing cancer 2.9 times compared to those who consume vegetables and fresh cucurbits daily. Also, results showed that milk and dairy product consumption was more than in the controls (74%) compared to cases (45%). Moreover, in a case-control study conducted by Cade

et al. in England to examine the nutritional factors of breast cancer, dairy consumption was introduced as a protective factor against developing breast cancer [28]. Knekt et al. indicated that milk consumption had a significant inverse association with breast cancer and called it a protective factor against breast cancer [29]. Inconsistencies have been observed in the conducted studies between fat consumption and increased risk of breast cancer so in investigating the nutritional causes of breast cancer, Knekt et al. introduced fat consumption as a risk factor for developing breast cancer [29]. Kour et al. also showed that a high-fat diet at postmenopausal age was proposed as the major risk factor for developing breast cancer [30]. In Koaks's study in 1998, fat consumption was not identified as a risk factor [31]. In the current research, consuming fried food containing higher fat in the two groups was also significantly different. Consuming boiled food, which has less fat, in this study, more than 53% of healthy individuals and about 9% of patients consumed boiled food. It seems that the way and amount of consumption of vegetables, fats and other food items in different societies are affected by different cultures, facilities and lifestyles. And these items cause different results in research in different areas. The sample size and the way of selecting the samples as the limitations in the study can be the reasons for the non-significance of differences in risk factors in different groups. In the present study, a significant difference was obtained between low and high menstruation age (13 years), so that 52% of patients had the age of onset of menstruation of 13 years and below, and in 27% of healthy people, it was 13 years or below. Numerous studies have been carried out to evaluate the association of breast cancer with fertility factors. Titus-Ernst off suggested the young age of first menstruation as the risk factor for breast cancer [32]. In a nested case-control study in Taiwan, Wu H.C. showed that the menstrual age of $\leq$ versus less than 13 years, and multiparity were associated with a decreased risk of developing breast cancer [33]. In the present study, significant association was observed between the high number of childbirths and breast cancer. Park et al showed that multiparity as a risk modifier could be heterogeneously related to breast cancer [34]. Huber D. showed no relationship was observed between 45-year-old and older women and the risk of using oral contraceptives [35]. The ratio of observed risks was higher for those who used oral contraceptives for five years after cancer diagnosis; this effect was more remarkable for women under 35 years. In the present study, there is a significant association between the history of using oral contraceptive hormones and developing breast cancer irrespective of other factors, taking these pills for more than six months enhances the odds of breast cancer.

The relationship between taking oral contraceptives was also stronger for cancers in advanced stages [35]. Kanadys W. claims that oral contraceptives do not seem to enhance the risk of developing breast cancer among users. However, taking contraceptives before the first pregnancy or for more than five years can change the development of breast cancer [36].

In this study, there is a statistically significant association between doing exercise in leisure time and the incidence of this disease. Exercise is an important factor in reducing the incidence of breast cancer more than 30% of healthy individuals have exercised for more than 30 minutes, which was 9% in the cases. Many studies have identified exercise and its duration as an inhibitory cause of developing breast cancer. Marcus et al. proved that sports activities at 12-15 years decreased the risk of developing breast cancer [37].

Among the limitations of this study are the use of convenient samples in cases and the low sample size. In conclusion results should be interpreted more cautiously. Moreover, the self-declaration of the answers to the questionnaire is another limitation of the present study. Considering the retrospective of the current study and the possibility of recall bias, the generalizability of the results is questionable. It is suggested to conduct research in a more extensive community using sampling methods with a low bias to obtain more credible results.

Conclusion

The present study showed that most of the demographic variables, Nutritional factors and physical activity, fertility and care factors were significantly associated with the risk of breast cancer. Also, given that the association of status with the incidence and consequences of cancer has also been shown in many studies, it should be noticed that modifiable risk factors for community-based interventions and breast cancer prevention planning. Cancer screening planning should be performed actively and passively. Also, training and holding training classes for girls of all ages, especially in schools, for nutrition and physical activity to prevent diseases can effectively improve women's health.

Ethical Consideration

The present research is the result of the master's thesis in community-based health education approved at Shahid Beheshti University of Medical Sciences with the ethical code IR.SBMU.SME.REC.1399.066.

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Conflict of interest

There is no conflict of interest between the authors.

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Authors' contributions:

SS and NS: Study design and conceptualization; SS: Statistic analysis and report; SS and NS: manuscript writing and evaluation manuscript.

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