An evaluation of the risk factors of breast cancer in women in Ilam Province: a case–control study based on hospital

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Aims: The present study aimed to identify the most associated risk factors of breast cancer in Ilam province in 2015–2016. **Materials & methods:** In this case–control study, the case group consisted of 50 women with breast cancer with a definitive diagnosis from date 23 September 2015 to 22 September 2016. The two groups were group matched in terms of age. Data were collected through interviews and medical records. **Results:** According to the results, there was a significant relationship between the disease status and variables of family history, history of irregular menstrual cycles, history of breastfeeding, menopausal status, history of oral contraceptive pill consumption, BMI, menarche and number of pregnancies ($p < 0.05$). **Conclusion:** Regarding decisive risk factors of breast cancer, more studies with larger sample sizes that take into account more risk factors are necessary.

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Keywords: breast cancer • Ilam • Iran • risk factors

Background

Breast cancer is one the most common types of cancer and the main cause of death from cancer in women worldwide. In 2012, around 1.7 million cases and 521,900 cases of death (i.e., 25% of all cancer cases and 15% of all mortality from cancer) occurred due to breast cancer [1]. Although breast cancer is the fifth highest cause of death from cancer worldwide. However, the most common cause of death from cancer among women in developing and developed countries has not been specified yet [2,3]. The incidence and mortality from breast cancer in 187 countries from 1980 to 2010 indicated that the incidence of breast cancer increased by 3.1% and the mortality from breast cancer increased by 1.8% every year [4]. The incidence and mortality from breast cancer in Iran follows the above mentioned trend. According to the latest report by national cancer registration system in 2008, breast cancer, with a prevalence of 24.8% of all cancers in women, is the most common type of cancer in women and constitutes 11.3% of all cancer incidences. Furthermore, it has an increasing trend in women; its crude incidence was 0.23 per 100,000 women in 2003–2004 and reached to 0.75 in 2008–2009. In addition, mean peak age of breast cancer in Iranian women is reported to be in their fourth and fifth decades of life, which is one decade lower than the global statistics [5] and doubles the importance of this issue for us. According to the latest report by the national cancer registration system in 2008, prevalence of breast cancer in Ilam province was around 12.04, which is considered a low prevalence along with provinces of Ardebil, Sistan and Baluchestan and Kohgiluyeh and Boyer-Ahmad [5]. Various risk factors are mentioned for breast cancer in different references including age (the incidence rate of breast cancer increases with age), genetic factors, family history of breast cancer, previous history of breast cancer, history of benign breast disease, early puberty before age 12 year, late menopause after age 55 year, previous history of chest radiation therapy and first delivery after age 30 year, obesity, alcohol consumption and consumption of high fat foods [6,7]. Since the above factors can be divided into two groups of modifiable and nonmodifiable factors,

it is important to identify the risk factors, particularly the modifiable factors. Identification of changeable factors provides the possibility to interfere and reduce the incidence of the disease, while identification of unchangeable factors provides the possibility to find the vulnerable groups and measures in primary and secondary prevention such as screening [8]. Therefore, the present study launched to identify the most associated risk factors of breast cancer via a case–control study.

Method

Materials & methods

From 23 September 2015 to 22 September 2016, a case–control study was conducted among 100 women (50 women involving with breast cancer and 50 women without breast cancer) referred to obstetrics and gynecology clinics in Ilam province. The name, phone number and address of all subjects were obtained from the Health Center of Ilam province. The definitive diagnosis of breast cancer was done through biopsy and pathologic examinations in involved samples. For each subject with breast cancer, one patient hospitalized in Imam Khomeini hospital (Tehran, Iran), was selected through convenience sampling as a control. For the control group, patients without a breast disease or any malignancy were selected. The inclusion criteria for the case group included no history of chemotherapy, radiotherapy and hormone therapy, no history of benign breast mass, no history of hormone-related diseases (hyperthyroidism, polycystic ovary syndrome and irregular menstruation), grade 1 and 2 malignancy, no change in dietary patterns in the last 5 years, not being in the period of pregnancy or breastfeeding and no consumption of certain drugs such as methotrexate, cyclosporine, metformin, aspirin, epileptics and contraceptives [9]. Moreover, data collection and completion of the questionnaire was done by a trained midwife based on face to face interview. In case a subject passed away, one of the informed women of the family was interviewed. The questionnaire included questions about age, marital status, education, history of pregnancy, age of first menstruation, age of menopause, history of using oral contraceptives and history of breastfeeding. Written informed consent was obtained from all participants. Personal information and results of the data were set without mentioning the personal characteristics.

Statistical analysis

Data analysis was conducted by chi-square (Fisher's exact test), t-test and regression logistic on SPSS₂₁ software was used and significance level considered as 0.05.

Results

In this case–control study, the case group consisted of 50 women with breast cancer with a definitive diagnosis based on pathology reports and eligible for the research and the control group included 50 women (hospital controls) referred to Imam Khomeini hospital without a neoplastic disease. Mean and standard deviation of age were 45.7 ± 8.7 and 45.2 ± 11.3 years in case and control groups, respectively. And illustrate the distribution of studied variables in both groups of case and control. Moreover, since age factor was a matched.

Data analysis showed that a significant relationship between breast cancer and family history, history of irregular menstrual cycles, history of breastfeeding, menopausal status, history of oral contraceptive consumption, BMI, menarche and number of pregnancies was revealed ($p < 0.05$). However, no significant relationship was found between the disease status and variables of marital status, age of marriage, age of first pregnancy, history of abortion, income, place of residence, smoking and career ($p > 0.05$; Tables 1 & 2).

Finally, the variables that showed a significant relationship with breast cancer and were appropriate for the model included: exercise, family history, irregular menstrual history, history of benign breast disease, history of breastfeeding, menopausal status, history of oral contraceptive pill (OCP) and BMI, Menarche and the number of pregnancies entered the multivariate logistic regression model. The results showed that controlling the effect of other factors like exercise, BMI, menarche, irregular menstrual history, history of benign breast disease, OCP Consumption history and breastfeeding history are important variables in predicting breast cancer in the subjects (Table 3).

Discussion

Breast cancer is the most common type of cancer among women and considering its risk factors and informing women about this disease is highly essential [10]. The analysis results demonstrated that women with family history of breast cancer had a greater chance of breast cancer. In a study entitled 'Risk factors of breast cancer in women under 40 years old' in Cancer Institute of Imam Khomeini hospital in Tehran, Tehranian *et al.* reported an odds

Table 1. The frequency distribution of qualitative variables in both case and control groups of breast cancer.

Variable		Disease		p-value
		Yes	No	
Education level	Under diploma	37 (52.1%)	34 (47.9%)	0.6
	Upper diploma	13 (44.8%)	16 (55.2%)	
Smoking	Ever smoker	3 (6%)	1 (2%)	0.61
	Never smoker	47 (94%)	49 (98%)	
	Current smoker	0 (0%)	0 (0%)	
Job	Housekeeper	46 (54.1%)	39 (45.9%)	0.09
	Employee	4 (26.7%)	11 (73.3%)	
Location status	Urban	36 (72%)	40 (80%)	0.48
	Rural	14 (28%)	10 (20%)	
Marital status	Single	5 (10%)	10 (20%)	0.26
	Married	45 (90%)	40 (80%)	
Income status	Under 1 million toman	28 (48.3%)	30 (51.7%)	0.68
	Upper 1 million toman	22 (53.7%)	9 (46.3%)	
History of irregular menstruation	Yes	36 (69.2%)	16 (30.8%)	0.0001
	No	14 (29.2%)	34 (70.8%)	
History of breastfeeding	Yes	17 (34%)	33 (66%)	0.0001
	No	28 (80%)	7 (20%)	
Menopause status	Yes	36 (72%)	16 (32%)	0.0001
	No	14 (28%)	34 (68%)	
History of OCP use	Yes	33 (73.3%)	11 (27.5%)	0.0001
	No	12 (26.7%)	29 (72.5%)	
History of abortion	Yes	10 (47.6%)	11 (52.4%)	0.60
	No	35 (54.7%)	29 (45.3%)	
Family history	Yes	31 (62%)	19 (38%)	0.027
	No	19 (38%)	31 (62%)	
Maternal age at the time of first pregnancy	>30 years	15 (60%)	10 (40%)	0.47
	<30 years	30 (50%)	30 (50%)	

OCP: Oral contraceptive pill.

Table 2. Comparing the quantitative variables between case and control groups of breast cancer.

		Mean $\pm$ SD	p-value
BMI	Case	27.6 $\pm$ 3.6	0.01
	Control	25.46 $\pm$ 4.4	
Menarche	Case	13.26 $\pm$ 1.6	0.0001
	Control	14.66 $\pm$ 1.23	
Number of pregnancy	Case	2.7 $\pm$ 1.9	0.02
	Control	3.9 $\pm$ 2.8	
Marriage age	Case	19.7 $\pm$ 4.6	0.2
	Control	18.6 $\pm$ 5	

SD: Standard deviation.

Table 3. Multivariate logistic regression statistical analysis.

Variable		OR	95% CI	p-value
Exercise	No	1	(0.00–0.32)	0.017
	Yes	0.002		
BMI		1.2	(1–2.3)	0.012
Menarche		4.6	(1.3–15.6)	0.013
History of irregular menstruation	No	1	(1.3–8.2)	0.026
	Yes	4.6		
History of benign breast disease	No	1	(3.1–69)	0.031
	Yes	10		
History of OCP use	No	1	(1.5–24.1)	0.019
	Yes	11.9		
History of breastfeeding	No	1	(0.002–0.8)	0.042
	Yes	0.04		

OCP: Oral contraceptive pill; OR: Odds ratio.

ratio (OR) of 7.07 in women with positive family history compared with those without family history [11]. Tavani *et al.* reported an OR of 1.85 in women with positive family history compared with those without family history [12]. Ebrahimi *et al.* in a study entitled 'Risk factors for breast cancer in Iran' demonstrated that risk factors in women with positive family history was more than others [13]. Jafarinia *et al.* in a study entitled 'Risk factors of breast cancer in Dezful' demonstrated that family history was one of the major risk factors of breast cancer [14]. The results of most of the studies in this field emphasized on the effect of family history as a risk factor for breast cancer, which are in line with the results of the present study.

Our study demonstrated that the risk of breast cancer was higher in women with lower age of menarche and this inverse relationship was significant according to univariate analysis. Tehranian *et al.* also demonstrated that the risk of breast cancer was higher in women with lower age of menarche [11]. Tavani *et al.* also demonstrated that age of menarche lower than 12 years was a risk factor of breast cancer [12]. However, Ebrahimi *et al.* reported that there was not a significant relationship between age of menarche and the risk of breast cancer [13]. Yankaskas *et al.* in a study entitled 'Epidemiology of breast cancer in young women', also reported an insignificant relationship between age of menarche and the risk of breast cancer [15]. Jafarinia *et al.* also demonstrated that there was not a significant relationship between age of the first menstruation (menarche) and risk of breast cancer [14]. The studies of Tehranian and Ebrahimi *et al.* were both conducted in Imam Khomeini Hospital in Tehran, and the first study confirmed a significant relationship between the age of menarche and risk of breast cancer but the second study reported a lack of significant relationship. In addition, our present study and some other studies confirmed the significance of the relationship, while some other studies did not confirm this significance and this inconsistency may be due to use of different methodologies applied in these studies. To prove the true relationship between the age of menarche and the risk of breast cancer, more accurate and prospective investigations with bigger sample sizes are required in the future.

The present study demonstrated that the mean number of pregnancies in case group was less than the control group and this relationship was significant according to univariate analysis, indicating that risk of breast cancer was lower in women with more pregnancies. Layde *et al.* in a study demonstrated that OR in women with more than seven pregnancies was 0.59 compared with nulliparous women (16). However, Tavani *et al.* demonstrated that OR in multiparous women under 40 years old was lower than nulliparous women [12]. Based on a univariate analysis, Tehranian *et al.* demonstrated that OR in women with more than four deliveries was 13.33 compared with nulliparous women [11]. These differences may be due to selection of samples with high mean age and using different methodologies. Proving the relationship between number of births and breast cancer requires more investigations.

The present study demonstrated that there was no significant relationship between age at the first birth and risk of breast cancer, which was in accordance with the study by Ebrahimi *et al.* Yankaskas *et al.* demonstrated that there was a significant relationship between age at the first birth and risk of breast cancer [15]. Tavani *et al.* also demonstrated that risk of breast cancer was higher in primiparous women older than 30 years [12]. This difference may be due to small sample size of the present study.

The present study also demonstrated that breastfeeding was a protective factor against breast cancer based on both univariate analyses. Jafarinia *et al.* also demonstrated that breastfeeding was a protective factor against breast cancer [14]. Toleutay *et al.* demonstrated that history of breastfeeding was a protective factor against breast cancer [17]. Layde *et al.* demonstrated that risk of breast cancer in women with history of breastfeeding longer than 25 months was lower than those with no history of breastfeeding [16]. Based on a study by Zheng *et al.* in China, risk of breast cancer in women with history of breastfeeding longer than 24 months was lower than those with history of 1–6 months breastfeeding [18]. In another study by Yuan *et al.* in China, risk of breast cancer in women with history of breastfeeding longer than 109 months was lower than those with no history of breastfeeding [19]. Study of Tehranian *et al.* demonstrated that the relative risk in women with history of breastfeeding was lower than those with no history of breastfeeding [11]. Similar to our study, several studies emphasized on the importance of breastfeeding as a protective factor for breast cancer.

The present study demonstrated that there was a significant relationship between taking contraceptive pills and risk of breast cancer and the prevalence rate of taking contraceptive pills among cases compared with controls was almost triple (73.3 vs 27.5%, respectively). According to univariate analysis, the OR of taking contraceptive pills and the risk of breast cancer were 7.2 and 11.9, respectively, compared with control group. Tehranian *et al.* also demonstrated that there was a significant relationship in taking contraceptive pills and risk of breast cancer between the two groups. They reported a prevalence rate of taking contraceptive pills as 38.8 and 18.5%, among case and control groups, respectively. Also based on their study, the OR in women who took contraceptive pills

was 2.83 compared with those who did not [11]. Sidoni *et al.* also demonstrated that history of taking contraceptive pills increased the risk of breast cancer [20]. However, Ebrahimi *et al.* demonstrated that there was no significant relationship between taking contraceptive pills and risk of breast cancer [13]. Marchbanks *et al.* also demonstrated that there was no significant relationship between taking contraceptive pills and risk of breast cancer [21]. Most studies emphasized on the positive relationship between taking contraceptive pills and risk of breast cancer and lack of such reports in some studies might be due to using different methodologies.

According to our results, there was no significant relationship between history of abortion and breast cancer. Tehranian *et al.* demonstrated that relationship between history of abortion and breast cancer was not statistically significant [11]. According to a study by Mahue-Giangreco *et al.* the risk of breast cancer did not increase in young women with a history of abortion [22]. However, a study evaluating the relationship between history of abortion and breast cancer demonstrated that the risk of breast cancer in women with a history of induced abortion before 12th week of pregnancy was 2.1–26.2-times more than that among women without a history of induced abortion [23]. In addition, the risk of breast cancer in women with a history of spontaneous abortion after 12th week of pregnancy was 2.5–16.3-times more than that among women without a history of spontaneous abortion. The risk of breast cancer in women with a history of spontaneous abortion, whose the first abortion occurred after 12th week of pregnancy was 4.7–55.7-times more than that among women without a history of spontaneous abortion. Proving the relationship between history of abortion and breast cancer requires more investigations.

The present study demonstrated that risk of breast cancer was higher in women with higher BMI, which was in accordance with the study of Holakouie *et al.* [24].

One of the limitations of this study was recall bias and women in case group were more likely to recall past events than women in control group. Another limitation was small sample size.

Conclusion

The overall results of the current study demonstrated that there was a significant relationship between the disease status and variables of family history, history of irregular menstrual cycles, history of breastfeeding, menopausal status, history of OCP consumption, BMI, menarche and number of pregnancies.

Authors contributions

SHR, MA, ZJ, NP and KHA acquired in idea and data. SHR analyzed and interpreted the data. SHR and MA drafted the manuscript; SHR critically revised the manuscript for important intellectual content. SHR supervised the study. All authors have read and approved the manuscript.

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Ethical conduct of research

The study was approved by Ilam University of Medical Sciences Ethical Review Committee; IR.MEDILAM.REC.1394.205.

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