Early marriage is a potential risk factor for female breast cancer in the Eastern Region of Saudi Arabia

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Abstract

This study investigates the potential risk factors of female breast cancer in the eastern region of Saudi Arabia. It is a hospital-based case control study of all Saudi women who were diagnosed with breast cancer during the period from 2010 to 2011. It includes 225 cases and 450 age-matched controls. The statistical analyses were conducted using descriptive statistics, the Student Sample t-test, the Mann-Whitney U test, Chi square test and matched logistic regression model. The factor of early marriage or early sexual intercourse, that is, for females under 18 years of age (OR = 13.9, 95% CI, 6.0 to 32.3), was the strongest risk factor for breast cancer among women in the eastern region of Saudi Arabia; this was followed by the factors of obesity with a high body mass index (BMI) greater than or equal to 30 (OR = 5.7, 95% CI, 2.53 to 13.0); and prolonged use of birth control pills ≥ 36 months (OR = 5.0, 95% CI, 2.13 to 11.8). This study concluded that early marriage is the strongest potential risk factor for female breast cancer among Saudi women. Therefore, it is recommended to increase family awareness and knowledge about the suitable age for marriage.

Keywords: Breast cancer; early marriage; early sexual intercourse; Case control study; Cancer epidemiology; Conditional logistic regression; Odds ratio

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1. Background

Breast cancer is a significant global health concerns. Every year, thousands of women are diagnosed with breast cancer.[1,2] It is considered to be the second most common causes of cancer in the world and the most frequent leading causes of cancer mortality among females.[3,4] It is estimated that more than one million new cancer cases diagnosed in 2012.[5] In the United State of America, it is estimated that the age-standardised incidence rate of breast cancer was 92.9 per 100,000, and the mortality 14.9 per 100,000 population. In Europe, the age-standardised incidence rate of breast cancer was 94 per 100,000, and the mortality 23 per 100,000 women.[5-7]

In Saudi Arabia, female breast cancer is the most common cancer among women since the year 1994.[8] The eastern region of Saudi Arabia is considered to be one of the most highly affected areas with female breast cancer, when compared to other parts of the country. From 2001 to 2008, the eastern region of Saudi Arabia had the highest overall age-standardised incidence rate of female breast cancer, at 26.6 per 100,000 women.[8] In 2012, the estimated age-standardised incidence rate of female breast cancer in Saudi Arabia was 29.6 per 100,000, and the mortality 9.1 per 100,000 population.[5]

The effect of early marriage was observed many years ago with regard to cervical cancer, but not with breast cancer.[9, 10] In addition, early age at first sexual intercourse has been identified as a risk factor for invasive cervical carcinoma.[11] To the best of our knowledge, there is no scientific study that investigates the association of early marriage with female breast cancer. Therefore, the main aim of this study is to examine the possible association of early marriage with breast cancer among Saudi women. In addition, we effort to identify the strongest potential risk factors of female breast cancer in the eastern region of Saudi Arabia, by conducting an observational, analytical, and hospital-based case control study. However, in Saudi Arabia and other countries, any sexual activity without marriage is basically prohibited and illegal. Further, there is no specific age for marriage, either for the husband or for the wife, but in late 2008, the Ministry of Justice prohibited marriage for females under the age of 14 years.[12]

2. Materials and Methods

Study design and data collection

The researchers conducted a retrospective and analytical observational hospital-based case control study of all Saudi women who were diagnosed with breast cancer in the King Fahad Specialist Hospital (KFSH) at Dammam, Saudi Arabia, from 1st January 2010 until December 31st 2011. According to the cancer registry centre, in KFSH-Dammam, Saudi Arabia, there were

225 incident cases who were confirmed to have a positive diagnosis of breast cancer from 2010 to 2011. The available data of all cases were collected from the cancer registry centre of KFSH-Dammam, through cancer survey forms in the patients' files. In addition, the cases of female breast cancer in the hospital were representative of all female breast cancer cases among the population of the eastern region. However, the inclusion criteria for cases were as follows: (A) Confirmation of the diagnosis of breast cancer, (B) No previous history of cancer, (C) No previous treatment with chemotherapy or radiotherapy, (D) Following ethical approval.

For the control group, they were randomly selected from the same hospital and were matched to the cases based on the age at diagnosis. The control group contained twofold cases, and involved 450 disease-free Saudi women. They were representative of the population of the eastern region, from which the cases came. Moreover, they were selected from different clinics of the hospital that were not related to cancer treatment departments. Furthermore, all the Saudi women who participated as controls in this study agreed to face-to-face interviews and they answered all the questions listed in the questionnaire. Before the beginning of the interview with the participants, the research project's investigator described the objectives of the study, and obtained the consent form to get started with the subjects. The questionnaire was depending on the data we have collected from cases, and included many questions, gathering information about the following variables: the socio-demographic characteristics of Saudi women (age, education level, marital status, occupation, weight, height and BMI), menstrual and reproductive factors (such as age at marriage, age at first pregnancy, age at menarche, age at menopause, breastfeeding, use of oral contraceptive pills, and parity). However, the inclusion criteria for the control group were as follows: (A) Age matched with an interval (± 4 years), (B) No previous history of cancer, (C) No prior treatment with chemotherapy and radiotherapy, (D) Following ethical approval.

Classification of continuous and categorical variables

The cut-off points for quantitative variables were selected for coding each group in the study. In the case of age at marriage (which pertains to sexual intercourse early in life), we identified the cut-off point, which is 18 years of age, as the upper limit of age of childhood, based on the Convention on the Right of the Child that provided by the United Nation of Human Rights.[13] The cut-off points for age at menarche and menopause were 12 and 50 years respectively. In addition, the BMI that used to measure the amount of fat in the body, was calculated for all cases, and controls, through measuring weight of the subjects in kilograms (kg) divided by their height in metres (m) squared. The BMI was categorized and defined as normal from 20 to 24.9 kg/m^2, overweight from 25 to 29.9 kg/m^2, and obese above 30 kg/m^2.[14] The age at first pregnancy for all subjects was divided into four groups, which involved 14-19, 19-23, 24-28, ≥29 years of age. Further, the educational level of the participants was divided into four categories, which included non-educated, primary/intermediate school, high school, 1and College or university. On the other hand, marital status was only classified into two groups, which were married and divorced/widowed. Actually, all cases and controls were married and no single-member in our study, therefore, we combined the group of divorced and widowed together. For breastfeeding, Saudi women were categorized into two groups of “Yes” or “No”. Furthermore, oral contraceptive use was divided into four groups, and included total absence of use, use for less than 12 months, use for 12 to 36 months, and use for more than 36 months.

Methods of statistical analysis

Statistical analysis of the data in this study was carried out using the Statistical Package for the Social Sciences Version 20.0 (SPSS), and divided into four stages, including the following:

Stage 1: Comparing the cases with the controls for continuous explanatory variables by using Student Sample t-test and Mann-Whitney U test.[15]

Stage 2: Univariate analysis was used to detect whether there is any significant relationship between the variable of breast cancer (for cases - controls) and all explanatory variables independently in the data, by conducting a chi-square test. This type of analysis helps to identify the explanatory variables that should be included in the conditional logistic regression model.[16]

Stage 3: Multicollinearity diagnosis was conducted to detect whether there is any significant relationship between independent variables. This procedure should be conducted before fitting the model of conditional logistic regression, in order to prevent interactions between the explanatory variables. The amount of collinearity in a model is estimated by the variance inflation factor (VIF), which is calculated as $1/(1-R^2)$, where R^2 is the multiple correlation coefficient. However, a VIF that is greater than or equal to 10 is a sign of collinearity, and it should exclude the explanatory variable from the fitted model.[17]

Stage 4: Using conditional logistic regression model that takes into account the matching process of cases with controls.[18,19] This procedure helps to control the confounding variable in the study, and so, the age of the participants was the most important confounding factor, because the probability of getting breast cancer increases with age. Therefore, the age of controls was very close to the age of cases at the time of diagnosis. However, the odds ratios, p-values, and the confidence intervals (CI) of all explanatory variables in this model were also obtained.

Ethical approval and consent form

The ethical approval for conducting this study was obtained from the committee of Institutional Review Board (IRB) in KFSH-Dammam, Saudi Arabia. In addition, the consent form was signed by all participants before beginning our study.

3. Results

Analysis of continuous explanatory variables

A total of 675 Saudi women, including 225 cases of women with breast cancer, were recorded in the cancer registry centre of the King Fahad Specialist Hospital - Eastern Region, Dammam, Saudi Arabia, and 450 women who were free of disease were included as controls. To begin with, from the data analysis obtained, it was noted that the average weight of women with breast cancer cases, at the time of diagnosis, was 75.2 Kg (95% CI, 73.0 to 77.3) with minimum and maximum weight being 43 and 112 Kg respectively. Furthermore, the average weight of the controls was 66.1 Kg (95% CI, 65.0 to 67.2) with minimum and maximum at 40 and 100 Kg respectively. The assumption of homogeneity of variances for weight was violated, as assessed by Levene's test for equality of variances ($p < 0.001$). However, there was a statistical difference in the mean weight between the cases and controls, $t(342.236) = -7.53$, $P < 0.001$. Therefore, the weight of Saudi women with breast cancer was higher than those who were free of disease (the controls) (Table 1).

Table 1: Comparing continuous variables between cases and controls by using Independent sample t-test. P-value < 0.05, indicates that the mean differences between cases and controls are statistically significant

Characteristics of Continuous variables	Cases (N = 225)				Controls (N = 450)				Parametric test Two sample t-test	
	Mean	**Median**	**SD**	**SE**	**Mean**	**Median**	**SD**	**SE**	**t-value**	**P-value**
Weight in Kg	75.2	75.0	16.1	1.1	66.1	65.8	11.5	0.5	-8.39	<0.001*
Height in cm	1.56	1.56	0.06	0.004	1.61	1.60	0.06	0.003	10.1	<0.001*
Body Mass Index	30.8	30.7	6.5	0.43	25.4	25.2	4.4	0.20	-12.7	<0.001*

The mean height of breast cancer cases was 1.56 m (95% CI, 1.55 to 1.57), with minimum and maximum height being 1.41 m and 1.73 m respectively. Furthermore, the mean height of controls was 1.61 m (95% CI, 1.60 to 1.61), with minimum at 1.44 m and maximum at 1.82 m. There was homogeneity of variances for height among the cases and controls, as assessed by Levene's test for equality of variances (p = 0.56). However, there was a statistical difference in the mean height between cases and controls, where t (673) = 10.0, P < 0.001. Therefore, the height of Saudi women with breast cancer was less than the control group. The mean BMI was documented as 30.8 (95% CI, 29.9 to 31.6) among the women with breast cancer, and 25.4 (95% CI, 25.0 to 25.8) among the control group of women, who did not have the disease. The assumption of homogeneity of variances for BMI was violated, as assessed by Levene's test for equality of variances (p < 0.001). However, there was a statistical difference in the mean BMI between the cases and controls, t (330.876) = -11.2, P < 0.001. Therefore, most of the cases were deemed obese, and the BMI was higher among the Saudi women with breast cancer compared to the group without breast cancer (Table 1).

The median age at marriage for the breast cancer cases and the controls was 16.0 and 19.0 years respectively. The variable of age at marriage was not normally distributed, even after making transformation for the data, and therefore, the non-parametric Mann-Whitney U test was used to determine if there were differences in the age at marriage between the cases and the controls. In addition, the median age at marriage was statistically significantly different between the cases and controls, where U = 28012.5, z = -9.527, P-value < 0.001. However, most breast cancer cases had early marriage (which resulted early sexual intercourse) at under 18 years of age, compared to the control group (Table 2).

The median age at first pregnancy for breast cancer cases and controls was 19.0 and 21.0 years. There was significant differences between the cases and controls, U = 32722.0, z = -7.544, P-value < 0.001, However, most Saudi women with breast cancer in eastern region of Saudi Arabia had their first pregnancy below 20 years of age compared to the controls group. In addition, the median age at menarche for cases and controls was 11.7 and 13.0 years respectively. It was also significantly different in both groups, U = 35885.0, z = -6.320, P-value <0.001. However, most Saudi women with breast cancer had early menarche, below 12 years, compared to the controls group. Finally, the median age at menopause was observed among cases and controls at 51 and 49 years respectively, where the differences between them was statistically significant, U = 5929.0, z = -5.238, P-value <0.001. In addition, the majority of cases had late menopause above 50 years of age, compared to those free of disease (Table 2).

Table 2: Comparing continuous variables between cases and controls by Mann-Whitney U test. P-value < 0.05, indicates that the median differences between cases and controls are statistically significant

Characteristics of Continuous variables	Cases (N = 225)				Controls (N = 450)				Non-parametric test Mann-Whitney U test	
	Mean	Median	SD	SE	Mean	Median	SD	SE	z-score	P-value
Age at marriage	17.5	16.0	3.8	0.25	19.5	19.0	2.7	0.12	-9.527	<0.001*
Age at first pregnancy	20.0	19.0	4.0	0.26	21.5	21.0	2.8	0.13	-7.544	<0.001*
Age at menarche	12.0	11.7	1.7	0.11	12.6	13.0	1.2	0.05	-6.320	<0.001*
Age at menopause	50.3	51.0	2.2	0.22	48.6	49.0	2.7	0.19	-5.238	<0.001*

Analysis of categorical explanatory variables

According to Table 3 and 4, the univariate Chi-square test was used to identify the independent association between breast cancer (case-control) and categorical explanatory variables that included the demographic characteristics, as well as the menstrual and other reproductive factors. The distribution of cases and controls by educational level, occupation, marital status, BMI, age at marriage, age at first pregnancy, age at menarche, age at menopause, breastfeeding, oral contraceptive use, and the number of children, was statistically investigated. However, the analysis of chi-square test showed that menopausal status was not associated with breast cancer independently, P-value >0.05, and all other categorical explanatory variables were appropriate to be included in the final model of conditional logistic regression.

Table 3: Univariate Chi-square test to determine the association between breast cancer and socio-demographic characteristics

Socio-demographic Characteristics of subjects	Cases (N = 225)		Controls (N = 450)		Chi-Square Test	
	N	%	N	%	Chi2 value	P-value
Education					34.4	<0.01
Non-educated	79	35.1	90	20		
Primary/Intermediate	66	29.3	94	20.9		
High School	41	18.2	136	30.2		
College/University	39	17.3	130	28.9		
Occupation					24.1	<0.01
Housewife	200	88.9	325	72.2		
Worker	25	11.1	125	27.8		
Marital status					31.5	<0.001
Married	334	74.2	208	92.4		
Divorced/Widowed	116	25.8	17	7.6		

Table 4: Univariate Chi-square test to determine the association between breast cancer and reproductive and other potential factors

Reproductive and other Characteristics of the subjects	Cases (N = 225)		Controls (N = 450)		Chi-Square Test	
	N	%	N	%	Chi2	P-value
Age at marriage (in Years)					150.2	<0.001
≥ 18	78	34.7	369	82.0		
< 18	147	65.3	81	18.0		
Age at first pregnancy (in years)					64.32	<0.001
14 – 18	83	36.9	53	11.8		
19 – 23	108	48.0	299	66.4		

24 – 28	25	11.1	89	19.8		
≥ 29	9	4.0	9	2.0		
Age at menarche (in years)					60.0	<0.01
≥ 12	119	52.9	366	81.3		
< 12	106	47.1	84	18.7		
Age at menopause (in Years)					18.3	<0.02
< 50	33	14.7	116	25.8		
≥ 50	65	28.9	77	17.1		
Menopausal status					0.02	0.86
Pre-menopause	127	56.4	257	57.1		
Post-menopause	98	43.6	193	42.9		
Breastfeeding					94.1	<0.001
No	118	52.4	75	16.7		
Yes	107	47.6	375	83.3		
Body Mass Index					140.1	<0.001
Normal	36	16.0	257	57.1		
Overweight	67	29.8	125	27.8		
Obese	122	54.2	68	15.1		
Oral contraceptive use (in					49.7	<0.01
Months)	64	28.4	230	51.1		
Never	24	10.7	42	9.3		
< 12	51	22.7	106	23.6		
12 - < 36	86	38.2	72	16.0		
≥ 36						
Number of children					45.5	<0.03
1-3	51	22.7	217	48.2		
4-6	126	56.0	183	40.7		
7-9	37	16.4	44	9.8		
≥ 10	11	4.9	6	1.3		

Multicollinearity diagnosis

One of the assumptions for using logistic regression is that the explanatory variables do not have a high degree of collinearity with another, and so, the table of diagnostic shows that there is no association between the explanatory variables, as indicated by the VIF closer to zero and less than the 10. In addition, the tolerance values are not close to zero, and that indicate collinearity. Thus, non-collinearity assumption can be met, and in other words, there is no need to involve interaction effect in the multivariate analysis (Table 5).

Table 5: Multicollinearity test for explanatory variables

Explanatory variables	Collinearity Statistics	
	Tolerance	Variance Inflation Factor (VIF)
Education	0.61	1.63
Occupation	0.70	1.42
Marital status	0.84	1.18
Age at first pregnancy	0.55	1.80
Age at menarche	0.81	1.23
Age at menopause	0.94	1.05
Menopausal status	0.47	2.11
Breastfeeding	0.86	1.16
Body Mass Index	0.76	1.30
Oral contraceptive use	0.75	1.32
Number of children	0.79	1.26

Dependent variable: Age at marriage

Matched multiple conditional logistic regression model

The first step of univariate chi2 analysis shows that all explanatory variables are each separately, but significantly (P-value <0.001), related to breast cancer. In the second step, the assumption of multicolonieарity is not violated in order to make interactive effect between the explanatory variables. Furthermore, the backward elimination procedure shows that the conditional logistic regression model, which includes all the potential variables, are statistically significant (P-value <0.05), except occupation, age at first pregnancy, age at menarche, age at menopause and the number of children (P-value >0.05), and therefore, these explanatory variables should be dropped from the model and the model should be re-fitted again. However, the final fitted model shows that the first highest odds ratio that indicated the increasing probability of getting breast cancer was observed in women who had early marriage, that is, below 18 years of age (OR=13.9, 95% CI, 6.0 to 32.3), followed by obesity with high BMI ≥30 (OR=5.74, 95% CI, 2.53 to 13.0), and using oral contraceptive ≥36 months (OR=5.0, 95% CI, 2.13 to 11.8), <12 months (OR= 4.0, 95% CI, 2.39 to 20.5). In contrast, the lowest odds ratio that showed a decreasing probability of getting breast cancer (protective factors) was observed in breastfeeding (OR=0.1, 95% CI, 0.03 to 0.22), in women with a high level of education (OR=0.05, 95% CI, 0.01 to 0.24), and women with marital status as divorced/widowed (OR=0.11, 95% CI, 0.04 to 0.34) (Table 6).

Table 6: (*) indicates: Simple conditional logistic regression model; (**) indicates: Multiple conditional logistic regression model for testing the association between breast cancer and other potential risk factors. P-value <0.05 indicates that the variable is statistically significant. Odds ratio (ORs) >1 indicated that there is a positive association to increase the probability of getting breast cancer. ORs <1 indicated a protective factor that means a negative association to decrease the probability of getting breast cancer

Explanatory variables Cases (N=225) Controls (N= 450)	Crude Odds ratio*	95% CI	P-value	Adjusted Odds ratio**	95% CI	P-value
Education						
Non-educated	1.0			1.0		
Primary/Intermediate	1.71	1.14 – 2.58	0.001	0.23	0.08 – 0.68	0.008
High School	0.48	0.32 – 0.73	0.001	0.03	0.01 – 0.15	<0.001
College/University	0.43	0.27 – 0.69	<0.001	0.05	0.01 – 0.24	<0.001
Occupation						
Housewife	1.0			1.0		
Worker	0.32	0.20 – 0.51	<0.001	0.95	0.33 – 2.68	0.92
Marital status						
Married	1.0			1.0		
Divorced/Widowed	0.21	0.12 – 0.37	<0.001	0.11	0.04 – 0.34	<0.001
Age at marriage (in Years)						
≥ 18	1.0			1.0		
< 18	14.9	8.54 – 25.9	<0.001	13.9	6.0 – 32.3	<0.001
Age at first pregnancy (in years)						
14 – 18	1.0			1.0		
19 – 23	0.45	0.32 – 0.63	<0.001	3.0	0.92 – 10.2	0.06
24 – 28	0.43	0.25 – 0.74	0.002	3.26	0.65 – 16.3	0.15
≥ 29	2.22	0.81 – 6.0	0.12	3.50	0.80 – 18.5	0.08
Age at menarche (in years)						
≥ 12	1.0			1.0		
< 12	3.82	2.64 – 5.54	<0.001	1.77	0.83 – 3.76	0.13

Age at menopause (in Years)						
< 50	1.0			1.0		
≥ 50	3.10	1.82 – 5.30	<0.001	2.21	0.72 – 6.82	0.16
Breastfeeding						
No	1.0			1.0		
Yes	0.14	0.89 – 0.21	<0.001	0.1	0.03 – 0.22	<0.001
Body Mass Index						
Normal	1.0			1.0		
Overweight	2.64	1.71 – 4.08	<0.001	2.12	1.04 – 4.33	0.03
Obese	7.62	4.75 – 12.2	<0.001	5.74	2.53 – 13.0	<0.001
Oral contraceptive use (in Months)						
Never	1.0			1.0		
< 12	1.16	0.68 – 1.97	0.58	4.0	2.39 – 20.5	<0.001
12 - < 36	1.0	0.63 – 1.40	0.78	1.7	0.71 – 4.31	0.21
≥ 36	3.56	2.37 – 5.34	<0.001	5.0	2.13 – 11.8	<0.001
Number of children						
1-3	1.0			1.0		
4-6	2.1	1.43 – 2.93	<0.001	4.66	-0.7 – 10.0	0.06
7-9	1.9	1.18 – 3.25	0.009	3.16	-0.9 – 7.16	0.10
≥ 10	3.66	1.35 – 9.91	0.01	5.54	0.63 – 48.4	0.12

4. Discussion

The results of this study are based on the data recorded by Cancer Registry Centre at King Fahad Specialist Hospital – Dammam, Saudi Arabia. The hospital-based case control study of female breast cancer in the eastern region of Saudi Arabia provides an important indicator for the strongest potential risk factors of breast cancer, that was involved the increase of its incidence rate among Saudi women.

Age matched multiple conditional logistic regression model indicates that early marriage or early sexual intercourse is the strongest risk factor for breast cancer among Saudi women, where the odds of breast cancer is 13.9 times higher among such women when compared with those above 18 years of age. Since there is no previous study in this context, therefore, we consider that the most likely explanation for the presence of breast cancer in women who had an early marriage and subsequently, had sex early, may be due to the discrepancy or elevation in the secretion of the female sex hormones (such as oestrogen hormone) among female teenagers. Therefore, early marriage may be considered to be inaudible risk factor of getting breast cancer in the future.

This study shows that most of the Saudi females who suffered from breast cancer were obese and their BMI was above (≥30). The odds of breast cancer are 5.74 times greater in women with high BMI than women within acceptable BMI (<25). Actually, the relation between obesity and the presence of breast cancer depends on the menopausal status. Obesity is a protective factor for premenopausal women, whereas in postmenopausal women, it is considered to be a high risk factor for the incidence of breast cancer. However, it has been noted that the risk of breast cancer decreases by 42% among premenopausal women who weigh above 80 kg, compared to those who weigh less than 60 kg.[21] Nonetheless, it has been suggested that the levels of oestrogen and progesterone are more likely to be decreased in obese women, and consequently, the reducing the chances of breast cancer risk.[22]

We found that prolonged use of oral contraceptive was a risk factor for breast cancer among Saudi women, where the odds of disease among contraceptive users was 5.0 times higher than those who never used the pill. A cooperative epidemiological analysis of 54 studies worldwide on the strength of association between contraceptive use and female breast cancer included 53,297 women with breast cancer and 100,239 women without breast cancer from 25 countries. It concluded that there was a little risk of breast cancer for women who used a combination of oral contraceptives for 10 years, and the risk was increased by 24% among the women who used oral contraceptives, compared to those who never used the pill.[23]

This study further reported that breastfeeding can be considered to be a protective factor for breast cancer among Saudi women, where the odds of disease is reduced by 99% among the breastfeeding women, when compared to those who are non-breastfeeding. Actually, the influence of breastfeeding was observed in many epidemiological studies, and the results showed that the longer time the women breastfed, the more they would be protected against breast cancer.[24,25]

According to the educational status, it was seen that a high level of education is considered to be a protective factor for breast cancer among Saudi women, where, the odds of disease is reduced by 95% among women who have a high level of education, when compared to those who did not have a high level of education, or were uneducated. Furthermore, a higher educational level may contribute to an increase in the awareness of women, when related to the appropriate age for marriage and sexual activity. Therefore, most of cases in our study were uneducated and they might not be aware the proper age to getting married.

Also the data collected indicate that the marital status as a divorced or widowed woman was also deemed to be a protective factor from breast cancer among Saudi women, where the odds of disease got reduced by 89% for divorced/widowed women. This finding may support the previous claim made that sexual intercourse early in one's life for women can become a potential risk factor for breast cancer, because the sexual activities for Saudi women after divorce or widowhood legally stops. Therefore, it can be suggested that the experts of breast cancer have generated a new hypothesis that is used to testify the age of women when they started or stopped sexual activity with their partners, and confirm its association with breast cancer.

Our results were not statistically significant for the association between age at menopause and breast cancer, while most epidemiological studies have observed that the odds ratio of breast cancer is higher for women who experienced a late menopause at age above 55 years, compared to those less than 45 years.[26,27] Despite the early menarche at age below 12 years was not a significant risk factor for breast cancer among Saudi women, the odds ratio was 77% higher than women who had late menarche ≥ 12 years of age. However, most of epidemiological studies have reported that women who had early age at menarche (<12 years) are more likely to get breast cancer, when compared to the women who had their first menstrual period above 12 years.[28,29] In addition, many epidemiological studies have shown that the women with early age at menarche had higher levels of oestrogens for a long time after menarche than of women with a later menarche.[27]

Finally, this study had some limitations and strengths like other epidemiological studies, it was limited by its small sample size, so a larger sample would have more accurate results. Furthermore, in case control study, the rare exposures cannot be studied, the incidence rate of the disease cannot be estimated and the investigation is limited to a single outcome. For strengths of this study, most of cases in were incident cases who had the disease in 2010 and 2011. The incident cases may decrease the recall bias that may occur when the information about the exposure is inaccurate. However, most women with breast cancer under investigation may recall the past history of their exposure than an individual without disease (control).[30] Furthermore, case control study is efficient for rare diseases with long latency periods, and multiple exposures can be examining very well. In this study, we tried to control the confounding factor that associated with increasing the probability of contracting breast cancer. Age of cases is considered to be the most important factor in epidemiological studies of breast cancer, therefore, we attempt to control it by conducting age-matched case control study.

5. Conclusion

This epidemiological study has revealed that early marriage is the strongest risk factor for breast cancer in the Eastern region of Saudi Arabia. We have concluded to increase family awareness and knowledge about the suitable age for marriage. Therefore, the Saudi government represented by ministry of justice, may contribute to ban underage marriage for female under 18 years of age.

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