Risk Factors of Breast Cancer in Hadramout Valley and Desert, Yemen

Abstract

Background: The incidence of breast cancer is on rise in low- and middle-income countries as populations increasingly adopt western lifestyles. Studies on risk factors of cancers including breast cancer are lacking in Yemen. Therefore, this study aimed to determine the risk factors of breast cancer among women registered at Hadramout Valley and Desert Oncology Center (HVDOC). **Methods:** A case–control study was conducted at HVDOC, Yemen. All women who were registered in HVDOC and diagnosed with breast cancer and confirmed by histopathology during 2011–2015 were selected as cases. Age-matched controls were selected from women who underwent mammography in HVDOC during 2011–2015 and were confirmed to be free of breast cancer. Data were collected using semi-structured questionnaire and clinical data were abstracted from the medical records. **Results:** A total of 105 patients and 210 controls were included in this study. About 70.5% of cases and 72.4% of control were 50 years old or younger. Compared with married women, divorced women had higher odds of breast cancer [odds ratio (OR) = 2.2]. The odds of breast cancer was higher for women who had never breastfed a child (OR = 1.7). Having hypertension (OR = 2.5), family history of malignancy (OR = 2.4), and postmenopausal status (OR = 2.0) were significantly associated with higher odds of breast cancer in multivariate analysis. **Conclusions:** The main risk factors for breast cancer among women in Yemen are divorced marital status, never breastfed a child, having hypertension, family history of malignancy, and postmenopause. Regular screening especially among women with high risk is needed.

Keywords: *Breast neoplasm, case–control study, risk factors, Yemen*

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Introduction

Breast cancer is the most common cancer in women worldwide, with an estimated 2.4 million incident cases in 2015,[1] accounting for 25% of all new cases of cancer in women.[1] It is the fifth most common cause of death from cancer in women with an estimated 523,000 deaths in 2015.[1,2]

The incidence of breast cancer is on rise in low- and middle-income countries as populations increasingly adopt western lifestyles. Mortality is disproportionately high in poor countries (mainly in Africa and Asia), where more than 60% of new breast cancer cases occur and 70% of the world's total deaths take place.[3] In the Eastern Mediterranean Region,[4-6] breast cancer is the most common malignancy, comprising 12%–30% of all cancer cases. In Yemen, breast cancer is the most common cancer among females where it constitutes about 21% of all cancer cases where the mean age at diagnosis is 47 years and about one-quarter of cases are diagnosed below the age of 40 years.[7-10]

Previous literature identified many personal and clinical risk factors associated with breast cancer. However, these studies included women of various ages, measured and reported risk factors in different ways, and provided wide ranges of risk estimates.[11] The most-studied known or suspected risk factors for breast cancer included advanced age, first-degree relatives with breast cancer, family history of early ovarian cancer, high endogenous estrogen or testosterone level (postmenopausal), first full-term pregnancy after age 35 years, alcohol consumption, early menarche (age <12 years), height (>5 feet 3 inches), high socioeconomic class, never breastfed a child, nulliparity (no full-term pregnancies), late menopause (age >55 years), type II diabetes mellitus, hypertension, obesity, recent and long-term use of hormone replacement therapy containing estrogen and progestin, oral contraceptive use, and tobacco abuse.[12-36]

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Studies on risk factors of cancers, including breast cancer, in Yemen are lacking. Therefore, this study aimed to determine the risk factors of breast cancer among women at Hadramout Valley and Desert Oncology Center (HVDOC) in Yemen.

Methods

A case–control study was conducted in HVDOC which is in Seiyun city, Hadramout Valley and Desert (HVD) governorate from October to December 2015. HVDOC receives all cancer cases from HVD governorate and the neighboring governorates where it provides diagnostic procedures and cancer care for all cancer patients.

All women who were registered in HVDOC and diagnosed with breast cancer and confirmed by histopathology during 2011–2015 were selected as cases. The total number of women who underwent mammography in HVDOC during 2011–2015 and confirmed to be breast cancer cases was 143. A total of 27 had died and 2 had moved to another governorate. Of the remaining 114 cases, 105 (92%) agreed to participate. All women who underwent mammography in HVDOC during 2011–2015 and confirmed to be free of breast cancer were considered as a source for controls. For each woman diagnosed with breast cancer, two control women were selected to match cases for age (±5 years), district residency, and year of diagnosis. All cases and control participants were living in HVD governorate and known to be of the same ethnicity and religion. Ethical approval was obtained from the Research Center at Ministry of Health and Population. All women gave an oral informed consent for their participation in the study.

Data were collected by face-to-face interview that took 20–30 min and that was conducted for cases during their monthly follow-up visits to HVDOC and for control at their houses. For cases who did not attend follow-up visits, the field workers visited them at their houses and interviewed them. A semi-structured questionnaire was used for the interview that included information on demographic data including age, education (illiterate/literate), employment, and marital status at the time of diagnosis for cases and at the time of last visit to HVDOC for mammography for controls. Clinical data were abstracted from the medical record. Other information was collected about other potential risk factors and included age at marriage, family history of breast cancer (first-degree relatives), menopausal status, age at menopause, age at menarche, parity, oral contraceptive use, hormonal replacement therapy, weight gain/loss, having breast biopsies, and so on. The questionnaire was pilot tested on 10 respondents who were not included in the study. Necessary changes were made according to the results from the pilot, for example, removing the question on income as the majority did not respond to it.

Data were analyzed using the Statistical Package for Social Science. The characteristics of breast cancer cases and control participants were compared using chi-square test. Multivariate binary logistic regression was used to determine the factors associated with breast cancer using forward selection method. A $P < 0.05$ was considered statistically significant.

Results

Participants' characteristics

This case–control study included a total of 105 women with breast cancer and 210 age-matched controls. Table 1 shows the sociodemographic characteristics of cases and control participants. About 70.5% of cases and 72.4% of controls were 50 years old or younger. Only 29.5% of cases and 38.1% of controls were literate, and 2.9% of cases and 8.1% of controls were employed. While there were no significant differences between cases and controls in age, education, and occupation ($P > 0.05$), cases and controls differed significantly in their marital status ($P = 0.015$) as the proportion of cases who were married was lower than the proportion for controls (64.8% vs. 78.6%). All interviewed women were non-smokers.

Univariate analysis

Table 2 shows the association between breast cancer and reproductive health of women, clinical and relevant characteristics in univariate analysis. Of all studied variables, postmenopausal status ($P = 0.020$), never breastfed a child ($P = 0.036$), oral contraceptive use ($P = 0.020$), family history of malignancy ($P = 0.012$), and hypertension ($P = 0.026$) were significantly associated with breast cancer in univariate analysis. All other studied variables were not significantly associated with breast cancer.

Multivariate analysis

Multivariate analysis of factors associated with breast cancer is shown in Table 3. Compared with married women,

Table 1: Sociodemographic characteristics of cases and control participants, Hadramout Valley and Desert, Yemen, 2011-2015

Variable	Cases (*n*=105)		Controls (*n*=210)		P*
	n	Percentage	*n*	Percentage	
Age (years)					
≤50	74	70.5	152	72.4	0.723
>50	31	29.5	58	27.6	
Education					
Illiterate	74	70.5	130	61.9	0.825
Literate	31	29.5	80	38.1	
Employment					
Housewife	102	97.1	193	91.9	0.072
Employed	3	2.9	17	8.1	
Marital status					
Divorced	17	16.2	15	7.1	0.015
Married	68	64.8	165	78.6	
Widow	20	19.0	30	14.3	

*Chi-square test

Table 2: The association between breast cancer and reproductive health of women, clinical and relevant characteristics in univariate analysis, Hadramout Valley and Desert, Yemen, 2011-2015

Variable	Cases (*n*=105)		Controls (*n*=210)		*P**
	n	Percentage	*n*	Percentage	
Age at menarche (years)					
≤12	33	31.4	54	25.7	0.285
>12	72	68.6	156	74.3	
Age at marriage (years)					
≤18	67	63.8	144	68.6	0.733
>18	35	33.3	66	31.4	
Age at first pregnancy (years)					
>23	7	6.7	19	9.0	0.587
≤23	87	82.9	184	87.6	
Menopausal status					
Postmenopausal	57	54.3	85	40.5	0.020
Premenopausal	48	45.7	125	59.5	
Age at menopause (years)					
>50	25	23.8	39	18.6	0.948
≤50	32	30.5	46	21.9	
Parity					
0-3	35	33.3	60	28.6	0.460
>3	70	66.7	150	71.4	
History of abortion	42	40.0	86	41.0	0.871
History of hysterectomy/oophorectomy	12	11.4	22	10.5	0.949
Breastfeeding	91	86.7	198	94.2	0.036
Any oral contraceptive method					0.020
No	53	50.5	93	44.3	
> 36 months	19	18.1	69	32.9	
≤36 months	33	31.4	49	23.3	
Family history of ovarian cancer	3	2.9	4	1.9	0.892
Family history of breast cancer	7	6.7	13	6.2	0.870
Family history of malignancy	17	16.2	15	7.1	0.012
Diabetes	10	9.5	25	11.9	0.526
Obesity	6	5.7	10	4.7	0.241
Hypertension	15	14.3	20	9.5	0.026
Dyslipidemia	6	5.7	10	4.7	0.302

*Chi-square test

divorced women had higher odds of breast cancer [odds ratio (OR) =2.2; 95% confidence interval (CI): 1.1–5.2; P = 0.048]. The odds of breast cancer was higher for women who had never breastfed a child (OR = 1.7; 95% CI: 1.1–5.0; P = 0.044). Having hypertension (OR = 2.5), family history of malignancy (OR = 2.4), and postmenopausal status (P = 2.0) were significantly associated with higher odds of breast cancer.

Discussion

This study showed that divorce, never having breastfed a child, having hypertension, family history of malignancy, and postmenopausal status were main risk factors of breast cancer for women in Yemen. Divorced women had higher risk of breast cancer compared with married women. An increased risk of breast cancer after divorce[15] and after husband's death[16] has been reported by previous studies. This finding might be explained by the psychosocial stress that results from these traumatic events. Inhibition of estrogen synthesis induced by chronic stress could explain the increased incidence of breast cancer in women exposed to stressful events such as divorce. Stressful life events in women have been reported to be associated with increased incidence of breast cancer.[17] It is also possible that several factors associated with divorce such as dietary habits and life style factors might confound the association between divorce and breast cancer. However, some case–control studies showed no or weak associations between divorce and breast cancer.[18,19]

Our findings clearly suggest that women who never breastfed their children have a higher risk of breast cancer. This finding is consistent with the findings of other studies.[22,26] Breastfeeding reduces a woman's number of menstrual cycles, and thus her cumulative exposure to endogenous hormones. These effects have been shown to

Table 3: Multivariate analysis of factors associated with breast cancer, Hadramout Valley and Desert, Yemen, 2011-2015

Variable	OR	95% Confidence interval		P*
Marital status				
Married	1.0			
Divorced	2.2	1.1	5.2	0.048
Widow	1.4	0.7	2.8	0.325
Breastfeeding				
Never breastfed a child	1.7	1.1	5.0	0.044
Breastfed a child	1			
Hypertension (yes vs. no)	2.5	1.4	5.0	0.005
Family history of malignancy	2.4	1.1	5.3	0.033
Menopause (yes vs. no)	2.0	1.2	3.5	0.009

OR=Odds ratio. *Multivariate binary logistic regression

be associated with a decrease in breast cancer risk.[20] In addition, breastfeeding has direct effects on breast cells, causing them to differentiate, or mature, so they can produce milk. Some researchers hypothesized that these differentiated cells are more resistant to becoming transformed into cancer cells than cells that have not undergone differentiation.[21,22]

This study showed that women with hypertension had an increased risk of breast cancer. Observational studies examining the relationship between hypertension and breast cancer risk have reported conflicting findings. A recent meta-analysis[23] suggested a significant association between hypertension and breast cancer risk, specifically for postmenopausal hypertensive women. This finding might be explained by the fact that hypertension and breast cancer risk may share common pathophysiological pathway mediated by adipose tissue, which could cause chronic inflammation and further increased the risk of both breast cancer and hypertension.[24] Another possible explanation is that hypertension may increase breast cancer risk by blocking and subsequently modifying apoptosis, thereby affecting the regulation of cell turnover.[25]

Our findings clearly suggest that postmenopausal status increased the risk of breast cancer which is consistent with some other studies.[26,27] This may be because some of the drugs used to manage menopausal symptoms (e.g., hormones) may be related to breast cancer.

We did not find age at menarche to be associated with breast cancer which is consistent with previous studies.[28,29] However, other studies reported early age at menarche as a risk factor which we could not show in this study may be due to the small sample size. A meta-analysis that included individual data from 117 epidemiologic studies showed an increased breast cancer risk by 5% for each year younger at menarche and by 2.9% for each year older at menopause.[29] The role of age at menarche and at menopause on breast

cancer risk was reassessed in a combined analysis of four Italian case–control studies including a total of 6,075 cases and 5,492 controls. The effect of age at menarche on breast cancer risk was small and the role of age at menopause was relatively moderate.[30] This study did not support the association between breast cancer and some other factors that were found to be associated with breast cancer in previous studies such as age at marriage,[31] age at first pregnancy,[31-33] parity,[34,35] abortion,[36] and family history,[32,36] which may be due to the small sample size in this study.

One of the limitations of this study is that the findings might not be generalizable to the whole population of Yemen. Another important limitation is the small sample size that may have affected power to detect significant differences. Furthermore, due to some logistical constraints, we did not collect information on other key factors such as nutritional status and physical activity.

Conclusions

Divorce, never breastfed a child, having hypertension, family history of malignancy, and postmenopausal status are the main risk factors of breast cancer in HDV. There is a need to increase public awareness regarding breast cancer and its possible risk factors as well as importance of regular screening especially among women with high risk.

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