Risk factors of breast cancer in a sample of Kurdish women of Kurdistan Region - Iraq: a comparative study between pre-menopausal and post-menopausal women

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Abstract

Background and objectives: To evaluate the difference between pre- and post-menopausal breast cancer regarding menstrual and reproductive risk factors for ca breast..
Methods: A prospective case-control study was conducted in Nanakaly Oncology Hospital in Erbil city-Kurdistan- Iraq, between September 2009 and April 2011. Cases were breast cancer patients admitted in the oncology floor of the hospital. Controls were hospital patients without breast cancer (other cancers). The study enrolled 300 cases and 600 controls. Menstrual and reproductive history was taken from both the cases and the controls. For every risk factor age-adjusted odds ratio (OR) and 95% confidence interval (CI) was calculated by logistic regression analysis, separate for pre- and post-menopausal women .
Results: Among the breast cancer patients, 42.7% were pre-menopausal and 57.3% were post-menopausal. Age at menarche had no association with breast cancer for both pre- and post-menopausal women. Nulliparity was a risk factor for both pre-menopausal (OR = 2.42, 95% CI (1.1-4.6) and post-menopausal breast cancer (OR = 3.7, 95% CI (2.04-6.87)). Among parous women only post-menopausal females having <3 children were at increased risk for breast cancer (OR = 2.18, 95% CL (1.45-3.27) compared with females having > 3 children. Younger age at first live birth decreased breast cancer risk in both pre- and post-menopausal women. Breastfeeding was not associated with both pre- and post-menopausal breast cancer.
Conclusion: Majority of risk factors for pre-menopausal breast cancer are also associated with post-menopausal breast cancer except less parity, which increased the risk for post-menopausal breast cancer only.
Keywords: Breast cancer, Case-control study, Risk factors. .

Introduction

With more than one million new cases in the world each year, breast cancer is the most common malignancy in women and comprises 18% of all women cancers.[1] Breast cancer incidence rates are increasing in most regions of the world, especially in the developing nations.[2] Breast cancer is the most common female cancer in Kurdistan -Iraq with an age-adjusted incidence rate of 68.9 per 100,000 per year.[3]

Globally there is a wide variation in age standardised breast cancer incidence across different populations ranging from 18 per 100,000 in south Africa to 88 per 100,000 women in Western Europe.[4]
This variation is mainly due to differences in reproductive and menstrual characteristics. Menstrual and reproductive factors are the most important risk factors for breast cancer. Younger age at menarche, nulliparity, older age at first live birth and

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no breastfeeding have been consistently found to increase breast cancer risk.[5-15] Menopause marks a crucial change in the reproductive life of a woman, bringing a decline in the levels of female sex hormones particularly estrogen and progesterone. There is also a marked increase in the levels of gonadotrophin hormones as a result of lack of feedback inhibition by the female sex hormones. Elevated FSH and LH levels lead to stromal stimulation of the ovary, with a resultant increase in estrone levels and a decrease in estradiol levels.[14] As hormonal factors play a significant role in causing breast cancer and the onset of menopause changes hormonal environment of females, therefore pre-menopausal women might not have the same hormonal risk factors as do the post-menopausal women. Many studies have tried to address this question and have found variable results.[5-9,11-15] A cohort study showed that younger age at menarche increased breast cancer risk only in pre-menopausal women, while nulliparity increased the risk only in post-menopausal women. Older age at first live birth increased breast cancer risk in both the menopausal groups.[7-15] The current study presented comparison between pre-menopausal and post-menopausal women regarding breast cancer risk associated with reproductive and menstrual factors.

Methods

Prospective case-control study was conducted in Nanakaly Oncology Hospital in Erbil city-Kurdistan Region- Iraq, between September 2009 and April 2011. Cases were breast cancer Kurdish patients from Erbil admitted in the oncology floor of the hospital. Controls were hospital patients without breast cancer (other cancers). As fewer cases than controls were available, it was decided to take cases and controls in a ratio of 1:2. We enrolled 300 cases and 600 controls.

After obtaining informed or verbal consent, both cases and controls were asked about their basic demographic factors. Menstrual and reproductive history was taken, including age at menarche, menopausal status, age at menopause, number of children born alive, age at first live birth and breastfeeding practice. Menopause was defined as absence of menstruation for at least six months before the diagnosis of breast cancer for cases and date of admission for controls.

In this study logistic regression was used to calculate age-adjusted odds ratio and 95% confidence interval for every hormonal factor, separate for pre- and post-menopausal women. The p-value was calculated using Chi-square test. All analyses were done with statistic program.

Results

Among the breast cancer patients 42.7% were pre-menopausal and 57.3% were post-menopausal. Age at menarche had no association with breast cancer for both pre- and post-menopausal women. Nulliparity was a risk factor for both pre- and post-menopausal breast cancer, but the association was stronger for post-menopausal women. Higher age at menopause did not increase breast cancer risk in post-menopausal women Table (1).

Among parous post-menopausal women, breast cancer risk was higher OR was 2.18 (95% CI (1.45-3.27)) for women having <3 children compared with women having > 3 children. No association was found between less parity and pre-menopausal breast cancer Table (2).

Among pre-menopausal parous women more cases than controls had age > 30 years at first live birth ($p < 0.001$). History of breastfeeding did not increase breast cancer risk for both pre- and post-menopausal women.

Table 1: Breast risk factor for all women

Variables		Case N	control N	Chi square	P value	OR, 95% confidence
Premenopausal		128	256			
Age at menarche	< 12	5	11	0.03	0.85	0.91 (0.27-2.9)
	≥ 12	123	245			
Parity	Nulliparous	21	20	6.61	0.01	2.42 (1.1-4.6)
	Parous	107	236			
Postmenopausal		172	344			
Age at menarche	< 12	7	15	0.02	0.877	0.93 (0.34-2.94)
	≥ 12	165	329			
Parity	Nulliparous	35	22	22.7	<0.0001	3.7 (2.04-6.87)
	Parous	137	322			
Age at menopause						
≥ 50		88	183	0.91	0.662	0.92 (0.63-1.35)
< 50		84	161			

Table 2: Breast risk factors for parous women t risk factor for all women

Variables		Cases N	Control N	Chi square	P Value	OR, 95% confidence
Premenopausal		128	256			
No of live biths	< 3	61	127	0.13	0.718	0.92 (0.95-1.45)
	≥ 3	67	129			
Age at first bith	< 30	49	194	51.6	<0.001	0.2 (0.12-0.32)
	≥ 30	79	62			
Lactation	Never	10	17	0.18	0.671	1.19 (0.49-2.85)
	Ever	118	239			
Postmenopausal		172	344			
No. of live birth	< 3	73	87	15.77	<0.001	2.18 (1.45-3.27)
	≥ 3	99	219			
Age at first birth	< 30	54	264	99.7	<0.991	0.14 (0.09-0.21)
	≥ 30	118	80			
Lactation	Never	11	18	0.29	0.588	1.24 (0.53-2.84)
	Ever	161	326			

Discussion

This study showed that younger age at menarche did not increase breast cancer risk for both pre- and post-menopausal women while nulliparity was a risk factor for both. Higher age at menopause was not a risk factor for post-menopausal women. Previous studies have reported inconsistent results regarding age at menarche and breast cancer risk. Lubin et al [8] found that younger age at menarche increased breast cancer risk only in pre-menopausal women, while Antoniou et al [13] reported increased risk only for post-menopausal women. In some studies, age at menarche was associated with both pre- and post-menopausal breast cancer[11, 15] while in another study it had no association with either pre- or post-menopausal breast cancer.[12] Majority of these studies relied on patient's recall for determining age at menarche. Correct recall of events that happened years ago depends on many factors, including age, education, and mental well-being. Recall-bias could be the reason for these inconsistent findings about age at menarche and breast cancer risk. A review article showed that age at menarche was associated with both pre- and post-menopausal breast cancer, but the association was stronger for pre-menopausal women. For each additional year of age at menarche, the risk of female breast cancer decreased by 9% for pre-menopausal women, and by 4% for post-menopausal women.[6] Similar findings were found in a study which showed that younger age at menarche explained 70% of pre-menopausal breast cancers while it explained only 27.5% of post-menopausal breast cancers.[15]

We found that both pre- and post-menopausal nulliparous women were at increased risk for developing breast cancer. A previous study has found that Nulliparity is associated with only post-menopausal breast cancer.[5] However, another study has reported increased risk for only pre-menopausal women.[12]

Areview article showed that pre-menopausal breast cancer risk was reduced by 3% per full-term pregnancy while the risk reduction was 12% for post-menopausal breast cancer.[6] It seems that the protective effect of parity against breast cancer is more for post-menopausal women than for pre-menopausal women. In a previous similar study, it was found that women who gave birth to a child before 24 years of age exhibit a decrease in their lifetime risk of developing breast cancer, and moreover additional pregnancies increase the protective effect. [14] The breast tissue of normally cycling women contains three identifiable types of lobules; the undifferentiated Lobules type 1 (Lob 1) and the more developed Lobules type 2 and Lobules type 3. The breast attains its maximum development during pregnancy and lactation (Lobules type 4). After menopause the breast regresses in both nulliparous and parous women and consists only of Lobules type 1. Despite the similarity in the lobular composition of the breast at menopause, in both the parous and nulliparous women, Lob 1 in these two groups of women are different biologically, and exhibit different susceptibility to carcinogenesis. It was suggested that Lob 1 found in the breast of nulliparous women and of parous women with breast cancer never went through the process of differentiation, retaining a high concentration of epithelial cells that are targets for carcinogens and are, therefore, susceptible to undergo neoplastic transformation.

In our study, increasing parity decreased breast cancer risk only in post-menopausal women while younger age at first live birth (FLB) decreased risk in both pre- and post-menopausal women. The findings about decreased risk for increasing parity are consistent with some previous studies.[14-16] Some studies have found that increasing parity decreased risk in both pre- and post-menopausal women.[11-13] In a local study increasing parity reduced breast cancer risk only in pre-menopausal women.[3]

The findings in this study about age at FLB are consistent with many previous studies which found that younger age at FLB decreased breast cancer risk in both pre- and postmenopausal women.[6,7,11] However, some studies found that a higher age at first live birth is protective only for postmenopausal women.[8,9] In a cohort study relative risk of breast cancer for age at FLB >30 years was 1.63 for pre-menopausal women and 1.35 for post-menopausal women.[7]

In younger age at FLB reduces breast cancer risk in two ways. First, early pregnancy results in early differentiation of mammary gland cells. Second, women with early age at FLB usually have longer cumulative duration of breastfeeding which further reduces breast cancer risk. Some studies have found that younger age at FLB is more important than increasing parity in reducing breast cancer risk. Lee showed that increasing parity no longer decreased breast cancer risk after adjusting for age at FLB.[15-16]

We found that breastfeeding was not protective against breast cancer for both pre- and post-menopausal women. Majority of Western studies have shown that breastfeeding is protective against pre-menopausal breast cancer.[10, 12] However; some studies found protective effect only for post-menopausal women.[15.] A collaborative re-analysis of 47 studies showed that breastfeeding was protective for both premenopausal and post menopausal women.[12]

Current study had some limitations. First, we studied prevalent breast cancer cases rather than incident ones. Second, the sample size was small which resulted in wider confidence intervals. We found only one local study similar to ours done in Sulaimani during 2006-2008, that assessed role of reproductive factors in causing breast cancer separate for pre- and post-menopausal women in sample of Kurd society.

Conclusion

Despite its limitations; the study will be a useful addition to current understanding of epidemiology of breast cancer in Kurdish women. Studies done on a wider scale are needed to establish the findings of the study related to risk factors for pre-menopausal and post-menopausal breast cancer in the country.

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