Reproductive risk factors of breast cancer

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Received: December 2019; Accepted: January 2020; Published: February 1, 2020.
Citation: Sarab K.Abedalrahman, Besmah M.Ali, Ali S. Al-Hashimi, Abid Issa Al-Khalidy. Reproductive risk factors of breast cancer. World Family Medicine. 2020; 18(2): 20-24. DOI: 10.5742MEWFM.2020.93764

Abstract

Background: Reproductive risk factors are important factors that have an effect on breast cancer risk, and incidence. This study aimed to study the effect of reproductive factors such as breast cancer risk factor.

Methods: Retrospective case control study, with a randomly selected 147 breast cancer cases compared with 161 non-breast cancer cases.

Results: Age at 1st delivery ≥30 years was significantly associated with increased risk of breast cancer OR 2.7. Nulliparity parity, had ≥ 3 full term pregnancies had no-significant association with increased risk of breast cancer1.28, and 1.97 respectively. Among those aged ≤ 45years having ≥3 children significantly had 2.7(1.02-7.3) risk than those who had 1-2 children, while among those aged > 45 years multiparty showed a non significantly protective effect with OR, 0.8(0.3-2.3). Age stratification show that age at first delivery ≥30 years had significant increased risk among those aged ≤ or > 45 years; OR 4.1, and 1.2, respectively. The Odds ratio for lactation for >12 month was 1.03(0.5-2.1), among those aged ≤ 45 years, with higher protective effect among those aged > 45 years, 0.6 (0.3-1.3).

Conclusion: Age at 1st full term pregnancy was an important factor affecting breast cancer risk. Parity has a dual effect in breast cancer risk.

Key words: Breast cancer. Risk factors, parity, age at 1st delivery, breast feeding

Introduction

Breast cancer is the chief and most commonly diagnosed cancer among women globally and the major reason of deaths related to cancer in the developing world[1].

The effect of reproductive factors strongly supports a hormonal role in the etiology of breast cancer [2].

Not breast feeding is another risk factor that is responsible for 5% of breast cancer cases in the UK [3] with lower risk among BRCA1 mutation carriers, while, it is not associated with BRCA2 carriers [4,5].

Full term pregnancy before age 20 years decreases breast cancer risk about 50%, than nulliparous or after 35 years [6] .

Alpha-fetoprotein, a protein produced by the fetus during pregnancy, helps regulate fetal growth. It can also help suppress breast cancer cells. Over the age of 30, alpha-fetoprotein works differently, and may actually help promote rather than inhibit breast cancer development. [7].

The risk of breast cancer declines with the number of children borne. Women who have given birth to five or more children have half the breast cancer risk of women who have not given birth [8].

The results of findings from analysis propose that the number of parities and the longer duration of breastfeeding were inversely associated with the risk of breast cancer [9].

Few detailed studies have been carried out on reproductive risk factors of breast cancer. The aim of this study was to estimate the effect of reproductive risk factors on breast cancer in Iraq.

Patients and methods

A retrospective case control study was done on patients of breast cancer registered in the women's health center, in Al-Elwyia maternity teaching hospital, during the period from 1st Jan- 30th October 2018. All 147 selected cases of breast cancer were included after documented histopathological examination and compared with 161 women registered in the women's health center, in Al-Elwyia Maternity Teaching Hospital, and proved not to have breast cancer by radiological, histopathological and cytological investigations.

Data was obtained through standardized questionnaire and follow up medical records to obtain the information about the demographic, characteristics, and different risk factors e.g. reproductive, hormonal and genetic risk factors of breast cancer. All breast cancer cases were included and a random sample of women without breast cancer attending the women's health center were included. The diagnosis of cases and controls done by consultant medical staff, using a Triple Assessment Technique (i.e. physical breast examination, ultrasonography, with or without mammography and fine needle aspiration cytology) according to the patient state.

The risk factors of age at menarche, age at menopause, age at 1st pregnancy and family history, were noted and categorized according to Centers for Disease Control and prevention CDC.[10]

The Statistical Package for Social Sciences (SPSS, version 18) was used for data entry and analysis. Pearson Chi- square ($\chi 2$) test was used to compare proportions of different factors among different groups of the study sample. Odds ratio, and adjusted OR was calculated using binary logistic regression using Enter method and were used to find the associations of risk factors. P value of ≤ 0.05 was regarded as statistically significant.

Results

The reproductive risk factors data show that : the Odds ratio was significantly associated with breast cancer regarding age at 1st delivery ≥30 years (2.7), while the number of full term pregnancies was non- significant as compared with the nulliparous with women who had 1-2 full term pregnancies (1.28), and (1.97) and for those had ≥ 3 full term pregnancies, as shown in Table 1.

Table 2 shows the age stratification of parity and breast cancer: the nulliparous were non-significantly associated with breast cancer with OR 0.7 (0.3-1.7), 1.6 (0.5-4.5) among those aged ≤ 45 years, and > 45 years, respectively.

Comparing the number of children, shows that among those aged ≤ 45years having ≥3 children significantly has 2.7(1.02-7.3) risk than those who had 1-2 children while among those aged > 45 years there is non- significant multiparity showing no significantly protective effect with OR, 0.8(0.3-2.3).

The Odds Ratio was significantly associated with breast cancer regarding age at 1st delivery ≥30 years, 4.1among those aged ≤ 45 years, with lower risk among those aged > 45 years, (1.2) as shown in Table 3.

The Odds Ratio was non-significantly associated with breast cancer regarding lactation for >12 month 1.03(0.5-2.1), among those aged ≤ 45 years, with higher protective effect among those aged > 45 years, 0.6(0.3-1.3), as shown in Table 4.

Table 1: The Reproductive risk factors among breast cancer cases and women without breast cancer

Reproductive factors		Cases	Controls	Total	OR	P value
Parity	Nulliparous	25	34	59	0.765(0.43-1.4)	> 0.05
		17.00%	21.10%	19.20%		
	Parous	122	127	249		
		83.00%	78.90%	80.80%		
No. of children	Nulliparous	25	34	59	1.28(0.62-2.62)	>0.05
		17.00%	21.10%	19.20%		
	1_2	23	40	63	1	
		15.60%	24.80%	20.50%		
	≥3	99	87	186	1.97(1.1-3.6)	0.022
		67.30%	54.00%	60.40%		
Lactation	<12 months	68	68	136	1.2 (0.75-1.84)	>0.05
		46.30%	42.20%	44.20%		
	≥12 months	79	93	172	1	
		53.70%	57.80%	55.80%		
Age at 1st delivery	<30	99	117	216	1	<0.05
		67.30%	72.70%	70.10%		
	≥30 years	23	10	33	2.7(1.2-5.98)	
		15.60%	6.20%	10.70%		

Table 2: The association between breast cancer and parity

	Controls No.%	Cases No.%	OR	P
Age ≤ 45 years				
Multiparous	88(73.3%)	32(26.70%)		
Nulliparous	29(80.60%)	7(19.40%)	0.7(0.3-1.7)	0.38
No. of births				
Nulliparous	29(80.6%)	7(19.4%)	1.4(0.4-4.5)	0.6
1-2 children	34(85%)	6(15%)	1	
≥3 children	54(67.50%)	26(32.5%)	2.7(1.02-7.3)	0.04
Age according to code 45 >45				
Multiparous	39(30.20%)	90(69.80%)		
Nulliparous	5(21.70%)	18(78.30%)	1.6(0.5-4.5)	0.4
No. of births				
Nulliparous	5(21.7%)	18(78.3%)	1.3(0.3-4.9)	0.7
1-2 children	6(26.1%)	17(73.9%)	1	
≥3 children	33(31.1%)	23(79.30%)	0.8(0.3-2.3)	0.6

Table 3: The association between breast cancer and age at 1st delivery

	Control	Cases	OR(CI)	P
Age at diagnosis ≤ 45 years				
Age of 1st delivery				
<30 years	112(77.20%)	33(22.80%)	1	
≥30 years	5(45.50%)	6(54.50%)	4.1(1.2-14.2)	0.02
Age at diagnosis >45				
Age at 1st delivery				
<30 years	38(29.50%)	91(70.50%)	1	
≥30 years	6(26.10%)	17(73.90%)	1.2(0.4-3.2)	0.7

Table 4. The association between breast cancer and duration of Breast feeding

	Control	Cases	OR(CI)	P value
Age at diagnosis ≤ 45 years				
Lactation				
≤12 months	52(75.40%)	17(24.60%)	1.03(0.5-2.1)	0.9
>12 months	65(74.7%)	22(25.3%)		
Age at diagnosis > 45 years				
Lactation				
≤12 months	16(23.90%)	51(76.1%)	0.6(0.3-1.3)	0.2
>12 months	28(32.9%)	57(67.1%)		

Discussion

The non-significant difference in parity among cases and controls reported in previous literature in Iraq [11,12] may be related to the fact that most of the Iraqi females get married at an early age and had mean family size of 5.5-6 persons.

Nulliparous was non-significant having 1.6 OR than parous among women aged > 45 years. This also reported in Iraq OR 2.1 [13] .

Women who had 3 or more children have OR of 1.97 compared to those who had 1-2 children. This goes along with what was found by Essiben F etal (1.43) for those had 3-5 children and 1.73 for > 5 children [14].

Previous studies done by, Lambe et al. [15], Liu et al. [16], Julie R et al [17] and Albrektsen G et al [18] demonstrated the presence of a transient increase in risk of breast cancer associated with each full-term birth, followed by a reduction in risk many years later.

Full-term pregnancy has several effects that could influence the risk of breast cancer [15,19].

The terminal differentiation of lobular mammary cells occurs at completion of a full-term pregnancy, leaving them less susceptible to malignant transformation. Women with 1st full term pregnancy at young age had less duration between menarche and pregnancy, thus reduced risk of breast cancer [20] .

The increased parity of more than 3 children is associated with decreased risk of breast cancer after age of 45 years. This may be explained by that found previously, that the increased risk with parity reaches its highest level at approximately 5 years after the birth and disappears approximately 15 years later [16] .

The transient increase in risk after birth was strongest after a late first birth, or subsequent pregnancies after age 30 years. [21]

The mother's age at births, as well as birth spacing, influenced the magnitude and timing of the transient increase in risk shortly after a delivery [18] . Most o Iraqi women in the cities tend to complete their families before age of 40 years, with little spacing, therefore this effect may be strong in early life and reduced after 45 years, especially if females married early.

All the above support the finding that late age (≥30 years) at 1st pregnancy had 2.7 fold of increased risk than those aged less than 30 years. Age stratification shows stability of increased risk of breast cancer with increasing age at 1st birth, this effect was more obvious in those aged≤ 45 years. This goes along with that found in previous studies in Iraq 3.4 [13] .

The promoting effect of pregnancy oestrogen was more prominent and the proportion of oestrogen and progesterone receptor positive breast tumours has been found to increase with age [22] with the highest proportion of oestrogen and progestron receptors at age 35–39 years [23].

Some studies found heterogeneity in reproductive risk factors for the distinct subtypes of breast tumors, as triple negative breast cancer had fewer consistent associations with reproductive factors and the only protective factor most consistently associated with TNBC was longer duration of breastfeeding [24] or the genetic hormonal pathways effect where it was reported that the number of deliveries at early age had a dose-response protective effect on breast cancer except for the women carrying C allele in rs2229712 who did not benefit from this protective effect [25] .

The changes in childbearing pattern during recent decades, with fewer children and higher age at births [26] will probably affect cancer incidence in the future.

From the findings of this study it is important to study the changes in reproductive behavior in relation to breast cancer risk, and the genetic subtypes of breast cancer.

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