Original Research Paper

REPRODUCTIVE RISK FACTORS OF BREAST CANCER: A CASE CONTROL STUDY

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ABSTRACT:

Background: Breast cancer is a multifactorial disease. This study was undertaken to study various reproductive risk factors associated with breast cancer.

Aim: to find out some of the reproductive risk factors of breast cancer and their association with breast cancer among patients attending the tertiary care centre

Methods: Cases were women with histopathological confirmed breast cancer. Controls were age-matched women without any current breast problems or previous breast cancer. A total of 138 cases and 138 controls were enrolled. They were interviewed for menstrual history, age at first child birth, breast feeding history, abortion history, family history etc after obtaining informed written consent.

Results: The significant risk factors were age >25 years at first child birth (OR 2.80, 95%CI 1.13-6.95), breast feeding history of < 2 years (OR 2.88, 95%CI 1.09-7.6), history of abortion (OR 3.35, 95%CI 1.37-8.18)

Conclusions: Age at first child birth >25 years, breast feeding duration of <2 years, history of abortion increases the risk of developing breast cancer.

Key words: breast cancer, case control study, breast feeding, risk factors.

INTRODUCTION

Breast cancer is the most common cancer among women worldwide. It was estimated that one in eight women in the Western world will develop the disease during their lifetime. According to GLOBOCON 2018, number of new cases of breast cancer in 2018 is 2,088,849 and number of deaths due to breast cancer in 2018 is 626 679.[1]

The burden of breast cancer is increasing in both developed and developing countries; it is now the most frequently occurring malignant disease in women and comprises 24.2% of all female cancer. Worldwide, breast cancer is the fifth most common cause of cancer death (after lung cancer, stomach cancer, liver cancer, and colon cancer).

Currently, in India, the incidence of breast cancer has steadily increased over the years. In 2018, number of new cases of female breast cancer of all ages is 162 468 (27.7% of all cancers in females).

Several studies showed certain risk factors are strongly correlated to development of breast cancer including: early menarche, null parity or late age at first birth, late menopause, family history as well as endogenous or exogenous hormonal factors. Other risk factors that may also be mediated through a hormonal pathway include obesity, diet, sedentary lifestyle, and alcohol consumption. Environmental factors such as xenoestrogens, radiation and pesticides have been also found to increase the risk of breast cancer development. Breastfeeding has proved to be a protective factor.

For a country like India with a huge population, diverse cultures, geographical variation and dietary habits the sources of information on breast cancer risk factors are considerably limited. The reasons for varying incidence of breast cancer among women are not fully understood. Most of the studies regarding breast cancer risk factors are western studies and there is only limited number of Indian studies.

Risk factors of breast cancer among Indian women are different from western population in many ways. The present study attempted to find out some of the reproductive risk factors of breast cancer and their association with breast cancer among patients attending the tertiary care centre Dr. B R Ambedkar Memorial Hospital Raipur (C.G.).

MATERIALS AND METHODS

This Case control study was conducted in the one year period of August 2017 to August 2018. Considering the delayed age at first delivery as a risk factor with an exposure of 30% in control group & an anticipated OR of 2 for a power of 80% & 5 % level of significance the sample size was calculated by epiTools software. Number of cases were138, for 1:1 allocation ratio the required number of controls were 138.

Cases were defined as all types of histopathologically confirmed cases of breast cancer irrespective of their stage and with age $\geq$ 25. All the stages of breast cancer, both preoperative and post-operative were included. Controls were females other than breast cancer in the hospital during the interview. Group matching was done with age with interval of ± 3 years. Male breast cancer, women with other proven malignancy, seriously ill patients, patients not willing to participate in study were excluded from the study.

Standard definitions were used for data collection. Mean and standard deviation were used to summarize data. Chi-square test, Odds ratio, Fisher's exact test were used to identify and quantify the risk of breast cancer.

RESULTS

Maximum number of cases was belonging to the age group of 45 to 54. The mean age of the cases was 48.7 Years (SD±10.6). The mean age of the controls was 47.4 years (SD± 10.6). (Figure 1)

Women who gave birth to their first child after 25 years of age had 2.8 times risk of breast cancer compared to women with first child birth before 25 years of age (OR 2.80, 95% CI 1.13-6.95, p value 0.025). Women who breast fed for less than 2 years had 2.88 times risk of breast

cancer than women who fed for more than 2 years (OR 2.88, 95% CI 1.09-7.6, p value 0.032). Women with history of abortion had 3.35 times risk of breast cancer (OR 3.35, 95% CI 1.37-8.18, p value 0.0077). (Table 1)

DISCUSSION

Breast cancer is rare before the age of 25. In our study maximum number cases were found in the age group of 45 to 54. Incidence of cases gradually increased with age up to 50 years and then decreased, this agrees with the result of Mitruen et al[3] The reduction in incidence of breast cancer around menopause could be related to ovarian and other hormones involvement in the development of breast cancer.

In our study we found that women who gave birth to the first child after 25 years of age had 2.8 times risk of breast cancer when compared to the women who gave birth before 25 years of age (Table 1)**.** There is similar Indian study by Rao et al [4] which showed delivering their first child after 30 years associated with increased risk of breast cancer.

In our study we have found that Women who breast fed their children for less than 2 years had 2.8 times risk of breast cancer than women who fed for more than 2 years (Table 1). This is in accordance with study by kuru et al [5] where they showed a significant association in Turkish women with breast feeding and decrease risk of breast cancer. Gajalakshmi et al [6], McCredie et al [7], Balasubramaniam SM et al [8] also found duration of breast feeding as a significant risk factor for breast cancer. In contrast there are studies by Riyadh K Lafta et al[9], Laufey Tryggvadottir et al [10] which found no association of breast-feeding practices with risk of breast cancer.

In our study we noted that women with history of abortion are at 3 times higher risk of breast cancer than women without history of abortion, this agrees with the study done by Alaa Darweesh et al [11], Tavani A et al [12]   Navneet Kaur et al [13] observed that women with two or more abortions had a 4.5-fold risk of breast cancer as compared to women with no history of abortions. Balasubramaniam et al [8] also found that women with history of at least one abortion had twice the risk of breast cancer than women with no history of abortion. Study done by Parameshwari et al[14] did not found history of abortion as a significant risk factor.

The mean age of menarche in cases was 13.86 with SD ±1.11 and the mean age of menarche in controls was 13.7 with SD±1.62. Age of menarche was not found to be a significant risk factor in our study (p value= 0.21) this agrees with the study by   Parkinson et al[15] and Laila Matalqah et al[16], Riyadh et al[9]. In contrast there are studies [14,17,18] which found significant association of early menarche as a risk factor of breast cancer.

CONCLUSIONS

Increasing age is the strongest risk factor for breast cancer. The rate of increase in incidence of breast cancer declines following menopause, suggesting a role for ovarian and other female hormones in the development of breast cancer. Reproductive history and menstrual cycle characteristics represent some of the most strongly established risk factors for breast cancer. Women with age at first child birth < 25 years, parity of > 3, duration of breast feeding for > 2 years have lower risk of breast cancer compared to women with age at first delivery > 25

years, parity of <3 and duration of feeding for < 2 years. Women with history of abortion have 3 times risk of developing breast cancer compared to women without history of abortion. Hence delayed age at first pregnancy should be avoided and breast feeding should be promoted. Breast cancer is a leading cause of mortality in developing countries like India. So, raising awareness about the above-mentioned reproductive risk factors help in reducing incidence of breast cancer.

Conflict of interest: None

Ethical approval: This study was approved by the institutional ethical committee.

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TABLES

Risk factors		Cases (%)	Controls (%)	O.R.	95% C.I.	P value
Age of menarche (years)	**≤15 years**	128 (92.7)	122(88.4)	1.67	0.73-3.84	0.22
	>15years	10 (7.24)	16 (11.5)	1(ref)		
Age at first child birth*	**≤25years**	120(86.9)	131(94.9)	1(ref)		**0.025****
	>25 years	18(8.69)	7(4.34)	2.80	1.13-6.95	
Parity	**Nulliparous**	6 (4.34)	1(0.72)	6.22	0.73-52.42	0.09
	Parous	132(95.6)	137(99.2)	1(ref)		
Duration of breastfeeding*	**≤ 2years**	16 (13.1)	06 (4.34)	2.88	1.09-7.6	**0.032****
	>2 years	122(88.4)	132(95.6)	1(ref)		
Age at menopause (For 75 cases and 73 control)	**Up to 50 years**	73 (97.3)	69 (94.5)	1(ref)		0.395
	More than 50 years	2 (2.66%)	4 (2.89%)	0.472	0.08-2.66	
Number of abortions*	**No abortions**	117(84.7)	131 (94.9)	1(ref)		**0.0077****
	Abortions	21 (15.21)	7 (6.52)	3.35	1.37-8.18	
Menstrual cycle	**Regular**	120 (86.9)	122 (88.4)	1(ref)	0.55-2.3	0.714
	Irregular	18 (13.04)	16 (11.5)	1.14		
Marital status	**Married**	136 (98.5)	137(99.2)	1(ref)		0.56
	Unmarried	2 (1.44)	1 (0.72)	2.01	0.18-22.48	

Table 1: Reproductive risk factors of breast cancer
* For statistical convenience unmarried women were also included
** Statistically significant
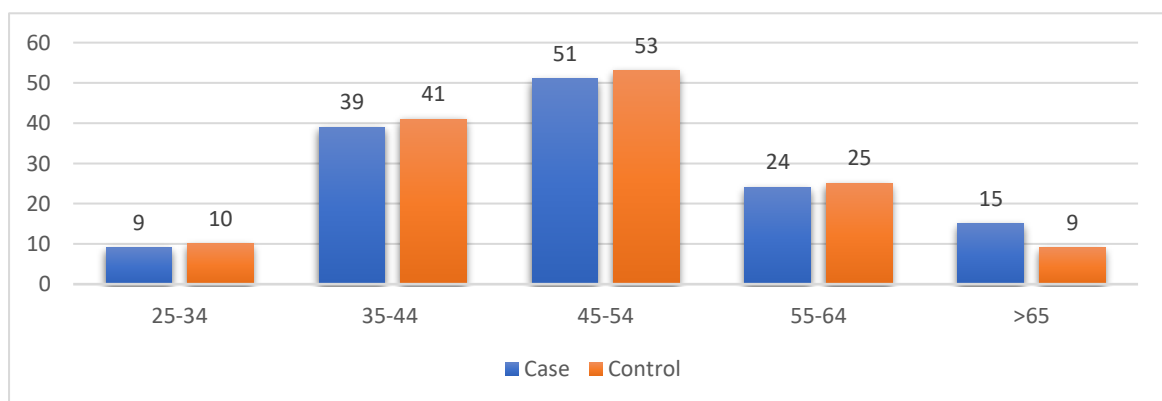
Figure 1: Age group-wise distribution among cases and controls