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Original Research Article

Risk factors associated with breast cancer among women attending a tertiary care hospital in Bangalore: a case control study

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ABSTRACT

Background: Breast cancer is one of the commonest cancers in both developing and developed countries. Owing to regional variations in distribution of risk factors, there is geographical variation in incidence of breast cancer. This study was attempted to assess the modifiable and non-modifiable risk factors associated with breast cancer among women attending a tertiary care hospital.
Methods: A hospital based case-control study was carried out in KMIO, Bangalore, India from May 2013 to February 2014. Newly diagnosed primary cases of female breast cancer of any age and one control per case matched by 5 years age class interval were interviewed, using a questionnaire until required sample was met. Statistical analysis was performed using SPSS software version 18.0.
Results: The study population consisted of 135 cases of breast cancer and 135 controls. The mean age was 50 years (SD±10.41) and 94 (34.8%) of them belonged to 45-54 years age group. After forward logistic regression, the risk factors significant at P<0.05 were age at first pregnancy >20 years OR 4.49 (95% CI 1.21-16.62), total duration of lactation <48 months OR 7.96 (95% CI 2.20-21.68), consumption of non-vegetarian diet OR 6.96 (95% CI 1.45-33.25), BMI ≥23 OR 4.91 (95% CI 1.25-19.23) and household physical activity ≤120 minutes/day OR 8.52 (95% CI 1.98-36.64), watching television during weekends >180 minutes/day OR 4.64(95%CI 2.71-7.78).
Conclusions: The modifiable risk factors of breast cancer include age at first pregnancy, total duration of lactation, non-vegetarian diet, increased BMI and lower household physical activity and non-modifiable risk factor being age at menopause.

Keywords: Risk factors, Breast cancer, Case control study

INTRODUCTION

Breast cancer is the most common cancer among females in the world.[1] Owing to regional variations in distribution of risk factors and differing lifestyles, there is geographical variation in incidence and mortality due to breast cancer.[2] In India, incidence of breast cancer is increasing rapidly due to population growth and increase in life expectancy leading to greater proportion of geriatric population.[3]

The risk factors for breast cancer are broadly classified into modifiable and non–modifiable factors. The non modifiable risk factors are age, gender, number of first

degree relatives suffering from breast cancer, menstrual history, age at menarche and age at menopause. The modifiable risk factors are body mass index (BMI), age at first child birth, number of children, duration of breast feeding, consumption of alcohol, dietary factors and number of unsuccessful pregnancies (abortions).[4,5]

Most of the breast cancer cases are usually diagnosed in the advanced stages despite availability of screening tests and biomarkers for early detection. Early detection can prevent complications, improve quality of life and increase survival period. Owing to the resource intensive nature of screening tests, it is imperative to identify women at risk and judiciously apply them for optimal benefits.[6] So, there is a need to determine the distribution of risk factors associated with breast cancer. Hence, this study had been attempted with an objective to assess the modifiable and non-modifiable risk factors associated with breast cancer among women attending a tertiary care hospital in Bangalore.

METHODS

A hospital based case control study was conducted in Kidwai Memorial Institute of Oncology (KMIO), Bangalore, India from May 2013 to February 2014. Cases were newly diagnosed (histologically confirmed) female breast cancer patients attending Kidwai Memorial Institute of Oncology, Bangalore and presenting at any stage (TNM) during the recruitment phase. For each case, one control was selected (1:1) who was matched by 5 years age class interval e.g. 30-34 years or 45-49 years etc. Controls were apparently healthy females i.e., attendants of other cases and who were not biologically related to the patients. Only cases with no history of any malignancy previously and controls, with no history of previously diagnosed or treated for any kind of malignancy were included in our study.

Sample size: A case control study carried out by Bala, to evaluate the role of dietary factors in breast cancer had revealed that 87% of the cases had >20% of energy derived from fat as compared to only 14% of controls.[7] Based on this, the sample size was estimated using N Master software version 1.2. To obtain a precision of 95% (α error of 5%), it was estimated that a minimum of 135 cases of breast cancer along with an equal number (1:1) of age and sex matched controls (135) was required.

Necessary permission was sought from the concerned authorities at Kidwai Memorial Institute of Oncology, Bangalore (KMIO) after obtaining clearance from Scientific and Ethical committee, M S Ramaiah Medical College, Bangalore, India. A pilot study was conducted to validate the pre designed questionnaire for content validity. After obtaining written informed consent from patients, newly diagnosed (histologically confirmed) primary cases of breast cancer attending KMIO, were interviewed using pre tested, semi structured questionnaire until the required sample was met. One control per patient matched by 5 years age class interval was interviewed, using similar questionnaire. Information regarding the socio-demographic factors and risk factors like age at menarche, age at marriage, age at first child birth, total duration of lactation (summation of duration of lactation in months during each child birth till date), history of abortion, history of hormone replacement therapy, history of oral contraceptive pills, history of diabetes, family history of breast cancer, details of physical activity, diet history with the help of food frequency questionnaire was collected from cases and controls. Body weight was measured in kilograms on the weighing scale with minimum outerwear (as culturally appropriate) and without any footwear. The reading was taken up to the nearest 0.5kg. Height was measured in centimetres using a non-stretchable tape with the subject in an erect position against a vertical surface, with the head positioned so that the top of the external auditory meatus was at the level of inferior margin of the bony orbit and the reading was taken up to nearest 1cm. Body mass index (BMI) was calculated by dividing the weight in kilograms with the square of height measured in meters. Asian cut off of BMI was used to categorize Normal weight and overweight/obesity.[8] The data thus obtained was entered in Microsoft Excel sheet and analysed in IBM SPSS version 18.0.

Statistical analysis

Descriptive statistics comprising of mean and standard deviation was calculated for the quantitative variables such as age, etc. Qualitative variables such as parity were expressed in terms of proportions along with 95% confidence intervals. Association of various risk factors of breast cancer between cases and controls was estimated through odds ratio with 95% confidence interval. Chi-square test of significance was used to test the significance of difference in proportions. Multivariate logistic regression analysis was carried out to assess independent risk factors to adjust for confounding variables.

RESULTS

Out of 270 participants, 135 were cases and 135 were controls. In our study, the mean age of the study subjects was 50years (SD±10.41) with age ranging from 25 to 69 years. Majority 94 (34.8%) of them belonged to the age group 45-54 yrs , 62.2% of the cases and 65.9% of the controls were from rural area and among cases 83.7% of them were Hindus as compared to 93.3% controls. It was revealed that 40.7% cases and 37.8% of controls belonged to lower middle class according to Modified BG Prasad Classification.[9] Majority of the cases 61 (45.2%) and controls 43 (31.1%) were not literate and 89 (65.9%) of the cases were not employed as compared to 91 (67.4%) of the controls (Table 1). In this study, it was observed that 62(45.9%) of the cases were in stage II followed by 59 (43.7%) in stage III, 9 (6.7%) in stage IV

and 5 (5.3%) in stage I breast cancer according to AJCC (TNM) classification.[10]

We did univariate analysis to know the significant variables associated with breast cancer. The variables which were found to be statistically significant ($p<0.05$) and taken for multivariate analysis are described in Table 2, Table 3 and Table 4. However, when forward logistic regression was done, the variables which were significant at $p<0.05$ were age at first pregnancy >20 yrs, total duration of lactation <48 months, age at menopause ≥50 yrs, non-vegetarian diet, BMI ≥23, watching television during weekends >180 min/day and household physical activity ≤120 min (Table 5).

Table 1: Distribution of study subjects by socio-demographic variables.

Variables	Study subjects		Chi square P value
Age (in years)	**Cases**	**Controls**	
	N (%)	**N (%)**	
25-34	11 (8.1)	11 (8.1)	Not applicable
35-44	28 (20.8)	28 (20.8)	
45-54	47 (34.8)	47 (34.8)	
55-64	34 (25.2)	34 (25.2)	
≥65	15 (11.1)	15 (11.1)	
Residence			
Rural	84 (62.2)	89 (65.9)	$\chi2=0.402$ P=0.526
Urban	51 (37.8)	46 (34.1)	
Religion			
Hindu	113 (83.7)	126 (93.3)	$\chi2= 6.614$ P=0.037
Muslim	17 (12.6)	8 (5.9)	
Christian	5 (3.7)	1 (0.7)	
Socio-economic status (SES)*			
Upper class	6 (4.4)	7 (5.2)	$\chi2= 6.614$ P=0.037
Upper middle class	20 (14.8)	22 (16.3)	
Middle class	40 (29.6)	40 (29.6)	
Lower Middle class	55 (40.7)	51 (37.8)	
Lower class	14 (10.4)	15 (11.1)	
Education			
Not literate	61 (45.2)	43 (31.9)	$\chi2=7.122$ P=0.212
Primary school	15 (11.1)	21 (15.6)	
Middle school	19 (14.1)	20 (14.8)	
High school	19 (14.1)	23 (17)	
Diploma/intermediate	13 (9.6)	22 (16.3)	
Graduate	8 (5.9)	6 (4.4)	
Occupation			
Not employed	89 (65.9)	91 (67.4)	$\chi2=0.067$ P=0.797
Employed	46 (34.1)	44 (32.6)	

*SES by modified BG Prasad classification.

Table 2: Association of reproductive factors with breast cancer.

Risk factors	Groups	Cases N (%)	Controls N (%)	Total (%)	Univariate analysis	
					Odds ratio (OR) (95% CI)	**P value**
Age at menarche (yrs)	≤13	73 (54.1)	36 (26.7)	109 (40.4)	3.23 (1.94-5.39)	0.001*
	>13	62 (45.9)	99 (73.3)	161 (59.6)	1 (ref)	
Marital status	Never married	8 (5.9)	0(0)	8(3)	Fischer's exact probability test = 0.007*	
	Ever married	127 (94.1)	135 (100)	262 (97)		
Age at marriage in years	>18	44 (34.6)	21 (15.6)	65 (24.8)	2.87 (1.59-5.20)	0.001*
	≤18	83 (65.4)	114 (84.4)	197 (75.2)	1 (ref)	
Age at menopause in years	≥50	50 (83.3)	33 (47.1)	83 (63.8)	3.89 (2.25-6.71)	0.001*
	<50	10 (16.7)	37 (52.9)	47 (36.2)	1 (ref)	
Age at first pregnancy in years	>20	79 (65.3)	33 (24.8)	112 (44.1)	5.7 (3.31-9.81)	0.001*
	≤20	42 (34.7)	100 (75.2)	142 (55.9)	1 (ref)	

Continued.

Risk factors	Groups	Cases N (%)	Controls N (%)	Total (%)	Univariate analysis	
					Odds ratio (OR) (95% CI)	P value
Total duration of lactation in months	<48	96 (80)	30 (22.6)	126 (49.8)	13.77 (7.50-25.13)	0.001*
	≥48	24 (20)	103 (77.4)	127 (50.2)	1 (ref)	
H/O Abortion	Yes	55 (45.5)	20 (15)	75 (29.5)	4.70 (2.59-8.53)	0.001*
	No	66 (54.5)	113 (85)	179 (70.5)	1 (ref)	
Family H/O breast cancer	Yes	19 (14.1)	7 (5.2)	26 (9.6)	2.99 (1.21-7.38)	0.013*
	No	116 (85.9)	128 (94.8)	244 (90.4)	1 (ref)	
Previous H/O lump in breast	Yes	5 (3.7)	0 (0)	5 (1.9)	Fischer exact probability test= 0.060*	
	No	130 (96.3)	135 (100)	265 (98.1)		

*Statistically significant.

Table 3: Association of physical activity and breast cancer.

Risk factor	Time taken/ day in minutes	Cases N (%)	Controls N (%)	Total (%)	Univariate analysis	
					Odds ratio (OR) (95% CI)	P value
Cleaning house	≤30	96 (71.1)	65 (48.1)	161 (59.6)	2.65 (1.60-4.38)	0.001*
	>30	39 (28.9)	70 (51.9)	109 (40.4)	1 (ref)	
Cooking	≤45	75 (55.6)	57 (42.2)	132 (48.9)	1.71 (1.05-2.76)	0.028*
	>45	60 (44.4)	78 (57.8)	138 (51.1)	1 (ref)	
Washing clothes (without washing machine)	≤20	105 (77.8)	93 (68.9)	198 (73.3)	1.58 (0.91-2.72)	0.099
	>20	30 (22.2)	42 (31.1)	72 (26.7)	1 (ref)	
Walking to buy things	≤15	128 (94.8)	114 (84.4)	242 (89.6)	3.36 (1.38-8.21)	0.008*
	>15	7 (5.2)	21 (15.6)	28 (10.4)	1 (ref)	
Carrying water	≤15	118 (87.4)	98 (72.6)	216 (80)	2.62 (1.39-4.93)	0.002*
	>15	17 (12.6)	37 (27.4)	54 (20)	1 (ref)	
Watching TV (week days)	>150	52 (38.5)	32 (23.7)	84 (31.1)	2.01 (1.19-3.41)	0.009*
	≤150	83 (61.5)	103 (76.3)	186 (68.9)	1 (ref)	
Watching TV (week ends)	>180	86 (63.7)	37 (27.4)	123 (45.6)	4.64 (2.71-7.78)	0.001*
	≤180	49 (36.3)	98 (72.6)	147 (54.4)	1 (ref)	
Total physical activity	≤120	101 (74.8)	45 (33.3)	146 (54.1)	5.94 (3.50-10.07)	0.001*
	>120	34 (25.2)	90 (66.7)	124 (45.9)	1 (ref)	

*Statistically significant.

Table 4: Association of dietary factors with breast cancer.

Risk factor	Groups	Cases N (%)	Controls N (%)	Univariate	
				Odds ratio (OR) (95% CI)	P value
Diet	Non veg	122 (90.4)	91 (67.4)	4.53 (2.30-8.91)	0.000*
	Veg	13 (9.6)	44 (32.6)	1 (ref)	
Total calorie in Kcal/day	>1200	81 (60)	71 (52.6)	1.35 (0.85-2.19)	0.220
	≤1200	54 (40)	64 (47.4)	1 (ref)	
Oil consumption of study subjects per month in grams	≥500	96 (71.1)	76 (56.3)	1.19 (1.15-3.16)	0.011*
	<500	39 (28.9)	59 (43.7)	1 (ref)	
Green leafy vegetable	≤weekly once	85(63)	57(42.2)	2.32(1.42-3.79)	0.001*
	>weekly once	50(37)	78(57.8)	1(ref)	
Fruits	≤weekly once	70(51.9)	57(42.2)	1.47(0.91-2.38)	0.113
	>weekly once	65(48.1)	78(57.8)	1	
Sweets	≥weekly once	43(31.9)	36(26.7)	1.28(0.76-2.17)	0.34
	<weekly once	92(68.1)	99(73.3)	1(ref)	
Bakery products	≥weekly once	56(41.5)	21(15.6)	3.84(2.15-6.85)	0.001*
	<weekly once	79(58.5)	114(84.4)	1(ref)	
Deep fried products	≥weekly once	42(31.1)	41(30.4)	1.03(0.617-1.73)	0.895
	<weekly once	93(68.9)	94(69.6)	1(ref)	

Table 5: Multiple logistic regressions for identifying independent risk factors associated with development of breast cancer.

Risk Factor	Groups	Study subjects		Univariate analysis	Multiple logistic regression
		Cases N (%)	Controls N (%)	Unadjusted OR (95%CI)	Adjusted OR (95%CI)
Age at 1st pregnancy	>20 years	79 (65.3)	33 (24.8)	5.7 (3.31-9.81)	4.49 (1.21-16.62)*
	≤20 years	42 (34.7)	100 (75.2)	1 (reference)	1 (reference)
Duration of total lactation	<48 months	96 (80)	30 (22.6)	13.77 (7.50-25.13)	7.96 (2.20-21.68)*
	≥48 months	24 (20)	103 (77.4)	1 (reference)	1 (reference)
Age at menopause	≥50 years	50 (83.3)	33 (47.1)	3.89 (2.25-6.71)	4.16 (1.10-15.74)*
	<50 years	10 (16.7)	37 (52.9)	1 (reference)	1 (reference)
BMI	≥23	79 (58.5)	29 (21.5)	5.15 (3.02-8.80)	4.91 (1.25-19.23)*
	<23	56 (41.5)	106 (78.5)	1 (reference)	1 (reference)
Diet	Non veg	122 (90.4)	91 (67.4)	4.53 (2.30-8.91)	6.96 (1.45-33.25)*
	Veg	13 (9.6)	44 (32.6)	1 (reference)	1 (reference)
Watching TV (week ends)	>180 min/day	86 (63.7)	37 (27.4)	4.64 (2.71-7.78)	5.34 (1.59-17.87)*
	≤180 min/day	49 (36.3)	98 (72.6)	1 (reference)	1 (reference)
Total physical activity	≤120 min/day	101 (74.8)	45 (33.3)	5.94 (3.50-10.07)	8.52 (1.98-36.64)*
	>120 min/day	34 (25.2)	90 (66.7)	1 (reference)	1 (reference)

*P<0.05.

DISCUSSION

In our study, the mean age of cases were similar to that of Meshram et al, while in the study by Kamath et al and Singh et al the mean age was slightly lower compared to the present study finding.[3,11,12] The cases and controls for the present study were enrolled from a hospital, which is the coordinating centre for Population Based Cancer Registry.[13] A majority of the cancer cases registered under the population based cancer registry are from Kidwai Memorial Institute of Oncology ensured greater representativeness. In this study, 62.2% of the cases and 65.9% of the controls were from rural area and 239(88.5%) of study subjects were Hindus. This reflects the figures of Census of India 2011, which shows that, 68.84% of total population in India resides in rural area and majority of people (80.5%) in India are Hindu by religion.[14] We found that majority of the cases 55 (40.7%), belonged to lower middle class and there was no statistically significant association of socio economic status with breast cancer in contrast to study by Thakur et al and Dutta et al where it was seen that women in upper socio economic status had increased risk of developing breast cancer.[15,16] Since Kidwai Hospital is a well known cancer institute run by the government with subsidized or free treatment, most people of lower socioeconomic strata prefer to come here.

In our study, we observed that 62(45.9%) of the cases were in stage II followed by 59 (43.7%) in stage III which was similarly seen in a study by Kapil et al, in which 40.65% of breast cancer cases presented in Stage II followed by 34.95% in Stage III.[17] However, in contrast to a study by Saxsena et al, which revealed that among cases 63.3% of them presented with stage III followed by 16.3% in stage II.[18] Since majority of breast cancer cases in our study were diagnosed in later stages, there is a need for ensuring early detection of breast cancer in our population through health education and access to appropriate health facilities.

Our study revealed that age at first pregnancy>20 years, was a significant risk factor of breast cancer with adjusted OR4.49 (95% CI: 1.21-16.62). This was similarly observed in a study by Reddy and Pakseresht et al.[5,19] Early age at first child birth reduces risk of breast cancer by bringing about cell differentiation in the breast tissue which makes it less susceptible to carcinogenesis. Women with total duration of lactation <48 months had 7.96 times increased risk of breast cancer. Similarly in a study by Thakur et al, there was increased risk of developing breast cancer in women who breast fed <36 months with OR 4.28 and adjusted OR 2.60.[15] However in a retrospective study by Bala, there was no association between total duration of lactation and breast cancer.[7] The oxytocin, which is released as a response to suction during lactation causes contraction of myoepithelial cells and inhibits cell proliferation and carcinogenesis of breast.[20]

It was found that age at menopause ≥50 years was significantly associated with breast cancer with adjusted OR 4.16 (95% CI: 1.10-15.74), which was similar to a study by Meshram et al, where the risk of breast cancer was 7.9 times more among women who had menopause at or after 50 years of age compared to women who had menopause before 50 years and a study by Bhadoria et al, where the risk of breast cancer increased 2.68 times in women having a menopause after 49 years.[3,21] In contrast, a retrospective study by Reddy revealed that there was no

association of age at menopause and breast cancer.[5] Late age at menopause increases the duration of exposure of estradiol, which may increase the likelihood of damage to DNA, hence causing breast cancer.[22]

It was noticed that the odds of those who had BMI ≥23 with breast cancer was 5.15 (95% CI: 3.02-8.80) as compared to women whose BMI was <23. Similar findings were observed in a case-control study conducted by Carpenter et al, which revealed that the risk of breast cancer increased with increasing BMI.[23] Overweight and obese women had OR of 1.14 and 1.22 as compared to women with normal weight. In women with high BMI, more sex hormones are synthesized in the fat leading to breast cancer.[24]

Our study also revealed that non vegetarian diet was significantly associated with breast cancer with Adjusted OR 6.96 (95% CI: 1.45-33.25). Similarly, a case control study by Bala and Harrison et al noted that diet was significantly associated with breast cancer.[7,25] The risk level for non-vegetarian diet was higher than vegetarian diet because non vegetarians consume more fat than vegetarians and a diet with a high animal fat intake has been shown to increase the risk of breast cancer.[11]

The study also revealed that the women who spent ≤120 minutes/day on total physical activity on household had increased risk of breast cancer with adjusted OR 8.52 (95% CI: 1.98-36.64). Similar findings were reported by Mathew et al, in which the risk of breast cancer declined with increasing time spent on household activities.[26] Decrease in physical activity can lead to obesity and hyperinsulinemia which triggers carcinogenesis in breast tissue.[27]

In our study, some of the variables like age at menarche, age at marriage, history of diabetes, family history of breast cancer, etc., which were statistically significant in univariate analysis did not have significant association with breast cancer in multiple logistic regression analysis. In contrast, a study by Thakur et al and Kaur et al revealed that early age of menarche was associated with breast cancer.[15,28] In a study by Reddy and Bhadoria et al it was found that late age of marriage was a risk factor for breast cancer.[5,20] History of abortion was also seen as independent risk factor in a study by Takalkar et al and Rai et al.[29,30] In a prospective study by Karin et al and Giovannucci et al women with diabetes had elevated risk of breast cancer.[31,32] However, we did not find these variables statistically significant in multivariate analysis, may be because of smaller sample size and many variables in the study.

A majority of the cancer cases in and around Karnataka are registered in KMIO, which is a Population Based Cancer Registry. Hence the cases included for this study were to be fairly representative of the population, thereby eliminating the possibility of selection bias. Matching of the cases and controls for age (5yr age group matching) and multiple logistic regression analysis (adjusted odds ratio) for the risk factors studied were done to minimize the bias due to confounding. In our study, only newly diagnosed cases without prior history of treatment were considered and the duration of interview of both cases and controls were same to minimize the possibility of recall and interviewer's bias.

Our study had few limitations. Controls were not confirmed by any diagnostic test for not having breast cancer. However, only apparently healthy females without any history of diagnosis or treatment of breast cancer were included. Since many variables were taken for analysis, numbers in the different subgroup were less and resulted in wide confidence interval.

CONCLUSION

The present study has revealed various modifiable and non-modifiable risk factors for breast cancer. The modifiable risk factors includes age at 1st pregnancy, total duration of lactation, non-vegetarian diet, increased body mass index and lesser household physical activity and non- modifiable risk factor being age at menopause. To recommend, health education must be provided to women regarding the risk factors for breast cancer and importance of lactation, optimum age at marriage, diet and physical activity to prevent the same. Since majority of patients presented in stages II (45.9%) and III (43.7%), there is a need for early detection of breast cancer in our population. Early detection of breast cancer has a good prognosis. Henceforth, along with health education on screening of breast cancer, the possibility of initiating cost-effective screening measures needs to be emphasized.

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