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## Predictors of breast cancer among women attending a tertiary care hospital in Puducherry-A case-control study

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### Abstract

**Introduction:** The incidence of breast cancer is increasing in developing countries over decades. Breast cancer is a public health problem in India. Identifying the risk factors helps to reduce the incidence and improve quality of life of people in future.

**Method:** A hospital based case control study was conducted among all the breast cancer cases newly diagnosed in a tertiary care teaching hospital in Puducherry. 40 cases of breast cancer were paired with age matched controls from the same hospital (ratio 1:2) with a total of 120 study participants. Data were collected by interviewing the participants using a pre tested structured questionnaire. Analysis was done using SPSS version 24.0

**Results:** Age group of participants ranged from 35-69 years. Age group of 46-55 years [OR-3.4; 95% CI: 1.1-11.2], homemaker [OR-0.4; 95% CI: 0.2-0.9], Early menarche <12 years [OR-2.8; 95% CI: 1.3-6], being unmarried [OR-2.3; 95% CI: 1.1-4.8], alcohol consumption [OR-4.5; 95% CI: 1.1-19], tobacco usage [OR-9; 95% CI: 2.9-27], increased waist circumference [OR-2.2; 95% CI: 1.1-4.9], severe perceived stress [OR-2.8; 95% CI: 1.1-7], were found to be the significant risk factors for the breast cancer.

**Conclusion:** The identified modifiable risk factors of breast cancer need to consider for screening as well as for health education program. Health care personnel should be trained to spread the awareness of breast cancer in the community and to identify the vulnerable groups at all levels of health care.

**Keywords:** Cancer breast, incidence, predictors, Puducherry

### Introduction

Breast cancer is a major public health problem that affects women in the developing as well as developed world. It is characterized by uncontrolled growth of cells, which results in the formation of lumps within the breast. It is one of the treatable forms of cancers however if not detected early, it can be a life threatening disease as it has the potential to metastasize to other parts of the body. It is the most common cancer in women in India and accounts for 14% of all cancers in women <sup>[1]</sup> It can occur at any age but the incidence rates in India begin to rise in the early thirties and peak at ages 50-64 years <sup>[2]</sup>.

Incidence rates vary greatly worldwide from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. In most of the developing regions the incidence rates are below 40 per 100,000 <sup>[3]</sup>. Breast cancer survival rates vary greatly worldwide, ranging from 80% or over in North America, Sweden and Japan to around 60% in middle income countries and below 40% in low-income countries <sup>[4]</sup>. The low survival rates in less developed countries can be explained mainly by the lack of early detection programmes, resulting in a high proportion of women presenting with late-stage disease, as well as by the lack of adequate diagnosis and treatment facilities.

Assessing various modifiable risk factors and implementing the necessary actions such as increasing disease awareness, detection, and management programs can impact in the reduction of morbidity and mortality associated with breast cancer. Thus, the present case-control study was conducted among women attending a tertiary care teaching hospital in Puducherry diagnosed with breast cancer to describe their socio-demographic profile and to find out various risk factors associated with cancer breast.

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## Materials and Methods

### Study Setting and Design

The case-control study was conducted in a tertiary care teaching hospital in Puducherry Union Territory (UT). It is located in the rural part of UT situated in the Cuddalore highway. It was an age matched case-control study. It is a 800 bedded teaching hospital. The average outpatient and inpatient load of General Surgery department per day is 80 and 20 respectively. Every year nearly 15 to 20 new cases of cancer breast are diagnosed in the department. The department maintains the registry of cancer patients getting diagnosed and treatment in the department.

### Study Population

Cases were women newly diagnosed with breast cancer attending the General Surgery Department for their treatment and follow up during the study period of two years from March 2017 to February 2019. The patients with proven cases of breast cancer by histopathology or cytopathology were included. Among them those who have undergone any treatment specific to breast cancer, have suffered from any major chronic illness in the past, before the diagnosis of breast cancer thereby leading to change their dietary pattern, have taken long course of any vitamin or mineral supplements during the last one year, on corticosteroid therapy or suffering from hepatic disorders and with severe malnutrition were excluded.

Controls were the normal healthy women accompanying the cases in the Department of Gastroenterology, Medicine and Surgery at the study hospital. Two controls were selected every time a new eligible case was recruited into the study in such a way that the age of the individual control was  $\pm 5$  years of the case. The exclusion criteria for selection of the controls were those who suffered from any major illness in the past, who had taken long course of any vitamin or mineral supplements during the last one year, who were on corticosteroid therapy or suffering from hepatic disorders and had severe malnutrition.

### Sampling and Sample Size

Sample size was calculated to be 120 using OpenEpi software version 3.0, taking the proportion of breast cancer cases that had risk of late marriage as 31% and exposure of controls to same risk factor as 8% and odds ratio of 0.19, based on previous study with 95% confidence interval and 80% power.<sup>5</sup> Cases and controls fulfilling the eligibility criteria were consecutively enrolled into the study in the ratio of 1:2 till the calculated sample size was reached over the study period of two years so that at the end 40 cases and 80 controls will be included into the study.

### Study Tool and Study Variables

Pretested structured proforma was developed for collecting information under three major headings namely

1. Socio-demographic details like age, education, occupation, residency, and religion
2. Reproductive factors like marital status, age at marriage, age at menarche, parity, breast feeding status
3. Life style related factors like diet, alcohol consumption, tobacco usage, hypertension status, diabetes status, perceived stress, family history of breast cancer and obesity status using waist circumference. Stress was assessed and classified into low, medium and high based on 10 item Perceived Stress Scale [6].

### Study Procedure and Data Collection

Cases and controls were selected as per the selection criteria mentioned above and details on study variables were collected after obtaining written informed consent from the study participants. Interview was conducted with the study subject to obtain information on risk factors under three major headings mentioned above using predesigned pilot-tested questionnaire by the principal investigator. Institute Human Ethics Committee clearance was obtained before initiating the study procedure. All

ethical principles have adhered throughout the study.

### Data Entry and Statistical Analysis

Data were entered into Microsoft Office Excel and analysed using SPSS software version 22. Description of categorical variables was done in frequency and proportion. Chi-square test was used to find out the association between various risk factors and breast cancer. Binary logistic regression was carried out with all risk factors to find out the unadjusted Odds ratio (OR), a measure of the strength of association and presented with its 95% confidence interval (CI). All tests were two-tailed and p-value  $< 0.05$  was considered statistically significant.

### Results

Totally there were 40 cases and 80 controls included in the study. Among cases 19 (47.5%) were in the age group of 46 – 55 years and among controls 48 (60%) participants were in the age category of more than 55 years. Most of the cases (90%) and controls (80%) were from rural background. Hinduism was the common religion of both cases (90%) and controls (85%). Only 5% were Muslims among cases and 7.5% among controls. Among cases 67.5% were labourer and 52.4% of the controls were involved in the same job. Homemakers constituted 22.5% of the cases and 43.8% of the controls. 80% of the cases and 71.2% of the controls were illiterate (Table-1).

The unmarried women were more (57.5%) among cases however married women were more (62.5%) among controls and this difference was statistically significant (p value=0.04). 62.5% of the cases had early age of menarche ( $< 12$  years) but it was 37.5% among controls and again this difference was statistically significant. Both case (75%) and controls (77.5%) had more people who got married less than 18 years. Nulliparous women were lesser in both group of study participants (7.5% in cases and 3.8% in controls) and no exclusive breast feeding status was also lesser in both groups (7.5% in cases and 3.8% in controls). But this difference was not statistically significant (Table-2).

Among cases 65% consume mixed diet and the same was consumed by 56.2% of the controls but this difference was not significant. 15% of the cases and 16.2% of the controls were known hypertensive on treatment and 22.5% of the cases and controls were known diabetes on treatment. There was significant difference in alcohol (15% in cases and 3.8% in controls) and tobacco (37.5% in cases and 6.2% in controls) consumption among cases and controls. Central obesity was higher among cases (47.5%) than controls (28.8%). Though cases (27.5%) had more positive family history of breast cancer than controls (16.2%) the difference was not significant. Moderate and severe level of perceived stress was significantly more among cases and controls (Table-3).

The unadjusted odds ratio for breast cancer according to socio-demographic risk factors was calculated and depicted in Table-1. Compared to women in the age group of 35-45 years those in the age group of 46-55 years had 3.4 times higher risk of developing breast cancer. Residency and religion was not associated with the incidence of breast cancer. 60% of the homemakers were protected against breast cancer compared with those involved in labour works (95% CI: 0.2-0.9). Though illiterate were found to be at risk the association was not statistically significant.

The association between reproductive risk factors with breast cancer was given in Table-2. Unmarried women had 2.3 times higher risk of developing breast cancer compared to married women (95% CI: 1.1-4.8). Women who had history of early age at menarche ( $< 12$  years) had 2.8 (95% CI: 1.3-6) times higher chance to develop breast cancer. Other reproductive factors were not associated with cancer breast among study participants. Among various life style related risk factors alcohol

consumption, tobacco usage, raised waist circumference and perceived stress happened to be associated statistically with the occurrence of breast cancer (Table-3).

## Discussion

The present study conducted at a tertiary care teaching hospital in rural Puducherry included 40 breast cancer cases and 80 age matched control subjects. The cases and controls were between the ages of 35 to 69 years. Majority of the participants in case and control group were in the age group of 46-55 years, rural setting, Hindus, labourer and illiterate. Among the various socio-demographic, reproductive and life style related risk factors studied, the significant predictors of breast cancer emerged out of the current study were age group of 46 to 55 years, homemaker, unmarried, lesser age at menarche, alcohol and tobacco consumption, central obesity and perceived stress in the unadjusted analysis.

Age is an important risk factor for breast cancer worldwide and the risk increases as the age progresses. In the current study cases with age group of 46-55 years had higher chance than the younger ones. Our finding is consistent with other studies done in India and also among studies done in other parts of world [7-10]. The reason for the above difference could be due to the various ethnic, socio-demographic, geographical and life style factors that are associated with advancement in the age which needs further exploration. Review of previous studies done in India and across world suggested that Indian women having breast cancer are found a decade younger in comparison to western women suggesting that breast cancer occurs at a younger premenopausal age in India [10].

In our study it was found rural women were at higher risk to develop breast cancer but it was not significant similar finding was obtained in a study conducted at China [9]. A review done on urban-rural disparities in female cancer incidence and mortality in Kerala revealed that breast cancers were more common among urban than rural residents and the mortality among rural women were more than urban.<sup>11</sup> This might be due to the disparity in the life style related risk factors and the availability of the medical services at these places. It was found homemakers were at lower risk than manual workers. Previous studies found that occupation like professionals and business were associated with higher risk.<sup>12</sup> The probable reason could be the level of physical activity associated with the occupation and also the socioeconomic status determined by the type of occupation. Previous studies had shown that women in the higher socio-economic status were associated with higher risk [7-9, 12, 13].

We found that the early menarche before attaining 12 years was significantly associated with increased risk of breast cancer. Many studies have shown that breast cancer risk is more among women who attained menarche at an early age, in India and also in other countries [5, 12-15]. Two main reasons behind this association are

1. Early menarche leads to an early opening of the first window and results in a substantial cumulative exposure to estrogens and the simultaneous presence of progesterone, an exposure theorized to increase the risk of breast cancer [16, 17]
2. Risk is probably indirectly associated, with nutrition being the possible common factor.<sup>5</sup> A statistically significant association was found in those women having a family history of breast cancer in the present study and the risk with genetic predisposition was similar to the other studies done within and outside India.

Unmarried women were found to have two fold increase risk for breast cancer in our study and it was significant too. The same finding that the single, unmarried women compared to married women had 2-6 fold higher risk for development of breast cancer was noted in the previous studies done across the world. [5, 9, 12, 18, 19]. Pregnancy induces terminal differentiation of human breast glands, which may have a smaller proliferative component and it induces irreversible changes that either render the breast tissue itself less susceptible to induction of cancer or reduced the carcinogenic stimulus to the breast [20]. Parity was found to be related to the risk of breast cancer in the present study however it was not significant. Results of earlier studies have reported a decrease in risk with higher parity [5, 7-9, 12, 14].

In our study, the life style related risk factors associated with breast cancer risk were alcohol consumption, tobacco usage, central obesity and perceived stress. Very few studies conducted around the world examined the association between these factors. In a study done in China it was shown that tobacco was positively associated and alcohol was associated with a decreased risk of breast cancer [9]. Study in Nigeria showed no association with tobacco usage [15]. In our study we found that central obesity was significantly associated with breast cancer. Similar results were found in studies done across countries [18, 19, 21, 22]. There were no previous studies done exploring the association between perceived stress and breast cancer however our study showed positive association with stress. Future studies are warranted to further explore the reason behind it. Vegetarian diet appeared to be negatively associated with breast cancer in our study but it was not significant. Though there was no study that directly supported our finding, one of the study showed that increased consumption of chicken was associated with increased risk.<sup>12</sup> However a meta-analysis carried out among Indian studies showed there was no significant association between vegetarian diet and cancer risk [23]. Chronic disease like hypertension and diabetes were not associated with the breast cancer in our study but a study done in China showed significant association with essential hypertension [9]. Future research can inform more about their association.

The study being a hospital based case control; there could be a chance of bias. The selection bias was minimized with prospective selection of incident case and controls at the same time point that were matched with age. Recall bias remained a challenge particularly when remembering the past events like age at menarche, family history of breast cancer, self-reported alcohol and tobacco consumption, and perceived stress, which might have influenced the outcome of these study variables.

## Conclusions

The study identified middle aged women, unmarried, women with early onset of menarche, labourer, alcohol consumption, tobacco use, increased waist circumference and perceived stress. Women with vulnerable risk factors need to be identified and appropriate preventive measures like awareness creation with regard to predictors, symptoms of breast cancer and breast self-examination. Suitable behaviour change communication activities must be formulated to sensitize the vulnerable population that improves the health seeking behaviour as and when the symptoms arise.

## Acknowledgements

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**Table 1:** Socio-demographic profile of study participants and their association with breast cancer (N=120).

Sl. No.	Study variable	Cases (N=40) n (%)	Controls (N=80) n (%)	X <sup>2</sup> value, df <sup>@</sup>	p value <sup>#</sup>	OR (95% CI) <sup>\$</sup>
1	Age group in years					
	35 – 45	5 (12.5)	15 (18.8)	8.7, 2	NA	1 (Reference)
	46 – 55	19 (47.5)	17 (21.2)		0.04*	3.4 (1-11.2)
	> 55	16 (40)	48 (60)		0.99	0.9 (0.3-3.2)
2	Residency					
	Rural	36 (90)	64 (80)	1.9, 1	0.17	2.3 (0.7-7.2)
	Urban	4 (10)	16 (20)		NA	1 (Reference)
3	Religion					
	Hindu	36 (90)	68 (85)	0.57, 1	0.58	1.6 (0.3-8.3)
	Christian	2 (5)	6 (7.5)		0.99	1 (0.1-9.6)
	Muslim	2 (5)	6 (7.5)		NA	1 (Reference)
4	Occupation					
	Labourer	27 (67.5)	42 (52.4)	6.1, 2	NA	1 (Reference)
	Homemaker	9 (22.5)	35 (43.8)		0.04*	0.4 (0.2-0.9)
	Others	4 (10)	3 (3.8)		0.36	2 (0.4-10)
5	Literacy					
	Literate	8 (20)	23 (28.8)	1.1, 1	NA	1 (Reference)
	Illiterate	32 (80)	57 (71.2)		0.30	1.6 (0.6 - 4)

**Note:** X<sup>2</sup>-Chi square value, @ df- degrees of freedom, # p value based on Chi square test, NA- Not Applicable, \* statistically significant (p value <0.05), \$OR-Odds Ratio, CI-Confidence interval.

**Table 2:** Reproductive factors profile of study participants and their association with breast cancer (N=120).

Sl. No.	Study variable	Cases (N=40) n (%)	Controls (N=80) n (%)	X <sup>2</sup> value, df <sup>@</sup>	p value <sup>#</sup>	OR (95% CI) <sup>\$</sup>
1	Marital status					
	Unmarried	23 (57.5)	30 (37.5)	4.3, 1	0.04*	2.3 (1.1-4.8)
	Married	17 (42.5)	50 (62.5)		NA	1 (Reference)
2	Age at menarche in years					
	< 12	25 (62.5)	30 (37.5)	6.7, 1	0.01*	2.8 (1.3-6)
	≥ 12	15 (37.5)	50 (62.5)		NA	1 (Reference)
3	Age at marriage in years					
	≥ 18	10 (25)	18 (22.5)	0.14, 1	0.71	1.2 (0.5-2.9)
	< 18	28 (75)	60 (77.5)		NA	1 (Reference)
4	Parity					
	Nulliparous	3 (7.5)	3 (3.8)	0.85, 1	0.36	2.1 (0.4-11)
	Parous	35 (92.5)	75 (96.2)		NA	1 (Reference)
5	Breastfeeding status					
	No	3 (7.5)	3 (3.8)	0.85, 1	0.36	2.1 (0.4-11.1)
	Yes	35 (92.5)	75 (96.2)		NA	1 (Reference)

**Note:** X<sup>2</sup>-Chi square value, @ df- degrees of freedom, # p value based on Chi square test, NA-Not Applicable, \* statistically significant (p value <0.05), \$OR-Odds Ratio, CI-Confidence interval.

**Table 3:** Life style related risk factors profile of study participants and their association with breast cancer (N=120).

Sl. No.	Study variable	Cases (N=40) n (%)	Controls (N=80) n (%)	X <sup>2</sup> value, df <sup>@</sup>	p value <sup>#</sup>	OR (95% CI) <sup>\$</sup>
1	Diet					
	Mixed	26 (65)	45 (56.2)	0.84, 1	0.35	1.4 (0.7-3.2)
	Vegetarian	14 (35)	35 (43.8)		NA	1 (Reference)
2	Hypertension status					
	Yes	6 (15)	13 (16.2)	0.03, 1	0.86	0.91 (0.3-2.6)
	No	34 (85)	67 (83.8)		NA	1 (Reference)
3	Diabetes status					
	Yes	9 (22.5)	18 (22.5)	0.001, 1	0.99	1 (0.4-2.5)
	No	31 (77.5)	62 (77.5)		NA	1 (Reference)
4	Alcohol consumption					
	Yes	6 (15)	3 (3.8)	4.9, 1	0.04*	4.5 (1.1-19)
	No	34 (85)	77 (96.2)		NA	1 (Reference)
5	Tobacco usage					
	Yes	15 (37.5)	5 (6.2)	18.7, 1	<0.001*	9 (2.9-27)
	No	25 (62.5)	75 (93.8)		NA	1 (Reference)
6	Waist circumference					
	High	19 (47.5)	23 (28.8)	4.1, 1	0.04*	2.2 (1.1-4.9)
	Normal	21 (52.5)	57 (71.2)		NA	1 (Reference)
7	Family history					

	Yes	11 (27.5)	13 (16.2)	2.1, 1	0.15	1.9 (0.7-4.8)
	No	29 (72.5)	67 (83.8)		NA	1 (Reference)
8	Perceived stress					
	Mild	11 (27.5)	42 (52.4)	6.7, 2	NA	1 (Reference)
	Moderate	12 (30)	15 (18.8)		0.03*	3 (1.1-8.3)
	Severe	17 (42.5)	23 (28.8)		0.03*	2.8 (1.1-7)

**Note:** X<sup>2</sup>-Chi square value, @ df- degrees of freedom, # p value based on Chi square test, NA- Not Applicable, \* statistically significant (p value <0.05), SOR-Odds Ratio, CI-Confidence interval.

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