

# A Hospital Based Case-Control Study on Risk Factors of Breast Cancer among Patients of Coastal Karnataka

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## Abstract

*Background:* Cancer is the third leading non communicable health issue after diabetes and hypertension worldwide. Breast cancer is the commonest cancer among women with a highly variable incidence between countries and regions. The present study aimed at studying the risk factors among breast cancer patients. *Materials & Methods:* 100 participants including 50 cases of breast cancer and 50 controls aged 25-70 years were included in the study considering the various inclusion and exclusion criteria. Association of various risk factors (general and reproductive variables) with breast cancer was studied. *Results:* Literacy level, social status, blood group, sedentary lifestyle, age at menarche and menopause were all significantly associated with breast cancer. ( $p < 0.05$ ). *Conclusion:* We conclude that low literacy, low socioeconomic status, O+ve blood group and early onset of menarche and late menopause were significantly associated with breast cancer.

**Keywords:** Blood Group; Breast Cancer; Menarche; Risk Factors.

## Introduction

Cancer is the third leading non communicable health issue after diabetes and hypertension worldwide. Breast cancer is the commonest cancer among women with a highly variable incidence between countries and regions. Nearly a million cases are diagnosed every year worldwide [1]. American cancer society predicted an approximate 232,340 to be newly diagnosed with invasive breast cancer and 39,620 women to die from breast cancer in 2013. In India, an estimated 1,44,937 women were newly detected with breast cancer according to International Agency for Research in Cancer (WHO) in 2012 with 50% mortality [2].

Though it was thought to be more common in developed countries, the number is steadily rising in the developing country as well. As against the lifetime risk, age specific risk of occurrence of breast cancer is found to be low. Carcinoma of the breast below the age of 20 years among females is almost unheard of. There is a steady rise thereafter. At 30 years, incidence rises to 1:622 females and at 60 years, it becomes 1:24 females [3].

Breast cancer incidence is found to peak after the age of 40 years in India as compared to 50 years elsewhere [4]. Breast cancer records have been maintained by various registries of national cancer registry project in India and it has been observed that there is an increasing trend in the incidence of breast cancer. Also, India is fast becoming the largest contributor of breast cancer deaths [5].

The primary risk factors for breast cancer are female gender and older age [6]. With rising incidence and awareness, breast cancer is found to be commonest cancer among urban Indian females and the second most common in rural India. Other potential risk factors include: genetics, lack or delayed childbearing or lack of breastfeeding, higher levels of certain hormones, certain dietary patterns and obesity [7-11].

The multifactorial risk factors are majorly dependent on the age of the woman [12]. Depending on the age of presentation, breast cancer can be grouped as reproductive-age (occurring at <40 years of age), peri menopausal - age (occurring between 40 to 55 years) and post menopausal (occurring at >55 years of age) [12]. This is mainly because the timing of reproductive events affects the hormonal and

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immunological status as well as the stage of breast tissue differentiation thus influencing the breast cancer risk [13].

India is a sub continent with huge diversity in culture, behavioural patterns, customs and practices, diet and lifestyle. Hence the information related to these factors which can potentially be a contributor for the occurrence of breast cancer is still limited. There is a need for mining more information on these factors which will give us an edge for the better understanding of science of breast cancer.

Increasing awareness and screening for the potential risk factors is the need of the hour. Since there are only few such studies done in coastal Karnataka, there is a need to study the association of various risk parameters on the occurrence of the disease.

### Materials and Methods

100 participants aged 25-70 years were included in the study. 50 patients had breast cancer and 50 were healthy age matched volunteers. 50 cases of breast cancer between the age groups of 25 to 70 years were taken as cases and  $\pm 2$  years age and gender matched 50 healthy volunteers who accompanied other patients to the hospital were considered as controls. All volunteers who were pregnant, with gynaecological problems and cases of male breast cancer formed the exclusion criteria for this study. Hundred cases and controls were recruited for this study to detect a minimum difference of 20% association of various risk factors with breast cancer with an alpha of 0.05 and power of 80%. Written informed consent was obtained from all the volunteers and ethical clearance for the study was also obtained from the Institutional Ethics Committee.

Study participants' age, anthropometric measurements and Body Mass Index (BMI) using Quetlet's formula were recorded. Socioeconomic status was ascertained by determining if the study participants were above or below poverty line. A pretested and duly validated questionnaire consisting of sets of questions pertaining to education level, employment status and income was administered to the study group and in accordance to Kuppuswamy classification all the participants were categorized as upper lower class, upper middle class and lower middle class. Information regarding the highest level of education was collected from all the study participants and

they were categorized as uneducated, 1<sup>st</sup> – 7<sup>th</sup> std, 8<sup>th</sup> – 12<sup>th</sup> std and >12<sup>th</sup> std. Status of employment was also noted for all the study participants. Blood sample of all participants were collected under aseptic precautions and blood group (ABO system and Rh system) was determined using standard agglutination method. Information regarding the type of diet (vegetarian diet/ mixed diet) consumed was recorded from all the study participants. Consumption of any form of tobacco or alcohol was also recorded.

A detailed history including past medical/ surgical history, personal history, drug history and family history were taken. Also, general physical examination, vital signs, and complete systemic examinations were done on all participants. A detailed history of reproductive variables such as age at menarche, age at marriage, age at first child birth, number of children, abortion history, use of oral contraceptive pills, age of menopause if attained, were taken and study samples were grouped appropriately for each of these reproductive variables.

Responses of socio-economic status, diet, physical activity, literacy and employment, use of tobacco and various reproductive variables were analyzed among the participants statistically. Age, BMI and blood group parameters among the study group were analyzed by using the statistical software SPSS version 21.0 and MS Excel 2007. Chi square test to compare the frequencies and unpaired t test to check the significance was used. All tests were two-tailed and  $p < 0.05$  was considered as significant.

### Results

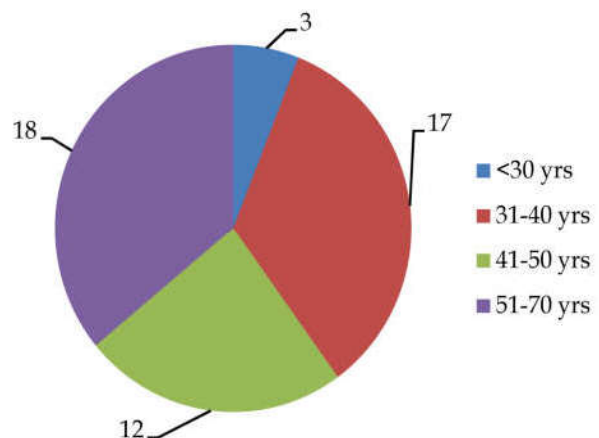
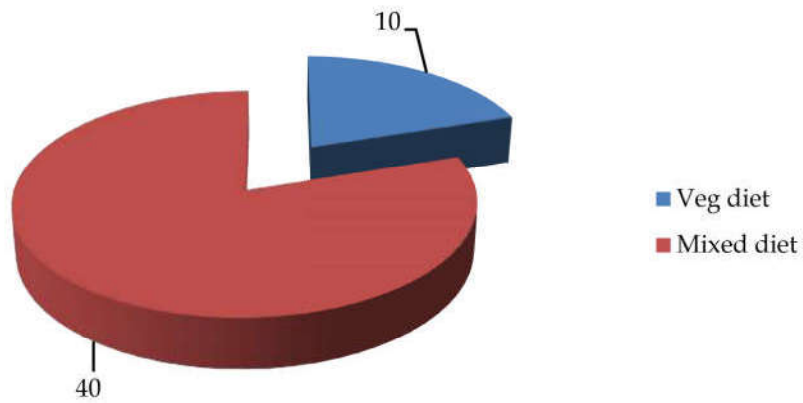


Fig. 1: Age wise distribution of breast cancer cases (n=50)

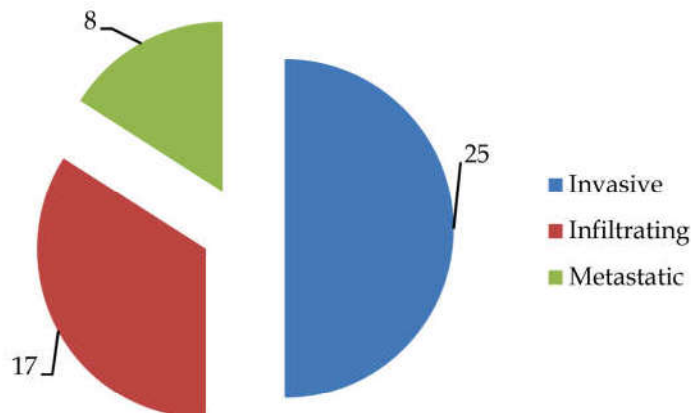
**Table 1:** Comparison of different general variables among cases and controls (n=100)

General Variables	Groups	Cases		Controls		p value
		N	%	N	%	
Level of education	Uneducated	11	22	3	6	0.01*
	1 <sup>st</sup> to 7 <sup>th</sup> std	22	44	15	30	
	8 <sup>th</sup> to 12 <sup>th</sup> std	13	26	21	42	
	>12 <sup>th</sup> std	4	8	11	22	
Social status	Upper lower class	14	28	13	26	0.01*
	Upper middle class	7	14	22	44	
	Lower middle class	29	58	15	30	
Occupational status	Unemployed	38	76	12	24	0.49
	Employed	35	70	15	30	
Blood group	A+	12	24	13	26	0.03*
	B+	14	28	16	32	
	AB+	04	08	04	08	
	O+	20	40	08	16	
	A-	0	0	03	06	
	B-	0	0	0	0	
	AB-	0	0	01	02	
BMI	Normal (18-24.9)	34	68	27	54	0.31
	Overweight (25-29.9)	13	26	20	40	
	Obese (>30)	03	06	03	06	
Physical activity	Sedentary	38	76	25	50	0.02*
	Non sedentary	12	24	25	50	
Tobacco use	Absent	41	82	50	100	0.00**
	present	09	18	0	0	

\*p<0.05 is considered to be significant, \*\*p<0.00 is considered to be highly significant



**Fig. 2:** Type of diet among the breast cancer cases (n=50)



**Fig. 3:** Distribution of type of breast cancer among cases (n=50)

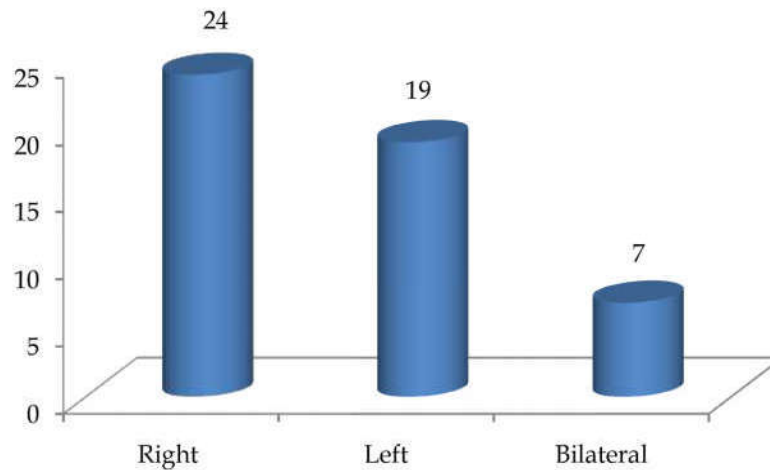


Figure 4: Side of breast involvement among cases (n=50)

Table 2: Comparison of various reproductive variables among cases and control (n=100)

Reproductive Variables	Groups	Cases		Controls		p value
		N	%	N	%	
Age at menarche	≤ 13 yrs	29	58	18	36	0.03*
	>13 yrs	21	42	32	64	
Menstrual cycle	Regular	41	82	40	80	0.79
	Irregular	9	18	10	20	
Age at marriage	Unmarried	3	6	0	0	0.13
	≤ 30 yrs	47	94	49	98	
Age at first child	>30 yrs	0	0	1	2	0.47
	No child	5	10	2	4	
	≤20 yrs	22	44	23	46	
	21 - 30 yrs	22	44	25	50	
Breast feeding	>30 yrs	1	2	0	0	0.14
	Not done	9	18	4	8	
Parity	Done	41	82	46	92	0.45
	Nulliparous	5	10	2	4	
	≤2 children	21	42	20	40	
Use of OCP s	>2 children	24	48	28	56	0.00**
	No	49	98	41	82	
Menopause	Yes	1	2	9	18	0.01*
	Not reached	21	42	27	54	
	<45 yrs	10	20	16	32	
	>45 yrs	19	38	7	14	

\*p<0.05 is considered to be significant, \*\*p<0.00 is considered to be highly significant

## Discussion

The present study was aimed to find out the association of various general variables and reproductive variables as risk factors contributing to the precipitation of breast cancer. In the present study, majority of the cases (36%) were distributed in the age group of 31–40 years followed by 34% of the cases occurring in the age group of 51–70 years (Figure 1). Number of cases in the age group of <30 years were the least, contributing to only 6% of the total cases. An American database confirms that 7% of the total

breast cancer is detected before the age of 40 years. It also emphasizes the fact that survival rates are lower among younger age group and young age is an independent predictor of adverse outcome [14].

When a comparison of level of education was done among cases and control (Table 1), it was found that the number of cases were significantly higher among lesser educated as compared to higher educated. Studies indicate that higher literacy has helped improve the knowledge and awareness amongst the masses about the cancer, our study showed a significantly higher incidence among lesser educated.

When socioeconomic status was compared between the cases and control, the number of cases was significantly high (58%) among lower middle class group of people. 86% of the cases were from upper lower class and lower middle class group of people. The need for spreading awareness is indeed very high among the lower rung of socioeconomic ladder of people.

There was no significant difference observed among the employed and unemployed group of people (Table 1). However, there was a significant increase in number of cases among the people with sedentary lifestyle as compared to people who were more physically active (Table 1). Sedentary lifestyle certainly plays an important role in development of non communicable disease like cancer. Earlier studies have however shown a positive association between body mass index and breast cancer in postmenopausal women and a large population based study concluded that obesity, high calorie intake and sedentary lifestyle all contribute to breast cancer in premenopausal women [15]. Adipose tissue is an extragonadal source of estrogen and increased exposure of estrogen to breast tissue may trigger the initiation and promotion of breast cancer [16]. It also increases the levels of insulin and insulin like growth factors which are a risk factor for breast cancer [17].

A significantly higher number of cases was seen among people with O+ blood group (40%) followed by B+ (28%) and then A+ (24%). There were no cases of breast cancer reported from people having negative blood group (Table 1). It is worthwhile to mention that majority of the Indian population belong to O+ and hence the majority of the cases might belong to this blood group. But the next highest number of cases belonged to B+ though the percentage of population having this blood group is quite low. Many studies have shown association of blood group to greater susceptibility to cancer. ABO antigen is mapped to 9q34 region and any mutation in this region is known to be associated with cancers [18].

Blood group antigens expressed on cancer cells are different from that of those expressed on normal cells. They have a role in systemic inflammatory response in pathogenesis of cancer. There is an altered motility of these cells which may lead to metastasis. They escape from apoptosis and from immune response which furthers cancer progress [19,20]. Majority of the sample population (91%) had no history of substance (tobacco) abuse, 9% of the women who had habit of tobacco consumption were found to have breast cancer (Table 1). Tobacco use is known to be associated with risk of developing various cancers.

Interestingly, when type of diet was compared among women suffering from breast cancer (Figure 2), it was found that 80% of the cases consumed mixed type of diet as compared to only 20% of the cases consuming vegetarian diet. Review of earlier studies has found that most of them found a positive association of improved survival among breast cancer cases with intake of vegetables, fruits and micronutrients [21].

It is very important to identify the signs and symptoms of breast cancer earlier on, so that appropriate treatment is provided at the earliest which improves the prognosis with minimum cost expenditure. Figure 3 shows that majority of the cases (50%) were found to be suffering from invasive type of breast cancer and metastatic type was found to be least prevalent (16%). Efforts should be made in enhancing the knowledge and awareness of these signs and symptoms of the disease amongst the population. Self breast examination should be taught and encouraged to achieve the goal of early detection. Involvement of right breast was highest (48%) as compared to left (38%) and bilateral involvement (14%) [Figure 4].

On comparing various reproductive variables, we found that (Table 2) earlier the age of menarche significantly higher was the incidence of breast cancer. 58% of the cases attained menarche lesser than or equal to 13 years of age. Early onset of menarche is found to be associated with increase in period of exposure of breast tissue to estrogen which is associated with increase in risk of breast cancer.<sup>22</sup> Type of menstrual cycle (regular/ irregular) was not found to be significantly associated with breast cancer. There was no significant association found between the age of marriage and breast cancer incidence. 88% of the breast cancer cases were aged less than or equal to 30 years at the time of birth of first child. Association of breast cancer with age at birth of first child was also not found to be significant. 10% of the cases were found to be nulliparous. More such studies are required on larger sample size. Earlier studies have revealed that the risk of breast cancer decreases with increase in the number of children. 82% of the cancer cases had done breast feeding when compared to 92% of those healthy volunteers. Studies show that the incidence of breast cancer is lower in breast fed women [23]. But alteration of lifestyle and increase in literacy and employment among Indian women is resulting in a change in breast feeding trend.

When use of oral contraceptive pills was determined, it was found that 90% of the sample population did not use pills. Earlier literature reveals

that, though pills are highly effective contraceptive measure, they are found to be associated with high incidence of breast cancer. Since our study was short term hospital based with limited number of sample size, we did not find any association of breast cancer and use of oral contraceptive pills. Larger population based studies for a longer duration need to be done to quantify the amount of this association.

Earlier attainment of menopause was significantly associated with lower incidence of breast cancer (Table 2). Only 20% of the breast cancer cases had attained menopause before the age of 45 years as compared to 32% of healthy volunteers. Also 38% of all breast cancer occurred in the cases that had attained menopause after the age of 45 years. However, the bulk of the cases i.e. 42% occurred among women who had not yet attained menopause. Though earlier studies are suggestive of occurrence of cancer in the elderly age group, the current scenario shows a rising incidence of cancer in earlier part of life itself. This is a disturbing trend, and more efforts need to be done in studying risk factors and drawing effective precautionary measures and screening tools to lessen the burden of this disease.

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