



## EPIDEMIOLOGICAL CHARACTERISTICS OF FEMALE BREAST CANCER PATIENTS OF SAURASTRA REGION OF GUJARAT-A HOSPITAL BASED STUDY

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### ABSTRACT

With the increase in adoption of westernization and sedentary life style in low- and middle-income countries like India, there is a significant increase in breast cancer incidence rate. The exact cause of breast cancer is yet unknown and there are limited studies available on the risk factors associated with breast cancer. Thus, this research work is carried out with an aim to study the region-specific contributing risk factors playing role in breast cancer incidence and their prognosis. We also aimed to study rural-urban disparity in risk factors associated with female breast cancer patients of Saurashtra region of Gujarat. This Cross Sectional, Single-Centre, Hospital-based study was conducted in Cancer Hospital at Rajkot, Gujarat India. One-to-one In-person interview of total 174 primary breast cancer patients were carried out and details were collected in pre-tested structured questionnaire. Data obtained from the patients were further analysed using Bürkner's BRMS package (R) interface and SPSS. In our study, majority of patients are from rural background and its subsequent relationship with other relevant parameters is found to be significant ( $p < 0.03$ ). The age of patients ranged from 22 to 76 years and the mean age at diagnosis of the breast cancer was 51.5 years. A positive association is observed between risk of breast cancer and BMI for both pre- and post-menopausal rural and urban women. 37% females were having premenopausal status and 62% females were postmenopausal. Out of total postmenopausal patients, 31% had attained late menopause at the age of 51 years, while 13% females had experienced menarche at <12 years of age. Our data is first of its kind studying risk factors playing role in breast cancer incidence in Saurashtra region of Gujarat. Even though having limited patients representing the population this region-specific study is useful for cancer projection and to understand treatment modalities.

**Keywords:** Breast Cancer, Epidemiology, Prognosis, Risk Factors, Socio-demographic.

### 1. INTRODUCTION

Worldwide, Breast Cancer (BC) accounts for approximately 30% of all cancers among women. The incidence of BC may vary between different geographic regions and is the leading type of cancer in terms of the number of new cases every year [1]. BC is ranked among the top 5 cancer types in terms of mortality and among the top 3 cancer types in terms of incidence rate as per WHO, 2018. It is the most frequently diagnosed cancer in the vast majority of the countries (154 of 185) and is also the leading cause of deaths in over 100 countries. The diagnosis of approximately 2.1 million cases was

estimated in 2018, contributing about 11.6% of the total cancer incidence burden throughout the world.

Considering the Indian scenario, the 3 most widely recorded malignancies are cancers of the breast, uterine cervix, and lip and oral cavity - together accounting for about 34% of all cancers in India each year. Increasing adoption of western life style in low- and middle-income countries like India, plays an important role in the increase of BC incidence [2]. BC is the most commonly diagnosed cancer among Indian women. With the population growth, changes in the lifestyle, and migration from rural to urban areas, there is

astatistically significant increase in the trends of incidence of BC in India. The mortality rates associated with BC have also increased many folds during the last two decades [3, 4].

Breast cancer is the most common type of cancer in females of urban India with the significant rise in incidence among rural females [5]. There is a substantial difference in BC incidence rates between rural and urban areas. The rates observed in urban registries range from 29/100,000 to 35/100,000 women, whereas those observed in rural registries vary from 10/100,000 to 12/100,000 women [6, 7]. Despite having lower rate of BC incidence in India (12.7/100,000), the rate of mortality is almost similar to worldwide rate (12.9/100,000) [8].

Breast cancer is a multifactorial disease and the exact cause is yet unknown but previous researches recognize many risk factors associated with its incidence, such as positive family history, genetics, age, sex, alcohol consumption, cigarette smoking among others and are broadly classified into modifiable and non-modifiable category. Other factors associated with increased BC incidence include increased life expectancy, reduction in competing risk of mortality from infections, change in reproductive patterns, and changes in lifestyles among individuals [9].

Reproductive risk factors are also associated with prolonged exposure to endogenous oestrogens, such as early menarche, late age at menopause, late age at first childbirth, nulliparity, number of children, and duration of breastfeeding are among the most important risk factors for BC [10, 11]. Exogenous hormones also exert a higher risk for BC occurrence. Oral contraceptive and hormone replacement therapy users are at a higher risk than non-users. Breastfeeding is hypothesized to have a protective effect [12].

The annual age-standardized rate for breast cancer incidence in India is 25.8/100,000 with a high mortality rate of 12.7/100,000 [13]. Several risk factors for BC have been well documented and studied worldwide but for the majority of women presenting with BC, it is not possible to identify specific risk factors [14]. Epidemiological characteristics such as sociodemographic profile, socioeconomic status and educational status have also been found to be associated with BC [15]. The risk of occurrence also increases with the changes in lifestyle such as low physical activity and consumption of high-fat diet [16, 17]. There are limited studies available on the risk factors associated with BC and despite the increasing trend in breast cancer among women in India,

there are no exclusive reports from Saurashtra region of Gujarat state.

Additionally, the incidence and prognosis of breast cancer may vary within the same society, and since a definite reason for BC is yet unknown, these differences are hypothetically linked to environmental factors, lifestyle and socioeconomic-cultural factors (SECF) contributing to diagnosis and mortality rate. Considering the Indian scenario, there is a difference in incident rates of breast cancer in different regions of our country. Thus, it is need of time to study the region-specific contributing risk factors playing role in breast cancer incidence and their prognosis.

## 2. METHODOLOGY

This Cross Sectional, Single-Centre, Hospital-based study was conducted between January 2017 and December 2019 at Shree Nathalal Parekh Cancer Hospital Rajkot, Gujarat India in order to study the risk factors associated with female breast cancer patients of Saurashtra region of Gujarat.

The study was reviewed and approved by institutional ethics committee. The patients were enrolled after explaining the purpose of the study and written informed consent was obtained from each patient. Terminally ill patients and the patients who did not give their consent for participation were excluded from the study. A total of 174 patients with primary breast cancer diagnosed and confirmed by histopathological and/or cytopathological reports were included in the study. One-to-one In-person interview of each participant was conducted in the hospital using a pre-tested structured questionnaire.

The questionnaire contained information on demographic and socio-economic factors, reproductive factors, household and occupational status, family history of cancer, smoking and chewing of tobacco, prior and current history of other chronic illness. Anthropometric measurements such as height (in cm) and weight (in kg) of each participant were measured using standard equipment at the end of the interview.

Socio-demographic factors noted were age, marital status, education, socio-economic status such as occupation, family income and residence status. Reproductive factors included were age at menarche, menopausal status, age at menopause, age at marriage, age at first pregnancy, number of live births/still births, parity (number of children), status of breastfeeding with tentative respective durations, hormone use and methods adopted to prevent pregnancy. Information

about clinical presentation and criteria for the diagnosis of breast cancer was also recorded. Patients' weight and height were recorded before surgery and for each study subject, we calculated body mass index (BMI) by dividing the weight in kilograms by the square of the height in meters (weight (kg)/height (m)<sup>2</sup>). Women were categorized according to the WHO Criteria: underweight BMI < 19 kg/m<sup>2</sup>; normal BMI ≥ 19 and <25 kg/m<sup>2</sup>; Overweight BMI ≥ 25 and <30 kg/m<sup>2</sup>; obese BMI ≥ 30.0 kg/m<sup>2</sup>. Data were analysed and presented as mean ± standard deviation and frequency tables.

### 2.1. Statistical Analysis

Data obtained from the patients were transferred to Microsoft Excel software and rationalized using Bayesian method. Further analysis was done using *Bürkner's BRMS package (R) interface* and SPSS (Statistical Package for Social Science), version 20.0 software (IBM SPSS Statistics, New York, USA). Data were analysed using descriptive statistical methods (number, percent, mean). The significance of background of the patients and relevance of other socio-demographic, anthropo-

metric and reproductive factors in breast cancer diagnosis among females of Saurashtra region were evaluated by Shapiro-Wilk test, Fligner Killeen test and Mann Whitney U test.  $p < 0.05$  was considered statistically significant and were subjected to a two-tailed test.

### 3. RESULTS

Data from total 174 newly diagnosed breast cancer patients were collected from Nathalal Parekh Cancer Hospital, Rajkot. The study duration is between January 2017 to December 2017 and details were collected using a structured questionnaire in order to study rural-urban disparity in risk factors associated with female BC patients of Saurashtra region of Gujarat.

Table-1 represents sociodemographic and socioeconomic characteristic of the cases. The age of patients ranged from 22 to 76 years and the mean age at diagnosis of the breast cancer was 51.5 years. 50 % of the patients were belonging to age group between 30 to 50 years whereas, 46.5 % were greater than 50 years of age. Youngest patient was of 22 years of age.

**Table 1: Sociodemographic and Socioeconomic characteristic of the Study Subjects.**

Variable	Categories	Frequency	Percentage (%)	Significance
Age	< 30 years	6	3.5	P<0.03
	30 - 50 years	87	50	
	> 50 years	81	46.5	
Side of breast affected	right	87	50	p <0.54
	left	83	47.7	
	bilateral	1	0.6	
	unknown	3	1.7	
Background	rural	98	56.3	p <0.02
	urban	76	43.7	
Educational status	illiterate	53	30.5	p <0.02
	below 8th std	36	20.7	
	below 12th std	68	39.1	
	graduate n above	10	5.7	
	unknown	7	4	
Employment status	housewife	101	58	p <0.03
	farming	44	25.3	
	others	19	10.9	
	unknown	10	5.7	
Marital status	married	144	82.8	p <0.79
	unmarried	2	1.1	
	unknown	28	16.1	
addiction	addicted	40	23	p <0.04
	not addicted	134	77.0	

56 % of the patients (n=98) were from rural areas and 44 % (n=76) patients were from urban localities of the Saurashtra region, and rural background of patients is further found to be significantly ( $p < 0.023$ ) playing role in other dependant variables because of significant rural-urban disparity. No significant disparity was observed among the incidence of breast cancer among side of breast affected as it possessed almost equal chance to become cancerous. Literacy ratio among females was subcategorized into different categories and it was found that, majority of females (92%, n=157) were having education below 12<sup>th</sup> std, and a very low percentages of females (6%) was found to have been graduated. Out of all, nearly 58 % females were engaged with different types of employment activities and 25% (n=44) were involved with farming work. Major portion of females (58%) were found to be home makers. Total 23% (n=40) of female patients were having an addiction

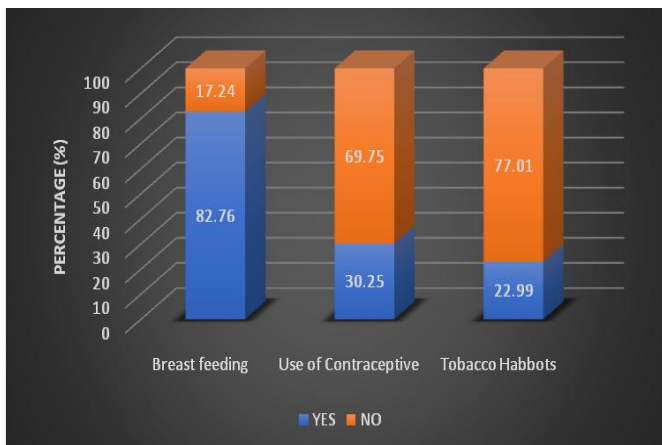
history with types of different products such as snuff, beetle nut and tobacco in majority of cases and some of the cases had habit of bidi and cigarette. More than 80% females were married and it was not significantly correlated with the incidence of breast cancer but further reproductive parameters based on this was found to be significantly associated with rural-urban disparity. The distributions of the hormonal, reproductive, and anthropometric characteristics of the 174 breast cancer cases are presented in table 2. The BMI revealed that 22% (n=77) female subjects were in each of the overweight (25-30 kg/m<sup>2</sup>) and obese (>30 kg/m<sup>2</sup>) categories. Whereas 46 % (n=80) were found to be having normal BMI range *i.e.* < 25 kg/m<sup>2</sup>. Thus, it can be stated that nearly 44 % patients ( $p < 0.0374$ ) were at a moderate and high-risk category as per WHO criteria since obesity is found to be closely associated with cancer incidence by multiple previous research data.

**Table 2: Hormonal, Reproductive, and Anthropometric characteristics of the study population**

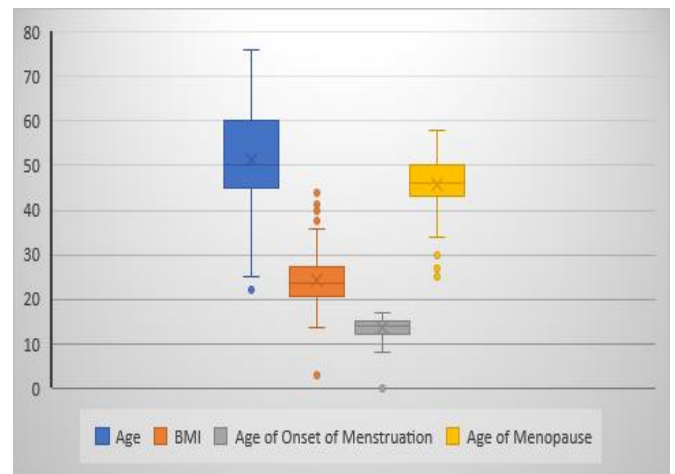
Variable	Categories	Frequency	Percentage (%)	Significance
BMI	normal <25 kg/m <sup>2</sup> low risk	80	45.9	p < 0.04
	overweight 25 - 30 kg/m <sup>2</sup> moderate risk	39	22.4	
	obesity >30 kg/m <sup>2</sup> high risk	38	21.8	
	unknown	17	9.7	
Age of marriage	below 15 years	9	9.6	p < 0.01
	below 20 years	66	70.2	
	20 - 30 years	16	17	
	above 30 years	2	2.1	
	no marriage	1	1	
Total parity	Nulliparity	2	1.8	p < 0.05
	1 to 3	52	47.7	
	> 3	55	50.5	
Age at first child birth	less than 20 years	38	41.3	p < 0.02
	between 20 - 30	49	53.3	
	> 30 years	3	3.3	
Breast feeding history	no	2	2.2	p < 0.02
	yes	15	17.2	
Use of contraceptives	no	72	82.8	p < 0.04
	yes	83	69.7	
Menopausal status	no	36	30.3	p < 0.19
	premenopausal	64	36.8	
	postmenopausal	107	61.5	
	amenorrhoea	1	0.6	
Age at menopause	unknown	2	1.1	p < 0.02
	< 50 years	60	56.1	
	> 50 years	33	30.8	
	unknown	14	13.1	
Age of onset of menstruation	<12 years	23	13.2	p < 0.31
	>12 years	68	39.1	
	amenorrhoea	1	0.6	
	unknown	15	8.6	
Menstrual pattern	regular	83	79.8	p < 0.29
	irregular	20	19.2	
	amenorrhoea	1	0.9	

Information regarding the known risk factors for breast cancer revealed that 37% (n = 64) of patients were premenopausal and 62% (n = 107) were postmenopausal category out of total patients. The mean age at menarche was found to be 13.68 years. 13% (n = 23) of patients experienced menarche at <12 years of age, whereas 39% (n = 68) of patients had menarche at >12 years of age. The mean age at menopause was 45.6 years and 31% (n = 33) of women attained late menopause at the age of 51 years and above. 80% breast cancer patients had regular menstrual and bleeding pattern during their reproductive age. 30% (n=36, p <0.03) females out of total subjects showed positive history of use of hormonal contraceptive pills as a birth control measures.

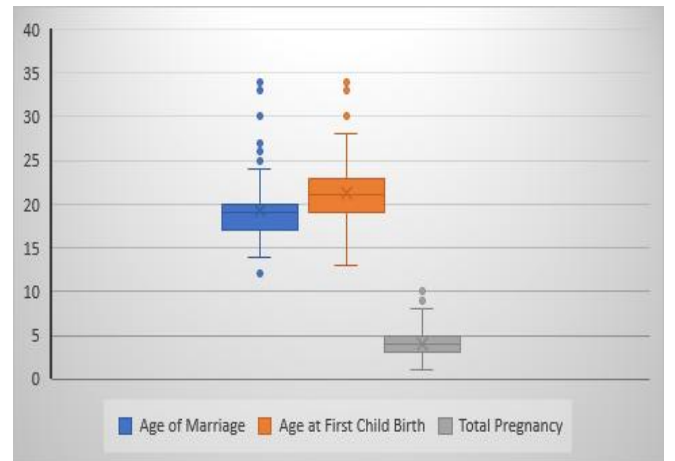
10% (n=9) out of total subjects were found to be married before 15 years of age, whereas 70% (n=66) patients were found to be married before 20 years of age indicating the scenario of early marriage among the study population (p<0.01). Early marriage resultantly leads to early age at primigravida. Out of 174, 98% (n=89) females were parous and only 3% gave birth to their first child at the age of 30 years and above. 41% (n=38) females gave birth to their first child before the age of 20 years, whereas 53% (n=49) gave birth to their first child between the age of 20 - 30 years. 48% females were having children between 1 to 3, and 51% females were found to be have more than 3 children in their reproductive age. In addition, it was also found that 83% (n=72, p <0.01) females had breastfed their children with a mean duration of at least one year from the birth of a child.



**Fig. 1: Graphical representation depicting frequency and percentage of breast feeding pattern, contraceptive use and tobacco habbits among Breast Cancer patients.**



**Fig. 2: Graphical representation by box whisker plot depicting frequency and percentage of age of diagnosis of breast cancer, reproductive factors (age of menarche and menopause) and anthropometric factor (BMI) observed in breast cancer patients.**



**Fig. 3: Graphical representation by box whisker plot depicting frequency and percentage of age of marriage with age of primigravida and total parity among breast cancer patients.**

**4. DISCUSSIONS**

As per NCRP (National Cancer Registry Program) data, breast cancer is the commonest cancer among urban Indian females, and the second commonest among the rural Indian women. In order to study rural-urban disparity, the present study is aimed to analyse the impact of sociodemographic factors, anthropometric factors and reproductive factors among breast cancer patients of Saurashtra region reporting to a major cancer hospital in Rajkot City of Gujarat, India.

## 4.1. Sociodemographic factors

### 4.1.1. Background

In our study, higher proportions of patients are from rural background and its subsequent relationship with other relevant parameters is found to be significant. ( $p < 0.03$ ). According to MacKinnon JA *et al.*, 2007 living place plays an important role in defining risk of advanced breast cancer and which is more likely to be diagnosed at earlier stages in urban women than in rural women, and thus, at a more treatable stage [18,19]. Our study is in accordance with the previous studies wherein, it is reported that the late stage at diagnosis and lower survival have been linked to poor access to healthcare facilities and lower awareness, especially among the urban poor and rural populations as well as to other demographic factors such as lower education and literacy [20-23].

### 4.1.2. Age

Age is also found to be having a statistically significant relationship with breast cancer, implying that the risk of BC increases with increase in age. As one gets old, the chances of suffering from BC get much higher probably due to the abnormal changes that occur in the breast through the aging process as a result of the hormonal changes such as the decrease in levels of oestrogen. In Western countries, the peak age of BC is 60-70 years while in Asian countries it is 40-50 years. Thus, in case of India, it peaks among women at a younger age [22, 24, 25]. Present study of ours observes result pattern of median age of diagnosis at 50 years while youngest patient of 22 years- pointing out the reporting of BC a decade earlier in Indian patients as compared to their western counterparts. Obtained results are in accordance with previous results that younger age at diagnosis tend to be more aggressive and possesses increased size of tumour, metastatic lymph node involvement, low hormone receptor status, and low survival rates [4, 24, 26, 27, 28].

### 4.1.3. Socioeconomic status

Socioeconomic status (SES) plays a massive role on a woman's health and in diagnosis of the breast cancer and education is a key factor influencing lifestyles, behavioural patterns, reproductive factors, such as parity and even stage at presentation [29, 30]. In our study, majority of patients belongs to rural background, 50% study population was found to be illiterate or had received only primary school education. Results are in accordance with previous research predicting that lower

education and income as one of the important factors leading to poor screening and delay in diagnosis of breast cancer among women of the developing countries [10, 20, 21, 22, 29-32].

## 4.2. ANTHROPOMETRIC FACTOR

### 4.2.1. Obesity

Significant association is found between being Overweight and obese with increased BMI and higher breast cancer incidence in the Asia- Pacific group than in European-Australian or North-American group [33-35]. In our study, a positive association is observed between risk of BC and augmented anthropometric factors for both pre- and post-menopausal rural and urban women. We found that more than 40% of patients are under Obese and overweight category as per WHO. Similar results are also observed in earlier research studies stating that high BMI is associated with worse long-term outcomes among obese women with breast cancer [15, 36-39]. It is hypothesized that obesity is affecting BC incidence by various mechanisms, including increasing oestrogen synthesis, causing insulin resistance, inhibiting the synthesis of sex hormone-binding globulin (SHBG), and promoting systemic inflammation and also thought to be associated to the greater number of irregular menstrual cycles, with decreased exposure to ovarian hormones in obese women leading to risk of breast cancer [37, 39, 40].

## 4.3. Reproductive Risk Factors

### 4.3.1. Onset of menstruation and menopause

The reproductive risk factors such as age of onset of menstruation, age of menopause, marital status, menstrual pattern, age at first childbirth, total number of children and breast feeding have been found to be associated with breast cancer which act early in life. Epidemiological studies in several countries suggest that the BC risk factors vary with ethnicity. Previous research studies suggest that age at first child birth, age at menarche and age at menopause are associated with the risk of BC and hypothesized to prolong the exposure period of oestrogen which is likely to be a key player in the initiation, progression, and promotion of BC enhancing overall risk among females acting in early life [41,42]. In the present study, 13% females had experienced menarche at <12 years of age whereas 39% had menarche at >12 years of age significantly correlating with the previous study [43, 44]. Late age at menopause in Indian women has been found associated with an increased risk of BC by Gilani GM *et al.*, 2004

[45]. In our study, 37% females were having premenopausal status and 62% females were postmenopausal. Out of total postmenopausal patients, 31% had attained late menopause at the age of 51 years and above. Similar results were obtained by other research study where the risk of BC was more for women who had menopause after 50 years compared to women who had menopause before 45 years of age [45-47].

#### 4.4. Marital Status and Parity

Marriage at an early age, early and multiple childbirths, and breastfeeding of all children for a longer period of time is the normal custom in most of the Indian societies. However significant disparity is observed among the rural and urban class as well as per regionality. In the present study, 83% of patients were married and nearly 80 % out of total was married before the age of 20 years. It has been found that owing to early marriage, the age at first pregnancy was also earlier among the subjects. 41% subjects had their first childbirth at the age <20 years. However, only 3% had older age at first pregnancy (>30 years). Moreover, 48 % females had fewer children's (1-3) whereas 50% females had >3 children. Pregnancy initiates cellular differentiation in mammary glands and lowers susceptibility to carcinogenesis. Previous studies have observed a negative relationship between parity and breast cancer risk and same is been observed in current study too [48-50].

#### 4.5. Breastfeeding

Most studies suggest that breastfeeding for a year or longer period of time slightly reduces a woman's overall risk of breast cancer [51]. As per Collaborative Group on Hormonal Factors in breast cancer, 2014 in a review of 47 studies in 30 countries, it was found that the risk of BC was reduced by 4% for every 12 months of breastfeeding [52]. As per Britt *et al.*, 2017, possible explanation for this effect may be that breastfeeding inhibits menstruation, thus reducing the lifetime number of menstrual cycles and lowers exposure of oestrogen [53]. Another possible explanation relates to the structural changes that occur in the breast following lactation and weaning by Faupel-Badger *et al.*, 2012 [51]. In present study, about 83 % females had breastfed their children with a duration of at least 12 months after birth suggesting a protective inverse relationship with breast cancer risk. Same results were observed in several previous studies also [46, 54].

#### 4.6. Oral contraceptives

Several studies suggest that the use of oral contraceptives (combined oestrogen and progesterone) which promote breast tumorigenesis, is associated with a small increase in breast cancer risk, particularly among women who begin their use before the age of 20 years or before first pregnancy [50,55]. In present study, 30% patients were having positive history of using oral contraceptives, while 70 % denied the use and were unable to answer properly because of social stigma. However, no exact role can be determined for it as a risk factor for breast cancer.

Few epidemiological studies conducted so far across India raise concern about increasing trends for breast cancer incidence and mortality across all parts of India mainly due to rapid urbanization, industrialization, population growth and ageing. Major risk factor contributing to the increasing incidence are marital status, reproductive factors, location (urban/rural), BMI, breast feeding, waist to hip ratio, low parity, obesity, alcohol consumption, tobacco chewing, smoking, lack of physical activity, high fat unhealthy diet and environmental factors. However, the reason behind increase in BC incidence at younger age is still mystery. Our data is first of its kind studying risk factors playing role in breast cancer incidence in Saurashtra region of Gujarat. Even though having limited patients representing the population, this region-specific study is useful for cancer projection and understanding treatment modalities. Larger patient study is recommended to exactly know the risk factors as a causative agent of higher breast cancer incidence.

#### 5. ACKNOWLEDGEMENT

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#### *Ethical approval*

The study is reviewed and approved by institutional ethics committee (approval no. 1621/17.18).

#### *Conflict of interest*

There is no conflict of interest between the authors.

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