# Review article

# Current scenario of epidemiology of breast cancer in India

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#### Abstract

Breast Cancer (BC) is the most predominant cancer affecting females in India. The prevalence of BC among young women between 15 to 39 years is on rise. The mortality rate is also high in India due to diagnosis at advanced stages. The burden of BC differs across states due to factors like demography, geography and culture. This narrative review delves into the state-wise prevalence of BC in India discussing the heterogeneity in incidence and mortality rates. The possible risk factors driving the rising incidence of BC are examined. The prevalence of various subtypes of BC in Indian population is covered with a special focus given to Triple Negative Breast Cancer (TNBC). The extent to which BC Screening is practised in India along with regional, cultural and socio-demographic factors that influence the screening practices is also addressed. It also delves into the economic burden caused due to expensive treatments and medications for treatment of BC particularly in low-income areas and calls for joint efforts to address all these aspects in order to curb the rising burden of BC. The review concludes with the necessary preventive and management measures which can be taken to reduce the burden and mortality rate in India.

Keywords: Breast Cancer, Prevalence, Triple-Negative Breast Cancer, Screening, Treatment

#### Introduction

Breast Cancer (BC) has become the commonest cancer among women. As per the World Health Organisation (WHO) records, Breast Cancer has affected 2.3 million women around the world and 6,70,000 women have died from it in the year 2022 [1]. The GLOBOCAN Statistics for India in 2022 also has pointed breast cancer as the leading cancer in women, accounting for 1,92,020 new cases (26.6%). The Age Standardized Incidence Rate (ASIR) comes around 26.6 per 1,00,000 women respectively [2].

From 1990 to 2019, the ASIR and the morbidity due to BC had been increasing gradually in Asian countries like India and China. A recent study revealed that the more recent cohort groups in these countries saw a rise in the likelihood of having BC. Forecasts reveal that the incidence will continue to increase through 2035 especially in low- and middle-income countries (LMICs) like India and other Asian Countries [3]. In India for every 4 minutes once, a woman is diagnosed with breast cancer and 1 in 28 women in India will be diagnosed with BC in her entire lifetime and this rate slightly differs in rural and urban areas [4].

This review brings out the existing landscape of BC in India giving an overview on regional differences, screening uptake, molecular subtypes, risk factors, economic burden due to breast cancer treatment and various management strategies which can be adopted.

## Risk factors contributing to rising breast cancer burden

Knowing the risk factors is essential to curb the rising cases. As the age progresses, the risk of BC increases. About 90% of the factors that cause BC are linked with lifestyle, environmental, reproductive factors which increase the risk of BC by disrupting the hormonal system. The remaining 10% of BC are caused due to Genetic Predisposition [5]. Apart from the risk factors, socio-economic development, cultural differences, income, healthcare advancements, education, and demographic changes also contribute to rising burden.

Lifestyle factors that increase the likelihood of breast cancer include consumption of unhealthy foods, physical inactivity, obesity, excessive alcohol consumption, and tobacco usage. A study reported an increase in the Age Standardized Mortality Rate (ASMR), Disability Adjusted Life Years (DALYs) of about 21.27 thousand over a period of 30 years till 2019 due to lack of physical activity. This emphasizes the need to incorporate physical activity into our daily routine. The possible reason could be attributed to socio-economic transition due to which people in low socio-demographic regions also take up regular income jobs and they find less leisure time to devote for physical activity [6].

The proportion of ageing population in the country will influence the prevalence of BC. As the age of women increases, the risk of BC also increases. Reproductive factors that increase the chances of BC are childbirth after 30 years, reduced number of live births, nulliparity, early menarche, late menopause, reduced duration of/no breastfeeding, use of oral contraceptives for longer duration [7]. Apart from the lifestyle and reproductive factors, genetic and hormonal factors also play a substantial role in increasing the BC burden. Genetic risk factors like BRCA ½ mutations, history of breast cancer in families, polymorphism in DNA repair genes contribute to about 70% risk of acquiring BC in Indian scenario [8].

During 1990 to 2019, substantial increase in the Age Standardized Incidence Rate (ASIR) was reported (EAPC = 0.59, 95% confidence interval (CI) = 0.5 to 0.68). In low and low-middle Socio-Demographic Index (SDI) countries like India, the mortality and the DALYs in young women are rising and second-hand smoke was reported to be the main risk factor that has caused increased mortality [9].

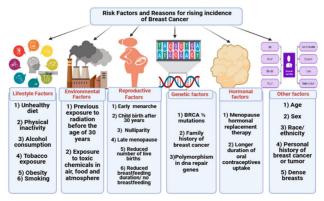


Figure 1: Risk Factors that contribute to rising Incidence of Breast Cancer in India. Regional and state-wise disparities in breast cancer burden

In the year 2019, India was one among the top three countries with highest BC incidences. It was in third position with 1,46,090 cases (95% UI: 112,452-183,482) after China and United States. India had second highest mortality cases after China with 83,510 deaths (95% UI: 64,550-105,994) [10]. ICMR and NCDIR based on Population based Cancer Registries (PRCRs) and Hospital Based Cancer Registries (HBCRs) reported that the overall incidence of cancer was very high in the North-Eastern Region from 2012 to 2016. The common cancers that affect the north east population are mouth and oesophagus cancer, lung, liver, stomach, gall bladder, breast and cervix. Another prominent finding reported increase in the incidences of life-style related cancers like colorectal and the breast cancers and the reduction of infection-related cancers like the cervical and the stomach cancers [11]. Currently, the major burden is due to oral, breast and cervical cancers which constitute to more than 50% burden [12]. Kerala ranks first in the highest incidence of BC cases followed by the states Mizoram,

Haryana, Delhi and Karnataka. Regarding the mortality rate, Mizoram tops the list, followed by Kerala and Haryana in the second and third positions respectively [4].

The burden of BC contributed by each state differs throughout India as each state in India differs in terms of socio-economy, culture, literacy and demography. Studying the state and region wise incidences of BC is important to effectively implement screening and treatment strategies based on the region's trends and needs. The PBCR is the primary source of cancer statistics for India which are reliable and consistent in terms of data that is being collected [13]. Epidemiological studies report cancer burden in terms of Years of Lives Lost (YLLs), Years lived with Disability (YLDs) and DALYs. During the period of 2012-2016, cancers of the breast contributed to the highest DALYs of 232.7 per 1,00,000 women among the other top sites like ovary, cervix, uterus, lung and gall bladder in females. About 63.5% of the DALYs were contributed by the breast alone between the age groups of 35-59 years. A PBCR based cancer burden study estimated that the regions north and northeast especially the state of Mizoram, Meghalaya and Delhi contributed to the highest cancer burden which is followed by south and central regions after adjusting for mortality to incidence ratio between the years 2012 to 2016 [14].

The regions and states with highest breast cancer burden in DALYs differ significantly from those with the highest overall cancer burden. Between the years 2012-2016, the region north contributed the highest age-adjusted BC burden followed by south, and then the central region and lastly north-east contributing to the lowest BC burden respectively [15]. In terms of states, Telangana contributed to the highest burden. Tamil Nadu and Karnataka also topped the list, both of which contributed to more than 700 DALYs per 1,00,000 women and Meghalaya reported the lowest number of BC cases [15]. On the basis of cancer registries, Chennai, Bangalore, Hyderabad and Delhi topped the list of highest breast cancer contributing registries with north-eastern registries contributing to the lowest [15].

## Prevalence of molecular subtypes of breast cancer in India

Breast Cancer is classified into several subtypes based on gene expression and molecular subtyping studies. The subtypes include Luminal A, Luminal B, HER-2 Positive, Basal like or TNBC. Molecular subtyping studies aid in opting for better treatment strategies based on the tumour characteristics. Epidemiological studies on the prevalence of molecular subtypes of BC in India can help researchers to find out the underlying factors influencing the distribution of these subtypes. A systematic review and meta-analysis study reported that Luminal A subtype is the most common among all subtypes followed by TNBC, Luminal B and HER2 in the second, third and fourth positions respectively [16]. A notable trend of increased prevalence of TNBC can be observed in our country. About 10-25% of tumours are of TNBC subtype in India. A prospective study analysed the incidence of molecular subtypes in 103 BC patients who underwent modified radical mastectomy in a hospital and it was found that 34% of the BC patients had TNBC subtype which equates to the general prevalence percentage of TNBC in India [17]. A similar pattern of Incidence rates of TNBC subtype can be observed in a retrospective observational study of 2062 BC patients attending a tertiary cancer centre present in western India. 26% of patients had TNBC subtype, 37% were Luminal A, 11% were HER2 Positive, 8% Luminal B and 18% belonged to unclassified type. Different subtypes affect different age groups. As age progressed the luminal A subtype incidence increased in patients. About 52% of TNBC subtype patient's age fell below 30 years. The age distribution of Luminal B subtype was even in age groups 50-59, 60-69 and greater than 70 years [18]. This highlights that luminal A subtype is commonest among Indian population and its prevalence increases as age increases. TNBC subtype is observed in younger population below 30 years which is highly aggressive, has poor prognosis, difficult to treat and advanced targeted therapies are used to treat them. The prevalence of TNBC subtype is higher in Indian women as compared to white women [16]. Further research on the reason behind the increasing prevalence of TNBC in India is warranted.

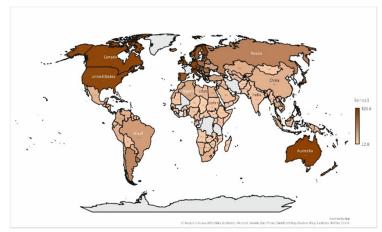


Figure 2: Geographic distribution of five-year prevalence rate (per 100,000 population) of Breast Cancer (Females).

# Breast cancer screening in India

It is quintessential to know what factors necessitate women to take screening tests and whether screening is given importance by people in all states. A district level analysis was performed in which information of breast examination of 6,99,000 women were collected from National Health Survey (NHS) 2015-2016. From the distribution curve of prevalence of BC screening, highest screening uptake was seen in Kerala. Apart from Kerala, the states Karnataka, Tamil Nadu, Punjab, Maharashtra, Jammu and Kashmir showed high uptake. Rest of the states showed only minimal uptake [19]. In the 2019-2021 National Family Health Survey study which targeted women in the age group of 30- 49 years, highest screening uptake was seen in Tamil Nadu (5781 per 1 lakh women). States like Mizoram, Kerala came next in the list with 2723 and 2429 per 1 lakh people respectively with states in the south and in the west showing higher screening rates in the country [20]. Screening uptake depends on several factors like education, income, awareness about BC, socioeconomic development, marriage status, age, employment, and previous history of BC in family. The screening uptake increased as the age progressed from 30 to 49 years in the reproductive age group women which reinforces that age plays a deciding factor for screening uptake [20].

A study examined the impact of these factors on the stage at diagnosis in 1210 patients who attended a cancer care hospital. Advanced stage of BC was diagnosed in 54% of patients. About 73% of screened people were from urban area and 27% from rural area, 83.7% belonged to Hindu religion, 9.7% were Muslims and 6.6% others, 81% were married, 15.2% were widowed/divorced, 3.5% unmarried, 18% were illiterate, 28.1% were pursuing higher education in college and above and 14% were employed/ working [21]. It could be noted that marital status plays a deciding factor for opting BC screening [19].

Wealth plays a significant deciding factor that further creates inequalities in the uptake of screening tests along with other socio-demographic factors. A study examined the impact wealth has on the uptake of BC screening along with the other parameters like age, area/region, religion, marital status, education. The most prominent finding was that wealthier sections of people opted for BC screening in each of the parameters like age, marital status, religion, education. Wealth differences among rural populations, religions like Christians and Muslims, Castes like Other Backward Caste (OBC) and Scheduled Caste (SC), people studying in secondary and higher education, people who are unemployed and people who are married had heavy impacts on the BC Screening uptake [22].

The positive impact education has on early screening of BC can be observed from a south Indian study involving 3,640 patients in which 1727 patients had BC. The entire study group was classified into illiterate/primary school, middle school and secondary school groups. The BC patients who studied till secondary school had increased 5-year survival rate of 73% when compared to 59% for primary school group and 68% for middle school group thereby emphasizing the fact that patients who had lower level of education had little awareness to be present earlier for screening programmes [23]. Presenting earlier to screening programmes might reduce the mortality rate due to treating BC at earlier stages.

The self-awareness about the symptoms, risk factors, screening, knowledge of self-breast examination (SBE) and other screening options for BC among people varies based on geography of the region (Rural/ Urban) as is

evident from the one-on-one interview study of 360 women residing in rural area in Karnataka. Out of the 360 women, 66.6% of them were unaware of SBE, 53.3% wanted female doctors to examine their breasts, 60.5% expressed that had they known about SBE before, they would have practised it now and then and 89.2% haven't taken screening tests before. A closer analysis of the data indicate that a considerable percentage of rural women lack awareness about SBE and other screening facilities [24].

The burden of cancer is likely to get doubled by the year 2040. Effective planning is required to reduce BC Incidence. Three steps can be implemented. Strengthening the Cancer Registries and allocating funds from the government to increase the number of registries and to effectively run them. Educating preventive steps to medical students, health care professionals and integration of Preventive Oncology course in medical books. Implementation of community-based screening programmes in hospitals and at the primary, secondary and tertiary heath care centres and increasing state led programmes keeping in view the economic, geographic, socio-demographic factors.[25].

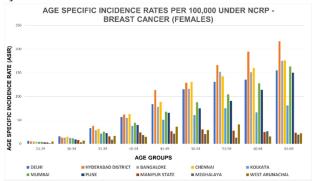


Figure 3: Age Specific Incidence Rates (ASIR) per 100,000 of Breast Cancer (females) across major regions in India.

## Economic burden due to breast cancer treatment

Currently, the cost of treatment for cancer is so high due to expensive medications, the utilization of complex multi-modal treatment strategies like surgery, chemotherapy, radiotherapy, hormonal therapy and targeted therapies [26]. An approximate amount of INR 20 lakhs (US\$27000) is required for multiple rounds of chemotherapy sessions along with patient specific treatment regimens [27. Patients tend to borrow money from their known circles, sell their assets, keep their jewellery in pawn shops, and take health loans often at a high interest rate [28]. The Out of Pocket (OOP) expenditure is greatly increased by factors like stage of cancer at diagnosis, age, the location of the patient's residence and the distance to the cancer speciality hospital (transportation costs), the type of hospital (government, private), the type of multimodal therapy based on the cancer stage, the extent of cancer treatment coverage in insurance if it is available (Blumen H et al, 2016)[29][30][31][32]. A prospective longitudinal study reported that the average expenses to undergo treatment was INR 258,095/US\$3531 (95% CI: 238,225, 277,934) and the average OOP expenditure for BC treatment was INR 186,461/US\$2551 (95% CI: 167,666, 205,257) which was about 72.2% of the total expenses. Although the patients could use some sort of insurance to cover their expenses, the total costs and the OOP expenditure were very high that the reimbursements given could not reduce the financial burden of the patients [28].

Despite the availability of advanced treatment options, the costs of these treatments are expensive. The mean direct cost of cancer treatment accounts to INR 25,606 and mean indirect cost accounts to INR 8772 and mean total costs comes around INR 34,378 in Vypin Block Panchayat of Ernakulam district, Kerala. The gap between the average income of the people and the average cost of cancer treatment is wide [33]. This emphasizes the fact that government must focus on providing cancer treatment at affordable costs especially to cancer patients in Panchayat and rural population.

#### Management of breast cancer

Breast Cancer Management measures must start from people who must be aware of the symptoms, risk factors, prognosis, and management of cancer. The presence of a multidisciplinary team consisting of surgeon, oncologist, radiologist, histo-pathologist, specialist nurse, allied health professionals and an administrator in Cancer Speciality hospitals and Clinics (Government/Private) enables more accurate diagnosis and aids in

efficiently devising patient specific treatment plans. This team is also called as Tumour Boards/Multidisciplinary Cancer Conferences. Such team of professionals will monitor the patients closely and often guide them through till the end of treatment with well-informed decisions [34]. The practice of Shared Decision Making (SDM) in Cancer Hospitals provides the best possible cancer care and treatment plans considering the individual patients situations. It is often practised in many developed countries. In India, the recommendation of Shared Decision Making in Clinical Practice Guidelines and in Consensus Statements is not sufficiently discussed. It is especially not adequately discussed in medical journals [35]. When it comes to taking measures to cure breast cancer in earlier stages, the importance and the practice of Self Breast Examination (SBE), must be made known to people. SBE can be performed by women after 20 years, once in a month after 5<sup>th</sup> day of the mensuration on a monthly basis. It is a very easy, tested, cost effective or cost reducing method that can reduce the mortality occurrence due to late diagnosis [24].

Management of Breast Cancer must be looked into in all possible ways. The integration of traditional system of medicine along with modern practices must be taken into consideration after having enough discussions among doctors, patients and field experts. In order to spread awareness, Internet can be used as a source to spread reliable and authenticated information about importance of screening and about BC. In regions of low-income and rural areas, the local community health workers and volunteers who are adequately trained to perform clinical breast examination and who can educate patients with available treatment options are invaluable to help control the increasing morbidity. These people need to be trained properly and paid regularly [36]. Screening Programmes must be regularly implemented in all of the government hospitals at affordable costs especially in rural areas in all of the states and districts. Enough awareness must be spread to people through advertisements and camps in rural as well as urban areas.

#### Conclusion

Breast Cancer has become the leading cancer among women especially among women aged 15-39 years in India. First of all, people must recognize that BC is increasing in alarming rates in India. The Indian Government and State Governments should organize numerous awareness programmes on early breast screening and should educate the importance of it in preventing mortality. Enough funds have to be allocated by the government for cancer treatment, care, infrastructure development in government hospitals all over the country covering all the regions. PBCRs must be set up in rural areas since more than 60% of the Indian population reside in these areas and it must be expanded in urban areas too since till now PBCRs cover only 10% of the Indian Population. Government must provide cost effective cancer control treatment options and medications so that patients from socio-economically weaker sections of the country can afford them. Smoking, alcohol consumption, exposure to toxic pollutants, physical inactivity, unhealthy diet are some of the modifiable risk factors people can take control of and modify them. Increasing People's participation into early screening programmes especially among rural people, adopting a healthy lifestyle, taking actions on modifiable risk factors, cost-effective screening and treatment options, shared decision making amongst various medical professionals to facilitate the best treatment option for each patient are some of the current options available to lower the incidence rates.

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