Breast Cancer Trends in India over the Last Ten Years: A Systematic Review

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By
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[Name of Institute]
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CERTIFICATE

This is to certify that the dissertation titled **"Breast Cancer Trends in India over the Last Ten Years: A Systematic Review"** for the partial fulfilment of the requirements for the award of the degree of **[]** in **[]** and submitted to **[]** is an authentic record of the research work carried out by **[]** during the period from "" under my supervision. The matter embodied in this thesis has not been submitted by me for the award of any other degree of this or any other University/Institute.

(Name of Supervisor)

DECLARATION BY THE SCHOLAR

I hereby certify that the work which is being presented in the thesis titled **"Breast Cancer Trends in India over the Last Ten Years: A Systematic Review"** for the partial fulfilment of the requirements for the award of the degree of **[]** in **[]** and submitted to **[]** is an authentic record of my own work carried out during the period from "" under the supervision of **[]**. The matter embodied in this thesis has not been submitted by me for the award of any other degree of this or any other University/Institute

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TABLE OF CONTENTS

ABSTRACT

Breast cancer is currently one of the most common cancers worldwide, and is the leading female cancer in India as well. Past population-based registries have shown that the incidence and prevalence of breast cancer in India is on the rise. However, the trends of this increase are unclear and the mechanisms are not well understood. The objective of this study was to conduct a systematic review to investigate and report the trends of breast cancer incidence and prevalence in India over the last 10 years. The databases PubMed, Science Direct, and Springer were searched using the keywords ‘breast cancer’, ‘India’, and ‘statistics’. Studies and reports published between the years 2013 and 2023 were included in the review. Following data extraction, it was seen that very few studies exist that report the incidence and prevalence of breast cancer specifically during the last 10 years. In contrast, several studies report the statistics of cancers in general. Also, surveys conducted for breast cancer are quite old and current statistics are missing. The data obtained from the review revealed that breast cancer is more prevalent in urban rather than rural areas, it has a higher incidence in the North Eastern part of India, it has recently become more common in the younger age group of 30 to 40 years, and is the leading cause of cancers in females. Future studies need to identify breast cancer trends in different parts of India to keep a track of the most recent updates.

LIST OF ABBREVIATIONS

AAR	Age-Adjusted Ratio
APC	Annual Percentage Change
ATM	Ataxia Telangiectasia Mutated gene
BBB	Blood Brain Barrier
BC	Breast Cancer
BRCA	Breast Cancer gene
BRIP1	BRCA1 Interacting Protein 1 gene
BSE	Breast Self-Examination
CBE	Clinical Breast Examination
CHEK2	Checkpoint Kinase 2 gene
CI	Confidence Interval
CSC	Cancer Stem Cell
DNA	Deoxyribonucleic Acid
ER	Estrogen Receptor
GLOBOCAN	Global Cancer Registry
HER2	Human Epidermal Growth Factor Receptor 2 gene
HR	Hormone Receptor
IARC	International Agency for Research on Cancer
ICMR	Indian Council of Medical Research
MRI	Magnetic Resonance Imaging
NCCN	National Comprehensive Cancer Network
NCDIR	National Centre for Disease Informatics and Research
NCRP	National Cancer Registry Programme
OR	Odds Ratio
PAH	Polycyclic Aromatic Hydrocarbons
PALB2	Partner And Localizer of BRCA2 gene
PBCR	Population-Based Cancer Registry
PR	Progesterone Receptor
PTEN	Phosphatase and Tensin homolog gene
RNA	Ribonucleic Acid
TNBC	Triple Negative Breast Cancer
TP53	Tumour Protein 53 gene

LIST OF FIGURES

LIST OF TABLES

1. Introduction

1.1 Background

Approximately 36% of all oncological patients worldwide suffer from breast cancer, which is the most common malignant tumour affecting women. There were an estimated 2.089 million women diagnosed with this debilitating condition in 2018 alone (Nardin et al., 2020). Globally, breast cancer is on the rise, with industrialized nations bearing the highest burden. The number of cases reported worldwide is shockingly high in affluent nations (Global Cancer Observatory, n.d.). There are many factors contributing to this worrying trend, including unhealthy eating habits, high levels of stress, and inactivity (Bellanger et al., 2018). In recent years, mammography has become a reliable and accepted method for screening breast cancer. The technique is especially beneficial to women aged 50 to 69 (Bellanger et al., 2018). A classical mammogram's sensitivity ranges from 75-95% and its specificity ranges from 80-95%, making it a highly effective tool for detecting breast cancer in its early stages. However, the magnetic resonance mammography is recommended as a screening test for women who have a family history of breast cancer. If a suspicious lesion is detected during a mammogram, a thick needle biopsy may be necessary, followed by a thorough histological evaluation (Elmore et al., 2005).

1.2 Risk factors

Several risk factors have been identified that increase the likelihood of developing breast cancer, but the exact cause of carcinogenesis remains elusive. These factors include gender, age, and economic development in a given country, as evidenced by the epidemiological data presented above. In addition to these factors, hormonal influences also play a crucial role, particularly those linked to the duration of exposure to estrogen. Breast cancer is also known to be associated with procreative factors, such as the number of pregnancies, age at the time of birth, and nursing (Smolarz et al., 2022).

1.2.1 Gender

Women are more likely to be diagnosed with breast cancer than men, with 99% of cases occurring in women. Among men, the incidence rate is 0.4/105, or 1% of all cases. There are no more than 100 documented cases per year (Religioni, 2020). In spite of this, breast cancer

incidence is on the rise in men, due to factors such as obesity and prolonged survival rates (Lima et al., 2021).

1.2.2 Age

Breast cancer incidence increases with age, with all age groups showing an upward trend. However, the most significant increase has been seen among younger women under 50 (Lima et al., 2021). Despite being relatively uncommon in this age group, breast cancer in young women is characterized by a higher histological malignancy, reduced expression of steroid receptors, frequent overexpression of the HER-2 receptor, or appears as a unique molecular subtype known as "basal-like" or "triple-negative". Moreover, breast cancer rates among premenopausal women are on the rise (Religioni, 2020).

1.2.3 Development status of a country

Globally, breast cancer incidence is increasing due to population aging and continued population growth (Torre et al., 2017). There is a high incidence rate in developed countries, in particular (Ghoncheh et al., 2016). As mentioned previously, this trend is attributed to the impact of the Western lifestyle. The morbidity rate in developing nations is also increasing as a result of economic growth and access to public healthcare, preventive and screening programs, and a decline in maternal, infant, and child mortality (Ghoncheh et al., 2016). In contrast, breast cancer risk factors such as delayed birth, low birth rate, hormone replacement therapy, obesity, inactivity, and poor diet are becoming more relevant (Torre et al., 2017). Although lower middle- and low-income countries have a lower incidence of breast cancer, their mortality rates are higher than their industrialized counterparts (Torre et al., 2017). A shortage of funding for primary prevention programs, diagnostic tests (primarily mammography), and the latest treatment modalities may be responsible for this trend, which has resulted in more cancers being detected at advanced stages (Ghoncheh et al., 2016).

1.2.4 Hormone status and reproductive factors

Factors associated with a woman's hormonal profile appear to have a significant impact on her likelihood of developing breast cancer. There is a link between estrogen exposure and an

increased risk of breast cancer, which is accentuated by factors like early menstruation, late menopause, delayed first childbirth, and a high number of children (Heer et al., 2020).

Oestrogen plays a critical role in breast cancer pathophysiology (Yue et al., 2010). Breast cancer, which is classified as a hormone-dependent tumor, is associated with elevated oestrogen levels and prolonged exposure to this hormone (Yue et al., 2010). All postmenopausal women have a higher risk of breast cancer when their circulating oestrogen levels are high. Various hormonal and reproductive factors influence the risk of developing breast cancer (Dall and Britt, 2017). The length of exposure to oestrogen and the effects of pregnancy are influenced by various factors, such as the age of menstruation, age of first pregnancy (especially after the age of 30), number of children, and age of menopause (Singletary, 2003).

1.2.5 Hereditary factors

Breast cancer is caused by hereditary factors in approximately 5-10% of cases. Mutations in the BRCA1 and BRCA2 genes are widely recognized genetic anomalies associated with this disease (Mehrgou and Akouchekian, 2016). The BRCA1 gene is located on chromosome 17 and encodes a nuclear protein involved in genomic stability. It interacts with histone deacetylase and binds to RNA polymerase II, regulating transcription, DNA repair, and recombination processes along with other tumor suppressor gene products and signal transduction genes. BRCA1 functions in conjunction with BRCA2, another tumor suppressor gene found on chromosome 13, in repairing double-strand DNA breaks via homologous recombination (Roy et al., 2011).

There are two additional suppressor genes that, when mutated with high-penetrance, increase the risk of breast cancer: the TP53 gene linked to Li-Fraumeni syndrome and the PTEN gene linked to Cowden syndrome. By age 70, 54% of women with Li-Fraumeni syndrome are likely to develop breast cancer, whereas 25% to 50% of women with Cowden syndrome are likely to develop breast cancer. In spite of the rarity of both genetic disorders (Angeli et al., 2020), mutations in ATM, BRIP1, CHEK2, PALB2, and CHEK2 genes are associated with a moderate predisposition to breast cancer, with carriers of these mutations 2-3 times more likely to develop it (Chamseddine et al., 2022).

Breast cancer is estimated to be caused by genetic predisposition in approximately 10% of cases (Armaou et al., 2009). Nevertheless, most breast cancers are caused by spontaneous somatic

mutations. Breast cancer is more likely to develop in women with a family history of the disease, particularly those with a mother or sister who has undergone treatment. In such cases, the risk is three to six times higher. The risk of breast cancer is lower, however, if the relative was diagnosed at an older age (Nardin et al., 2020).

1.3 Types of breast cancer

Five molecular subtypes of breast cancer have been identified through gene expression analysis: luminal A, luminal B, HER2-positive non-luminal, basal-like, and special histological types. Based on pathological criteria, these subtypes represent the immunophenotypes of cancer cells. Genes associated with proliferation and the HER2 receptor are low expressed in luminal A tumors, while genes associated with estrogen receptor function are highly expressed (Smolarz et al., 2022). Luminal type B is characterized by positive ER status, but with lower expression of genes associated with this receptor and higher expression of genes associated with proliferation, as measured by the Ki-67 marker. Luminal type A has a more favorable prognosis for evaluation according to the St. Gallen panel of experts' analysis of the Ki-67 gene expression and breakdown (Curigliano et al., 2017). HER2, oestrogen, and progesterone receptors, as well as genes associated with these receptors, are not expressed in basal-like breast carcinomas, also known as triple-negative cancers. Patients with cerebellar metastases with this type of cancer are particularly interesting, and biological markers such as CK 5/6, HER1, and c-KIT can be useful in identifying both similar and dissimilar basal subtypes, but their clinical utility remains unclear. HER2-positive breast cancer is characterized by overexpression of HER2 in the absence of ER and PR (Smolarz et al., 2022).

1.4 Pathogenesis of breast cancer

The breast is made up of specialized glandular tissues along with connective tissue for support which comprises of fibrous tissue, neurovascular bundles, and adipose. The glandular tissue comprises of an epithelial layer along with supporting stroma which is made up of blood vessels, fibroblasts, and lymphoid cells. The epithelial layer is lined by myoepithelial cells at the outer end and luminal cells at the inner end (Fentiman and D’Arrigo, 2004). Several types of tumours and cancers can occur in the breast which include systemic neoplasms, Hodgkin’s disease, and lymphomas. Breast cancer may begin in the epithelial layer where it is called a carcinoma or in the connective tissue layer where it is called a sarcoma. Breast carcinoma occurs in two phases:

in situ phase where the cancer is restricted to the epithelial layer and can be easily removed from the breast, and invasive phase where it leaves the epithelial layer and enters the connective tissue of the breast leading to metastasis (Fentiman and D'Arrigo, 2004).

Tumours are usually heterogeneous in nature and comprise of a small but significant population of cancer stem cells (CSCs) which are capable of self-renewal, expansion, differentiation, and organogenesis (Clarke and Fuller, 2006). The initial tumour stages are regulated by various transcription factors and signalling pathways which downregulate epithelial markers such as E-cadherin and upregulate mesenchymal markers such as vimentin. These markers have been shown to play an important role in metastasis (Fazilaty et al., 2013). As the initial tumour begins to spread from the primary site, it secretes angiogenic factors which cause extensive vascularization within the tumour. Eventually, it breaches the extracellular matrix and stroma to leave the primary site and establish in secondary sites (Sarrio et al., 2008). Some tumour cells may also enter the lymphatic vessels or the blood vessels to reach distant secondary sites. At the same time, these cells interfere with apoptosis and immune defences of the host in order to survive in a foreign environment (Thiery, 2002). When the tumour cells reach the blood vessels in the brain, they cross the blood-brain-barrier (BBB), move into the parenchyma, and establish themselves as secondary tumours (Fidler et al., 2002).

1.5 Diagnosis of breast cancer

One of the first means of diagnosis of breast cancer is breast self-examination (BSE) and women are encouraged to perform this on a monthly basis to detect anomalies (Kosters and Gotzsche, 2003). Furthermore, clinical breast examination (CBE) is also recommended for women above the age of 40 years (McCready et al., 2005). Mammography remains the gold standard for the diagnosis of breast cancer as it can detect non-palpable masses at early stages. According to medical guidelines, mammography is recommended annually for women over the age of 40 for all women and over the age of 25 for those women with an increased hereditary susceptibility to breast cancer (NCCN, 2013).

Magnetic Resonance Imaging (MRI) is also an important technique to detect, assess, stage, and manage breast cancer. It has higher sensitivity but lesser specificity for the detection of breast cancer as compared to mammography. According to medical experts, women over the age of 25

who have an increased risk of breast cancer should undergo annual mammography as well as MRI (Warner et al., 2008). In high risk patients, adjunctive screening through ultrasound may be performed; however, its utility in the detection of breast cancer is not well documented. It may be particularly useful for detecting cancers in dense breasts where traditional screening methods may not yield results (Kelly et al., 2010).

1.6 Treatment of breast cancer

Once breast cancer is detected and staged, several treatment options are available. Total mastectomy, lumpectomy, or radical mastectomy may be carried out with or without radiation depending on the status of the cancer. In order to be eligible for breast-conserving surgery, neo-adjuvant chemotherapy may be administered comprising of doxorubicin and cyclophosphamide. Radiation therapy may be used to prevent relapse of the tumour after lumpectomy. Systemic targeted therapy may also be used to reduce tumour relapse, and various compounds have been tested such as trastuzumab and tamoxifen (Shah et al., 2014).

1.7 Aim and objectives

The aim of this study is to understand the incidence, prevalence, and relative proportion of breast cancer in India during the past 10 years.

The objectives of this study are as follows:

1. To identify and report breast cancer statistics in India over the last 10 years
2. To identify and report breast cancer statistics in different regions of India over the last 10 years
3. To identify and report breast cancer statistics in different age-groups in India over the last 10 years
4. To identify and report breast cancer statistics in males and females in India over the last 10 years

2. Literature Review

Breast cancer (BC) is the leading cancer affecting women worldwide. Breast cancer was projected to account for 11.7% of all cancer cases worldwide in 2020, according to estimates (Sung et al., 2021). It is now the most prevalent form of cancer in the world, surpassing lung cancer. By 2030, epidemiological studies suggest that 2 million people will be diagnosed with breast cancer, which is alarming (DeSantis et al., 2011). In addition, between 1965 and 1985, the incidence of breast cancer in India increased by around 50%. In order to combat the increasing rates of breast cancer, this trend requires urgent attention (Saxena et al., 2002). A total of 118,000 new cases of breast cancer were reported in India in 2016, of which 98.1% were women. In addition, there were 526,000 prevalent cases in the country. In all 50 states, the age-standardized incidence rate of breast cancer among females increased by 39.1% from 1990 to 2016. Globocan data from 2020 shows that breast cancer caused 10.6% (90,408) of all cancer deaths and 13.5% (178,361) of all cancer cases (IARC, 2020). The cumulative risk of breast cancer in India is 2.81, indicating it poses a significant threat to women's health and wellbeing (IARC, 2020).

Indian women are at a higher risk of developing breast cancer at a younger age than western women. Data from cancer registries were analyzed by the National Cancer Registry Programme to determine changes in cancer incidence rates between 1988 and 2013. All population-based cancer registries reported a significant increase in breast cancer prevalence over time (NCRP, 2016). In 1990, the cervix was the most common site of cancer in India, followed by breast cancer, according to the registries of Bangalore (23.0% vs. 15.9%), Bhopal (23.2% vs. 21.4%), Chennai (28.9% vs. 17.7%), Delhi (21.6% vs. 20.3%), and Mumbai (24.1% vs. 16.0%). However, breast cancer has increased sharply over time, and it has now become the most prevalent cancer among Indian women. In comparison with previous prevalence rates of cervical cancer in India, these statistics highlight the concerning trend of breast cancer prevalence in the country. To combat this growing public health issue, it is crucial to raise awareness and take preventive measures (Takiar and Srivastav, 2008).

Breast cancer patients' overall survival rates vary depending on their stage of cancer, according to a study. Patients in stage I had a survival rate of 95%, those in stage II had a survival rate of 92%, those in stage III had a survival rate of 70%, and those in stage IV had a survival rate of

only 21% (Arumugham et al., 2014). Various factors, including early age at onset, advanced illness at presentation, delay in definitive management, and insufficient or fragmented care, contribute to a lower survival rate for Indian patients with breast cancer compared to their Western counterparts (Maurya and Brahmachari, 2020). Breast cancer management requires early detection and timely treatment, according to the World Cancer Report 2020. A systematic review of 20 studies published in 2018 found that the cost of breast cancer therapy increases with the stage of the disease at diagnosis (IARC, 2020). Breast cancer survival rates and healthcare costs can be improved by early detection and prompt treatment. Therefore, raising awareness and educating people about breast cancer screening and timely treatment is essential to combating this disease's growing burden in India (Sun et al., 2018).

Using data from six major population-based cancer registries (PBCRs), a study published in 2012 examined time trends for breast cancer incidence over the past three decades. Statistical significance was determined by calculating the slope and p-value based on simple linear regressions in the five PBCRs of Bangalore, Barshi, Bhopal, Chennai, Delhi, and Mumbai for each year. Across all PBCRs, the AARs for breast cancer increased consistently between 1982 and 2014. Further evidence of the rise in breast cancer incidence over time was provided by Joinpoint Regression Model Graphs for the same registries. To address this growing health problem in India, efforts must be made to prevent and manage breast cancer (ICMR, 2016). There has been a steady rise in age-adjusted rates of breast cancer per 100,000 population in all PBCRs except Barshi between 1982 and 2014. PBCRs with significant increases in AARs included Bangalore with an APC of 2.84 %, Bhopal with an APC of 1.35 % from 1988 to 2007 and 5.64 % from 2008 to 2013, Chennai with an APC of 1.51% from 1982 to 1993 and 2.83% from 1994 to 2013, and Delhi with an APC ranging from 0.91% for 1988 to 2007 to 5.31% for 2008 to 2012. For all PBCRs except Barshi, average AARs have significantly increased over the past 3 and 5 years. Breast cancer incidence is on the rise in urban Indian areas, according to these findings (Malvia et al., 2017).

The risk of breast cancer among Indian women has been linked to various risk factors in several research studies. Among women from north India, factors such as location (urban or rural), higher body mass index, and breastfeeding are strongly associated with breast cancer (Pakseresht et al., 2009). Physical exercise and breastfeeding are generally beneficial to both ER+ and ER-

breast cancer patients (Dey et al., 2009). Moreover, breast cancer risk is negatively associated with the frequency of breastfeeding over a woman's lifetime (Gajalakshmi et al., 2009). Compared to urban lifestyles, rural lifestyles are associated with a lower risk of breast cancer. It is possible that this is due to differences in lifestyle habits between the two populations (Nagrani et al., 2014). Women living in urban and rural areas with waist-to-hip ratios below 0.95 (versus less than 0.84) are more likely to develop breast cancer. The significant variation in breast cancer incidence between urban and rural areas in India cannot be explained by body size and obesity (Mathew et al., 2008).

It has been demonstrated by several studies that breast cancer risk in Western and South India is associated with factors such as ageing, low parity (having three or more pregnancies reduces breast cancer risk by 40-50%), and obesity (Augustine et al., 2014). There is no difference between rural and urban women who perform household tasks, but spending more time doing household work lowers the risk of developing breast cancer. Premenopausal women engaged in household tasks for 5-6 hours per day had odds ratios (ORs) of 0.48 (95% confidence interval, 0.32-0.72) and postmenopausal women had odds ratios (ORs) of 0.49 (95% confidence interval, 0.34-0.72). As for ORs for more than 6 hours a day, they were not statistically significant (0.70, 95% confidence interval, 0.48-1.02 and 0.51, 95% confidence interval, 0.35-0.73, respectively) (Mathew et al., 2009). Breast cancer rates are higher among women with low levels of education and they tend to seek treatment at a later stage. The odds ratio (OR) for illiterate women was 2.72, whereas the OR for women with primary school education was 2.32, whereas the OR for women with middle school education was 2.07, whereas the OR for postmenopausal women had an OR of 1.45 with a 95% CI of 0.97-2.19, which indicates an increased risk for the disease (Ali et al., 2008).

It has been shown that breast cancer is the most prevalent form of cancer in north-eastern India, and that its occurrence is significantly correlated with factors such as smoking and consumption of betel nut, age at marriage, age of first childbirth, and menarche age (Paul et al., 2015). There is also a mild correlation between the number of children and breast cancer incidence. Breast cancer is more likely to develop in women who experience menarche before their 12th birthday. Furthermore, women who reach menopause after age 55 are at greater risk because of the

prolonged exposure to oestrogen and progesterone during their menstrual cycle (Surakasula et al., 2014).

There has been a sharp increase in the number of younger people being diagnosed with breast cancer in India, despite the fact that the disease is generally associated with older women (Chopra et al., 2014). There is a higher rate of triple-negative and oestrogen receptor-negative subtypes in early-onset breast cancers than in late-onset breast cancers (Anders et al., 2008). As young women have denser breast tissue, routine screening programs may have difficulty detecting tumors, which tend to present as a palpable mass with nodal involvement. The early detection of breast cancer is crucial to its management and treatment (Das and Lokanatha, 2015). Triple negativity is a serious prognostic indicator for younger women with breast cancer (Gogia et al., 2014). India has a significantly higher prevalence of triple-negative breast cancer (TNBC) than Western countries, according to several meta-analyses. Compared to other subtypes of breast cancer, TNBC patients in India are more likely to present with locally advanced stage, histologically more aggressive (grade 3) and larger tumours (Ghosh et al., 2011). Consequently, two-thirds of patients with TNBC in India have advanced disease when they are diagnosed, which reduces overall survival. In order to reduce the negative outcomes associated with TNBC, early detection and timely treatment are crucial (Akhtar et al., 2015).

Breast cancer risk has been linked to environmental factors such as polycyclic aromatic hydrocarbons (PAHs), which are highly emitted in India. It is thought that PAHs can interact with cellular estrogen receptors because they are lipophilic, which means they have an affinity for fat tissues in the breast (Bonner et al., 2005). A family history of breast cancer is also associated with 5% of cases. Breast cancer risk is heavily influenced by genetic factors, such as mutations in BRCA1 and BRCA2. In Indian patients with familial breast cancer, the prevalence of BRCA1/2 mutations ranges from 2.9% to 24.0% (Vaidyanathan et al., 2009). In addition, 2.8% of Indian individuals diagnosed with breast cancer at a young age have BRCA1/2 mutations. The BRCA2 mutation rate in India was lower than the BRCA1 mutation rate (Kim and Choi, 2013). The 185delAG founder mutation is characteristic of Ashkenazi Jews although several studies have identified distinct sequence variants in BRCA1 and BRCA2. In the Indian population, breast cancer has a complex genetic profile, making genetic testing important for individuals with a family history of breast cancer (Saxena et al., 2002). Several genes have also

been associated with breast cancer, including ATM, TP53, CHEK2, PTEN, CDH11, and STK11. Moreover, a community-based breast cancer survey revealed that despite nearly half of the women believing breast cancer was incurable, nearly half were aware of its various aspects. As a result of their socioeconomic status, 40.5% of women had a better understanding of breast cancer (Dey et al., 2015).

3. Methods

A systematic review of the published literature was performed to fulfill the objectives of the study. Relevant studies were searched in the PubMed, ScienceDirect, and Springer databases using a combination of the keywords – “breast cancer”, “India”, and “statistics”. Studies were included in the literature review if they reported statistics of breast cancer in India either based on geographic region, age, gender, and/or other characteristics. Only studies that reported incidence, prevalence, and relative proportion of cases were included; studies that reported on statistics related to screening or treatment were excluded. Apart from original research articles, reports published by government and non-government organizations involved in cancer research were also included. Review articles, case reports, editorials, and clinical guidelines were excluded. Publications between the years 2013 and 2023 were included because statistics pertaining to the last 10 years was the focus of the study. Studies that did not directly report statistical data were not included in the study.

Studies were evaluated by scanning titles, abstracts, and methods section (where relevant) to check if they met the inclusion criteria. The reference lists of the selected articles were also checked to find relevant studies that could be included in the literature review. Each selected study was thoroughly scanned to assess study characteristics such as the first author’s last name, year of publication, study location, type of statistical data available, aims of the study, and relevant findings.

4. Results and Discussion

4.1 Breast cancer burden in India

Breast cancer accounts for 28.8% of all cancers in females, making it the top site for cancers in women (Sathishkumar et al., 2022). For both males and females, breast cancer is on the second position contributing to 10.5% of all cancer cases (Kulothungan et al., 2022). It has been found that at least 45% of all diagnosed breast cancer cases in India are present at advanced stages, which in turn contributes to increased mortality (Malvia et al., 2017). Annually, more than 100,000 women in India develop breast cancer and they demonstrate a case fatality ratio of 40% (Thakur et al., 2018). According to the National Cancer Registry Programme statistics, the incidence of breast cancer during the period of 2012 to 2016 was 2,21,757 (Sathishkumar et al., 2022) or 232.7 per 100,000 (Kulothungan et al., 2022). In 2016, the incidence of breast cancer was estimated to be 1,18,000 cases and the prevalence was estimated to be 5,26,000 cases (Mehrotra and Yadav, 2022). The increase in incidence of breast cancer has been 39.1% from 1990 to 2016 (Mehrotra and Yadav, 2022). According to estimates taken in 2020, breast cancer accounted for 13.5% of all cancers and 10.6% of all cancer-related deaths with a risk of 2.81 (Mehrotra and Yadav, 2022). Table 4.1 provides an overview of breast cancer statistics in India over the past decade.

The incidence of Triple-Negative Breast Cancer (TNBC) is on the rise and accounts for 20 to 43% of all breast cancer cases diagnosed in India (Thakur et al., 2018). India currently has the highest incidence of TNBC (27.9%) among other countries of the world (Thakur et al., 2018). A meta-analysis carried out by Sandhu et al. (2016) found the prevalence of TNBC to be 31% as compared to the prevalence of HR-positive breast cancer (48%) and HER-2 positive breast cancer (27%). The prevalence of TNBC varied from 27 to 35% in different regions of India (Sandhu et al., 2016).

Table 4.1: Breast cancer statistics in India from 2012 to 2020

Year	Incidence	Mortality	5-year prevalence	Source
2012	1,44,937	70,218	11,25,960	GLOBOCAN, 2012

2018	1,62,468 (15.46%)	87,090 (12.11%)	4,05,456	GLOBOCAN, 2018
2020	1,78,361 (13.5%)	90,408 (10.6%)	4,59,271	GLOBOCAN, 2020

4.2 Breast cancer trends based on geographic location

During the period of 2012 to 2014, breast cancer ranked number one in major cities such as New Delhi, Mumbai, Chennai, Bangalore, and Dibrugarh, and the relative proportion varied between 19% and 30% (Table 4.2) (Malvia et al., 2017). The highest crude rate of breast cancer was found to occur in Thiruvananthapuram (43.9 per 100,000) and the lowest crude rate was found in Mumbai (33.6 per 100,000) (Malvia et al., 2017). The age-adjusted rate of breast cancer was highest in New Delhi (41 per 100,000) and lowest in Dibrugarh (13.9 per 100,000) (Malvia et al., 2017). Despite the high incidence of breast cancer in New Delhi, it was found to have a low mortality/incidence ratio (8.0) (Malvia et al., 2017). Statistics from the National Cancer Registry Programme conducted from 2012 to 2016 revealed an increase in incidence of breast cancer cases over the years (Mathur et al., 2020). The highest Annual Percentage Change (APC) was seen in Aurangabad (6.8%) closely followed by Sikkim (5.8%) and Kamrup urban (5%), and the lowest APC was seen in Nagpur (0.4%) (Mathur et al., 2020).

Among the breast cancer cases, TNBC accounts for 72.61% cases in Bangalore, 65% cases in Hyderabad, 62% cases in Srinagar, and 58.33% cases in Pune (Figure 4.1) (Thakur et al., 2018). In all these cities, TNBC is mostly diagnosed in women below the age of 50 years (Thakur et al., 2018). In contrast, New Delhi is the only city where TNBC is more prevalent among older women (54.6%) as compared to younger women (51.5%) (Thakur et al., 2018). Considering all age groups, TNBC has the highest incidence in Nagpur at 43.5%, followed by Srinagar at 34.4% and North East India at 31.1% (Thakur et al., 2018). The lowest incidence of TNBC occurs in Hyderabad at 22.8% (Thakur et al., 2018). Considering the prevalence of TNBC, Mumbai has the highest at 32.1% followed by New Delhi at 24.2% (Thakur et al., 2018). The lowest prevalence of TNBC is seen in Hyderabad at 22.8% (Figure 4.1) (Thakur et al., 2018).

In Barshi rural area, breast cancer ranks second after cervical cancer (Table 4.2) (Malvia et al., 2017). Despite its low crude rate (13.2 per 100,000) and low age-adjusted rate (12.4 per 100,000), it has a very high mortality/incidence ratio (66.3) (Malvia et al., 2017). According to

the National Cancer Registry Programme statistics, the APC of breast cancer in Barshi rural was 0.5% (Mathur et al., 2020).

Table 4.2: Breast cancer distribution based on geographic location during 2012 to 2014 (APC – Annual Percentage Change) (Source: Breast Cancer India, 2020; Malvia et al., 2017; Mathur et al., 2020)

City	Relative proportion (%)	Rank	APC (%)	Crude rate (per 100,000)	Age-adjusted rate (per 100,000)
Ahmedabad	31.5	1			
Aurangabad	30.6	1	6.8		
Bangalore	27.5	1	3.1	29.3	34.4
Bhopal	31.2	1	2.1		
Chennai	30.7	1	2.6	40.6	37.9
Delhi	28.6	1	1.5	34.8	41
Dibrugarh	19.0	1	4.1	12.7	13.9
Imphal West			3.0		
Kamrup Urban			5.0		
Kolkata	25.4	1			
Kollam			2.7		
Mizoram			4.6		
Mumbai	28.8	1	1.4	33.6	33.6
Nagpur	31.9	1	0.4		
Pune	31.4	1	3.8		
Sikkim			5.8		
Thiruvananthapuram	28.5	1	3.3	43.9	33.7
Barshi Rural	20	2	0.5	13.2	12.4

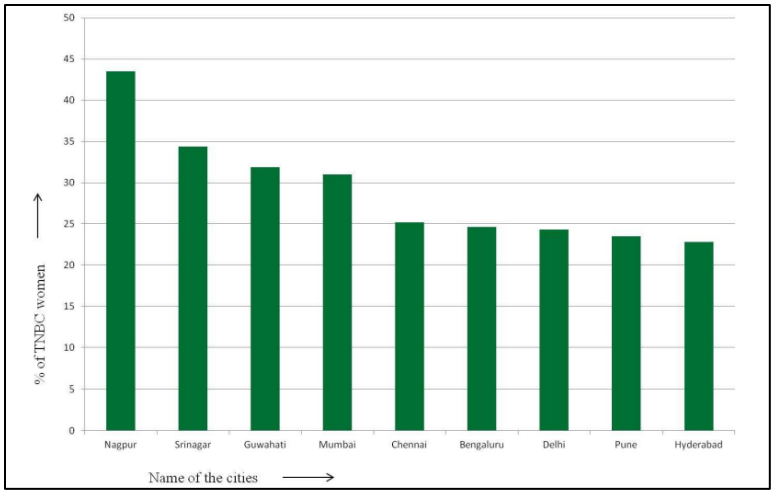

Figure 4.1: Distribution of TNBC in Indian women based on geographic location (Source: Thakur et al., 2018)

In urban areas, the high incidence of breast cancer is associated with a change in lifestyle and diet, westernization, and urbanization (Malvia et al., 2017). Despite this, urban areas have a low mortality/incidence ratio as compared to rural areas which may be attributed to increased awareness and literacy, and better medical infrastructure (Malvia et al., 2017). On the other hand, rural areas have a high mortality/incidence ratio because most cases are diagnosed at advanced stages and have metastasized to a large extent, indicating that these areas need more awareness and better medical facilities for timely diagnosis and treatment (Malvia et al., 2017).

4.3 Breast cancer trends based on age

Women diagnosed with breast cancer are found to occur at least 10 years younger in recent years with the age group of 15 to 34 years having an APC of 0.8 to 4.24% and the age group of 35 to 44 years having an APC of 0.37 to 2.97% (Malvia et al., 2017). For women above 64 years, the APC was found to be between 0.53 and 2.64% (Malvia et al., 2017). The peak relative proportion of breast cancer was found to occur in the age group of 45 to 49 years in all regions except for North East India where it was found to occur in the age group of 35 to 39 years (Figure 4.2) (Malvia et al., 2017). Breast cancer diagnoses experiences an increasing trend in women aged 30 and above and it peaks at 60 to 65 years, indicating that women below 40 have a high risk of being diagnosed with breast cancer (Malvia et al., 2017). With regards to TNBC, the

peak age of diagnosis is 40 to 55 years in Indian women as compared to 50 to 70 years in other parts of the world, and the mean age of diagnosis is 47 years (Thakur et al., 2018).

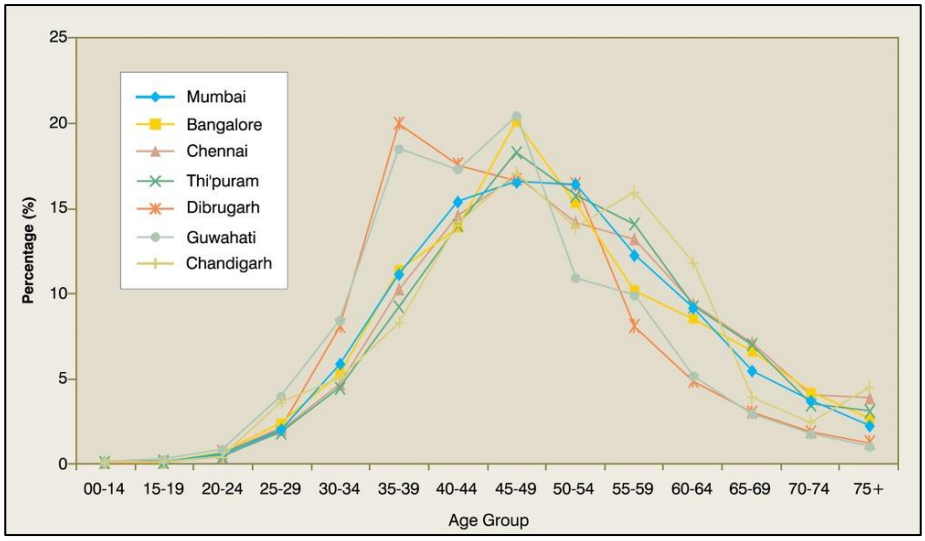

Figure 4.2: Distribution of breast cancer in Indian cities based on age group (Source: Malvia et al., 2017)

4.4 Breast cancer trends based on gender

Results from the National Cancer Registry Programme conducted from 2012 to 2016 revealed that breast cancer is the most common cancer in females contributing to 57% of all cancer cases in women (Mathur et al., 2020). In contrast, the prevalence of breast cancer in Indian males is extremely low at 0.5 to 2.8% of all male cancers (Chhabra et al., 2021).

4.5 Projection of breast cancer burden in India

The estimated burden of breast cancer by the year 2020 was 2,05,424 cases, which is slightly higher than the recorded 1,78,361 cases in 2020 (NCDIR, 2020). By the year 2025, it is estimated that 2,32,832 women would be diagnosed with breast cancer (Sathishkumar et al., 2022).

5. Conclusions

This systematic review aimed to provide statistical data with respect to the incidence and prevalence of breast cancer in India over the last 10 years. It differentiated the statistical data to represent breast cancer incidence and prevalence with respect to geographic region, age group, and gender. Overall, this study revealed that detailed statistical data pertaining to breast cancer in India is quite old, making it difficult to understand trends currently. Most population-based registries have carried out surveys before the year 2020, and so, the present data may not be completely representative of the current trends. Also, a lot of surveys have covered cancers in general, and very limited studies have focused on breast cancer in particular, despite the fact that breast cancer is the leading cancer afflicting women in urban areas and the second most common cancer affecting women in rural areas after cervical cancer.

Breast cancer is found to be highly prevalent in the North Eastern parts of India, probably owing to the high consumption of tobacco in this region. Following this, metro cities and other industrial cities such as Mumbai, Chennai, Delhi, Bangalore, and Dibrugarh have a high incidence and prevalence of breast cancer. On the other hand, rural areas such as Barshi rural have an overall low prevalence of breast cancer as compared to urban areas. However, given the high rates of breast cancer in India, updated data regarding breast cancer statistics is unavailable.

With respect to age group, statistics showed that in recent years, breast cancer is becoming more common in the younger age group of 30 to 40 years. This is alarming because India has a considerable population in this age group which is vulnerable to breast cancer. Furthermore, exposure to tobacco and drugs has also made this age group susceptible to breast cancer. With regards to gender, breast cancer is primarily a female disease, being the leading cancer among females in urban areas and the second leading cancer among females in rural areas. However, it also affects males to a small extent.

This study has several limitations. First of all, the range of studies included in the review was limited to 2013 to 2023 as we wanted to study data from the last 10 years. However, this limited the number of studies that could be included in the review as very limited research exists that has focused specifically on the statistics of breast cancer in India. The second limitation is that the data obtained was quite old as most population-based surveys have been conducted between

2008 and 2018. Therefore, no data could be derived for the years 2020 to 2023 leaving gaps in our knowledge of the current status of breast cancer in India. The third limitation was that statistics related to risk factors, screening, and treatment-related factors were not included in this study.

Future studies need to carry out extensive population-based investigations on age and region-related incidence and prevalence of breast cancer in India. It also needs to understand the risk factors for the observed trends so that appropriate measures can be taken to prevent the development of breast cancer in susceptible women. Also, families of women diagnosed with breast cancer should be counselled about regular screening and should be encouraged to undergo annual check-ups to diagnose and treat breast cancer at early stages.

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