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Systematic Review on the Trends in Breast and Cervical Cancer in India, Especially in North East India

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Abstract

Background: Every country's leading cause of mortality is cancer, which also poses a significant obstacle to raising life expectancy. In nations like India, it is the top cause of mortality, with high rates in the north-eastern regions. Therefore, economic growth has resulted in rising cancer costs, which have caused financial hardship and higher mortality rates.

Objective: In order to provide helpful insights for developing countries and emerging nations, this article analyses India's cancer prevalence trends, survival rates, and treatment regimens for breast and cervical cancer in North East India.

Method: This systematic review evaluates existing literature on breast and cervical cancer trends in India and North East India with an emphasis on citations and original research. Without using patient names or other direct connection, the review uses the PubMed and Google Scholar databases.

Results: In Southern India since 2003, Aizawl and Kamrup had the highest Age-standardized cancer incidence Rate (AAR) per 100,000 residents. Papumpare has the highest incidence among women. Mizoram's Aizawl district has the highest incidence rate (30.7%). Data from the HBCR show that loco regional spread is responsible for 60.0% of instances of cervical cancer and 57% of cases of female breast cancer. Early detection increased overall 5-years survival rates for breast and cervical cancers compared to late detection. According to statistics from South India, the average duration between self-detection of breast cancer symptoms and the first visit to a general practitioner is 60 days, with over 90 days being the usual in 38.7% of cases. The primary therapy for cervical cancer symptoms begins 123 days after the first symptoms.

Conclusion: There are high death rates and low survival rates as more than 70% of patients with advanced cancer seek diagnostic and therapeutic treatments. Cancer has an impact on families' day-to-day operations, financial stability, stigma, and anxiety in LMICs like India. It is absolutely necessary to expand cancer care facilities in urban and rural regions in order to close the gap.

Keywords: Carcinoma; Cancer; Ultrasonography; Chemotherapy; Vaccination

Introduction

Cancer is the main cause of death in every country and a major impediment to extending life expectancy. 2019 figures from the World Health Organisation (WHO) show that cancer is the third or fourth top cause of death before the age of 70 in 23 countries and the 1st or 2nd main cause in 112 of 183. In 2020, there will likely be 10.3 million cancer deaths and 19.3 million new cases. According to estimates, Asia, home to 59.5% of the world's population, accounts for half of all instances of cancer overall and 58.3% of cancer fatalities for both sexes combined. Despite making up just 9.7% of the world population, Europe accounts for 19.6% of cancer fatalities and 22.8% of all cancer incidences [1]. It is becoming more prevalent in Low and Middle Income Countries (LMICs), where two-thirds (65%) of the world's 8 million cancer related fatalities occur each year [2]. India's urban and rural areas, respectively, cancer is the second and fourth most common cause of adult mortality that has doubled from 1990 to 2016 because of low knowledge, limited access to cheap care, and poor prognosis. In India, all cancers combined caused 5% of all DALYs and 8% of all fatalities in 2016, an increase of 90% and 112% from 1990. The states of Mizoram, Kerala, Assam, Haryana, and Meghalaya had the highest crude cancer DALY rates in 2016, whereas theNorth-Eastern states of Mizoram, Meghalaya, Arunachal Pradesh, and Assam had the highest age standardized rates [3]. Over the last two decades, India has seen significant economic expansion and today, cancer is the leading cause of catastrophic medical costs, financial hardship, and escalating costs before death [4]. The growing cancer burden in the nation is partially attributable to the nation's shifting lifestyle related habits. Due to the adoption of lifestyle practices that are known to increase the risk of developing cancer, such as smoking, a poor diet, inactivity, and changes in reproductive behaviour (such as lower parity and later ages

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at first birth), the prevalence of cancer has increased even more in less economically developed countries.

Significance of the study

Lessons and insights from the past about the rise in cancer can be extremely helpful for less developed Indian states, India's neighbours, and other emerging nations that will undoubtedly experience this issue in the future. Therefore, this paper provides an overview of India's trends of cancer prevalence and explores the survival rate and treatment regimen of breast and cervical cancer in India and North East India.

Literature Review

This is a systematic review where a comprehensive critical assessment of several papers that have been published was assessed to compile as many relevant citations as possible in order to locate original research on the patterns of breast and cervical cancer, diagnosis, treatment, and survival rate in India and North East India. The review of literature was conducted on PubMed and Google scholar databases along with references from pertinent papers to track down more studies for cancers. No patient identifiers or direct interaction with the patients were used in the study.

Cancer database in India and North East India

Population based cancer registry: The National Cancer Registry Programme in India started in 1982, and since then, a number of urban and a few rural Population-Based Cancer Registry (PBCRs) have been added. There are 29 Population Based Cancer Registries (PBCRs) which represent 10% of all people in India. Of them, the North-East (NE) area is home to 11 PBCRs [5]. However, PBCRs and reliable population-based statistics continue to be lacking in India's most populated and least developed states, known as the Empowered Action Group (EAG) states. The most current estimates of India's cancer burden given in the GLOBOCAN 2018 database were produced by extrapolating data from a number of regional PBCRs, with little representation from rural areas and no data from EAG states [6].

Hospital-based cancer registry: The Hospital Based Cancer Registries (HBCRs), which concentrate on clinical care, treatment, and outcome, keep records of information on cancer patients who visit a certain hospital. Their main goal is to support patient care and administrative operation, while they could also be somewhat useful for epidemiological research. Currently, there are now 29 hospital-based cancer registries in India. These HBCRs are often found in general or multi-specialty hospitals (public and private) serving the local urban or rural population.

Trends in breast and cervical cancer: Globally, breast cancer is the most prevalent cancer that affects women. With a projected 2.3 million new cases, or 11.7% of all cancer cases, it will now overtake lung cancer as the most common kind of cancer worldwide in 2020 [7]. Within the last 25 years, breast cancer has become the second most prevalent kind of malignancy in India, and it is more frequently diagnosed in younger people. The incidence has rapidly grown, with an estimated 5,26,000 prevalent cases and 98.1% female incident cases in 2016 [8-10]. In case of cervical cancer, with a global age-standardized incidence rate of 13.1 and 6.9 per 100,000, respectively, it is the ninth most common and ninth most lethal form of cancer [11]. According to the GLOBOCAN survey from 2018, cervical cancer diagnoses made up 3.2% of all new cancer cases globally, with Asia accounting for the highest number (55.3%) [12].

The prevalence of cancer is rising in India, with breast and cervical cancer among Indian women accounting for 39.4% of all cancer cases [7]. A combined analysis of the North-East Hospital-based Cancer Registry (HBCR) data indicated Aizawl district in Mizoram and Papumpare district in Arunachal Pradesh having the highest overall Age-Adjusted Rates (AARs) of 269.4 and 219.8 per 100,000, respectively, the NE region of India had the highest incidence of cancer [8]. To fulfil the demand for cancer care, there are not enough hospitals in the NE area that treat cancer. While Manipur and Tripura, which have populations larger than Nagaland, each only have one cancer treatment facility, whereas Nagaland has six cancer treatment facilities. Additionally, Sikkim (98.3%), Nagaland (78.7%), and Manipur (62.4%) had the highest percentages of patients seeking care outside the NE area [9].

Diagnostic methods for breast and cervical cancer: Currently, early detection of cancer and prompt treatment after diagnosis are the two main pillars that must be addressed in order to control the illness effectively and preserve lives. Testing for abnormal calcifications or masses on mammograms, lumps, or nodules found *via* clinical or self-examinations, or during lump or nodule finding procedures, are all part of the evaluation process for breast cancer. Ultrasonography has long been an essential technique for breast cancer screening, image-guided biopsies, and lymph node identification. Other frequently used imaging techniques include Positron Emission Tomography (PET), which uses a radioactive substance called a tracer to look for disease in the body, Magnetic Resonance Elastography (MRE), which combines MRI imaging with low-frequency vibrations to create a visual map that shows stiffness of body tissues, and sentinel lymph node biopsy to determine whether there is cancer in the lymph nodes (Figure 1) [13].

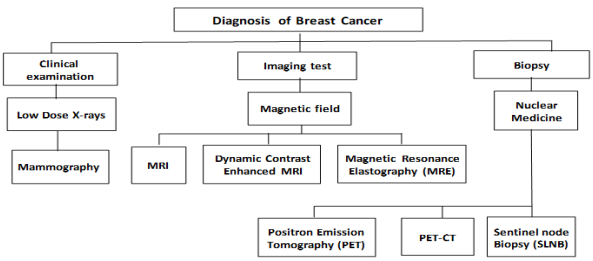

Figure 1: Representation of various types of diagnostic methods for breast cancer.

Early identification of cervical cancer has been attempted using a variety of methods, including Pap smear analysis, visual assessment of the cervix, and HPV-DNA testing. Visual screening procedures, such as VIA, Visual Inspection with Lugol's Iodine (VILI), and Visual Inspection with Magnification Devices-Magnavisualizer (VIAM), provide results that are instantly available, allowing for diagnosis and/or therapy to be administered during the same session. Other diagnostic methods include colposcopy, a specialised magnifying device used to look for abnormal cells, punch biopsy, which uses a sharp tool to pinch off small samples of cervical tissue, and endocervical curettage, which uses a small, spoon-shaped instrument

(curet) or a thin brush to scrape a tissue sample from the cervix (Figure 2) [14].

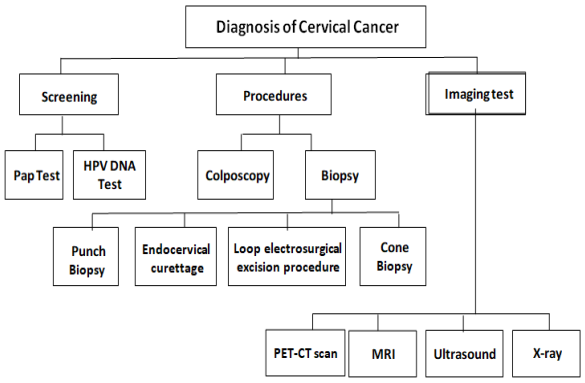

Figure 2: Representation of various types of diagnostic methods for cervical cancer.

Treatment modalities–breast and cervical cancer: Breast cancer treatment has progressed from mastectomy followed by adjuvant chemotherapy through endocrine therapy, chemotherapy, anti-HER2 therapy, bone stabilisation medicines, polymerase inhibitors for BRCA mutation carriers, and immunotherapy at present [7]. Most women with breast cancer in stages I, II, or III are treated with surgery, frequently followed by radiation therapy. Each stage of breast cancer has a particular therapeutic technique via which doctors can relieve patients. The following figure outlines the treatment option available by stages and type of treatment for breast cancer (Figure 3).

On the other hand, radiation therapy, chemotherapy, and surgery are the most frequent forms of treatment for cervical cancer. The most common surgical procedures used to treat early stage cervical cancer include radical trachelectomy, which removes the cervix, nearby tissue, upper part of the vagina, and ligaments and tissues that closely surround these organs, total hysterectomy, which removes the uterus and the cervix, and modified radical hysterectomy, which removes the uterus, cervix, upper part of the vagina, and ligaments and tissues that closely surround these organs. As shown in Figure 4, other treatment options include radiation therapy, which involves shining a radiation beam at the affected area of the body, and internal radiation therapy (also known as brachytherapy), which involves inserting a device containing radioactive material into your vagina for a brief period of time. Chemotherapy, usually known as "chemo," is the use of chemicals to either kill or prevent the division of cancer cells in order to stop the spread of the disease.

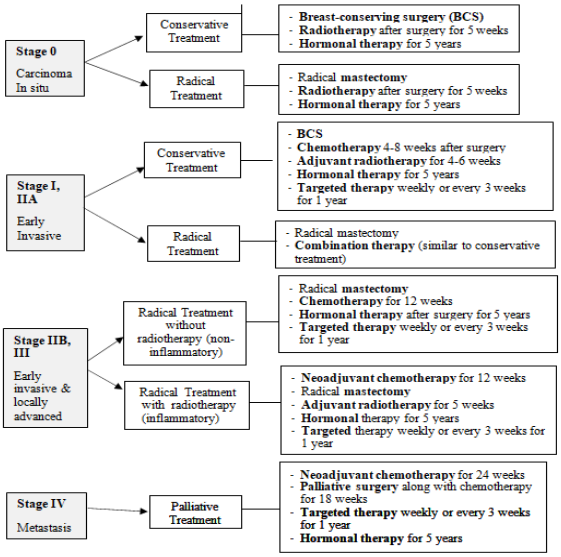

Figure 3: Treatment modalities for breast cancer according to clinical stages.

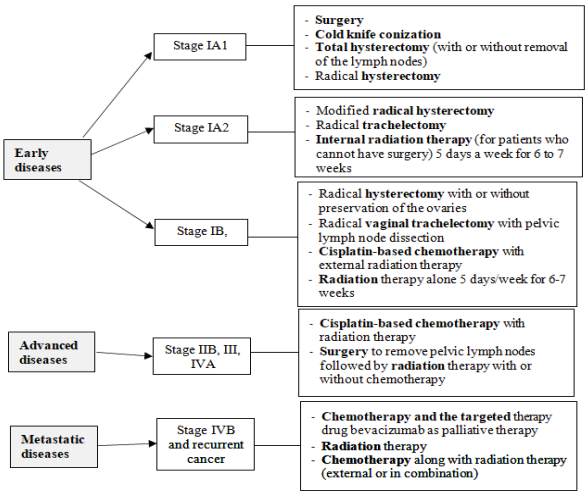

Figure 4: Treatment modalities available for cervical cancer by clinical stages.

Survival rate of breast and cervical cancer in India: In order to provide the most accurate survival prognosis for breast cancer, which is regarded as a heterogeneous disorder, it is necessary to evaluate as many clinical and pathological variables as feasible. The duration of survival for cancer patients is a key indication for understanding the effectiveness of treatment. In low-middle income nations like Brazil (58.4%) and India (52%) as opposed to the United States (83.9%), Japan (81.6%), and Australia (80.7%), breast cancer survival rates are low. Breast cancer is the second most frequent malignancy in women in Madras, where survival rates at 1, 3, and 5 years are respectively

80%, 58%, and 48% whereas, according to the major Indian cancer registries, the incidence rates for cervical cancer in 2012-2014 were 15.3 in Bengaluru, 16.1 in Barshi, 15.9 in Chennai, and 19.0 in Mumbai.

Assessing the review studies

Breast and cervical cancer: Age-Standardized Cancer Incidence Rate (AAR) per 100,000 population from PBCR in different areas of India showing highest in Southern part of India. Since 2003, Aizawl and Kamrup urban (Assam) have had the highest rates of cancer incidence, however according to NCRP statistics from 2012 to 2016, Papumpare had the highest incidence among women [8]. Among all the NE PBCRs, the Aizawl district in Mizoram had the highest incidence (30.7%). The three districts with the highest cervical cancer incidence rates were Papumpare (27.7%), Aizawl (27.4%), and Pasighat (20.3%). Bangalore had the highest AAR (146.8) among the other areas (apart from NE), followed by Delhi (146.8) for men and Delhi (141.0) for women.

Clinical stage and treatment of breast and cervical cancer: According to the data provided by the HBCRs, 2012-16, locoregional spread accounted for the majority of female breast cancer cases (57%), followed by localised illness (29.0%) and distant metastases (10.3%) instances. On the other hand, the clinical extent of carcinoma of the cervix uteri was loco regional in 60.0% of patients, with 32.8% localised and 5.1% distant metastases. With respect to treatment, breast and cervical cancer treatment modalities is presented in Figures 5 and 6 according to clinical stages of disease.

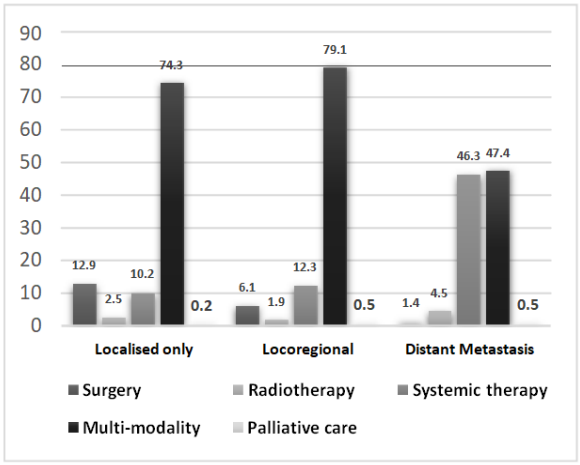

Figure 5: Proportion (%) of breast cancer by type of treatment, clinical extent of disease-females.

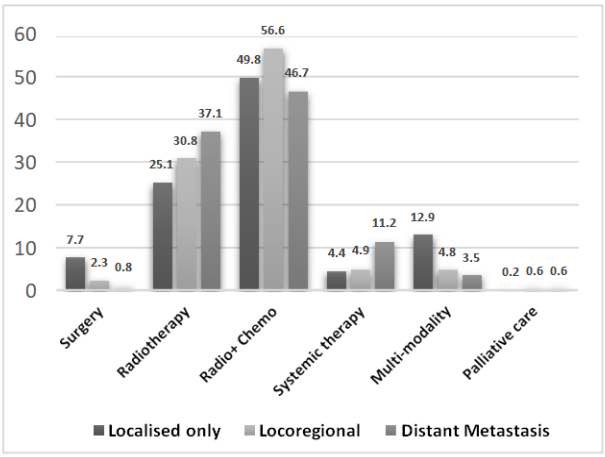

Figure 6: Proportion (%) of cervical cancer by type of treatment, clinical extent of disease females.

Survival rate of breast and cervical cancer in India: The overall 5-year survival rates for cervical cancer (Figure 7) when diagnosed at an early stage is 91%, after it has spread to nearby tissues, organs, or regional lymph nodes (60%), spread to a distant part of the body (19%) and for all people with cervical cancer is 67%, whereas, for breast cancer when diagnosed at an early stage (Figure 8) is higher compared to when diagnosed at late stage.

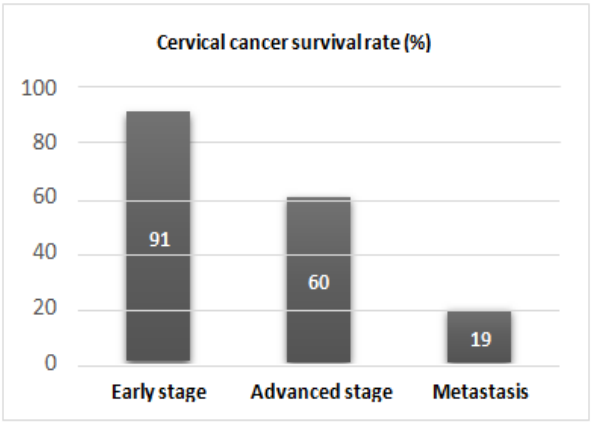

Figure 7: Overall survival rate of cervical cancer.

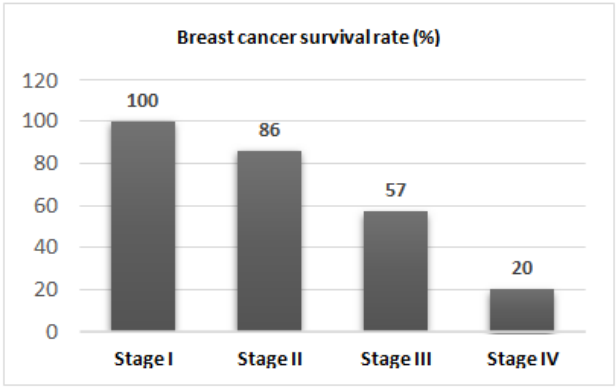

Figure 8: Overall survival rate of breast cancer.

Another study based on 3-years survival rate of breast cancer at state cancer hospital, Guwahati reported overall 3-years survival rate as 63% for people >50 years of age compared to people <50 years of age (60%) followed by stage III and IV as 60% and 24% respectively (Figures 9 and 10).

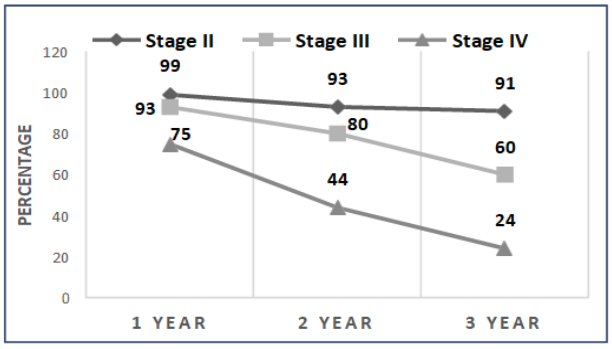

Figure 9: Survival rates of breast cancer by clinical stages.

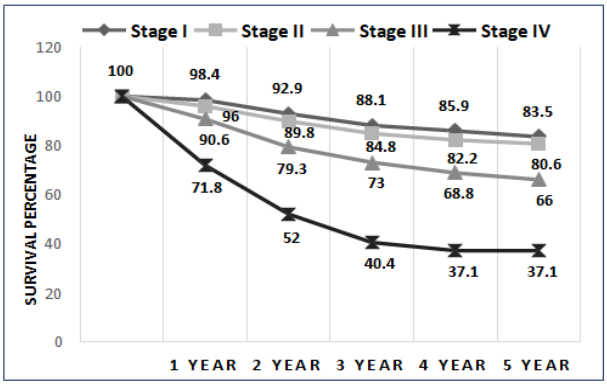

Figure 10: Survival rate of cervical cancer by clinical stages.

In case of cervical cancer, the results of a survival research done in a major cancer hospital in Mumbai show that patients under 50 had a better prognosis than patients over 50. Also, with the severity of the disease worsening, survival rates fell, with stage-IV exhibiting the lowest rates. The 5-years survival rates for stage I, stage II, stage III, and stage IV, respectively, were 83.5%, 80.6%, 66.0%, and 37.1% (Figure 11).

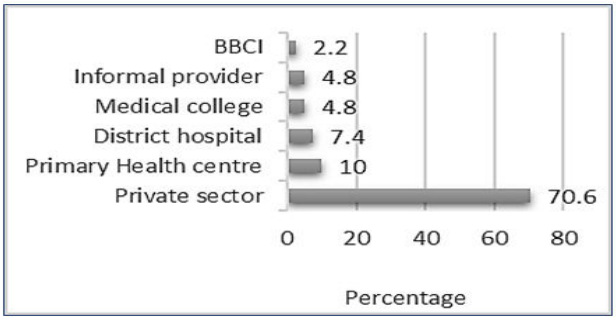

Figure 11: Type of healthcare provider preferred by the patients.

In comparable research, among cancer patients enrolled at the Dr. Bhubaneswar Borooah Cancer Institute (BBCI), Guwahati, between February and June 2019, due to BBCI's inaccessibility and challenging terrain and geography, the bulk of patients sought care from several private providers before moving on to district hospitals and medical colleges before arriving at the cancer care facility.

Additionally, some patients sought out non-medical professionals as their initial point of contact, such as traditional healers from the religious community, maybe as a result of misunderstandings and preconceived notions about the illness, a lack of confidence in the legal system, or a sense of social shame associated with the condition.

Time interval from detection of symptoms to treatment: According to research from South India, there was an average delay of 60 days between the self-detection of breast cancer symptoms and the initial visit to a general practitioner (Figure 12) with a delay of more than 90 days occurring in 38.7% of cases. On the other hand, the average median period from self-detection of cervical cancer symptoms to the start of primary therapy, according to research from a regional cancer facility in the south of India was 123 days. After the initial contact, a diagnosis was made on average 25 days later (Figure 13).

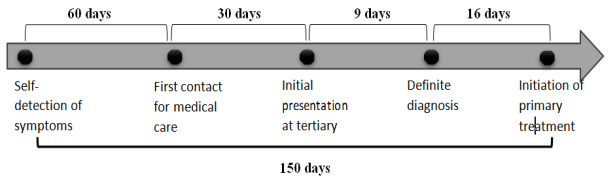

Figure 12: Median Time between Self-detected Breast cancer symptoms and treatment.

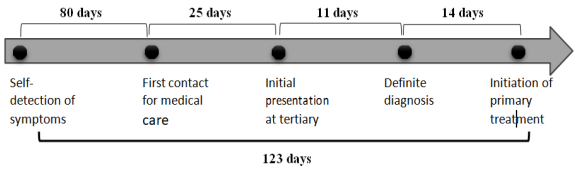

Figure 13: Time between self-detected cervical cancer symptoms and treatment.

Challenges

Breast cancer: The majority of patients only visit the hospital when a big palpable mass or secondary alterations such local skin or chest wall changes are evident. Due to their domestic duties, women often overlook small symptoms and wait until they are intolerable before visiting the hospital. Lack of knowledge about the illness, particularly in rural regions, is another factor that can be responsible for the late presentation [10]. In 50% to 70% of patients in rural regions, the earliest sign of breast cancer, a lump, is not often painful, which further contributes to the delay in seeking treatment. The availability of a diagnostic or treatment facility in the area, the patient's preference for and trust in the healthcare provider, the travel time to the service centre, and the amount and availability of financial resources for the treatment are additional variables that may affect the early detection and treatment of breast cancer. Another issue related to the high attrition rates/loss to follow-up of breast cancer therapy is unacceptable out-of-pocket expenses [14].

Cervical cancer: India currently lacks a proper cervical cancer screening plan despite having a much too high incidence of cervical cancer-related mortality. The absence of community mobilisation and widespread misunderstandings make it difficult to have more women tested for preventive healthcare. Many women are unaware of the need of preventative healthcare and do not understand the need to visit the doctor if they are symptom-free. In a study conducted in Delhi, just a small percentage of people who were aware of cervical cancer had any idea about its mode of transmission.

Cytological assays, physical examination, or an HPV test can all be used for cervical cancer screening. The most popular test for spotting precancerous lesions is the PAP test, however it has several drawbacks and is frequently avoided due to accessibility issues, social shame, and side effects. The Pap smear test is also an intrusive one, which makes it uncomfortable for many women. Beside various screening methods, the HPV vaccine is the most effective method of preventing cervical cancer. It is recommended for both boys and girls between the ages of 9 and 14 since it can protect against certain HPV strains that might cause cancer. Unfortunately, many Indian women do not have access to regular screening and preventative programmes, especially those who reside in rural areas without access to healthcare or who might not be able to afford the diagnostic cost. Most people also believed that cervical cancer could be prevented despite not knowing about the HPV vaccine. Due to concerns about consequences following immunisation and the vaccine's relative newness on the market, many were reluctant to vaccinate either themselves or their daughters.

Discussion

Since the 1982 launch of India's national cancer registry programme, several urban and rural PBCRs have been added. A systematic collection of information on reportable neoplasms from diverse sources in a population with a defined geographic region is known as a Population-Based Cancer Registry (PBCR) whereas, Hospital Based Cancer Registries (HBCRs) handle data on the administration, therapy, and outcomes of patients who present to a certain institution. A significant prevalence of malignancies is seen in the country's northeast, according to trends in regional distribution. The most prevalent cancer sites in women were the breast and cervix [5]. This is mainly as a result of a lack of qualified employees and reliable information on specialised medical personnel. The lack of effective screening and awareness among these women, biological factors linked to more aggressive disease, and delays in diagnosis as a result of the relative rarity of breast cancer in younger women and the prevalence of symptoms linked to benign breast disorders are some of the factors that contribute to this [9].

In India, cervical cancer affects more women than any other type of cancer, with HPV infection through sexual activity being the leading risk factor. As seen in our study, it is associated with behaviours such as unhygienic genitalia, early marriage, multiple partners, multiple pregnancies, long-term use of contraceptives, smoking, young marriage age, young first encounter age, and greater parity. On the other hand, a few unrelated factors have an impact on cervical cancer prognosis and patient survival. The most important characteristics are the size, stage, and histology of the cancer, with sociodemographic factors and the availability of efficient prevention and treatment methods playing less of a role. However, age, diet, Waist to Hip Ratio (WHR), Body Mass Index (BMI), high-density lipoprotein cholesterol, triglycerides, more than three pregnancies, and number of menstrual cycle years are risk factors for breast cancer, which is the second most common cancer in women. In order to accurately identify the risk variables and prepare for early measures to decrease the cancer-related mortality, an immediate intervention by the regulatory authorities is necessary.

Our study discovered that there was a delay in seeking treatment after a diagnosis at the tertiary care level because of the fear of treatment, financial dependence on the family, physical deformity, stigma connected with the ailment, and the drawn-out treatment procedure. According to a similar study, the delay in cancer identification is one of the main reasons for the patients' poor prognosis and low survival rate. The fear of the therapy, the family's financial dependence, the concern over physical deformities, and the stigma attached to the disease all contributed to this delay. Following a tertiary diagnosis, these circumstances led to the delay in receiving treatment.

Conclusion

Despite advancements in detection and treatment, cancer continues to be one of the major causes of death in many nations. More than 70% of patients with advanced illness seek diagnostic and treatment services, which results in low survival rates and high fatality rates. Cancer may have a substantial effect on the family's daily life and finances, due to out-of-pocket costs and inadequate government facilities, the condition is strongly associated with stigma and anxiety in LMICs like India. Therefore, in order to reduce the gap between cancer diagnostic and treatment services, there urgently has to be an increase in the number of cancer care facilities that are reachable by residents especially in rural areas. Additionally, to lessen anxiety and promote acceptance of cancer prevention and care seeking, interventions and education to counteract the stigma associated with

cancer screening are required. Furthermore, women need to be educated on the importance of early identification of precancerous lesions and how to prevent them. In terms of HPV vaccination, training medical staff on how to approach parents and advocate HPV vaccination will significantly increase uptake.

Ethical Clearance

Was not obtained as this is a review article.

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