



A REVIEW ON BREAST CANCER IN INDIA AND OTHER DEVELOPING COUNTRIES

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ABSTRACT

This article reviews breast cancer in India and other developing countries. Developing countries including India are facing a breast cancer epidemic over the last few decades. Changing life-styles of women has made them more prone to cancer of the breast in the metropolitan cities than in the rest of the country. The implications of the disease are serious when measured in terms of family hardship, disablement, and loss of life. Breast cancers are generally detected at advanced stages when a cure is not possible. Earlier detection by screening can save many lives. Types of breast cancer, stages of breast cancer, breast cancer risk factors, screening of breast cancers, breast self examination, diagnosis and treatment facilities & palliative care facilities have been reviewed in this article to address suitable solution to fight against the disease.

Key words : Breast cancer, India, risk-factors, stage, screening, palliative care

INTRODUCTION

Breast cancer is the most common form of cancer among women worldwide, accounting for 458,000 deaths each year. The incidence of breast cancer is higher in developed countries and it is also increasing in the developing countries [1].

Breast cancer incidence peaks among women in their forties in Asia, while in the United States and Europe, it peaks among women in their sixties. In India premenopausal patients constitute about 50% of all breast cancer patients. Breasts perform the vital function of breast feeding which is an emblem of mother hood. Therefore, it is necessary that women look after the health

of their breasts. If detected at an early stage, breast cancer can be treated effectively. This is why breast cancer awareness is very much necessary for the people [2].

In 2001 there were approximately 80,000 new breast cancer cases in India [3]. In South Asia, out of 200,000 new breast cancer cases about 97,500 patients died in the year 2012. In Bangladesh, 14,836 new breast cancer cases were diagnosed in 2012 with an age-standardized incidence rate (ASR) of 21.4 per 100,000. In West Bengal, the ASR data is 25.2 per 100,000, which is somewhat similar to that of Bangladesh [4].

In developing countries like Japan, Singapore and Korea, breast cancer rates have doubled or tripled in the past 40 years while an increased rate of 20% to 30% breast cancer rates have been documented by China's urban cancer registries [5]. By 2020, breast cancer cases might be increased by 26% and most of these will be seen in developing countries [6].

Breast Cancer in Indian States

In India, breast cancer is most prominent in the women of Delhi, Rajasthan, Himachal Pradesh, Nagaland and Goa, and the second most common form of malignancy is found in females of Maharashtra, Gujarat and Punjab. In Tripura the third most common form of cancer among women folks is breast cancer [7].

According to the Population Based Cancer Registry at Dr. B.R. Ambedkar Institute Rotary Cancer Hospital, AIIMS, New Delhi during 2008-09 a total of 29027 incident cases of cancer were registered with 15189 (52.3%) males and 13838 (47.7%) females. Out of the female cancer patients 26.8% suffered from breast cancer [8]. In Maharashtra, the increasing industrialization and changes in the lifestyles has seen cancer to be emerging as one of the most threatening diseases and it has to be controlled immediately [9]. In eastern India, breast cancer is the most frequently reported cancer (22.7%) in females and the age-specific incidence rate is 25.1 per 100,000 populations [10]. According to Poona Cancer Registry, a division of Indian Cancer Society, breast was the leading site of cancer among females in Pune in the year 2009. The data were collected from Govt. and private hospitals, diagnostic centres and nursing homes of Pune [11].

In 1963, the first population-based cancer registry (PBCR) in India was organized in Mumbai. A PBCR was organized in Kolkata in the Department of Epidemiology and Biostatistics of the Chittaranjan National Cancer Institute (CNCI), one of the premier Regional Cancer Centres in India, to collect information on cancer incidence from January 1st 1997 on the resident population of the city. The objective of this organization is to collect data on the prevailing cancer patterns in Eastern

India which help in the planning and evaluation of cancer control activities [12].

In the period of 1982-1999, the Bangalore, Chennai and Mumbai PBCRs showed significant increase in annual average age adjusted incidence rates (AARs) of breast cancer over time across the age groups starting in the 35-44 age groups and in Delhi starting in 45-54 age groups. Additionally, in Mumbai PBCR, an increase in AARs was also observed in the age group of 0-24 [13].

Types of Breast Cancer

The most common type of breast cancer is the Ductal cancer which affects the cells of the thin tubes called ducts connecting the lobes and lobules of the breast. Cancer that starts in lobes and lobules is called lobular cancer which is also more often found than other types of cancer. Breast cancer can also be classified as invasive (infiltrating) and non invasive (in situ). Invasive breast cancer has a tendency to metastasize to other tissues or regions of the breast or body while in situ refers to cancer that has not spread past the area where it developed initially. Other breast cancer types are inflammatory breast cancer, tubular carcinoma, mucinous carcinoma, medullary carcinoma, etc [14].

Stages of Breast Cancer

Breast cancer generally has five stages when diagnosed. They are:

- Stage 0 – Non-invasive breast cancer, with no spreading out of duct or lobules
- Stage 1 – Tumours smaller than 2 cm, without involvement of lymph nodes in armpit
- Stage 2 – Tumours between 2 cm and 5 cm in size, with or without involvement of lymph nodes in armpit
- Stage 3 – Tumours larger than 5 cm
- Stage 4 – Tumour spread to other parts of body such as bones, lung, liver or brain [15].

Breast Cancer risk factors

Greater urbanization and changing lifestyles is an important cause of increasing breast cancer in India. Higher education level and economic independence of women also leads to increased breast cancer risk (15.9%) because these factors encourage them to marry late or remain single [6].

Some reproductive factors of breast cancer risk are early menarche, late menopause, nulliparity and late age of childbirth, etc. Early age of menopause, late age of menarche, multiparity, early age of 1st child birth, history of ever breast feeding and increased duration of breast feeding were found to be important protective factors for breast cancer [16]. Non reproductive factors include menopausal hormone therapy, greater alcohol intake, positive family history of cancer, higher body mass index and others [4].

The risk of breast cancer is higher in middle-aged and elderly women than in young women. Women have more breast tissue than men and so they are at a higher risk of breast cancer. Also, estrogen promotes the development of breast cancer [17,18]. The breast cancer risk is higher in women who have a close blood relation like mother, sister or daughter who have had the disease. The risk increases if the relative developed breast cancer before the age of 50 or in both breasts [19].

It has been shown recently that germ line mutation in the BRCA1 and BRCA2 genes account for a large proportion of cases of hereditary breast cancer [20]. Women who reach menarche at a relatively early age (12 or younger) and those who reach menopause at a relatively late age (55 or older) are slightly more likely than other women to develop breast cancer. These relationships are believed to be mediated through estrogen production [21]. Women who never have children (nulliparous) or have children at a relatively late age are more prone to breast cancer than those who have children (parous) or have their first pregnancy at an early age of life. First full term pregnancy after 30-35 years of age raises the risk of breast cancer [22].

The long-term (more than 5 years) use of postmenopausal estrogen ((ERT) or combined estrogen/progestin hormone replacement therapy (HRT) may be associated with an increase in breast cancer risk [23]. Studies have shown that premature termination of pregnancy increases breast cancer risk while use of oral contraceptives does not have a large effect on the same [24]. Obese women have a 30% higher risk of post menopausal breast cancer than women with a healthy weight [25,26]. The relation between body mass index and breast cancer risk is heterogeneous according to hormonal receptor status. Higher body mass index associates with higher risk of hormone receptor positive tumors in post menopausal women and has a protective effect in premenopausal women with breast cancer [27].

Alcohol increases risk, whereas physical activity is probably protective against breast cancer. Mutations in certain genes greatly increase breast cancer risk, but these accounts for a minority of cases [28]. Plant substances called isoflavones found in soy products have some protective effect against breast cancer. Diets low in fat and calories and high in fruits and vegetables are healthful for many reasons, and they may indirectly reduce the risk of breast cancer by helping to prevent obesity [29].

Screening of breast cancer

Almost all breast cancers can be clinically detected. Breast cancer can be detected at earlier stages by simple breast self-examination but most of the patients seek medical attention at advanced stages: i.e., stages III and IV [4].

Most low and middle-income countries (LMICs) do not have organized breast cancer screening programs. Due to increasing life expectancy, dietary habits and changes in reproductive risk factors the incidence of breast cancer is rising rapidly in LMICs. Limited breast cancer awareness leads to detection at relatively advanced stages when treatment is less likely to be successful. This is why more than half the breast cancer deaths globally occur in LMICs in spite of relatively low incidence [30].

Mammographic screening is the most effective method for identification of breast cancer at an early stage often before any symptoms can be identified by physical examination [31]. But in LMICs mammographic screening may not be an appropriate screening test because it is a complex and costly test requiring skilled manpower, stringent quality control and also because mammography is less effective in women below the age of fifty years [30].

Studies suggest that Mammographic Tata Memorial Hospital has been involved in a randomized controlled trial (n=150,000) which compares the efficacy of health education and clinical breast examination (CBE) provided by trained primary health care workers with just health education provided by the same workers in women aged 30-6 years living in the slums of Mumbai. This study has now entered its 6th year and 3rd round of screening. The study already shows a good compliance-to screening rate (70%) and down staging is already evident. The principal objectives of the study i.e. demonstration of a reduction in incidence and mortality will however become evident only after another 10-15 years [6].

Breast self-examination (BSE) has been employed as a way of screening for breast cancer, with the aim of reducing breast cancer mortality. BSE usually refers to a standardized technique of self-examining the breasts in a prescribed pattern such as a grid or clock pattern of touching the breast on a specific monthly schedule. It is possible that by noticing a change in her breast a woman could find a breast cancer before its detection otherwise. Therefore, BSE is a reasonable health practice especially for younger women who do not receive mammograms. It is not always necessary to use a specific method in checking the breasts and underarms but to be familiar with how they look and feel. If any changes are noticed other than those that occur normally during the monthly cycle, they can be reported to a health care provider. Finding such changes doesn't necessarily mean that cancer is present, but occasionally one will be detected [32].

Most breast cancer in low resource countries (LRCs) present with the paradigmatic self-discovered "painless breast lump", due to absence of systematic screening

programs. In these countries, it is common for a woman to be aware of this symptom for many months or even years and not disclose it until complications such as pain, ulcer, foul-smelling purulent discharge or symptoms of metastatic disease occur. A woman may suspect that the change is due to cancer but avoid seeking a diagnosis out of fear of cancer or its treatment. A significant proportion of women seeks guidance primarily from alternative health care providers for long periods and decides to see a medical professional only when the cancer has advanced [33].

Diagnosis and Treatment

Apart from regular BSE, there are certain investigations which help in diagnosing breast cancer such as mammograms, ultrasonography, fine needle aspiration cytology (FNAC), needle biopsy, surgical biopsy, etc. BSE should be performed on regular basis by all women for detection of lumps at an early stage to help physicians in making a diagnosis. Mammograms are X-ray photographs of the breast used for early diagnosis even before symptoms appear, done by placing the breast in direct contact with an ultra sensitive film. Ultrasonography, using high frequency sound waves can often show whether a lump is a solid mass (which may or may not be cancer) or a fluid filled cyst (not cancer). In FNAC, a thin needle is put into the lump or mass on the breast to remove fluid or cells which are smeared on to a slide to be checked by a pathologist.

Needle biopsy is done using a fine needle such as Trucut or Corecut biopsy device under local anaesthesia, where tissue can be removed from the lump or suspicious area and checked by a physician for cancer cells. In case of surgical biopsy the surgeon cut out a portion or all the lumps/suspicious area and a pathologist examines the tissues under microscope to check for cancer cells [34].

Breast cancer is treated using three main modalities: surgery, radiotherapy and systemic therapy [6]. Surgical treatment is the most widely available treatment modality for breast cancer in LRCs and mastectomy is the most common surgical treatment option. But there are few quality control or assurance programs for surgical

treatments in most LRCs and mastectomies are sometimes incorrectly and improperly done, leading to poor outcome. This may spread distrust among the general public for the medical treatment of breast cancer. It is often deployed whenever the patient is deemed operable because late-stage presentation/diagnosis is the norm and lack of radiation therapy services, good quality diagnostic oncology services and noncompliant patients make breast conservation surgery of limited value. Patients with metastatic disease are associated with significant morbidity and mortality and in such cases patients must be carefully selected for surgical mastectomy. Preoperative systemic therapy followed by mastectomy has been recommended for carefully selected patients with advanced breast cancer who are deemed likely to benefit from it based on adequate clinical response [33].

Patients with advanced breast cancer require radiotherapy for palliation and symptom control of locally advanced and metastatic disease. Radiation therapy is also used in curable breast cancer to reduce incidence of loco-regional relapse and improve overall survival [33]. In radiotherapy, high-energy X-rays are produced by a machine called a linear accelerator which is able to damage and destroy cancer cells in the area to be treated in the body [15]. The International Atomic Energy Agency (IAEA) inventory of radiotherapy machines in 34 low income countries, representing 946 million people, identified 93 radiotherapy centers with a total of 39 linac machines and 96 Co⁶⁰ radiotherapy machines. The countries of Vietnam, Bangladesh and Uzbekistan, accounted for 43% of these radiotherapy centers. As estimated by IAEA, an additional 5000-7000 radiotherapy machines are needed worldwide to adequately care for the current needs of cancer patients and this figure may be higher with increased incidence of cancer in future [33]. Out of about 1100 million populations in India, 1155 radiotherapy machines are required to cater to all cancer patients but presently there are only 400 teletherapy machines located in large cities only [6].

In the presence of detectable metastatic disease, systemic therapy can provide palliation of symptoms and modest prolongation in overall survival of breast cancer.

The application of chemotherapy, endocrine therapy, and/or biological therapy in the adjuvant or neo-adjuvant treatment of primary breast cancer substantially decreases the risk of recurrence and increases overall survival [33]. Chemotherapy uses cytotoxic drugs to destroy cancer cells that may have spread to other parts of the body from the original tumour. This is called systemic treatment as the whole body is exposed to this drug. Hormone therapy is useful in cases where women have hormone dependent breast cancer like oestrogen and progesterone receptor positive breast cancer. Here, drugs are used which either block the hormone receptors or block the oestrogen and progesterone production [15].

More than 90% of patients with breast cancer require either chemotherapy or hormonal therapy but due to high expense of the recently launched anti breast cancer agents these are beyond the reach of most patients with breast cancer in developing countries [6]. Combination of chemotherapy based on old but effective regimes like cyclophosphamide, methotrexate and 5-fluorouracil (CMF) provide cheap systemic treatment opportunities in LRCs. In patients with metastatic disease, optimal treatment is the sequential use of endocrine therapy if the tumor is HR positive in addition but not concurrently with combination chemotherapy and use of the latter alone if tumor is HR negative. If the tumor is HER2 positive, most patients in LCRs cannot afford the HER2 targeted agents. In such cases preference is given to anthracycline-based chemotherapy [33].

Palliative care in breast cancer

Palliative care is patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Palliative care includes addressing physical, intellectual, emotional, social, and spiritual needs and facilitating patient autonomy, access to information, and choice. Services are provided by a team of doctors, nurses, and other specialists who work with a patient's other physicians to provide additional support [35].

In low- and middle-income countries (LMCs), breast cancers are commonly diagnosed at late stages and women may receive inadequate treatment, pain relief, or

palliative care [5]. Limited availability of medical oncologists in LRCs often results in non-specialist providing chemotherapeutic services, which requires additional supervision and training. Palliative care is an emerging field in LRCs that requires investment in training and infrastructure development. A commitment and investment in the development of breast cancer care services by LRC governments and health authorities remains a critical need in LRCs. More than 80% of cancer patients in LRCs will require palliative care because here high percentage of patients present with advanced disease. Several middle resource countries like Chile, Uganda, South Africa, Mongolia, and Georgia have adopted national palliative care policies and national health plans that include palliative care. In LRCs like Malaysia, Jordan, Nepal, India, Bangladesh and Albania, home palliative care programs have been shown to be cost-effective and feasible.

In Malaysia, the Sarawak Palliative Care Program showed that the primary health care centre nurses can provide home-based care even in remote rural regions if good communication is maintained with the central hospital Palliative Care system [33]. The long-term and late effects of cancer survivors will also be provided by knowledgeable nurses who can anticipate and integrate palliative care into survivorship care early in their treatment plan. Primary symptoms may vary depending on disease, age, treatment, and other co morbidities. A multidisciplinary palliative care team can help manage the primary late effects for cancer survivors including fatigue, depressive symptoms, anxiety and distress, pain, and sleep disturbance [36].

CONCLUSION

Government hospitals, NGOs and Medias like TV, radio, newspapers, journals and magazines etc. can play major role in increasing awareness of breast cancer among the general public. Awareness campaign in regional language has a good impact. Teachers of school and colleges after proper training can educate their students about risk factors of breast cancer. Protectiveness of breast feeding against risk of breast cancer could be promoted by celebrities. In the syllabus of life science of

higher classes of school and colleges cancer awareness chapter could be included.

In medical collages, nursing institutes, pharmacy institutes etc, cancer related curriculum should be given importance highlighting on breast screening procedure along with awareness. Protocols relating to breast lump can avoid mismanagement at primary and secondary health care facilities. In developing countries including India, women in late 30s should plan for breast cancer screening.

Public health workers should be trained in CBE to cover huge population of the developing countries. Continued medical education and training of the general surgeons can help to increase skills of breast surgery. Guidelines for breast cancer management for developed countries are not feasible for LRCs and therefore suitable management guidelines should be implemented. Regulatory authority should regulate the cost of chemotherapy drugs which are relevant in providing complete treatment to the patients.

Suitable infrastructure for medical insurance to cover cancer patients is urgently required. To cover remote villages, hilly areas etc. free mobile mammography units may help to address the problem.

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