

Research Article

Breast Carcinoma in women - A Rising threat

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Abstract

Breast cancer continues to be the commonest cancers among women all over the world. Incidence is more in developed countries as compared to underdeveloped countries. Life style changes ,late marriages,genetic predisposition and unopposed action of oestrogen have been documented to be the risk factors. Infiltrating ductal carcinomas form the most common pathological type. Diagnostic modalities like sonomamography,fine needle aspiration and histopathology of breast tumours help in the detection of breast carcinoma. Self breast examination and regular preventive check ups by trained health workers have helped in early diagnosis of cancers in developed countries. Ignorance,reluctance in examining own breasts and inadequate screening facilities are responsible for diagnosis in late inoperable stages in underdeveloped world. Early diagnosis and prompt treatment in the form of surgery,chemotherapy or radiation therapy can result into reduction in breast cancer related mortality.

Keywords:Breast carcinoma ,Mammography, Oestrogen ,Self breast examination

1. Introduction

Blame modern lifestyle for it, but breast cancer has overtaken cervical cancer in India in numbers. According to ICMR (Indian Council for Medical Research), the incidence of breast cancer is on the rise, while cervical cancer is beginning to come down. Social taboos regarding breast cancer prevent women from talking to friends and families, let alone doctors. This poses a big problem in early detection .¹

Global and Indian Scenario - Breast cancer is the most common cancer in women worldwide, comprising 16% of all female cancers. Although breast cancer is thought to be a disease of the developed world, a majority (69%) of all breast cancer deaths occurs in developing countries (WHO Global Burden of Disease, 2004).² Incidence rates vary greatly worldwide, with age standardized rates as high as 99.4 per 100 000 in North America. Eastern Europe, South America, Southern Africa, and western Asia have moderate incidence rates, but these are increasing. The lowest incidence rates are found in most African countries but here breast cancer incidence rates are also increasing. Breast cancer is the most common of all cancers and is the leading cause of cancer deaths in women worldwide, accounting for >1.6% of deaths and case fatality rates are highest in low-resource countries. A recent study of breast cancer risk in India revealed that 1 in 28 women develop breast cancer during her lifetime. This is higher in urban areas being 1 in 22 in a lifetime compared to rural areas ,where this risk is relatively much lower being 1 in 60 . In India, almost 80 percent patients are in advanced stages when they come to hospitals.³ The average age of the high risk group is 43-46 years unlike in the west, where women aged 53-57 years are more prone to breast cancer. Breast cancer is the most common cancer among women in the the developed

countries, other than skin cancer. It is the second leading cause of cancer death in women, after lung cancer. The chance of a woman having invasive breast cancer some time during her life is about 1 in 8. The chance of dying from breast cancer is about 1 in 36. Breast cancer death rates have been going down in developed countries. This is probably the result of finding the cancer earlier and better treatment.

2. Risk Factors

The factors influencing breast cancer risk are broadly classified into modifiable and non-modifiable factors. The non-modifiable risk factors are age, gender, number of first degree relatives suffering from breast cancer, menstrual history, age at menarche and age at menopause. While the modifiable risk factors are BMI, age at first child birth, number of children, duration of breast feeding, alcohol, diet and number of unsuccessful pregnancies (abortions). Having a 1st-degree relative (mother, sister, and daughter) with breast cancer doubles or triples the risk of developing the cancer. About 5% of women with breast cancer carry a mutation in one of the 2 known breast cancer genes, BRCA1 or BRCA2. If relatives of such a woman also carry the gene, they have a 50 to 85% lifetime risk of developing breast cancer.

3. Patho- physiology and role of oestrogen

The breast is a highly modified sweat gland that develops as an ingrowth from ectoderm. Anatomically, the primary secreting units consist of groups of terminal ductules with sac-like ends (alveoli), which are embedded in a fine specialized connective tissue to form the breast lobules. It is now firmly believed that breast cancer commonly starts in the epithelium which lines the terminal ductules within the lobule. Physiologically, the human female breast is under the primary control of different hormones; the role of estrogen appears to be central. Estrogen is responsible for the development of the ductal system, whereas progesterone is necessary for lobular development. Therefore, the etiology of breast cancer has a strong hormonal component. Once an epithelial cell of ductal system is transformed into a malignant phenotype, it is no longer subject to normal growth controlling mechanisms. A malignant cell may be noninvasive, i.e. unable to penetrate the basement membrane (*in situ* cancer). Ductal carcinoma *in situ* (DCIS) is the most common histological variant of the non-invasive stage of breast cancer. Similarly, invasive or infiltrating duct carcinoma (IDC) is the commonest form of breast cancer accounting for 85 to 90% of all cases. These phenomena signify the important role of estrogen in the development of breast cancer. The most common types of breast cancer are: a) Infiltrating (invasive) ductal carcinoma. This cancer starts in the milk ducts of the breast. It then breaks through the wall of the duct and invades the surrounding tissue in the breast. b) Ductal carcinoma *in situ* is ductal carcinoma in its earliest stage (stage 0). *In situ* refers to the fact that the cancer hasn't spread beyond its point of origin. In this case, the disease is confined to the milk ducts and has not invaded nearby breast tissue. If untreated, ductal carcinoma *in situ* may become invasive cancer. It is almost always curable. c) Infiltrating (invasive) lobular carcinoma. This cancer begins in the lobules of the breast where breast milk is produced, but has spread to surrounding tissues or the rest of the body. It accounts for 10% to 15% of breast cancers. This cancer can be more difficult to diagnose with mammograms. Lobular carcinoma *in situ* is a marker for cancer that is only in the lobules of the breast. It isn't a true cancer, but serves as a marker for the increased risk of developing breast cancer later, possibly in both or either breasts. Thus, it is important for women with lobular carcinoma *in situ* to have regular clinical breast exams and mammograms. Cancers can also form in other parts of the breast but are less common.

4. Warning symptoms and signs

A lump or thickening in or near the breast or in the underarm that persists through the menstrual cycle, a mass or lump, which may feel as small as a pea, a change in the size, shape, or contour of the breast, a blood-stained or clear fluid discharge from the nipple, a change in the look or feel of the skin on the breast or nipple (dimpled, puckered, scaly, or inflamed), redness of the skin on the breast or nipple, an area that is distinctly different from any other area on either breast, a marble-like hardened area under the skin.

5. Available diagnostic modalities

a) Breast examination: b) Mammography: c) Digital mammography. d) Ultrasonography: Based on the results of these tests, a biopsy of the breast mass cells or tissue may be required. Laboratory tests, such as hormone receptor tests (estrogen and progesterone) and human epidermal growth factor receptor (HER2/neu), can show whether hormones or growth factors are helping the cancer grow. If the test results show that they are (a positive test), the cancer is likely to respond to hormonal treatment or antibody treatment. These therapies deprive the cancer of the estrogen hormone or use a monoclonal antibody known as herceptin to treat the cancer.

Other diagnostic tests -e) Scintimammography: A technique in which radioactive contrast agents are injected into a vein in the arm. An image of the breast is taken with a special camera, which detects the radiation (gamma rays) emitted by the dye. Tumor cells, which contain more blood vessels than benign tissue, collect more of the dye and project a brighter image. **f) Positron emission tomography (PET) scanning:** A technique that measures a signal from injected radioactive tracers that migrate to the rapidly dividing cancer cells. The PET scanner picks up the signal and creates an image. **g) Magnetic resonance imaging (MRI):** A test that produces very clear pictures, or images, of the human body without the use of X-rays. MRI uses a large magnet, radio waves, and a computer to produce these images. **h) Needle Biopsy / FNAC** Confirmation of malignancy with cytology or histology is the minimum requirement for “indeterminate” or “high-risk” solid lesions. Fine-needle aspiration / Tru cut / core biopsy / surgical excision/ Incision biopsy / percutaneous breast biopsy for non-palpable disease are the various methods used to obtain tissue for pathological confirmation.

6. Treatment options

Breast cancer can be treated using a multimodality approach of surgery, chemotherapy, radiotherapy and targeted therapy. The treatment options vary as per the stage of the tumor. The TNM staging is traditionally used to stage breast cancer. Patients are clinically grouped into one of the following categories -Operable Breast Cancer, Large Operable Breast Cancer, Locally Advanced Breast Cancer and Metastatic Breast Cancer. There are multiple ongoing clinical trials in breast cancer. The type of treatment recommended will depend on the size and location of the tumor in the breast, the results of lab tests done on the cancer cells, and the stage, or extent, of the disease. Breast cancer treatments are local or systemic. Local treatments are used to remove, destroy, or control the cancer cells in a specific area, such as the breast. Surgery and radiation treatment are local treatments. Systemic treatments are used to destroy or control cancer cells all over the body. Chemotherapy and hormone therapy are systemic treatments. A patient may have just one form of treatment or a combination, depending on her needs.

7. Preventive measures

Breast cancer is one of the curable cancers, if detected early. Cancer subjects the family to unimaginable emotional stress. Following steps are suggested for early detection:

1-Get a mammogram. The American Cancer Society recommends having a baseline mammogram at age 35, and a screening mammogram every year after age 40. Mammograms are an important part of health history. Recently, the US Preventive Services Task Force (USPTF) came out with new recommendations regarding when and how often one should have mammograms. These include starting at age 50 and having them every two years.⁴

2-Examine breasts each month after age 20. Breast self-examination should be performed at the same time each month, three to five days after your menstrual period ends. If one has stopped menstruating, it is advised to perform the exam on the same day of each month. One gets familiar with the contours and feel of the breasts and will be more alert to changes.

3-Have breast examined by a healthcare provider at least once every three years after age 20, and every year after age 40. Clinical breast exams can detect lumps that may not be detected by mammogram.⁵

8. Developments in breast cancer research

Research into the causes, prevention, and treatment of breast cancer is being done in many medical centers throughout the world.

a-Causes of breast cancer- Some studies are looking at the effect of exercise, weight gain or loss, and diet on breast cancer risk. A large, long-term study is now going on to help find the causes of breast cancer. It is known as the Sister Study and it will follow 50,000 women whose sisters (not they themselves) have had breast cancer. Over 10 years, information will be gathered on many factors that might cause breast cancer.

b- Chemoprevention- Fenretinide, a drug related to vitamin A, is being studied as a way to reduce the risk of breast cancer. In a small study, this drug reduced breast cancer risk as much as tamoxifen. Other drugs are also being studied to reduce the risk of breast cancer.

c-New lab tests:

i) Gene studies- In recent years, scientists have been able to link certain patterns of genes with more aggressive cancers — those that tend to come back and spread to distant sites. Some lab tests based on these findings are already available, but

doctors are still trying to figure out the best way to use them.

ii-Tumor cells in the blood -Researchers have found that in many women with breast cancer, cells may break away from the tumor and enter the blood. These tumor cells can be found with sensitive lab tests.

d-Treatment :

i) Oncoplastic surgery-Sometimes after breast surgery the breasts can be different sizes or shapes. Some doctors are trying to address this problem by combining cancer surgery and plastic surgery. This is called *oncoplastic surgery*. It involves reshaping the breast at the time of first surgery, and may mean operating on the other breast as well to make them look more alike. The main concern is whether or not oncoplastic surgery might be more likely to leave tumor tissue behind.

ii-Breast reconstruction surgery-Advances in re-attaching blood vessels (microvascular surgery) have led to improvements in breast reconstruction.

iii-Radiation treatment-For women who need radiation after breast-conserving surgery, newer methods such as hypofractionated radiation or accelerated partial breast irradiation are being studied to see if they work as well as standard treatment in keeping breast cancer from coming back. They can make it easier to get treatment since the treatment can be done on in a shorter time.

iv-New chemotherapy drugs-Because advanced breast cancers are often hard to treat, researchers are looking for newer, better drugs. A drug class has been developed that targets cancers caused by *BRCA* mutations. This class of drugs is called PARP inhibitors and they have shown promise in clinical trials treating breast, ovarian, and prostate cancers that had spread and were resistant to other treatments. Further studies are being done to see if this drug can help patients without *BRCA* mutations.

v-Targeted therapies- Targeted therapies are a group of newer drugs that take advantage of gene changes in cells that cause cancer.

Drugs that target HER2: Three drugs approved for use target excess HER2 protein: trastuzumab (Herceptin) and lapatinib (Tykerb), and pertuzumab (Perjeta). Researchers are also looking at using a vaccine to target the HER2 protein.

Anti-angiogenesis drugs: For cancers to grow, blood vessels must be made to feed the cancer cells. Some studies have found that breast cancers with many new, small blood vessels are likely to spread more quickly. Bevacizumab (Avastin) is an example of anti-angiogenesis drug. New drugs are being made that may be useful in stopping breast cancer growth by keeping new blood vessels from forming.

Other targeted drugs: Everolimus (Afinitor) is a targeted therapy drug that seems to help hormone therapy drugs work better. It is approved to be given with one certain hormone therapy drug to treat advanced hormone receptor-positive breast cancer in women who have gone through menopause. Other possible targets for new breast cancer drugs have been identified in recent years. Drugs based on these targets are now being studied, but most are still in the early stages of clinical trials- Bisphosphonates, Denosumab and Vitamin D.

9. Conclusion

There is rising threat of development of breast cancer in women from developing countries. Life style changes ,late marriages and shorter duration of breast feeding have been documented to be the emerging risk factors. Self breast examination and regular preventive check ups by trained health workers will help in early diagnosis of the dreaded condition.Early diagnosis and prompt treatment in the form of surgery,chemotherapy or radiation therapy can result into reduction in breast cancer related mortality.Non government organizations can play an important role in arranging various awareness activities and screening programmes for high risk population.

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