

A Review on Breast Cancer: Its epidemiology, Pathophysiology, Treatment, and Diagnosis

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ABSTRACT

As of 2020, breast cancer has become the most diagnosed cancer globally, overtaking lung and prostate cancers. Breast cancer incidence is increasing globally with cases in the United States expected to reach 364,000 in the year 2040. Part of this increase may be attributed to improved detection but some, especially in lower developed countries, may be due to changes in female fertility patterns along with lifestyle changes. Developed countries have the highest incidence of breast cancer. Mortality rates vary widely from global region to region but are highest in socio-economically low areas, reflecting a lack of access to early screening and timely treatment. Even in developed countries, the disproportionately high mortality rate among black women and white women further underscores existing health inequality. This chapter aims to provide a global epidemiological overview of breast cancer incidence and mortality.

Keywords: epidemiology of breast cancer, incidence of breast cancer, mortality from breast cancer, breast cancer, risk factors for breast cancer

I. INTRODUCTION

Breast cancer is a disease in which abnormal breast cells grow out of control and form tumours. If left unchecked, the tumours can spread throughout the body and become fatal.

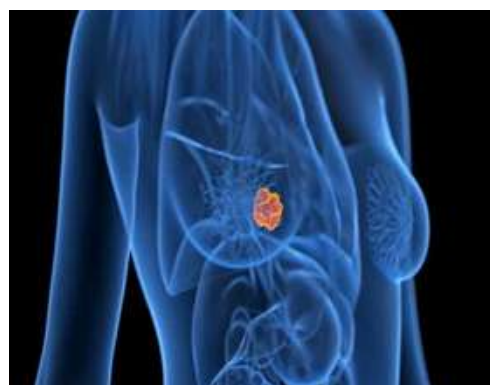
Breast cancer cells begin inside the milk ducts and/or the milk-producing lobules of the breast. The earliest form (in situ) is not life-threatening and can be detected in early stages. Cancer cells can spread into nearby breast tissue (invasion). This creates tumours that cause lumps or thickening.

Invasive cancers can spread to nearby lymph nodes or other organs (metastasize). Metastasis can be life-threatening and fatal.

Treatment is based on the person, the type of cancer and its spread. Treatment combines surgery, radiation therapy and medications. (1)

Breast cancer is cancer that starts in cells in the breast. The ducts and the lobules are the two parts of the breast where cancer is most likely to start.

Breast cancer is one of the most common types of cancer in the U.S. Health care providers don't yet know exactly what causes it. Once breast cancer forms, cancer cells can spread to other parts of the body (metastasize), making it life-threatening. The good news is that breast cancer is often found early, when it's small and before it has spread. (2)



Epidemiology

Worldwide, breast cancer is the most common invasive cancer in women.⁽³⁾ Breast cancer comprises 22.9% of invasive cancers in women^[2] and 16% of all female cancers.^[4]

In 2008, breast cancer caused 458,503 deaths worldwide, which is 13.7% of cancer deaths in women and 6.0% of all cancer deaths for men and women together.^[2] Lung cancer, the second most common cause of cancer-related death in women, caused 12.8% of cancer deaths in women, which is 18.2% of all cancer deaths for men and women together.^[3]

The number of cases worldwide has significantly increased since the 1970s, a phenomenon partly attributed to the modern lifestyles.

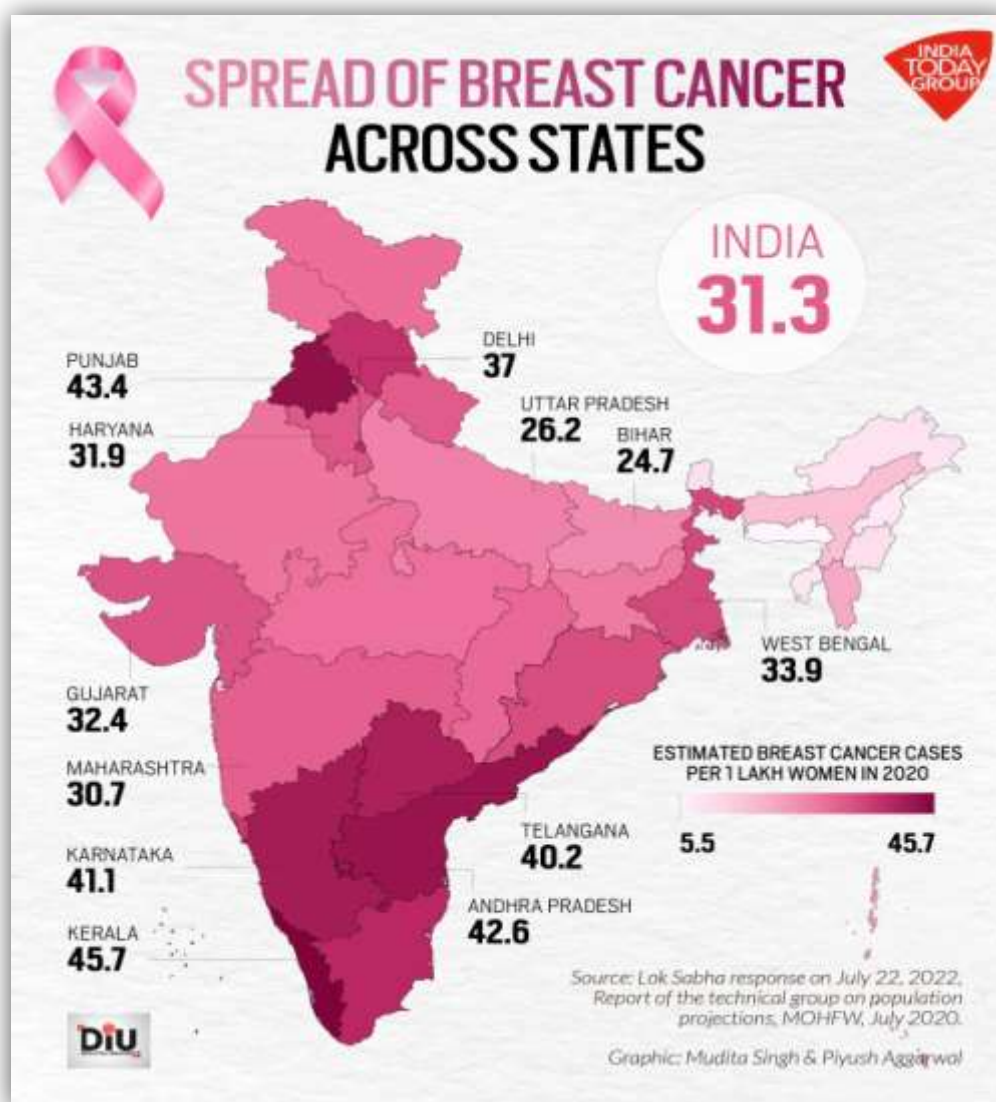
By age group

Breast cancer is strongly related to age, with only 5% of all breast cancers occurring in women under 40 years old.^[6]

By Region

The incidence of breast cancer varies greatly around the world: it is lowest in less-developed countries and greatest in the more-

developed countries.^[7] In the twelve world regions, the annual age-standardized incidence rates per 100,000 women are as follows: in Eastern Asia, 18; South Central Asia, 22; sub-Saharan Africa, 22; South-Eastern Asia, 26; North Africa and Western Asia, 28; South and Central America, 42; Eastern Europe, 49; Southern Europe, 56; Northern Europe, 73; Oceania, 74; Western Europe, 78; and in North America, 90.^[8]



Different Types of Breast Cancer

Breast cancer is not just one disease — it can be classified into different types of breast cancer depending on how the cells in the breast look under a microscope. Different types of breast cancer include:

- 1. Ductal Carcinoma In Situ (DCIS):** DCIS is considered a non-invasive form of breast cancer, meaning it has not spread beyond the milk ducts into any surrounding normal tissue.
- 2. Invasive Ductal Carcinoma (IDC):** This is the most common type of breast cancer, accounting for

70% to 80% of all breast cancers where cancer cells have invaded the surrounding tissue.

3. **Inflammatory Breast Cancer:** This type of breast cancer is considered aggressive and can often be hard to diagnose because it does not always form a lump.

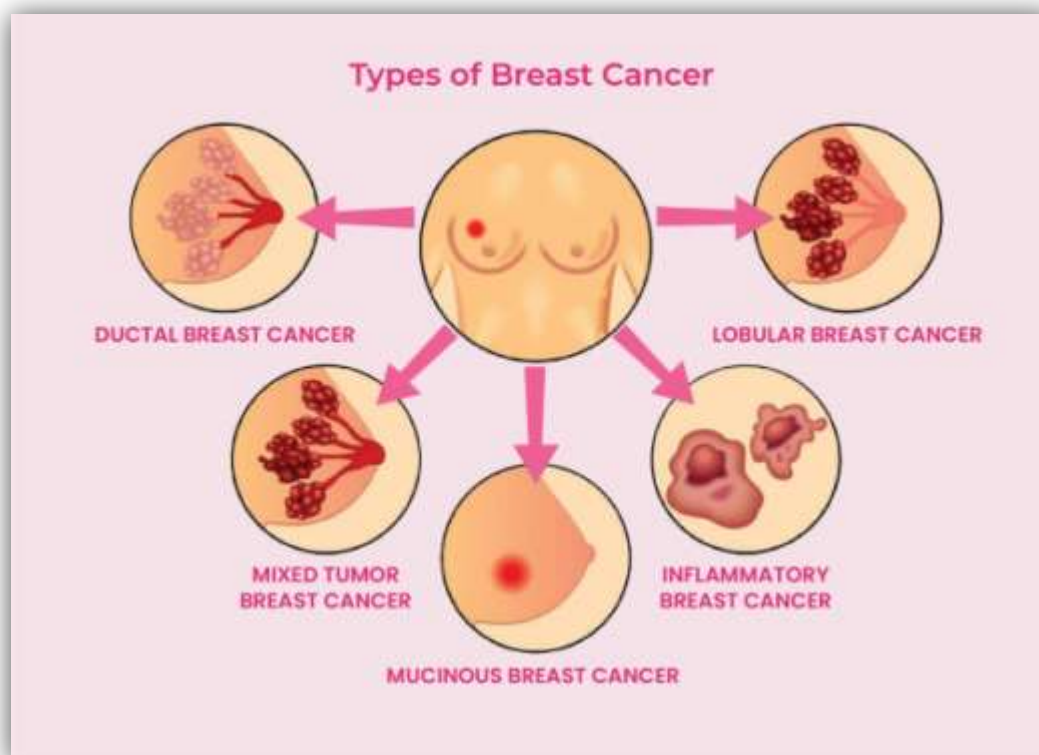
4. **Lobular Carcinoma In Situ (LCIS):** LCIS is considered a non-invasive type of breast cancer which means that the cancer cells are contained within the lobules and have not spread to surrounding normal tissue. 5. **Invasive Lobular Carcinoma (ILC):** This type of cancer starts in the milk-producing lobules and can spread beyond them into other parts of the breast.

6. **Mucinous Carcinoma:** This type of breast cancer is slow growing and is often found in older women.

7. **Metaplastic Breast Cancer:** This rare form of breast cancer can be aggressive, but treatment options are often effective.

8. **Angiosarcoma:** This type of cancer is very rare and can occur in any part of the body, but it is most commonly found in the breast tissue.

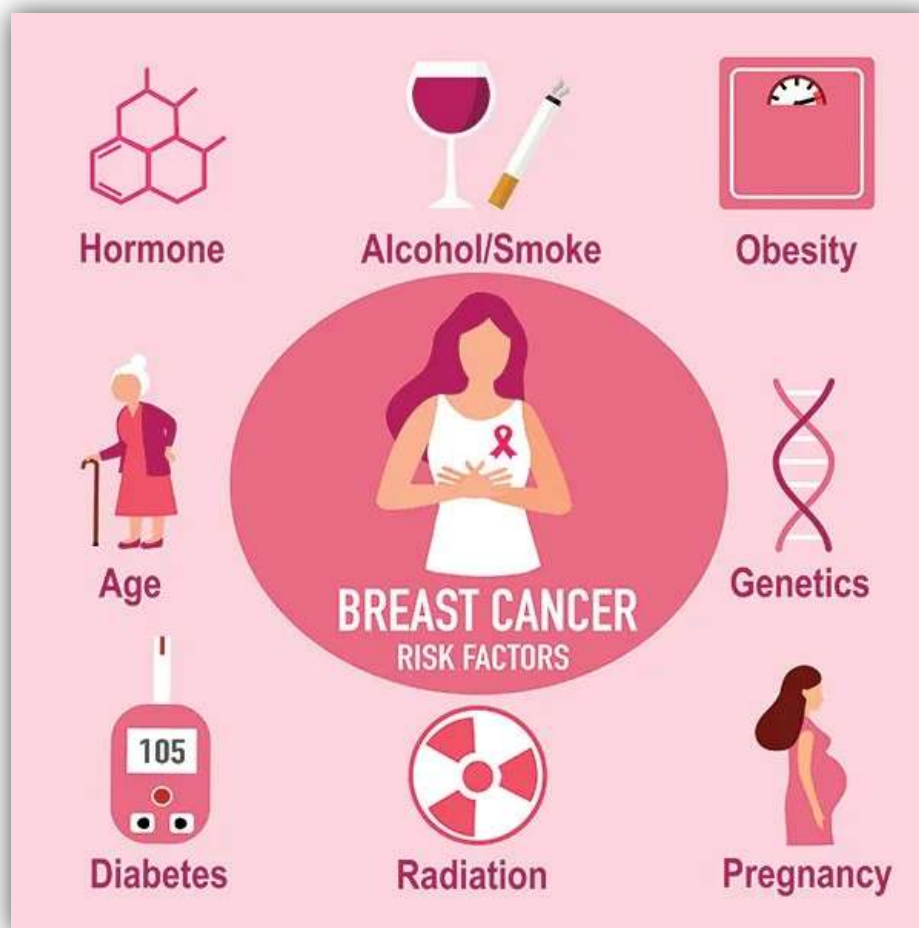
9. **Phyllodes Tumor:** This type of tumor is not considered cancer, but it can still be dangerous if not treated promptly. 10. **Page's Disease:** This is a rare form of breast cancer that starts in the nipple and can spread to other parts of the breast if left untreated. (9)



Risk Factor

Factors that influence risk of developing breast cancer include:

- Prior History of Breast Disease
- Family History of Breast Disease
- Age
- Race
- Reproductive and Menstrual History
- Radiation Exposure
- Dietary Factors



Symptoms

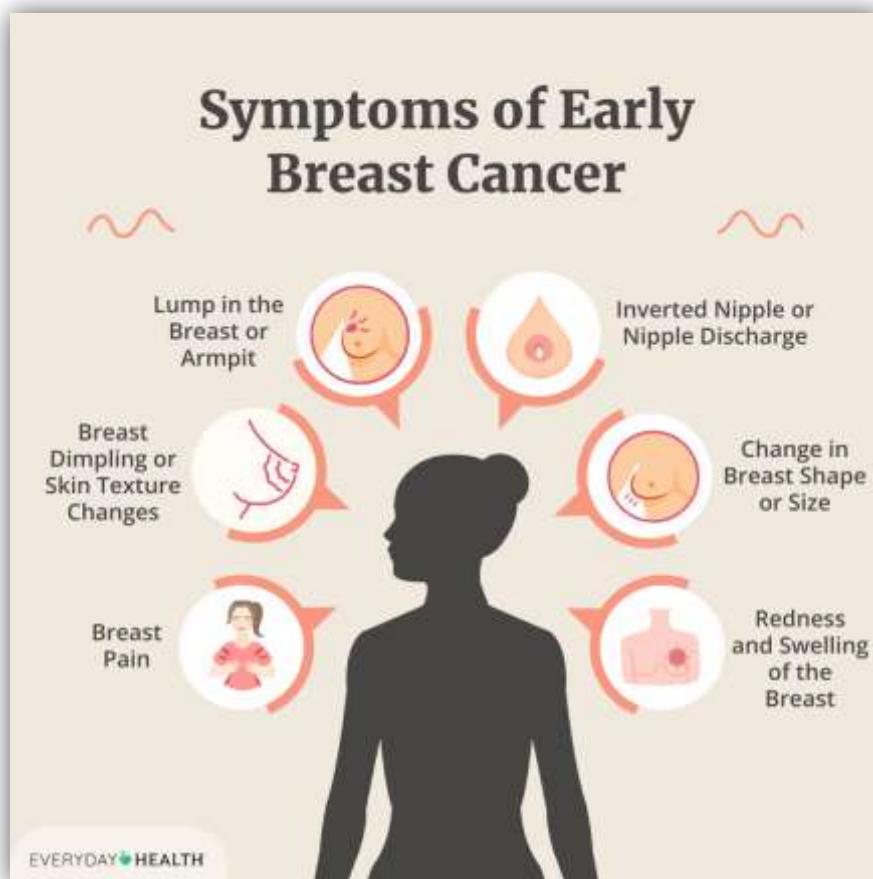
Signs and symptoms of breast cancer may include:

- A breast lump or thickened area of skin that feels different from the surrounding tissue.
- A nipple that looks flattened or turns inward.
- Changes in the color of the breast skin. In people with white skin, the breast skin may look pink or red. In people with brown and Black skin, the breast skin may look darker

than the other skin on the chest or it may look red or purple.

- Change in the size, shape or appearance of a breast.
- Changes to the skin over the breast, such as skin that looks dimpled or looks like an orange peel.
- Peeling, scaling, crusting or flaking of the skin on the breast. (12)

source such as lymphatic spread, military dissemination, or contiguous spread (e.g.,



In lactational mastitis, it is likely that bacteria (often originating from the mouth of the infant) gain entry via cracks or fissures in the nipple surface. Once the primary defences are breached, organisms have an ideal culture environment in nutrient rich maternal milk leading to rapid replication. This can be augmented by milk stasis and overproduction leading to mastitis. In neonates, transient breast enlargement secondary to maternal hormones can make them vulnerable to mastitis.

In duct ectasia, the mammary duct-associated inflammatory disease sequence involves squamous metaplasia of lactiferous ducts, causing blockage (obstructive mastopathy) with peri-ductal inflammation and possible duct rupture. Inflamed ducts are prone to bacterial infection.

In tubercular mastitis, mycobacterium tuberculosis can enter the breast from a direct inoculation (via a nipple abrasion) or more commonly from secondary spread from a distal

empyema necessitans). Clinical presentation is usually of a solitary, ill-defined, unilateral hard lump situated in the upper outer quadrant of the breast. Primary TB of the breast is rare. Necrotizing granulomas are the histopathological hallmark of TB infection.

In granulomatous mastitis, granulomas are usually non-necrotizing, inflammation is focused around breast lobules that clinically may present as a painless mass.

Left untreated, mastitis may cause tissue destruction resulting in an abscess. Lactational abscesses tend to be located in the peripheral breast and are often a progression of mastitis or lactational breast inflammation. Occasionally spread is hematogenous from an infection elsewhere. Risk factors for lactational breast abscess formation include the first pregnancy at maternal age over 30 years, pregnancy more than 41 weeks of gestation, and mastitis. Early infection is usually localized to a single segment within the breast, extension to another segment is a late sign. Lactose-rich milk

provides an ideal growth environment, so bacterial dispersion in the vascular and distended segment is easy. The pathological process is similar to any acute inflammatory event, although the nature of the lactating breast architecture; with its loose parenchyma and stagnation of milk in an engorged segment may allow the infection to spread quickly both within the stroma and through the milk ducts.

Non-lactational breast abscesses are often sub-areolar and were first described as fistulas of lactiferous ducts by Zusaket al. It was noted that this results in chronically draining sinuses and abscess formation near the areola. This form has a known association with squamous metaplasia of the lactiferous duct epithelium, duct obstruction and subareolar duct dilation or duct ectasia. This is proceeded by inflammation of the surrounding duct, infection of these terminal lactiferous ducts, duct rupture and subsequent peri-areolar fistula and sub-areolar breast abscess formation. These abscesses have a chronic course, often with recurrent obstruction of the ducts with keratin plugs and tend to form extensive fistulas. Central (peri-areolar) non-lactational abscesses are usually due to periductal mastitis. Smoking and Diabetes mellitus are significant risk factors for periductal mastitis and non-lactational abscesses (10)

Stage 1

Breast Cancer Symptoms

Stage 1 breast cancer is the earliest form of invasive breast cancer – at this stage, cancer cells are contained but still affect breast tissue. Patients may have a tumor up to 2 cm across that has not spread to lymph nodes, a tumor under 2 cm with small clusters of cancer cells in the lymph nodes, or cancer cells in lymph nodes with no tumor in the breast.

In this stage, it is still possible to not experience symptoms prior to diagnosis. However, there are still signs to look for that, while they are not surefire indicators of breast cancer, warrant a visit with a health care professional. These include:

- A lump that does not go away after a period
- Hard lump with irregular edges
- Changes to the shape of the nipple
- Nipple discharge that is clear or red, brown, or yellow in color
- Unexplained redness, swelling, and itchiness around the breast

Detecting breast cancer at this stage is incredibly important for a patient's survival. Between 2012 and 2018, the 5-year survival rate

for patients with localized invasive breast cancer was 99%.

Stage 2

Breast Cancer Symptoms

In stage 2 breast cancer, the tumor has grown from stage 1 and/or has seen the cancer spread to nearby lymph nodes. Stage IIA may feature no tumor or a tumor in the breast up to 2 cm with cancer spreading to lymph nodes under the arm, or a tumor ranging from 2 to 5 cm where cancer has not spread to lymph nodes. Stage IIB may be a tumor from 2 to 5 cm with cancer spread to nearby lymph nodes or a tumor over 5 cm across but the cancer has not yet spread to lymph nodes.

As cancer at this stage either has not spread to lymph nodes or has not spread to distant nodes, patients who experience symptoms at this stage are likely facing those similar to that of stage 1.

Stage 3 Breast Cancer Symptoms

There are three subcategories to stage 3 breast cancer. With stage IIIA, either the cancer has spread to 4 to 9 lymph nodes or the tumor is over 5 cm and has spread to 1 to 3 lymph nodes. In stage IIIB, the cancer has spread to the chest wall. Here, it may have spread to the skin or even broken through to create an ulcer or wound. This may also be the case in stage IIIC, or the cancer has spread to at least 10 lymph nodes under the arm or to lymph nodes near the collarbone.

At stage 3

Other symptoms may appear depending on where the cancer has spread. If it has spread to the skin, patients may experience a new lump, additional redness and swelling, and possible ulcerations.

Stage 4 Breast Cancer Symptoms

Stage 4 breast cancer is also known as metastatic breast cancer. Here, the cancer has spread to other lymph nodes and distant parts of the body, potentially including organs. The lungs, liver, bones, and brain may be affected at this point.

The effects of metastasized breast cancer may include not only existing breast cancer symptoms that can start at earlier stages, but also symptoms that may affect the parts of the body where the cancer has spread. If the cancer has metastasized to the lungs, patients may experience chest pains or a chronic cough. Metastasis to the liver could cause jaundice, nausea, and abdominal

pain. Cancer that has spread to the bone can cause additional swelling and susceptibility to breaks. If it has spread to the brain, patients could potentially experience seizures, headaches, and even behavioural changes.

At stage 4, patients with breast cancer may also experience symptoms not necessarily specific to the affected organs, such as fatigue and unexplained weight loss. Breast cancer classified as distant (spread to other areas of the body) has a 5-year survival rate of just 30%.

Stage 0 Breast Cancer Symptoms (Non-invasive)

A non-invasive stage 0 breast cancer is known as a carcinoma in situ, in which abnormal cells have not reached tissue or become invasive. This can include ductal carcinoma in situ (DCIS), where the abnormal cells form inside the milk duct of the breast.

DCIS is most often found via mammogram, as it is rare to experience symptoms in this form of breast cancer that has not yet made it to breast tissue. However, it has at times caused symptoms that include a breast lump and bloody discharge from the nipple. (11)

Signs of breast cancer include a lump or change in the breast.

These and other signs may be caused by breast cancer or by other conditions. Check with your doctor if you have:

- A lump or thickening in or near the breast or in the underarm area.
- A change in the size or shape of the breast.
- A dimple or puckering in the skin of the breast.
- A nipple turned inward into the breast.
- Fluid, other than breast milk, from the nipple, especially if it's bloody.
- Scaly, red, or swollen skin on the breast, nipple, or areola (the dark area of skin around the nipple).
- Dimples in the breast that look like the skin of an orange, called peau d'orange. (13)

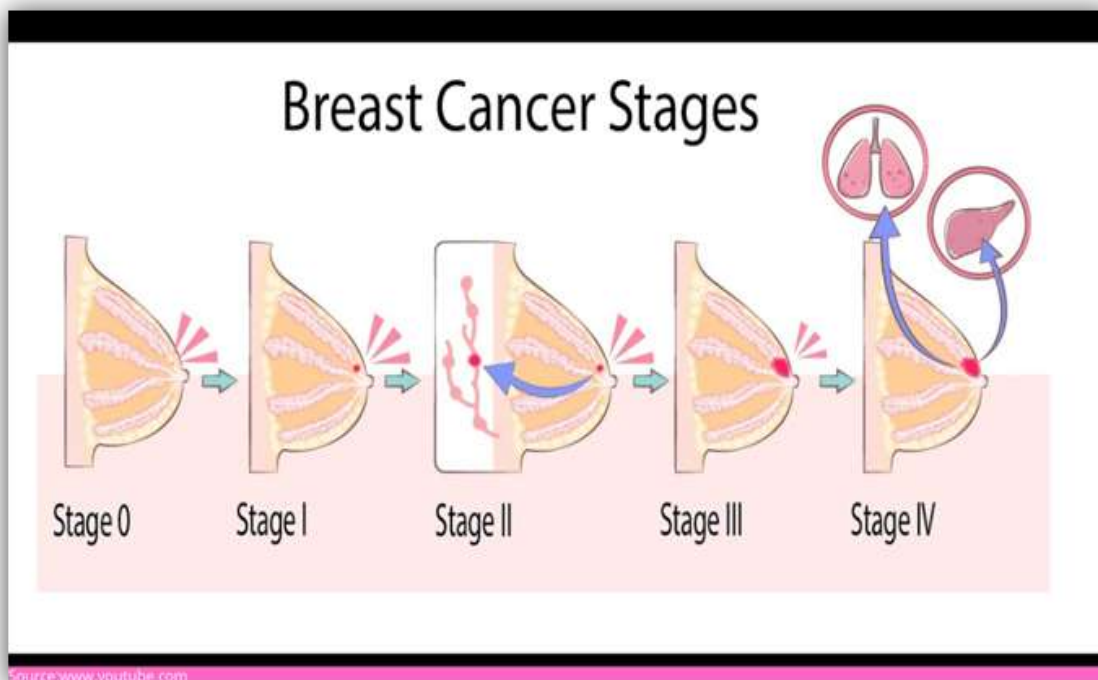
Tests that examine the breasts are used to diagnose breast cancer.

Check with your doctor if you notice any changes in your breasts. The following tests and procedures may be used:

- **Physical exam and health history**: An exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.
- **Clinical breast exam (CBE)**: An exam of the breast by a doctor or other health professional. The doctor will carefully feel the breasts and under the arms for lumps or anything else that seems unusual.
- **Mammogram**: An x-ray of the breast.
- **Ultrasound exam**: A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram. The picture can be printed to be looked at later.
- **MRI (magnetic resonance imaging)**: A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of both breasts. This procedure is also called nuclear magnetic resonance imaging (NMRI). **ENLARGE**
- **Blood chemistry studies**: A procedure in which a blood sample is checked to measure the amounts of certain substances released into the blood by organs and tissues in the body. An unusual (higher or lower than normal) amount of a substance can be a sign of disease.
- **Biopsy**: The removal of cells or tissues so they can be viewed under a microscope by a pathologist to check for signs of cancer. If a lump in the breast is found, a biopsy may be done.

There are four types of biopsy used to check for breast cancer:

- **Excisional biopsy**: The removal of an entire lump of tissue.
- **Incisional biopsy**: The removal of part of a lump or a sample of tissue.
- **Core biopsy**: The removal of tissue using a wide needle.
- **Fine-needle aspiration (FNA) biopsy**: The removal of tissue or fluid, using a thin needle.



II. CONCLUSION

Breast cancer was and continues to be among the most prevalent and growing malignant diseases among Iranian women in the past four months. Breast cancer is a disease that involves the patient, family, and community, and wastes many financial and spiritual resources. This cancer is developed in breast tissues including ducts (tiny tubes that carry the milk) and lobules (milk-producing glands). Breast cancer is not gender-specific, but rarely develops in men. Although the exact cause of breast cancer is unknown, specific risk-factors have been identified. Different types of cancer have different risk factors. Some of these risk factors such as cigarette-smoking, alcohol use, and diet can be changed and depend on life style. However, other factors like age, race, gender, and family history are fixed and unchangeable. Having one or more of these risk factors does not necessarily mean infliction.

Although many of these risk factors increase the chance of breast cancer development and progress, its exact mechanism is not clear. It seems that hormone plays a very important role in some types of breast cancer; however, its development and progress mechanisms are not very clear. In general, it can be said that such factors as aging, history of breast cancer development in family, certain changes in breasts, genetic changes, history of productivity and menopause, lack of physical activity, alcohol-use, diet and nutrition,

race, and radiation therapy to chest are risk factors of breast cancer.

This disease affects different physical, mental, and social aspects of women life. On the other hand, such factors as social and family supports during the illness can reduce its negative impacts.

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