

# A Review Literature on Science of Breast Cancer

Neda Fatima<sup>1</sup>, Shweta Singh<sup>2</sup>

Prasad Institute of Technology, Utter Pradesh- Jaunpur, India

**Abstract:** *This article include review of breast cancer literature, introduction, pathophysiology, highly risk factors for development of breast cancer, types, stages along with its causes and symptoms , diagnosis, targeted delivery system, and vaccines used in breast cancer treatment. Breast cancer is one of the leading disease among women in India. There are several diagnosis, prevention and treatment of breast cancer. But it is a noticeable issue in public health and medical practice. Current scenario risk of breast cancer is enhancing day -by -day because of family history [13-58%], tobacco and smoking were reported to be a risk of developing a breast cancer [20- 40% ],obesity and over -weight were consider to be risk factor by [11-51%]. Breast cancer is not found only in those Person who are addicted to alcohol and tobacco. Sometimes imbalance of hormone cause breast cancer due to which mother does not have tendency for breast feeding a small cyst is developed in the breast which cause breast cancer .The mortality rate of breast cancer affected in younger (below age 35) and in older (greater than 75).There are various treatment of breast cancer but in the new era targeted drug delivery is the excellent treatment*

**Keywords:** Introduction, pathophysiology, signs of breast cancer risk, types of breast cancer, stages, diagnosis, targeted drug delivery, vaccines

## 1. Introduction

Breast cancer is one of the most common cancer in female about 23% women are affected from breast cancer [1]. There are 30% cases seen at different cancer centre in India and 60% to 70% of cases in the developed world-wide [2].One of the extensive reason cause breast cancer.

Cancer cause by late presentation and high morbidity/mortality is lack of breast cancer awareness in the population compounded with a lack of population level method. The main identification procedure of screening / early detection include mammography, clinical breast examination (CBE) and breast self examination (BSE),the American cancer society and other leading cancer agencies have suggest monthly breast self examination in women to be strongly associated with early presentation in our studies[3]. According to National cancer register and regional cance centre. It is the most common cancer in Delhi, Mumbai, Ahmadabad and Kolkata.

In India the number of new breast cancer cases is about 115,000 per year and this is expected to rise to 250,000 new cases per year. In the developed countries the breast cancer are take place above the age of 50 year, as compared to India where it occur in younger age group. A total of 7066 women aged 15–70 year showed varied level on risk factor such as family history (13-58%), reproductive factor (1-88%) and obesity (11- 15%) [4].

## 2. Pathophysiology

There are trillions of cells are found in our body. These cells have a rapidly regulated cell cycle that control growth, maturity, division and death.

Breast cancer is a type of malignant tumor that starts from the cell of breast. There are several factor raise the level of breast cancer such as predisposing factor (Genetic/hereditary) and precipitating factor (Life style,

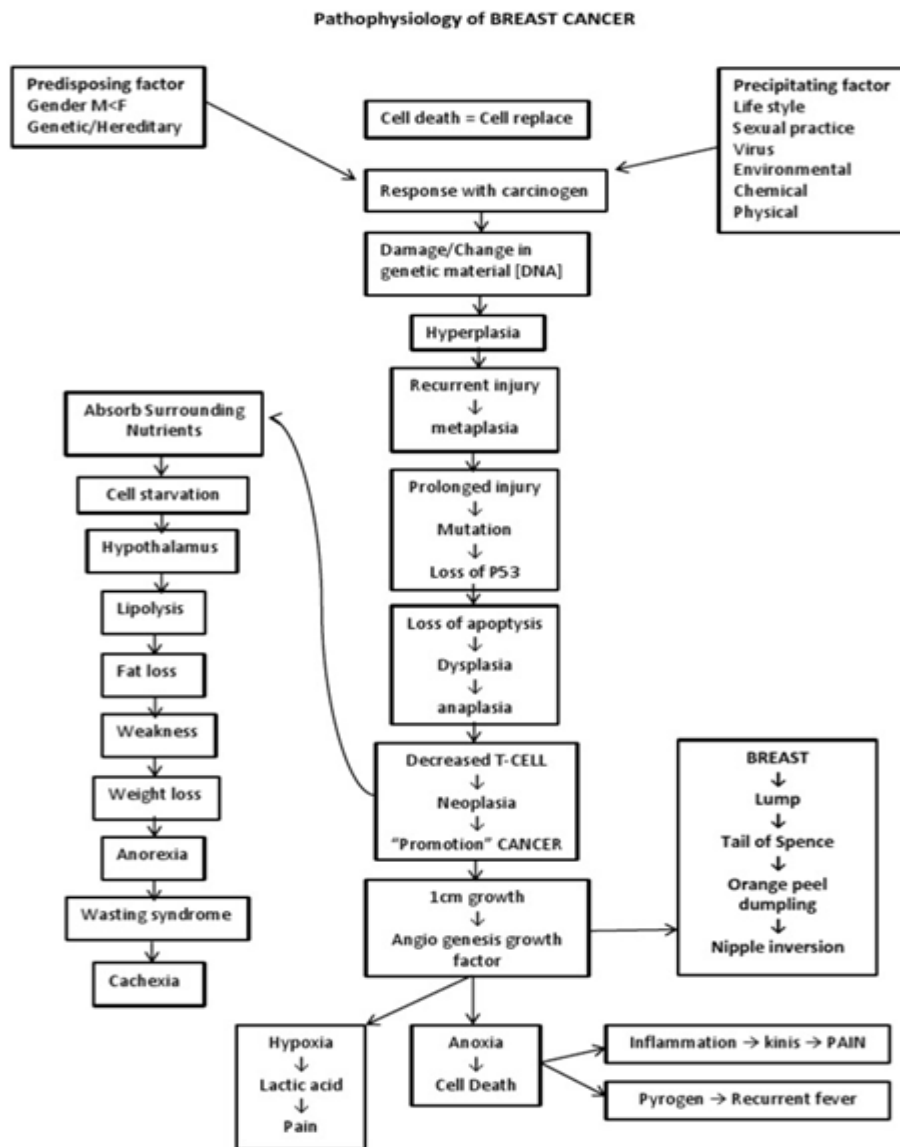
sexual practice, virus , environment, chemical and physical). Both factor give response to carcinogen which may cause damage to the DNA and genetic mutation can lead to the breast cancer.

The breast cancer starts from the initial step that is known as hyperplasia. They are involved in increase the number of cell. It is found in the duct (ductal hyperplasia) or lobules (lobular hyperplasia) it can be graded as mild, moderate, florid.

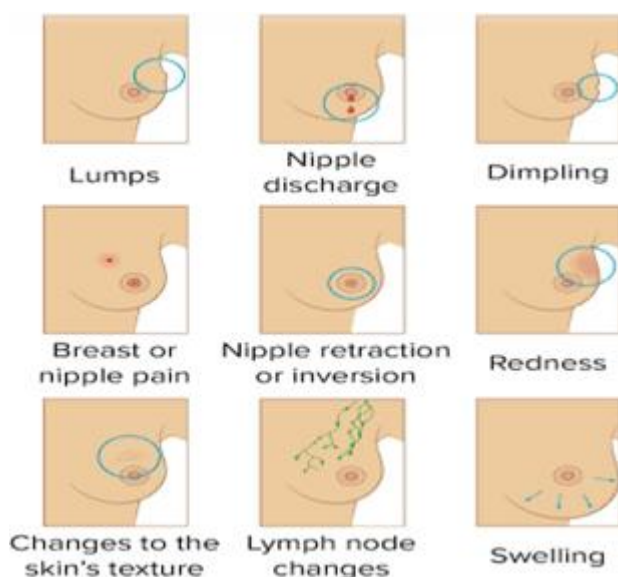
After the stage of hyperplasia breast can be injured. It may cause brushing and swelling to the breast, which can be tender and painful to touch and then the cause abnormal change in the nature of tissue this term is known as metaplasia.

Sometime, mutation found in the breast results behind is decrease the level of P53. This is the tumor suppressor gene after decreasing the level of P53. Tumor size rapidly increases and less blood cell are develop in bone marrow. Which affect the abnormal growth or development of a tissue or organ and implies dedifferentiation or loss of structural and functional differentiation of normal cell then they decrease the level of t-cell. So, our immune system does not have ability fighting to the cancerous cell and the place of tumor formation of new abnormal tissue it can be benign and malignant.

A carcinogen works in a series of stage to produce cancer. A complete carcinogen a tumor cell in all stage of development; on incomplete carcinogen is one which may not have the ability to initiate a tumor but which act accelerates its growth, promotion, progression and malignanat conversion. At the stage 0 tumor become less than 1 cm or 1 cm in length. Essential steps for tumor progression and dissemination are following steps. Sometime, absence of oxygen cells might be dead which cause hypoxia, inflammation etc.



### 3. Sign of Breast Cancer



- 1) Age
- 2) Reproductive factor
- 3) Personal or family history
- 4) Genetic pre-disposition
- 5) Environmental factor

#### 1) Age

Grow the age also enhance the risk of breast cancer. According to the surveillance, epidemiology and end results (SEER) database, the prospect of breast cancer of women in the united state developing breast cancer threat lifetime 1 in 8, 1 in 20 from birth to age 39 years of age, 1 in 26 from 40 to 59, and 1 in 28 from 60 to 69 years [5].

#### 2) Reproductive factor

Reproductive factor are known the risk of breast cancer. The main affect of reproductive factor (age at menarche, age at first full- term pregnancy, the time interval between these two ages and parity) enhance the risk of breast cancer [6].

- a) Age at menarche
- b) Pregnancy
- c) Parity and breast cancer
- d) Lactation and breast cancer
- e) Age at menopause and breast cancer

#### Risk Factor

There are various factor have been associated with an increased the risk of breast cancer.

- f) Oral contraceptive pills
- g) Other hormonal contraceptives

#### a) Age at menarche

Age at menarche is a most prevalent factor which influencing the risk of breast cancer. Research predict that the risk of breast cancer reduce 10 to 20 % for every year menarche is delayed. The result of broad study revealed that for each two year delay in onset of menstruations, breast cancer risk was reduced by about 10 %. Increase in the breast cancer rate have been occurring in recent year is decrease age at menarche, due to improving nutritional status in adolescence [7].

#### b) Pregnancy

The pregnancy may increase the risk of breast cancer, pregnancy effect depends on your age when you first give birth. Breast cancer risk is moderate increased for about ten year. Women have first child at later ages are at an increase risk of breast cancer as compared to women who have their first child in younger age [8].

#### c) Personal or family history

The breast cancer risk connect to family history may be due to the inherited gene mutation or shared lifestyle factor. More than first degree relative (mother, sister, or daughter) with breast cancer at an early age.

The family history of cancer was divided in to two mutual exclusive categories.

- Family history of breast cancer
- Family history of other cancer

#### d) Family history of breast cancer

Family history of breast cancer was coded in to three categories.

No family history of breast cancer; sister, daughter or any first degree male relative (father, brother, and son) mother and sister are mutually exclusive.

#### e) Family history of other cancer

The family history of other cancer was divided in to six categories-

- No cancer history
- Cancer diagnosed in- *son or brother*
  - Father
  - Daughter
  - Sister
  - Mother [9].

#### f) Genetic

Genetic risk factor underlying both familial and sporadic breast cancer, much of the genetic contribution of breast cancer etiology remains unknown. The discovery of BRCA1 and BRCA2 over 20 years ago remains the seminal event in this field. Research describe there are 10 % women suffer from breast cancer because of family history. More recently, genome – wide association studies (GWAS) have identified over 80 loci significantly association with sporadic breast cancer. BRCA1 and BRCA2 respectively will develop breast cancer by age 70 and risk increases to 84 to 85 % respectively [10]

#### g) Environmental factor

Environment and lifestyle risk factor that could play a role in the breast cancer. Increasing the epigenetic factor being recognized as playing role in the development of cancer. Literature in the area of research, there are known physiological, lifestyle and environmental risk factor that play a vital role in the development of breast cancer. Alcohol consumption, obesity, physical activity and parity are some of the factor known to the effect the risk of breast cancer [11].

#### Types of Breast Cancer

The two main types of breast cancer-

- 1) Ductal carcinoma in situ
- 2) Invasive ductal carcinoma

**Ductal carcinoma in situ:** Ductal carcinoma in situ (DCIS) is a non-invasive form of breast cancer. DCIS have an enhancing the risk of breast cancer malignancy and breast cancer death compared with general population [12].

#### Symptoms

Ductal carcinoma in situ does not typically have any signs and symptoms. However, DCIS can sometimes cause signs such as-

- A breast lump
- Bloody nipple discharge

#### Causes

DCIS are formed when the genetic mutation are found in the DNA of breast duct cells. The genetic mutation growth of abnormal cell, but the cell don't have affinity to break out of the breast duct. Researches don't know activation of abnormal cell growth that lead to DCIS that may play a part include your lifestyle, your environmental factor and also genetic factor included.

#### Risk factor

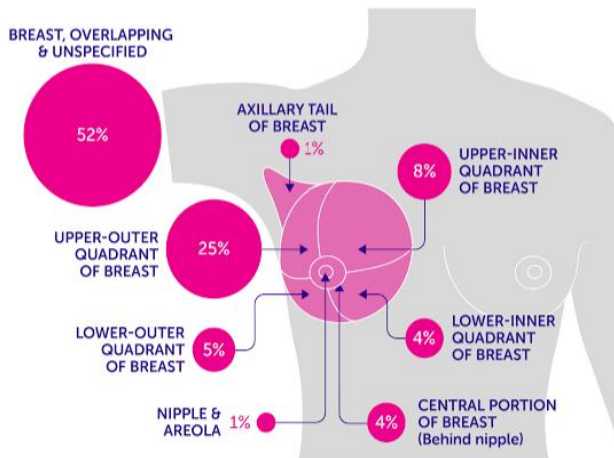
Factor that may increase your risk of DCIS included-

- Increase age
- Never having been pregnant
- Having your first period before age 12
- Beginning menopause after age 55
- Genetic mutation [13].

#### Invasive ductal carcinoma

Invasive means that the cancer has “invaded” or spread to the surrounding breast tissues. Invasive ductal carcinoma (IDC), sometime called invasive ductal carcinoma, is the most comcommon type of breast cancer. About 80% of breast cancers are invasive ductal carcinoma.

### INVASIVE BREAST CANCER CASES: PERCENTAGE DISTRIBUTION BY ANATOMICAL SITE



#### Symptoms

- Swelling of all part of the breast
- Skin irritation or dimpling
- Breast pain
- Nipple pain or the nipple turning inward
- Redness or thickness of the breast skin
- Nipple discharge
- A lump in the under arm area [14].

#### 4. Stages of Breast Cancer

There are five stages of breast cancer. Stage 0 followed by stage 1 to 4. In situ the cancer cells are only in the duct or lobules where they started and have not grown in to nearby breast tissue (non – invasive) it is stage 0.

##### Stage 0 (Carcinoma in situ)

- There are cancer cell only in the lining of breast duct and this in known as ductal carcinoma in situ.
- When it is build up abnormal cells in breast lobules there is called as lobular carcinoma in situ.

##### Stage 1A

The tumor size is 2cm.

##### Stage 1b

The tumor size is 2cm or smaller or no tumor seen in the breast.

A small number of cancer cell are found in the lymph nodes. Each lymph node with cancer cells in it is no larger than 2mm.

##### Stage 2A

- The tumor is 2 cm or smaller, or no tumor can be seen in the breast.
- Cancer cells are found in 1 to 3 lymph node under the arm (axillary lymph nodes), in lymph node inside the c

##### Stage 2B

The tumor is larger than 5cm. The tumor has spread to 1 to 3 axillary lymph node, internal memory lymph node in both area.

##### Stage 3A

The tumor is 5cm and no tumor has been seen in the breast cancer cell are found in 4 to 9 axillary lymph nodes or in the internal memory lymph node.

##### Stage 3B

The tumor has grown in to the muscles of the chest wall and also the skin. The cancer may have also spread to 1 to 9 axillary lymph node or to internal mammary lymph node.

##### Stage 3C

The cancer has spread to 10 or more axillary lymph nodes or to lymph node below the collarbone.

##### Stage 4

The cancer has spread other parts of the body such as liver, bone, lungs or brain. This is also called metastatic cancer [15]

#### 5. Diagnosis of Breast Cancer

Breast cancer is the main cause death among women. Early detection and diagnosis through regular screening and timely treatment can be preventing from breast cancer.

##### Test and procedure used to diagnose breast cancer:-

- a) Breast self examination
- b) Mammogram
- c) Breast ultrasound
- d) Biopsy
- e) Breast magnetic resonance

##### a) Breast self – examination

Self examination is very simple, quick, cost less procedure that can be carried out by women themselves.

##### Benefit of breast self examination in to two ways-

- Women become familiar with both the appearance and the feel of their breast.
- Detect any change in their breast as soon as possible.

Researches describe about 90% the times breast cancer is noticed by patients itself. Also various studies exhibit that barrier to diagnosis and treatment can be increasing women awareness of breast cancer. In developed and developing countries reported 54% of population practiced breast self examination (BSE)[16].

##### b) Mammography

Mammography (also called mastography). This is help to detect the human breast diagnosis and help to early detection of cancer masses [17]. Although the screening mammography reduce mortality from breast cancer among women aged 40 to 47 years [18]. Advanced breast cancer rate (ABCR) allow the effect of early detection help to improve the mortality rate. The relation between reduction in breast cancer mortality and advanced breast cancer mortality has start on the basis of screening trials [19].

##### c) Breast ultrasound

Ultrasound is safe and widely available, through ultrasound of the breast should be performed by clinician. Ultrasound is



useful in these circumstances, in both characterizing the area of concern and guiding a biopsy (tissue sample) of area [20].

#### d) Biopsy

It is a medical test commonly used for extraction of sample cells or tissue for examination to determine about the disease. Core needle biopsy has the obvious and specificity, high negative and positive predictive value, low inadequate rate. Core needle biopsy (CNB) has been performed by radiologist under guidance with good yield material and low inadequacy rate [21]

#### e) Magnetic resonance imaging (MRI)

Mammography and ultrasound are the most commonly imaging tool used for the detection. MRI is very superior technique as compared to mammography and ultrasound. Breast abnormalities, (CE-MRI) with its high soft tissue contrast, multi-planar sectioning and three dimensional representation of the breast provide high sensitivity cover 90% in the detection of breast cancer. An additional value of MRI is the detection of invasive component in DCIS lesions [22].

#### Targeted Drug Delivery

Targeted delivery May be defined as the supply of therapeutic amount of drug to a target site in a body. It is ideally should be non- immunogenic, biochemically inert (non-toxic), physically stable and chemically in vivo and vitro condition and predict rate drug during transit [23].

#### Types of targeted drug delivery system

- a) Systemic drug delivery
- b) Organic drug delivery
- c) Inorganic drug delivery
- d) Localized drug delivery
- e) Receptor based drug deliver

#### a) Organic drug delivery

- Micelles
- Polymers
- Dendrimers

#### b) Inorganic drug delivery

- Gold nanoparticles
- Super magnetic iron oxide(SPI-NPs)
- Quantum dots (QD)

#### c) Localized drug delivery

- Nanofibres
- Hydrogels
- Intraductal injection

#### d) Receptor based drug delivery

- HER-2
- EGRF
- IGRF-IR[24]

#### Nanoparticle drug delivery system

Nanoparticle based delivery system provides many potential profit, including increased biocompatibility, multifunctional encapsulation of active agent, the work of nanoparticle tumor targeting and enhanced collection of active agent.

#### Example- Doxil (doxorubicin)[25]

#### How to deliver doxil?.

- A tumor marker is a substance found in the body that can help to elevate the cancerous cell.
- Oncomarker is a signature of cancerous cell, and modern nanoparticle develop to conjugate to various molecular marker.
- Doxil is the most efficient anti cancer dr
- But doxil cause death healthy cell too.
- That's why nanoscale capsule can deliver inside cancer cell by using oncomarker signature.
- It consists of a DNA- origami shell by covered by immune factor with molecular binding sites on its surface.
- Nanoparticle delivery start from blood stream.
- Doxil nanoparticle penetrate inside the cancer marker on its surface.
- When nanoparticle conjugated with several marker its DNA-origami shell opens releasing doxil inside the cell.
- Doxil successfully delivered.

#### Vaccines against Breast Cancer

Breast cancer vaccines may provide extra palliative benefit to patients with metastatic disease, the approaches will likely to combine with chemotherapy an immune-modulator to improve outcome. Cancer vaccine differ from shown in cytotoxic agents, the clinical development paradigm for vaccine should be tolerated dose or response rate measure by traditional response evaluation criteria in solid tumor (RECIST). Criteria may not applied to early phase of cancer.

#### Vaccines designed for cancer preventions and treatment

- a) Autologous tumor cell-based vaccine.
- b) Allogenic tumor cell-based vaccines
- c) Viral vector – based vaccine
- d) DNA vaccine
- e) Dendritic cell vaccine
- f) Peptide based vaccine
- g) Whole cell vaccine.

#### Two to three vaccination are discussed below

#### a) Autologous tumor cell- based vaccine

Vaccine is used to train the immune system to detect and kill cancer cell. Autologous tumor based vaccine (ATCBV) are based on the tumor cells lysate obtained from patients. The advantage of vaccine are their safety, multivalency, and patient patients safety.

#### b) Allogenic tumor cell- based vaccine

Allogenic vaccine are another kind of vaccine that use the collected cell lines from similar class of cell. This type of vaccine is cost effective , reproducible and easily designed.

#### Viral vector – based vaccine

The viral vector have also been used vaccination, is part due to their ability in the efficient delivery of genes. They show high in vitro and vivo trans-gene expression and elicit low toxicity, they have been used to serve as Ag- specific vaccines for the activation of immune response in the tumor microenvironment [25]

## 6. Conclusion

Breast cancer is the most leading cancer. Women need to be aware of both modifiable and non-modifiable risk factors. In this article review discuss about general knowledge regarding breast cancer, furthermore review highlight the targeted drug delivery system and vaccines used in the treatment of breast cancer.

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