# "A STUDY OF HER2Neu STATUS IN PRIMARY BREAST CANCER AND METASTATIC AXILLLARY LYMPH NODES WITH BEARING ON POST OPERATIVE TARGETED THERAPY"


**By**

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**In partial fulfillment of the requirements for the degree of**

**MASTER OF SURGERY**

**IN**

**GENERAL SURGERY**

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**APRIL/MAY2020**

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**Signature of the candidate**

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# LIST OF ABBREVATION

| | | |
|---|---|---|
| BC | : | BREAST CANCER |
| CB | ; | CARCINOMA BREAST |
| MC | : | MONOCLONAL ANTIBODY |
| EGFR | : | ENDOTHELIAL GROWTH FACTOR RECEPTOR |
| OS | : | OVERALL SURVIVAL |
| HRT | : | HORMONAL REPLACEMENT THERAPY |
| OCPS | : | ORAL CONTRACEPTIVE PILLS |
| BMI | : | BODY MASS INDEX |
| DC | : | DUCTAL CARCINOMA |
| IHC | : | IMMUNOHISTOCHEMISTRY |
| LC | : | LOBULAR CARCINOMA |
| DCIS | : | DUCTAL CARCINOMA IN SITU |
| LCIS | : | LOBULAR CARCINOMA IN SITU |
| ALH | : | ATYPICAL LOBULAR HYPERPLASIA |
| ADH | : | ATYPICAL DUCTAL HYPERPLASIA |
| FNAC | : | FINE NEEDLE ASPIRATION CYTOLOGY |
| BCS | : | BREAST CONSERVATIVE SURGERY |
| MRM | : | MODIFIED RADICAL MASTECTOMY |
| FISH | : | FLUORESCENT IN SITU HYBRIDIZATION |

# ABSTRACT

**Background:** Carcinoma breast is the second most common cancer (11.6%) worldwide in 2018, around 2.1 million were newly diagnosed with BC accounting for almost 1 in 4 cancer cases among women. Molecular markers play a vital role in treatment of carcinoma breast. The status of gene encoding human EGF-like receptor 2 (HER2) is an important prognostic and predictive marker in carcinoma breast, for treatment with targeted therapy i.e trastuzumab. Discrepancies in HER2 status between primary tumors and metastatic axillary lymph node have been unclear. Here we explore the prevalence of discrepancies in primary and metastatic axillary in the given population.

**Objectives**:

To asses HER2 expression in primary breast tumor tissue.

To asses HER2 expression nodal metastatic tissue.

To see for any variability of HER2 expression in primary tumor and lymph node.

To identify patients with positive her2neu expression, who might be benefited from targeted therapy.

**Methods**: Prospective observational study.

**SOURCE OF DATA**: This study will be conducted in the Department of General Surgery, R.L. Jalappa Hospital, Kolar. Thirty patients admitted with diagnosis of locally advanced carcinoma of breast will be included in the study in the period of Dec 2017 to June 2019. Specimen will be sent in 10% buffered formalin. The paraffin blocks of primary tissue and metastatic lymph node will be sent for HER2neu tumor marker study using IHC, along with the regular appropriate treatment. The similarity and variability will be studied and compared with other randomized studies, using appropriate statistical analysis methods. Patient with positive discordance i.e positive

in metastatic lymph node were treated with targeted therapy for a duration of 12 months.

All cases were regularly followed up for response of treatment and also recurrence.

**Results:** In our study we assessed her2neu expression from the primary tumor in 30 patients with positive results in 8 patients i.e 26.7% of the patients and assessed her2 neu in the nodal metastasis(axilla) in 30 patients and positive in 9 patients i.e 30% and ER /PR positive in 19 patients. 5 patients had her2 (tumor nodes) discordance amounts to 16.6%. 5 patients also received targeted therapy.

**Conclusion:** Our study shows that there was significant change in discordance of her2neu receptor in primary breast tumor and metastatic axillary lymph node, so assessment of her2neu from a metastatic site helps patients in receiving targeted therapy.

**Keywords:** carcinoma breast , her2 neu, discordance, metastatic axillary lymph node

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# INTRODUCTION

# INTRODUCTION

Carcinoma breast is the second most common cancer (11.6%) worldwide in 2018, around 2.1 million were newly diagnosed with carcinoma breast accounting for almost 1 in 4 cancer cases among women. [1] The disease is the most frequently diagnosed cancer in the vast majority of the countries and is also the leading cause of cancer death in over 100 countries. [1] In India, although age adjusted incidence rate of carcinoma breast is lower (25.8 per 100 000) than United Kingdom (95 per 100 000) but the mortality is very high. [2] There is a recent **i**ncrease in the incidence and cancer-associated morbidity and mortality in Indian subcontinent. Carcinoma breast crude rate (CR) among different registries showed highest rate in Thiruvananthapuram 43.9 (per 100 000) followed by Chennai (40.6), New Delhi (34.8) and Mumbai (33.6). [2] Globocan 2018, India along with United States and China collectively accounts for almost one third of the global carcinoma breast burden. [1]

The status of gene encoding human EGF-like receptor 2 (*HER2*) is an important prognostic and predictive marker in carcinoma breast, for treatment with targeted therapy i.e trastuzumab. Discrepancies in *HER2* status between primary tumours and metastatic axillary lymph node have been unclear. Here we explore the prevalence of discrepancies in primary and metastatic axillary in the given population. [3]

# OBJECTIVES

## OBJECTIVES OF THE STUDY

To asses HER2 expression in primary breast tumour tissue.

To asses HER2 expression nodal metastatic tissue.

To see for any variability of HER2 expression in primary tumour and lymph node.

To identify patients with positive her2neu expression, who might be benefited from targeted therapy.

# REVIEW OF LITERATURE

## REVIEW OF LITERATURE.

The surgical treatment of CB has evolved substantially over the past few decades. Extensive surgical resection has now been less preferred in favour of a more conservative approach [4, 5]

Axillary lymph node involvement is still single important factor in determining the metastatic spread of carcinoma breast [4,5,6]. Advancement in molecular techniques, targeted therapies are slowly becoming main stay of adjuvant therapy of carcinoma breast.

Carcinoma breast is a diverse disease and most patients present with advanced stage. There are multiple mechanisms put forth in change in biomarkers a switch in the biology of the disease; sampling error in focally receptor-positive cancers; limited reproducibility of receptor assays; heterogeneous tumour with different clinical characteristics, disease course, and responses to specific treatment; and previous treatment that may change in receptor status. [3]

Assessment of these receptors is done using tumour tissue from the primary tumour, post mastectomy. In recent years, studies have shown that HER2 status may varies in metastases compared to primary tumour. [5, 8, 9, 10, 11]

HER2 receptor is one such genetic entity which has a huge bearing over the prognosis and also gives great option for treatment with MC like Trastuzumab post-surgery, by virtue of its expression in tumour tissue. [7, 8]

HER2 is a transmembrane receptor and belongs to the EGFR family. This feature of HER2 expression is significant because it may modify patient's sensitivity to targeted therapy, which may be appropriate for primary tumour but not metastases, or vice versa. [9, 10]. This reason, some authors have suggested a need for assessment of HER2 status in metastasis. [7, 9, 10]

Her2 neu status is assessed on primary tumour to avoid the biopsy of metastasis it could be a her2 neu positive primary tumour or her2 neu negative metastatic lymph node or either way. The latter set of patients can be benefited with prolonged disease-free survival time post mastectomy.

Most targeted therapy are based on molecular markers for hormone receptors and HER-2/neu. A variability in biomarkers could have a huge impact on systemic therapy. Certainly, patients possessing HER-2/neu in tumour biomarkers are negative and subsequent tumours are rendered positive provide great opportunity for additional targeted systemic management with hormone manipulation or HER-2/neu-targeted treatments.

According to study, (16%) with HER-2/neu negative primary tumours had either their first or second metastases reported as HER-2/neu positive. HER-2/neu-positive. BC is associated with high virulence and poor survival, treatment with HER-2/neu-targeted therapies including trastuzumab is quite effective in reducing the impact HER-2/neu on survival. [11]

Similar study conducted by Nikura et al. evaluated 182 subjects with HER2-positive primary BC with recurrence and found that those with a loss of HER2 receptor at recurrence had significantly shorter OS than those with concordance in their HER2 status.[12]

## SURGICAL ANATOMY OF BREAST [13]

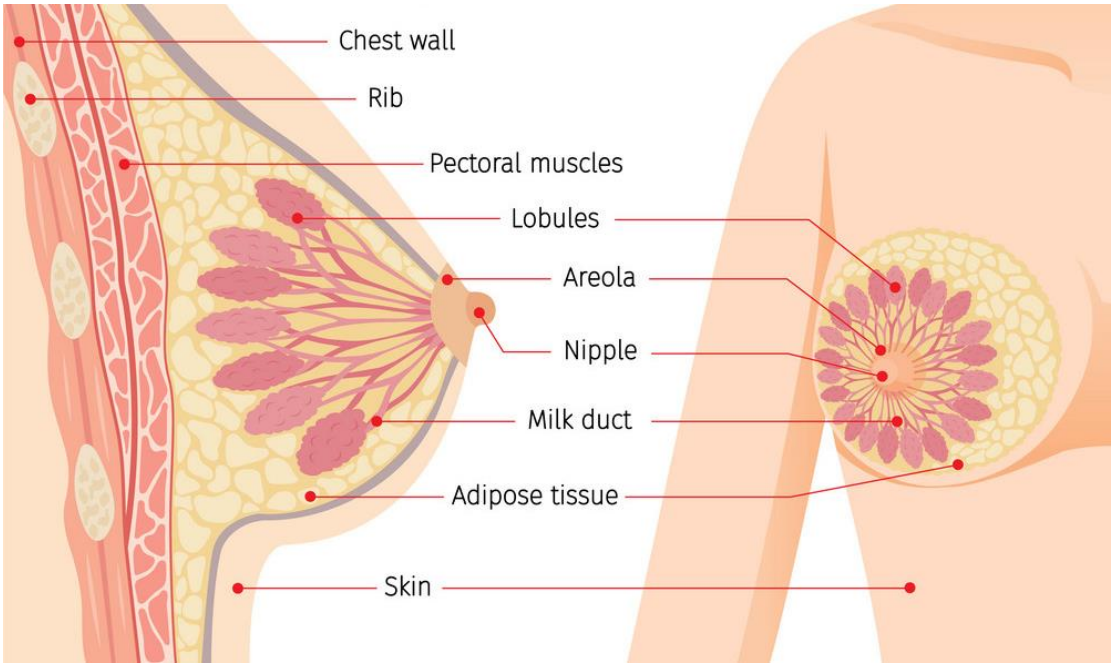



**Fig 1 : Anatomy of breast**

The breasts are modified sweat glands, situated on the anterior and also along the lateral aspects of the thorax. Each breast extends superiorly to second rib, inferiorly to sixth costal cartilage, medially to sternum, and laterally to mid-axillary line. The nipple–areola complex is located between fourth and fifth ribs.

Natural lines of skin, known as Langer lines, extend outwards circumferentially from nipple–areola complex. lines of Langer assume particular clinical significance for surgeon, when determining where to place the incision for breast biopsy.

Shape of breast is of a teardrop, with an extension of breast tissue towards axilla known as tail of Spence, which has a surgical importance while performing a mastectomy. Breast, it can extend as high as clavicle, inferiorly beyond inframammary fold, into axilla, or beyond border latissimus dorsi.

Breast is more conical in nulliparous woman and pendulous in women who have had children. Contour and volume of breast however, varies accordingly. Average volume of breast is roughly 300-400ml.

Breast mainly comprises of skin, the subcutaneous tissue, and fibro glandular breast tissue. The skin of breast is thin and contains hair follicles, sebaceous glands, and eccrine sweat glands. The nipple-areolar complex is typically located over the fourth intercostal space. Both the nipple and areola consist of a keratinizing stratified squamous epithelium with basal melanin deposition, which accounts for the pigmentation.

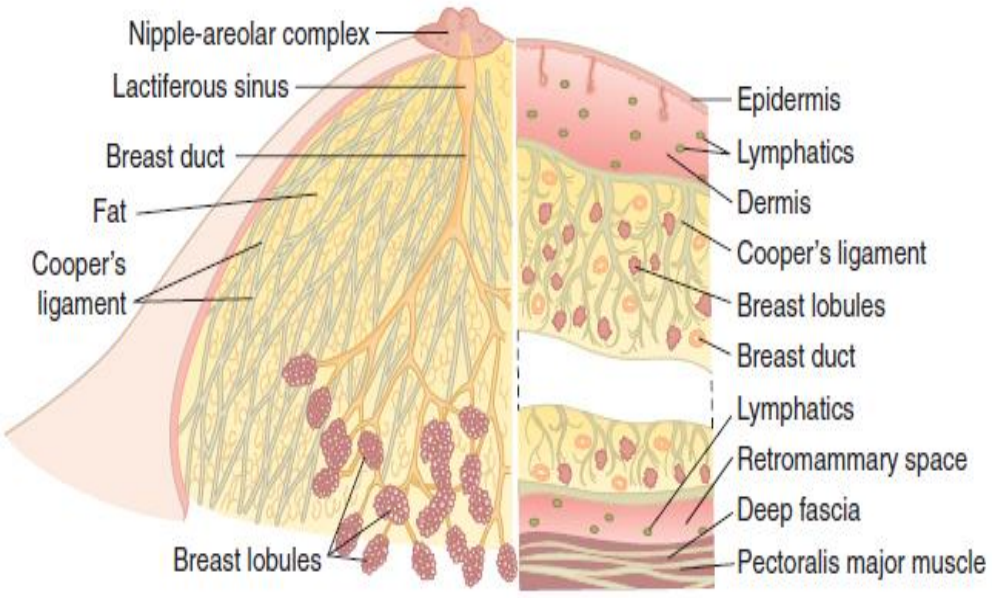



**Fig 2: Histological representation of breast**

The areola contains hair follicles, sebaceous glands, and sweat glands. Along periphery of areola are the Morgagni tubercles, elevations formed by openings of ducts of Montgomery glands. These glands are a fusion

between sweat and mammary glands, and are reasonable for producing milk.

Beneath skin is subcutaneous fat, defines the size of breast. Underneath is superficial pectoral fascia. The gland of the breast lies within superficial fascia, with anterior layer between skin, mammary gland, and posterior layer between the gland and the fascia of pectoralis major muscle. Two fascial layers are suspended by fibrous bands i.e. Cooper ‘s ligaments which help and give breast its shape and also anchor gland to skin. Deep layers of the breast are related to deep investing fasciae of the pectoralis major, serratus anterior, and external oblique muscles, and a part of rectus sheath.

**AXILLA**

The axilla is a pyramidal having apex, a base, and 4 walls. Apex is a triangular space bordered by clavicle, upper border of scapula, and first rib.

Base is formed by axillary fascia and skin. The anterior wall is composed of 3 muscles pectoralis major, pectoralis minor, and subclavius and clavipectoral fascia. Posterior wall is formed by scapula and 3 muscles: subscapularis, latissimus dorsi, and teres major. Medial wall consists of lateral thoracic wall. The lateral wall is created by structures of arm. The axilla contains lymph nodes; axillary sheath which covers blood vessels and nerves.

## Arterial Supply

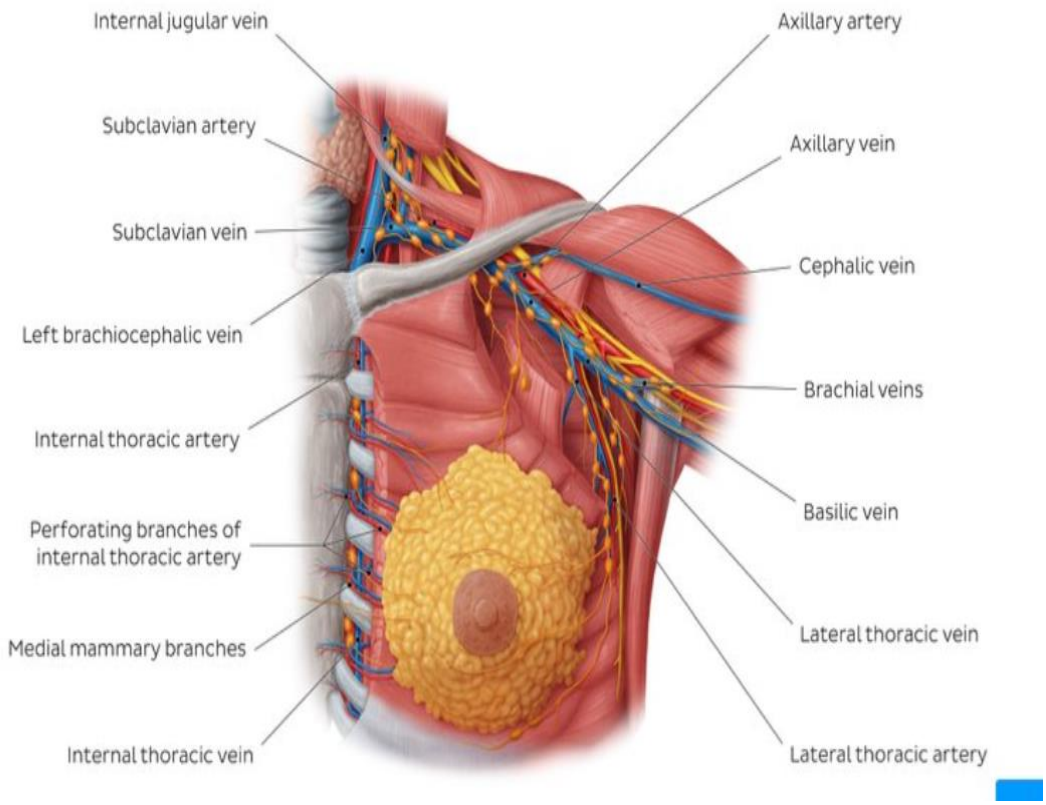



**Fig 3: Arterial supply and venous drainage of breast**

Blood supply of breast is derived mainly from the internal mammary artery (internal thoracic artery), and lateral thoracic artery.

Entire breast both superomedial and superolateral are supplied by internal thoracic artery.

Internal mammary artery also gives rise to posterior intercostal arteries, and branches of intercostal arteries penetrate deep surface of the breast.

**Branches of Axillary Artery**

(1) Supreme thoracic branch.

(2) Pectoral branches of thoracoacromial artery.

(3) Lateral thoracic arteries.

Lateral thoracic artery is most important of these vessels. Axillary vasculature supplies lateral portion of breast.

**Venous drainage**

**A**xillary, internal thoracic, and 3 to 5 intercostal veins drain mammary gland. These veins follow arteries.Perforating tributaries from medial half of breast carry greater part of venous drainage. They enter internal thoracic vein, joins brachiocephalic vein.

Basilic and Brachial veins together form axillary vein. Axillary vein lies medial or superficial to axillary artery and receives 1 or 2 pectoral branches from breast. As it crosses lateral border of 1 rib, the axillary vein becomes subclavian vein.

Intercostal veins communicate posteriorly with vertebral venous system, enters azygos, hemiazygos, and accessory hemiazygos veins, which in turn drain to superior vena cava. This pattern of venous drainage explains distant metastasis.

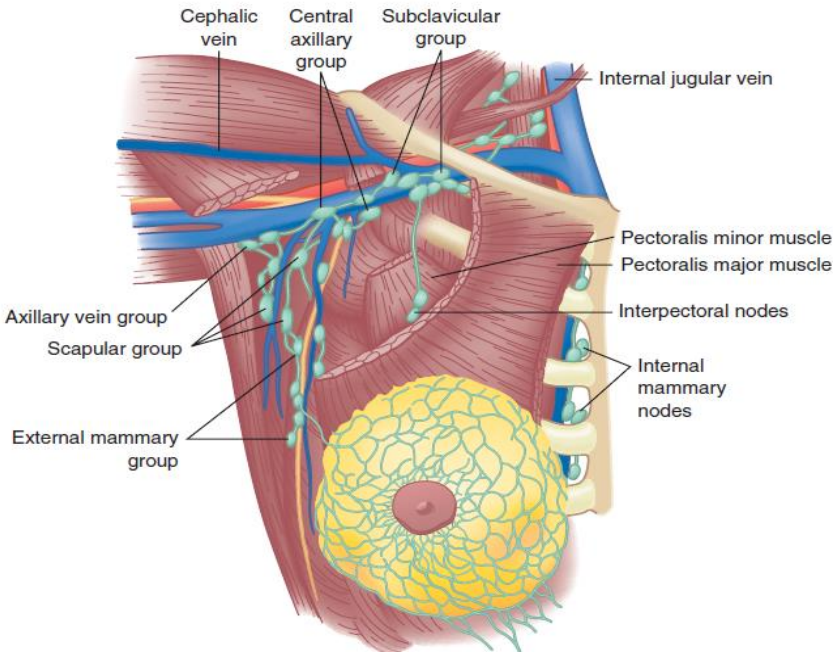



**Fig 4 ; Lymphatic drainage of the breast**

## Lymphatic Drainage [13]

Lymphatic drainage of the breast accompanies blood supply. Drainage from any quadrant of breast passes to axillary nodes (75 %) and to the internal mammary chain (25 %).

**Axillary drainage**

**Group 1. Anterior pectoral nodes.**

Deep to areola there is network of lymphatic vessels, called subdermal lymphatics also known as Sub areolar Plexus of Sappey. These plexuses receive lymph from both medial and lateral part of breast parenchyma.

**Group 2. Scapular nodes**

Lymphatics from these intercommunicate with intercostal lymphatic vessels. They lie along the subscapular vessels and their thoracodorsal branches.

**Group 3. Central nodes**

Largest group of lymph nodes; they are palpated easily in axilla.

**Group 4. Interpectoral nodes (Rotter's nodes)**These lie between pectoralis major and minor muscles. They are smallest group of axillary nodes.

**Group 5. Axillary vein nodes**

This is second largest group of lymph nodes in axilla. They lie on the caudal and ventral surfaces of lateral part of axillary vein.

**Group 6. Sub clavicular nodes**.

They along lie on anterior and posterior surfaces of axillary vein medially. These nodes are inaccessible for dissection.

**Internal Thoracic (Mammary) Drainage**

Lymphatic vessels arise from medial aspect of breast over pectoralis fascia. They run along perforating blood vessels, which, pierce pectoralis major and intercostal muscles to reach internal thoracic nodes. These

nodes also receive lymphatic from skin of opposite breast, liver, diaphragm, rectus sheath, and upper part of rectus abdominis. The nodes, about four to five on each side, are small and are usually in fat and connective tissue of intercostal spaces. Internal thoracic trunks empty into thoracic duct or right lymphatic duct. This route to venous system is shorter than axillary route.

Breast lymphatics drain by way of 3 major routes:

1) Axillary,

2) Trans pectoral

3) Internal mammary.

Inframammary lymph nodes are considered are as axillary lymph nodes for staging purposes; metastasis to any other lymph node is considered distant (M1), including supraclavicular, cervical, or contralateral internal mammary.

Interpectoral (Rotter's) nodes and lymph nodes along axillary vein and its tributaries that may be (but are not required to be) divided into the following levels:

a. Level I : lymph node lateral to lateral border of pectoralis minor muscle.

b. Level II : lymph nodes between the medial and lateral borders of pectoralis minor muscle and Interpectoral (Rotter's) lymph nodes.

c. Level III : lymph nodes medial to medial margin of pectoralis minor muscle including those designated as sub clavicular, infraclavicular, or apical.

Internal mammary (ipsilateral): lymph nodes in intercostal spaces along edge of sternum in endothoracic fascia .

Pathway of metastasis follows direction of lymph flow to lymph nodes (I, then to II and III). Between two muscles there may be a few Interpectoral nodes (of Rotter)

**Nerve supply of breast**[14]

Breast is supplied by motor and sensory nerves. Thoracic nerves provide cutaneous sensation to breast via anterior and lateral perforating branches. Most sensitive portion of breast is nipple, which is innervated by branches of fourth thoracic nerve.Pattern of distribution of these nerves is medial and lateral to nipple, due to which circum areloar incisions along superior and inferior margins are preferred as nerves are unlikely to be damaged.

Pectoralis major muscle is innervated by medial and lateral pectoral (anterior thoracic) nerves.

Dissection of these while performing mastectomy is very important as denervation causes muscle atrophy

Long thoracic nerve (**also called external respiratory nerve of Bell)** innervates serratus anterior muscle. Nerve can be identified by stripping fascia along serratus anterior.

The thoracodorsal nerve innervates latissimus dorsi muscle, during axillary dissection functional integrity should be maintained for reconstructive purpose.

**Nerve to Subscapularis.**

Function of muscle is to both stabilize the humerus in glenoid fossa and flexion, extension, abduction, and adduction of arm, injury to nerve can lead devastating complications. Skin over axilla and upper medial aspect of arm is mainly supplied by intercostal brachial nerve

## EMBRYOLOGY [13]

Mammary gland is derived from epidermal thickenings that develop along anterior surface of body, so-called milk line. Breast undergoes various structural and functional changes from the intrauterine life to aging, which have various implications on developmental anomalies and surgical approach to benign and malignant diseases.

Development of breast occurs after birth growth, further development of branching of the mammary glands progress slowly during the prepubertal years.

Breast increases at puberty with further branching of ducts, formation of acini buds, and proliferation of intraductal stroma.

Major ducts are formed at birth. Mammary glands remain essentially undeveloped until puberty. At puberty, the mammary glands develop rapidly, to stromal and connective tissue around ducts. Growth of duct system is mainly influenced by oestrogen & progesterone.

At time of pregnancy breast achieves both structural and functional activity. Onset of menopause, acini regresses, with loss of both interlobular and intralobular connective tissue, So morphologic appearance of breast in postmenopausal women is much different.

## Physiology of Breast [14]

Lactation is main purpose of mammary gland, which supplies nutrients in new born. Alveoli, small saccules of the lactiferous ducts controlled by interaction of various hormones causes stimulation of milk, any change in these hormonal levels can cause severe histologic changes in breast. Changes occur both in epithelium and stroma and immensely influence morphology.

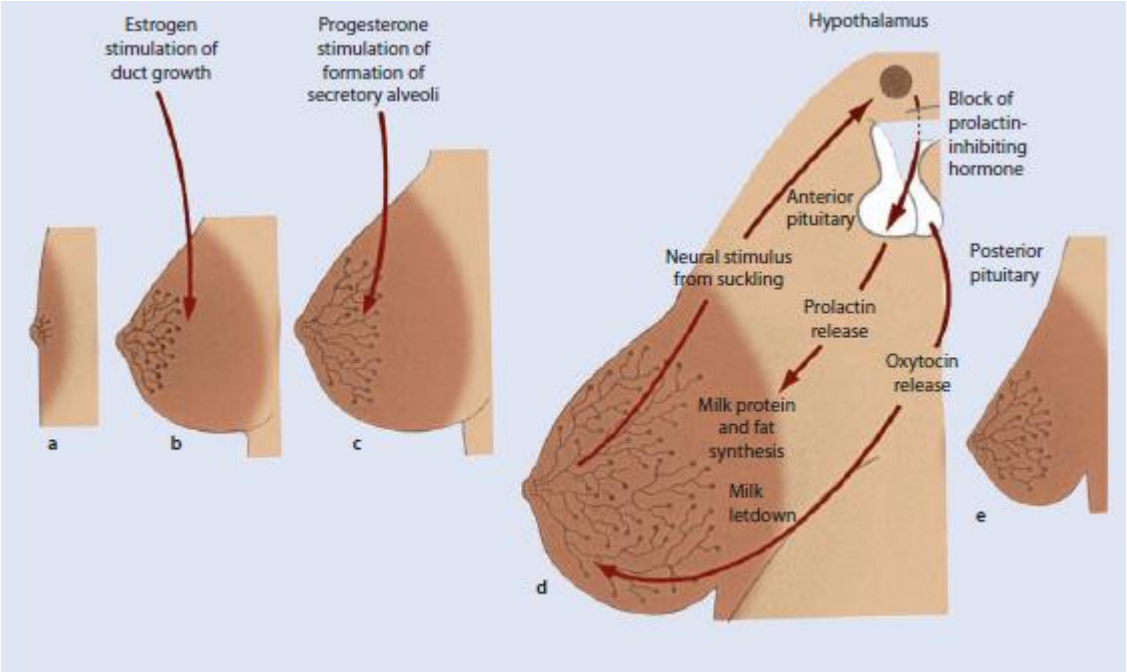



**Fig 5: Physiology of breast**

## Hormones affecting breast

| HORMONES | FUNCTIONS |
|---|---|
| ESTROGEN | Required for lobuloalveolar growth |
| PROGESTERON | Lobuloalveolar differentiation and growth |
| GLUCOCORTICOIDS | Enhances lobuloalveolar growth |
| GROWTH HORMONE | Lactational Stimulus, Maintains mammary epithelial cell survival |
| INSULIN | Growth of mammary epithelium, Enhances ductal alveolar growth |
| PROLACTIN | Lactogenesis and lactation |

| | |
|---|---|
| HUMAN PLACENTAL LACTOGEN | Stimulates alveolar growth |
| THYROID HORMONES | Increases epithelial secretory response to Prolactin |
| OXYTOCIN | Causes contraction of myoepithelial cells and milk ejection |

## Risk Factors for Breast Cancer [14]

### Hereditary Risk Factors

### Racial factors

BC incidence and mortality are relatively higher in western nations like USA, UK and Canada compared to Asians but recently there is also increase in Asian population.

### Family history

All women having first degree relative with breast cancer are a higher risk of developing cancer. There is always double risk of breast cancer with risk increasing age, more with younger age group. Risk also increases with number of relatives affected, age of diagnosis, unilateral, bilateral.

**Genetic Mutations:**

| Gene (Syndrome) | BC risk by Age 70 | Other Associated Cancers |
|---|---|---|
| P53 (Li Fraumeni | >90% | Sarcoma (soft tissue and osteo), brain tumours, adrenocortical carcinoma, leukaemia, colon |
| PTEN (Cowden) | 25-50% | Thyroid, endometrial, genitourinary |
| STK11/LKB1 (Peutz-Jeghers) | 45% to 50% | Small intestine, colorectal, uterine, testicular, ovarian sex cord |
| BRCA1 (HBOC | 45% | Ovarian, pancreatic |
| BRCA2 (HBOC) | 35% | Ovarian, prostate, pancreatic, male BC |

Most well-known genes for increased susceptibility to breast cancer are BRCA 1 and BRCA2. Risk of developing breast cancer by the age of 70 years is 46% to 65%. ATM (ataxia-telangiectasia), BRIP1 (Fanconi 's anaemia), PALB2 are the other genes associated with an increased risk

**Menstrual and Reproductive Factors**

Prolonged exposure to both exogenous and endogenous oestrogen will increase the risk of breast cancer.

**Age at Menarche**

Later onset of regular menstrual cycles, less exposure to the oestrogen. Approximately 10% reduction in BC risk for every 2-year.

**Age at Menopause**

Prolonged exposure to oestrogen due delayed menopause can cause more chances of BC.

**Pregnancy**

Number of pregnancies a woman has and age at which she has her first full-term pregnancy can influence breast cancer risk as well. Protective effect comes from the full cellular differentiation in breast that occurs during and after pregnancy.

Nulliparous women have a RR of about 1.5 due to prolonged and uninhibited oestrogen action.

**Hormone Levels**

Association between hormonal levels and BC risk play a vital role in development of BC. Association is strongest when looking at ER- and PR positive tumours.

**HRT**

It is a relatively modest risk, estimated to be about a 1.24-fold increase. Length of time a woman uses HRT is also important. concurrent use of HRT is associated with highest risk of hormone-positive BC.

**OCPs**

There is significant difference in OC users versus non users. Prolonged usage of the drugs increased the risk by 14%. oestrogen containing pills are associated with increased risk of breast cancer.

**Personal habits**

**Obesity**

High BMI is associated with increased levels of oestrogens. Obesity is strongly associated with increased risk of BC in post-menopausal women.

**Physical Activity**

Exercise has been linked to a decreased production of oestrogen metabolite there by reducing risk of cancer in both premenopausal and postmenopausal women. It helps reduce obesity and reduces serum oestrogen levels in postmenopausal women.

**Diet**

Dietary fat is more significant in younger women, particularly in prepubertal years. This may have more impact on age of menarche and subsequent BMI.

Alcohol consumption is also associated with an increased risk of breast cancer. Effect may be additive with HRT.

**Breast Feeding**

Breast feeding has been protective factor for women. A 4.3% decrease in risk for every 12 months of breast-feeding. Addition to a decrease of 7% for each birth. It is most likely due to a delay in the return of ovulatory cycles and a decrease in oestrogen production.

**Proliferative Lesions without Atypia**

Benign lesions can be categorized as proliferative or non-proliferative. Non-proliferative lesions are not associated with increased risk for BC, whereas proliferative lesions may be associated with an increased risk of either non-invasive or invasive disease.

Risk depends upon degree of atypia associated with lesion

**Other Factors**

Cigarette smoking has been implicated as increasing carcinoma breast. Silicone breast implants, electromagnetic fields, electric blankets, antiperspirants, and hair dyes have all been implicated as causes of carcinoma breast. Ionizing radiation at a young age is associated with increased risk of carcinoma breast. Women treated previously for Hodgkin ‘s lymphoma in younger age are more prone for carcinoma breast.

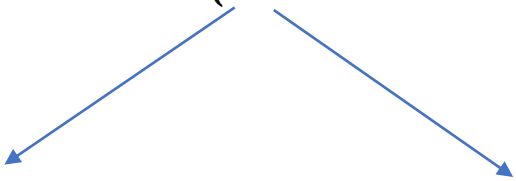
**Pathology of carcinoma breast**

Carcinoma breast arises from the epithelium of the duct system anywhere from nipple end of major lactiferous ducts to terminal duct unit, of each breast lobule. Disease in situ initially which may progress over a period of time.

Degree of differentiation of tumour is usually described using 3 grades:

1. Well differentiated,
2. Moderately differentiated, or
3. Poorly differentiated

**Pathology of carcinoma breast (Foot and Stewart classification)**



| **Non-invasive carcinoma** | **Invasive carcinoma** |
|---|---|
| Ductal carcinoma in situ | Invasive ductal carcinoma (80%) |
| Lobular carcinoma in situ | Invasive lobular carcinoma- 10% |
| Paget's disease of the nipple | Mucinous carcinoma -2% |
| | Medullary carcinoma -5% |
| | Papillary carcinoma -1% |
| | Tubular carcinoma -1% |
| | Adenoid cystic carcinoma |
| | Secretory (juvenile) carcinoma |
| | Apocrine carcinoma |
| | Carcinoma with metaplasia |
| | Inflammatory carcinoma |

Ductal carcinoma is most common type than Lobular carcinoma next making in up to 15% of cases. Various subtypes of LC including the classical type, which has a better prognosis than the pleomorphic type.
There are various patterns depending on histological type. If there is doubt whether a tumour is predominantly lobular in type. Diagnosis of variants of lobular type is mainly done by IHC assay by using e-cadherin.

Colloid carcinoma a rare variant has better prognosis. the cells of this variety produce abundant mucin, whereas medullary type variant has sheets of large cells often associated with a marked lymphocytic reaction.

Invasive LC are often multifocal and/or bilateral. screening programme have made earlier detection of smaller tumours and better differentiation than presenting at advance stage.

Inflammatory carcinoma is a aggressive cancer presents as painful, swollen, with cutaneous oedema and erythematous breast. As a result of blockage of the sub dermal Lymphatics with carcinoma cells. Inflammatory cancer usually involves at least one-third of the breast and may mimic a breast abscess. A skin biopsy will confirm the diagnosis and show undifferentiated carcinoma cells. It's a fatal form but with aggressive salvage surgery and chemoradiotherapy the prognosis has improved considerably.

Carcinoma in situ is pre-invasive cancer that has invaded basement membrane. This is a rare entity usually asymptomatic, found during breast biopsies. There is a increase in incidence due to advent of mammographic screening. Carcinoma in-situ may be ductal (DCIS) or lobular (LCIS), latter often being both multifocal and bilateral. Both are precursors of invasive cancer, seen in at least 20% of patients

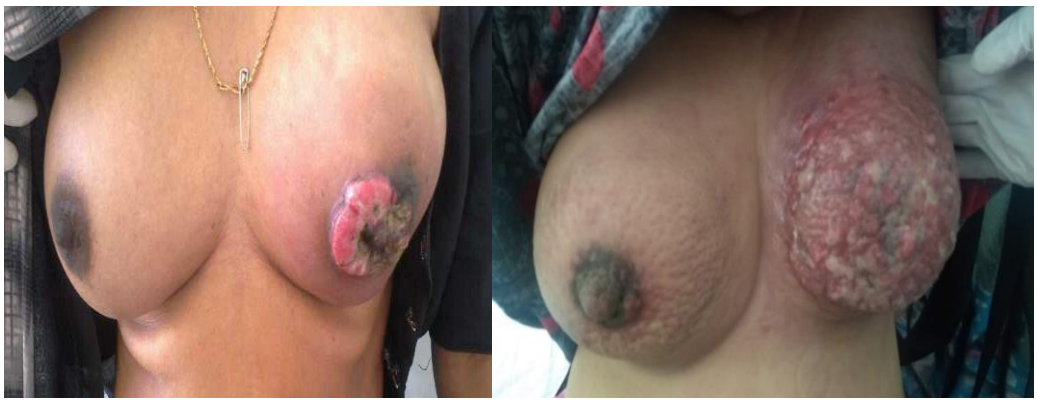


**Fig 6: Paget's disease of nipple**

Paget 's disease of nipple is a superficial manifestation of an underlying BC. It presents as eczema-like condition of nipple and areola. Nipple is

eroded slowly. The underlying carcinoma will sooner become clinically evident. Nipple eczema should be biopsied if there is any doubt about its cause. Paget ‘s disease is characterised by presence of large, ovoid cells with abundant, clear, pale-staining cytoplasm in the Malpighian layer of the epidermis.

**Spread of carcinoma breast**

**Local Spread**

Local spread is by penetration of tumour cells into skin, portions of breast and pectoral muscles. Tumour size increases in advanced stage in can involve chest wall.

**Distant Metastasis**

**Through Lymphatic route**

Axillary & internal mammary lymph nodes are main source of lymphatic metastasis occurring primarily from tumours in posterior one third of the breast. Represents not only mode of spread of carcinoma but is also signifies the virulence of metastatic potential of that tumour. Involvement of supraclavicular nodes and of any contralateral lymph nodes represents advanced disease.

**Mechanisms involved**:

By Permeation: Malignant cells proliferate through lymphatic vessels up to lymph node level.

By Embolization: Cells get dislodged from lymphatic vessels and freely travel to spread into further lymph nodes. i.e. From Axillary node to Supraclavicular node.

**Haematogenous Route**

Homogenous route is mainly responsible for skeletal metastasis, spine metastasis is through batsons venous plexuses.

Order of frequency is lumbar vertebrae, femur, thoracic vertebrae, rib and skull.

**Trans celomic spread**

Metastatic deposits can be seen on functional ovaries in premenopausal women known as krukenbergs tumour.

**Clinical Presentation:**

Lump in breast – location- Most commonly in Upper Outer Quadrant, irregular shape, hard in consistency.

Recent onset of nipple Retraction

Nipple discharge – Serosanguinous, Bloody discharge

Ulceration / fungating

Painful lump- inflammatory carcinoma breast

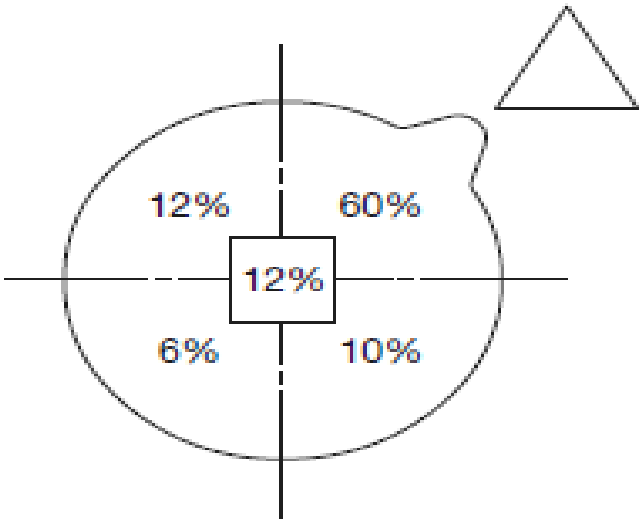



**Fig 7 ; The relationship of carcinoma of the breast to the quadrants of the breast**.

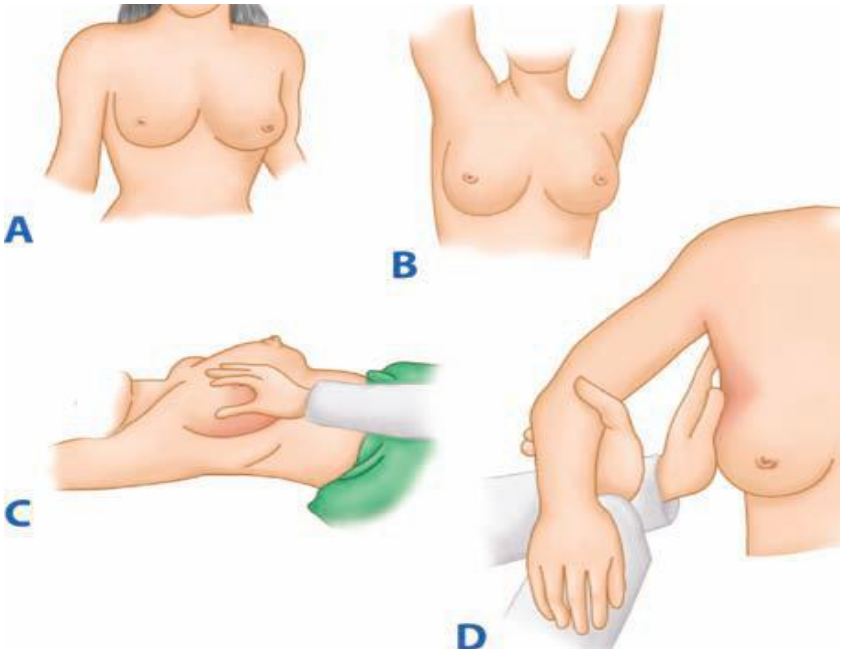



**Fig 8 : Examination of the breast.**

**A. Inspection of the breast with arms at sides.**

**B. Inspection of the breast with arms raised.**

**C. Palpation of the breast with the patient supine.**

**D. Palpation of the axilla**.

**Signs to See:**

Peau d'Orange – Blockage of Subdermal Lymphatics

Recent onset of Nipple Retraction.

Puckering and dimpling of skin

Axillary: Central, subscapular, anterior, posterior apical, Supraclavicular Lymphadenopathy.

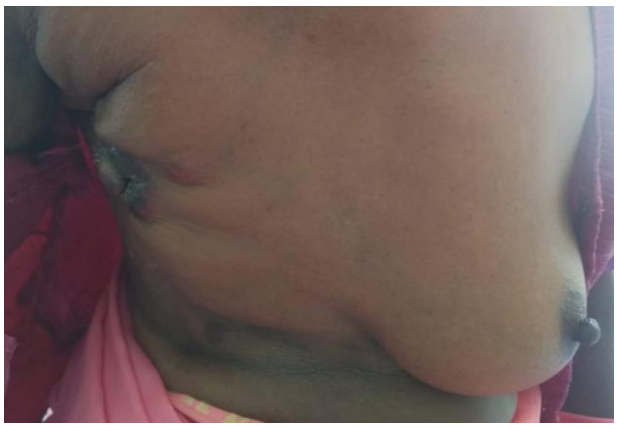


**Fig 9 : Retraction of the right nipple areola complex**

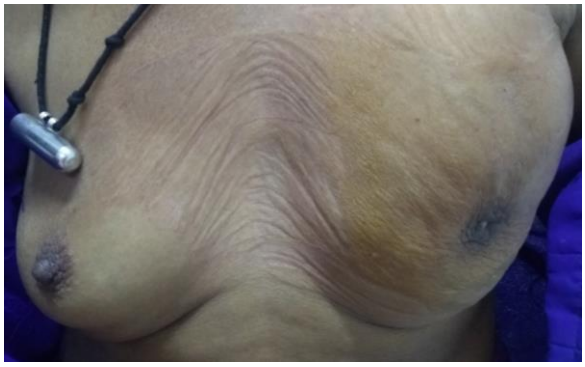


**Fig 10: Left Nipple retraction**

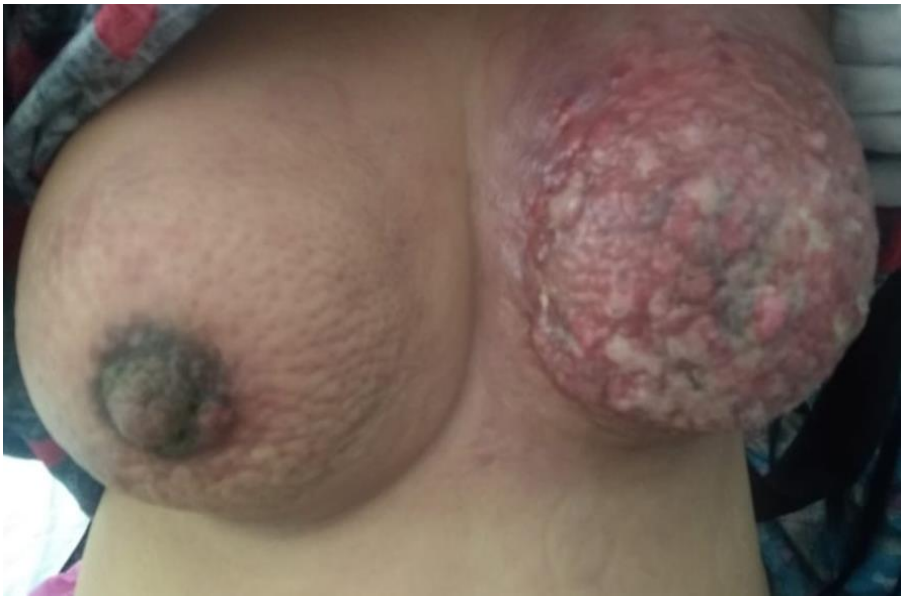


**Fig 11: Cancer en cuirasse**

**Fig 12 : Lump in upper inner quadrant**

## STAGING SYSTEMS IN CARCINOMA BREAST

## MANCHESTER CLASSIFICATION OF CARCINOMA BREAST

Stage 1: Growth is confined to breast

Stage 2: Growth is confined to breast but palpable axillary lymph nodes are present.

Stage 3: Growth extends beyond parenchyma, skin invasion or fixation over large area in relation to size.

Stage 4: Growth extends beyond breast area as shown by fixing or matting of axillary nodes, complete fixation of tumour to chest, deposits in supraclavicular fossa nodes or in opposite breast, distant metastasis

## TNM STAGING SYSTEM OF CARCINOMA BREAST

### Primary tumor (pT)

- **pTX**: cannot be assessed
- **pT0**: no evidence of primary tumor
- **pTis**: ductal carcinoma in situ, Padget disease, encapsulated papillary carcinoma and solid papillary carcinoma
  - **pTis (DCIS)**: ductal carcinoma in situ without invasive carcinoma
  - **pTis (Paget)**: Paget disease without invasive carcinoma
- **pT1mi**: tumor ≤ 1 mm
- **pT1a**: tumor > 1 mm but ≤ 5 mm
- **pT1b**: Tumor > 5 mm but ≤ 10 mm
- **pT1c**: Tumor > 10 mm but ≤ 20 mm
- **pT2**: Tumour > 20 mm but ≤ 50 mm
- **pT3**: Tumour> 50 mm
- **pT4a**: Extension to chest wall (not including pectoralis muscle)
- **pT4b**: Edema (including peau d orange), ulceration of skin or ipsilateral satellite skin nodules
- **pT4c**: both T4a and T4b
- **pT4d**: inflammatory carcinoma (involves > 1/3 of the breast skin, primarily a clinical diagnosis)

### Regional lymph nodes (pN)

- **pNX**: Cannot be assessed
- **pN0**: No regional lymph node metastasis histologically
- **pN0(i-)**: No regional lymph node metastasis by histology or IHC
- **pN0(i+)**: Isolated tumor cells (cluster ≤ 0.2 mm and < 200 cells)
- **pN0(mol+)**: RT-PCR positive but negative by light microscopy
- **pN1mi**: Micro metastasis (tumour deposit > 0.2 mm and ≤ 2.0 mm or ≤ 0.2 mm and > 200 cells)

- **pN1a**: metastasis in 1 - 3 axillary lymph nodes with at least 1 tumour deposit > 2.0 mm
- **pN1b**: metastasis in internal mammary sentinel lymph node with tumour deposit > 2.0 mm
- **pN1c**: pN1a and pN1b
- **pN2a**: metastasis in 4 - 9 axillary lymph nodes with at least 1 tumour deposit > 2.0 mm
- **pN2b**: metastasis in clinically detected internal mammary nodes with pathologically negative axillary nodes
- **pN3a**: metastasis in ≥ 10 axillary lymph nodes with at least 1 tumour deposit > 2.0 mm or metastasis to infraclavicular lymph node
- **pN3b**: positive internal mammary node by imaging with pN1a or pN1b
- **pN3c**: metastasis in ipsilateral supraclavicular lymph node
- **Distant metastasis (M)**
- **pM1**: distant metastasis histologically proven > 0.2 mm

## ANATOMIC STAGE PROGNOSTIC GROUP

| | |
|---|---|
| 0 | Tis N0 M0 |
| IA | T1 N0 M0 |
| IB | T0 N1mi M0 |
| | T1N1mi M0 |
| IIA | T0 N1 M0 |
| | T1 N1 M0 |
| | T2 N0 M0 |
| II B | T2 N1 M0 |
| | T3 N0 M0 |
| IIIA | T0 N2 |
| | T1 N2 M0 |
| | T2 N2 M0 |
| | T3 N1 M0 |
| | T3 N2 M0 |
| III B | T4 N0 M0 |
| | T4 N1 M0 |
| | T4 N2 M0 |
| III C | Any T N3 M0 |
| IV | Any T Any N M1 |

## Screening and Diagnosis of Breast Carcinoma [14]

Principles of Screening:

Disease should be prevalent and serious enough to justify cost and effort of screening. Screening test must have of both sensitivity and specificity.

Disease has to have an asymptomatic phase where it is detectable.

Early Intervention offers a better prognosis and survival if treatment is initiated soon.

Screening Recommendations

Begin self-examinations and every 3 years clinical breast examination at age 20. Begin annual mammograms and yearly clinical breast examination at age 40.

**Modalities of Breast Imaging**:

**1.Mammogram**

Begin annual mammograms & yearly clinical breast examination at age

Used both for screening in asymptomatic patients and diagnosis of symptomatic patients.

**Technique:**

Two standard views are taken – MLO & CC.

Optional views: Magnification, Spot Compression, Exaggerated CC, Rolled & Tangential Views.

**Suggestive of Malignancy:**

Indistinct / amorphous micro calcifications

Pleomorphic /heterogeneous calcifications

Fine linear / branching calcifications.

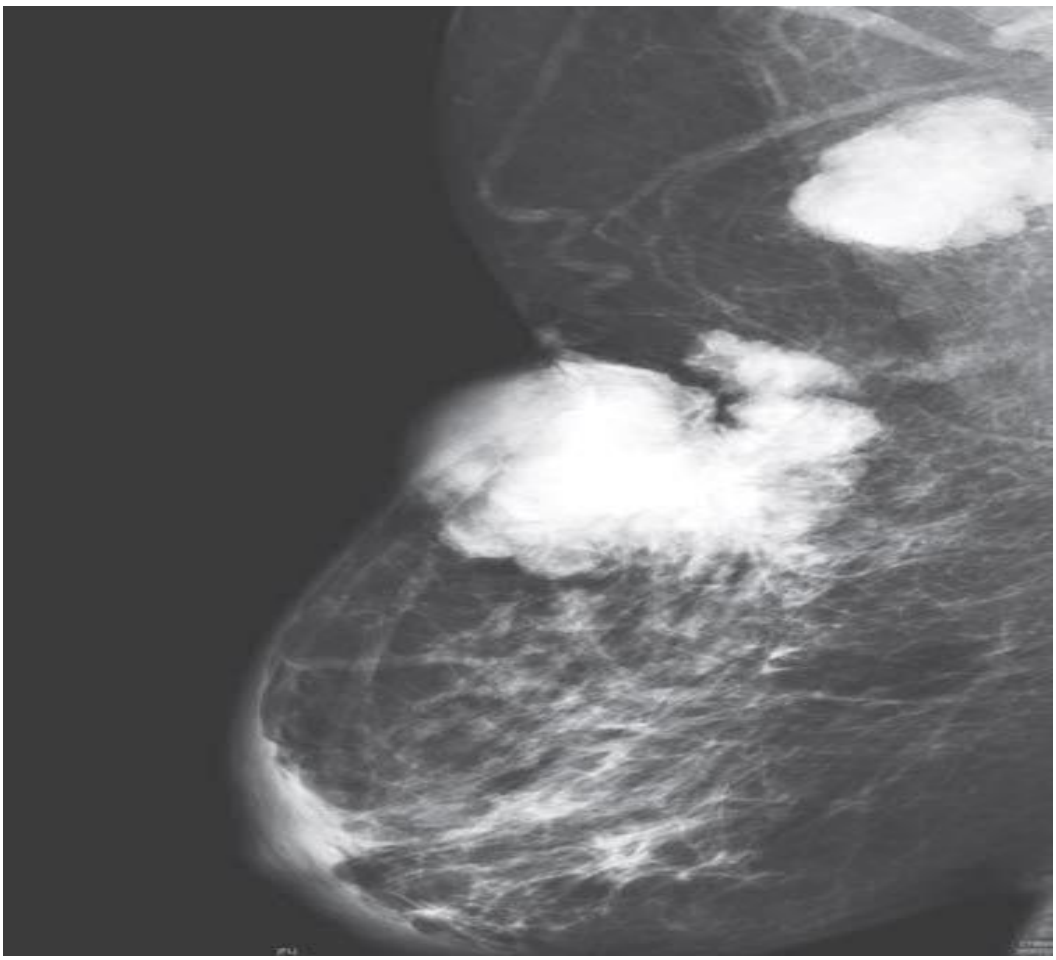


**Fig 13: Extensive calcifications seen throughout the breast on CC view**

**BREAST IMAGING REPORTING AND DATA SYSTEM**

(BIRADS)

| | |
|---|---|
| Category 0 | Incomplete Assessment. |
| Category 1 | Negative. Breasts are normal in appearance. |
| Category 2 | Benign Finding |
| Category 3 | Probably benign finding / high probability of lesion being benign. |
| Category 4 | Suspicious abnormality. |
| Category5 | Highly suggestive of malignancy |

**2**. **Guided Interventional Radiology (Stereotactic Biopsy**): Allows for percutaneous biopsy of lump detected on mammography.

**3**. **Ultrasound (Sonomammography**): Ultrasound now plays a vital role in diagnosis and treatment of breast cancer. Even though it is less reliable to detect micro calcifications, plays a important role in BC screening and also to detect benign conditions.

USG is performed with high-resolution linear array transducer with a frequency of at 7.5 MHz.

**4. Magnetic Resonance Imaging** (MRI):

Recommended Annually Based on Evidence

- BRCA Mutation Carriers
- Untested first-degree relative of BRCA carrier
- Lifetime risk>20% to 25% defined by BRCAPRO or other family history model
- Radiation to chest from age 10 to 30
- Li-Fraumeni syndrome and first-degree relatives
- Cowden syndrome (and variants) and first-degree relatives.

**Insufficient Evidence to Recommend for or Against**

Lifetime risk 15% to 20%

LCIS

ALH or ADH

Personal history of Intraductal or invasive breast cancer

Lifetime risk<15%

Differentiation of benign and malignant lesion.

**Indications and Uses**:

Imaging of Silicone Breast Implants

Occult Primary breast cancer

Assessing candidacy for breast conservation

Screening as adjunct to Mammogram

Response to Neoadjuvant Therapy

Follow up of CB patients

**5. Positron Emission Tomography:**

Principle & Technique: Are anatomic in nature; PET scanning demonstrates physiologic changes.

Indications and Uses:

Detection of distant disease with minimal radiation

## TRIPLE TEST ASSESSMENT [15, 16, 17]

Term ―triple diagnosis refers to combination of physical examination, mammography, and fine-needle aspiration biopsies for diagnosing palpable CB.

Triple assessment helps in differentiating benign from malignant breast lesions sensitivity of triple assessment ranges (0% to 0.6%).

Patients suggestive of benign breast lesions, should follow up for 4 to 6 months for a repeated clinical examination. Follow up of 1-year mandates to confirms lesion as benign. If either mammogram or FNAB is suggestive of malignancy, then a more definitive tissue biopsy is indicated.

## BIOPSIES OF PALPABLE LESIONS

### Fine needle aspiration cytology. [18]

Fine needle aspiration is a quick way to diagnose malignancy in a patient with a breast mass. Surgeon then fixes the tumour with his using the thumb and index finger. Syringe attached to a 21- gauge needle is then placed into breast mass while suction on the syringe is maintained Needle is passed through breast mass in various directions, suction is then released and the needle brought out of breast mass. Tissue debris on needle and tip of syringe is sprayed onto glass slides.

FNAC results are in conclusive or fails at least twice, surgeon can consider for frozen section for tissue diagnosis intraoperatively.

## Fine Needle Aspiration Cytology (FNAC) [18]

| | |
|---|---|
| Benign | No signs of malignancy |
| Atypical / Indeterminate | Non-diagnostic cellular findings |
| Suspicious | Significant Atypia or architectural distortion |
| Malignant | Diagnostic of malignancy |
| Unsatisfactory | Scant cellularity or artefact precluding |

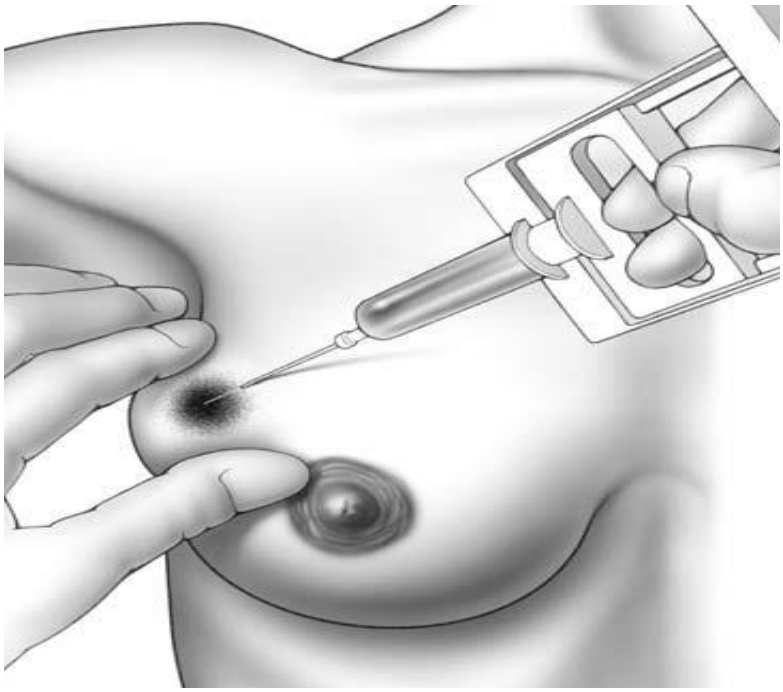


**Fig:14: Fine needle aspiration**

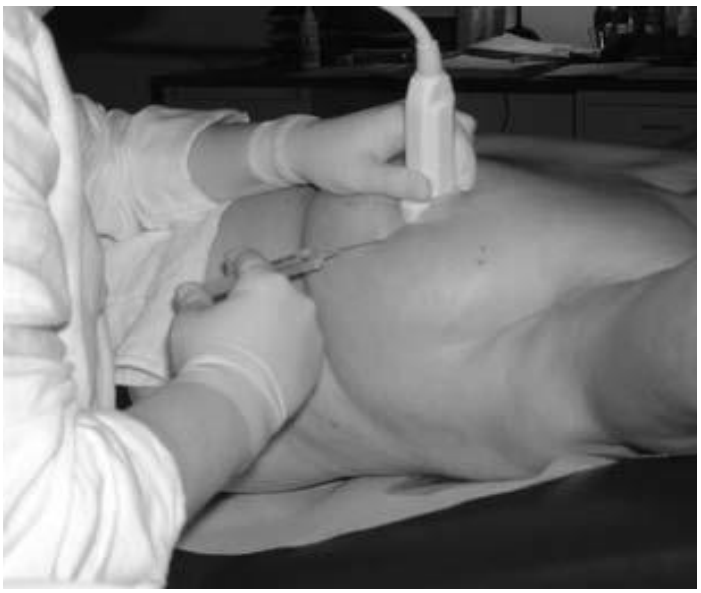


**Fig 15 : Fine needle aspiration under ultrasound guidance**

## 2. Core Needle Biopsy [18]

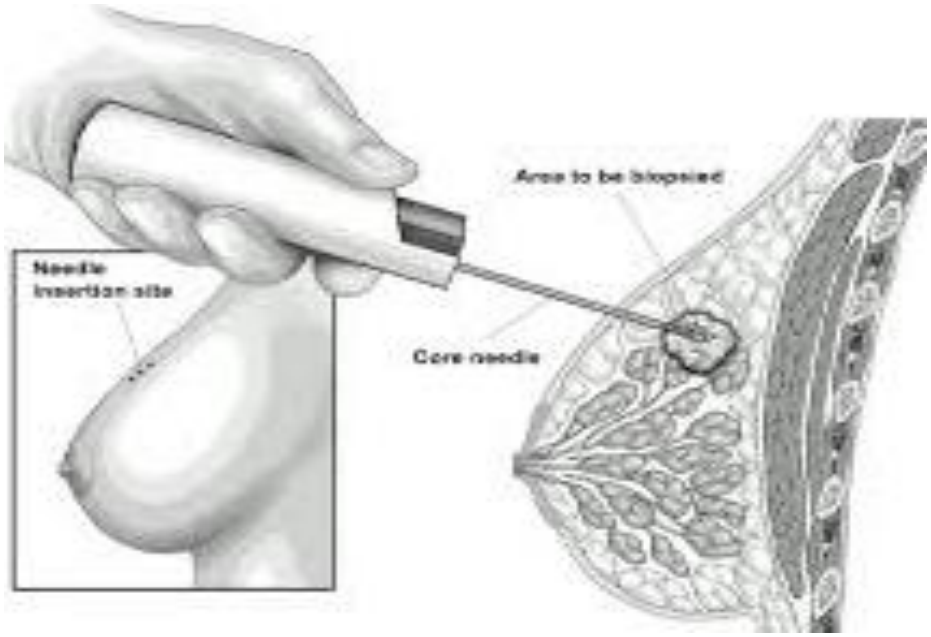



**Fig 16: Core biopsy of the breast lump**

Technique of core needle biopsy can be applied to both palpable and nonpalpable breast lesions. Lesion is palpable, image guidance is not

necessary. Skin overlying breast mass is cleaned with rubbing alcohol and local anaesthetic is injected around intended biopsy site.

A small cut is made on skin overlying breast mass using an 11-blade knife, and tip of biopsy instrument is placed against mass.

Breast mass is then stabilized with one hand, & biopsy instrument fired with other hand. Tissue samples are analysed.

Other biopsies are : Excisional Biopsy, Incisional Biopsy, Frozen Section Biopsy

**Biopsies for Non-palpable lesions**

1. USG Guided Biopsy
2. Stereotactic Needle Biopsy
3. Wire localized Excisional Biopsy
4. MRI guided biopsy

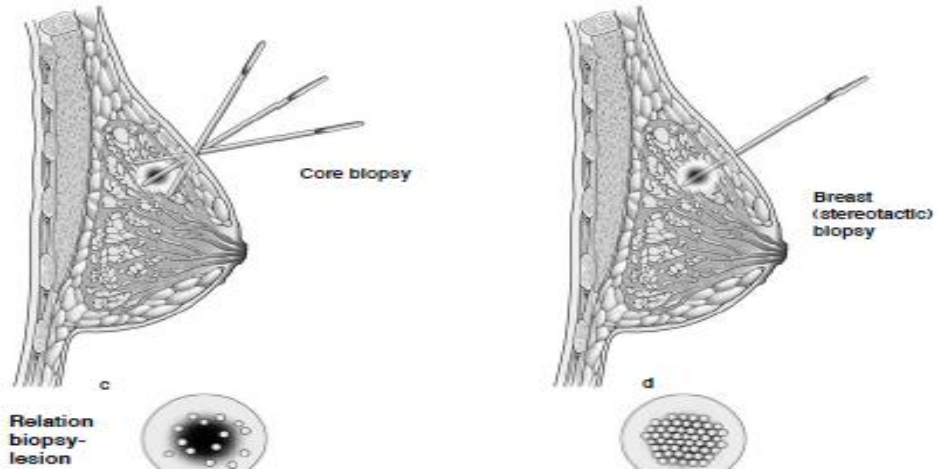



**Fig 17: Comparison of different biopsy techniques, their invasiveness, and amount of tissue sampled.**

**c ) Core biopsy;**

**d) Stereotactic vacuum-assisted biopsy device**

## Needle-localised biopsy [18]

Needle-localized biopsy is performed to assess abnormalities of the breast that are not palpable but are seen on mammogram.

The patient is first transported to the radiology suite, where the mammographic abnormality is localized with a hooked wire. Mammograms with two views are obtained showing the wire and its relationship to the abnormality. These mammograms guide the surgeon during dissection. The needle-localized biopsy can be performed using either local or general anaesthetic, depending on preferences of the patient and surgeon. A curvilinear incision is made immediately adjacent to the wire, along direction of one of natural skin crease lines. Hooks are lifted up with breast tissue at edges of skin. The tissue samples are subjected for analysis.

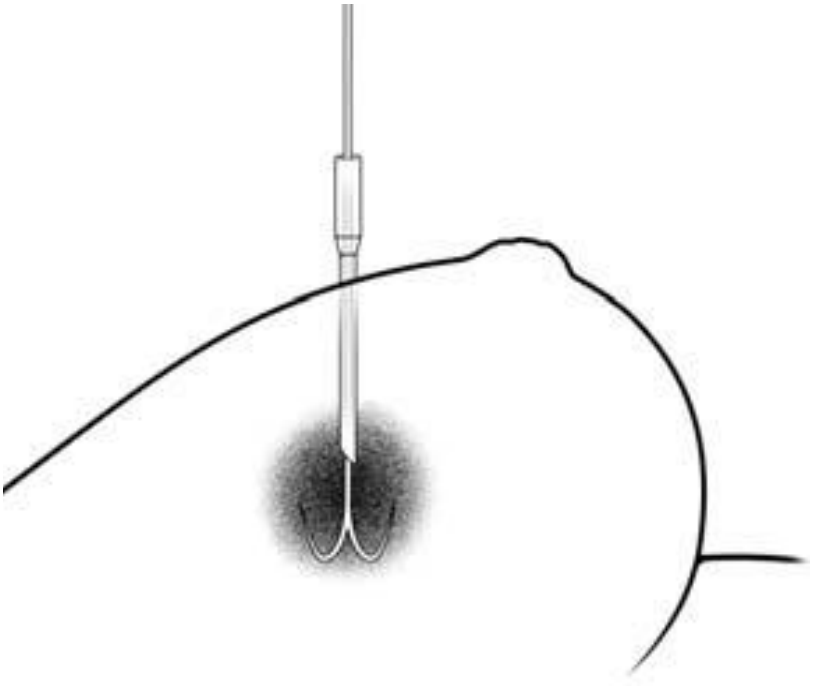


**Fig 18: Needle-localized biopsy**

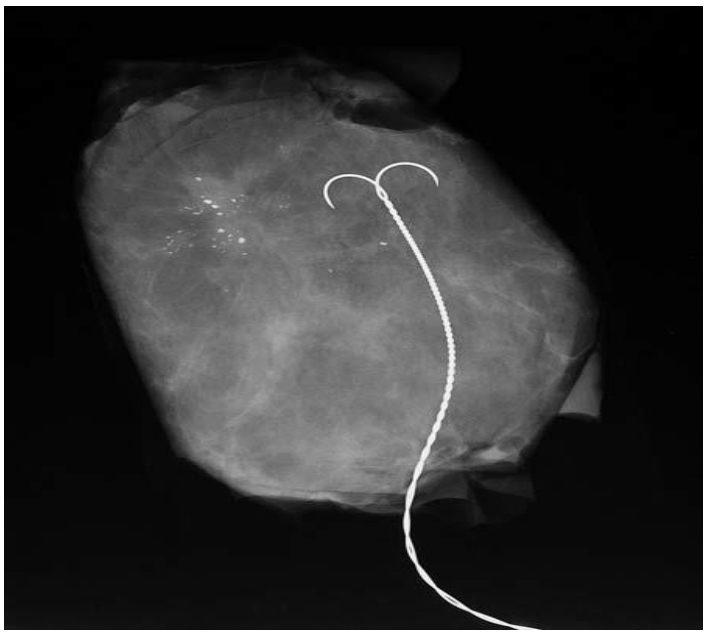


**Fig 19: Radiograph of the breast tissue specimen with microcalcifications**

**Sentinel lymph node biopsy [18]**

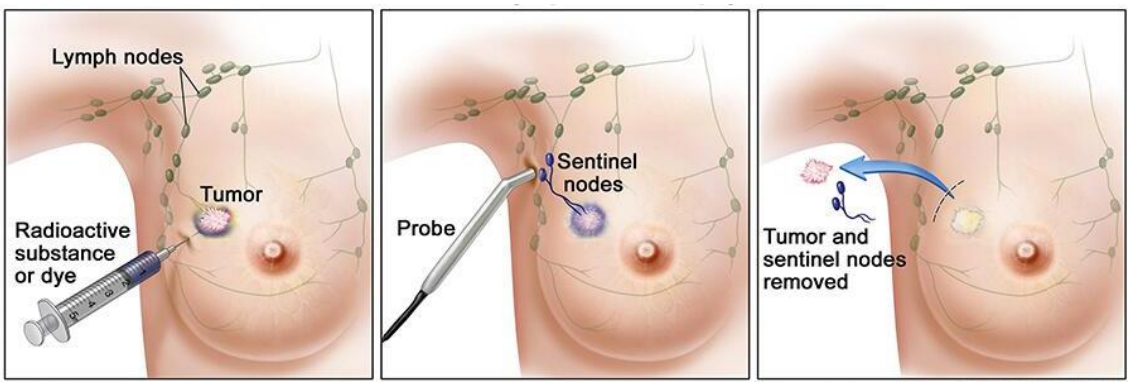



**Fig 20: sentinel lymph node biopsy**

The sentinel lymph node biopsy is a diagnostic test that is used to determine status of regional lymph nodes. sentinel node is first lymph node to receive drainage from a tumour.

Surgeon identifies sentinel lymph node by injecting blue dye and/or radioactive colloid into breast parenchyma around tumour.

Lymphatic mapping agents are carried from breast by afferent lymphatics, & lymph node that initially traps dye and/radiocolloid is identified as sentinel lymph node. Surgeons who use only blue dye will generally make a small incision in the axillary crease, and dissect down into the axilla. If radiocolloid is used, then sentinel lymph node is identified by radioactivity counts emitted from node and recorded by a hand-held gamma probe.

The sentinel node is submitted for histological evaluation. There is no evidence of metastatic disease in sentinel lymph node, then perform a complete axillary lymph node dissection, & the small axillary wound is closed with a running subcuticular stitch.

**Tumour Size**

Measure at least 2 tumour dimensions; however, indicate only size of the invasive lesion, at its greatest dimension.

Always verify tumour size under microscope; in case of difference between tumour sizes, determine gross & at microscopic examination.

In case of multiple tumours, tumour size should not be determined as sum of individual tumour sizes; individual tumour sizes should be reported, and most voluminous tumour will be taken into account for staging. Tumour size greater than 2 cm compared to <0.9 cm was associated with increased risk of local recurrence. Extent >1.5 cm was shown to be a risk for local recurrence. [19]

**Margin Status**

The goal in margin-negative resection is to remove the targeted lesion with a margin of normal breast tissue which recommend a minimum 2 mm radial margin for patients undergoing BCS for DCIS.

A margin of 2 mm between the DCIS and resection appears to be superior to 1mm. [19]

## Tumour Grade

### Nottingham grading system ( Elston-Ellis modification of the Scarff-Bloom-Richardson grading system)

This system grades breast tumours based on the following features:

1. Tubule formation: how much of the tumour tissue has normal breast (milk) duct structures.
2. Nuclear grade: an evaluation of size and shape of the nucleus in the tumour cells .
3. Mitotic rate: how many dividing cells are present, which is a measure of how fast the tumour cells are growing and dividing

Each of categories gets a score between 1 and 3; a score of "1" means cells and tumour tissue look the most like normal cells and tissue, and a score of "3" means the cells and tissue look the most abnormal. The scores for the three categories are then added, yielding a total score of 3 to 9. Three grades are possible:

Total score = 3–5: G1 (Low grade or well differentiated)

Total score = 6–7: G2 (Intermediate grade or moderately differentiated)

Total score = 8–9: G3 (High grade or poorly differentiated)

## ROLE OF HORMONE RECEPTORS, HUMAN EPIDERMAL GROWTH FACTOR (HER-2) ONCOGENE [14, 15, 17]

Receptors status over breast tissue are studied by immunohistochemistry (IHC) or FISH (fluorescent in situ hybridisation) in which cells are stained based on the oestrogen progesterone receptors, her 2neu status.

Critical analysis of these receptors is very important as these help in planning of adjuvant treatment and prognosis of the patient**.**

**ER / PR Status**

ER and PR are steroid receptors located on nucleus of breast tissue. These hormonal receptor statuses of a tumour signify on planning of hormonal therapy. Also predicts response to endocrine therapy (more specifically to anti-oestrogenic tamoxifen) or in-patient selection for alternative first line treatment.

**HER-2 (neu / Erb-2 / Epidermal Growth Factor)**

**T**ransmembrane cell surface glycoprotein receptor with intrinsic tyrosine kinase activity that helps regulate normal growth, division.

HER2 it's an oncogene regulating tumour proliferation, its over expression is linked with increased cell proliferation and independent growth as well as assistance to pro-apoptotic stimuli. It increases tumorigenicity, angiogenesis and metastasis. All these characteristics of the receptor HER2 plays a vital role in cancer biology. HER-2 gene is frequently amplified protein over expressed in many cancers including Breast, Ovarian, Lung, Gastric and Oral. Patients expressing Her-2 neu definitely benefit from monoclonal antibodies directed against such tumours i.e. Herceptin (Trade name: Trastuzumab)

## MOLECULAR BIOMARKERS

Hormone receptors and Her-2 neu expression are evidently used as Prognostic and Predictive indicators in carcinoma breast.

Gene expression profiling has identified 5 molecular subtypes of carcinoma breast.

ER/PR+, Her-2+ = Luminal B

ER/PR+, Her-2- = Luminal A

ER/PR-, Her-2+ = Her-2 Over expression

ER/PR-, Her-2- = Triple Negative Breast Cancer (TNBC)

## TRIPLE NEGATIVE CANCER [15, 16, 17]

i.e. ER-,PR-,Her-2- carcinoma breast also called as Basal-like cancer. Consistent trend across studies confirming unfavourable clinical outcomes. It is usually seen in women who carry a disease associated mutation in BRCA1 but not BRCA2. Patients with TNBC do not benefit from hormonal therapy.

Score for proportion staining multiplied by score for staining intensity is equal to score.

Score 0 - ineffective endocrine treatments.

Score 2–3 indicates a 20% chance of response to endocrine treatment.

Score 4–6 indicates a 50% chance of response to endocrine treatment.

Score 7–8 indicates a good (75%) chance of response to endocrine treatment.

## PROTOCOL FOR IHC

Formalin-fixed, paraffin-embedded tissue blocks were sectioned at 3-4 um thickness.

Cut and mount thin paraffin sections on slides coated with (3-Aminopropyl) Triethoxysilane.

Place sections in hot air oven overnight at 58C prior to start deparaffinization.

Deparaffinize sections in a fresh Xylene for 2 changes into 15 minutes each.

Rinse sections in absolute alcohol for 2 changes into 2 minutes each.

Transfer sections to running tap water for 5 minutes.

Rinse sections in distilled water for 5 minutes.

Bring sections to a pressure cooker containing Tries-EDTA buffer at pH – 9.0. Heat until the pressure cooker reaches 4 whistles.

Allow to cool sections from 15-20 minutes at room temperature.

Rinse sections in distilled water for 2 changes, 2 minutes each. 66

Placed sections in 0.3% hydrogen peroxide in distilled water for 20 minutes, to inhibit the endogenous peroxidase activity.

Wash sections in 0.05 Molar Tri-buffered saline wash buffer at pH – 7.6 for 2 changes, 2 minutes each. Place sections in 2% skimmed milk prepared in TBS buffer for 30 minutes, to inhibit the non-specific background staining.

Transfer diluted primary antibody to sections and incubate for 1.30 hours at room temperature.

Wash sections in TBS buffer for 2 changes, 2 minutes each.

Place sections in 2% skimmed milk prepared in TBS buffer for 3 minutes.

Apply super enhancer to sections and incubate for 30 minutes at room temperature.

Wash sections in TBS buffer for 2 changes, 2 minutes each.

Place sections in 2% skimmed milk in TBS buffer for 3 minutes.

Apply Polymer HRP-reagent and incubate for 30 minutes at room temperature.

Wash sections in TBS buffer for 2 minutes, 2 minutes each

.

Apply m substrate to sections and allow for 5-10 minutes.

Wash sections in TBS buffer for 2 minutes.

Rinse in distilled water for 2 changes, 2 minutes each.

Counterstain with Haematoxylin for 20-30 seconds.

Blot and mount the sections in DPX. 67

**Scoring for Her-2 was as follows**

**Her 2 nu 1+**

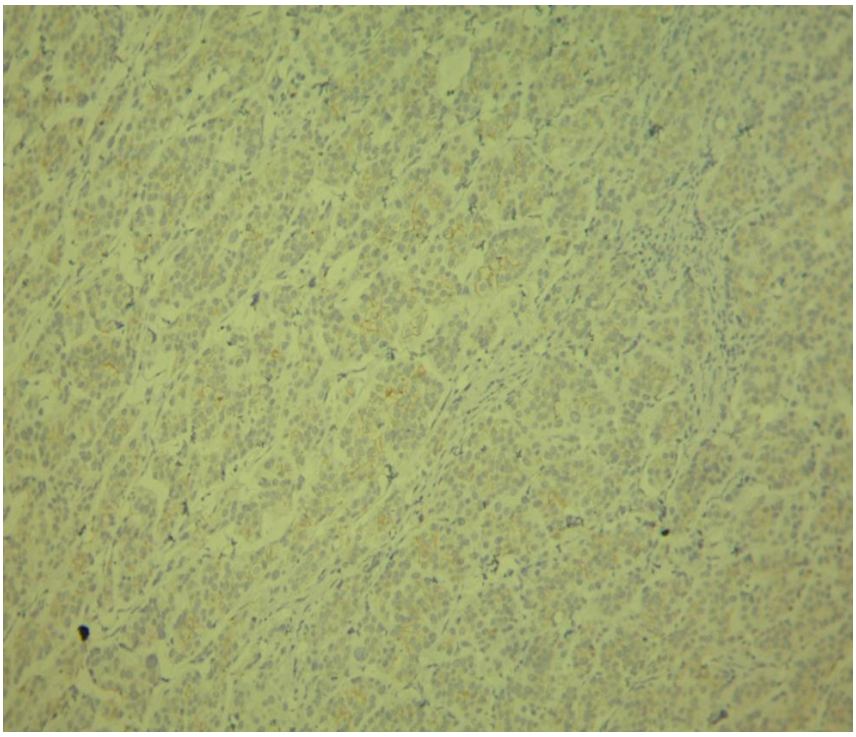


**Fig 21: Faint/ barely perceptible and in >10% of tumor cells. 40x. IHC stain.**

**Her 2 nu 2+**

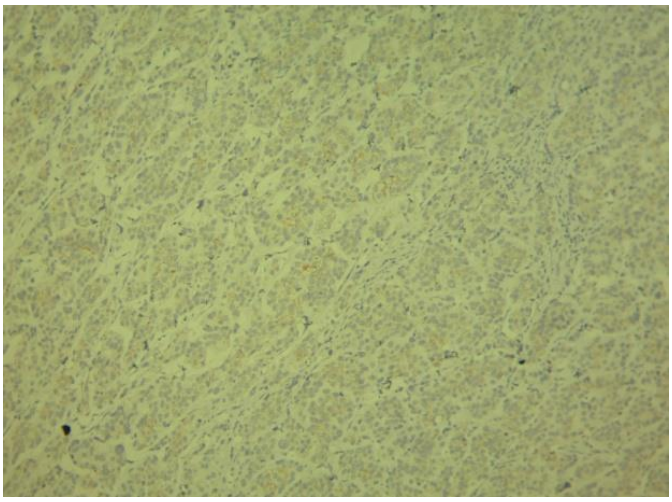


**Fig 22:Faint/ barely perceptible and in >10% of tumor cells. 40x. IHC stain.**

**Her 2 nu 3+**

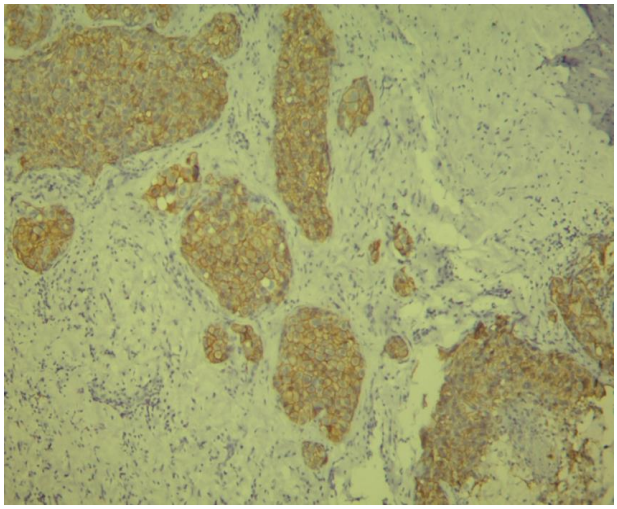


**Fig 23: Intense staining in >10% of tumor cells. 100x IHC stain.**

**Management of carcinoma breast**

**Classification of staging**

| | |
|---|---|
| Early Breast Cancer | Stage I, IIa, IIb. |
| Locally Advanced | Stage IIIa, IIIb, IIIc |
| Distant Spread | Stage IV |

**Early Breast Cancer** [21,22,23]

Stage I, IIA, or IIB are known as early breast cancer.

All patients should undergo a full clinical examination, bilateral mammogram, tissue diagnosis with local regional workup in form of CT.

Lumpectomy, modified radical mastectomy and radiation therapy are preferred method of treatment for women of stage I and II.

Accelerated partial breast irradiation (APBI) is also option for carefully selected patients with DCIS and early stage breast cancer. Lower total dose compared with standard course of 5 to 6 weeks of radiation (50 Gray with or without a boost) was given to patients in early BC.

**Advanced Local-Regional Breast Cancer** [24,25, 26]

Women with stage II , IIIA and IIIB BC have advanced local-regional BC but have no clinically detected distant metastases.

In LABC surgery is integrated with radiation therapy and chemotherapy.

Surgical therapy for women with operable stage IIIa disease is usually a modified RM. followed by adjuvant chemotherapy: followed by adjuvant radiation therapy.

ACT is used to maximize distant disease-free survival, while radiation therapy is used to maximize locoregional disease-free survival.

For inoperable stage IIIa and for stage IIIb breast cancer, NCT is used to decrease the locoregional cancer burden and can permit subsequent surgery to establish locoregional control.

In an advanced form of disease, it usually has a prolonged clinical course; nevertheless, LABC represents a relatively common presentation in our country.

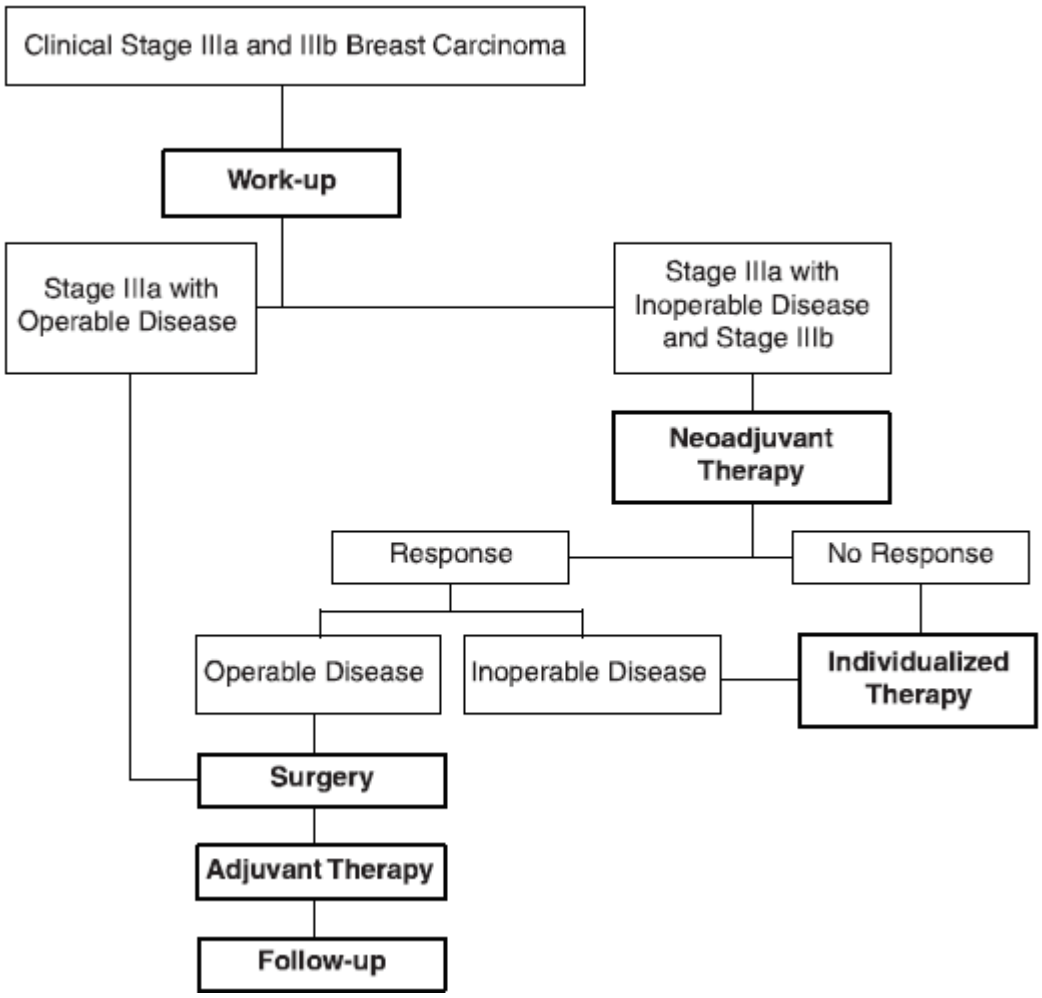



**Fig 24: Schematic representation of management of carcinoma breast**

**Distant Metastases (Stage IV)** [27, 28]

Treatment for stage IV BC is not curative but may prolong survival and enhance a woman's quality of life.

Clinical manifestation of metastatic breast cancer depends on the site and size of metastasis. MC organs that metastasises are the bone, lung, liver and brain.

Metastases to bone usually manifest with progressive pain which is usually a dull ache, often worse at night and often affects the back, pelvis and hips. Pathological fracture is a relatively common

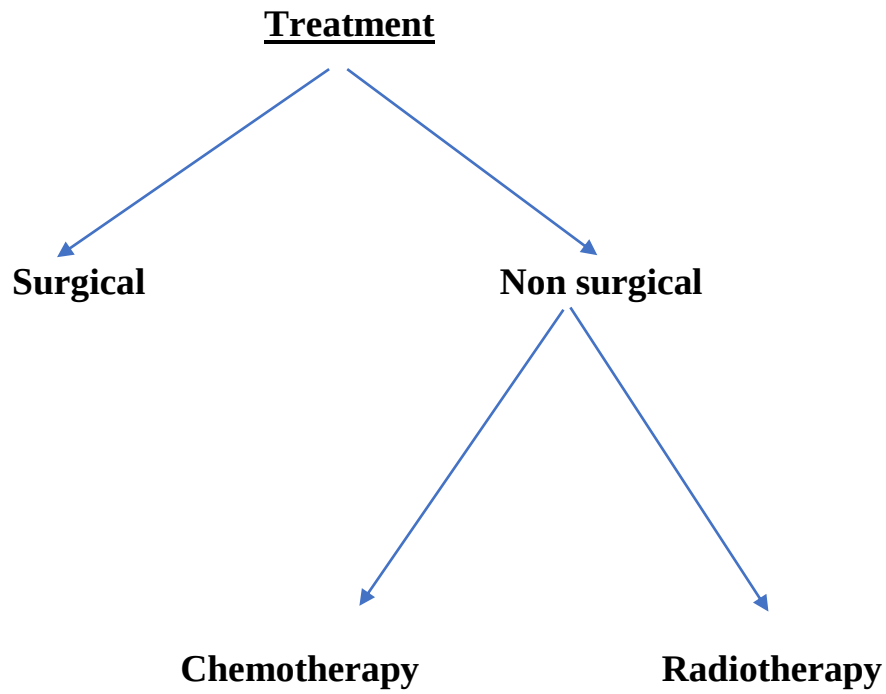
Women with stage IV breast cancer may develop anatomically localized problems that will benefit from individualized surgical or radiation treatment such as Bisphosphonates, which may be given in addition to chemotherapy or endocrine therapy, should be considered in women with bone metastases.

1.More serious is impending or actual spinal cord compression due to spinal metastases, and suspicion of this (back pain, loss of bladder or bowel control, perineal numbness) is a medical emergency.

2. Metastasis to lung is associated with chronic non-productive cough, breathlessness or chest pain due to pleural involvement.

3. Metastasis to liver is associated with abdominal pain, abdominal swelling, anorexia, nausea, vomiting, jaundice and pruritus.

4. Metastasis to brain may have several neurological consequences including progressive headache (typically worse in the morning), vomiting, visual disturbance, loss of balance, seizures, personality change and focal symptoms.




**Surgeries for Breast Carcinoma**

Surgery still has a vital role in the management of BC but there has been a gradual shift towards more conservative techniques. There is equal efficacy between mastectomy and local excision followed by radiotherapy.

**Principles**

Achieve local control + Appropriate surgery

1. Breast conservative surgery
2. Mastectomy and axillary dissection
3. Modified radical mastectomy
4. Reconstruction of breast and chest wall.

## SURGICAL MANAGEMENT OF BREAST CANCER

### Breast conservative surgery

Breast conservation involves resection of the primary breast cancer with a margin of normal-appearing breast tissue, adjuvant radiation therapy, and assessment of regional lymph node status.

Breast conservation surgery is currently the standard treatment for women with stage 0, I, or II with N02 breast cancer.

Resection of the primary breast cancer is alternatively called segmental mastectomy, lumpectomy, partial mastectomy, wide local excision, and tylectomy.

**Contraindications**

a) prior radiation therapy to breast or chest wall.
b) Involved margins or unknown margin status following re excision.
c) Multicentric disease.
d) Scleroderma or connective tissue disease.

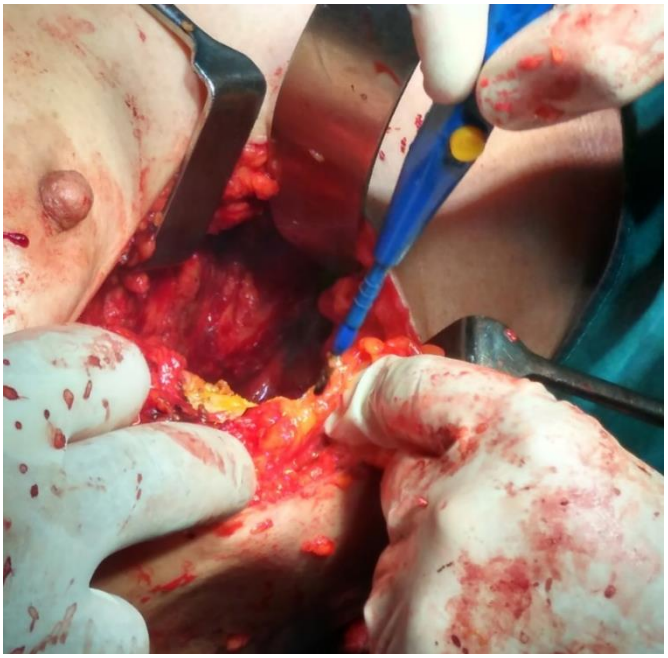


**Figure 25 : Breast conservative surgery**

## Mastectomy

A skin-sparing mastectomy removes all breast tissue, the nipple-areola complex with the tumour. Recurrence rate of less than 6% to 8%.

A total (simple) mastectomy without skin sparing removes all breast tissue, the nipple-areola complex, and skin.

An extended simple mastectomy removes all breast tissue, the nipple-areola complex, skin, and the level I axillary lymph nodes.

**Complications of mastectomy**

Wound Infection

Seroma

Hematoma / Haemorrhage

Chronic Pain

Flap Necrosis

Chronic Breast Lymphedema / Cellulitis

## MODIFIED RADICAL MASTECTOMY

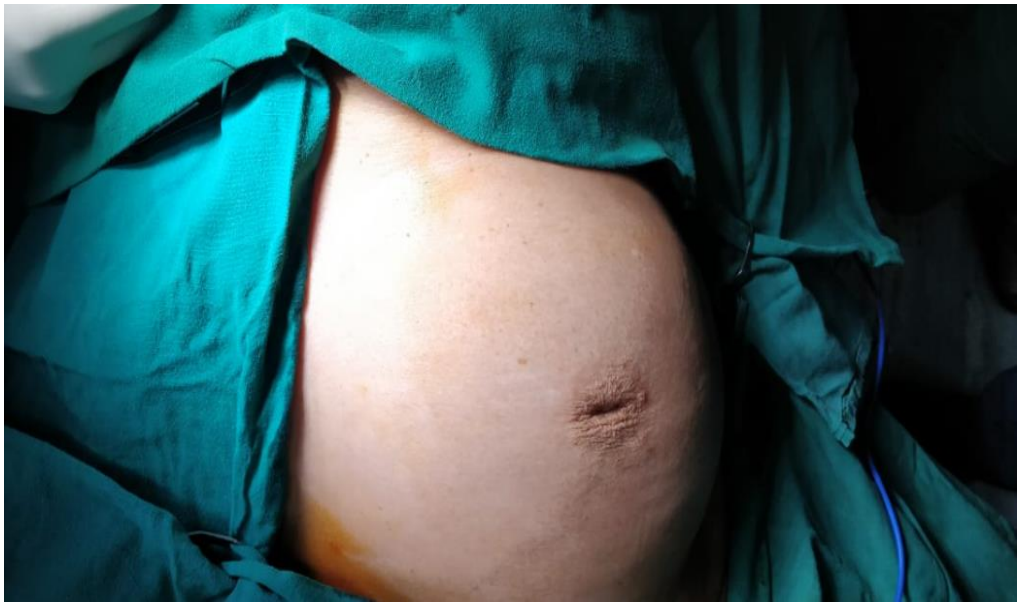


**fig ;26  Lump in left breast**

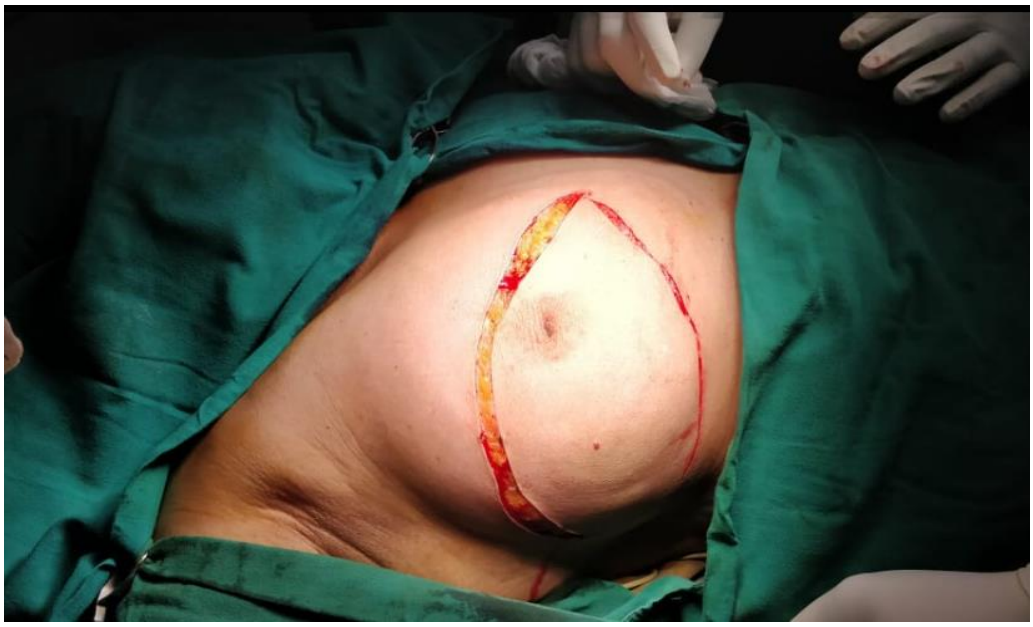


**Fig 27 : Left Stewart Incision**

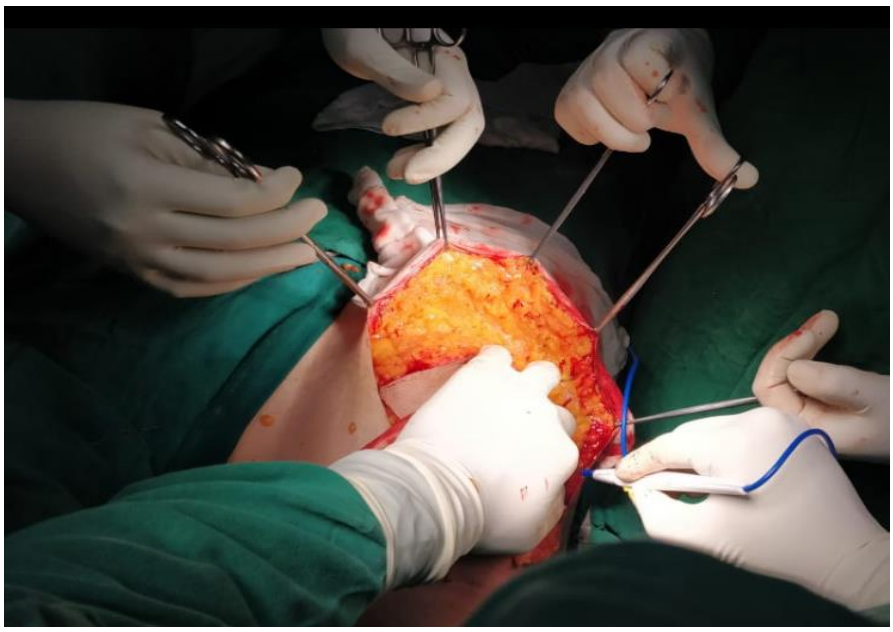


**Fig 28: Upper skin flaps in Left MRM**

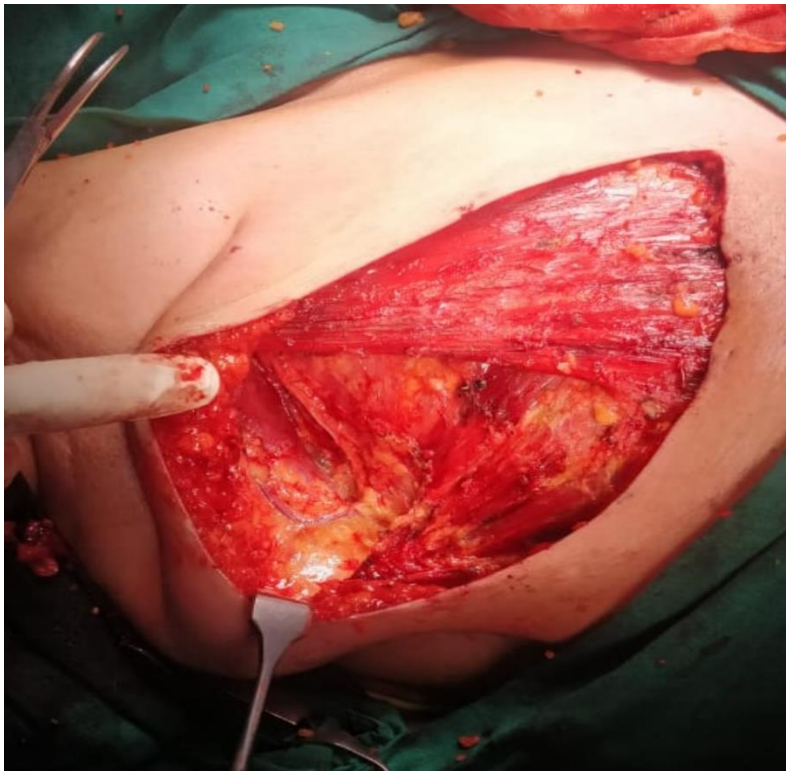


**Fig 29 : Demonstration of axillary vein**

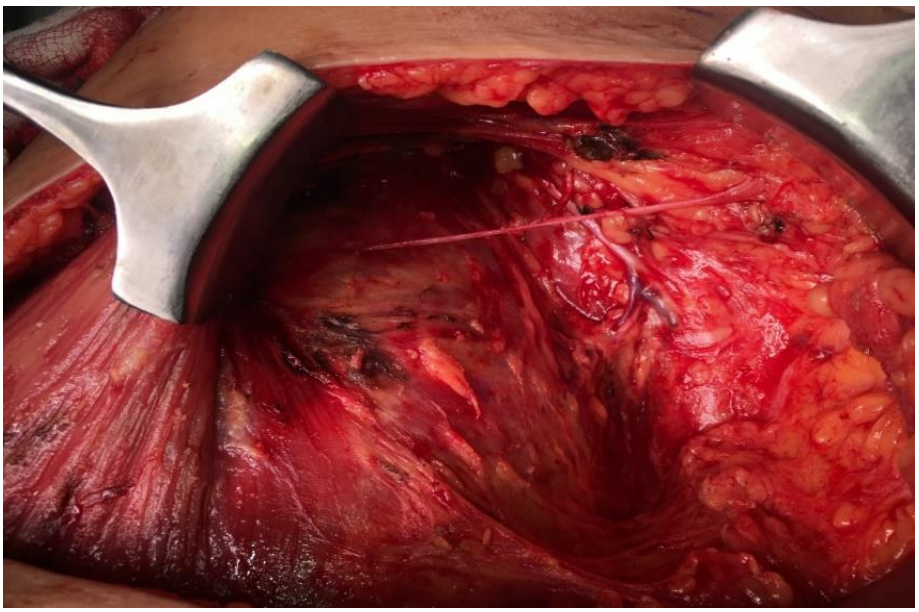


**Fig 30 ; Demonstration of thoraco dorsal nerve**

- A Patey's MRM removes all breast tissue, the nipple-areola complex, skin, and the levels I, II and III axillary lymph nodes: pectoralis minor which was divided giving improved access to level III nodes.
- MRM (Auchincloss) is more commonly performed. It is total mastectomy along with clearance of all levels of axillary lymph nodes and preservation of pectoralis minor muscle.
- The Halsted radical mastectomy removes all breast tissue and skin, nipple-areola complex, pectoralis major and pectoralis minor muscles, and level I, II, and III axillary lymph nodes.

**COMPLICATIONS OF MASTECTOMY**

- Wound Infection
- Seroma
- Hematoma
- Chronic Pain
- Flap Necrosis
- Chronic Breast Lymphedema / Cellulitis

## COMPLICATIONS OF AXILLARY DISSECTION:

- Nerve Injuries
- Cording or limited range of motion
- Lymphedema
- Lymphangiosarcoma (Stewart-Treve's Syndrome)

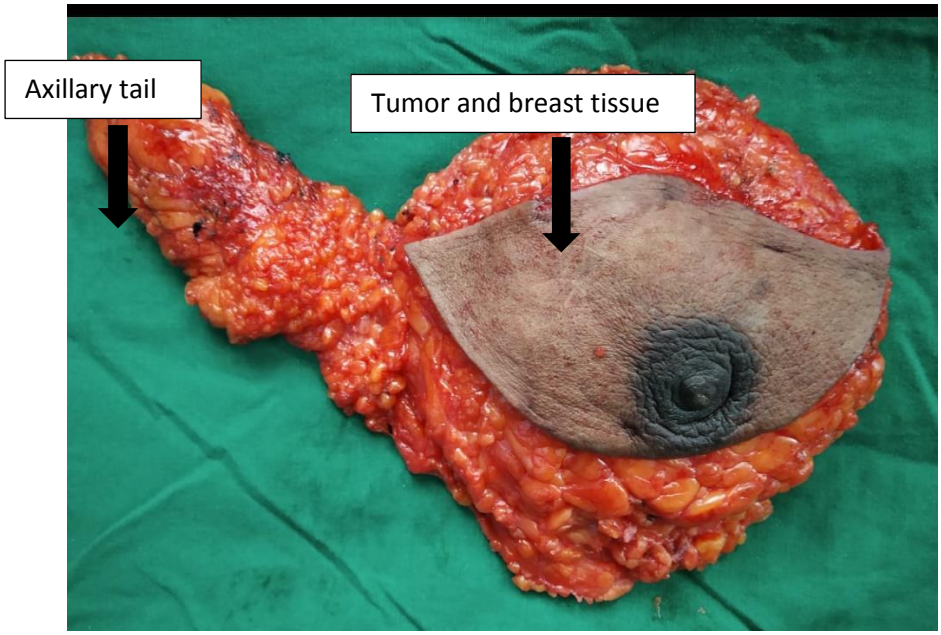



**Fig 31 : Breast tissue with tumour and axillary lymph nodes**

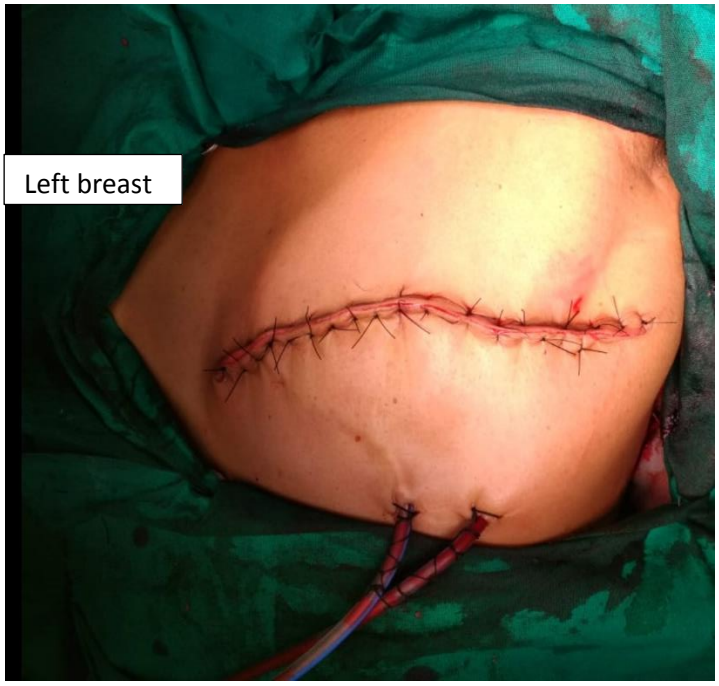



**Fig 32 : Flap closure**

**Reconstruction of breast and chest wall**

1. Adverse tumour volume to breast volume ratio.
2. Adverse tumour location (superomedial central/subareolar, inferior).
3. Multifocal and multicentric disease.
4. Macromastia.

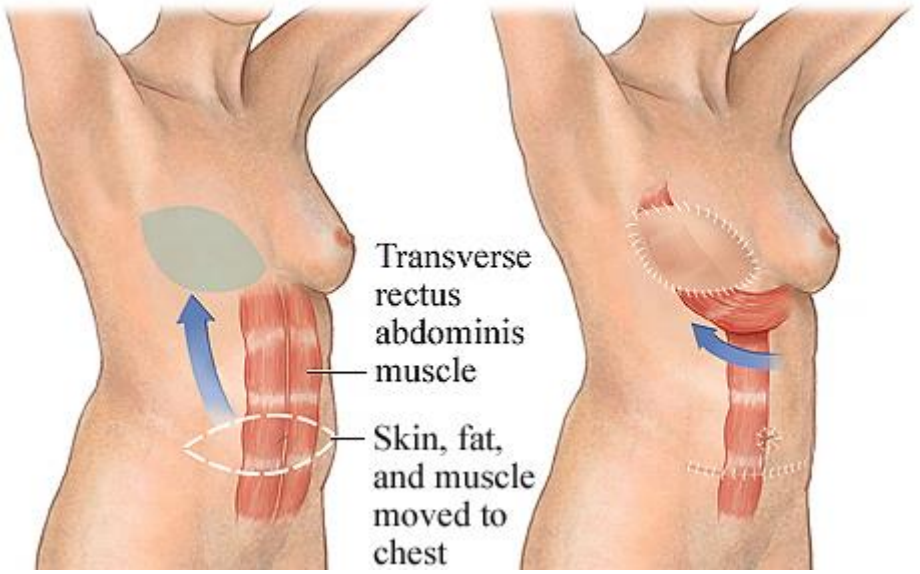



**Fig 33: TRAM flap**

The goals of reconstructive surgery after a mastectomy for BC are wound closure and breast reconstruction.

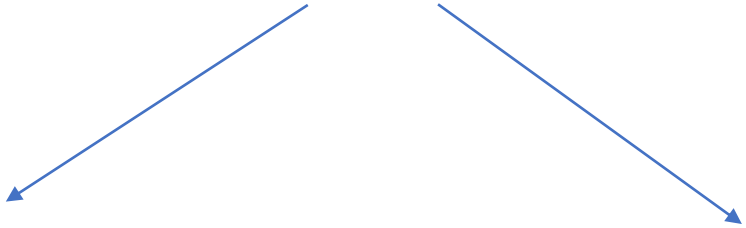
Wound closure after mastectomy is accomplished with simple approximation more radical removal of skin and subcutaneous tissue is necessary, a pedicled myocutaneous flap from the latissimus dorsi muscle is generally the best approach for wound coverage.

Reconstruction can proceed with an expander/implant reconstruction or with autologous tissue such as a pedicled myocutaneous flap or a free flap using microvascular techniques.

The **latissimus dorsi myocutaneous flap** (LD)is appropriate for immediate breast reconstruction because of the favourable donor site and predictable wound healing.

A **transverse rectus abdominis myocutaneous** (TRAM) flap consists of a skin paddle based on the underlying rectus abdominis muscle, which is supplied by vessels from the deep inferior epigastric artery.

## SYSTEMIC THERAPIES IN BREAST CARCINOMA



**Neo-adjuvant Chemotherapy** [15, 17]

For operable tumours to downgrade tumour size and control nodal metastasis before definite surgical treatment.

**Adjuvant Chemotherapy** [15, 17]

Given after surgery to achieve control of nodal/occult micro-metastasis and increases overall survival and reduces recurrence sometimes possibly achieving cure.

**Systemic therapy**

Cyclophosphamide

Methotrexate (M)

5-Fluorouracil (F)

Adriamycin (A) Epirubicin

Paclitaxel (T)

**TABLE : 5**

| Drug Used | Mechanism of Action | Side Effects | Dosage |
|---|---|---|---|
| Cyclophosphamide (C) | Anthracycline: Interferes with DNA synthesis; DNA break | Myelosuppression<br>Nausea/vomiting<br>Alopecia<br>Infertility<br>Haemorrhagic cystitis<br>Syndrome of inappropriate antidiuretic hormone (SIADH)<br>Second-degree malignancies | Cyclophosphamide 600 mg/m<br>2 IV |
| 5-Fluorouracil (F) | Antimetabolite | Myelosuppression<br>Blepharitis<br>Cardiac ischemia | 5-FU 600 mg/m<br>2 IV |
| Adriamycin (A) | | Myelosuppression<br>Nausea/vomiting<br>Cardio toxicity<br>Alopecia<br>Mucositis<br>Diarrhoea<br>Rash (radiation recall) | Doxorubicin 60 mg/m<br>2 IV |
| Paclitaxel (T) | Taxane: Cell death by microtubule break | Myelosuppression<br>Hypersensitivity<br>Neurotoxicity<br>Alopecia<br>Mucositis<br>Diarrhoea | 175 to 225 mg/m2<br>IV |

| | | | |
|---|---|---|---|
| | | Cardiac arrhythmia<br>Hepatotoxicity | |
| Methotrexate (M) | Antimetabolite | Myelosuppression<br>Mucositis<br>Hepatotoxicity<br>Renal failure<br>Pneumonitis<br>Arachnoiditis(when given intrathecally) | Methotrexate<br>40 mg/m2 IV |
| Docetaxel(T) | Taxane: Same as above | Myelosuppression<br>Hypersensitivity<br>Fluid retention<br>Neurotoxicity<br>Alopecia<br>Arthralgias<br>Myalgias<br>Mucositis<br>Diarrhoea<br>Rash | 75 mg/m2 IV |

**Drug Regimens (Standard)** [14, 17, 29]

FAC: 6 cycles every 21 days

AC: 4 cycles every 21 days

TC: 4 cycles every 21 days

FEC: 6 cycles every 28 days

AC -> P: 4 cycles of AC every 21 days -> 12 cycles of Paclitaxel weekly

AC -> D: 4 cycles of AC every 21 days -> 4 cycles of Docetaxel every 21days.

Patients on neoadjuvant chemotherapy and adjuvant chemotherapy are regularly monitored for renal functions, thrombocytopenia and

haemoglobin levels as chemotherapy effects the bone marrow and causes bone marrow suppression.

**Endocrine Therapy**

Presence of the ER and/or PR; interruption of the production of oestrogen or the ability of oestrogen to interact with the ER has been associated with improved disease-free and overall survival for women with metastatic BC.

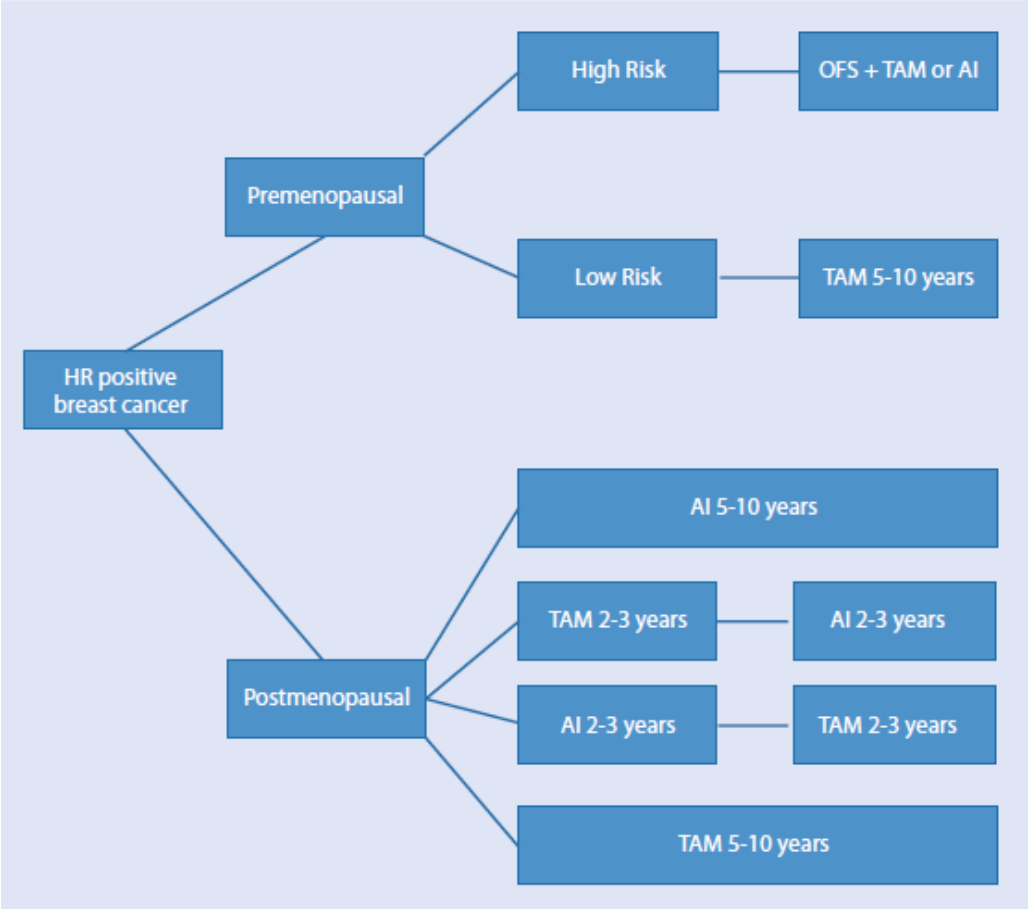



**Fig 34: Algorithm of endocrine therapy**

Premenopausal women

Tamoxifen is a selective oestrogen receptor modulator that has antagonistic and weak agonistic effects.

Within the cytosol of breast cancer cells are specific proteins (receptors) that bind and transfer steroid moieties into the cell nucleus to exert specific hormonal effects

1. Tamoxifen 20mg in two divided or OD dose for 10 years
2. Ovarian ablation by surgery/radiation
3. Progestogens – Medroxyprogesterone 400mg
4. Androgens – Fluoxymestrone.

Side effects of tamoxifen

1. Thromboembolic events, in particular deep vein thrombosis and pulmonary embolism.
2. Cerebrovascular accidents.
3. Tamoxifen use can also lead to hot flushes, vaginal discharge and sexual dysfunction.
4. An increased risk of endometrial cancer seems to be more frequent in women over 55 years

Postmenopausal women:

Postmenopausal women with hormone receptor-positive breast cancer, the use of AI therapy at some point during adjuvant treatment, either as upfront therapy or as sequential treatment after tamoxifen, is recommended.

Aromatase inhibitor like Anostrazole, Letrozole 2.5mg OD

i. Progestogens.
ii. Androgens

Side effects of AIs

AIs are associated with a higher risk of osteoporosis, fractures, cardiovascular risk and hypercholesterolemia but with a lower risk of

thromboembolic events and endometrial cancer when compared to tamoxifen.

**HERCEPTIN MONOCLONAL ANTIBODY (TRASTUZUMAB) [14,16]**

The epidermal growth factor receptor (EGFR) family of tyrosine kinases regulates a complex signalling cascade that controls the proliferation, survival, adhesion, migration, and differentiation of cells.

MECHANISMS FOR TRASTUZUMAB:

Inhibition of tumour cell proliferation / Reduces signalling through cell proliferative pathways (MAPK) / Promotes apoptosis / Reduces signalling through cell survival pathways (Pt3K/Akt) / Inhibits angiogenesis / Induces G1 arrest / Induces p27 cell cycle inhibitor / Reduces cyclin D1 levels / Initiates ADCC

Drugs : Trastuzumab (Herceptin

Ado-trastuzumab emtansine (kadacyla)

Lapatinib (Tykerb)

Neratinib (nerlynx)

Pertuzumab (perjeta )

Dacomitinib

**Indications:**

Her-2 neu positive tumours, Metastatic tumours

Trastuzumab 440 mg/kg intravenously every 3 weeks after completion of paclitaxel for 1 year.

Combined regimen

Trastuzumab-Based Regimens

AC followed by paclitaxel weekly + trastuzumab → trastuzumab maintenance

AC followed by docetaxel + trastuzumab → trastuzumab maintenance

TCH (docetaxel, carboplatin, trastuzumab) → trastuzumab maintenance

Chemotherapy followed by trastuzumab maintenance ERA.

Neoadjuvant Therapy

Paclitaxel weekly + trastuzumab followed by FE C + trastuzumab.

Complications:

Cardio toxicity, Myelosuppression.

## RADIOTHERAPY IN CARCINOMA BREAST

Indications

- To Chest wall
- T3 tumour > 5cm
- Residual disease LABC
- Positive Margin/close surgical margin of < 2 cm.
- After conservative surgery
- High Risk Group
- Inflammatory Carcinoma
- 4 or more nodes positive
- Extra nodal spread
- Axillary status not known / Not assessed

Used to reduce tumour size preoperatively and downstage disease so that operability is better. External Beam RT is given over the breast area, Axilla (in selected patients if ALND is not done or more than 4 positive axillary nodes), internal mammary and supraclavicular area .Total Dosage: 5000 cGY units 200 cGY units daily 5 days a week for 6 weeks.

**Indications:**

Advanced carcinoma breast.

In postoperative period after modified radical mastectomy in stage III carcinoma breast with fixed axillary nodes in inflammatory carcinoma breast.

# METHODOLOGY

# MATERIALS AND METHODS

**STUDY DESIGN**: Prospective observational study.

**SOURCE OF DATA**: This study will be conducted in the Department of General Surgery, R.L. Jalappa Hospital, Kolar. 30 patients admitted with diagnosis of locally advanced carcinoma of breast will be included in the study in the period of Dec 2017 to June 2019. Specimen will be sent in 10% buffered formalin. The paraffin blocks of primary tissue and metastatic lymph node will be sent for HER2neu tumour marker study using IHC, along with the regular appropriate treatment. The similarity and variability will be studied and compared with other randomized studies, using appropriate statistical analysis methods. Patient with positive discordance i.e positive in metastatic lymph node were treated with targeted therapy for a duration of 12 months.

All cases were regularly followed up for response of treatment and also assessed for recurrence.

**INCLUSION CRITERIA**:

All carcinoma breast patients with locally advanced disease undergoing MRM or lumpectomy with axillary clearance.

All metastatic carcinoma breast patient with clinically or radiologically identifiable lymph nodes under (trucut) biopsy for evaluation of hormone status before planning adjuvant chemotherapy or neoadjuvant chemotherapy

**EXCLUSION CRITERIA**:

All carcinoma patients with early BCs with no clinically/ radiologically identifiable lymph nodes.

All male carcinoma breast patients.

## STATISTICAL ANALYSIS

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data. [30, 31, 32. 33]

# RESULTS

# RESULTS

**Table 1: Age distribution among subjects**

| | | Count | % |
|---|---|---|---|
| Age | <40 years | 5 | 16.7% |
| | 41 to 50 years | 11 | 36.7% |
| | 51 to 60 years | 9 | 30.0% |
| | >60 years | 5 | 16.7% |
| | Total | 30 | 100.0% |

In the study 16.7% were in the age group <40 years, 36.7% were in the age group 41 to 50 years, 30% were in the age group 51 to 60 years, 16.7% were in the age group >60 years.

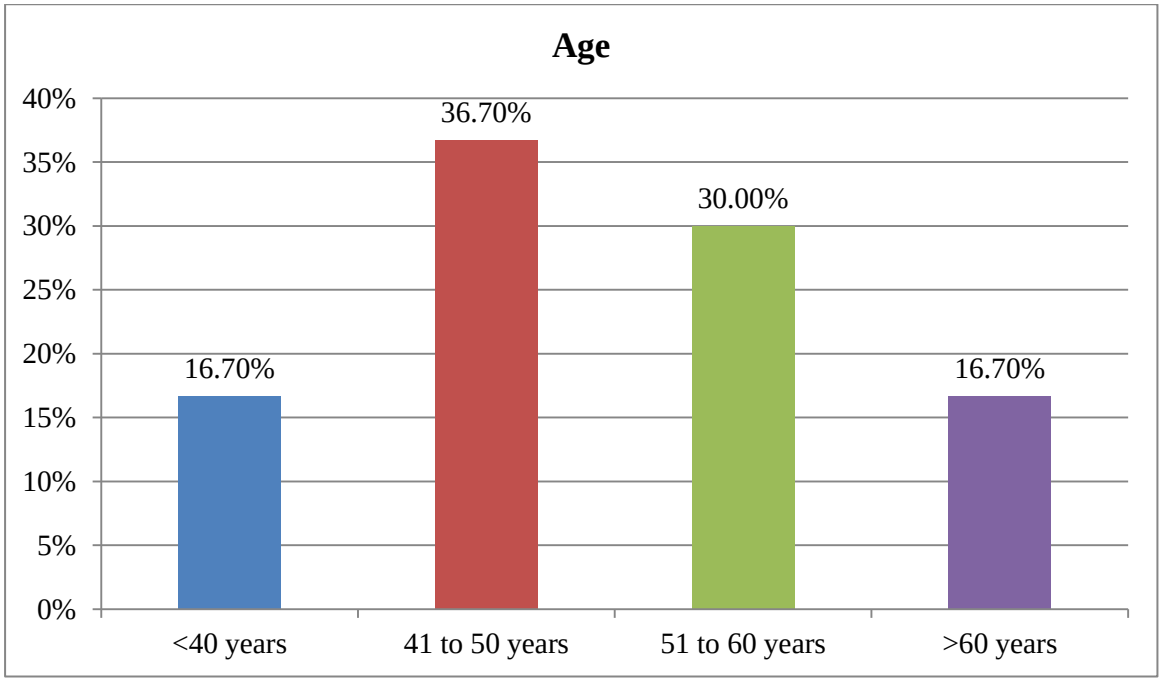



*Figure 1: Bar diagram showing Age distribution among subjects*

**Table 2: Side distribution**

| | | Count | % |
|---|---|---|---|
| Side | Left | 15 | 50.0% |
| | Right | 15 | 50.0% |

In the study 50% were on left side and 50% were on right side.

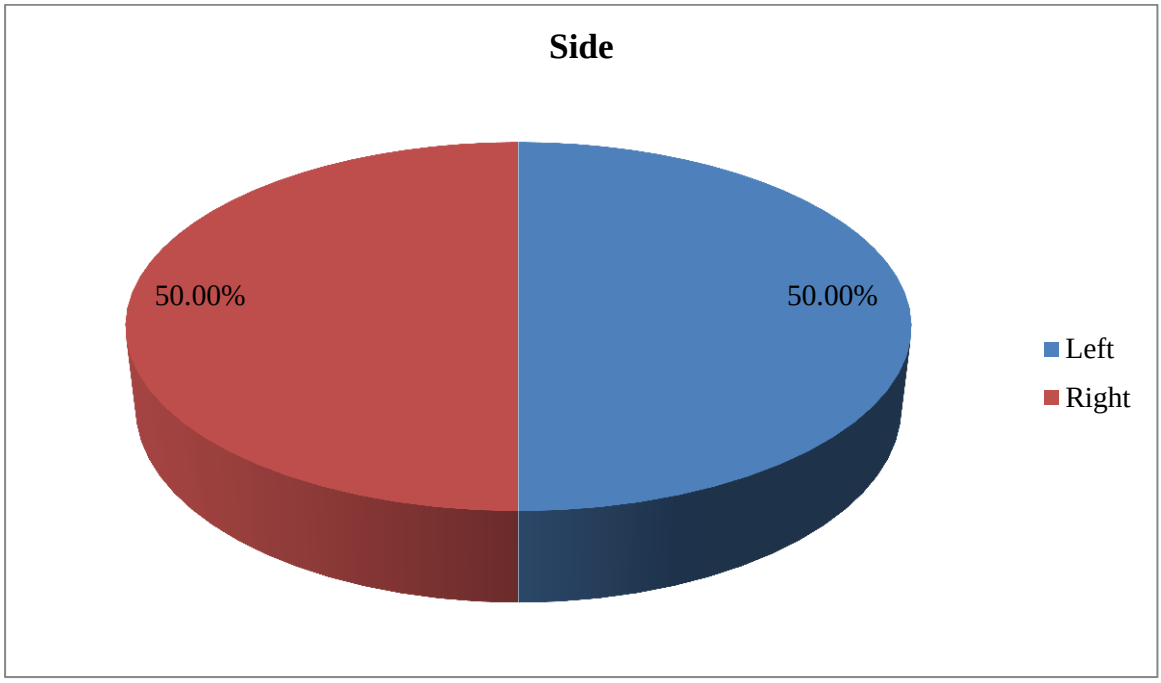



*Figure 2: Pie diagram showing Side distribution*

**Table 3: Quadrant affected in the study subjects**

| | | Count | % |
|---|---|---|---|
| Quadrant | Central | 4 | 13.3% |
| | Lower | 5 | 16.7% |
| | Upper Outer | 21 | 70.0% |

In the study 13.3% had Central lesions, 16.7% had lower quadrant lesions and 70% had upper outer quadrant lesions.

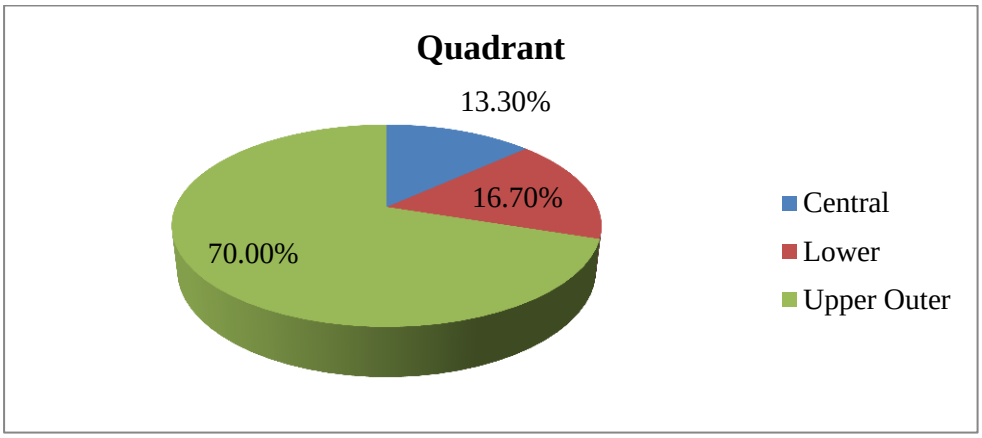



*Figure 3: Pie diagram showing Quadrant affected in the study subjects*

**Left breast**

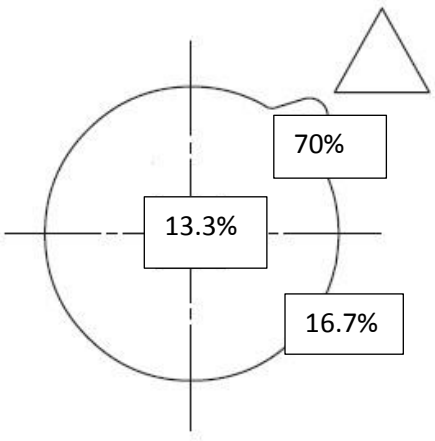


**Table 4: Premenopausal and post-menopausal distribution**

| | | Count | % |
|---|---|---|---|
| PRE/POST | Post | 26 | 86.7% |
| | Pre | 4 | 13.3% |

In the study 86.7% were pre and 13.3% were post-menopausal.

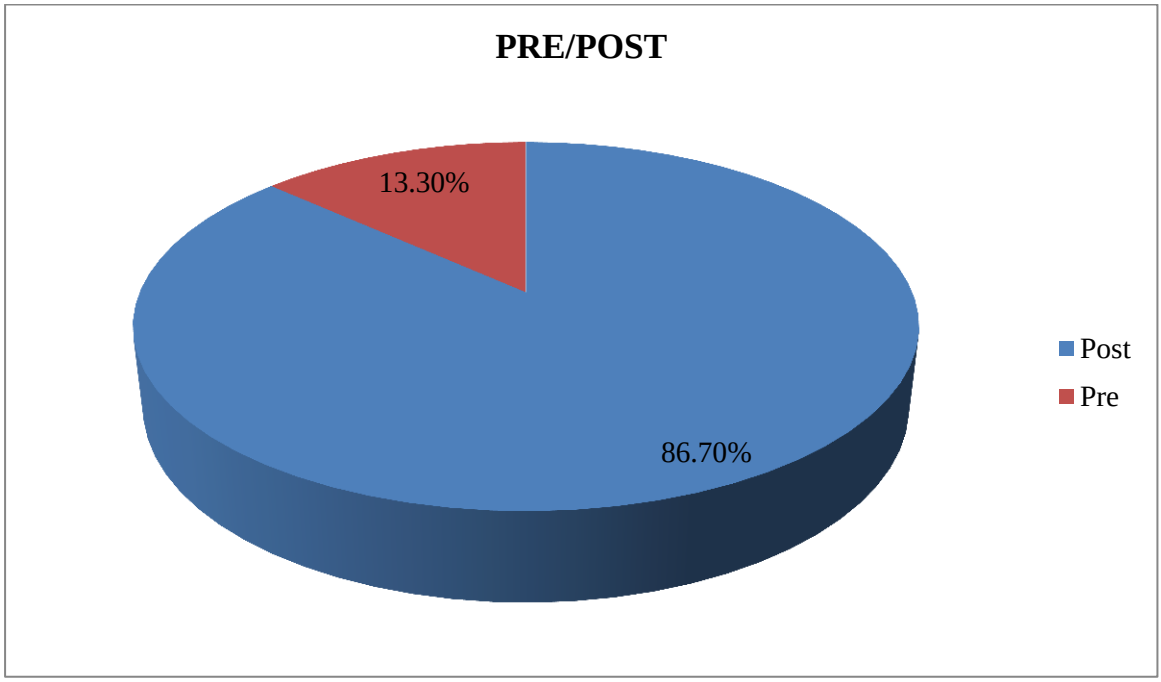



*Figure 4: Pie diagram showing Pre or Post Treatment distribution*

**Table 5: Stage of Tumour distribution among subjects**

| | | Count | % |
|---|---|---|---|
| Stage | II | 16 | 53.3% |
| | III | 11 | 36.7% |
| | IV | 3 | 10.0% |

In the study 53.3% were in stage II, 36.7% were in stage III and 10% were in stage IV.

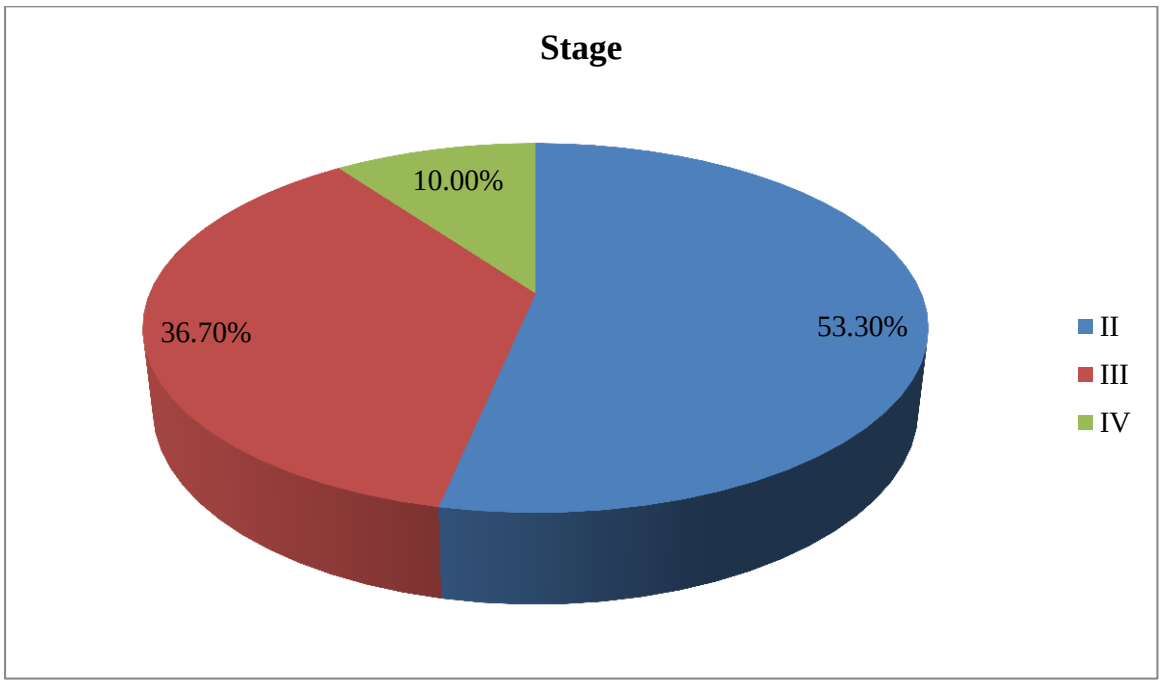



*Figure 5: Pie diagram showing Stage of Tumour distribution among subjects*

**Table 6: HPR diagnosis distribution among subjects**

| | | Count | % |
|---|---|---|---|
| HPR | Infiltrating Ductal Carcinoma | 27 | 90% |
| | Lobular | 1 | 3.3% |
| | Squamous Cell Carcinoma | 2 | 6.7% |

In the study 90% had Infiltrating Ductal Carcinoma, 6.7% had Squamous Cell Carcinoma and 3.3% had Lobular carcinoma.

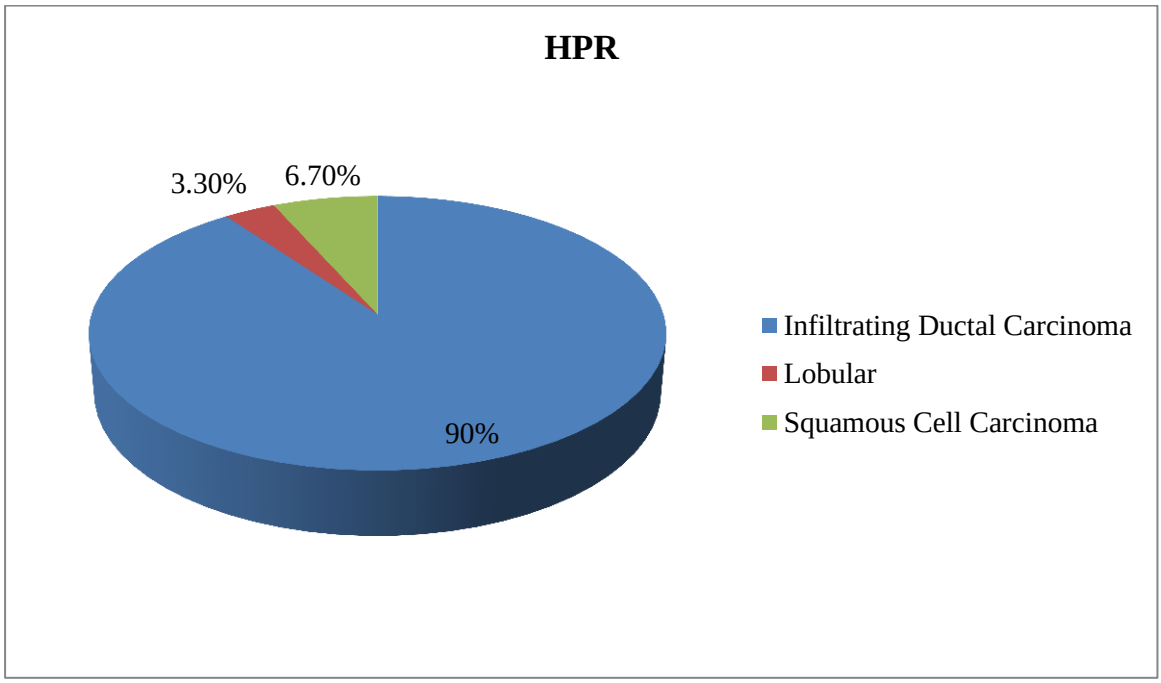



*Figure 6 : Pie diagram showing HPR diagnosis distribution among subjects*

**Table 7: Clinical Staging distribution among subjects**

| | | Count | % |
|---|---|---|---|
| Clinical Staging | T2N0M0 | 2 | 6.7% |
| | T2N1M0 | 3 | 10.0% |
| | T2N2M0 | 2 | 6.7% |
| | T3aN1M0 | 1 | 3.3% |
| | T3N0M0 | 8 | 26.7% |
| | T3N1M0 | 8 | 26.7% |
| | T3N1M1 | 1 | 3.3% |
| | T3N2M0 | 3 | 10.0% |
| | T4BN1M0 | 1 | 3.3% |
| | T4BN1M1 | 1 | 3.3% |

In the study on Clinical staging majority of subjects were in stage T3N0M0 and T3N1M0 (26.7% respectively).

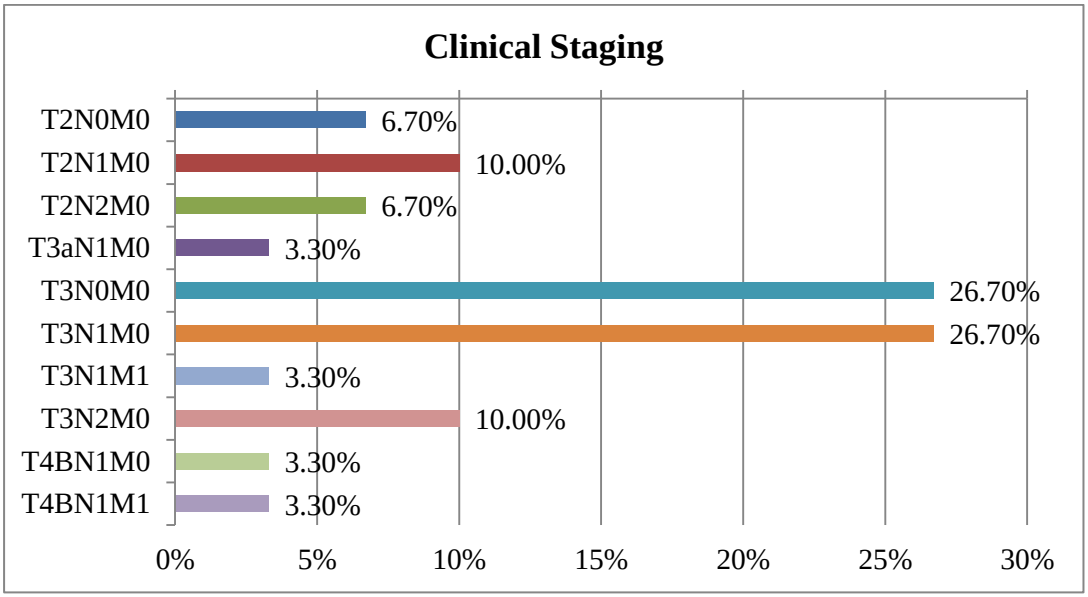



*Figure 7: Bar diagram showing Clinical Staging distribution among subjects*

**Table 8: Pathological Staging distribution among subjects**

| | | Count | % |
|---|---|---|---|
| Pathological Staging | T2N1MX | 3 | 10.0% |
| | T3N0Mx | 5 | 16.7% |
| | T3N1aMx | 4 | 13.3% |
| | T3N1M0 | 3 | 9.9% |
| | T3N1Mx | 8 | 26.7% |
| | T3N2m0 | 2 | 6.7% |
| | T3N2mx | 1 | 3.3% |
| | T3N3mx | 2 | 6.7% |
| | T4N1mx | 2 | 6.7% |
| | Total | 30 | 100.0% |

In the study on pathological staging, majority were in the stage, T3N1Mx (26.7%).

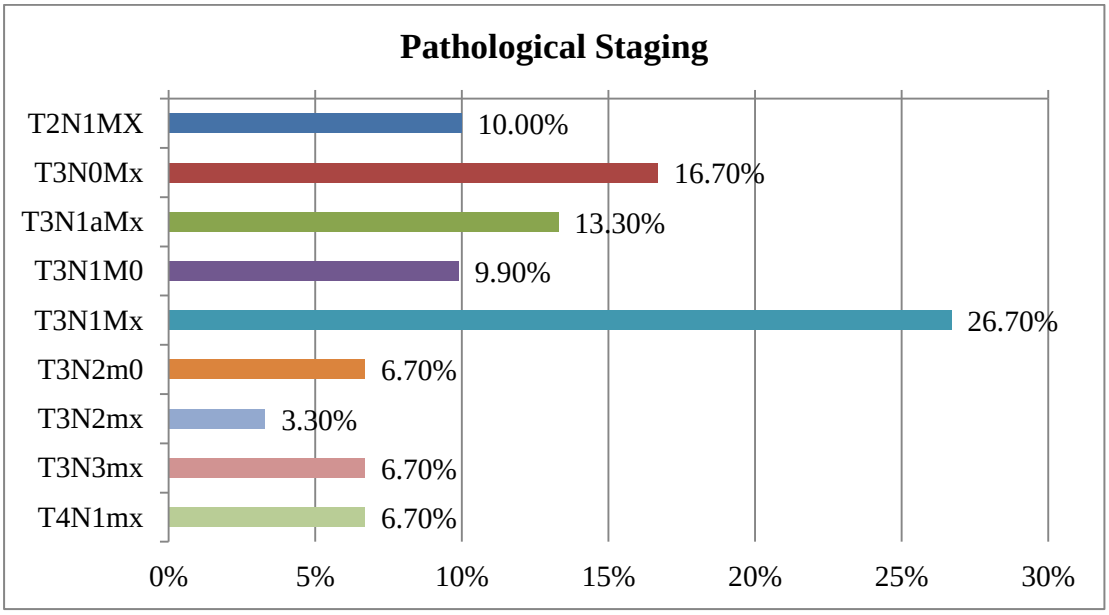



*Figure 8 ; Bar diagram showing Pathological Staging distribution among subjects*

**Table 9: Operative Procedure done in the study subjects**

| | | Count | % |
|---|---|---|---|
| Operative Procedure | Lumpectomy+ axillary dissection (BCS) | 1 | 3.3% |
| | | | |
| | MRM | 29 | 96.6% |

In the study 96.6% underwent MRM, 3.3% underwent lumpectomy+ axillary dissection (BCS).

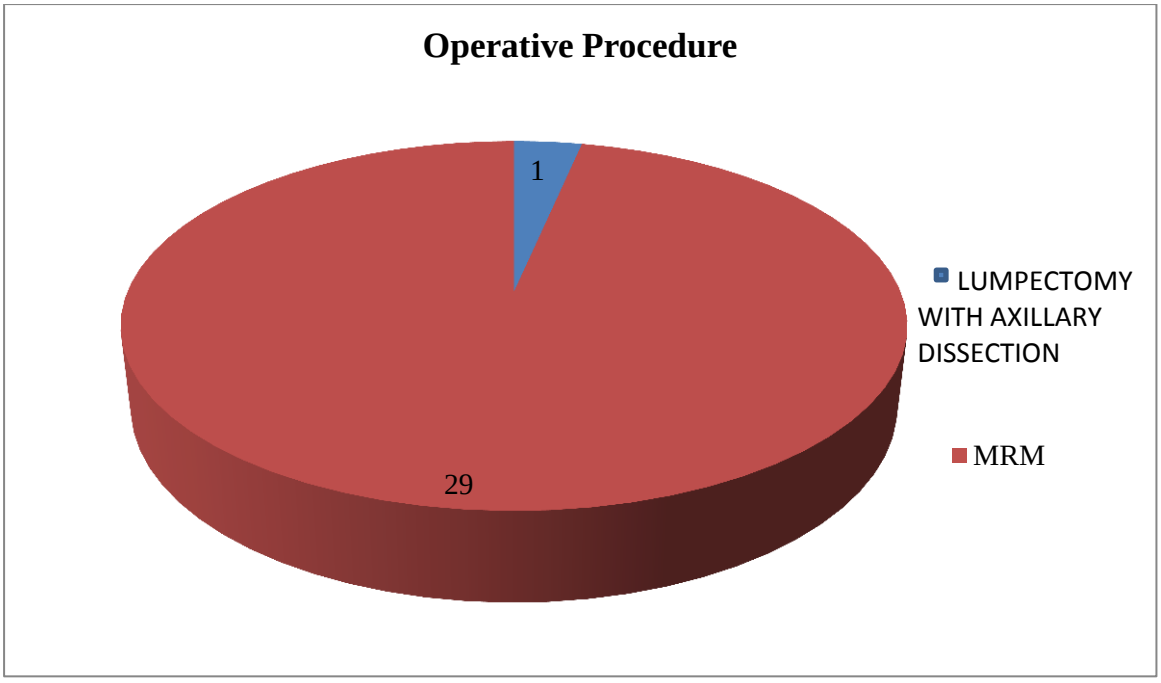



*Figure 9 : Pie diagram showing Operative Procedure done in the study subjects*

**Table 10 : ER and PR Receptor status distribution**

| | | Count | % |
|---|---|---|---|
| ER | Negative | 11 | 36.7% |
| | Positive | 19 | 63.3% |
| PR | Negative | 11 | 36.7% |
| | Positive | 19 | 63.3% |

In the study 63.3% were positive for ER and PR respectively.

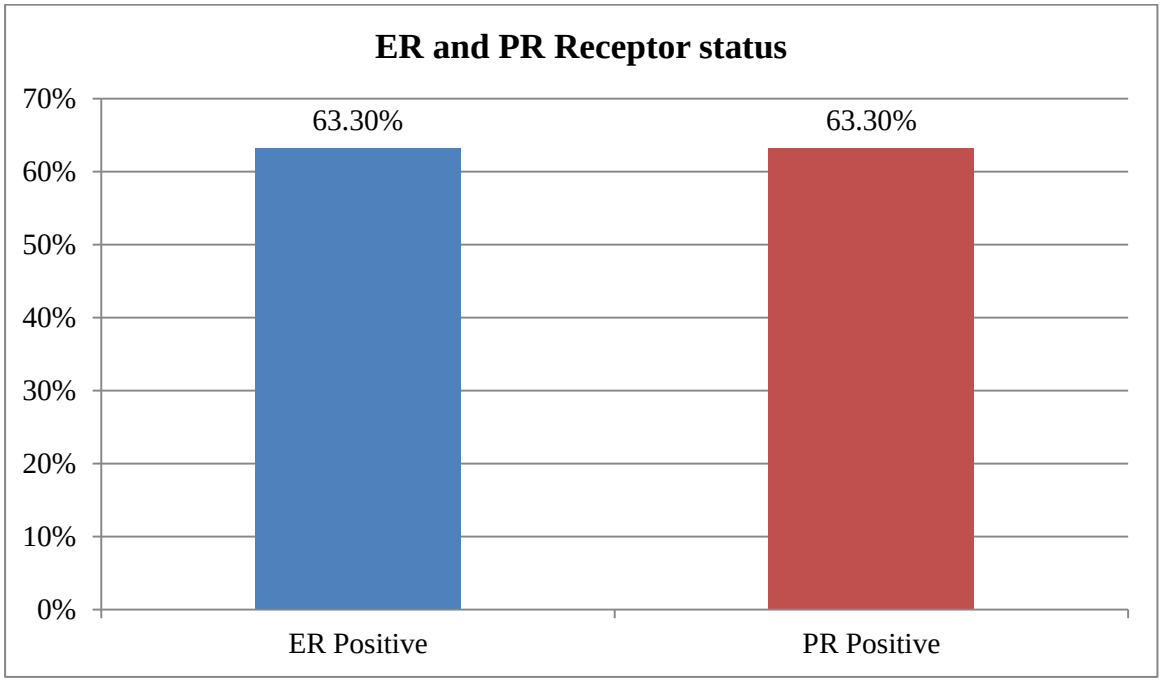



*Figure 10 : Bar diagram showing ER and PR Receptor status distribution*

**Table 11: HER2 expression in primary tumour distribution**

| | | Count | % |
|---|---|---|---|
| HER2NEU | Equivocal | 6 | 20.0% |
| | Negative | 16 | 53.3% |
| | Positive | 8 | 26.7% |

In the study 26.7% were positive for HER2Neu and 20% had equivocal for primary tumour.

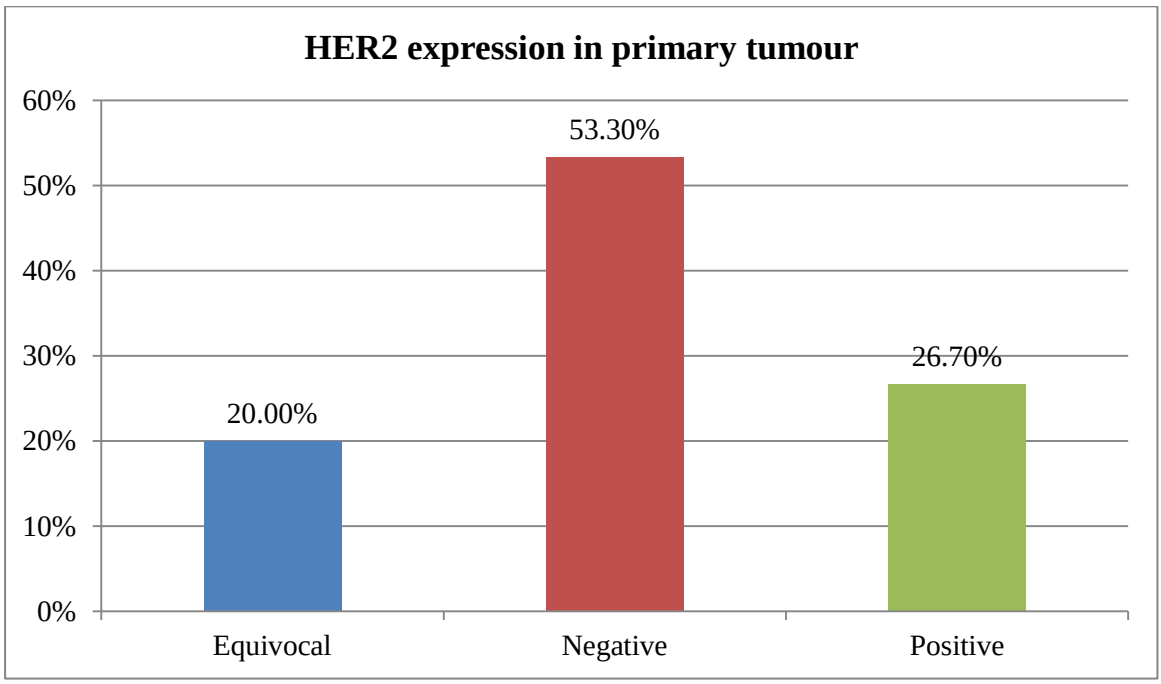



*Figure 11: Bar diagram showing HER2 expression in primary tumour distribution*

**Table 12: HER2 expression in lymph node distribution**

| | | Count | % |
|---|---|---|---|
| HER2NEU in Lymphnode | Equivocal | 4 | 13.3% |
| | Negative | 17 | 56.7% |
| | Positive | 9 | 30.0% |

In the study 30% were positive for HER2Neu and 13.3% had equivocal for Lymph nodes.

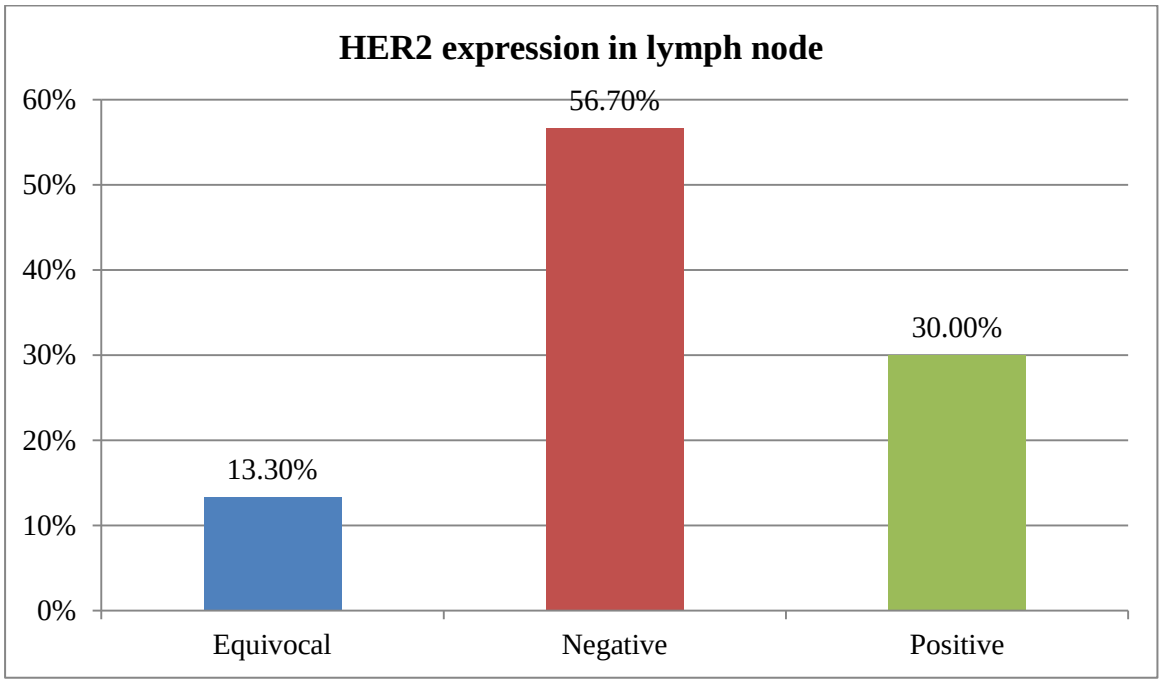



*Figure 12: Bar diagram showing HER2 expression in lymph node distribution*

**Table 13 : Association between HER2 expression in Tumour and lymph node**

| | | HER2NEU in Tumour | | | | | |
|---|---|---|---|---|---|---|---|
| | | Equivocal | | Negative | | Positive | |
| | | Count | % | Count | % | Count | % |
| HER2NEU in Lymphnode | Equivocal | **3** | **50.0%** | 1 | 6.2% | 0 | 0.0% |
| | Negative | 2 | 33.3% | **11** | **68.8%** | 4 | 50.0% |
| | Positive | 1 | 16.7% | 4 | 25.0% | **4** | **50.0%** |

$\chi 2 = 10.326$, df =4, p =0.035*

In the study there was significant association between HER2Neu status between primary tumour and Lymph node.

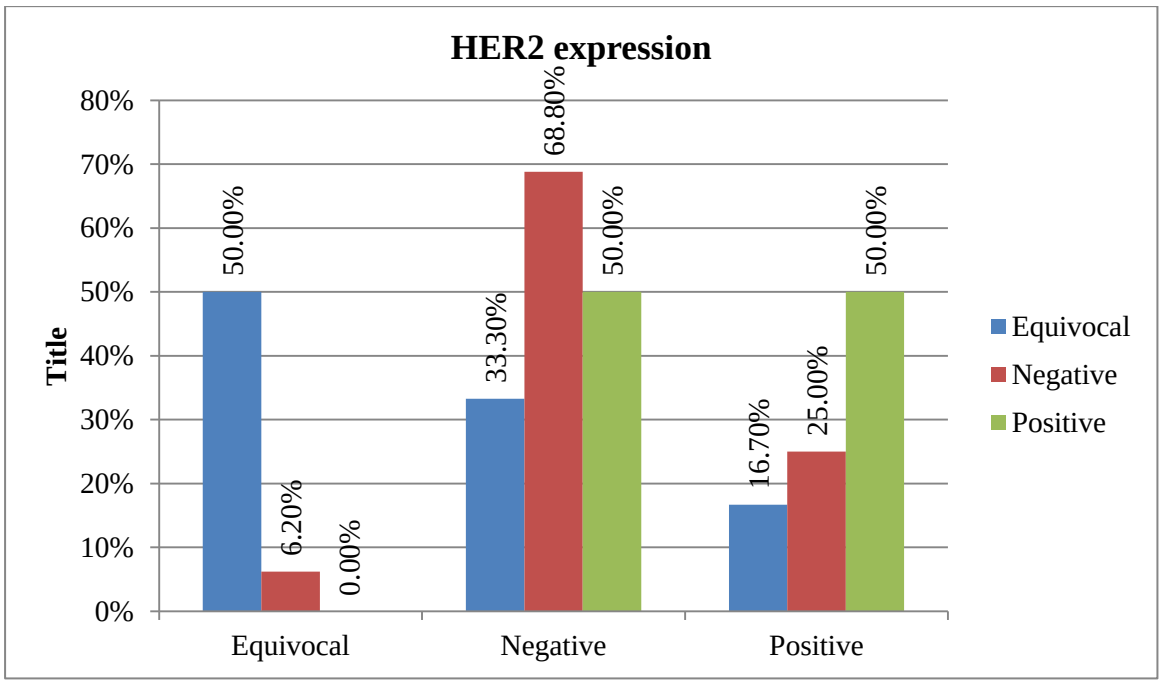



*Figure 13: Bar diagram showing Association between HER2 expression in Tumour and lymph node*

**Table 14: Chemotherapy, Radiotherapy, Hormonal therapy and Targeted therapy distribution among subjects**

| | | Count | % |
|---|---|---|---|
| Chemotherapy | 12cycles | 9 | 30.0% |
| | 8cycles | 21 | 70.0% |
| RT | 15# | 30 | 100.0% |
| Hormonal | Not received | 12 | 40.0% |
| | Received | 18 | 60.0% |
| Targeted | Nil | 25 | 83.3% |
| | 10cycles | 1 | 3.3% |
| | 12cycles | 4 | 13.3% |

In the study 30% received 12 cycles and 70% received 8 cycles of chemotherapy, 100% of subjects received Radiotherapy with 15#, 60% received Hormonal therapy and 5 subjects received targeted therapy.

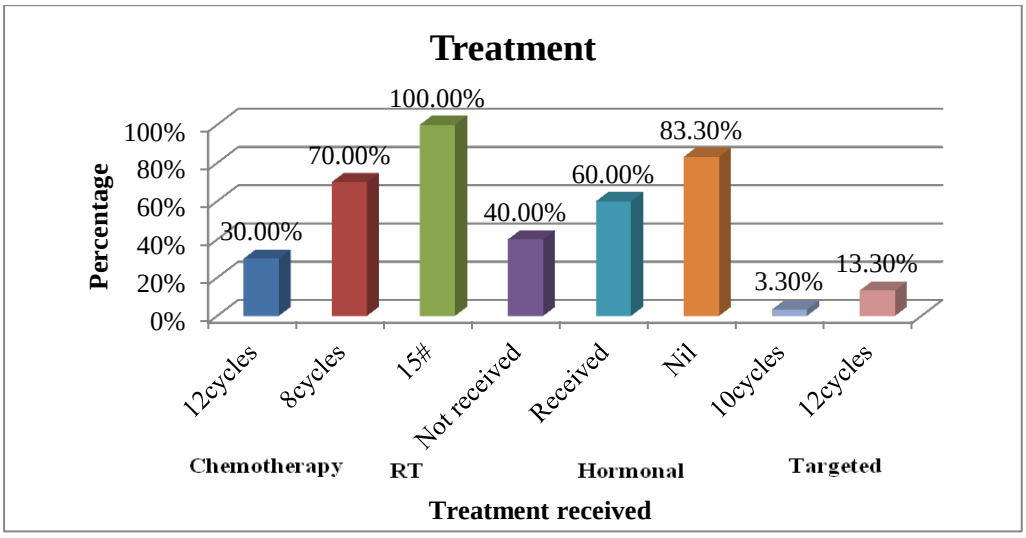



*Figure 4: Bar diagram showing Chemotherapy, Radiotherapy, Hormonal therapy and Targeted therapy distribution among subjects*

**Table 15: Herceptin given in tumour positive patients distribution among subjects**

| | | Count | % |
|---|---|---|---|
| Herceptin given | Yes | 5 | 16.7% |
| | No | 25 | 83.3% |
| | Total | 30 | 100% |

In the study 16.7% of subjects received Herceptin.

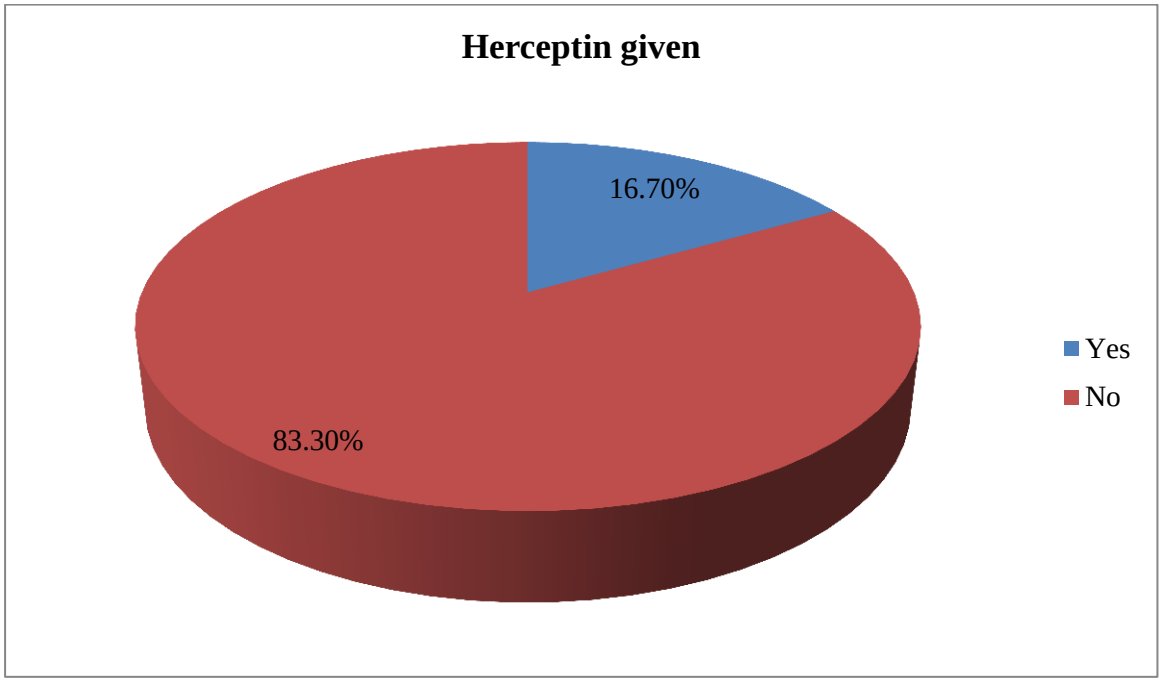



*Figure 15: Pie diagram showing Herceptin given distribution among subjects*

# DISCUSSION

# DISCUSSION

This present study, conducted in the department of RL Jalappa hospital & research Centre. this study helps in assessing her2neu expression in primary breast tissue and metastatic axillary lymph node and its variability. This study included total of 30 patients. All patients diagnosed with carcinoma breast included in study, early carcinoma, locally advanced and metastatic diagnosed by triple assessment.

## Comparison of Age

A study conducted by gogia at al. in 2019 Median age of presentation was 47 years (range,26 to 72 years) [34]. A study conducted by dieci et all median age is 51 years(26–87)[35]. Median age according to de Duenas et al was 57(30-92) [36]. A study by sari et al showed median age 57(30-92)[37]. Similar to this study conducted Chan et al. in 2012 median age was 50 (range3-48)[5]. A similar study conducted by Hoefnagel et al in 2012 median age was 53.9 (25-89) [38]. Similar this to study curtit et al median age 53(range 29-93)[39]. In our study patients were seen between the age of 40- 50 (36.7%) years age group.

## Comparison of histopathology

Sari*et all a total of 78 subjects were included in study of which 40 patients were diagnosed with infiltrating ductal carcinoma and 5 patients were invasive lobular carcinoma [37]. According to study conducted by Tapia et all a total of 105 patients were included in study 82 patients had ductal carcinoma, 12 had lobular carcinoma[3] . In our study 27(90%) had infiltrating ductal carcinoma, 1(3.3%) patient had lobular carcinoma and 2(6.2%) had squamous cell carcinoma.

**Comparison of premenopausal and post-menopausal distribution**

According to gogia et al 42(41.6 were pre-menopausal women and 59(58.4) were post-menopausal women [34.] Similar study by deice et al showed 57.7 were premenopausal and 37.2 were post-menopausal [35]. Similar study conducted by de Duenas showed 31.3% of pre-menopausal women and 69.2 were post-menopausal [36]. Similar study sari et al showed 57.7% of premenopausal and 47.2 were post-menopausal [37.] In our study pre-menopausal women were 4(13.3% ) and post-menopausal were 26(86.7%).

**DEMOGRAPHIC TABLE**

| | Present study | Gogoia [34] et all | Dieci et all [35] | De Duenas et al [36] | Sari et al [37] | Hoefnagel et al [38] | Chan et al [39] |
|---|---|---|---|---|---|---|---|
| **Total** | 30 | 103 | 119 | 196 | 78 | 233 | 50 (31–85) |
| Median age, years(range) | 50(28-65) | 47 (26-72) | 51(26-87 | 57(30-92) | 44.5(21-76) | 53.9(25-93) | |
| Sex<br>Male<br>Female | <br><br>30 | <br>2 (1.9)<br>101 (98.1) | | | | | |
| Menopausal Status<br>Premenopausal female<br>Postmenopausal female | <br>4(13.3% )<br>26((86.7%) | <br>42 (41.6)<br>59 (58.4) | <br>57.7<br>37.2 | <br>31<br>69 | <br>57.7<br>47.2 | | |
| Side<br>Right<br>Left | <br>15(50%)<br>15 (50% | <br>48 (46.6)<br>55 (53.4) | | | | | |
| Histology<br>IDC<br>ILC<br>others | <br>27(90%)<br>1(3.3%)<br>2(6.7%) | <br>92 (95.1)<br>19 (4.9)<br>8 | <br>77.3<br>16<br>6.7 | | | <br>82.4<br>8.6<br>9 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Staging<br>I<br>II<br>III<br>IV | <br><br>16 (53.3%)<br>11(36.7%)<br>3(10.0%) | <br><br>7 (6.8)<br>33 (32)<br>63 (61.2) | <br><br>34<br>43<br>2.5 | <br><br>16<br>50<br>22 | <br>4(5.10<br>28(35.9)<br>23(29.5)<br>23(29.50 | <br>73<br>80<br>12<br>68 | |

## PATHOLOGICAL TABLE

| Receptor status | Present study | Gogoia [34] et all | Dieci et all [35] | De Duenas et al [36] | Sari et al [37] | Hoefnagel et al [38] | Chan et al [39] |
|---|---|---|---|---|---|---|---|
| ER Positive<br>Negative | 11(36.7%)<br>19(63.3%) | 45.7 | 79 | 62.8 | 49(60.2)<br>27(34.61) | 74.7 | 74 (63.8) |
| PR positive<br>Negative | 11(36.7%)<br>19(63.3%) | 58.9 | 61 | 62.8 | 49(60.2)<br>24(30.7) | 74.2 | 74(63.8) |
| Her2neu((LN)<br>Negative<br>Positive | <br>17<br>9 | 41.7 | 17.7 | 25.6 | 20(25.6)<br>46(58.9) | 20.2 | 37 (31.8%) |

**Expression of hormonal receptors in primary tumour**

Santinelli et all conducted a study which had patients with 12 (27%) positive, 26 (57%) Negative, 7 (16%) Not determined oestrogen receptors and 17 (37), Positive 21 (47) Negative, Not determined 7 (16) Progesterone receptors [39].

Gogia et al showed 45.7% of ER positivity, 58.9 had progesterone positivity and her2 was 41.7% [34]. Dieci et al had a similar study showed 79% with ER positivity, 61% with progesterone positivity and her2neu

with 17.7%[35]. Duenas et al showed 62.8 % with ER positivity, 62.8 % positivity for progesterone. 25.6 % with Her2neu positivity [36].

In this study 11 patients had negative expression of oestrogen in primary tumour and 19 patients had positive expression of oestrogen, similarly 11 patient's negative expression of progesterone and 19 had positive expression of progesterone in primary tumour.

**Expression of her2neu in primary tumour.**

Aitken et all conducted a study in which HER2 expression in nodal disease was significantly higher than primary disease with significant

P =0.00001. 3 patients had negative expression of her2 neu in primary tumour and positivity in lymph node. [4]

In the study conducted by Chan et al, 79 patients had negative her2nue in primary tumour and 37 were positive in primary tumours [5]

In Lower et al, 12 of the total patients showed her2nue positivity in the primary tumour, and 7 cases showed positivity in the lymph nodes [11].

In the present study that was conducted, 8 (26.7%) were positive in the primary tumour, 16(53.3%) were negative and 6 were equivocal (20.0%)

**Comparison of her2 in metastatic lymph node**

In the study that was conducted by Atkin el al there were 3 cases that were positive for her2neu in the lymph node and 14 were negative [4].

In the present study that was conducted total positive were 9 , 17 negatives and equivocal were 4.

## TREATMENT TABLE

| **Surgery** | Present study | Gogoia [34] et all | Dieci et all [35] | De Duenas et al [36] | Sari et al [37] | Hoefnagel et al [38] | Chan et al [39] |
|---|---|---|---|---|---|---|---|
| MRM | 96.6% | 85 (82.5) | | | | | |
| BCS | 3.3% | 18 (17.5 | | | | | |
| **Chemotherapy** | | | | | | | |
| Paclitaxel | 30 (100%) | 81 (78.64) | | | | | 11 |
| Ac regimen | 30(100%) | 5 (4.85) | | | | | 38 |
| Radiotherapy | 30(100%) | 7 (6.8) | | | | | |
| Hormonal therapy | 19 (63.3%) | 10 (9.7) | | | | | |

## ANALYSIS OF HER2NEU RECEPTOR

| | **Type of receptor** | **Positive to Negative** | **Negative to Positive** |
|---|---|---|---|
| **Present study** | **Her2** | **14 (46.6%)** | **5(16.6)** |
| **Gogia et all [34]** | **Her2** | **7(6.8)** | **9 (8.7)** |
| **Dieci et all [35]** | **Her2** | **10 (10.2)** | **4(19)** |
| **De Duenas et al [36]** | **Her2** | **11(20.8)** | **13(100)** |
| **Sari et al [37]** | **Her2** | **12(41.1)** | **10** |
| **Hoefnagel [38]** | **Her2** | **6%** | **5.2%** |
| **Chan et all [5]** | **Her2** | **3** | **2** |

**Comparison of variability of her2neu between primary and lymph node**

In a study that was conducted by Nishimura et al. positive to negative conversion of receptor status was 14.4% and negative to positive was 3.1%. [40]

Amir et al.- 9% positive to negative conversion of receptor status was seen, negative to positive was 2.1% [41]. In Shin et al 10.3% positive to negative conversion of receptor status was seen, negative to positive was 2.8% [42]. Meng et al 11% positive to negative conversion of receptor status was seen, negative to positive was 4.4% [43]. In the study that was conducted by Ba et al, 14.1%positive to negative conversion of receptor status was seen, negative to positive was 8.8% [44]. Similar results were seen in a study that was conducted by El et al 30%positive to negative conversion of receptor status was seen, negative to positive was 15% [45]. Kinwe et al showed 13.5% positive to negative conversion of receptor status was seen, negative to positive was 12.5% [46].

A study by gogia et al showed positive to negative conversion of 7(6.8%) and negative positive conversion of 5(16.6%) [34].

According to dieci at all 10(10.2 %) positive to negative conversion and 4(19%).[35]De Duenas et all had 11(20.8%) positive to negative conversion and 13(86.7%).[36]

Sari et al had 12 (41.1%) positive to negative conversion [37]

Hoefnagel et al 6% positive to negative conversion and negative 5.2%. [38]

In the above study that was conducted 43% positive to negative conversion of receptor status was seen, negative to positive was 16.6%.

# SUMMARY

## SUMMARY

In the above study conducted in Department Of General Surgery, 30 patients diagnosed with carcinoma breast were included. All patient's demographic history was obtained with informed consent. All patients were staged accordingly and underwent, surgery, chemotherapy and radiotherapy based on IHC. All patients were analysed for ER PR and Her2neu receptor status in primary breast tissue and Her2neu was also analysed in metastatic axillary lymph node.

Out of 30 patients studied most common age group of presentation was between 41-50 years. There was equal distribution of lump in both left and right breast.26(86. 7%) post- menopausal women and 4 (13.3%) were pre-menopausal women.

Most common presentation of lump was in upper outer quadrant 21(70%). Patients had infiltrating ductal carcinoma 90% as the common histological presentation, lobular was seen in 3.3% and squamous was seen in 2 patients(6.7%). In above study conducted ,patients in stage II were 16(53.3%). Of the 30 patients studied 1 patient (3.3%) underwent (BCS) 29 (96.6%) underwent modified radical mastectomy.

19(63.3%) were positive for ER & 19(63.3%) were PR positive. 8 patients (26.7%) were her2neu positive in primary tumour, 16(53.3%) were negative in primary tumour & 6(20.2%) were equivocal.

Her2neu negativity was seen in 17 patients (56.7) in the lymph node, and positivity was seen in 9 patients (30.0%) in lymph node and 4(13.3%) were equivocal.

In the study there was a significant association of her2neu in primary tumour and metastatic axillary lymph node (table 12) with significant p value = 0.0035.

In our present study 9 patients (30%) received 8 cycles chemotherapy and remaining 21(70%) received 12 cycles of chemotherapy.

All the 30 subjects were treated with adjuvant radiotherapy. 18 patients (60%) received hormonal therapy. 11 patients had similarity of receptor study in both primary breast tumour and metastatic axillary lymph node.

14 (43%) had negative discordance or variability i.e positive in primary breast tumour and negative in metastatic axillary lymph node.

5 patients (16.6%) had positive axillary lymph node i.e there is negative expression of her2ue receptor in primary breast tissue but her2neu was positive in metastatic axillary lymph node.

5 patients with positive her2neu in metastatic axillary lymph node were treated with targeted therapy. During the course of the treatment patients were on regular follow up for analysis for local recurrence and systemic metastasis.

# CONCLUSION

# CONCLUSION

In the above prospective study that was conducted in Department Of General Surgery Of R L Jalappa Hospital.

In our study we assessed her2neu expression from the primary tumour in 30 patients with positive results in 8 patients (26.7%) and assessed her2 neu in the nodal metastasis(axilla) in the same which showed positivity in 9 patients (30%) and ER /PR positivity in 19 patients (63.3%).

5 patients (16.6) had her2neu positive discordance in metastatic lymph node. The her2neu results were compared with HPR and a total of 5 patients (16.6%) underwent targeted therapy, and were benefited in our study. These patients receiving targeted therapy at regular intervals and are still being followed up.

Response to treatment is to be calculated after completion of the treatment. The sample size that is taken is 30 and is a small group, and needs a bigger group to analyse the outcome.

Our study, has helped in subjecting, 5(16.6%) patients for targeted therapy i.e. her2neu expression in metastatic lymph node. Our study shows that analysis of metastatic node for her2neu other than primary tumour helps patients in receiving targeted therapy.

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## BIBLIOGRAPHY


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# ANNEXURES

## PROFORMA

**PARTICULARS OF THE PATIENT**

**NAME :**

**AGE :**

**SEX :**

**UHID NUMBER :**

**OCCUPATION:**

**DOA:**

**DOD:**

**CHIEF COMPLAINTS :**

**HISTORY OF PRESENTING ILLNESS:**

**PAST HISTORY :**

**FAMILY HISTORY:**

**PERSONAL HISTORY:**

**MENSTRUAL HISTORY :**

**GENERAL PHYSICAL EXAMINATION:**

**PULSE : BP: TEMP : RR:**

**PALLOR : ICTERUS: LYMPHADENOPATHY : CYANOSIS:**

**CLUBBING : OEDEMA :**

**LOCAL EXAMINATION**

**INSPECTION :**

**PALPATION:**

**TUMOUR SIZE AND LATERALITY :**

**LYMPH NODE STATUS**

**SYSTEMIC EXAMINATION**

**CVS:**

**RS:**

**P/A:**

**CNS:**

**INVESTIGATIONS**

**HB :**

**RBC :**

**PCV:**

**WBC:**

**PLATELETS:**

**RBS :**

**BLOOD UREA:**

**SERUM CREATININE :**

**SERUM SODIUM :**

**SERUM POSTASSIUM:**

**LIVER FUNCTION TEST**

**CHEST X RAY :**

**USG ABDOMEN AND PELVIS :**

**FNAC :**

**TRUCUT BIOPSY :**

**CT THORAX :**

**HISTOPATHOLOGY:**

**IMMUNO HISTOCHEMISTRY :**

| NATURE OF TISSUE | ESTROGEN | PROGESTERONE | HER2neu |
|---|---|---|---|
| Primary breast tissue | | | |
| Axillary lymph node | | | |

**CLINICAL STAGING :**

**PATHOLOGICAL STAGING :**

**HISTOPATHOLOGICAL STAGING :**

**DATE OF SURGERY :**

**SURGERY PERFORMED:**

**CHEMOTHERAPY:**

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**RADIOTHERAPY:**

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## HORMONAL THERAPY:

## PATIENT INFORMATION SHEET

Study title: A STUDY OF HER2neu STATUS IN PRIMARY BREAST CANCER AND METASTAIC AXILLARY LYMPH NODE WITH BEARING ON POST OPERATIVE TARGETED THERAPY

GUIDE: DR P N.SREERAMALU

STUDY CONDUCTED BY: DR VARSHA A

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

INVESTIGATIONS: -Cbc ,Renal function test, serum electrolytes, chest radiograph and ECG.FNAC of breast tissue and lymph node.ER, PR Status ,USG abdomen and pelvis, Mammography Immunohistochemistry marker study from the tumour tissue and nodal tissue for HER2Neu receptor and treatment with targeted therapy.

COMPLICATIONS: haemorrhage, infection, inadequate sample, need for redo of procedure.

Patients presenting with complaints of lump in breast and locally advanced disease will be included in this study.

Patients in this study will have to undergo routine preoperative investigations, cbc ,rft ,core needle biopsy of breast tissue and axillary lymph node Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity

will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact: Dr Varsha .A [post graduate]

PHONE NO:9916974081

PATIENTS SIGNATURE:

PATIENTS ATTENDERS SIGNATURE:

## INFORMED CONSENT FORM

I Mr/ Mrs …… Have been explained in my own understanble language , that , i will be included in study of her2neu status in primary breast cancer and metastatic axillary lymph node with bearing on post operative targeted therapy.

I have been explained that my clinical findings , investigations , intraoperative findings , post operative course , will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary and I can withdraw from the study any time and this will not affect my relation with my doctor or the treatment for my ailment.

I have been explained about the follow up details and possible benefits and adversities due to interventions , in my own understandable language.

I have understood that all my details taken during the study are kept confidential and while publishing or sharing of the findings , my identity will be masked.

I in my sound sound , mind give full consent to be included in this study.

Signature of patient — Dr Varsha. A

Name ; — ph no ; 9916974081

Signature of witness ; — signature ;

Name ;

# ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ:

**ಶೀರ್ಷಿಕೆ:** ಪ್ರಾಥಮಿಕ BREAST CANCER, ಮತ್ತು METATSTATIC AXILLARY LYMPH NODES ನ HER 2-NEU ಸ್ಥಿತಿ ಅಧ್ಯಾಯನ ಮತ್ತು ಅದರ ಶಸ್ತ್ರ ಚಿಕಿತ್ಸೆ ನಂತರದ ಚಿಕಿತ್ಸೆಯಲ್ಲಿ ಬಳಕೆ.

**ಅಧ್ಯಯನದ ಸ್ಥಳ**: ಕೋಲಾರದ ಶ್ರೀ ಆರ್. ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ ಶ್ರೀ ದೇವರಾಜ ಅರಸ್ ವೈದ್ಯಕೀಯ ಮಹಾ ವಿದ್ಯಾಲಯ ಟಮಕ.

**ಮಾರ್ಗದರ್ಶಿ:** ಡಾ. ಶ್ರೀರಾಮುಲು ಪಿ.ಎನ್

ಡಾ. ವರ್ಷ.ಎ ಮೂಲಕ ನಡೆಸಲ್ಪಟ್ಟ ಅಧ್ಯಯನ

ಪ್ರಕ್ರಿಯೆ ಪ್ರಾಥಮಿಕ BREAST CANCER , ಮತ್ತು METATSTATIC AXILLARY LYMPH NODES ಯಿಂದ ಅಂಗಾಂಶ ಐ.ಎಚ್.ಚಿ ಅಧ್ಯಯನಕ್ಕೆ ಒಳಪಡಿಸಲಾಗುತ್ತದೆ.

**ವಿಷಯದ ಆಯ್ಕೆ :** ಎಲ್ಲಾ ಸ್ಥಳೀಯವಾಗಿ ಹರಡಿರುವ ಬ್ರೆಸ್ಟ್ ಕ್ಯಾನ್ಸರ್.

ಈ ಅಧ್ಯಯನದ ರೋಗಿಗಳು ಸಿಬಿಸಿ, ಬಿಟಿ ಸಿಟಿ,ಬ್ಲಡ್ ಗ್ರೂಪಿಂಗಗೆ ರಕ್ತದ ಸಕ್ಕರೆ , ರಕ್ತದ ಯೂರಿಯಾ, ಸೀರಮ್ ಕಿಯಟಿನ್, ಸೀರಮ್ ಎಲೆಕ್ಟ್ರೋಲೈಟ್ಸ್, ಎಚ್.ಐ.ವಿ, ಎಚ್.ಬಿ.ಅಸ್.ಅ.ಜಿ, ಎದೆಯ ಎಕ್ಸರೇ, ಇಸಿಜಿ ಮ್ಯಾಮೋಗ್ರಾಫಿ ಮತ್ತು ಎಫ್.ಎನ್.ಎ.ಸಿ ಪರೀಕ್ಷೆಗಳಿಗೆ ಒಳಗಾಗಬೇಕಾಗುತ್ತದೆ.
ತೊಡಕುಗಳು: ರಕ್ತಸ್ರಾವ, ಗಾಯದ ಸೋಂಕು, ಕಡಿಮೆ ಅಂಗಾಂಶ ಮತ್ತು ಪರೀಕ್ಷೆ ಮತ್ತೆ ಮಾಡುವುದು ಅನಿವಾರ್ಯ.
ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಈ ಮೇಲೆ ವರ್ಣಿಸಿರುವ ಕಾಯಿಲೆಯುಕ್ತ ರೋಗಿಗಳನ್ನು ಸೇರ್ಪಡಿಸಲಾಗುತ್ತದೆ.
ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ, ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಒಪ್ಪಿಕೊಂಡರೆ, ನಿಮ್ಮಿಂದ ಅಥವಾ ಇಬ್ಬರಿಗೂ ಜವಾಬ್ದಾರರಾಗಿರುವ ಮಾಹಿತಿಯನ್ನು ನಾವು (ಮಾಹಿತಿ ಪ್ರಕಾರ) ಸಂಗ್ರಹಿಸುತ್ತವೆ. ಸಂಬಂಧಿತ ರೋಗಲಕ್ಷಣಗಳನ್ನು ತೆಗೆದುಕೋಳ್ಳಲಾಗುವುದು. ಸಮಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರೌಢಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗಾಗಿ ಮಾತ್ರ ಬಳಸಳಾಗುತ್ತದೆ. ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿರಿಸಲಾಗುವುದು ಮತ್ತು

ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಗೊಳ್ಳುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವು ಸಾಂಸ್ಥಿಕ ನೀತಿ ಶಾಸ್ತ್ರ ಸಮಿತಿಯಿಂದ ಪರಿಶೀಲಿಸಲ್ಪಟ್ಟಿದೆ ಮತ್ತು ನೀವು ಸಂಸ್ಥೆಯ ಎಥಿಕ್ಸ್ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತವಾಗಿರುತ್ತೀವಿ. ಈ ಅಧ್ಯಯನಕ್ಕೆ ಒಪ್ಪಿಗೆ ನೀಡಲು ಯಾವುದೇ ಕಡ್ಡಾಯವಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಆರೈಕೆ ಬದಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಸ್ವಯಂ ಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಕೊಳ್ಳುವುದಾದರೆ ಮಾತ್ರ ಹೆಬ್ಬೆರಳ ಗುರುತು / ಸಹಿ, ಅನಿಸಿಕೆ ನೀಡಬೇಕಾಗಿದೆ.

**ಹೆಚ್ಚಿನ ವಿವರಗಳಿಗೆ ಸಂಪರ್ಕಿಸಿ:**

೧. ಡಾ. ವರ್ಷ.ಎ (ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿನಿ)

ಶಸ್ತ್ರಚಿಕಿತ್ಸೆ ವಿಭಾಗ,

ಮೊ: 9916974081

ಶ್ರೀ ದೇವರಾಜ ಅರಸ್ ವೈದ್ಯಕೀಯ ಮಹಾ ವಿದ್ಯಾಲಯ ಟಮಕ, ಕೋಲಾರ.

ರೋಗಿಯ ಸಹಿ / ಹೆಬ್ಬೆರಳು ಗುರುತು ಸಾಕ್ಷಿ / ಹೆಬ್ಬೆರಳು ಗುರುತು

# ಮಾಹಿತಿದಾರರ ಒಪ್ಪಿಗೆ ಪತ್ರ

**ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ:** ಪ್ರಾಥಮಿಕ BREAST CANCER, ಮತ್ತು METATSTATIC AXILLARY LYMPH NODES ನ HER 2-NEU ಸ್ಥಿತಿ ಅಧ್ಯಾಯನ ಮತ್ತು ಅದರ ಶಸ್ತ್ರ ಚಿಕಿತ್ಸೆ ನಂತರದ ಚಿಕಿತ್ಸೆಯಲ್ಲಿ ಬಳಕೆ.

ನಾನು ಶ್ರೀ / ಶ್ರೀಮತಿ_____ ಈ ಒಪ್ಪಿಗೆ ಪತ್ರದಲ್ಲಿ ತಿಳಿಸಿರುವ ಎಲ್ಲಾ ಕ್ರಮಗಳನ್ನು ಅರಿತುಕೊಂಡು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿರುತ್ತೇನೆ.

ನನಗೆ ತಿಳಿದಿರುವ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ಎಲ್ಲವನ್ನೂ ಓದಿ ವಿವರಿಸಿರುತ್ತಾರೆ. ಮತ್ತು ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶವನ್ನು ಅರಿತುಕೊಂಡಿರುತ್ತೇನೆ. ಈ ಅಧ್ಯಯನ ಸಂದರ್ಭದಲ್ಲಿ ಸಂಗ್ರಹಿಸಲ್ಪಡುವ ಎಲ್ಲಾ ವಿಷಯಗಳು ಗೋಪ್ಯ ರೀತಿಯಾಗಿರುತ್ತವೆ. ಮತ್ತು ಅಧ್ಯಯನಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸಲ್ಪಡುತ್ತದೆಂದು ಗೊತ್ತಿರುತ್ತದೆ. ಈ ಸಂದರ್ಭದಲ್ಲಿ ನನ್ನಲ್ಲಿ ಉದ್ಭವಿಸಿದ ಎಲ್ಲಾ ಪ್ರಶ್ನೆಗಳನ್ನು ಸಮರ್ಪಅವಾಗಿ ಉತ್ತರಿಸಿರುತ್ತಾರೆ. ಮತ್ತು ಸಂಗ್ರಹಿಸಿದ ಮಾಹಿತಿಗಳನ್ನು ಸಂಶೋಧನೆಗಾಗಿ ಬಳಸುವರೆಂದು ತಿಳಿದಿರುತ್ತೇನೆ.

ಡಾ. ವರ್ಷ.ಎ (ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿನಿ)

ಶಸ್ತ್ರಚಿಕಿತ್ಸೆ ವಿಭಾಗ,

ಮೊ: 9916974081

ಭಾಗವಹಿಸುವ ಡಾಕ್ಟರ್ ಸಹಿ:

ಸಾಕ್ಷಿಗಳು:

1. ಸಹಿ/ ಹೆಸರು ದಿನಾಂಕ

2. ಸಹಿ/ ಹೆಸರು ದಿನಾಂಕ

| AGE | UHID NO | SIDE | | PRE/POST | CLINICAL STAGING | PATHOLOGICAL SLN | stage | op | HPR | LN | ER | PR | HER2NEU | lymph n | chemo | RT | hormonal | targeted |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 68 | 461171 | LEFT | upper outer | POST | T2N1M0 | Pt2n1mx | II | mrm | infiltrating ductal carcinoma | 2 of 11 | NEGATIVE | NEGATIVE | equivocal | euivocal | 8cycles | 15# | | |
| 50 | 582129 | RIGHT | central | POST | T2N1M0 | pT3N2mx | II | mrm | infiltrating ductal carcinoma | 3 OF 8 | positive | positive | equivocal | negative | 8cycles | 15# | received | |
| 53 | 582456 | LEFT | upper outer | POST | T3N0M0 | pt2n1mx | II | lumpectomy | infiltrating ductal carcinoma | 3 OF 14 | POSITIVE | POSTIIVE | NEGATIVE | positive | 8cycles | 15# | received | 12cycles |
| 65 | 586568 | RIGHT | lower | POST | **T3N1M0** | T3 N1a Mx | III | mrm | infiltrating ductal carcinoma | 2 OF 7 | POSTIVE | NEGATIVE | NEGATIVE | negative | 12cycles | 15# | | |
| 66 | 575376 | RIGHT | upper outer | POST | T2N2M0 | pt3n2m0 | III | mrm | infiltrating ductal carcinoma | 2 OF 12 | POSITIVE | POSITIVE | POSITIVE | negative | 8cycles | 15# | received | |
| 46 | 584126 | RIGHT | lower | PRE | T2N2M0 | pT3N1aMx | III | mrm | infiltrating ductal carcinoma | 2 of 10 | NEGATIVE | NEGATIVE | NEGATIVE | positive | 12cycles | 15# | | 12cycles |
| 65 | 581449 | LEFT | upper outer | POST | T3N1M1 | pT3N0Mx | IV | mrm | infiltrating ductal carcinoma | 2 OF 8 | NEGATIVE | NEGATIVE | NEGATIVE | negative | 12cycles | 15# | | |
| 50 | 537450 | LEFT | upper outer | POST | T3N1M0 | pt3n1Mx | II | mrm | infiltrating ductal carcinoma | 3 OF 16 | POSITIVE | POSITIVE | NEGATIVE | positive | 8cycles | 15# | received | 12cycles |
| 55 | 560942 | LEFT | upper outer | POST | T3N1M0 | pt3n1Mx | III | mrm | infiltrating ductal carcinoma | 3 OF 4 | POSITIVE | POSITIVE | POSITIVE | negative | 8cycles | 15# | received | |
| 60 | 543952 | LEFT | upper outer | POST | T4BN1M1 | pT3N1MX | IV | mrm | infiltrating ductal carcinoma | 3 OF 10 | NEGATIVE | NEGATIVE | NEGATIVE | positive | 8cycles | 15# | | 12cycles |
| 42 | 612034 | RIGHT | upper outer | POST | T3N2M0 | pT3N3mx | III | mrm | infiltrating ductal carcinoma | 11 OF 16 | NEGATIVE | NEGATIVE | POSITIVE | euivocal | 12cycles | 15# | | |
| 60 | 603691 | RIGHT | upper outer | POST | T3aN1M0 | pT4N1mx | III | mrm | infiltrating ductal carcinoma | 2 OF 8 | positive | positive | NEGATIVE | negative | 8cycles | 15# | received | |
| 55 | 678651 | LEFT | upper outer | POST | T3N1M0 | pt3n2m0 | III | mrm | infiltrating ductal carcinoma | 6 OF 13 | positive | positive | POSITIVE | negative | 8cycles | 15# | received | |
| 30 | 647618 | RIGHT | lower | POST | T2N1M0 | pt3n1m0 | II | mrm | ductal carcinoma | 10 | positive | positive | negative | euivocal | 8cycles | 15# | received | |
| 30 | 6681638 | left | upper outer | post | t3nom0 | pt3n1mx | II | mrm | infiltrating ductal carcinoma | 3 of 10 | negative | NEGATIVE | NEGATIVE | negative | 12cycles | 15# | | |
| 60 | 611791 | RIGHT | upper outer | POST | T3N0M0 | pT3N1aMx | II | mrm | infiltrating ductal carcinoma | 3 of 10 | positive | positive | NEGATIVE | positive | 8cycles | 15# | received | 10cycles |
| 32 | 618298 | RIGHT | lower | PRE | T3N0M0 | pt3nomx | II | mrm | infiltrating ductal carcinoma | 1 OF 23 | NEGATIVE | positive | NEGATIVE | negative | 8cycles | 15# | | |
| 50 | 601433 | LEFT | upper outer | POST | T3N1M0 | pT3N1aMx | III | mrm | lobular | 3 OF 10 | NEGATIVE | NEGATIVE | euivocal | positive | 12cycles | 15# | | |
| 75 | 501731 | LEFT | upper outer | POST | T3N2M0 | pt3n1mx | III | mrm | smous cell carcinoma | 7 | positive | positive | euivocal | negative | 8cycles | 15# | received | |
| 53 | 582456 | LEFT | upper outer | POST | T2N0M0 | pT3N1MX | II | mrm | infiltrating ductal carcinoma | 3 OF 12 | positive | positive | NEGATIVE | negative | 8cycles | 15# | received | |
| 59 | 601433 | LEFT | lower | POST | T3N1M0 | pt3n1mx | II | mrm | infiltrating ductal carcinoma | 11 | NEGATIVE | NEGATIVE | POSITIVE | positive | 12cycles | 15# | | |
| 50 | 570525 | RIGHT | upper outer | POST | T3N1M0 | pT2N1MX | II | mrm | infiltrating ductal carcinoma | 3 OF 11 | positive | positive | NEGATIVE | negative | 8cycles | 15# | received | |
| 35 | 622345 | RIGHT | upper outer | PRE | T3N0M0 | pT3N1MX | II | mrm | smous cell carcinoma | 11 | positive | positive | equivocal | negative | 8cycles | 15# | received | |
| 48 | 664790 | RIGHT | upper outer | POST | T3N2M0 | pt3n3mx | III | mrm | infiltrating ductal carcinoma | 11 of 15 | NEGATIVE | NEGATIVE | POSITIVE | positive | 12cycles | 15# | | |
| 54 | 767363 | left | central | post | T3N1M0 | pT3N1M0 | III | mrm | infiltrating ductal carcinoma | 2 of 10 | positive | positive | POSITIVE | positive | 8cycles | 15# | received | |
| 38 | 761094 | left | upper outer | pre | T2N0M0 | pT3N0Mx | II | mrm | infiltrating ductal carcinoma | 3 of 7 | positive | positive | POSITIVE | euivocal | 8cycles | 15# | received | |
| 44 | 529217 | right | upper outer | post | T3N0M0 | pt3nomx | II | mrm | infiltrating ductal carcinoma | 2 0f 10 | positive | positive | negative | negative | 8cycles | 15# | received | |
| 45 | 678900 | left | central | post | t3nom0 | pt3nomx | II | mrm | infiltrating ductal carcinoma | 3 of 2 | negative | NEGATIVE | euivocal | negative | 12cycles | 15# | | |
| 42 | 738555 | right | upper outer | post | T3N0M0 | pT3N1m0 | II | mrm | infiltrating ductal carcinoma | 2 of 8 | positive | positive | NEGATIVE | negative | 8cycles | 15# | received | |
| 45 | 735987 | right | central | post | T4BN1M0 | pT4N1mx | IV | mrm | infiltrating ductal carcinoma | 4 of 5 | positive | positive | NEGATIVE | negative | 8cycles | 15# | received | |