STUDY OF CORRELATION OF ER, PR, HER2 RECEPTOR STATUS IN BREAST CANCER AT A SINGLE TERTIARY CARE HOSPITAL WITH EMPHASIS ON CLINICAL UTILITY OF PR RECEPTOR

Dissertation Submitted to

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M.S GENERAL SURGERY

BRANCH-I

REG NO : 221911208

DEPARTMENT OF GENERAL SURGERY

THANJAVUR MEDICAL COLLEGE AND

HOSPITALTHANJAVUR - 613 004

MAY – 2022

CERTIFICATE – I

This is to certify that this dissertation entitled "**STUDY OF CORRELATION OF ER, PR, HER2 RECEPTOR STATUS IN BREAST CANCER AT A SINGLE TERTIARY CARE HOSPITAL WITH EMPHASIS ON CLINICAL UTILITY OF PR RECEPTOR"** is the bonafide original work of **DR. T. Livin** in partial fulfillment of the requirements for award of the Degree M.S General Surgery Branch-I Examination of the Tamilnadu Dr. M.G.R Medical University, to be held in May- 2022. The period of the study is from January 2021 to December 2021.

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Title of the study: study of correlation of ER, PR, Her2 receptor status in breast cancer at a single tertiary care hospital with emphasis on clinical utility of PR receptor.

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This to certify that the protocol submitted by the principal investigator of the above mentioned study has been reviewed as per standard ethical guidelines and the same has been **APPROVED** by the members of the Institutional ethical committee at its meeting held on 13/01/2020.

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CERTIFICATE-II

This is to certify that this dissertation work titled **"STUDY OF CORRELATION OF ER, PR, HER2 RECEPTOR STATUS IN BREAST CANCER AT A SINGLE TERTIARY CARE HOSPITAL WITH EMPHASIS ON CLINICAL UTILITY OF PR RECEPTOR"** of the candidate **Dr. T. Livin** with Registration Number **221911208** for the award of **M.S** in the branch of **General Surgery**. I personally verified the **urkund.com** website for the purpose of plagiarism Check.

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DECLARATION

I, declare that this dissertation titled, **"STUDY OF CORRELATION OF ER, PR, HER2 RECEPTOR STATUS IN BREAST CANCER AT A SINGLE TERTIARY CARE HOSPITAL WITH EMPHASIS ON CLINICAL UTILITY OF PR RECEPTOR"** done at Thanjavur Medical College, Thanjavur represent a genuine work of mine. I also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other university board, neither in India nor abroad. This is submitted to the The Tamil Nadu Dr.MGR Medical University, Chennai in fulfillment of the rules and regulations for the award of Master of Surgery Degree Branch 1 [General Surgery].

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Date :

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INTRODUCTION

Breast cancer is a major public health problem for women throughout the world. In the United States, breast cancer remains the most frequent cancer in women and the second most frequent cause of cancer death. In 2017, it was estimated there were 255,180 new cases of breast cancer, with 41,070 deaths.1

Worldwide, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females, accounting for 25% of cancer cases and 15% of the cancer deaths.

Among the Indian women carcinoma of the breast and cervix account for 60% of total cases, of which breast carcinoma accounts for 10.4%.

A study conducted by WHO revealed that Chennai has the highest incidence among all leading centres in India accounting for 26/1, 00,000 women [7]. The mean age of occurrence is 42 years.

The approach to the management of breast carcinoma has undergone enormous changes over the last 20 years [13]. Today, the choice of conservative and reconstructive surgery is more popular than mastectomy. Such changes are accompanied by increasing range of systemic, hormonal and cytotoxic drugs used in both adjuvant and neoadjuvant settings [6, 13.] Prognosis and management of breast carcinoma are influenced by the classic variables such as histological type and grade, tumor size,lymph node status, Estrogen, Progesterone receptor status and HER-2/neu overexpression .[11]

Identification of biomarkers plays a paramount role in the treatment, management and prognosis of breast carcinoma. Determination of hormonal status is an important primary assessment at the time of diagnosis of breast carcinoma. Testing for Estrogen and Progesterone receptor status is critical to plan optimal treatment for breast cancer.[1, 2]

Estrogen receptor is a well established predictive and prognostic factor in breast cancer.Patients with ER-positive/PR-positive tumors have a better prognosis than patients with ER- negative/PR-negative tumors. Hormone receptor test is done routinely in these cases since hormone treatment has fewer side effects and it prevents recurrence in 25% of cases.[1]

HER2/neu status became clinically relevant with the demonstration that HER-2/neu positive tumors have a worse prognosis than HER2/neu negative tumors.[2] It has been recognised that HER2/neu overexpression served as both a marker of aggressive disease and a target for treatment. HER2/neu status not only predicts poor outcome, but predicts sensitivity to treatment with Trastuzumab (Herceptin), a humanized monoclonal anti- HER2/neu antibody .

With these prognostic implications, the need for accurate and precise assessment of ER, PR, and HER2/neu expression in breast carcinoma is critical in the determination of patients appropriate for treatment with these drugs. Immunochemistry is an important tool in precise histopathological diagnosis. Immunohistochemistry (IHC) is the most commonly used method of testing for ER, PR, and HER2/neu status.[2]

Survival and response to hormone therapy are most favourable among women who are receptor positive, intermediate for tumors discordant on receptor status and least favourable for receptor negative patients. The interrelationship of Estrogen, Progesterone receptor status and HER-2/neu overexpression has an important role in management of breast carcinoma. It has been shown that patients with HER-2/neu overexpression do not respond to tamoxifen therapy, while they serve as a candidates for trastuzumab therapy.

OBJECTIVES OF THE STUDY

:

- To Analyse the incidence of
  - age, sex,
  - stage at presentation
  - the modality of treatment given and
  - hormone receptor status.

- It is a retrospective and prospective analysis of women with breast cancer
- Patients considered restrospectively from January 2017
- Prospectively till December 2021

- To determine the clinical utility of PR receptor study.

REVIEW OF LITERATURE

INCIDENCE AND EPIDEMIOLOGY

Carcinoma afflicts all the communities worldwide. Approximately 10 million people are diagnosed with carcinoma and more than 6 million people die of the disease every year.[4] Breast carcinoma is the most common non-skin malignancy in women. It causes 3,76,000 deaths in a year worldwide and every year 9,00,000 new cases are diagnosed. [5, 6]

Among the Indian women cancer cervix and breast carcinoma accounts for 60% of total cases, of which breast carcinoma incidence is 10.4%. A study conducted by WHO [7] (1999) denotes that Chennai accounts for the highest incidence among all the leading centres in India (ie) 26/1,00,000 women. The mean age of occurrence is 42 years.

There has been a sharp increase in the detection of breast carcinoma, owing to the widespread use of mammography. [3, 7] However the mortality from breast carcinoma is beginning to fall, presumably because of earlier diagnosis and improved therapy.

Survival rates in women with breast cancer have steadily improved over the last several decades, with 5-year survival rates of 63% in the early 1960s, 75% during the years 1975 to 1977, 79% during 1984 to 1986, and 90% during 1995 to 2005.

The largest decreases in death rates from breast cancer have been in women younger than 50 years (decreases of 3.2% per year), although breast cancer death rates have also decreased in women older than 50 years (by 2% per year). The decreased mortality from breast cancer is thought to be the result of earlier detection via mammographic screening, a decreased incidence of breast cancer, and improvements in therapy. The survival rate for stage I breast cancer is 98.7%. The current treatment of breast cancer is guided by pathology, staging, and more recent insights into breast cancer biology. There is an increased emphasis on defining disease biology and status in individual patients, with the subsequent tailoring of therapies.

RISK FACTORS

The frequency of the disease has prompted an intensive study of risk factors. It has been proposed that the common denominator for most of these factors is strong and **prolonged estrogen stimulation** operating in a genetically susceptible background.

1. Country of birth: Incidence of breast carcinoma is more in developed countries than in developing countries.

2. Family history: Women who have first degree relatives with breast carcinoma have a risk two to three times that of the general population.

3. Menstrual and reproductive history: Increased risk is correlated with

- early menarche - < 12 years
- nulliparity
- age at first birth – after 30 years
- late menopause after 55 years owing to hyper estrogenic stimulation

4. Breast biopsies: Increased risk is associated with prior biopsies showing atypical hyperplasia.

5. Race and socio economic group: Incidence of breast carcinoma is high among the high socio- economic group

The risk of developing invasive carcinoma within the next 20 years at age 50 is 1 in 26 for Asian / Pacific islanders.

Additional risk factors as follows are also recognized, but there is a lack of definitive correlation.

1. Estrogen exposure: Post menopausal hormone replacement therapy and use of oral contraceptive drugs are associated with increased risk of breast cancer. Oophorectomy reduces the risk of breast carcinoma by 75%.

2. Radiation exposure: Those who are exposed to therapeutic radiation and atom bomb survivors have a high incidence of breast cancer.

3. Carcinoma of contralateral breast and endometrium: Increased risk is associated with the above mentioned factors.

4. Geographic influence: Breast cancer incidence rates are increased about four times in the United States and Europe than in other countries.

5. Diet: High fat diet and obesity carry increased risk.

6. Exercise: Reduced risk is associated with premenopausal women who exercise regularly.

7. Breast feeding: The longer the women breast feed their children the greater is thereduction in the risk of breast carcinoma.

ETIOLOGY AND PATHOGENESIS

The major risk factors for the development of breast carcinoma are hormonal and genetic (family history)

. Breast carcinoma can therefore be divided into

1) Sporadic breast carcinoma. 2) Hereditary breast carcinoma.

HEREDITARY BREAST CARCINOMA:

About 25% familial cancers can be attributed to two highly penetrant autosomal dominant genes BRCA1, and BRCA2, located in 17q21 and 13q12.3 respectively. BRCA1 and BRCA2 do not show sequence homology.

They function on similar pathways and interact with multiprotein complexes. Both act as tumour suppressor genes that confers the risk of malignancy. Loss of these function leads to breast carcinoma perhaps due to intermittent proliferation of breast epithelium.

BRCA1 interacts with Estrogen receptor and is involved in X- Chromosome activation. BRCA1 associated breast cancers are most common in medullary carcinoma (67%) and mucinous carcinoma (55%), BRCA2 mutation does not have a distinct morphologic appearance.

SPORADIC BREAST CARCINOMA:

The major risk factors for sporadic breast cancer are related to hormone exposure, gender, age at menarche and menopause, reproductive history and exogenous estrogens. These carcinomas are associated with post menopausal women and they overexpresses the estrogen receptor.

Incidence of sporadic, familial, and hereditary breast cancer	
Sporadic breast cancer	65%–75%
Familial breast cancer	20%–30%
Hereditary breast cancer	5%–10%
BRCA1[a]	45%
BRCA2	35%
p53[a] (Li-Fraumeni syndrome)	1%
STK11/LKB1[a] (Peutz-Jeghers syndrome)	<1%
PTEN[a] (Cowden disease)	<1%
MSH2/MLH1[a] (Muir-Torre syndrome)	<1%
ATM[a] (Ataxia-telangiectasia)	<1%
Unknown	20%

MICROSCOPIC TYPES OF BREAST CARCINOMA:

The two key determinations to make in the morphologic study of breast carcinoma are

1) whether the tumour is confined to the epithelial component of the organ (in situ carcinoma) or has invaded into the stroma (invasive carcinoma).

2) whether it is ductal or lobular type.

Noninvasive Epithelial Cancers

Lobular carcinoma in situ

Ductal carcinoma in situ or intraductal carcinoma

- Papillary, cribriform, solid, and comedo types

Invasive Epithelial Cancers (Percentage of Total)

Invasive lobular carcinoma (10%)

Invasive ductal carcinoma

- Invasive ductal carcinoma, not otherwise specified (50%–70%)
- Tubular carcinoma (2%–3%)
- Mucinous or colloid carcinoma (2%–3%)
- Medullary carcinoma (5%)
- Invasive cribriform carcinoma (1%–3%)
- Invasive papillary carcinoma (1%–2%)
- Adenoid cystic carcinoma (1%)
- Metaplastic carcinoma (1%)

Mixed Connective and Epithelial Tumors

Phyllodes tumors, benign and malignant

Carcinosarcoma

Angiosarcoma

Adenocarcinoma

Salient characteristics of in situ ductal (DCIS) and lobular (LCIS) carcinoma of the breast

	LCIS	DCIS
Age (years)	44–47	54–58
Incidence[a]	2%–5%	5%–10%
Clinical signs	None	Mass, pain, nipple discharge
Mammographic signs	None	Microcalcifications
Premenopausal	2/3	1/3
Incidence of synchronous invasive carcinoma	5%	2%–46%
Multicentricity	60%–90%	40%–80%
Bilaterality	50%–70%	10%–20%
Axillary metastasis	1%	1%–2%
Subsequent carcinomas:		
Incidence	25%–35%	25%–70%
Laterality	Bilateral	Ipsilateral
Interval to diagnosis	15–20 y	5–10 y
Histologic type	Ductal	Ductal

INVASIVE CARCINOMA:

Tumours included in this category are all those in which stromal invasion is detectable, whether an insitu component is identifiable or not.

Invasive tumours can be divided into two major categories: ductal type and lobular type. [14, 15]

INVASIVE DUCTAL CARCINOMA –NOS TYPE:

Rosen (1975) 18 accounts that this type constitutes 65-80% of mammary carcinomas. WHO classification of Invasive ductal carcinoma -NOS type tumour is one of exclusion:

"Invasive ductal carcinoma is most frequently encountered malignant tumour, not falling into any other categories of invasive mammary carcinoma".[17]

Microscopically WHO classification requires a non-specialized pattern in over 50% of the tumour area to be classified as NOS- type. Typically combinations of infiltrative margins, trabecular, diffuse sheet like, acinar and nested patterns are noted. Histological grading of the tumour depends on tubular formation, pleomorphism and mitotic count.

They are graded into well differentiated, moderately differentiated and poorly differentiated grades. [14, 15]

Predictive value of Estrogen receptor is evaluated by quantitative immunohistochemical analysis in breast carcinoma.[19,23]

Hormone receptor studies of IDC-NOS type shows 70-80% Estrogen, Progesterone positivity and 15-30% HER-2 / neu positivity [14,15,]

INVASIVE LOBULAR CARCINOMA: (ILC)

Foote and Stewart (1946) 20 introduced the term Infiltrating Lobular carcinoma. Tavassoli (1992) 21 described that ILC of breast composed of small cells with linear growth pattern. Over 90% of the carcinoma should have a lobular morphology to be classified in this group. This type represents 4.9-15% of all invasive breast carcinomas. [22]

There is some evidence that increased risk of lobular carcinoma occur in postmenopausal women and it is frequently multicentric when compared with other sub-types. 1[6,22]

Microscopically the cell type characteristic of invasive lobular carcinoma is non-cohesive with relatively round or oval eccentrically placed nuclei with small nucleoli and small amount of cytoplasm. The classical pattern of single file and targetoid arrangements were noted. [14,17]

Dixan J M (1985) 22 conducted receptor assay that reveals

Estrogen, Progesterone receptor positivity in 67 -92% of cases, [14,15]

E-Cadherin negative 15 and HER-2/neu negativity. [21]

MUCINOUS CARCINOMA:

In 1852 Robinson RR has described about gelatinous carcinoma of breast. The incidence ranges from 0.8 -6% probably reflecting the applied diagnostic criteria.17 The tumor type is characterized by a mucinous morphology in over 90% of the tumour. WHO classification describes “large amount of extracellular mucin sufficient to be visible both grossly and microscopically surrounding the tumour cells”. [17]

Diab SG (1999) 26 in his study concluded Estrogen receptor positivity in 73-95%,progesterone receptor positivity 79-84% and HER-2/neu negativity of mucinous carcinoma.

Mucinous carcinoma tends to be negative for HER-2/neu and for EGFR [24,25]

MEDULLARY CARCINOMA:

Geschicker C F (1945) described about high grade tumor as a different entity in breast carcinoma. Grossly the tumor appears as a well circumscribed mass and soft in consistency. WHO defined as "well circumscribed carcinoma composed of poorly differentiated cells with scant stroma and prominent lymphocytic infiltration". Despite the high grade of tumor it carries relatively good prognosis. [17]

Immunohistochemical studies of Estrogen expression are found to be negative [14,27,28] and they also exhibit characteristic immunophenotype (i.e) p53 positive, HER-2 / neu negative [27]

NEUROENDOCRINE CARCINOMA;

In 1975 Coombes RC has described neuroendocrine carcinoma in his study. WHO defines this type of carcinoma with neuroendocrine marker positivity noted in more than 50% of the cell population. [17] A study confirmed that 10-18% breast carcinoma showed evidence of neuroendocrine differentiation. This type has an infiltrative morphology with component cells arranged in nests, sheets or trabecular formation and peripheral palisading of cell groups. [1]

Immunohistochemical studies by LeeAK31 show neuroendocrine marker positivity in 82% of the cases.

However 67% show Estrogen receptor positivity and 56% exhibits Progesterone receptor positivity. [30, 32]

HER-2/neu overexpression is found to be negative in this type of tumour [32]

PAPILLARY CARCINOMA:

Foote and Stewart [20] (1946) defined it as "A rare carcinoma whose invasive pattern predominantly is in the form of papillary structures."
Estrogen, Progesterone receptor positivity and HER-2/neu negativity are characteristic of this tumour. [31,33] Zekiglu.O.ErhanY et al (2004)[34] conducted immunohistochemical analysis of papillary carcinoma and interpreted receptor positivity in upto 89% of cases and HER-2/neu in 27 % of cases.

CARCINOMA WITH METAPLASIA:

In 1984 Kaufman M.W [35] described special edition of mammary carcinoma with pseudosarcomatous metaplasia. WHO (2003) publication defines metaplastic carcinoma breast as "heterogeneous group of neoplasm with spindle cells, squamous cells or with mesenchymal differentiation"

TNM STAGING OF BREAST CARCINOMA:

- Tis: DCIS[a]: Ductal carcinoma in situ
- Tis (Paget): Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.
- T1: Tumor ≤20 mm in greatest dimension
- T1mi: Tumor ≤1 mm in greatest dimension
- T1a: Tumor >1 mm but ≤5 mm in greatest dimension (round any measurement >1.0–1.9 mm to 2 mm)
- T1b: Tumor >5 mm but ≤10 mm in greatest dimension
- T1c: Tumor >10 mm but ≤20 mm in greatest dimension
- T2: Tumor >20 mm but ≤50 mm in greatest dimension
- T3: Tumor >50 mm in greatest dimension
- T4: Tumor of any size with direct extension to the chest wall and/or to skin (ulceration or skin nodules); invasion of the dermis alone does not qualify as T4
- T4a: Extension to chest wall; invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not quality as T4
- T4b: Ulceration and/or ipsilateral macroscopic satellite nodules and/or edema (including peau d'orange) of the skin that does not meet the criteria for inflammatory carcinoma
- T4c: Both T4a and T4b are present
- T4d: Inflammatory carcinoma

Regional Lymph Nodes—Clinical (cN)

- cNX[b]: Regional lymph nodes cannot be assessed (e.g., previously removed)
- cN0: No regional lymph node metastases (by imaging or clinical examination)
- cN1: Metastases to movable ipsilateral level I, II axillary lymph node(s)
- cN1mi[c]: Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
- cN2: Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted *or* in ipsilateral internal mammary nodes in the absence of axillary lymph node metastases
- cN2a: Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures
- cN2b: Metastases only in ipsilateral internal mammary nodes in the absence of axillary lymph node metastases
- cN3: Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; *or* in ipsilateral internal mammary lymph node(s) with level I, II axillary lymph node metastases; *or* in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
- cN3a: Metastases in ipsilateral infraclavicular lymph node(s)
- cN3b: Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
- cN3c: Metastases in ipsilateral supraclavicular lymph node(s)

Note: (sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or FNA/core needle biopsy, respectively

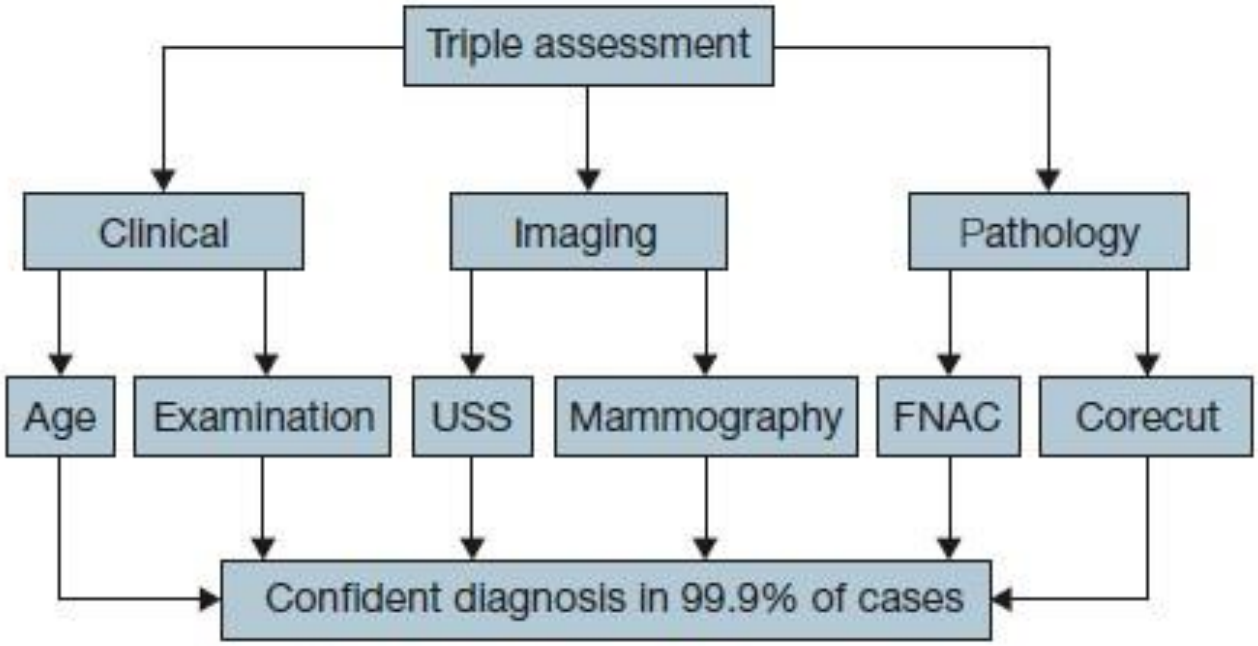
Regional Lymph Nodes—Pathologic (pN)

- pNX: Regional lymph nodes cannot be assessed (e.g., previously removed or not removed for pathologic study)
- pN0: No regional lymph node metastasis identified or ITCs only
- pN0(i+): ITCs only (malignant cell clusters no larger than 0.2 mm) in regional lymph node(s)
- pN0(mol+): Positive molecular findings by RT-PCR; no ITCs detected
- pN1: Micrometastases; or metastases in 1–3 axillary lymph nodes; and/or clinically negative internal mammary nodes with micrometastases or macrometastases by SLNB
- pN1mi: Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
- pN1a: Metastases in 1–3 axillary lymph nodes, at least one metastasis >2.0 mm
- pN1b: Metastases in ipsilateral internal mammary sentinel nodes, excluding ITCs
- pN1c: pN1a and pN1b combined
- pN2: Metastases in 4–9 axillary lymph nodes; or positive ipsilateral internal mammary lymph nodes by imaging in the *absence* of axillary lymph node metastases
- pN2a: Metastases in 4–9 axillary lymph nodes (at least one tumor deposit >2.0 mm)
- pN2b: Metastases in clinically detected internal mammary lymph nodes with or without microscopic confirmation; with pathologically negative axillary nodes
- pN3: Metastases in 10 or more axillary lymph nodes; *or* in infraclavicular (level III axillary) lymph nodes; *or* positive ipsilateral internal mammary lymph nodes by imaging in the *presence* of one or more positive level I, II axillary lymph node(s); *or* in more than 3 axillary lymph nodes and micrometastases or macrometastases by SLNB in clinically negative ipsilateral internal mammary lymph nodes; *or* in ipsilateral supraclavicular lymph nodes
- pN3a: Metastases in 10 or more axillary lymph nodes (at least one tumor deposit >2.0 mm); or metastases to the infraclavicular (level III axillary lymph) nodes
- pN3b: pN1a or pN2a in the presence of cN2b (positive internal mammary nodes by imaging); or pN2a in the presence of pN1b
- pN3c: Metastases in ipsilateral supraclavicular lymph nodes

Note: (sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or FNA/core needle biopsy, respectively, with no further resection of nodes.

DIAGNOSIS:

TRIPLE ASSESSMENT



CLINICAL:

Examination

Inspection.

The clinician inspects the woman's breast with her arms by her side, with her arms straight up in the air , and with her hands on her hips (with and without pectoral muscle contraction).

Symmetry, size, and shape of the breast are recorded, as well as any evidence of edema (peau d'orange), nipple or skin retraction, or erythema.

With the arms extended forward and in a sitting position, the woman leans forward to accentuate any skin retraction.

Palpation.

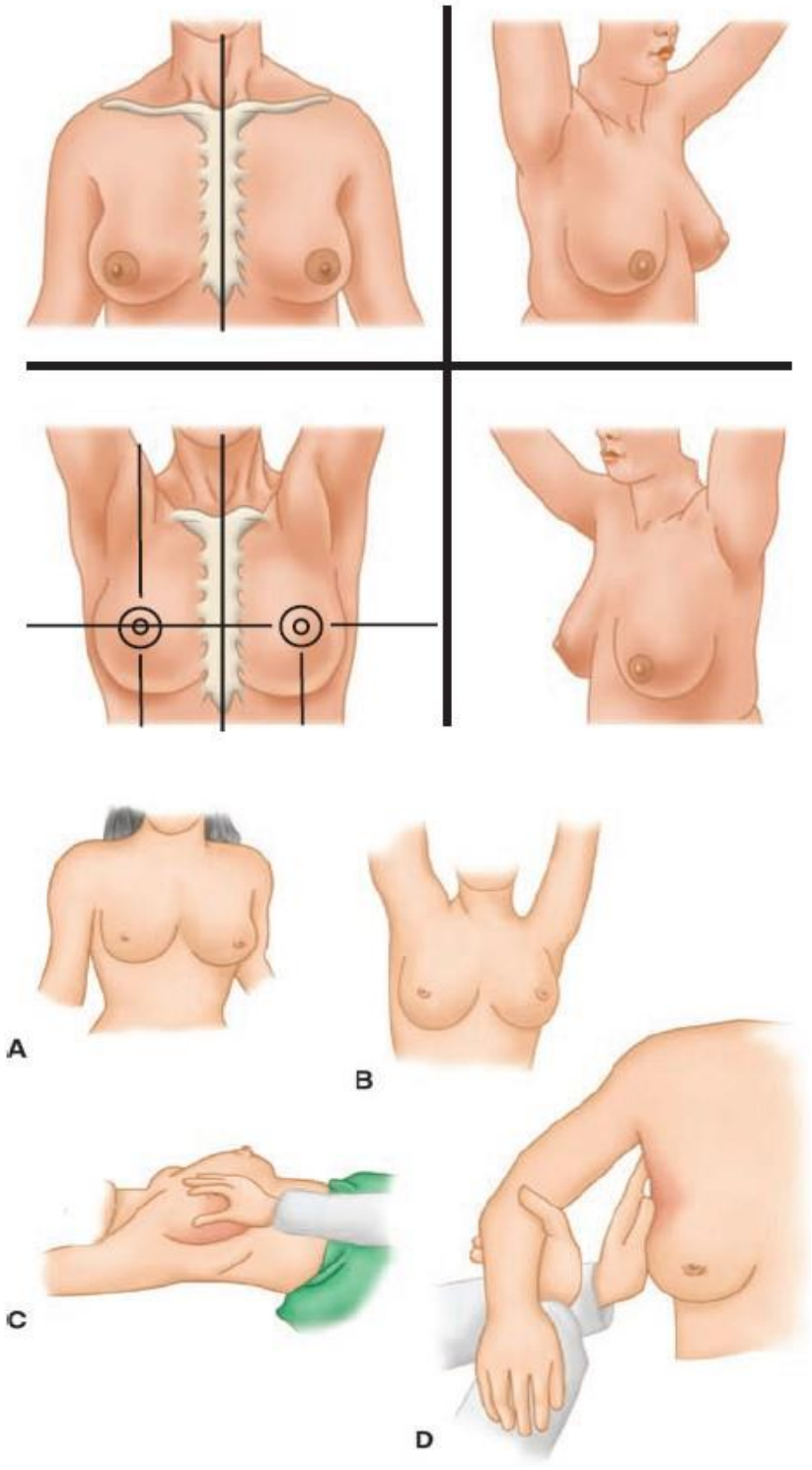
As part of the physical examination, the breast is carefully palpated. With the patient in the supine position ,the clinician gently palpates the breasts, making certain to examine all quadrants of the breast from the sternum laterally to the latissimus dorsi muscle and from the clavicle inferiorly to the upper rectus sheath.

The examination is performed with the palmar aspects of the fingers, avoiding a grasping or pinching motion. The breast may be cupped or molded in the examiner's hands to check for retraction.

A systematic search for lymphadenopathy then is performed.

By supporting the upper arm and elbow, the examiner stabilizes the shoulder girdle. Using gentle palpation, the clinician assesses all three levels of possible axillary lymphadenopathy.

Careful palpation of supraclavicular and parasternal sites also is performed. A diagram of the chest and contiguous lymph node sites is useful for recording location, size, consistency, shape, mobility, fixation, and other characteristics of any palpable breast mass or lymphadenopathy



SPECIMENS TAKEN FOR diagnosis & ER/PR/Her2 status:

- **Fine needle aspirationCytology:**

- **Core Needle Biopsy (trucut)**

CNB is the method of choice to sample breast lesions. Biopsies can be performed with trigger devices requiring multiple entries or with vacuum-assisted devices that require only single insertion.

The size of a CNB ranges from 8 to 14 gauge. CNB can be performed under mammographic (stereotactic), ultrasound, or magnetic resonance imaging (MRI) guidance.

Mass lesions that are visualized on ultrasonography can be sampled under ultrasound guidance; calcifications and densities that are best seen on mammography are sampled under stereotactic guidance.

- **Mastectomy Specimens:**

Modified Radical Mastectomy

Toilet / Simple Mastectomy

Radical Mastectomy

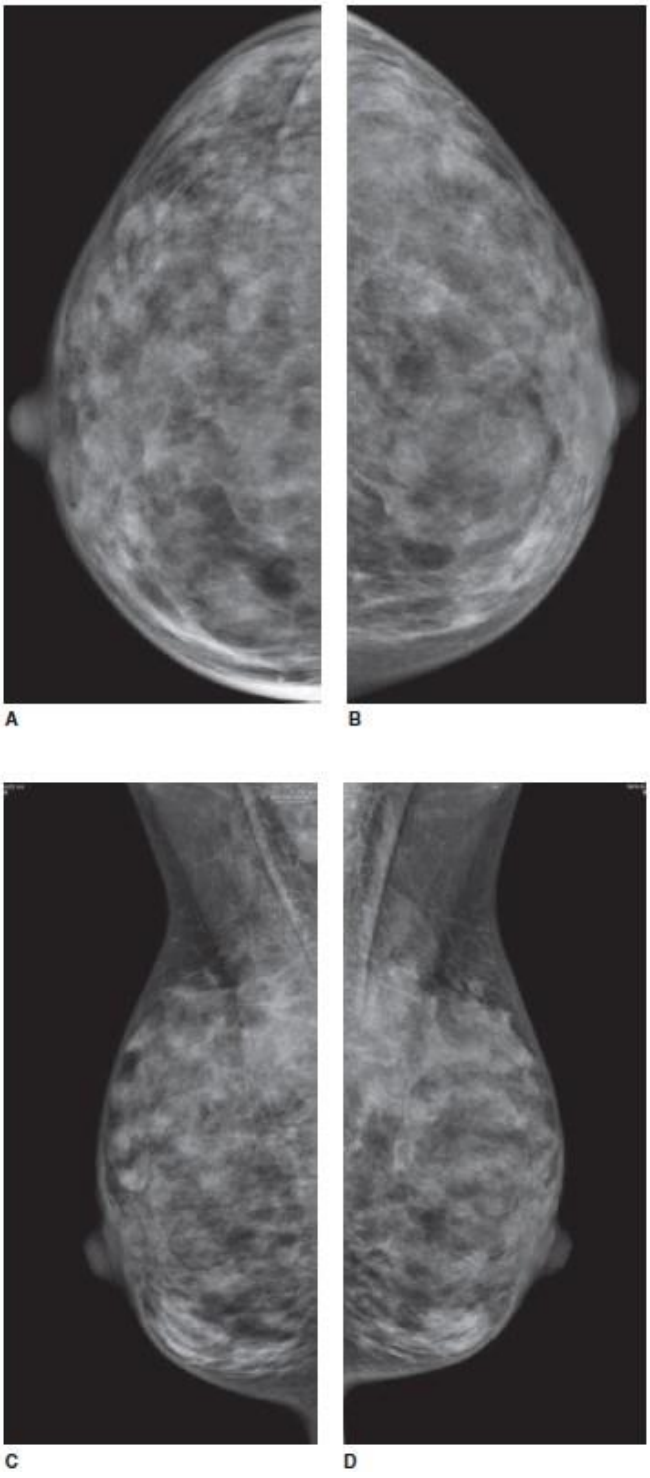
Extended Radical Mastectomy

Skin sparing Mastectomy

IMAGING STUDIES

Mammography

With screening mammography, two views of the breast are obtained: the craniocaudal (CC) view and the mediolateral oblique (MLO) view



Ductogram:

B

Figure 17-22. Ductogram. Craniocaudal (**A**) and mediolateral oblique (**B**) mammographic views demonstrate a mass (*arrows*) posterior to the nipple and outlined by contrast, which also fills the proximal ductal structures. *(Used with permission from B. Steinbach.)*

Ultrasonography:

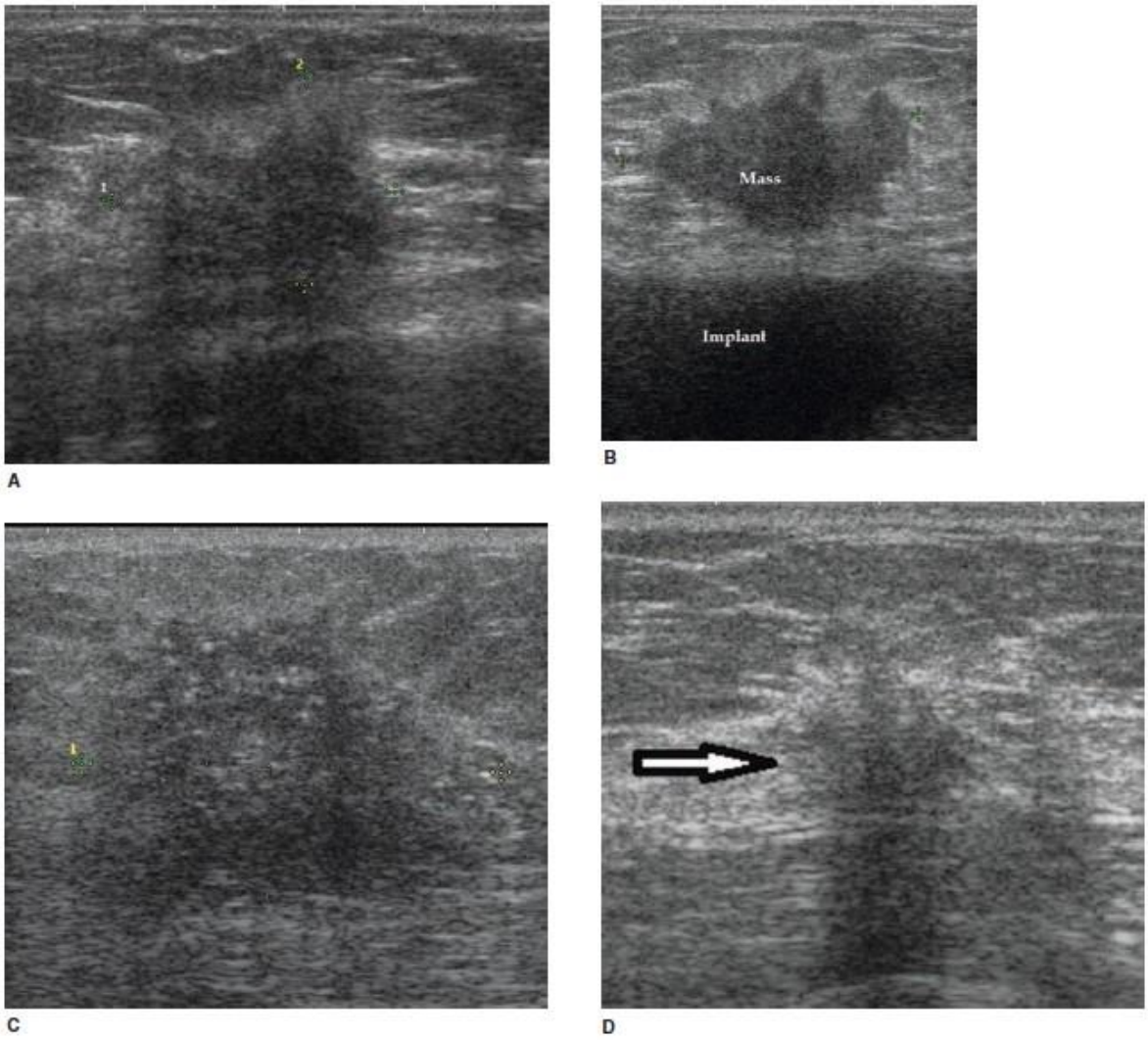


Figure 17-25. Ultrasonography images of malignant breast lesions. **A.** 25 mm irregular mass. **B.** Ultrasound 30 mm mass anterior to an implant. **C.** Ultrasound breast cancer with calcification. **D.** Ultrasound shows a 9 mm spiculated mass (see arrow) with attenuation. *(Used with permission from Dr. Anne Turnbull, Consultant Radiologist/Director of Breast Screening, Royal Derby Hospital, Derby, UK.)*

PROGNOSTIC AND PREDICTIVE FACTORS

Prognosis is determined by the pathologic examination of the primary carcinoma and the axillary lymph nodes.

Major prognostic factors are the strongest predictors of death from breast carcinoma and are incorporated into the American Joint committee cancer (AJCC) staging system.

Predictive factors are used to determine the likelihood of response to a particular therapy.

1. Invasive carcinoma or in situ disease:

By definition, in situ carcinoma is confined to the ductal system and cannot metastasize. In contrast, at least half of invasive carcinomas will have metastasized locally or distantly at the time of diagnosis**.** 15

2. Distant metastases:

Once distant metastases are present, cure is unlikely, although long- term remissions and palliation can be achieved, especially for women with hormonally responsive tumors. Favoured sites for dissemination are the lungs, bones, liver, adrenals, brain and meninges. 6,13

3. Lymph node metastases:

Axillary lymph node status is the most important prognostic factor for invasive carcinoma in the absence of distant metastases. The sentinel node is highly predictive of the status of the remaining nodes. Sentinel node biopsy can spare

women the increased morbidity associated with a complete axillary dissection. Macrometastases (>0.2 cm) are of proven to be prognostic importance.

4. Tumor size:

The size of the carcinoma is the second most important prognostic factor and is independent from lymph node status.

5. Locally advanced disease:

Tumors invading into skin or skeletal muscle are frequently associated with concurrent distant disease.

6. Inflammatory carcinoma:

Women presenting with the clinical appearance of breast swelling and skin thickening have a particularly poor prognosis.

MINOR PROGNOSTIC FACTORS:

In this group, minor prognostic factors can be used to decide among chemotherapy regimens and/or hormonal therapies. Three of these factors estrogen receptor, progesterone receptor, and HER2/neu-are most useful as predictive factors for response to specific therapeutic agents.

1. Histologic subtypes:

The 30-year survival rate of women with special types of invasive carcinomas (tubular, mucinous, medullary, lobular, and papillary) is greater than 60% compared with less than 20% for women with cancers of no special type.

2. Tumor grade:

The most commonly used grading system to assess the degree of tumor differentiation (Scraff Bloom Richardson) combines nuclear grade, tubule formation, and mitotic rate.

3. Estrogen and Progesterone Receptors:

Current assays use immunohistochemistry to detect the receptor status in the nucleus. [19] Women with hormone receptor-positive cancers have a slightly better prognosis than do women with hormone receptor-negative carcinomas. The evaluation of hormone receptors is most valuable to predict response to therapy. [39]

4. HER-2/neu:

HER2 (human epidermal growth factor receptor 2) or c-erb B2 is a transmembrane glycoprotein involved in cell growth control. HER2/neu is overexpressed in 20% to 30% of breast carcinomas.

Overexpression of HER-2/neu is associated with a poor prognosis.

Transtuzumab is a humanized monoclonal antibody to HER-2/neu developed to specifically target tumor cells and it is hoped to spare normal cells. [24]

5. Lymphovascular invasion (LVI):

Tumor cells may be seen within vascular spaces (either in lymphatic or in small capillaries surrounding tumours). This finding is strongly associated with the presence of lymph node metastasis and is a poor prognostic factor. [38]

6. Proliferative rate:

Proliferation can be measured by flow cytometry (as the S-phase fraction), by thymidine labelling index, by mitotic counts, or by immunohistochemical detection of cellular proteins (e.g.,cyclins, Ki-67) produced during the cell cycle. Tumours with high proliferation rates have the worst prognosis. [12]

7. DNA content:

The amount of DNA per tumour cell can be determined by flow cytometric analysis or by image analysis of tissue sections. Aneuploid tumours are those with abnormal DNA indices and have a slightly worse prognosis.

Despite the numerous prognostic indicators currently in use or under investigation, it is impossible in an individual case to predict the outcome. 14For this reason, there are continuing searches for better or more refined biologic markers of prognosis and more effective treatment modalities.

Current therapeutic approaches include local and regional control using combination of surgery (mastectomy or breast conservation) and postoperative radiation and systemic control using hormonal treatment or chemotherapy or both. Newer therapeutic strategies include inhibition (by pharmacologic agents or specific antibodies) of membrane-bound growth factor receptors (e.g., HER-2/neu), stromal proteases, and angiogenesis. [1,2]

TREATMENT REGIMEN for SYSTEMIC THERAPY

The two basic principles of treatment are

1. to reduce the risk of local recurrance
2. chance of local recurrence and the risk of metastatic spread
3. 

STAGE	SYSTEMIC THERAPY	COMMENTS
I (<1 cm)		
Hormone receptor–positive	Endocrine therapy ± chemotherapy	Consider genomic testing
Hormone receptor–negative	Consider chemotherapy	
HER-2–positive	Strongly consider trastuzumab and chemotherapy	
I (>1 cm)		
Hormone receptor–positive	Endocrine therapy ± chemotherapy	Consider genomic testing
Hormone receptor–negative	Chemotherapy	
HER-2–positive	Trastuzumab and chemotherapy	
II (Lymph Node–Negative)		
Hormone receptor–positive	Endocrine therapy ± chemotherapy	Consider genomic testing
Hormone receptor–negative	Chemotherapy	
HER-2–positive	Trastuzumab and chemotherapy	
II (Lymph Node–Positive), III		
Hormone receptor–positive	Chemotherapy + endocrine therapy	Endocrine therapy should be recommended for all patients
Hormone receptor–negative	Chemotherapy	Decision-making for chemotherapy may be influenced by results from ongoing clinical trials
HER-2–positive	Trastuzumab and chemotherapy	Consider neoadjuvant chemotherapy with dual HER-2–targeted therapy

Local treatment of early breast cancer

Local control is achieved through surgery and/or radiotherapy.

SURGERY

Surgery still has a central role to play in the management of breast cancer but there has been a gradual shift towards more conservative techniques.

Mastectomy is indicated for large tumours (in relation to the size of the breast), central tumours beneath or involving the nipple, multifocal disease, local recurrence or patient

preference. The radical Halsted mastectomy, which included excision of the breast, axillary lymph nodes and pectoralis major and minor muscles, is no longer indicated as it causes excessive morbidity with no survival benefit. The modified radical (Patey) mastectomy is more commonly performed and is thus described below.

Simple mastectomy involves removal of only the breast with no dissection of the axilla, except for the region of the axillary tail of the breast, which usually has attached to it a few nodes low in the anterior group.

Patey mastectomy

The breast and associated structures are dissected *en bloc* and the excised mass is composed

of:

- the whole breast;
- a large portion of skin, the centre of which overlies the tumour but which always includes the nipple;
- all of the fat, fascia and lymph nodes of the axilla.

The pectoralis minor muscle is either divided or retracted to gain access to the upper two-thirds of the axilla. The axillar vein and nerves to the serratus anterior and latissimus dorsi (the thoracodorsal trunk) should be preserved. The intercostal brachial nerves are usually divided in this operation and the patient

should be warned about sensation changes postoperatively. The wound is drained using a wide-bore suction tube.

Early mobilisation of the arm is encouraged and physiotherapy helps normal function to return very quickly;

most patients are able to resume light work within a few weeks.

Conservative breast cancer surgery (BCS)

This is aimed at removing the tumour plus a margin of normal breast tissue. This is commonly referred to as a wide local excision.

The term lumpectomy should be reserved for an operation in which a benign tumour is excised and in which a large amount of normal breast tissue is not resected. A quadrantectomy involves removing the entire segment of the breast that contains the tumour.

Both of these operations are usually combined with axillary surgery, usually via a separate incision in the axilla.

There are various options that can be used to deal with the axilla, including sentinel node biopsy, sampling, removal of the nodes behind and lateral to the pectoralis minor (level II) or a full axillary dissection (level III).

The width of the margin has attracted much controversy, with some units adopting a 1-cm margin and others 1 mm.

A recent consensus meeting has suggested that no tumour at the inked margin is sufficient, although the trials upon which this is based have been challenged and many still regard 1 mm as a safer margin. There is no need for wider margins than this.

There is a somewhat higher rate of local recurrence following conservative surgery, even if combined with radiotherapy, but the long-term outlook in terms of survival is unaffected.

Local recurrence is more common in younger women and in those with high-grade tumours and involved resection margins.

Patients whose margins are involved should have a further local excision (or a mastectomy) before going on to radiotherapy**.**

Local excision of a breast cancer without radiotherapy isassociated with an unacceptably high local recurrence rate.

The role of axillary surgery is to stage the patient and to treat the axilla. **The presence of metastatic disease within the axillary lymph nodes remains the best single marker for prognosis;**

however, treatment of the axilla does not affect long-term survival, suggesting that the axillary nodes act not as a ‘reservoir’ for disease but as a marker for metastatic potential. It used to be accepted that only premenopausal women should have their axilla staged by operation as there was a good case for giving chemotherapy to lymph node-positive patients; however, it is now clear that postmenopausal women also benefit from chemotherapy and so all patients require axillary staging.

In postmenopausal patients, tamoxifen was once given regardless of axillary lymph node status, but it is now known that only hormone receptor-positive patients, irrespective of age, benefit from this. Axillary surgery should not be combined with radiotherapy to the axilla because of excess morbidity. Removal of the internal mammary lymph nodes is unnecessary.

RADIOTHERAPY

Radiotherapy to the chest wall after mastectomy is indicated in selected patients in whom the risks of local recurrence are high.

This includes patients with large tumours and those with large numbers of positive nodes or extensive lymphovascular invasion.

There is some evidence that postoperative chest wall radiotherapy improves survival in women with node-positive breast cancer.

It is conventional to combine conservative surgery with radiotherapy to the remaining breast tissue. Recurrence rates are too high for treatment by local excision alone except in special cases (small node-negative tumours of a special type).

Trials are under way to investigate whether radiotherapy can be given intraoperatively at one sitting or as an accelerated postoperative course. This would have considerable advantages in making conservative surgery available in areas where radiotherapy is not currently used.

It would also relieve the burden of the current demand for radiotherapy, which accounts for up to 40% of activity in some departments.

Extrapolation from the Oxford overviews of systemic therapy (carried out every 5 years) suggests that for every four local recurrences avoided, one additional life will be spared at 15 years.

Adjuvant systemic therapy

Over the last 25 years there has been a revolution in understanding of the biological nature of carcinoma of the breast.

It is now widely accepted that the outcomes of treatment are predetermined by the extent of micrometastatic disease at the time of diagnosis. Variations in the radical extent of local therapy might influence local relapse but probably do not alter long-term mortality from the disease.

However, systemic therapy targeted at these putative micrometastases might be expected to delay relapse and prolong survival.

As a result of many international clinical trials and recent world overview analyses it can be stated with statistical confidence that the appropriate use of adjuvant chemotherapy or hormone therapy will improve relapse-free survival by approximately 30%, which ultimately translates into an absolute improvement in survival of the order of 10% at 15 years. Bearing in mind how common breast cancer is in Northern Europe and the USA,

these figures are of major public health importance.

Who to treat and with what are still questions for which absolute answers have yet to found, but the data from overviews of recent trials show that lymph node-positive and many higher-risk node-negative women should be advised to have adjuvant combined chemotherapy.

Women with hormone receptor-positive tumours will obtain a worthwhile benefit from at least 5 years of endocrine therapy, either 20 mg daily of tamoxifen if premenopausal or the AIs (anastrozole, letrozole and exemestane) if postmenopausal.

It is no longer appropriate to give hormone therapy to women who do not have oestrogen or progesterone receptor-positive disease.

Recent trials have shown that longer durations of endocrine therapy provide a small extra benefit but with increased toxicity.

HORMONE THERAPY

Tamoxifen has been the most widely used ‘hormonal’ treatment in breast cancer.

Its efficacy as an adjuvant therapy was first reported in 1983 and it has now been shown to reduce the annual rate of recurrence by 25%, with a 17% reduction in the annual rate of death. Beneficial effects of tamoxifen in

reducing the risk of tumours in the contralateral breast have also been observed, as has its role as a preventative agent (IBIS-I and NSABP-P1 trials).

Trials studying the optima lduration of treatment suggest that 5 years of treatment is preferable to 2 years.

Other hormonal agents that are also beneficial as adjuvant therapy have been developed. These include the LHRH agonists, which induce reversible ovarian suppression and thus have the same beneficial effects as surgical or radiation-induced ovarian ablation in premenopausal receptor-positive women, and the oral AIs for postmenopausal women.

AIs are now licensed for treatment of all stages of disease and have been shown to be superior to tamoxifen.

A large trial comparing anastrazole to tamoxifen in the adjuvant setting has shown beneficial effect for the AI in terms of relapse-free survival, although no benefit for overall survival. There is an additional reduction in contralateral disease, which makes this drug suitable for a study of prevention, and the side-effect profile is different from that of tamoxifen.

AIs are more expensive than tamoxifen but are coming off patent protection and generic copies may allow more widespread use.

There is an increase in bone density loss with patients taking an AI and a bone density scan is advised prior to commencement with treatment of underlying osteopaenia or osteoporosis.

CHEMOTHERAPY

Chemotherapy using a first-generation regime such as a 6-monthly cycle of cyclophosphamide, methotrexate and 5-fluorouracil (CMF) will achieve a 25% reduction in the risk of relapse over a 10–15-year period.

It is important to understand that this 25% reduction refers to the likelihood of an event happening. For example, a woman with a 96% chance of survival at, for example, 5 years only has a 4% chance of death over this time and the absolute benefit from chemotherapy would be an increase in survival rate of 1%, to 97%. This would not be a sufficient gain to offset the side effects of this potentially toxic therapy.

However, for a woman with a 60% chance of dying (40% survival rate) a 25% reduction in risk would increase her likelihood of survival to 55% and thus treatment would be worthwhile. CMF is no longer considered adequate adjuvant chemotherapy and modern second- and third-generation regimes include an anthracycline (doxorubicin or epirubicin) and the newer agents such as the taxanes.

Chemotherapy used to be prescribed only to premenopausal women with a poor prognosis (in whom its effects are likely to be the result, in part, of a chemical castration effect) but it is now also offered to postmenopausal women with poor prognosis disease.

Chemotherapy may be considered in node-negative patients if other prognostic factors, such as tumour grade, imply a high risk of recurrence.

The effect of combining hormone and chemotherapy is additive, although hormone therapy is started after completion of chemotherapy
to reduce side effects.

High-dose chemotherapy with stem cell rescue for patients with heavy lymph node involvement has now been shown in controlled trials to offer no advantage and has been abandoned.

Primary chemotherapy (neoadjuvant) is being used in many centres for large but operable tumours that would traditionally require a mastectomy (and almost certainly postoperative adjuvant chemotherapy).

The aim of this treatment is to reduce tumour volume to enable breast-conserving surgery to be performed. This approach is successful in up to 80%

of cases, but is not associated with improvements in survival compared with conventionally timed chemotherapy.

Patients who achieve a complete pathological response have increased survival rates. Patients with Her-2-positive disease will receive Herceptin as part of their management and have high complete response rates. It is important that tumours have a metallic clip placed into them at the onset of therapy as otherwise there will be uncertainty about which area to resect once chemotherapy has been completed. There is debate about the safety and utility of sentinel node biopsy preinduction of chemotherapy; however, it can be safely performed after completion of chemotherapy.

Neoadjuvant therapy is also used in the triple negative cohort of patients (Er, PR and Her-2 negative). In patients with breast cancer strongly positive for hormone receptors, a similar effect can be seen following 3 months of endocrine treatment.

Newer 'biological' agents will be used more frequently as molecular targets are identified – the first of these, trastuzamab (Herceptin®), is active against tumours containing the growth factor receptor c-erbB2.

Other agents currently available are lapitinab, an oral combined tyrosine kinase inhibitor (TKI).

Other TKIs are in development such as, pertuzumab. T-DM1 is a drug used in Her- 2-positive disease where a chemotherapy agent, emestane, is bound to an anti-Her-2 agent to allow targetedndelivery of the chemotherapy to Her-2-positive cells.

The antivascular growth factor bevacizumab initially showed promise but is now no longer routinely used for adjuvant therapy.

Treatment of advanced breast cancer

Breast cancer may occasionally present as metastatic disease without evidence of a primary tumour (that is with an occult primary). The diagnosis is made partly by exclusion of another site for the primary tumour and may be confirmed by histology with special immunohistological stains of the metastatic lesions.

Management should be aimed at palliation of the symptoms and treatment of the breast cancer, usually by endocrine manipulation with or without radiotherapy.

Locally advanced inoperable breast cancer

Locally advanced inoperable breast cancer, including inflammatory breast cancer, is usually treated with systemic therapy, either chemotherapy or hormone therapy. Occasionally, ‘toilet mastectomy’ or radiotherapy is required to control a fungating tumour but often incision through microscopically permeated tissues results in a worse outcome.

Metastatic carcinoma of the breast

Metastatic carcinoma of the breast will also require palliative systemic therapy to alleviate symptoms. Hormone manipulation is often the first-line treatment because of its minimal side effects.

It is particularly useful for bony metastases. However, only about 30% of these tumours will be hormone responsive and, unfortunately, in time even these will become resistant to treatment.

First-line hormone therapy for postmenopausal women is now anastrazole or one of the other third-generation AIs. Tamoxifen, ovarian suppression by surgery (for premenopausal women), radiotherapy and medical treatment are all in common use. When resistance to these has developed, other hormonal agents can prove useful, with about one-half of the response rate seen in the

first-line therapy. The newer agents such as antiprogestins, pure antioestrogens and growth factor TKIs are all candidates for this role.

Cytotoxic therapy is used particularly in younger women or those with visceral metastases and rapidly growing tumours. A variety of regimes is available and, although none prolongs survival, contrary to expectations, quality of life and symptom control is often better with more aggressive treatments, with responses being seen in up to 70% of patients.

Local treatment may also prove useful for some metastatic disease, such as radiotherapy for painful bony deposits and internal fixation of pathological fractures.

IMMUNOHISTOCHEMISTRY (IHC)

Immunohistochemistry has over the years evolved into a revolutionary diagnostic tool for the pathologist. The necessity for some special training method can be recognized from the fact that surgical pathology is a subjective discipline. Despite the presence of various diagnostic criteria, there is overlapping among different entities and dissimilarities among the same entity. This when compounded with subjective disparity among the pathologists, reproducibility of diagnosis become difficult.[40]

This prompted the development of special staining technique to stain cells of particular lineage, marking the beginning of histochemistry in the mid nineteenth century. Francois Vincent Raspard was the first botanist to use immunochemistry. Advent of aniline dyes revolutionized immunochemistry from 1862 to 1929. [41]

With the development of immunology, a new method of staining was developed incorporating immunologic techniques. Here antibodies labelled with special stains are used to identify specialantigen in the tissue.

The antigen –antibody reaction imparts a particular colour to the cells. Immunochemistry is an important adjuvant method in histopathologic diagnosis. The origin of Immunohistochemistry techniques lies in the pioneering work of Albert Coons, starting in 1941. He described his first attempts to label antibodies directly with fluorescent isocyanate. Later the indirect technique was introduced by Nakane and Pierce in 1966, in that an unlabeled antibody is followed by second antibody or substrate. Various stages of development of Immunohistochemistry from peroxidase –antiperoxidase (1970), Alkaline phosphatase labelling (1971), Avidin-biotin technique (1977, 1979) and to two layer dextrin polymer technique (1993) carries both advantages and disadvantages for each techniques. [5]

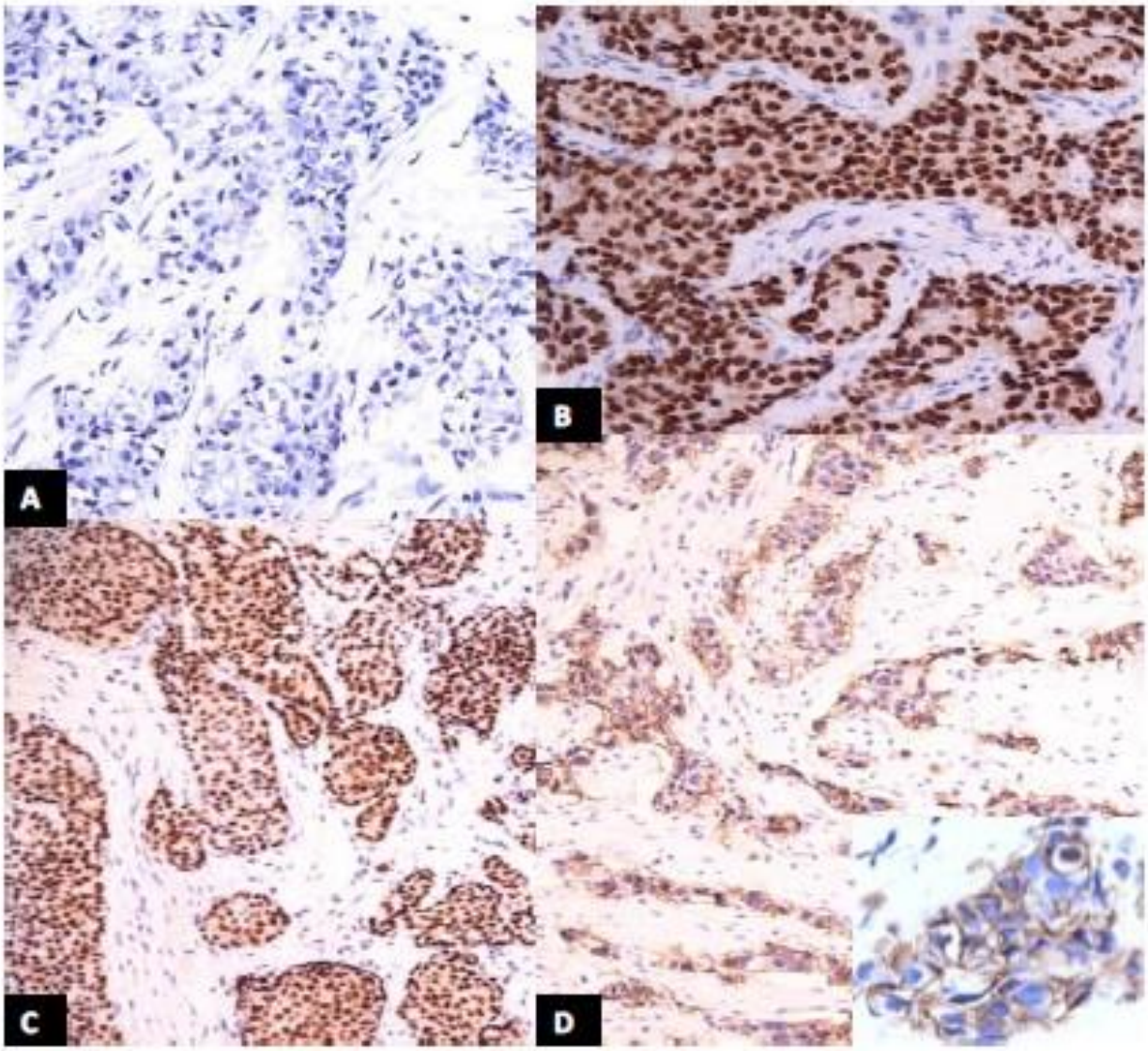


Figure1: (A) Negative staining for ER/PR, 10X (B) strong nuclear staining for ER, 20X (C) strong nuclear staining for PR, 20X; (D) HER 2 –Score 3,10X and inset showing complete membranous staining, 40X.

USES OF IMMUNOHISTTOCHEMISTRY IN BREAST PATHOLOGY [5,43]

1. Assessment of Estrogen and Progesterone status by using specific antibodies to the receptor proteins.
2. Assessment of HER-2/neu protein overexpression by using specific antibodies to the HER-/2 neu protein
3. Distinguishing in situ from invasive carcinoma by using antibodies to myoepithelial markers (e g. Actins, calponin, smooth muscle myosin heavy chain, P63) and basement membrane proteins (eg type IV collagen, laminin)
4. Assessment of metastatic lesions of possible breast origin by using antibodies to ER, GCDFP, CK 7/ CK 20 and other marker.
5. Evaluation of spindle cell lesions (metaplastic carcinoma Vs mesenchymal lesions).
6. Distinguishing ductal from lobular in situ carcinoma by using antibodies to E- cadherin.

HORMONE RECEPTORS

In 1950s Elwood V Jensen [47] identified Estrogen Receptor, further in 1996 Kuiper identified Estrogen receptor gene. [48] Estrogen and Progesterone receptors are localized in the nuclei of approximately 7% of epithelial cells of normal breast tissue. They are found in higher proportion in the lobular than the ductal cells. [48] Shoker at al [49] reported the tendency of contiguous Estrogen receptor positive pattern of valuable size in lobular unit. Variation in expression during menstrual period was also reported. [50]

Estrogen and Progesterone receptors belong to super family protein. They are nuclear transcription factors that are involved in breast development, growth, differentiation and tumorigenesis.

Estrogen receptor regulates the expression of other genes such as Progesterone & bcl2 [48.] Thus Progesterone receptor is an indicator for intact Estrogen receptor functional pathway. There are two forms of Estrogen receptor referred to as Estrogen receptor alpha & Estrogen receptor beta encoded by 6p25.1 and 14q respectively. [51] Estrogen receptor alpha is found in endometrium, breast cancer cells, ovarian stroma and hypothalamus. Estrogen receptor beta distribution is seen in kidney, brain, bone, heart and lungs [48,49.]

Walker D (1999) described that Estrogen receptors are regarded as cytoplasmic receptor in unliganded state. Since they are steroid receptors, they do not require membrane bound receptors for their activation.

During activation Estrogen receptor rapidly diffuses into the cytoplasm, it migrates from cytosol to nucleus, then dimerisation of the receptor occurs and subsequently it binds into HREs (Hormone Response Elements).

The DNA – receptor complex activates MAPK/P13K pathway and induces cell proliferation. Two hypotheses have been proposed for its action. One hypotheses states that Estrogen receptor induces transcription activity by alternative RNA splicing of Estrogen receptor alpha subunit thereby inducing rapid uncontrolled proliferation and accumulation of genetic mutation.

The other hypotheses states that it acts by producing by genomic waste. [48,51] Hormone receptors are well established biomarkers in breast carcinoma and their assessment helps in predicting the response to endocrine therapy. [52, 53,54] Receptors can be assessed by either Ligand Binding Assay (LBA) on frozen sections or by immunohistochemistry on paraffin sections. [23] No laboratories offer LBA, but immunohistochemistry method is done worldwide. This assay is found to be superior to LBA. [55]

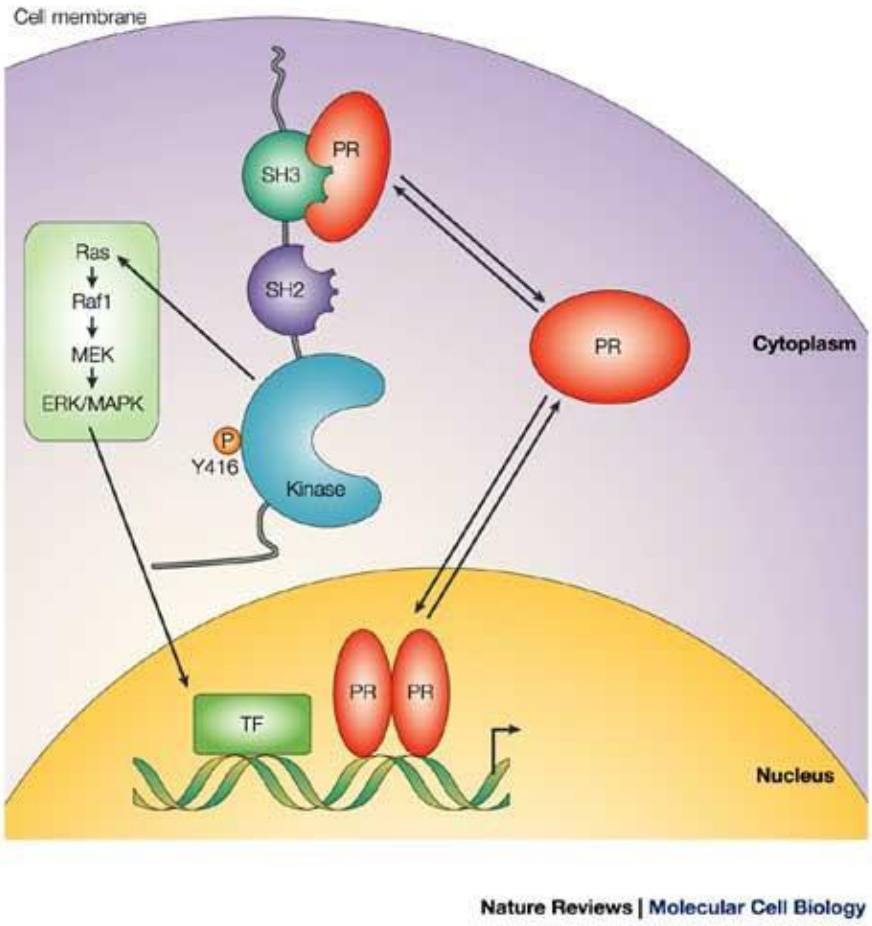
PROGESTRONE RECEPTOR :

Progesterone receptor is an intracellular steroid receptor that specifically binds to progesterone.

Progesterone receptor is encoded by a single gene PGR 11q22 and regulated by Estrogen receptor.

Estrogen receptor is always necessary to induce Progesterone receptor. Binding of hormone to the receptor induces structural changes whereby inducing cell proliferation. Estrogen and Progesterone receptor share a common structural and functional organization. WHO consensus development conference (1980) found that Progesterone receptor expression is a predictive marker. Hence it is estrogen regulated; most Progesterone receptor positive carcinomas are Estrogen receptor positive also.

Clarks et al[57] (1988) demonstrated Progesterone receptor by immunohisto-chemistry in formalin fixed paraffin embedded section. It is seen visually in the same cells which are positive for Estrogen receptor. Scoring system is the same as adopted for Estrogen receptor.



SCORING SYSTEM:

Estrogen and Progesterone receptors express nuclear positivity. They are scored by the proportion of tumour cells showing positivity and intensity of the reaction. Both are summated to give a total score.

1. H – SCORE SYSTEM:

Goulding et al58 (1995) used a semiquantitative method. It is based on the proportion of tumour cells showing different degree of reactivity. A score of 0-3 was given based on the following expression.

0- No reaction

1-Weak reaction

2 – Moderate reaction

3- Strong reaction

Score calculation

= % weakly positive cells x 1 + % moderately positive cells x 2+ % strongly positive cells x 3

Total score comes about 0-300.

Using H-score the positive score defined 51-300 and for negative upto 50 or less. The main disadvantage of this score is that it is time consuming and hence impractical for most pathologists.[81]

2. QUICK SCORE SYSTEM:

Barnes et al59 (1998) used another scoring method called **Quick score** .A score for theproportion of stained cells and intensity of staining as follows:-

Intensity of Staining Proportion of Staining

This comes to a maximum score of 8. Score of more than 2 is considered as positive. [71]

Advantage of this score is that it correlates into probability of response to endocrine therapy. [5]

The Intensity score, scored as mentioned above and the Proportion score as follows.

0 No positive cells

1 1-25% of positive cells

2 26-50% of positive cells

3 51-75% of positive cells

4 76-100% of positive cells

This gives total score about 0-7.

The lower cut-off of less than 10% cells is considered to be positive.

HER-2 /neu RECEPTORS

Her-2/neu (c-erb B -2) is an oncogene that encodes a transmembrane glycoprotein with tyrosinekinase activity. The proto-oncogene is encoded with 17q 11.2 –q12. HER-2/neu belongs to EGFR family [63] Overexpression in breast carcinoma leads to recurrence and worst prognosis [24,25]

It can be assayed by Florescent In situ Hybridization (FISH) for gene amplification and Immunohistochemical method for protein over expression. In over 90% gene amplification is associated with protein expression.

Food and Drug Administration approves two tests, one is Hercep test for immunohistochemistry and another is Pathvysion for FISH. [54].

When compared to each other immunohistochemistry is relatively easy to perform and is less expensive. [63,64]

If the immunotest gives 1+ or 2+ it can be confirmed with FISH. Reliability for both the tests depends on laboratory experience [54,64]

SCORING SYSTEM [65]

Staining pattern score HER-2/neu expression

No staining or membrane staining in

<10% of cells

A faint staining only a part of membrane

> 10 % of cells

A weak to moderate complete staining in

> 10% tumour cells

A strong complete membrane staining

> 10% tumour cells

0 Negative

1+ Negative

2+ Weakly positive

3+ Strongly positive

BENEFITS OF ESTROGEN AND PROGESTERONE RECEPTOR ASSESSMENT IN BREAST CARCINOMA :[52,53,54]

1. Estrogen and Progesterone receptors are weak prognostic factors but strong predictive factors for tumor behaviour in breast carcinoma.

2. Estrogen and Progesterone receptor positive tumours are benefited by hormone therapy in 50-60% of cases.

3. Estrogen and Progesterone receptor positive tumours are associated with reduced risk of recurrence and mortality.

4. Estrogen and Progesterone receptor negative tumors are not found to respond to endocrine therapy.

MATERIAL AND METHODS

This is a descriptive study of cases of breast carcinoma during the period of January 2017 – December 2021 in the Department of General Surgery, Thanjavur Medical College Hospital, Thanjavur.

One hundred and fifty breast specimens have been received in our department. during this period, .A detailed history regarding age, parity, socio-economic status, family history, menstrual history, lactational history, and previous biopsy reports are reviewed in all cases.

A detailed history regarding neo-adjuvant therapy is also noted.

Inclusion criteria

1. Patients in the age group between 15 to 95 years
2. Patients – both female and male
3. Retrospective Patients who is already on treatment before Jan 2017
4. Case sheets of patients from January 2017 for retrospective study
5. Both Mastectomy and corecut biopsy specimens were taken into consideration.
6. Patient who went neoadjuvant chemotherapy, on adjuvant and palliative chemotherapy were taken into considerations.

Exclusion criteria:

1. Patients admitted in department of General Surgery Department before January 2017

All the mastectomy specimens received are properly sliced and fixed in 10% formalin for about 16-18 hours. Detailed gross examination pertaining to overall size of the specimen, appearance of skin measurements of scars or incisions, appearance of nipple and areola, margins, nodal status are carefully noted.

The specimens are cut into thin slices and examined .The tumor size, consistency and distance from cut margins are noted.

The representative sections are taken from the tumor, nipple, cut margins, deep margins and palpable lymph nodes. The tissue slices are processed in various grades of alcohol and xylol and subsequently embedded in paraffin. Paraffin sections of 4 μm thickness are subjected to haemotoxylin and eosin staining [24].

Histological assessment of tumor grade is done by Modified Richardson – Bloom Scoring system .Nodal status and margins involvement are recorded in each case.

IMMUNOHISTOCHEMICAL ANALYSIS OF HORMONE RECEPTOR:

Immunohistochemical analysis of hormone receptor assay is done in paraffin embedded tissue blocks, by using the Supersensitive Polymer HRP system based on non-biotin polymeric technology that makes use of two major components, Super enhancer and poly- HRP reagent

. The retrieved antigen is bound to primary antibody and then detected by the addition of secondary antibody conjugated with horse radish peroxidase polymer and DAB substrate. The score was calculated after adequate color development which can be more readily visualized under a light microscope.

SCORING SYSTEM:

Immunohistochemically stained slides are evaluated for the presence of reaction, cellular localization (nuclear or cytoplasm), pattern of staining (focal or diffuse) and intensity of reaction in individual tumor cells (Strong or weak). Scoring for Estrogen &Progesterone receptors is done by using Quick score system [59] and for HER-2/neu according to the guideline published by Ellis et al.[65]

Estrogen, Progesterone receptors and HER-2/neu with tumor size, nodal status, histological variants and grades.

The study is conducted after obtaining the ethical approval from the Ethical Review Committee of Thanjavur Medical College Hospital, Thanjavur.

OBSERVATION AND RESULTS

INCIDENCE OF BREAST TUMORS

In the two year study period from January 2020 – December 2021, 150 cases were studied

Both retrospectively from case sheets January 2017 and prospectively.

TABLE 1.

AGE WISE DISTRIBUTION OF CA BREAST

S.No. (In years)	
1. Less than 20 Yrs	2
2. 21-30 Yrs	4
3. 31-40 Yrs	27
4. 41-50 Yrs	52

5. 51-60 Yrs

42

6. 60-70 Yrs

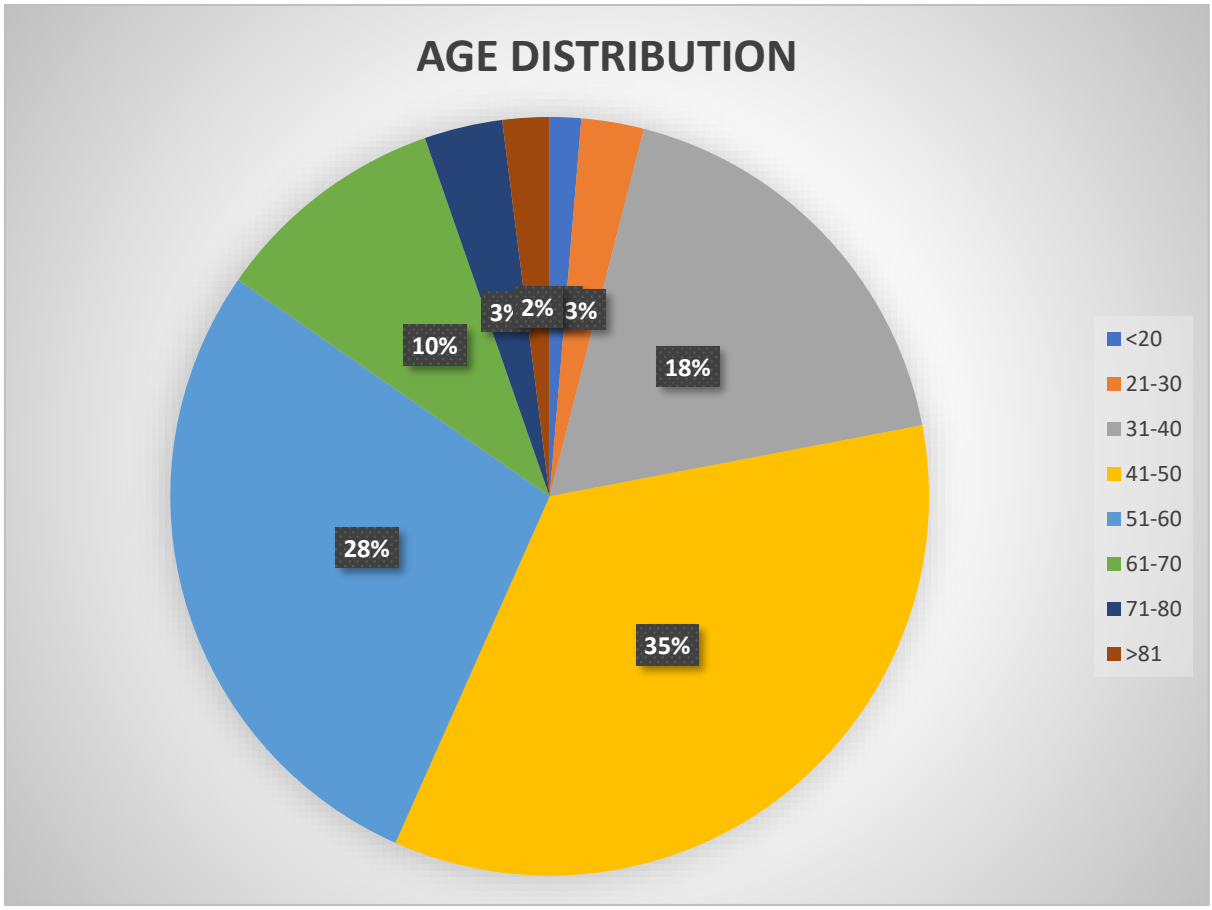
15

7. 71-80 Yrs

5

8.Greater than 81

3



Total No. of cases

150

The above shows the distribution of breast tumors according to age.

The carcinoma breast had a peak incidence in the age group **41-50 years.**

TABLE 2.

DISTRIBUTION OF HISTOLOGICAL VARIANTS IN BREAST CARCINOMA

S.No. Histological Variants No. of Cases Percentage

1. Invasive Ductal Carcinoma - NOS type – 94.67% - 142

2. Invasive Lobular Carcinoma 0% - 0

3. Mucinous Carcinoma 0.67 % - 1

4. Papillary Carcinoma 0.67% - 1

5. Metaplastic Carcinoma 0.67% - 1

6. Apocrine Carcinoma 0.67% - 1

7. Medullary Carcinoma 0.67% - 1

8. Invasive Ductal Carcinoma with mucinous differentiation – 1.33% - 2

142 (94.67%) were Invasive Ductal Carcinoma NOS type, 2 (1.33%) were Invasive Ductal Carcinoma with mucimous differentiation – 1.33% and

in other special sub – types including Papillary carcinoma, Metaplastic carcinoma, Apocrine, medullary carcinoma were 1 each (0.67%)

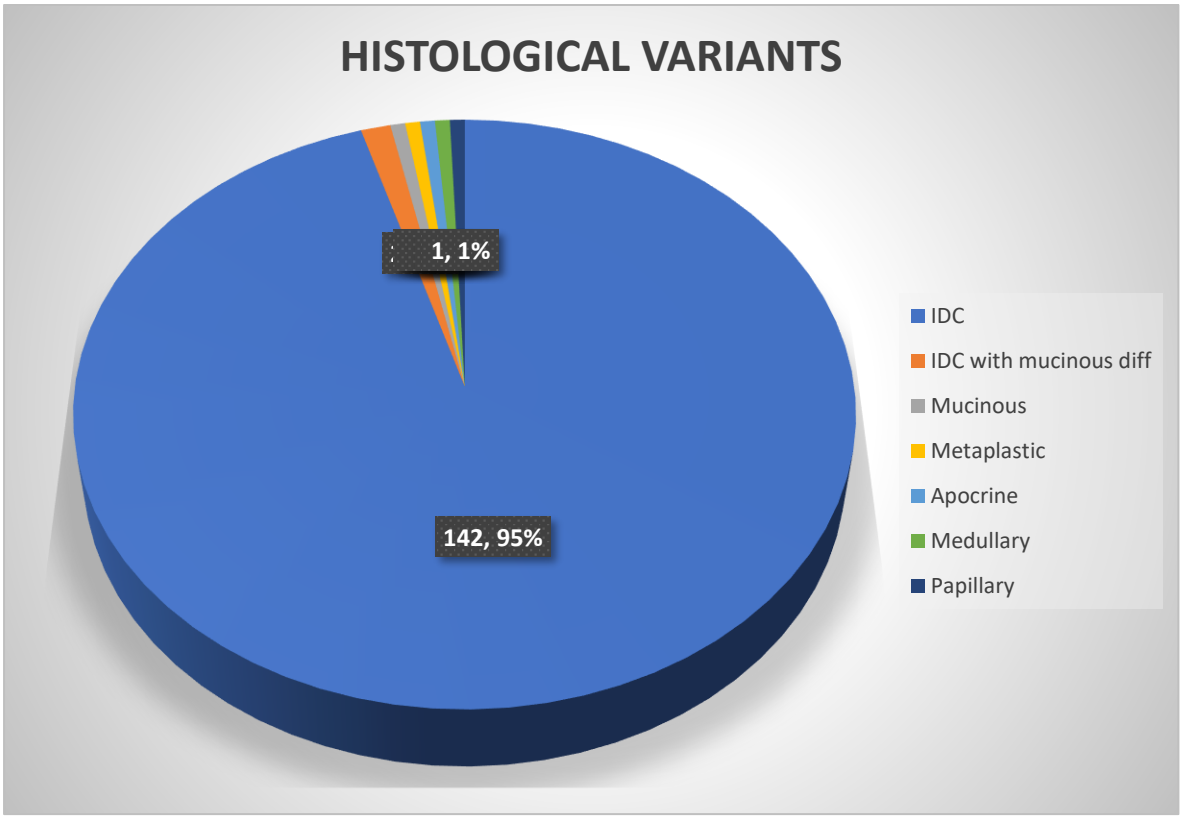


TABLE 3.

.SCORING SYSTEM FOR HORMONAL RECEPTORS

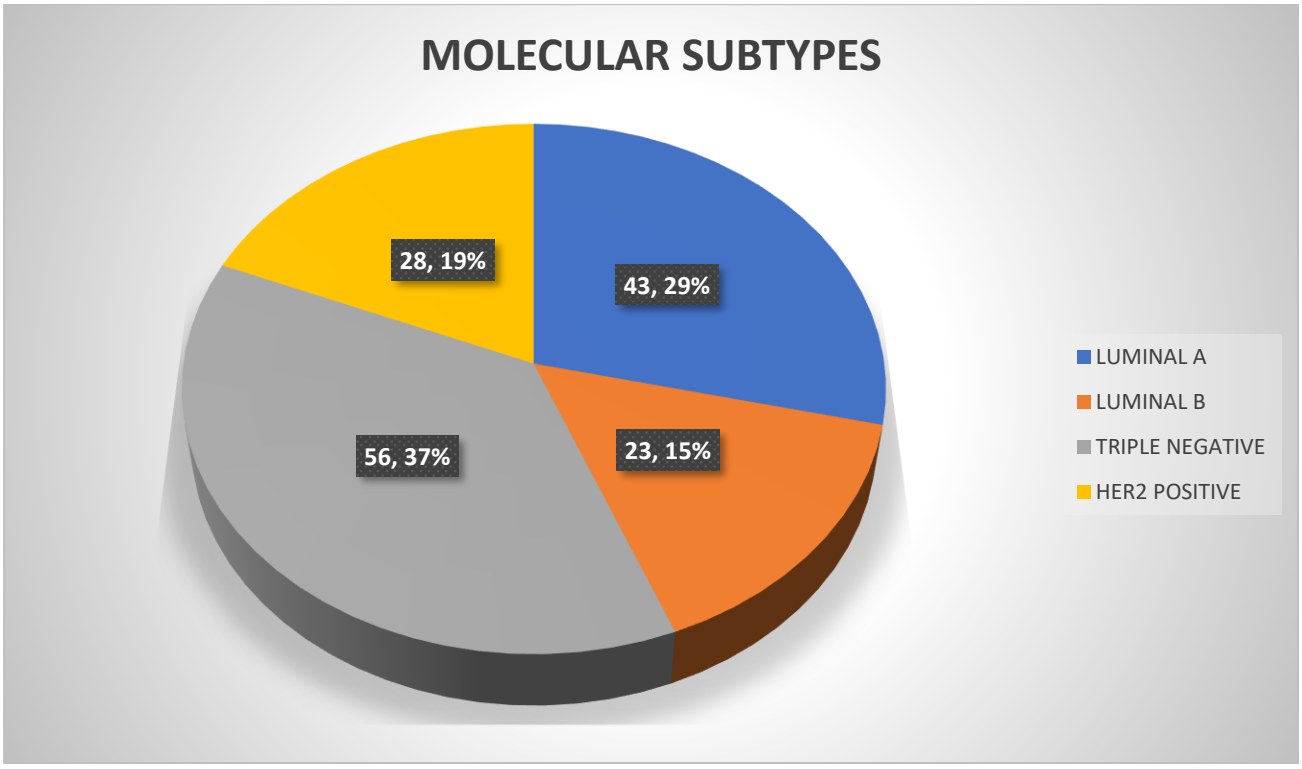
Of the total 150 cases in the study period, cases were analyzed on the basis of inclusion and exclusion criteria. All the cases were processed, immunohistochemically analyzed and carefully examined under the light microscope. Dark brown colour of the nuclei was interpreted as positive score for Estrogen and Progesterone receptor. For scoring Quick score system was adopted.

A total score of more than 2 was considered as positive.

Dark brown membrane positivity was scored for HER -2/neu. Intensity of staining, percentage of cells positivity were included and scored. A score of complete membrane positivity in >10% of the tumor cells were considered as positive.

ER, PR, HER-2/neu TABLE

Molecular subtype	Percentage
LUMINAL A	43 (28.66%)
LUMINAL B	23 (15.33%)
TRIPLE NEGATIVE	56 (37.33%)
HER2 POSITIVE	28 (18.66%)



Total No of cases 150 100%

In our study, luminal A shows 28.66%, luminal B shows 15.33%, triple negative (basal like) shows 37.33% and her2 positive type shows 16.66%

TABLE 4

EXPRESSION OF HER-2/neu IN BREAST CARCINOMA

S.no HER-2/neu expression

Total No. of cases -150

Percentage %

1. **Positive 50 – 33.33%**
2. **2. Negative 100 – 66.67%**

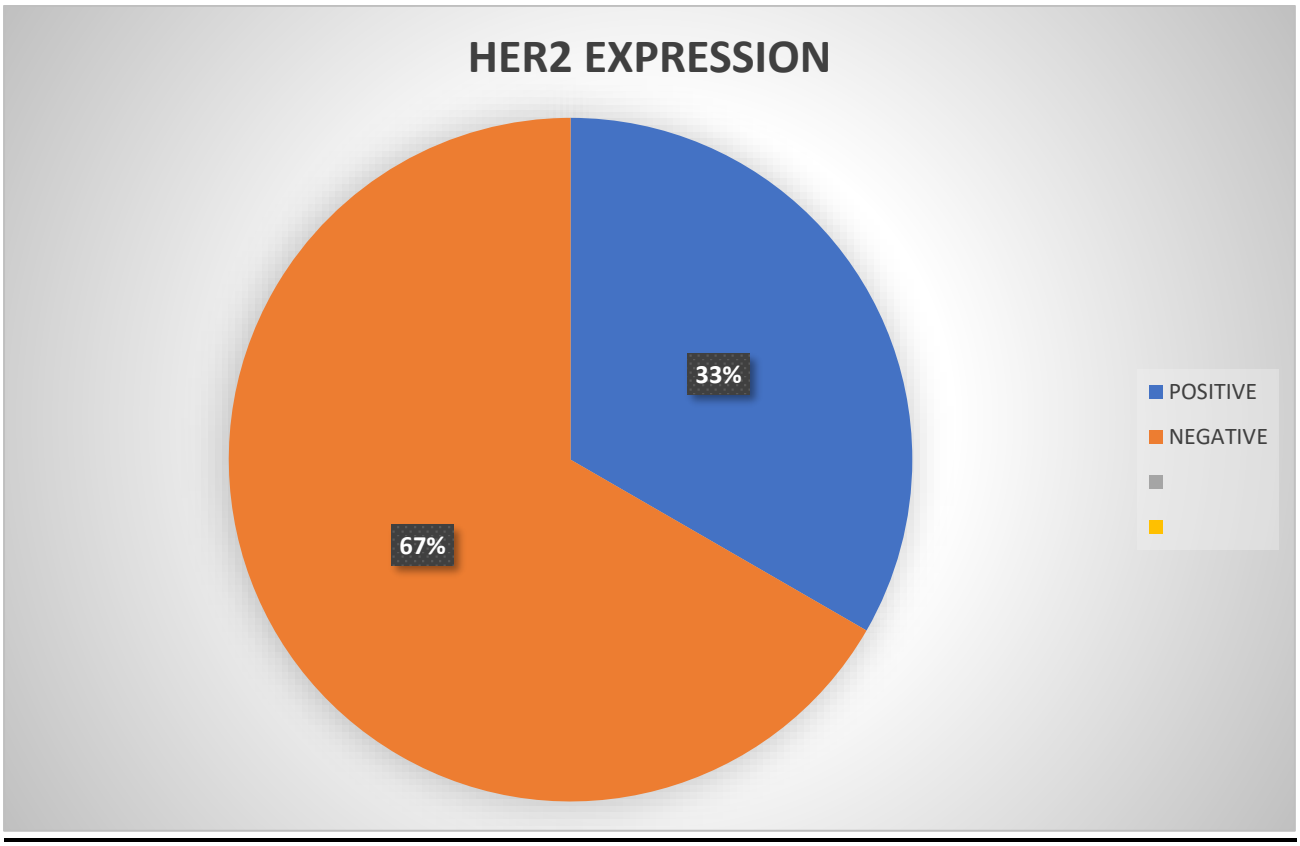


Table 4. shows HER-2/neu overexpression in 150 breast carcinoma patients, among them 50 cases (33.33%) were found to be positive, while 100 cases (66.67%) were found to be negative.

TABLE 5.

CORRELATION OF TUMOUR SIZE IN BREAST CARCINOMA

TUMOR SIZE STAGING

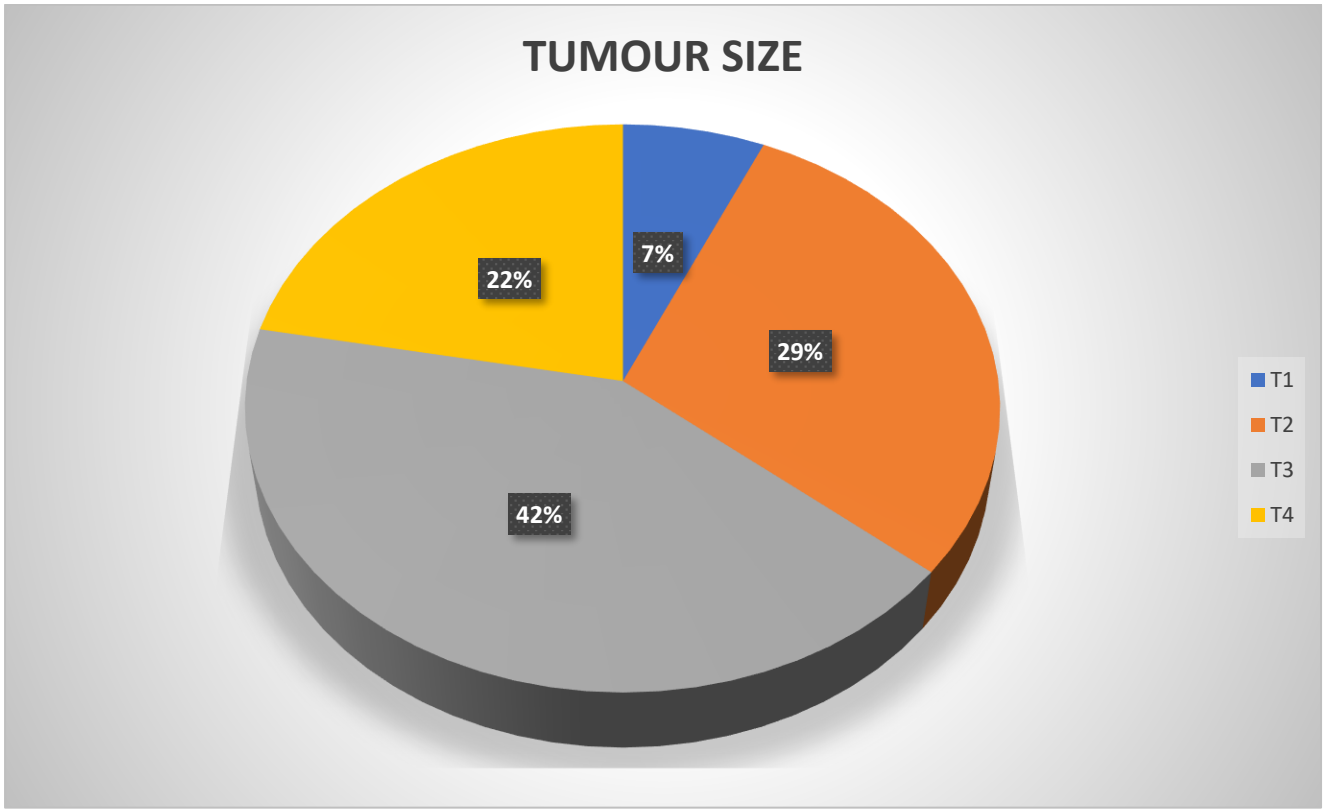
Percentage %

1. T1 < 2 cm 10 – 6.67%

2. T2 2- 5 cm 44 - 29.33%

3. T3 >5 cm 63- 42%

4. T4 – 33 – 22%



Total No. of Cases 150

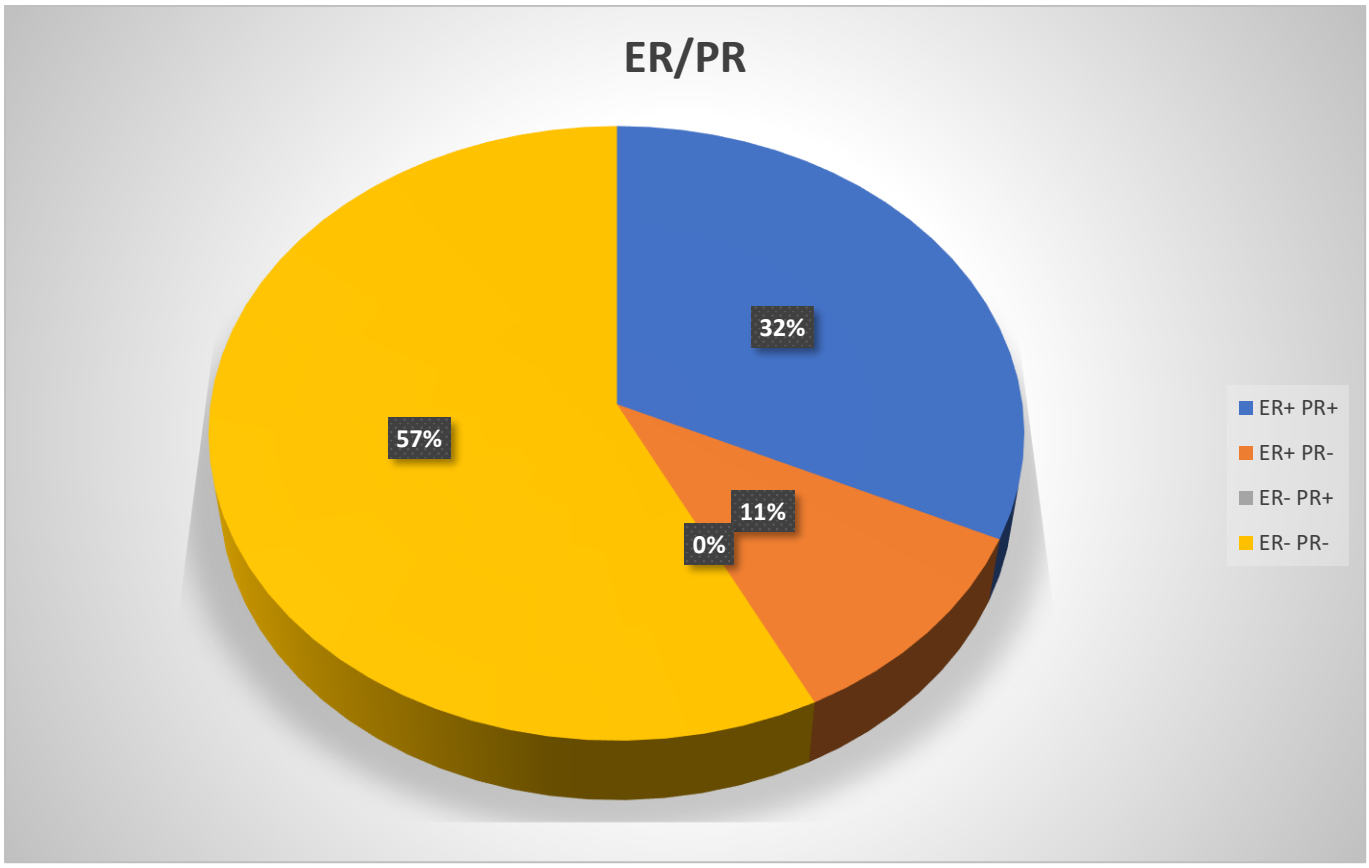
Table 5. shows correlation of tumor size staging..

10 cases had Tumor of size < 2cm, 44 cases had tumor size between 2 cm and 5cm, 63 cases had size more than 5 cm, 33 cases had t4 staged tumour.

TABLE 6

EXPRESSION OF ER/PR IN BREAST CARCINOMA

ER+ PR+	48
ER+ PR-	16
ER- PR+	0
ER- PR-	86



Estrogen receptor and Progesterone receptor positivity was noted in 32% of tumors,

The receptor status of oestrogen and progesterone was found to be comparatively reduced in larger sized tumors as depicted in 84 cases in which most them are t3/t4 staged.

TABLE 7 . CORRELATION OF TREATMENT REGIMENS SPECIFIC TO PR RECEPTOR STATUS

Total; cases 150

Out of total 150 cases, 102 found to have PR negative status

And 48 found to have PR positive status

- most treatment guidelines centered around ER-positive *v* ER-negative pathways); 2) to assist in prognostication, such as classification of breast cancer, for the most appropriate overall prognostic stage group (eg, American Joint Committee on Cancer [AJCC] eighth edition prognostic stage groupings) and as a diagnostic aid in metastatic breast cancer.

SL.NO	PR STATUS	N	PERCENTAGE
1.	**POSITIVE**	**48**	**32%**
2.	**NEGATIVE**	**103**	**68%**

To the total 150 cases, there were no specific treatment carried out for PR status as neoadjuvant, adjuvant and palliative chemotherapy.

DISCUSSION

- In our study, The carcinoma breast had a peak incidence in the age group **41-50 years.**

- 142 (94.67%) were Invasive Ductal Carcinoma NOS type, 2 (1.33%) were Invasive Ductal Carcinoma with mucimous differentiation – 1.33% and in other special sub – types including Papillary carcinoma, Metaplastic carcinoma, Apocrine, medullary carcinoma were 1 each (0.67%)

- **In our study, luminal A shows 28.66%, luminal B shows 15.33%, triple negative (basal like) shows 37.33% and her2 positive type shows 16.66%**

- 10 cases had Tumor of size < 2cm, 44 cases had tumor size between 2 cm and 5cm, 63 cases had size more than 5 cm, 33 cases had t4 staged tumour.

- Estrogen receptor positivity and Progesterone receptor positivity was noted in 32% of tumors,

- The receptor status of oestrogen and progesterone was found to be comparatively reduced in larger sized tumors as depicted in 84 cases in which most them are t3/t4 staged.

- Our study shows HER-2/neu overexpression in 150 breast carcinoma patients, among them 50 cases (33.33%) were found to be positive, while 100 cases (66.67%) were found to be negative.

To the total 150 cases, there were no specific treatment carried out for PR status as neoadjuvant, adjuvant and palliative chemotherapy.

Western literature showed that by immunohistochemistry, about 70-80% of invasive breast carcinoma express nuclear ER in a proportion ranging from ≥1% to 100% positive cells and like ER, PR is expressed in the nuclei of 60-70% of invasive breast cancers, with expression that varies in continuum ranging from 1% to 100% positive cells.[9,10]

- **most treatment guidelines centered around ER-positive *vs* ER-negative pathways)**; 2) to assist in prognostication, such as classification of breast cancer, for the most appropriate overall prognostic stage group (eg,

American Joint Committee on Cancer [AJCC] eighth edition prognostic stage groupings) and 3) as a diagnostic aid in metastatic breast cancer

Another interesting finding in our study is that we have none of the case expressing PR but not ER (ER-/PR+). Low percentage of ER-/PR+ cases was described in previous study from India and Kaul et al in their study also from north India revealed 0% ER-/PR+ cases.[14,15]

Added clinical benefit of PR evaluation in breast cancers is uncertain and debate is going among western researches whether ER-/PR+ tumors are actually exist. Role of PR status in the management of breast cancer remains controversial and to date relatively few studies have been performed to find an association between PR status and prognosis of breast cancer.

In a study by Hefti et al by incorporating gene expression profiling data, clinical and immunohistochemistry data across two large and diverse datasets found PR expression at low level in ER- breast cancer. They clearly mentioned that ER-/PR+ breast cancers are not a reporoducible subtype and PR expression is not associated with prognosis in ER- breast cancer.

Similarly Olivotto et al in their study observed that with modern IHC method most breast tumors that are ER− are also PR−. They concluded that as PR testing is no longer useful in clinical decision-making and it is time to stop progesterone receptor testing in breast cancer management.

In clinical practice, it is very complex to use PR as a biological marker. Despite progress in understanding the structure and function of PR, it is still not widely used as either a predictive or prognostic marker in the treatment of cancer.

However data from the large ATAC (Arimidex, Tamoxifen, Alone or in combination) adjuvant trial, a worldwide clinical trial comparing the efficacy of tamoxifen with that of the aromatase inhibitor showed that patients with ER+/PR+ tumors had a lower recurrence rate than those with ER+/PR- tumors (7.6% vs. 14.8%, respectively).

Yao et al in their study found that patients with ER positive invasive breast cancers with low PR expressing tumors have a worse prognosis than those with high PR expressing tumors.

Further research is also needed to investigate the Role of Tamoxifen in ER-/PR+ tumors and clear guidelines are essential when to evaluate PR receptor in

invasive breast carcinoma. In developing countries, finances used for PR receptor evaluation can be better utilized for management in breast cancer patients.

Percentage of triple negative breast cancers (TNBC) in our study was 56 (37.33**%)** while triple positive breast cancers constitute only 15.33%. This percentage is considerably higher compared with that seen in Western populations, where TNBC accounts only 12% to 17% of all invasive breast cancers. Another study from one tertiary care centre in India revealed 22.7% triple negative cases. And one large study by Sandhu et al by combining the data from seventeen studies from India involving 7,237 breast cancer patients found 31% incidence of TNBC.

This finding is also alarming because the targeted therapy to ER, PR, HER2 receptor are of no use in TNBC causing lower disease free survival and overall survival. Extensive research is needed not only to understand the determinants of TNBC in India but also in finding newer and better treatment options.

CONCLUSION

This single institutional study of 150 cases of breast cancer patients from Thanjavur (Delta region) suggest that ER positivity of 48 %, not grossly different from rest of the country but significantly lower than western studies.

- The carcinoma breast had a peak incidence in the age group **41-50 years.**

- **In our study, luminal A shows 28.66%, luminal B shows 15.33%, triple negative (basal like) shows 37.33% and her2 positive type shows 16.66%**

- **Triple receptor negative cases (TNBC) is on the rise**

- **ER-/PR+ tumors was not identified in this study** and on analyzing the various research data we have an opinion that PR testing is highly unlikely to alter therapeutic decisions, the resources could be saved or better allocated. We encourage others to question the value of continuing a test, initiated for good reasons, but which today has little use in guiding therapy decisions.

Further studies are also required in larger group taking into account various clinical parameters along with molecular study and survival pattern analysis to substantiate these immunohistochemical findings.

Similarly with high incidence of triple negative breast cancers an additional research is needed to understand the determinants of TNBC in India for future better outcome in these patients.

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PROFORMA

Serial No. : Name :

HPE No. : Age :

IP No. : Sex :

Chief complaints:

Past H/o: previous surgery/ chemo/ radiotherapy/ ocp pills

No of child births/ breast feeding h/o

Menstrual H/o:

Menarche –

Age at first child birth –

Nulliparity –

Menopause -

Clinical diagnosis :

Breast : Right / Left

Clinical staging:

T:

N:

M:

Specimen : Excisional (Lumpectomy / Mastectomy/trucut biopsy)

Macroscopic Examination :

Specimen Size :

Skin and Nipple :

Tumor Size :

Tumor margins : Circumscribed / Infiltrative

Posterior margin :

Lymphnode :

Number :

Size :

C/S :

Histological type of lesion :

Skin : Free / Involved

Nipple : Free / Involved

Muscle : Free / Involved

LYMPHNODES

Total Number :

No.of nodes involved :

Other Findings :

Receptor Study :

ER Status:

Proportion Score :

Intensity Score :

Total Score :

PR Status:

Proportion Score :

Intensity Score :

Total Score :

HER – 2/ neu Status :

Weak :

Moderate :

Strong Positive :

Molecular subtype:

Pathological staging :

PATIENT CONSENT FORM

STUDY TITLE:

"STUDY OF CORRELATION OF ER, PR, HER2 RECEPTOR STATUS IN BREAST CANCER AT A SINGLE TERTIARY CARE HOSPITAL WITH EMPHASIS ON CLINICAL UTILITY OF PR RECEPTOR"

STUDY CENTRE:

Government Thanjavur Medical College and Hospital

PATIENT NAME:

Age: Sex:

IP/ OP NO:

I confirm that I have understood the purpose of treatment and procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the possible complications that may occur during the interventional procedure. I understand that my participation in the study is voluntary and I am free to withdraw at any time without giving any reason.

I understand that the investigator, regulatory authorities and the ethical committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to the study. I understand that my identity will not be revealed to third parties or published, unless

as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to participate in this study of "**STUDY OF CORRELATION OF ER, PR, HER2 RECEPTOR STATUS IN BREAST CANCER AT A SINGLE TERTIARY CARE HOSPITAL WITH EMPHASIS ON CLINICAL UTILITY OF PR RECEPTOR"**

Date:

Place:

Patient's name: Signature/ thumb impression of patient

Name of the investigator: Signature of the investigator

INFORMATION SHEET

We are conducting a study on "**STUDY OF CORRELATION OF ER, PR, HER2 RECEPTOR STATUS IN BREAST CANCER AT A SINGLE TERTIARY CARE HOSPITAL WITH EMPHASIS ON CLINICAL UTILITY OF PR RECEPTOR"** among patients attending Government Thanjavur Medical college and Hospital, Thanjavur and for that your information is valuable to us.

We are selecting certain cases and if you are found eligible we may be using your information which in any way do not affect your final report or management. The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation, resulting from the research, no personallly

identifiable information will be shared. Taking part in this study is voluntary. You are free to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of the patient:

Signature of the investigator:

Date:

Place:

ஆராய்ச்சிக்கான ஒப்புதல் கடிதம்

புறநோயாளி எண் : தேதி:

பெயர் : வயது:

இனம் : ஆண் / பெண்

இந்த ஆய்வின் நோக்கம் மற்றும் விவரங்கள் எனக்கு தெளிவாக அறிவிக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துக்கொண்டு நான் என் விருப்பத்தினைத் தெரிவிக்கிறேன்.

இந்த ஆய்வில் நன்மைகளைப் பற்றி மருத்துவர் மூலம் தெரிந்துக்கொண்டேன்.

இந்த ஆய்வில் பிறரின் நிர்பந்தமின்றி என்னுடைய சொந்த விருப்பத்தின்பேரில் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆய்விலிருந்து எப்போது வேண்டுமானாலும் விலகிக் கொள்ளலாம் என்பதனையும் அறிந்துக்கொண்டேன்.

நான் என்னுடைய விருப்பத்தின்பேரில் முழு ஒப்புதலுடன் இந்த மருத்துவ ஆய்வில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

மருத்துவர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள் :

இடம் : தஞ்சாவூர்

SL.NO	NAME	AGE	IP.NO	IHC NO	HPE NO.	ER	PR	HER2	MOLECULAR SUBTYPE	HPE TYPE	CLINICAL STAGING	PATHOLOGICAL STAGING	SIDE	NEOADJUVANT CHEMO	MRM/BCS	TRUCUT	ADJUVANT TREATMENT	ANY TREATMENT SPECIFIC TO PR STATUS
1	THAIYALNAYAGI	55 F	33438	5//17	2188/17	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N0M0	T2N0MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
2	MANIMEGALAI	45 F	44553	8//17	2901/17	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T4BN1M0	T4BN2MX	LEFT	YES	YES	NO	YES	NO
3	RANI	40 F	39132	10//17	2545/17	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N0M0	T2N0MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
4	VALLI	42 F	55345	53/17	4163/17	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N0M0	T3N0MX	RIGHT	NO	YES	NO	YES	NO
5	SARASWATHI	55 F	7576	56/17	4243/17	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T4AN2M0	T4ANXMX	RIGHT	NO	YES- SIMPLE	NO	YES	PR NEGATIVE
6	BAMA	38 F	34295	58/17	2425/17	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T3N1M0	T2N1MX	LEFT	NO	YES	NO	YES	NO
8	TAMILRANI	58 F	22185	111/17	1797/17	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	YES	NO
9	THULAMAMAML	44 F	10626	112/17	783/17	POSITIVE	POSITIVE	POSITIVE	LUMINAL A	IDC	T3N1M0	T2N1MX	LEFT	NO	YES	NO	NO	NO
10	VELLAIAMMAL	60 F	24890	113/17	31/17	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N1M0	T2N1MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
11	CHITRA	37 F	7254	114/17	32/17	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T1N0M0	T1N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
12	YELAMBAL	40 F	18339	254/17	1249/17	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N0M0	T3N0MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
13	RADHA	65 F	6772	134/17	928/17	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T4AN2M0	T4AN1MX	RIGHT	YES	YES	NO	YES	PR NEGATIVE
16	SHANTHI	56 F	86754	145/17	8227/17	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T2N1M0	T2N1AMX	LEFT	NO	YES	NO	NO	NO
17	PAKKIRIYAMMAL	65 F	3864	78/17	355/17	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T1N0M0	T1N0MX	LEFT	NO	YES	NO	NO	NO
19	JEYAPARVATHY	60 F	36785	145/17	886/17	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N0M0	T3N0MX	RIGHT	NO	YES	NO	YES	NO
20	GANDHIMATHI	40 F	6843	56/17	595/17	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N0M0	T2N1MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
21	REVATHI	39 F	43303	198/17	1784/17	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T1N1M0	T1N1MX	RIGHT	NO	YES	NO	YES	PR NEGATIVE
24	RUKMANI	55 F	61417	245/18	4120/18	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
26	AVAMANI	85 F	52253	157/18	3551/18	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC WITH MUCINOUS	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	NO
27	PANTHANAM	55 F	50841	155/18	3603/18	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	YES	NO
28	NAGAMMAL	51 F	55497	154/18	3604/18	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
29	PUSHPA	45 F	52034	143/18	3474/18	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N1M0	T4N1MX	LEFT	NO	YES	NO	YES	NO
30	RAMAMIRTHAM	45 F	52744	144/18	3468/18	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N2M0	T2N2MX	RIGHT	NO	YES	NO	YES	PR NEGATIVE
32	YOGAMBAL	70 F	51968	176/18	3665/18	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	YES	NO
33	JAYALAKSHMI	50 F	50052	175/18	3210/18	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N1M0	T2N1MX	LEFT	NO	YES	NO	NO	NO
34	SHANTHI	53 F	46788	165/18	2876/18	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
36	KALAISELVI	45 F	34567	160/18	2255/18	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T1N0M0	T1N0MX	LEFT	NO	YES	NO	NO	NO
38	BABY	50 F	42766	159/18	2427/18	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N1M0	T2N1MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
39	JANAKI	79 F	7169	36/18	622/18	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	APOCRINE	T2N0M0	T2N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
41	THANGAMMAL	53 F	5910	19/18	367/18	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N0M0	T2N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
43	SHANTHI	47 F	3726	34/18	294/18	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1M0	T2N1MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
44	GLORYA MARY RANI	54 F	15467	156/18	1892/18	POSITIVE	NEGATIVE	POSITIVE	LUMINAL B	IDC	T1N0M0	T1N0MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
45	ESTHER MARY	38 F	1088	7//18	155/18	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N0M0	T2N1MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
46	ALAGAMMAL	59 F	1527	5//18	150/18	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T3N0M0	T3N1MX	RIGHT RECURRENT	NO	YES	NO	NO	PR NEGATIVE
47	ABARANAM	55 F	71888	2//18	06//18	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T4AN0MX	RIGHT	NO	YES	NO	YES	NO
48	SELVI	50 F	72911	1//18	59/18	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N0M0	T2N1MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
50	BANUMATHI	50 F	661	2//19	39/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	YES	NO
51	THENGAJAYANTHI	45 F	715	3//19	137/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	PAPILLARY	T2N1MX	T2N0MX	LEFT	NO	YES	NO	NO	NO
52	SASIKALA	41 F	4563	7//19	412/19	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T3N2M0	T2N2MX	LEFT	YES	YES	NO	YES	NO
54	VIJAYA	37 F	9576	9//19	655/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T2N1M0	T2N2MX	RIGHT	NO	YES	YES	YES	NO
55	KALAISELVI	52 F	11092	16/19	1197/19	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T2N0M0	T2N1MX	RIGHT	NO	YES	NO	YES	NO
56	DHARMAMBAL	60 F	20202	17/19	1193/19	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T3N1M0	T2N1MX	LEFT	NO	YES	NO	YES	NO
57	VAIJAYANTHIMELA	38 F	15101	18/19	1013/19	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T3N2M0	T2N0MX	LEFT	NO	YES	NO	YES	NO
59	KALPANA	40 F	34578	49/19	1928/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T4BN3M1	NOT DONE	RIGHT RECURRENT		YES	YES	PALLIATIVE	NO
60	SUNDARAMBAL	45 F	37890	50/19	2269/19	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T3N0M0	T4BN0	RIGHT	NO	YES	NO	YES- RT	PR NEGATIVE
61	RENGANAYAKI	45 F	45900	55/19	3305/17A	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	MEDULLARY	T1N0M0	T1N0MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
62	LOGAMBAL	55 F	46754	57/19	2498/19	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	NO
63	BANUMATHI	50 F	51002	58/19	3572/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N1M0	T4N1MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
64	JANAKI	48 F	51278	61/19	3672/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
65	AROKIYAMARY	50 F	62189	63/19	3807/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N1M0	T2N1MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
66	LAKSHMI	35 F	67866	70/19	3440/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T4BN3M1	NOT DONE	LEFT		YES	YES	PALLIATIVE	PR NEGATIVE
67	AMMALU	68 F	67911	71/19	3582/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T1N0M0	T1N0MX	LEFT	NO	YES	NO	NO	NO
68	RAJESWARI	38 F	70201	72/19	3831/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	NO
69	DEIVANAYAGI	45 F	71209	73/19	1609/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N1M0	T2N1A	RIGHT	YES	YES	NO	YES	NO
70	NITHYA	28 F	72819	74/19	3846/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
71	GOWSALYA	52 F	72989	75/19	3437/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N0M0	T4BN0	LEFT	NO	YES	NO	YES- RT	NO
72	SUBBULAKSHMI	66 F	74563	75A/19	3886/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1M0	T2N1AMX	LEFT	NO	YES	NO	NO	PR NEGATIVE
74	JEYAMANI	45 F	75673	77/19	495/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	NO
75	HASINA BEGUM	46 F	79031	78/19	3862/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL B	IDC	T3M1N0	T3N1AMX	RIGHT	NO	YES	NO	YES	NO
77	PERIAMAYIL	55 F	84579	83/19	4218/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N2M0	T3N2AMX	RIGHT	YES + RT	YES	NO	NO	NO
78	POTHUMATHI	32 F	87899	84/19	4270/19	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T1N0M0	T1N0MX	LEFT	NO	YES	NO	NO	NO
79	SANGEETHA	21 F	89139	85/19	4239/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3M1N0	T3N1AMX	RIGHT	NO	YES	NO	YES	PR NEGATIVE
80	ALAMELU	65 F	5432	4//20	407/20	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
81	KAVERIAMMAL	74 F	6786	7//20	127/20	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1MX	T2N1AMX	LEFT	NO	YES	NO	YES	PR NEGATIVE
83	LAKSHMI	53 F	9100	10 //20	540/20	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
84	VIJAYA	36 F	15019	17//20	852/20	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T1N0M0	T1N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
86	VANITHA	37 F	5923	4//21	467/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T3M1N0	T3N1AMX	RIGHT	NO	YES	NO	YES	PR NEGATIVE
87	KALAISELVI	36 F	5800	471/21	471/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N2M0	T2N2AMX	RIGHT	NO	YES	NO	YES	PR NEGATIVE
88	SUGUNA	56 F	6783	07//21	3917/19	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
89	AMUDHA	35 F	8764	13/21	1405/20	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
90	AMSAVALLI	43 F	11092	21/21	1062/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
91	MARIYAMMAL	18 F	14678	22/21	1076/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N2M0	T2N2AMX	RIGHT	NO	YES	NO	YES	PR NEGATIVE
92	SAROJA	41 F	19906	23/21	1083/21	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N1MX	LEFT	NO	YES	NO	NO	NO
93	VATCHALA	50 F	17243	24/21	1109/21	NEGATIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T2N1MX	T2N1AMX	LEFT	NO	YES	NO	YES	PR NEGATIVE
94	AROKIYAMARY	44 F	12455	25/21	125/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T4AN2M0	T4BN2M0	LEFT	YES	YES	NO	YES	PR NEGATIVE
96	ANANDAVALLI	52 F	13738	20/21	853/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T4AN2M0	T4BN2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
97	SAROJA	60 F	19876	31/21	1223/21	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	NO
98	JOTHI	55 F	22258	32/21	1248/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N0M0	T1BN0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
99	THENMOZHI	43 F	19347	33/21	1229/21	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	IDC	T4BN1M0	T4BN0MX	RIGHT	YES	YES	NO	YES	NO

100	PRAGADAMMAL	70 F	27048 39/21	1467/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N2M0	T2N3AMX	LEFT	NO	YES	NO	YES	PR NEGATIVE
102	SELINA MARY	60 F	17682 45/21	2008/21	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	MUCINOUS ADENOCARCINOMA	T2N0M0	T2N0MX	RIGHT	NO	YES	NO	NO	NO
103	RUKMANI	60 F	12578 35/21	35/21	POSITIVE	NEGATIVE	POSITIVE	LUMINAL B	IDC	T4BN1M0	T4BN0MX	RIGHT	YES	YES	NO	YES	PR NEGATIVE
104	AMSAVALLI	45 F	22609 41/21	1355/21	POSITIVE	POSITIVE	POSITIVE	LUMINAL B	MIXED WITH MUCINOUS	T3N1M0	T3N0MX	RIGHT	NO	YES	NO	YES	NO
106	GOKILA	50 F	29673 43/21	1625/21	POSITIVE	NEGATIVE	POSITIVE	LUMINAL B	IDC	T2N0M0	T2N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
107	ANANDHAM	60 F	52437 49/21	2133/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N0M0	T3N0MX	LEFT	NO	YES	NO	YES	PR NEGATIVE
111	PADMAVATHY	55 F	55380 55/21	2273/21	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T2N1M0	T2N1AMX	LEFT	NO	YES	NO	YES	PR NEGATIVE
112	SUSEELA	70 F	55459 56/21	2277/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T4BN2M0	T4BN3AMX	LEFT	YES	YES	NO	YES	PR NEGATIVE
113	BANUMATHI	45 F	58246 67/21	2357/20	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N0M0	T2N0M0	RIGHT	NO	YES	NO	YES	PR NEGATIVE
114	GANDHIMATHI	40 F	26895 68/21	1533/20	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N0M0	T2N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
115	THAIYALNAYAGI	40 F	28731 65/21	2801/20	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N0MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
117	ARUL JANY MARY	35 F	35672 79/21	2631/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
118	ANJALI DEVI	45 F	41567 80/21	2755/21	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N0M0	RIGHT	NO	YES	NO	YES	NO
120	REVATHY	50 F	54263 72/21	2350/21	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T2N0M0	T2N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
121	REVATHY	41 F	55708 173/21	2392/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T3N0M0	T3NOMX	LEFT	YES	YES	NO	YES	PR NEGATIVE
122	VANAROJA	60 F	70250 174/21	2807/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	PAPILLARY	T2N0M0	T2N0MX	RIGHT	NO	YES	NO	NO	PR NEGATIVE
123	MEENA	33 F	54789 78/21	3027/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1M0	T2N1AMX	LEFT	NO	YES	NO	NO	PR NEGATIVE
125	MANIMEGALAI	48 F	61428 82/21	2809/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N1M0	T2N1AMX	LEFT	NO	YES	NO	NO	PR NEGATIVE
127	RAMYA	42 F	71236 88/21	2906/20	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
132	THANGAPONNU	60 F	83386 99/21	3766/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T2N1M0	T2N1A	LEFT	NO	YES	NO	YES	PR NEGATIVE
133	SAROJA	75 F	80991 100/21	3881/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	METAPLASTIC	T3N0M0	T4BN0	RIGHT	NO	YES	NO	YES- RT	PR NEGATIVE
134	GUNASUNDARI	65 F	85083 101/21	3886/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N1M0	T2N1A	RIGHT	YES	YES	NO	YES	PR NEGATIVE
135	RAJESHWARI	53 F	85654 103/21	2067/20	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1M0	T2N2M0	LEFT	NO	YES	NO	YES	PR NEGATIVE
136	NAGAMMAL	65 F	86747 104/21	4118/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T1N0M0	T1N0MX	LEFT	NO	YES	NO	NO	PR NEGATIVE
140	MAHESWARI	39 F	22902 113/21	1534/20	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T4BN1M0	T4N1MX	LEFT	YES	YES	NO	YES	NO
142	MUNIYAMMAL	52 F	14875 122/21	926/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1M0	T1CN2AMX	RIGHT	NO	YES	NO	YES	PR NEGATIVE
143	SAKUNTHALA	55 F	91846 123/21	4464/21	POSITIVE	NEGATIVE	NEGATIVE	LUMINAL A	IDC	T3N1M0	T3N1MX	RIGHT RECURRANCE		YES	NO	NO	PR NEGATIVE
146	YAGULA MARY	53 F	93672 126/21	4552/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T3N2M0	T3N2M0	RIGHT	YES	YES	NO	YES	PR NEGATIVE
147	BELLA MARY	50 F	97747 127/21	4554/21	POSITIVE	POSITIVE	NEGATIVE	LUMINAL A	IDC	T3N1M0	T2N1A	RIGHT	YES	YES	NO	YES	NO
148	SUNDARI	47 F	98729 128/21	4549/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1M0	T2N2M0	LEFT	NO	YES	NO	YES	PR NEGATIVE
149	PARVATHI	44 F	91672 129/21	4659/21	NEGATIVE	NEGATIVE	NEGATIVE	TRIPLE NEGATIVE	IDC	T2N1M0	T2N1AMX	LEFT	NO	YES	NO	NO	PR NEGATIVE
150	JESINA	42 F	96272 131/21	4637/21	NEGATIVE	NEGATIVE	POSITIVE	HER2 POSITIVE	IDC	T4BN2M0	T4BN2MX	RIGHT	NO	YES	NO	YES	PR NEGATIVE