A Dissertation on

MANAGEMENT OF LOCALLY ADVANCED BREAST CANCER FIFTY CASES

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CERTIFICATE

This is to certify that this dissertation in **"MANAGEMENT OF LOCALLY ADVANCED BREAST CANCER"** is a work done by **Dr.B.JAYA SAI SEKHAR** under my guidance during the period 2004 - 2006. This has been submitted in partial fulfillment of the award of M.S. Degree in General Surgery (Branch - I) by the Tamil Nadu Dr.M.G.R. Medical University, Chennai - 600 032.

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Last but not the least , my heartfelt thanks to all my beloved patients without whom this study would not have happened.

CONTENTS

1. INTRODUCTION

Breast cancer is a major and important malignant disease in the Western World. In North America it was the most common malignancy among women, accounting for 27 per cent of all female cancers. One in 14 women can expect to develop breast cancer.

Breast cancer is one of the more slowly growing tumours which therefore renders it suitable for screening programmes. The evolution of breast cancer, especially in its preclinical phases, can be measured in years or even decades, although there are exceptions to this rule in which the disease takes on a more aggressive form.

The disease progresses from normality to hyperplasia, atypia, carcinoma in situ, and finally to invasive cancer. This progression is by no means inevitable and, in theory, stages may be missed out. It is also possible that a given stage may be permanent or may even regress to a more normal state. Serial mammography has indirectly indicated that the **doubling time for human breast cancer is usually of the order of 100 to 300 days**, although exceptions to this are frequently seen.

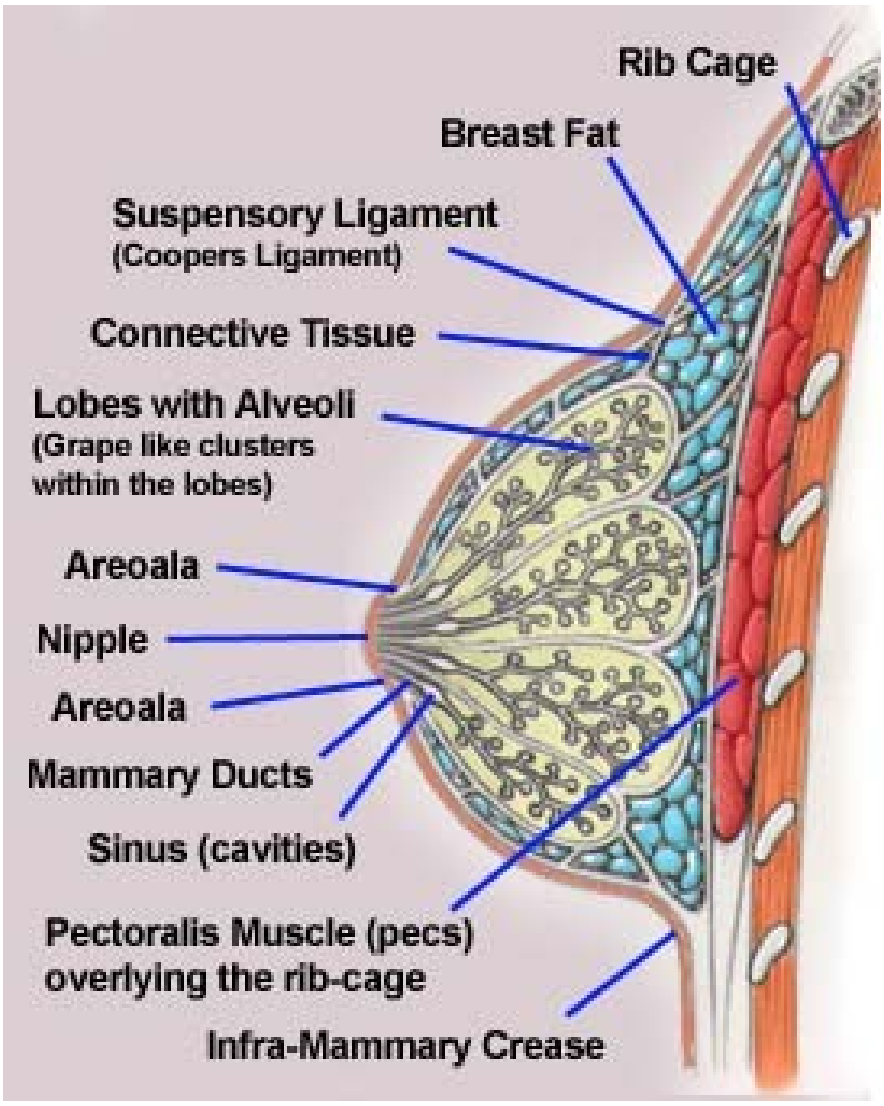
2. AIMS AND OBJECTIVES

This study was conducted on patients who were treated at the Government Royapettah Hospital ,Royapettah , Chennai 14 and Government Kilpauk Medical college Hospital , Kilpauk, Chennai 10 during the period 2004 – 2006 . This is a prospective study the aims of which are :

1. **To find the Age incidence of Locally Advanced Breast Cancer(LABC).**
2. **To study the various presentations of LABC.**
3. **To study the management protocol used , its rational and relevance to our system of medical care.**
4. **To study the awareness of the present management protocol of surgeons through the cases referred to the institution.**
5. **To analyze the Disease free survival of patients with LABC.**

REVIEW OF LITERATURE

CROSS SECTION OF THE BREAST



3.REVIEW OF LITERATURE

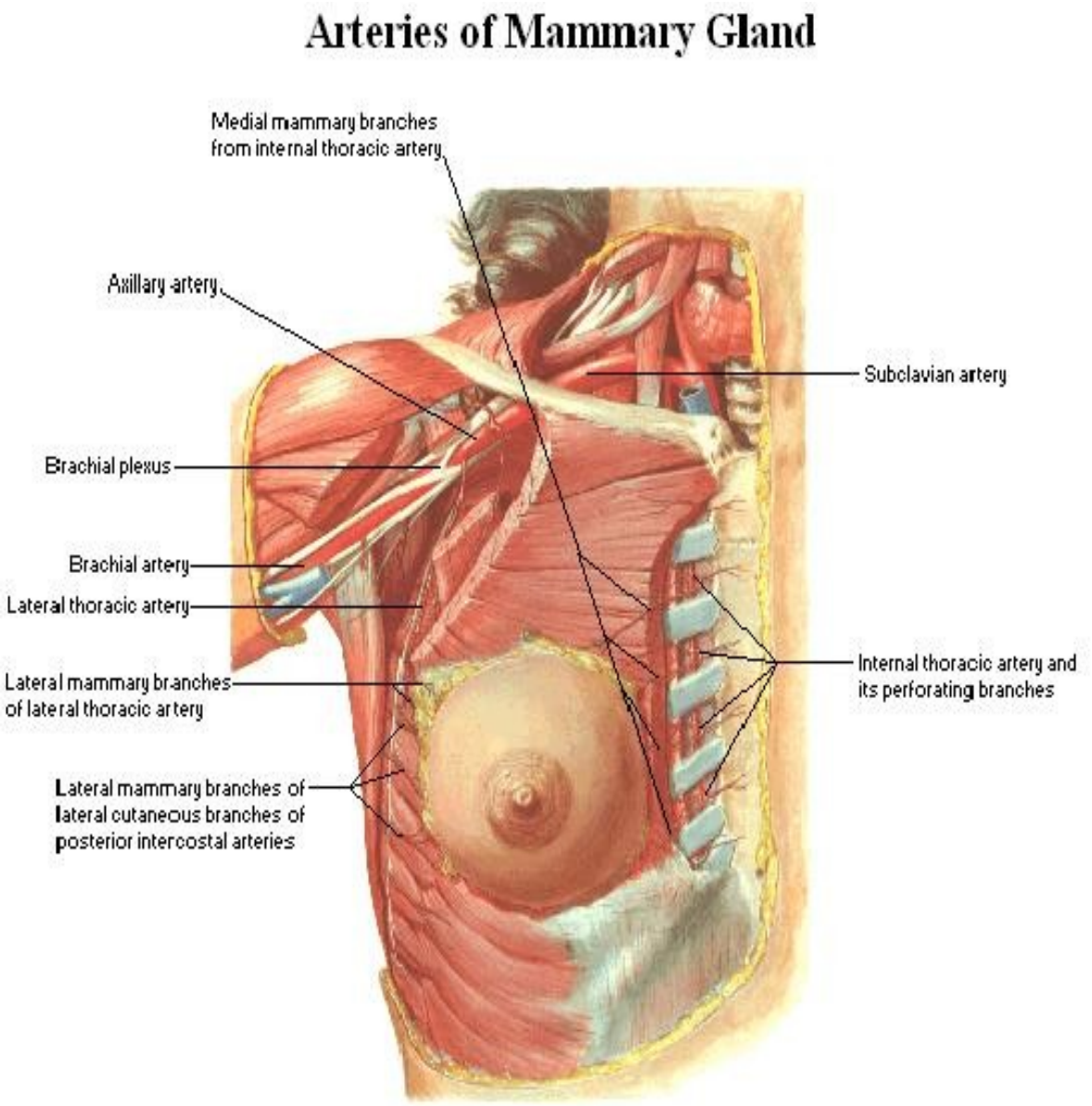
3.1 ANATOMY OF THE BREAST

The breast is a modified sweat gland and extends vertically from 2nd to 6th rib and horizontally from lateral part of sternum to anterior axillary line. Surgical extent is from the clavicle to the 7th rib and from midline to lateral edge of latissmus dorsi. The axillary tail of the breast(Spence) is of importance and its sometimes normally palpable, in lactation and also pre menstrually.

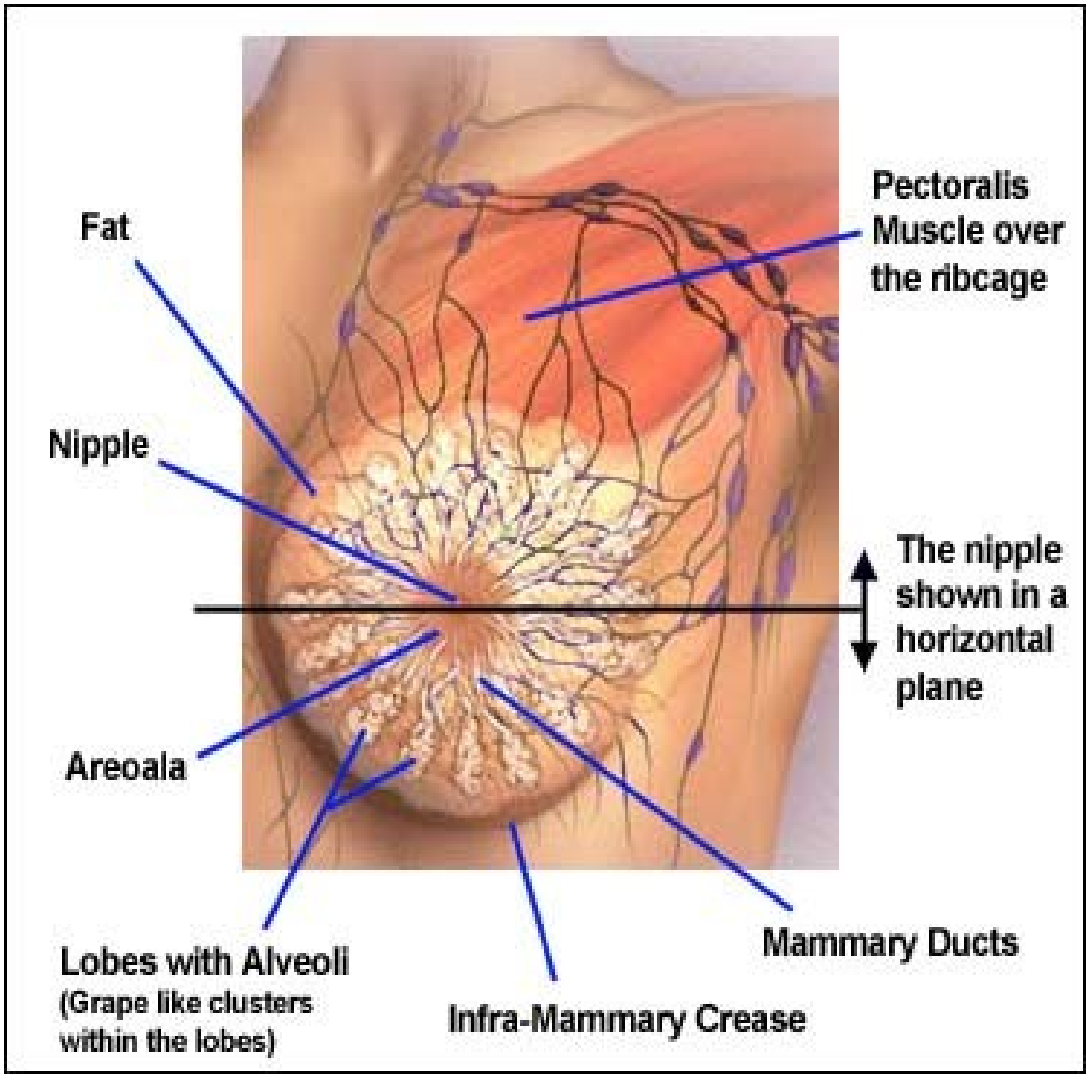
The lobule is the basic structural unit of the gland and their number and size varies considerably . Over 10 to 100 lobule drain into the nipple through 15- 20 lactiferous ducts. Each duct is lined by myo – epithelial cells and has a terminal ampulla which can contain milk or abnormal secretions.

The ligaments of cooper are fibrous strands which run from the skin into the gland substance and account for the skin changes in malignancy. The areolar epithelium has both sweat glands and sebaceous glands.

The nipple is covered by thick skin and at its apex contains the openings of the lactiferous ducts. It has smooth muscle fibres and is an erectile structure.



LYMPHATICS OF THE BREAST


Fat
Pectoralis Muscle over the ribcage
Nipple
The nipple shown in a horizontal plane
Areoala
Lobes with Alveoli
(Grape like clusters within the lobes)
Infra-Mammary Crease
Mammary Ducts

3.2 RISK FACTORS

The cause of breast cancer is unknown. Risk factors for breast cancer fall into three main groups: genetic, endocrine, and environmental; each may be of **major, intermediate, or minor importance**

3.2.1 Major risk factors

I, Sex:

Breast cancer is **100 times more common in women than in men**. In strict epidemiological terms, therefore, female sex is a major risk factor for breast cancer, although it is often forgotten as such.

II, Age:

As for other epithelial cancers the incidence of breast cancer increases with age. Breast carcinoma shows rapid rise in age-specific rates. Breast cancer rate continues to rise until old age

III, Previous breast cancer:

The development of a second breast cancer may be a clinical manifestation of multifocal origin of the first cancer or may be an entirely new cancer. There appears tobe an overall increased risk of 0.75 per cent to 1 per cent per year. This risk appears greatest in young women if their initial breast cancer is diagnosed before the age of 40.

IV, Family history:

A family history breast cancer is associated with an increased risk of the disease.The risk is greatest in patients with first-degree

relatives (mother or sister) affected,especially if they were under the age of 50 when the disease developed. The relative risk of developing breast cancer is

1.7 to 2.5 – breast cancer in a first-degree relative

1.5 among those with an affected second-degree relative.

V, Parity:

Nulliparity removes a protective effect against breast cancer. Single and nulliparous married women have a relative risk rate of 1.4 compared to parous women;.

Women whose first birth occurred after the age of 30 there appeared to be virtually no protective effect, with a relative risk of 0.94.

If the age at first birth is taken into account, subsequent pregnancies appear to have no influence on the risk of developing breast cancer. The protective effect occurs only if the pregnancy continues to full term.

3.2.2 Intermediate risk factors

I, Age of menarche and menopause:

Women whose menarche occurs before the age of 12, have a relative risk of 2.30 compared to those starting menstruation after this age. This decreases as the age of onset of menstruation increases. The risk of developing breast cancer also relates to the age of the menopause. Artificial menopause by oophorectomy or irradiation also reduces the risk of breast cancer.

II, Irradiation:

An increased risk of breast cancer has been demonstrated in survivors of atomic explosions, women treated by radiation for postpartum mastitis, and patients receiving multiple chest radiographs during assessment of tuberculosis. This increased risk becomes apparent after a latent period of 10 to 15 years: the effect is most obvious in women exposed to irradiation when under the age of 35; there is little increased risk in women exposed after the age of 40.

III, Body weight:

There is a strong relationship between body weight and breast cancer although this is critically dependent on age. In women under age 50 there is little correlation. However, in the 60 to 69 age group an increase in weight from less than 60 to 70 kg or greater increases breast cancer risk to 1.8.

IV, Benign breast disease:

Severe atypia with hyperplasia is associated with a moderately increased risk of developing breast cancer.

3.2.3 Minor and controversial risk factors

I, Alcohol:

Evidence for an association between consumption of alcohol and increased liability to breast cancer is becoming stronger, although the risk is small (1.5).

II, Diet:

Although weight correlates with breast cancer risk the relationship between dietary factors such as fat or cholesterol intake have not been shown to be an important factor in the development of breast carcinoma.

III, Contraceptive pill:

The risk with the present day pill with low dose estrogen is small. Those most at risk are women taking oestrogen-based oral contraceptives early in life and taking them for at least 8 to 10 years.

IV, Hormone replacement therapy:

Small doses of exogenous oestrogen therapy for short periods of time in premenopausal women appear to be safe. However, when hormone replacements are taken for 8 years or longer there may be an increased risk of 1.5 to 2.0.

V, Benign breast disease:

Some pathological entities, such as multiple papillomatosis and hyperplasia with gross atypia, are certainly associated with an increased risk of breast cancer (3.0).Patients with recurrent macroscopic apocrine cysts may also have a slightly increased risk of breast cancer.There is no increased cancer risk for fibroadenoma and fibrocystic change.

3.3 PATHOLOGICAL FEATURES OF BREAST CANCER

The histological assessment of breast cancer is of paramount importance in establishing the diagnosis of the tumour. It also helps determine the patient's prognosis and allows a greater understanding of the biology of the disease in any one case. There are many methods of pathologically classifying breast cancer whether it is derived from the duct system or the lobule .

3.3.1 DUCTAL CARCINOMA OF THE BREAST:

This is the most common form of breast cancer accounting for 85 to 90 per cent of all cases. It can conveniently be subdivided into in situ and invasive types.

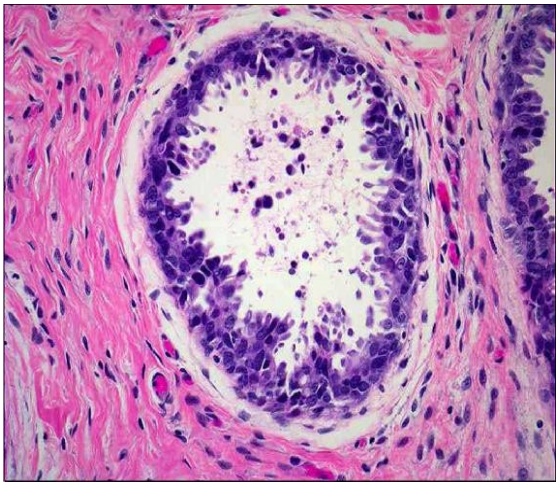
I ,Ductal carcinoma in situ:

It is a preinvasive form of breast cancer. It is characterized by a proliferation of malignant breast epithelial cells, is **confined to the duct system, and does not invade the basement membrane** or surrounding tissues.

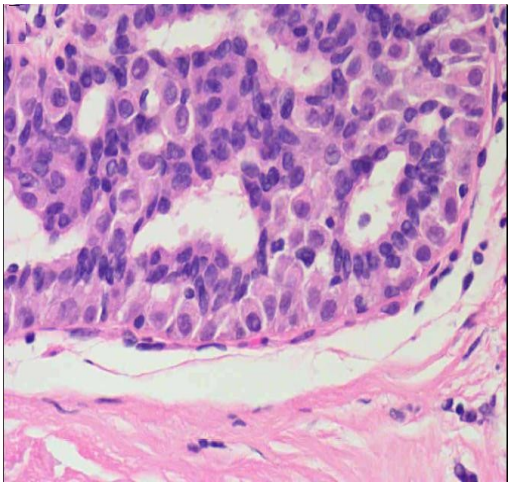
The most important aspect of ductal carcinoma is its malignant potential. Studies demonstrate a 30 to 50 per cent of ipsilateral invasive cancer, usually in the same quadrant, after an interval of some 10 to 15 years. The risk of developing invasive cancer depends on the extent of ductal carcinoma in situ.

HISTO- PATHOLOGY OF BREAST CANCER

DUCTAL CA IN SITU



LOBULAR CA IN SITU



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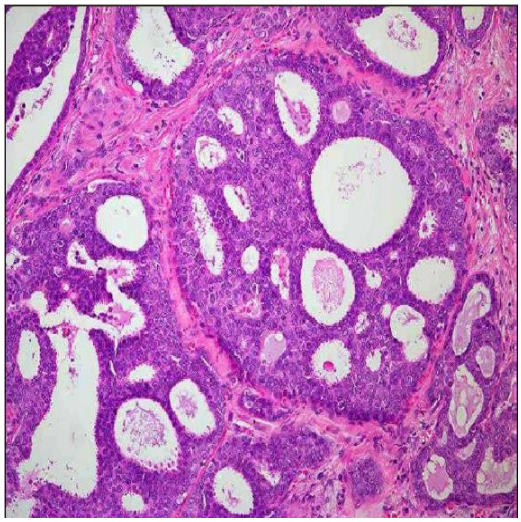
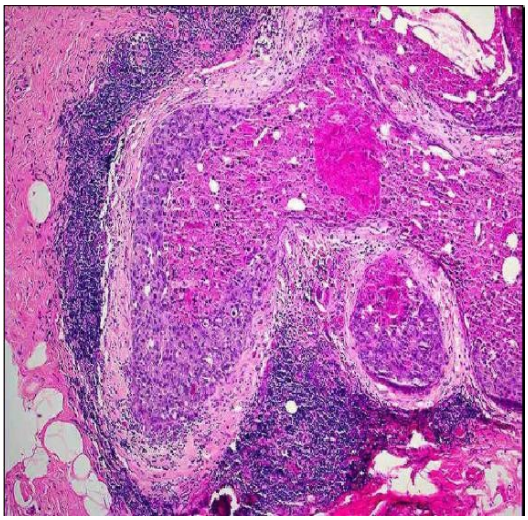
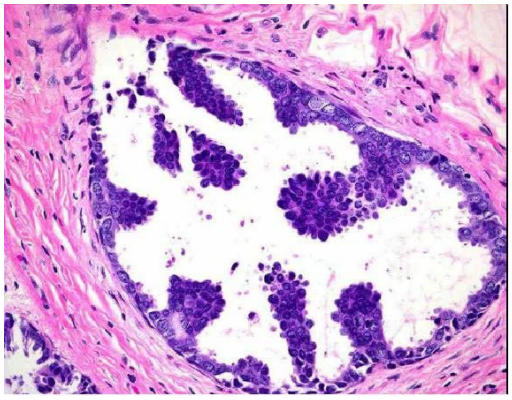


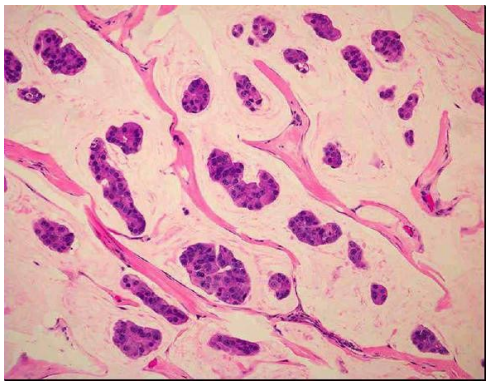
COMEDO CA



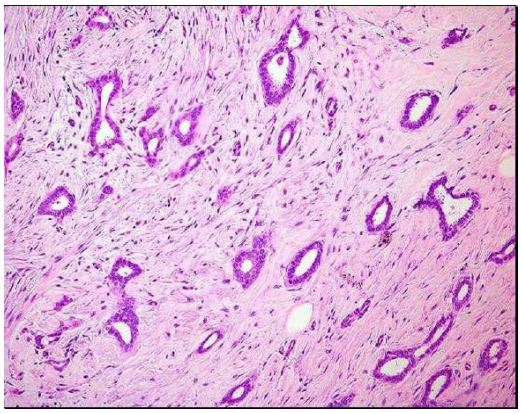
MICRO PAPILLARY CA



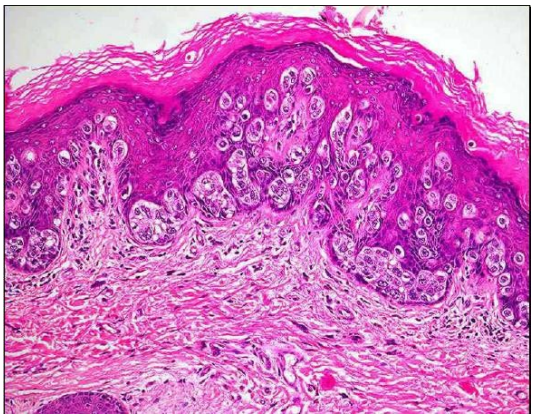
MUCINOUS CA



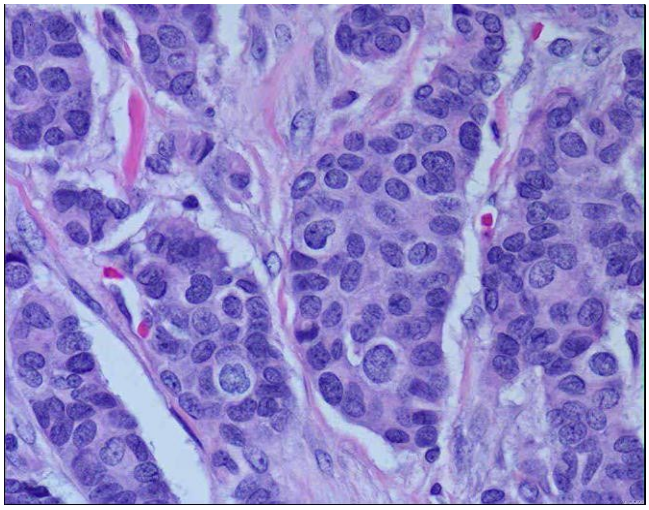
TUBULAR CA



PAGETS DISEASE OF NIPPLE



INFILTRATING DUCTAL CA



There are five main histological types of intraductal carcinoma:

1. Solid type: Duct lobular unit filled with malignant cells
2. Comedo type : The lesions undergo central necrosis
3. Cribriform type : They have a sieve-like appearance.
4. Papillary/micro-papillary :They show papillary projections
5. Clinging type: They may cling to the duct wall

Comedo and papillary forms are the most common and are both associated with multicentric disease;

Comedo carcinoma has the greatest expression of both DNA aneuploidy and of the C- erb2 oncogene.

II, Invasive / Infiltrating ductal cancer :

Invasion of the basement membrane of the duct is the most important criterion for all malignant tumours – the ability to infiltrate into surrounding tissue.

The majority of invasive ductal cancers fall into the group with no characteristic microscopic appearance . These are described as infiltrating ductal carcinoma, not otherwise specified (NOS).

III, Infiltrating ductal carcinoma (NOS):

This is essentially a diagnosis of exclusion, but it accounts for about 65 per cent of all invasive mammary cancers. The lack of specific and consistent histological features .

IV, Special types of infiltrating ductal carcinoma

A**,** Medullary carcinoma

B, Tubular carcinoma

C, Mucinous (mucoid) carcinoma

D, Papillary carcinoma

E, Cribriform carcinoma

V, Other types of Infiltrating ductal carcinoma:

A, Signet ring tumours

B, Clear cell tumours

C, Secretory carcinomas

Inflammatory carcinoma:

-- occurs in all age groups but more common in middle age

-- tumour emboli in dermal lymphatics, giving rise to the red infiltrative appearance of this condition.

-- must be differentiated from peau d'orange

-- Its prognosis is very poor.

3.3.2 LOBULAR CARCINOMA OF THE BREAST:

Lobular carcinoma can also be conveniently subdivided into in-situ and invasive forms, depending on whether the basement membrane of the lobule has been invaded by tumour.

I, Lobular carcinoma in situ

Lobular carcinoma in situ, is also a preinvasive form of breast cancer. The **microscopic criteria are**: uniform proliferation of cells , no interstitial spaces and expansion of at least half of the acini in the lobular unit

It has a high potential for becoming invasive. Lobular carcinoma in situ rarely expresses the C- erb2 oncogene.

The risk of invasive cancer after diagnosis of lobular carcinoma in situ (relative risk, 10) relates equally to both breasts. It is a risk factor for tumour development rather than a direct precursor. Atypical lobular hyperplasia has a 4-fold increased risk of cancer.

II, Invasive lobular cancer

It accounts for about 10 per cent of all cases of breast carcinoma, although its incidence varies quite widely.

Five main subtypes of Invasive lobular cancer are described:

A, classical

B, solid

C, alveolar

D, mixed

E, pleomorphic.

Histologically there is **Indian filing** in a **targetoid pattern** in the classical variety. In others there is a **lack of a specific histologic architecture** .

Frequently produces **distortion of the breast rather than a lump**. The prognosis of classic type better than that of invasive ductal cancer and other types of lobular carcinoma

III ,Labelling index

It is the percentage of cells undergoing cell division at any particular time.

High labelling indices → short doubling times →more aggressive. Median labelling index is about 3 per cent;

High labelling indices → poor prognosis and outcome

3.4 THE SPREAD OF BREAST CANCER

3.4.1 LOCAL SPREAD WITHIN THE BREAST:

Within the breast there are three main mechanisms of spread.

I, Direct infiltration (The most important)

This occurs by the ramifying projections that give the characteristic macroscopic stellate appearance of breast cancer. If uncontrolled, direct infiltration of overlying skin or the underlying fascia occurs.

II ,Direct infiltration along ducts

Multifocality is due to wide spread in situ cancer. The incidence and extent of multifocality depends on the size of the primary tumour..

Multifocality is presence of cancer within the same quadrant as the primary tumour.

Multicentricity is the presence of carcinoma outside the quadrant containing the primary tumour.

III, Local lymphatic and vascular spread

Lymphatic pathways extending into the pectoral fascia and sub-areolar regions.

3.4.2 REGIONAL SPREAD OF BREAST CANCER

The regional spread of breast cancer is defined as that to the axillary, internal mammary, and supraclavicular nodes.

I, Axillary Nodal Spread

The axillary nodes represent the most important site of regional spread from breast cancer.

Spread to axillary nodes is the most important prognostic indicator of breast cancer: approximately 45 per cent of all patients have nodal disease at presentation.

The likelihood of axillary nodal spread is a function of the size of the primary tumour

SIZE OF PRIMARY In cm	INCIDENCE OF AXILLARY NODES
< 2cm	< 20 %
2 to 5cm	35%
>5 cm	50%

About 30 per cent of palpable and apparently diseased nodes are found to be histologically free of metastases and vice versa

Techniques such as clearing the axillary fat with xylene to increase nodal yield and more thorough sectioning of the nodes themselves increase the positivity rate.

The relationship between axillary nodal spread and prognosis depends on three factors:

A,Number of nodes involved

According to studies National Surgical Adjuvant Breast Project (NSABP) the number of positive nodes correlates directly with survival with 4 or more nodes being associated with worse prognosis.

The number of negative nodes have no prognostic importance. To ensure that the axilla is clear of metastases at least four, and possibly up to 10, negative nodes must be isolated.

B, Level of nodal disease

The axillary nodes are conveniently divided into three groups depending on their relationship to the pectoralis minor muscle. Prognosis relates to the level of axillary node affected, although this is a less powerful factor than the total number of nodes affected by the tumour.

Level of nodes	5 yr survival rate
I	65 %
II	31 %
III	< 3 %

C, The extent of disease in individual axillary nodes

In practice the prognosis for patients with a single micrometastasis can be regarded as similar to those with node-negative disease. **Extra nodal disease is associated with bad prognosis.**

II, Internal Mammary Nodal Spread

Internal mammary nodes are more commonly associated with **medial or periareolar tumours.** They are involved in 20 per cent of cases. Internal mammary nodal disease alone is rare and is only 8 %

It has the same prognostic implication as axillary nodal disease. However, if both the internal mammary and axillary nodes are affected 10-year survival rate is only 25%.

III, Supraclavicular Nodes

Involvement of Supraclavicular nodes implies extensive involvement of the internal mammary or axillary nodes. Supraclavicular nodal disease is associated with a **poor prognosis**.

3.5, THE CLINICAL PRESENTATION OF BREAST CANCER

The majority of women presenting with breast cancer complain of a lump. Classically this is **hard, painless, immobile, fixity to surrounding tissues, skin, underlying pectoral muscle**.

Not all breast cancers are hard: they are often firm.

The degree of mobility can also vary . It is therefore, advisable to undertake histological and cytological examination of any discrete lump

in a woman over the age of 25. A diagnosis of a fibroadenoma or cystic change without such confirmation is extremely dangerous.

A, Lump:

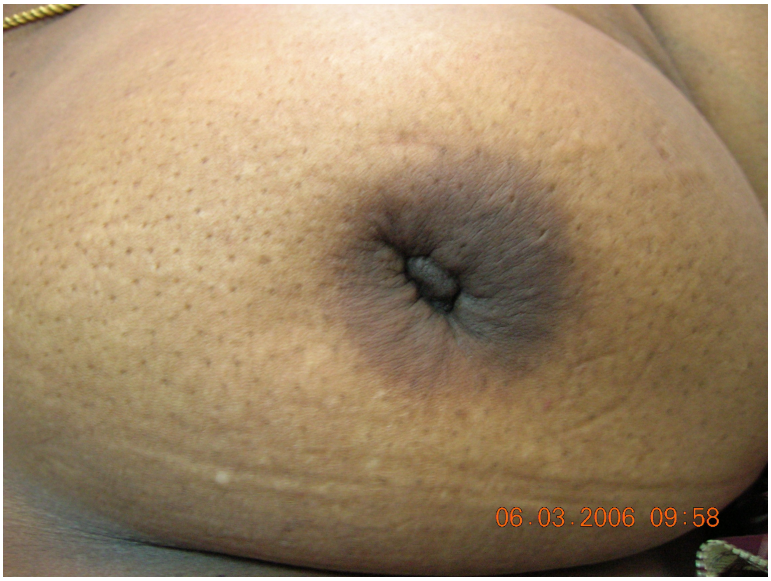
A lump is **the presenting feature in 85 % of cases** . This is not the case in lobular carcinoma. The diffuse nature of the tumour produces **distortion**, puckering, and the eventual **feeling of heaviness** . Later there may be **nipple retraction** and **discomfort.**

B, Pain :

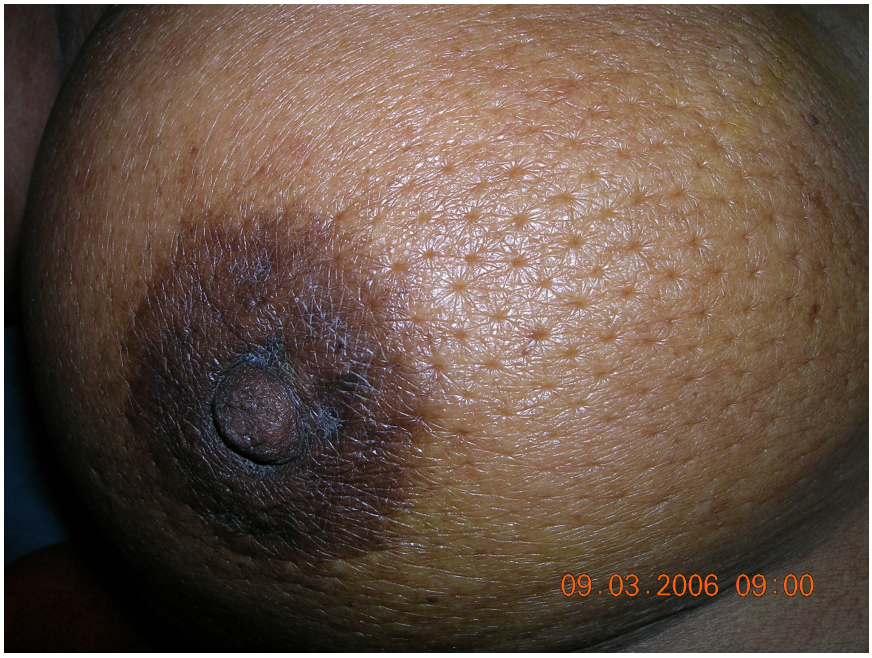
Pain is not a common feature in carcinoma of the breast. It usually indicates an inflammatory process.

Not all cancers are painless and have occasionally increased discomfort in the lump prior to menstruation.

NIPPLE RETRACTION WITH PEAU D' ORANGE



CLASSICAL PEAU D' ORANGE



C, Changes in the skin:

It may present with dimpling tethering or Puckering.

Peau d'orange is a feature of advanced cancer. The cause of this characteristic clinical sign is oedema of the skin: this is not due to direct infiltration of the skin by tumour but **represents lymphatic obstruction of the breast** as a result of axillary metastasis.

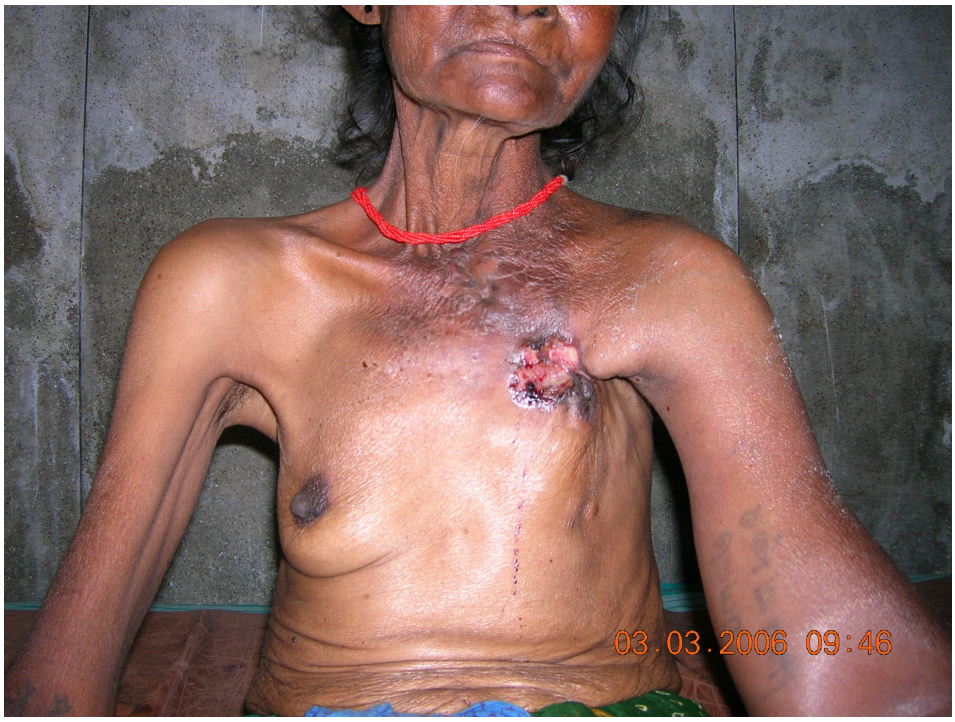
It is **differentiated from inflammatory breast cancer**, in which cutaneous lymphatics contain tumour emboli. In advanced, untreated cases there may be ulceration and fungation.

D, Changes at the nipple

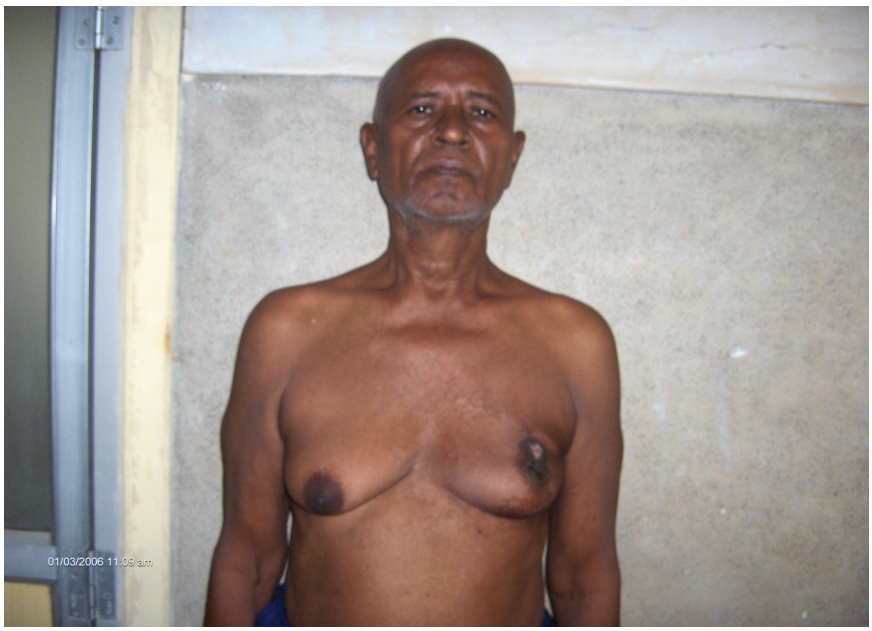
Nipple distortion and retraction are common presenting features in patients with breast cancer. The discharge associated with intraductal cancer is unifocal ,**watery or blood-stained**. It is multifocal, tenacious, and coloured in duct ectasia.

Paget's disease is usually a presenting feature of breast cancer in the elderly, although it is occasionally seen in other age groups**. It usually represents an underlying intraductal carcinoma** which may be quite extensive in the breast and which may also exhibit an invasive component. There are characteristic, **large, clear Paget cells** origin of which is unknown.

LOCALLY ADVANCED BREAST CANCER WITH LIMB LYMPHEDEMA



LOCALLY ADVANCED CA DEVELOPING IN GYNAECOMASTIA



3.6, DIAGNOSIS OF BREAST CANCER

There is no indication for a purely clinical diagnosis of breast cancer. Confirmatory diagnosis is by pathology and radiology.

3.6.1, PATHOLOGICAL DIAGNOSIS

A, Fine needle aspiration cytology

This method is performed as an outpatient procedure and today can also find ER/PR status with immunohistochemistry.

The false-negative rate is about 15 per cent and are usually due to sampling errors.

The false positive results occur in about 2 per cent of cases and could be due to hyper cellular fibroadenoma, effects of hormone therapy, pregnancy, or lactation on normal breast tissue.

Aspiration cytology cannot differentiate in-situ or invasive cancer but can distinguish ductal from lobular carcinoma

B, Trucut/Core biopsy

It is performed under local anaesthesia and gives a histological rather than a cytological specimen. It differentiates insitu from invasive disease , detects ER/PR status and the grade of the tumour

C, Incision / Excision biopsy

It is rarely used only if FNAC or core biopsy fails. **It can confirm or exclude malignant disease. Incision biopsy only when the tumour > 3 cm in size.**

3.6.2 RADIOLOGICAL DIAGNOSIS

A, Mammography

A high level of sensitivity and specificity is now available using modern mammographic techniques.

The classic features of breast cancer on mammography are:

A. Tissue Asymmetry

B. Mass Effect

C. Microcalcification

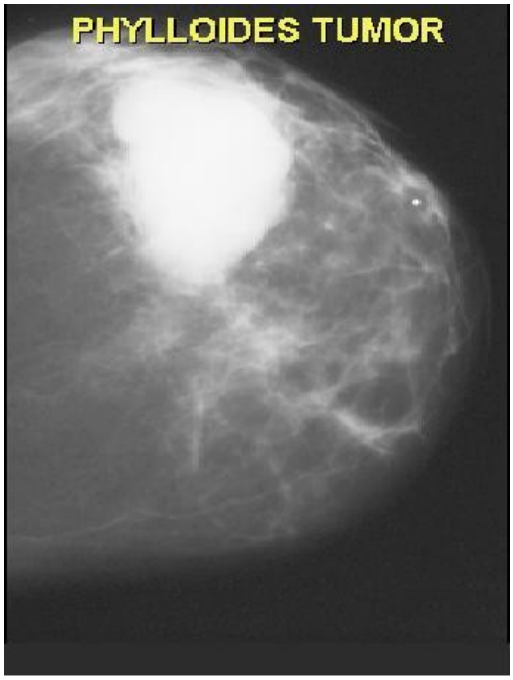
D. Skin Thickening

E. Nipple Inversion

The combination of **mass effect with localized microcalcification has the highest predictability for a malignancy.** It detects **potential multicentricity** and acts as a **base-line for radiological evaluation** of the breast in the years after initial diagnosis.

MAMMOGRAM

PHYLLODES TUMOUR



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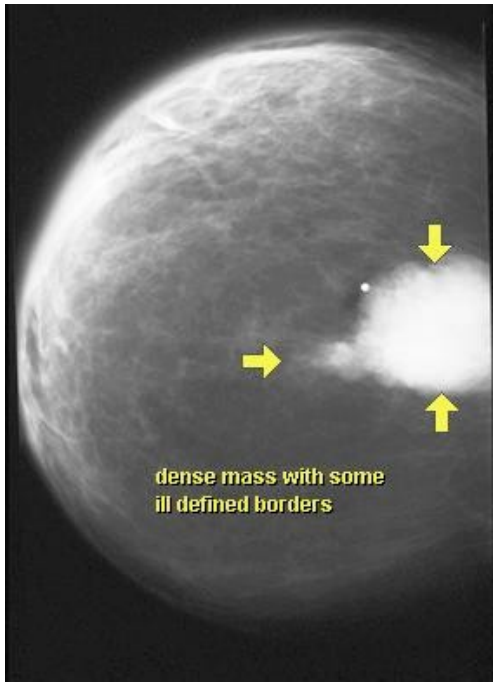
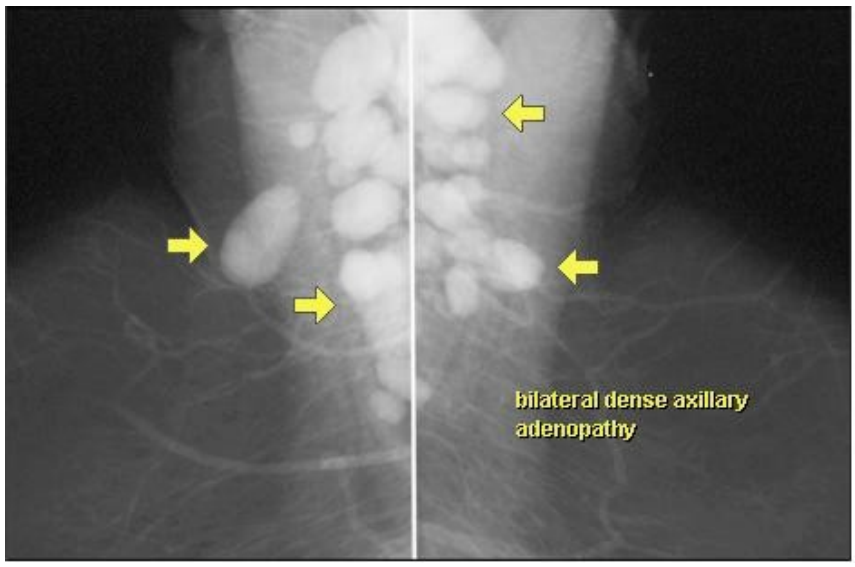
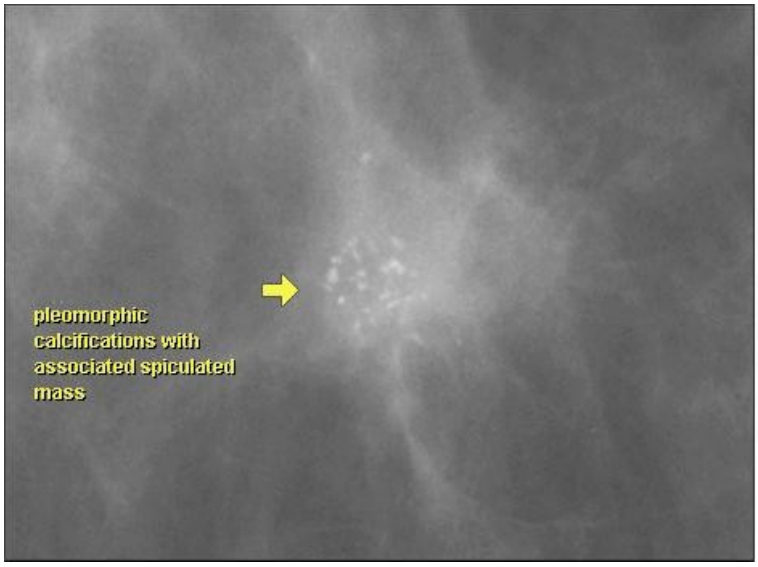


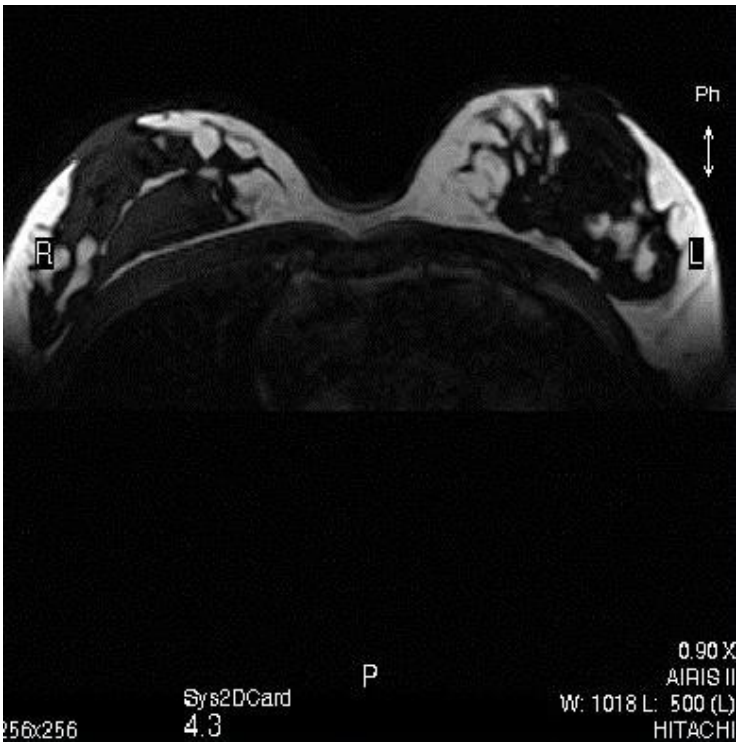
AXILLARY NODES- MLO VIEW



DCIS- PLEOMORPHIC CALCIFICATIONS



MRI OF THE BREAST



LOCALLY ADVANCED BREAST CANCER WITH LIMB LYMPHEDEMA

B, Ultrasound:

Ultrasound remains the primary means of differentiating a cystic or solid nature of a lesion. Sensitivity of the ultrasound today helps to pick up a 3 mm lesion.

Its main uses today are:

A. In a nipple discharge a duct ectasia or ductal papilloma can be identified.
B. In finding fluid collections post lumpectomy
C. In diagnosing breast abcesses
D. Breast implant rupture and leak
E. Preferred modality in pregnant women
F. Combined with mammogram in dense breasts
G. Can guide aspirations or biopsies in small areas

C, Magnetic resonance imaging:

Magnetic resonance imaging has an established role in breast imaging. It exploits the difference in relaxation times of various types of tissue. The breast fat appears bright on T1 weighted image whereas a fluid filled cyst appears bright on a T2 weighted image.

Its definite uses are :

A. Clarifies if both USG and Mammogram fail
B. In isolated axillary metastases with negative breast imaging
C. Distinguishes scar from recurrence in post mastectomy status
D. Gold standard in post reconstruction follow up

3.7, STAGING

The purpose of staging is to aggregate cases having an approximately similar prognosis.

Many staging systems have been proposed. The older systems used were **The Manchester And Columbia Systems** .Today only the TNM system is used.

3.7.3 THE TNM CLASSIFICATION :

The TNM classification as released in 1954 by the International Union against Cancer (Union Internationale Contre Cancere) attempted to classify breast cancer on a description based on the primary tumour (T), the regional lymph nodes (N), and distant metastases (M). This system is the most popular system used till date.

Tumour size(T):

Tx : primary tumour cannot be assessed
T0 : no evidence of primary tumour.
Tis : carcinoma in situ (DCIS,LCIS, pagets disease of nipple with no palpable tumour)
T1 : < 2cm in greatest dimension
T2 : 2 to 5cm in greatest dimension
T3 : > 5cm in greatest dimension
T4 : fixation to chest wall or skin
T4a : Extension to chest wall
T4b : Skin→edema (including peau d orange), Ulceration and satellite nodules
T4c : both

T4d : inflammatory carcinoma

Nodal stage (N):

Nx: regional lymph nodes cannot be assessed

N0: axillary nodes do not contain tumour

N1: mobile involved axillary nodes

N2: fixed axillary nodes

N3: a, infraclavicular nodes

b, internal mammary and axillary

c, supraclavicular lymph node and/ or arm swelling.

Metastasis (M):

Mx: presence of distant metastases cannot be assessed

M0: no distant metastases.

M1: distant metastases present.

Stage grouping:

STAGE	TUMOUR	NODE	METASTASIS
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage Iia	T0 T1 T2	N1 N1 N0	M0
Stage Iib	T2 **T3**	N1 **N0**	**M0**
Stage IIIa	**T0** **T1** **T2** **T3**	**N2** **N2** **N2** **N1,N2**	**M0**
Stage IIIb	**T4**	**N0,N1,N2**	**M0**
Stage IIIc	**ANY T**	**N3**	**M0**
Stage IV	ANY T	ANY N	M1

3.8 TREATMENT OF CARCINOMA OF THE BREAST

The treatment of carcinoma breast has changed, more so in the past few years. We have witnessed fundamental changes in our approach, with decreasing reliance on radical surgical excision of the primary tumour and associated regional lymph nodes.

This is mainly due to a **better understanding of the spread of breast cancer**, a greater appreciation of the **systemic aspects of the disease**, and increased realization that variations in local regional treatment are unlikely to alter prognosis.

Hence a multi- modal approach is adopted to obtain the best results in terms of patient survival and disease free survival

The modalities are surgery, chemotherapy, radiotherapy and hormone therapy and immunotherapy . Surgery is the main modality in all stages except when systemic disease is present .

3.8.1 SURGERY :

The surgical options available today are

A, Breast conservation surgery

B, modified radical mastectomy (patey's)

C, palliative simple mastectomy

A, Breast conservation surgery : (BCS)

Patient choice is one of the important criteria in electing this modality .

I, Indications for breast conservative therapy

Tumour characteristics, the position of the cancer in the breast, and the nature of the breasts themselves. Mammography is an essential preoperative investigation to determine the presence of multicentric tumours.

1,Tumour size :

Tumour is less than 4cm in diameter (mastectomy if the tumour is more than 3 or 4cm in diameter).

2, Tumour fixity :

No fixation to the underlying muscle or overlying skin.

3, Tumour breast ratio :

Favourable tumour breast ratio allows breast conservation surgery to be an option.

II, Contraindications to breast conservation surgery

1, Absolute :

A, Multicentricity.

B, Patients with a second tumour in the breast,

C, Collagen vascular diseases

D, Prior irradiation

E, Pregnancy

F, Positive lumpectomy margins

2, Relative :

A, Multifocality

B, Centrally located tumours

C, Poor tumour differentiation

B, Modified Radical Mastectomy (Patey's)

Modified radical mastectomy refers to a procedure **combining total mastectomy with removal of axillary lymph nodes in continuity with the mastectomy specimen**. It is the most widely used procedure to treat operable breast cancer and is the alternative to breast-sparing procedures.

The patient is left with intact musculature around the shoulder and a situation that is well suited to prosthetic reconstruction.

The structures removed in a modified radical mastectomy are :

A. The whole breast

B. Skin overlying the tumour with nipple areola complex

C. All of fat, fascia and lymph nodes of the axilla.

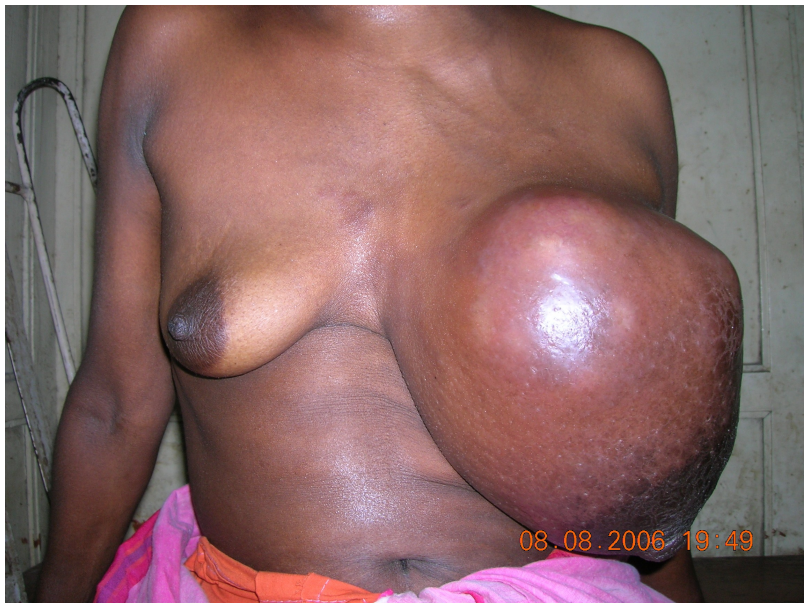
D. The pectoralis minor is either divided or retracted or removed .

E. Axillary vein, nerve to serratus, subscapular neurovascular bundle are preserved

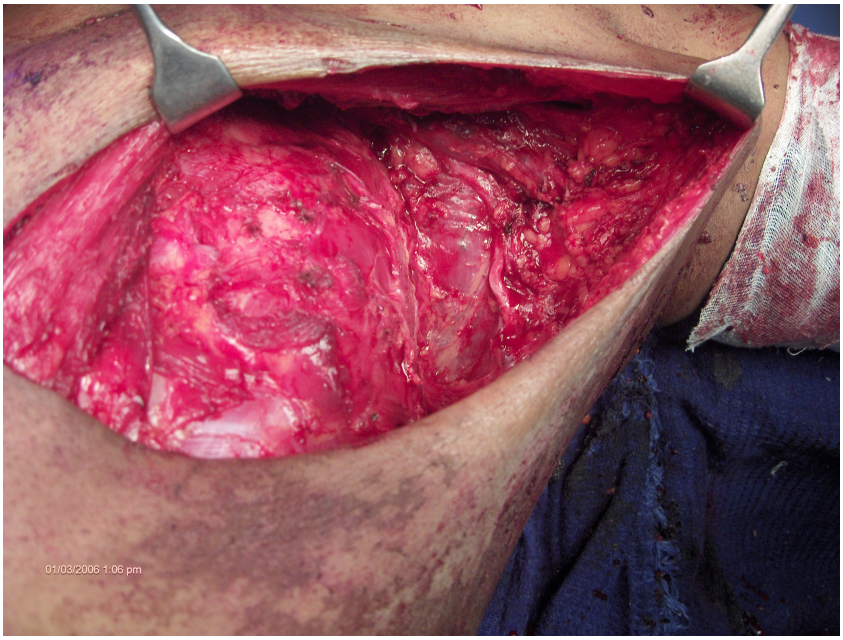
The survival of patients with negative axillary nodes was 82% at 10 years with a local recurrence rate of 5%. For patients with positive

nodes, the survival was 48%, very similar to results with radical mastectomy.

SARCOMA OF THE BREAST



POST MRM FIELD



Scanlon modified the Patey procedure by dividing the pectoralis minor muscle,allowing removal of apical (level III) nodes and preservation of the lateral pectoral nerves to the major muscle.

Auchincloss differs from the Patey procedure by retracting the pectoralis minor muscle. This modification limits the complete removal of high axillary nodes but is justified by Auchincloss, who calculated that only 2% of patients will potentially benefit by removal of the highest level nodes

Management of axillary nodes

Axillary dissection acts as a **guide to staging and prognosis**. It dictates the need for adjuvant therapy with chemotherapy, irradiation, or hormonal therapy. It provides good local control of disease in the axilla as untreatable axillary metastases can cause much morbidity.

Axillary nodal clearance

Block dissection of axillary nodes accurately stages the axilla, both qualitatively and quantitatively, and has the advantage that it provides a good mechanism for tumour control.

However, **if there is bulk nodal disease with metastases greater than 2cm in diameter full surgical axillary clearance is usually preferred.**

Axillary nodal sampling:

If done properly it provides qualitative data as good as those obtained from clearance, allows appropriate patients to be treated with radiotherapy, and provides a rational basis for systemic treatment.

Sentinel lymph node biopsy

The **sentinel lymph node is the first node to receive lymphatic drainage from the tumour**. Blue dye or radio-active colloid is injected around the tumour and the first node to show a blue colour or high radio-activity is sent for histopathological examination.

Positive → a Complete axillary dissection

Negative → Further exploration is abandoned and

Complications of limb edema and arm stiffness are avoided

Absolute contraindications are palpable axillary lymph node metastases, multi focal breast cancer or prior breast or axillary surgery

3.8.2 Local recurrence after treatment of breast cancer

Locally recurrent disease must be distinguished from regional recurrence; the two are often confused. **Local recurrence is that seen in the breast after conservative therapy or on the chest wall after mastectomy**; regional recurrence denotes recurrent disease in regional lymph nodes.

Regional recurrence associated with widespread metastatic disease and it is therefore mandatory to identify distant metastases.

In general, the more radical the treatment the lower the incidence of local recurrence. The lowest local recurrence rate (2 per cent for stage I disease) has been recorded after extended radical mastectomy. **The overall incidence of local recurrence after breast conservation is about 10 %.**

Factors predisposing to local recurrence:

A, Positive axillary nodes :

Recurrence is more common in patients with positive axillary nodes. It has therefore been suggested that as well as giving radiotherapy to all patients after partial mastectomy, **the chest wall should be irradiated after total mastectomy if disease has spread to the nodes.**

B, Tumour size:

Tumour size has been shown to be associated with increased incidence of local recurrence after both total mastectomy and breast conservation. Therefore in T3 and T4 lesions adjuvant irradiation is recommended.

Again, there is no evidence that this improves survival, although it reduces local recurrence.

C, Positive surgical margins:

Positive surgical margins are an important risk factor for recurrence. Reason being either inadequate surgical technique or extensive in-situ disease. **Hence multifocality is an important factor predisposing to local recurrence.**

D. Other factors :

High tumour grade, lymphatic or vascular invasion, and young age are also associated with recurrent disease.

Rationale of systemic approach :

Systemic metastatic disease has a median survival after diagnosis of 14 months. The systemic component of breast cancer, as described above, indicates that either the patient is cured by local treatment or that death occurs from metastatic disease at about the same time that she would have died without local intervention.

3.8.3 ADJUVANT CHEMOTHERAPY

A combination of **cyclophosphamide, 5-fluorouracil, and methotrexate has been most widely used .** The initial study evaluating this combination therapy in breast cancer showed a **30 per cent reduction in mortality in patients receiving** and the effect was

most clearly apparent in premenopausal women with 1 to 3 positive nodes.

Adjuvant polychemotherapy is now recommended for all node-positive women aged less than 50. Chemotherapy causes a pharmacological castration and ovarian ablation.

Non-Metastatic Breast Cancer

A, Node-Negative Patients :

- CMF / FAC /AC

B, Node-Positive Pateints

- FAC/ CMF / AC
- CEF / EC where E = Epirubicin
- TAC where T = Docetaxel

Recurrent or Metastatic Breast Cancer

- CAF/ CMF/ CEF /AC / EC / AT

DRUG	ABBREVIATION	DOSE
Cyclophosphamide	C	500 mg/m^2 /IV 100-200 mg/m^2 /PO
Adriamycin	A	40-50 mg/m^2 /IV
5-Flourouracil	F	400-500 mg/m^2 /IV
Epirubicin	E	110-120 mg/m^2 /IV
Docetaxel	T	60-100 mg/m^2 /IV

- FAC → all on DAY1 → repeat every 28 days
- CMF classical→ Cyclophosphamide PO 14 days
  M & F on DAY 1 and 8
  Repeat every 28 days
- CMF → all on DAY 1 → Repeat every 21 days
- AC → A on DAY1, C on DYAS 3-6
  Repeat every 21 days

3.8.4 ADJUVANT HORMONAL THERAPY

Hormone therapy is offered to **all women with hormone receptor-positive invasive breast cancer** regardless of size or the number of lymph nodes involved.

The effect is greatest in patients age over 50 with positive nodes, in whom there is a **20 per cent reduction in annual mortality**.

This translates to an **8 per cent reduction in 10-year mortality**. There is a small, yet still significant, effect in node-negative individuals.

Tamoxifen:

An important effect of adjuvant tamoxifen is that it **reduces the risk of contralateral breast cancer by 39 per cent.** The role of **adjuvant tamoxifen is now well established in women over the age of 50**. Newer generation drugs like raloxifene and toremifene are available but tamoxifen is most widely used.

Tamoxifen at 10 mg bi daily for 5 years is considered standard in all women > 50 yrs especially if node positive. Aromatase inhibitors have an additive effect if used with tamoxifen.

Side effects of tamoxifen include thrombo embolic phenomenon , hot flushes , endometrial cancer and particularly in premenopausal patients experience menopausal symptoms, nausea, weight gain, vaginal dryness, or discharge.

Aromatase inhibhitors:

New study results now confirm that aromatase inhibhitors (Eg. Letrozole) are either better than or equal to tamoxifen in cancer that is locally advanced or has spread to other parts of the body. These drugs function by preventing estrogen from being produced, but they are **only effective in women who are past menopause.**

Despite these results these drugs are not presently the standard in the government setup because of the cost factor and poor follow up to draw any conclusions.

LHRH agonists :

Goserelin and leuprolide act on the pituitary –ovarian axis and block estrogen production from the ovaries.

3.8.5 ADJUVANT RADIOTHERAPY:

Radiation is used to destroy cancer cells left behind in the breast, chest wall, or lymph nodes after surgery. Radiation treatments are usually given at 40 -50 Gray, 5 days a weekin divided doses for 6 to 7 weeks.

Indications :

- All cases of breast conservation therapy.
- Tumour size larger than 5 cm in size,
- Positive margins after mastectomy
- 4 or more positive lymph nodes and / or extra capsular spread
- High grade with lymphatic / vascular invasion

Types of therapy :

A, External beam radiation**:** Most common method

B, Internal radiation / brachytherapy/ interstitial radiation.

Field of therapy:

A,Post lumpectomy: The entire breast , infraclavicular/ internal mammary nodal areas withextra boost to tumour bed

B, Post mastectomy : The entire chest wall + /- axilla

Side effects:

Skin changes and lymphedema of the ipsilateral arm

Partial breast radiation : Radiation over a much shorter period only to the part of the breast with the cancer is still experimental.

3.8.6 IMMUNOTHERAPY

Trastuzumab (Herceptin) is a drug that is an antibody directed against the HER-2/neu receptor on the surface of the breast cancer cells

Indication :

Metatstatic disease with breast cancer with HER-2/neu receptor and nodal positivity.

It is cardiotoxic as heart muscle cells also have the HER-2/neu receptor. It should be used cautiously when combined with other heart-damaging drugs such as anthracyclines (doxorubicin and epirubicin).

3.9 LOCALLY ADVANCED CANCER (STAGE III)

Locally advanced tumours are defined as those more than 5cm in diameter or those with fixed axillary nodes in which there is no evidence of distant metastases. The management of these cancers has been somewhat disappointing because of poor local tumour control and the high incidence of subsequent metastatic disease, resulting in an **overall survival rate of 20 per cent or less**.

Role of neoadjuvant therapy :

Preoperative systemic chemotherapy gives the best results. Postoperative chemotherapy and radiotherapy did not improve the survival rate as compared to the control group(2). The agents and their dosages used are the same as that of adjuvant setting.

Data from the NSABP B-27 and GEPAR-duo trials strongly support a combined **anthracycline / docetaxel (AT)** regimen in the neo-adjuvant setting with improved overall and disease-free survival(3), although cardiac toxicity underlies the necessity to optimize the schedule of AT combination(4).

This is particularly the case in more aggressive tumors or those women with lymph node involved cancers. The length of these regimens ranges from four months to six months.

Role of Surgery in LABC :

Surgery following neo adjuvant therapy is usually a modified radical mastectomy although presently the role of breast conservation is being evaluated in this situation. Other procedures are not recommended.

3.10 FOLLOW-UP OF WOMEN WITH BREAST CANCER

Physical evaluation is directed towards the detection of local regional recurrence as well as distant metastases. The evaluation of local regional recurrence should include detection of new primary breast cancers.

Mammography is therefore recommended every 1 to 2 years after initial diagnosis.

Local recurrence in the breast or in regional lymph nodes can be treated or at least palliated with further surgery, irradiation, or chemotherapy.

3.11 MALE BREAST CANCER

Breast cancer occurring in the mammary gland of males is rare and less than 1% of the incidence in women. The average age at diagnosis is 10 years older in men than in women. Since breast tissue is scant in men, breast tumors in males involve the pectoralis major muscle more commonly.

Histologically, tumors of the male breast are **most commonly infiltrating ductal carcinomas** that are similar in appearance to their counterparts in females. **Lobular carcinoma, is rarely seen** in males. Interestingly, male breast cancer **very often contains steroid hormone receptors.**

Studies found that **84% of tumors arising in male mammary glands contain estrogen receptor**, and support the high incidence of receptors and the frequent hormone sensitivity of male breast tumors.

TREATMENT

The treatment of carcinoma in the male breast depends on the **stage and local extent of the tumor**. If the underlying pectoral muscle is involved, **radical mastectomy is the procedure of choice**.

For **smaller mobile tumours, a modified radical mastectomy** appears to be the procedure of choice with postoperative radiation therapy.

Node-positive disease portended a worse prognosis in men than in women. There is little experience with adjuvant chemotherapy or hormonal therapy in male breast cancer.

Because the majority of these tumors are hormone sensitive, the use of adjuvant tamoxifen for node positive and high-risk node-negative patients seems logical.

3.12 THE PROGNOSIS OF BREAST CANCER

The natural history of breast cancer is uncertain and survival, even after the development of metastases, may be prolonged without treatment. Recurrence and subsequent death may occur as long as 25 years after the original diagnosis.

Despite these limitations the analysis of **5 year/10 year survival** demonstrates that

STAGE	5 YR SURVIVAL	10 YR SURVIVAL
I	80 %	50 %
II	50 %	35 %
III / IV	30 %	< 25 %

Prognostic factors in breast cancer

They act as a guide to overall prognosis, but they may also determine the need for adjuvant treatment.

Overall **clinical stage is, therefore, only a relatively poor prognostic indicator**, and is less important than specific pathological and certain biochemical parameters.

Multivariant analysis of the various clinical and pathological features show that **axillary nodal disease, tumour size, and differentiation are the most important** .

A, Lymph node metastases

Nearly all studies show that the presence of **axillary lymph node metastases is the most important prognostic determinant.**

Prognosis is a function of the number of lymph node metastases, although other factors such as level of disease, extranodal spread, or size of tumour metastases may be of some minor significance.

Number of involved nodes	Relative survival rate at 5 yrs
0	82 %
1-2	60 %
5-6	47 %
11-12	31 %
20	8 %

B, Tumour size

Tumour size is the second most important prognostic determinant. Although tumour size and lymph node metastasis are closely related they are also independent of each other in terms of prognosis..

C, Histological grade

Grade is classified as I, II, or III on the basis of tubule formation, nuclear pleomorphism, and mitotic rate. Mitotic rate is the most powerful factor.

Tumour grade	% distribution
Grade I	20 %
Grade II	40%
Grade III	40%

D, Tumour type

There is a relationship between tumour type and prognosis. Special types of breast cancer such as **pure tubular, mucinous, and invasive cribriform carcinoma have an excellent prognosis**

Infiltrating lobular and medullary carcinoma appear to have an intermediate prognosis

The grading of classic lobular cancer is also difficult because of the nature of the tumour cells and lack of histological pattern in this particular type of cancer.

E, Hormonal receptor status

Such endocrine sensitive tumours can be identified by measurement of oestrogen or **progesterone receptors(PR)** within the cancer itself.

The oestrogen receptor(ER) is a cytosol protein that can be identified using a variety of methods.

Previously, the most common method of detection involved the incubation of the supernatant fluid of a tissue homogenate with radiolabelled oestrogen. The unbound label is then removed by **dextran-coated charcoal or sucrose density centrifugation** and an assay performed.

More recent methods use monoclonal antibodies against the receptor; such methods require smaller specimens.

F, The Hormonal Axis

Estrogen → ER → Nucleus → Mrna → ER +PR+ Cell growth

The presence of oestrogen or progesterone receptors within the cell has been associated with **an improved short-term prognosis** in some studies. They are weak indicators of overall prognosis

G, Other factors

Other histological features with doubtful prognostic importance:

1. Vascular or lymphatic invasion in the breast,
2. Perineural invasion
3. Tumour necrosis
4. Mucin production.

F, Newer prognostic factors

(a) Growth factor indicators:

EGFR (growth factor receptor)

ErbB&sub2; oncogene

(b)Factors relating to tumour invasion:

Cathepsin D

Collagenase activity

(c) Factors relating to growth rate:

p53

S-phase fraction

(d) Factors relating to cell adhesion:

CD44 glycoprotein

3.13, THE MANAGEMENT OF METASTASES

The management of metastases demands a multimodality approach by surgeons, radiotherapists, and medical oncologists.

A, Assessment of patients with metastatic disease

A full series of staging investigations:

A, Chest Radiography, CT Scan

B, Abdominal Ultrasound/ CT Scan

C, Bone Scintigraphy

Brain scanning is not recommended: the likelihood of this investigation detecting asymptomatic recurrence is small.

Carcino-embryonic antigen at present does not have any significant role in assessment of metastatic breast cancer or the evaluation of response to treatment.

B, Prognostic indicators in metastatic disease

1,Disease free interval

The most important prognostic indicator in metastatic disease.The median survival of women who relapse in a single site within 1 year of diagnosis is about 11 months; those who experience a disease-free interval of more than 5 years have a survival of up to 40 months.

2,The site of metastatic disease

Prognosis is better in patients with local regional or bony metastases than in those with recurrence in the liver or central nervous system. The

3,Number of metastatic sites

The more the number of sites the worser the prognosis. Survival of patients with three sites of metastases is only 50 per cent of those with one affected site.

C, TREATMENT OF METASTASES

The majority of patients with metastases can be regarded as suffering from widespread systemic disease, the use of systemic therapy is nearly always appropriate. Breast cancer is responsive not only to radiotherapy and chemotherapy but also to various endocrine therapy.

1, Endocrine therapy

The effect is mediated by oestrogen receptors .**The overall response to endocrine therapy in breast cancer is about 30 per cent**. Ranges from 60 per cent in ER+Ve and 10 per cent in ER-Ve tumours. Response is proportional to level of oestrogen receptors. If the level of progesterone receptors is also elevated the response rate is likely to be increased.

Present Recommendations:

-- Tamoxifen is the ideal first-line endocrine therapy

-- Failure to respond is an indication to stop endocrine therapy.

-- Relapse following an initial response is treated with progesterone

-- Subsequent treatment failure is treated by **Aminoglutethimide**

-- Oophorectomy is a second-line treatment

2, Chemotherapy:

Response and time for it depend on the site of metastatic disease**: better responses are seen in soft tissue and bone than in the liver or central nervous system**.

Cutaneous or lymphatic metastases →3 to 6 weeks;

Bony metastases → 4 or 5 months

Vincristine : Although no survival advantage,**it is not myelosuppressive** and hence preferred.

Mitomycin C is most commonly used in combination with methotrexate and mitozantrone **.(MMM) as a second-line treatment.**

CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) **is most commonly used regimen** which has an overall response rate of up to 60 per cent.

CAF (Adriamycin, cyclophosphamide and 5-fluorouracil) is **a second-line treatment following failure of initial chemotherapy,** especiall in younger patientswith a poor prognosis, such as those with liver metastases. Its toxicity precludes its use in older patients.

3.14, SPECIFIC MANAGEMENT OF METASTATES

A,Local regional recurrence

Regional recurrence is always of clinical importance and **implies a worsening of prognos**is. However, it is particularly important if it occurs in a treated rather than an untreated field.

The management of regional recurrence depends on the site of relapse.

Internal mammary or supraclavicular areas

Radiotherapy with endocrine/ chemotherapy as appropriate.

Axillary relapse :

No previous surgery → full surgical clearance

Previous surgery → Radiotherapy / chemotherapy.

Metastases in the gastrointestinal tract

B, The liver

--Common site of metastatic spread of breast cancer

-- Surgical resection has no role

-- The prognosis of hepatic metastases is poor,

-- Poor response to hormone therapy.

-- In young patients with good performance status

combination chemotherapy, including adriamycin

C, Peritoneal metastases

-- Present as acites or intestinal obstruction.

-- Particularly common in patients with lobular carcinoma.

-- Systemic combination chemotherapy is required

--Surgical intervention should be avoided if possible

D, Respiratory system

-- Metastatic lymphangitis can cause distressing dyspnoea

-- No role for surgery or radiotherapy.

-- Systemic combination chemotherapy

-- Endocrine treatment in older poor-performance patients.

-- Steroids for symptomatic relief.

-- Pleurodesis is indicated for persistent pleural effusion

E, Bony metastases

-- **Most common form of secondary spread** of breast cancer

-- **Pain and pathological fracture** are the most common

-- Radiotherapy for symptomatic relief

-- Chemotherapy – as risk of developing multiple

metastases

--Endocrine therapy with tamoxifen is first-line treatment,

-- **Pathological fractures–surgical fixation**

-- **Hypercalcaemia** –Rehydration with forced diuresis with steroids .Resistant cases – mithramycin or diphosphonates

F, Central nervous system metastases

-- Brain, Spinal cord, Meninges, Epidural space causing cord compression. Primary Radiation therapy with Surgery only for cord compression

G, Bone marrow metastases

-- Often associated with bony deposits

-- Potential leucopenia and thrombocytopenia

-- Endocrine / chemotherapy based on performance status, age, and ease of administration.

4.MATERIALS AND METHODS

This study was conducted on patients with locally advanced breast cancer who were admitted and treated at both **Government Royapettah Hospital ,Chennai – 14,** And **Government Kilpauk Medical College and Hospital, Chennai -10.**

Pathological diagnosis was by FNAC for all cases, TRUCUT and OPEN BIOPSY as appropriate for each case.

CASE SELECTION CRITERIA:

All cases with breast cancer with T stage of T3 and above and /or nodal stage of N2 and above were chosen**.**

Metastatic breast cancer was ruled out from each system by appropriate investigations such as :

A, Abdomen and Pelvis : Ultrasound , CT scan for doubtful lesions

B, Respiratory : X ray chest, CT scan for doubtful lesions

C, Skeletal : X ray of part, Bone scan if normal X ray

D, Brain And Spinal Cord : CT/ MRI as per affordability.

No case of Inflammatory breast cancer was encountered in this study.

In cases that had particular symptoms the same investigations as those done to rule out metastases were performed. Cases were reviewed monthly for the first year and two monthly for the second year.

Clinical examination at every visit, Liver function tests every 3 months, and an ultrasound abdomen every 3 months were routinely performed in cases where there were no specific complaints.

An Echo cardiogram was done in patients to evaluate cardiac status before and during the course of chemotherapy with cardiotoxic agents such as adriamycin and taxanes.

5. PROFORMA

NAME

AGE DATE OF ADMISSION

SEX DATE OF SURGERY

IP NO: DATE OF DISCHAGE

PRESENTING COMPLAINTS**:**

Lump

Nipple Discharge

Pain

Loss Of Weight /Appetite

H/O Previous Breast Disease

H/O Previous Procedures

MENSTRUAL H/O :

Pre/Post Menopausal

Age At Menarche /Menopause

Age At First Child Birth /Breast Feeding

FAMILY H/O : Breast / Ovarian / Colonic Cancer

H/O Oral Contraceptive Intake

EXAMINATION:

GENERAL EXAMINATION:

Build And Nutrition

Jaundice

Pallor

Vital Signs

SYSTEMIC EXAMINATION:

Cardiovascular System

Respiratory System

Central Nervous System

Abdomen

LOCAL EXAMINATION:

LUMP: Site , Size , Shape , Skin Over The Lump

Warmth, Tenderness, Consistency , Borders

Chest Wall Fixity

NIPPLE: Ulceration , Discharge, Retraction

NODES: Axilla , Supraclavicular of both sides

OTHER BREAST

CLINICAL STAGE: T__ N__ M__

INVESTIGATIONS:

Hemogram

Renal Parameters,Blood Sugar

Mammogram , Ultrasound Of Breast

Biopsy- Fnac, Trucut, Incision Biopsy

Er/Pr Status

X Ray Chest,Ultrasound Abdomen And Pelvis

Liver Function Test

PRIMARY TREATMENT MODALITY

CHEMOTHERAPY :Drugs Used, No Of Cycles , Duration

RADIOTHERAPY : Total Dose, Fractions/ No Of Sittings

HORMONE THERAPY:

OTHER: Surgery

RESPONSE TO PRIMARY TREATMENT

Partial/ Complete / No Response

Nature Of Response : Size , Edema , Nodes

SECONDARY TREATMENT MODALITY

SURGERY : MRM

CHEMOTHERAPY :Drugs Used, No Of Cycles ,Duration

RADIOTHERAPY : Total Dose, Fractions/ No Of Sittings

HORMONE THERAPY

RESPONSE TO SECONDARY TREATMENT

Response / Failure

RELAPSE :

Nature,

Time Interval Since Treatment

Asymptomatic Interval

Disease Free Interval

PERIOD OF FOLLOW UP: _____ months

6. OBSERVATIONS AND DISCUSSION

In this study 50 patients were diagnosed to have locally advanced breast cancer and followed during the period 2004 – 2006.

Age:

The youngest patient in this study was 26 yrs old and the oldest patient 82 years of age with the maximum number of cases(58%) occurring in 40- 60 years interval.

Sex:

There was 1 male in this study for whom a radical mastectomy was the surgical treatment given.

Menopausal status:

Majority of cases(55 %) were post menopausal . Peri-menopausal (two) patients were considered as pre menopausal and treated similarly .

Mode of presentation:

Post mastectomy status was the most common presentation to our hospital with a painless lump being the next most common presentation.

Stage of presentation:

Majority of the cases belonged to the TNM stage IIIA (38%) . The remainder presented as stage IIB (24%) and IIIB (28%). Very few cases presented as stage III C (10%).

ER/PR status:

Estrogen / progesterone receptor status was done only for 7 cases and hence no particular inference could be obtained from it in this study.

Treatment modalities:

I, Surgery followed by adjuvant chemotherapy : 33/ 50 (66%)

A, Surgery: Modified radical mastectomy/ simple mastectomy/ lumpectomy

B, Adjuvant therapy:

Chemotherapy – FAC/ CMF

Radiotherapy – 45Gy/ 50 Gy

Hormone therapy – Tamoxifen

II, Neo adjuvant therapy followed by surgery:13/ 50 (26%)

Chemotherapy – CMF / FAC

Radiotherapy – 70 Gy (1 case)

Surgery – modified radical and radical mastectomy

III, Chemo-endocrine manipulation only : 4 out of which 3 cases showed poor response and one patient was not fit for surgery

Margins:

Surgical margins were positive in 7 cases and out of which 4 cases had a loco-regional recurrence and a recurrence rate of 57 %.

Pathology:

Infiltrating ductal carcinoma (NOS) was the most common pathological diagnosis with one case being a medullary carcinoma .

Recurrence:

A total of 17 patients had recurrences in which 12 cases (70%) had loco- regional recurrences and 4 patients(23%) had pure systemic (distant) recurrences. One patient (7%) had both loco-regional and systemic recurrence occurring at the same time.

Of the 12 loco- regional recurrences 7 cases (58%) occurred in the chest wall, 1 case (8%) had pure axillary recurrence, 2 cases (16%) had both. 2 cases(16%) had supraclavicular nodal recurrence .

Systemic recurrence were 5 of the total 17 cases , 2 occurred in the liver(40%) and 3 cases had bone secondaries (60%).

Of the 17 recurrences , 15 cases belonged to the arm which had surgery with adjuvant therapy as the treatment modality whereas only 2 cases belonged to the neo-adjuvant therapy followed by surgery arm.

10 out of those 15 cases (66%) had recurrence in the first 6 months following initiation of adjuvant treatment. The remaining 5 cases (34%) relapsed within the subsequent 6 months .

The arm which had only chemo-endocrine manipulation did not have an attempt to cure although one case had a distant metastasis identified during follow up and considered as a recurrence.

Recurrence interval :

The shortest recurrence interval was 3 months and the longest was 10 months leading to a Mean Recurrence interval of 6.05 months. The mean recurrence interval in the arm with surgery followed by adjuvant therapy was 5.5 months and in the arm with neo-adjuvant therapy as the initial treatment was 7 months.

Treatment of recurrences:

Chest wall and or axillary disease was treated with radiotherapy +/- chemotherapy . Revision surgery was done in case of pure axillary relapse with chemotherapy .

Supraclavicular recurrences with radiotherapy +/- chemotherapy.

Bone secondaries were treated with radiotherapy .

Liver secondaries with chemotherapy (CEF/CMF).

Follow up:

The period of follow up ranged from a minimum of 3 months to a maximum of 20 months with a mean follow up period of 8.3 months. The mean period of follow up in patients without recurrences:

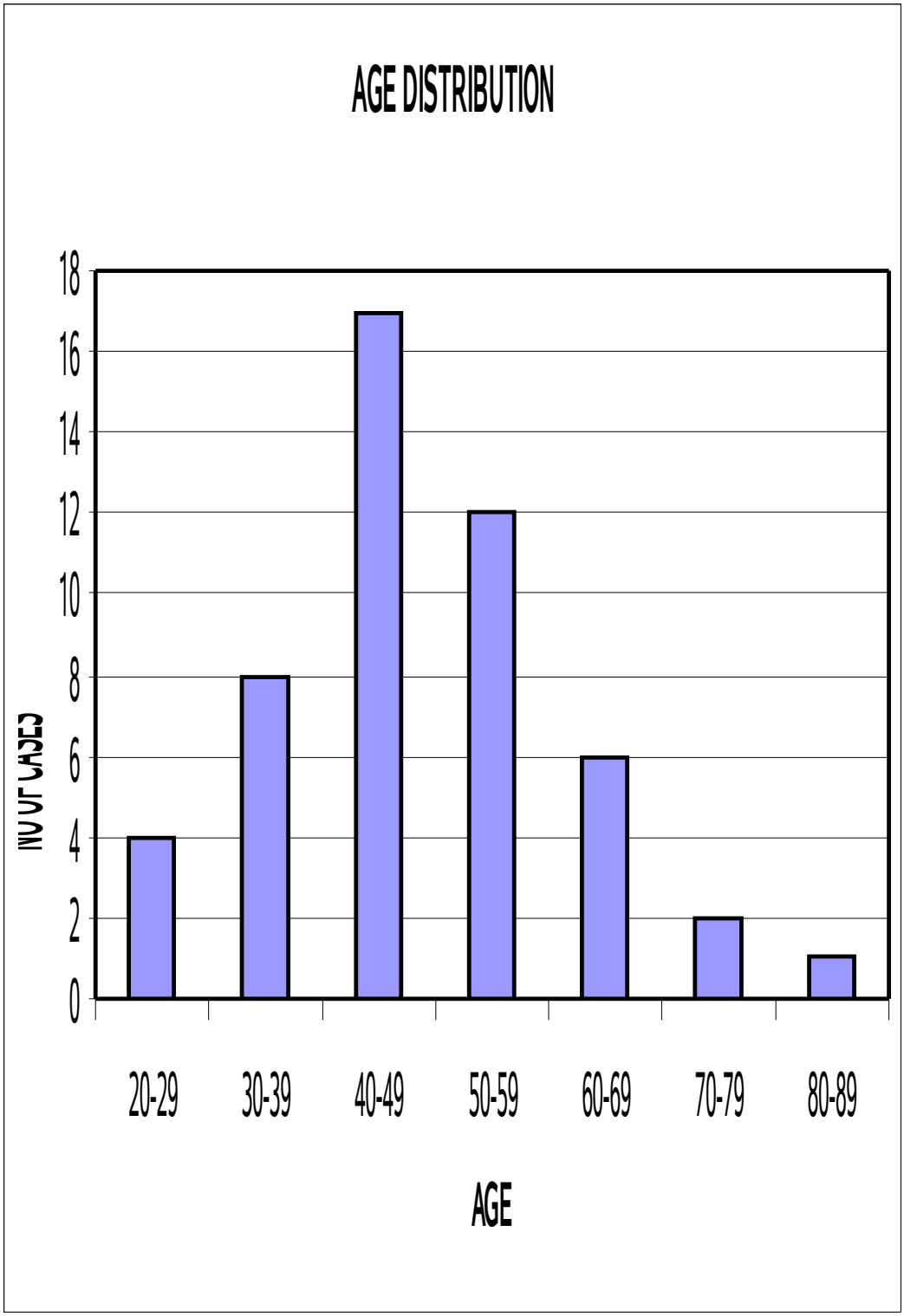
A, Surgery followed by adjuvant chemotherapy : 7 months

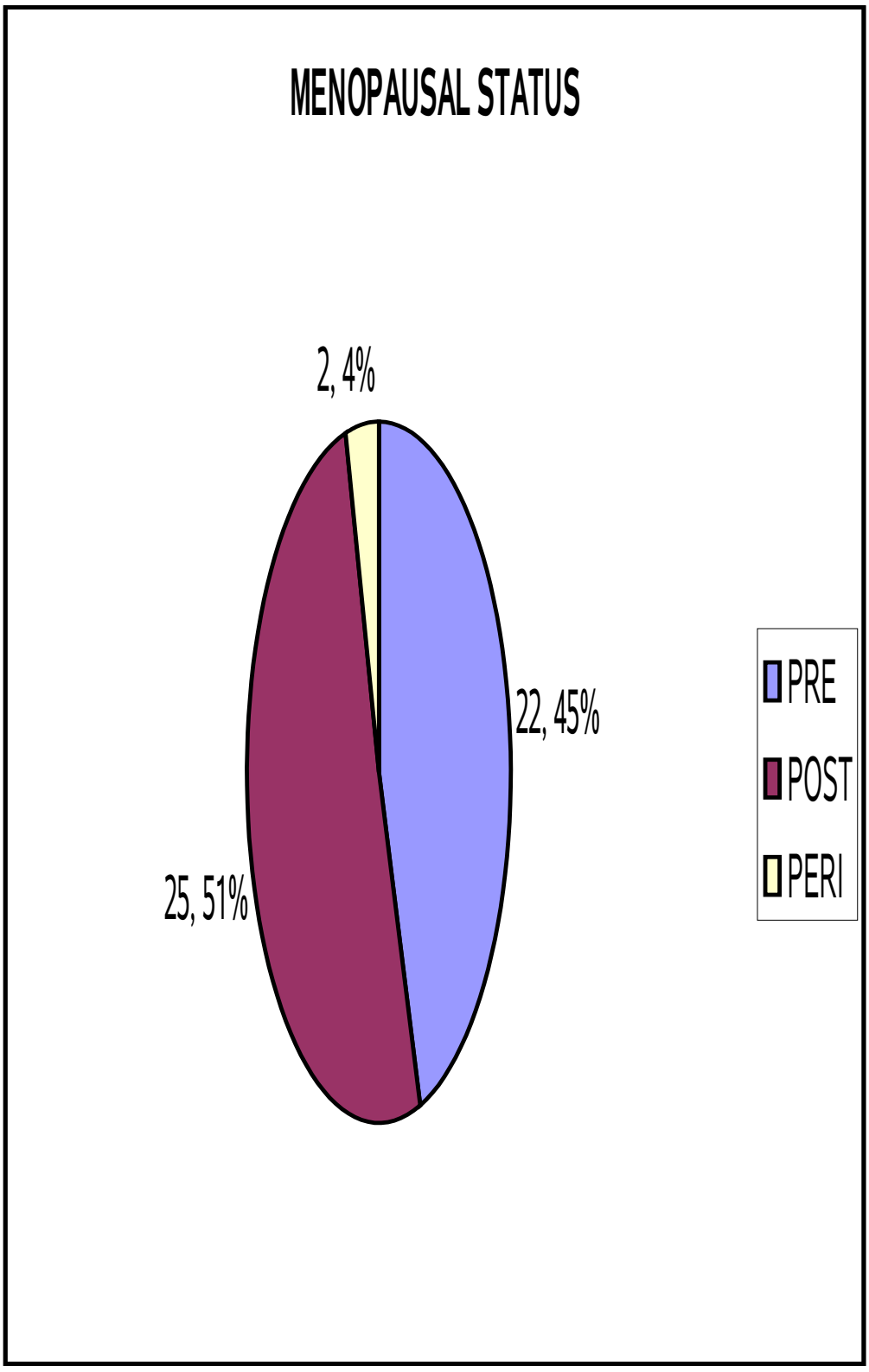
B, Neo-adjuvant therapy followed by surgery : 11 months.

Disease free survival:

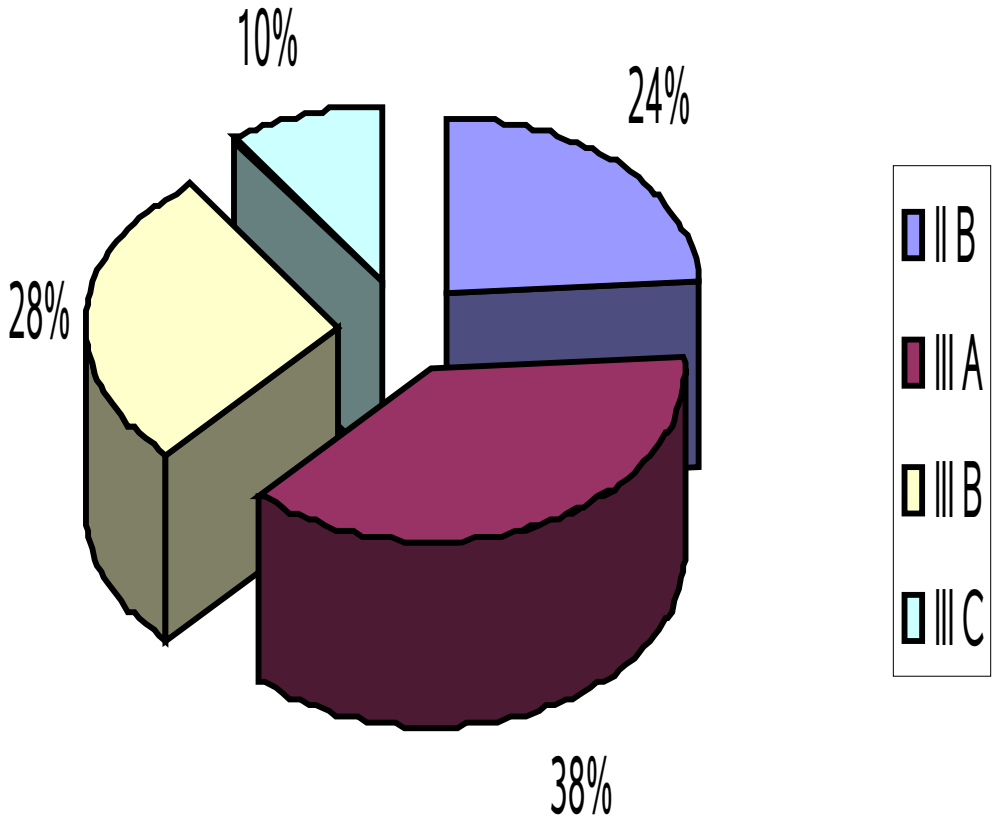
The number of months between the discharge from secondary treatment to that of occurrence of symptoms was taken as disease free interval. The average disease free survival was 7.2 months with a minimum period of 3 months and a maximum of 20 months.

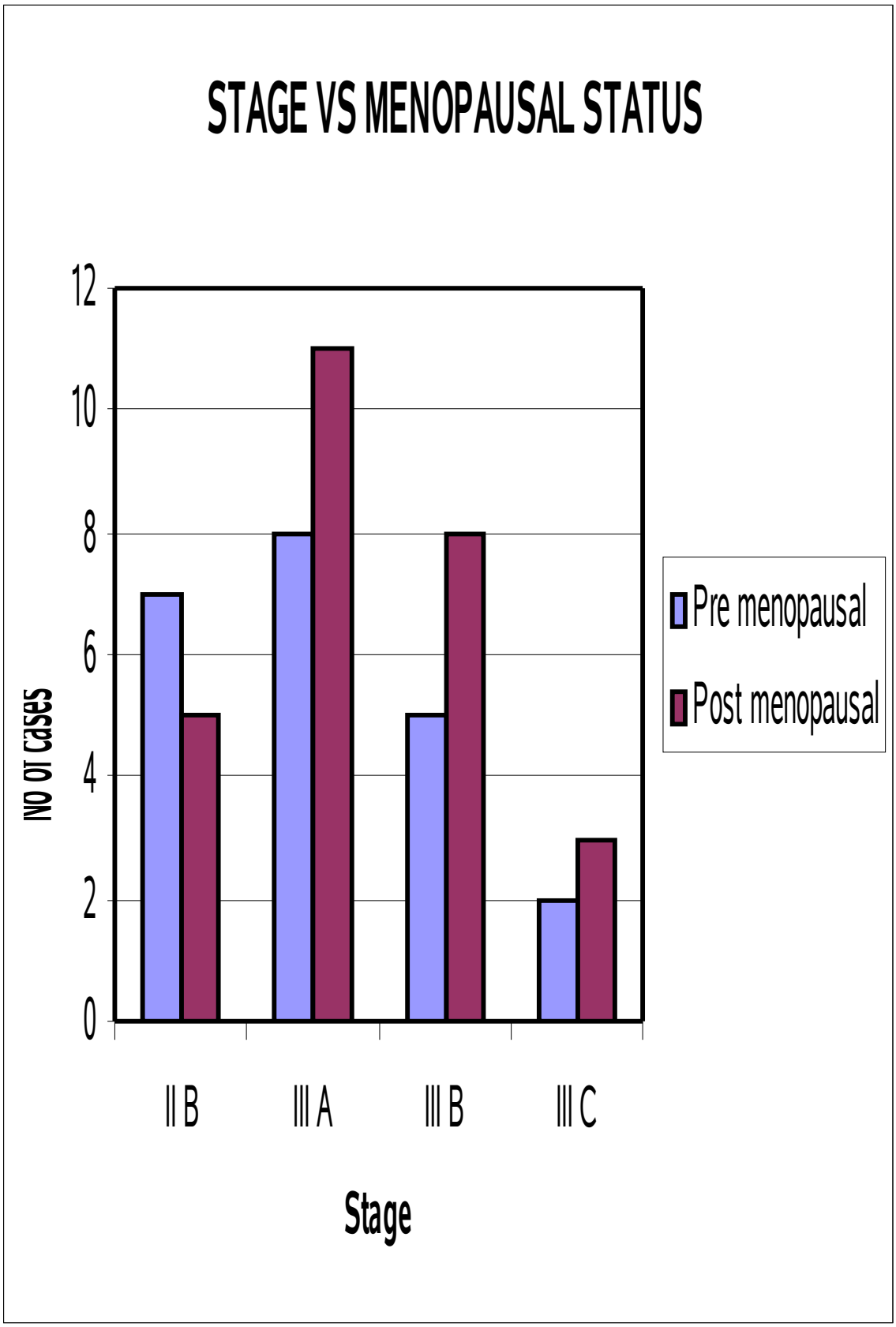
ANALYTICAL DATA

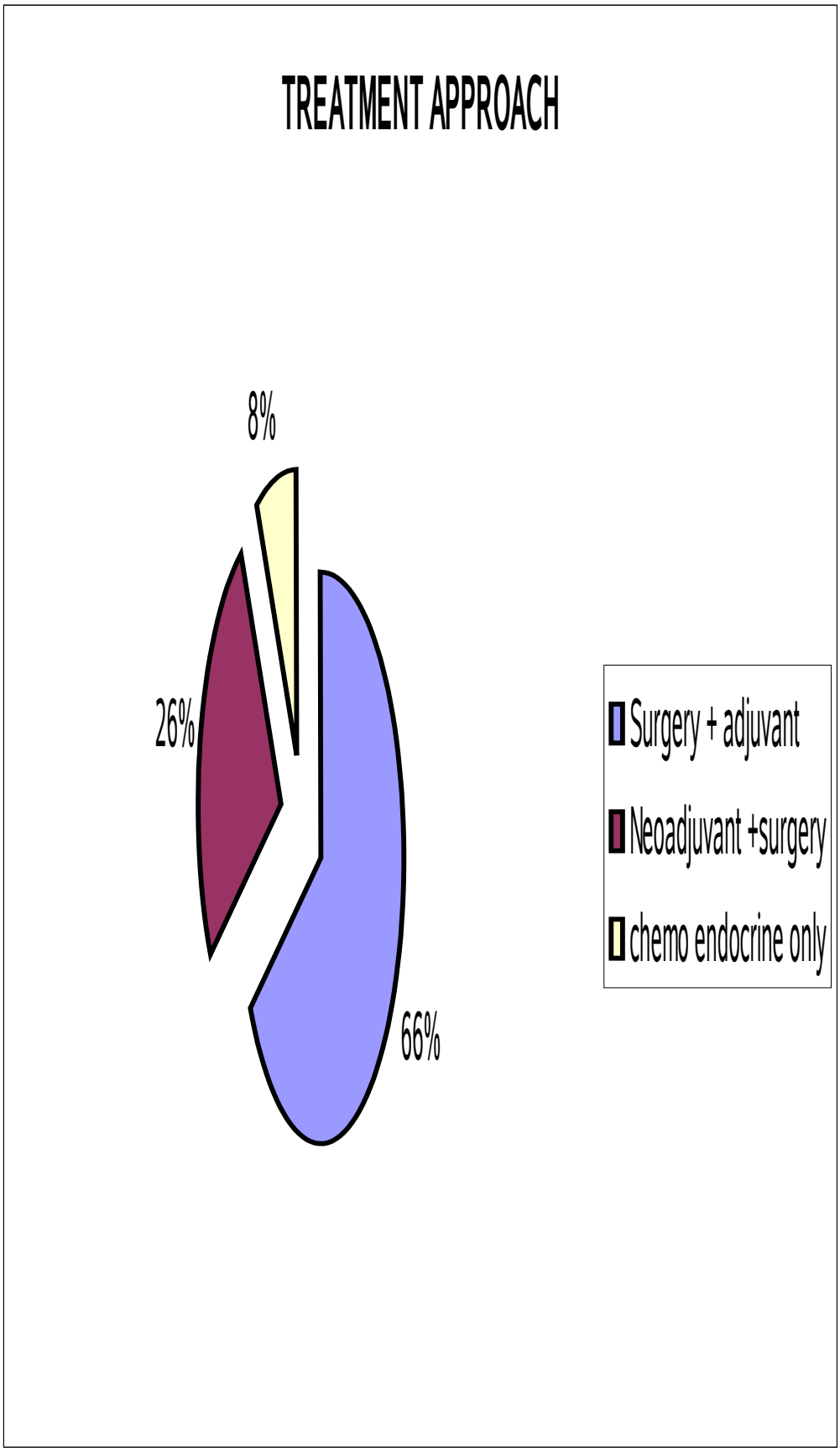


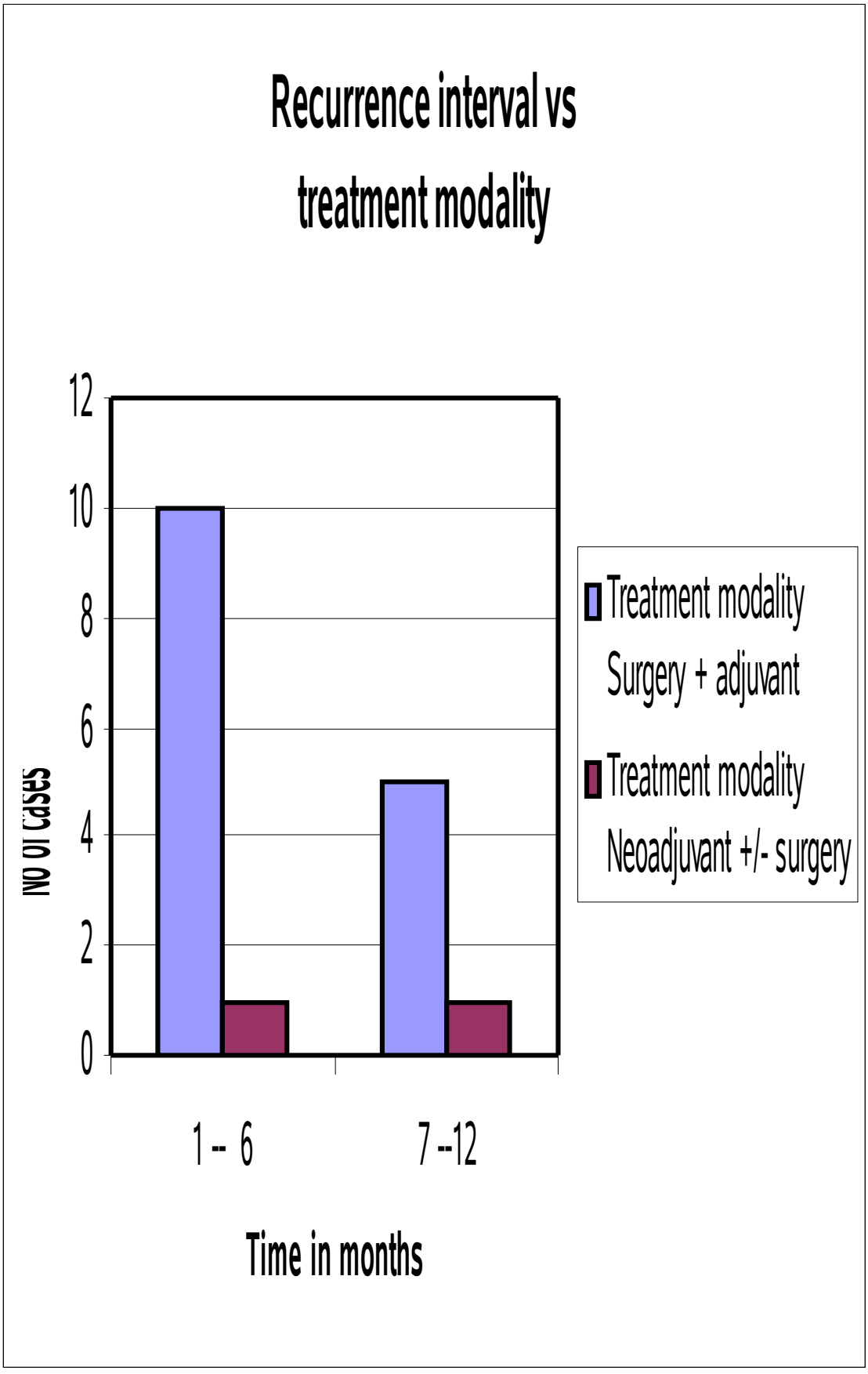

MENOPAUSAL STATUS
2, 4%
22, 45%
25, 51%
PRE
POST
PERI

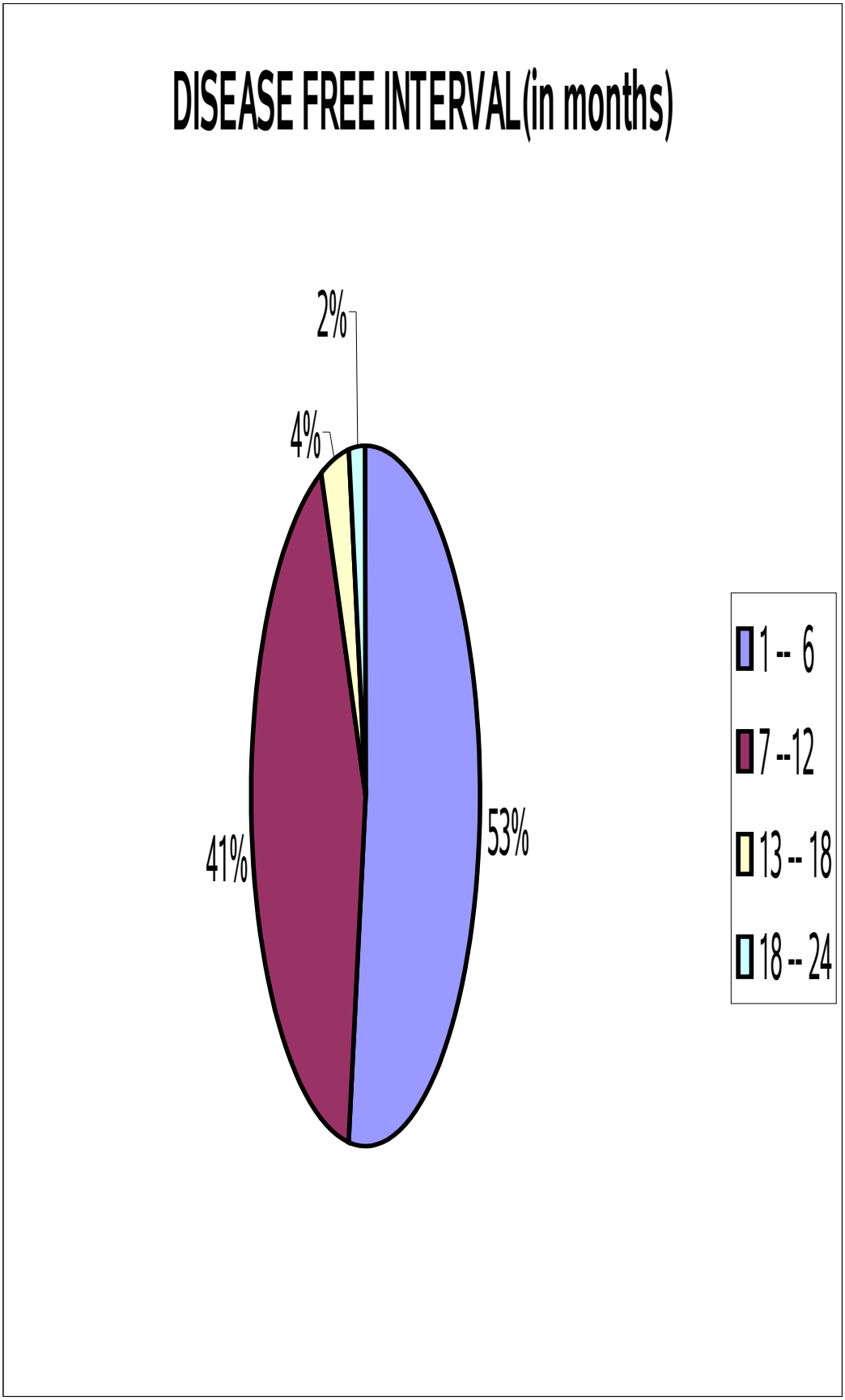
STAGE WISE DISTRIBUTION




STAGE VS MENOPAUSAL STATUS
12
10
8
6
4
2
0
NO OF CASES
II B
III A
III B
III C
Stage
Pre menopausal
Post menopausal


TREATMENT APPROACH
8%
26%
66%
Surgery + adjuvant
Neoadjuvant +surgery
chemo endocrine only


Recurrence interval vs
treatment modality
12
10
8
6
4
2
0
NO OF CASES
1 -- 6
7 --12
Time in months
Treatment modality
Surgery + adjuvant
Treatment modality
Neoadjuvant +/- surgery


DISEASE FREE INTERVAL(in months)
2%
4%
41%
53%
1 -- 6
7 --12
13 -- 18
18 -- 24

7.CONCLUSIONS

Age:

The most common age for presentation of LABC was from 40 to 60 years of age.

Sex:

It is most common in female sex. Male breast cancer most commonly presents as LABC.

Menopausal status:

Post menopausal cases comprised the largest group of patients presenting with LABC.

Mode of presentation:

Post mastectomy status was the most common presentation with a painless lump being the next most common presentation.

Stage of presentation:

Majority of the LABC cases belonged to the TNM stage IIIA .

Treatment modalities:

Surgery with or without adjuvant chemotherapy was the most common treatment(66 %) given to patients outside our hospital as per this study

Neo adjuvant therapy (26 %) followed by surgery was the treatment offered to patients treated primarily in this institute.

Margins:

Positive Surgical margins led to high rate of loco-regional recurrences .

Pathology:

Almost all cases were Infiltrating ductal carcinoma (NOS) type

Recurrence:

Recurrence rate was found to be 88% in the arm with surgery with adjuvant therapy of which 66% (10/ 15) recurred in the first six months and remaining 34% in the subsequent 6 months.

A recurrence rate of 12 % (2/17) in the arm with neo-adjuvant therapy followed by surgery of which 50% recurred in first six months and 50% in next six months.

Recurrence interval :

The time interval for recurrence to occur was on an average 6 months.

8.SUMMARY

Locally advanced breast cancer commonly:

- Presents in the fifth to sixth decade of life.
- Presents as a painless lump in un-intervened cases.
- Presents in the post menopausal group and with a higher stage.
- Has a good disease control if treated first by neo-adjuvant therapy followed by surgery.
- Has early loco-regional and distant recurrences if managed by non standard protocols.

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ABBREVIATIONS USED IN THE MASTER CHART

R	-- Right
L	-- Left
C/F	-- Clinical features
Rec. int	-- Recurrence interval
Dis free	-- Disease free interval
Post mastec	-- Post mastectomy status
Rec lump	-- Recurrent lump
Simple mast.	-- Simple mastectomy
Axi. Dis	-- Axillary dissection
SCLN	-- Supraclavicular nodes
Multi bone mets	-- Multiple bone metastases
ND	-- Not done
NA	-- Not applicable
Neg	-- Negative
Posi	-- Positive
Re MRM	-- Revision modified radical mastectomy
Spinal	-- Spinal metastases
Pelvic	-- Pelvic metastases
Gy	-- Gray
Cy	-- Cycles