A STUDY OF EPIDEMIOLOGICAL & PROGNOSTIC PROFILE OF CARCINOMA BREAST

Submitted to

TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In Partial fulfillment of the

Requirement for the award of Degree

MASTER OF GENERAL SURGERY

BRANCH I

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DEPARTMENT OF GENERAL SURGERY

KILPAUK MEDICAL COLLEGE & HOSPITAL

CHENNAI – 600 010.

CONTENTS

CERTIFICATE

This is to certify that this study on **Epidemiological & Prognostic profile of Carcinoma Breast** is a Bonafide dissertation done by **Dr. R. JEYAKUMAR,** and submitted in partial fulfillment of the requirement for the award of degree of M.S., General Surgery Branch –1 of the **Tamil Nadu M.G.R. Medical University, Chennai.**

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It would have been impossible for me to get this done without the whole hearted co-operation of the patients and relatives of this study.

I thank my family members and the almighty for seeing this through.

INTRODUCTION

Carcinoma Breast is one of the commonest malignancies in women all over the world.

It causes about 20% cancer deaths among females. It is commonest malignancy of the female in India.[i]

The age standardized incidence rate of breast cancer in Indian population based registration varies from 17-21.6 per 1, 00,000 population. It is estimated that about 75,000 new cases of breast cancer occurs in India every year[ii]

Carcinoma breast is a systemic disease even on initial presentation. The heterogeneous nature of the disease necessitates individualized treatment. In spite of major advances in oncology and multimodality approach towards treatment of Carcinoma Breast there is not much decrease in mortality. This study is undertaken to find out the various prognostic and risk factors for Carcinoma Breast in Patients who attended Kilpauk Medical College Hospital Department of Surgery & Surgical Oncology.

Fig. 3.4(b): Ten Leading Sites of Cancer - Females (Contd...)

Age Adjusted Rates given in parentheses

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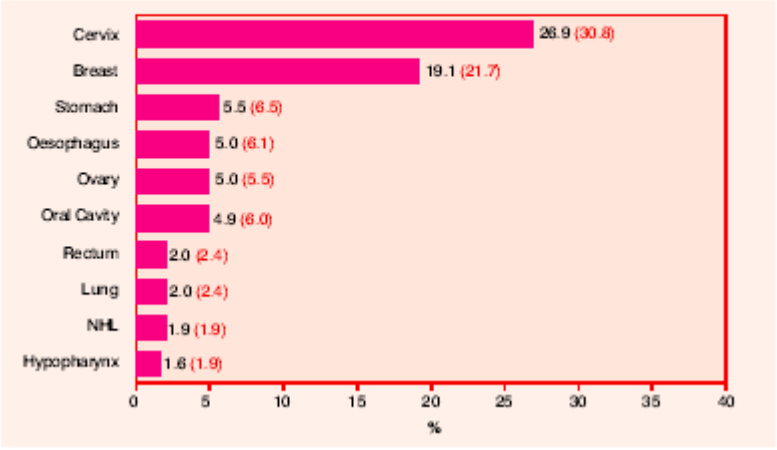
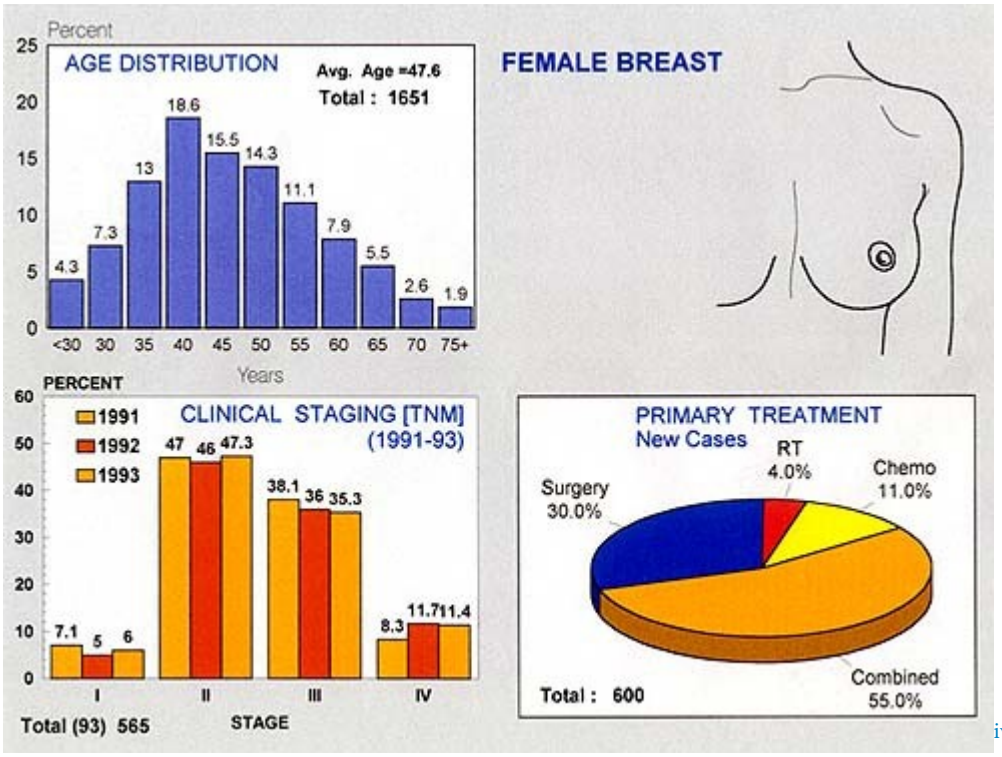



Percent
AGE DISTRIBUTION
Avg. Age =47.6
Total : 1651
4.3
7.3
13
18.6
15.5
14.3
11.1
7.9
5.5
2.6
1.9
<30 30 35 40 45 50 55 60 65 70 75+
Years
FEMALE BREAST
PERCENT
1991
1992
1993
CLINICAL STAGING [TNM]
(1991-93)
7.1 5 6
47 46 47.3
38.1 36 35.3
8.3 11.7 11.4
I II III IV
Total (93) 565
STAGE
PRIMARY TREATMENT
New Cases
RT
4.0%
Chemo
11.0%
Surgery
30.0%
Combined
55.0%
Total : 600

iv

AIMS AND OBJECTIVES

1. To study the incidence, geographic pattern and other epidemiological factors of Carcinoma Breast.

2. To study the role of possible environmental factors in the genesis of Carcinoma Breast in our region.

3. To study the various prognostic factors of Carcinoma Breast.

4. To study the histopathological types of Carcinoma Breast.

REVIEW OF LITERATURE

Embryology[v]

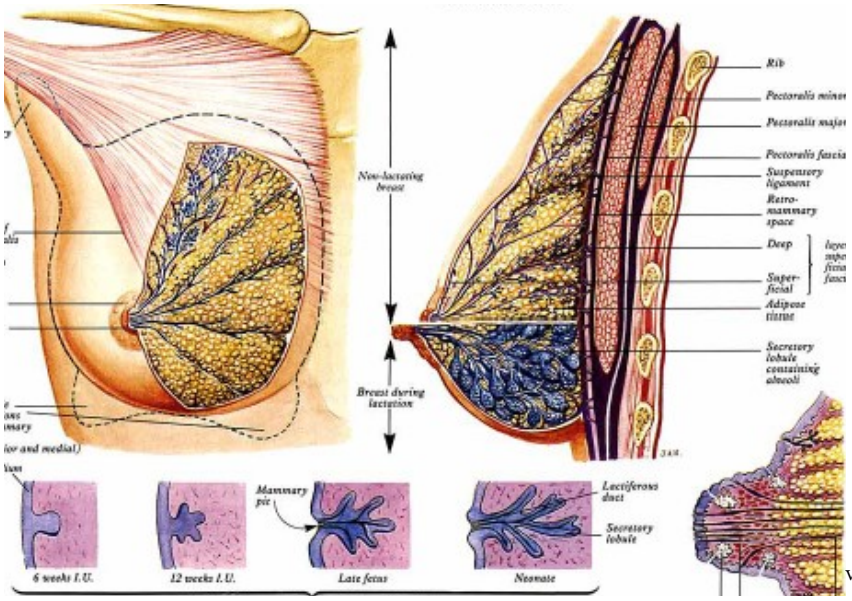
Breast is a modified sweat glands embryologicaly derived from down growth of ectoderm into underlying mesenchyme

Anatomy[vi]

It is extended from the 2nd rib to 6th rib. Blood supply lateral thoracic artery, perforating cutaneous branches of internal mammary artery from 2nd, 3rd, 4th spaces, lateral branches of 2nd, and 3rd, 4th intercostal arteries

Nerve supply

Secreting tissue supplied by sympathetic nerves which reach via 2nd, to 6th intercostal nerve. Overlying skin is supplied by anterior and lateral branches of 4th, 5th, 6th intercostal nerve.



Physiology

Appreciation of stages of breast development is necessary to understand the benign and malignant condition of breast tissue.

During adolescence, breast is composed of lobular stoma scattered ducts lined by epithelium. During puberty increased deposition of fat and formation of new ducts by branching, elongation and first appearance of lobular units. The progress of growth entails cell division and is under the control of estrogen, progesterone, adrenal hormone, pituitary hormone, thyrotrophic hormone, and insulin.

During phases of menstrual cycle or in response to exogenous hormones, the breast epithelium and lobular stroma under go cyclic stimulation. It appears that the dominant process is hypertrophy and alteration in morphology rather than hyperplasia.

In late luteal phase there is accumulation of fluid and interlobular edema that appears to correspond to breast engorgement.

It is only with the onset of pregnancy that the breast assumes its complete morphologic maturation and functional activity. By the end of pregnancy the breast is composed entirely of glands separated relatively scanty amount of stroma. The secretary glands are lined by cuboidal cells, in third trimester secretary vacuoles of lipid material are found with in the cell.

Following lactation the glands once again regress and atrophy, ducts shrink .at menopause ducts and glands further atrophied with more shrinkage of inter and intralobular stroma. The gland almost totally disappears leaving only the ducts.[viii]

Risk factors[ix]

They are genetic, endocrine and environmental.

Age

Cumulative risk between 20-40 years is 0.5%

From 20 to 30 years there is a steep rise in age specific cancer

Family history

If the first degree relative has Carcinoma Breast, relative risk is 1.7% -2.5%. If the second degree relative had Carcinoma Breast, risk is 1.5 %.Direct genetic factor risk is about 5%.

Parity

In single para and nullipara relative risk is 1.4% compared to multipara

Genetic[x]

High incidence of Carcinoma Breast is seen in women with inherited mutation of two breast cancer gene BRCA1, BRCA2. Risk is 7%

It is estimated that approximately 5%of all women with Carcinoma Breast may have the recently identified germ line mutation in a gene BRCA1, located in chromosome 17q21. Their relatives if carriers of BRCA 1 mutation may have 85%life

time for breast cancer with 50% of Carcinoma Breast occurring before 50 years of age.

Menarche

Before 12 years relative risk is 2.3 %. Duration of the menstrual life is important factor for breast cancer. Artificial menopause by oopherectomy or irradiation reduces the risk.

Body weight[xi]

Women under the age of 50 years there is little correlation between the body weight and cancer.

Diet

Alcohol increase the risk 1.5%. High fat in diet increases the risk.

Oral contraceptives

Risk is 0.4% and up to 5 years risk is 1.2%.

Ionizing radiation

Thymus radiation, nuclear war, professional exposure increased the risk apparent

after a latent period of 10 to 15 years, if the women were exposed before the age of 35.

Benign breast lesion[xii]

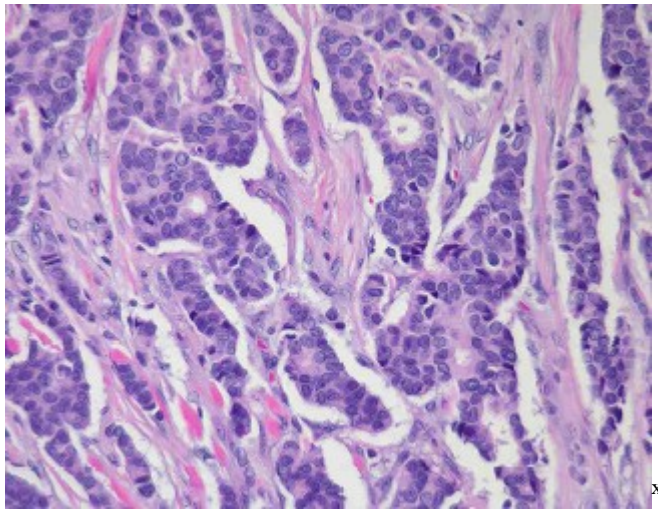
Fibrocystic disease with atypia is more prone for Carcinoma Breast.

Pathology[xiii]

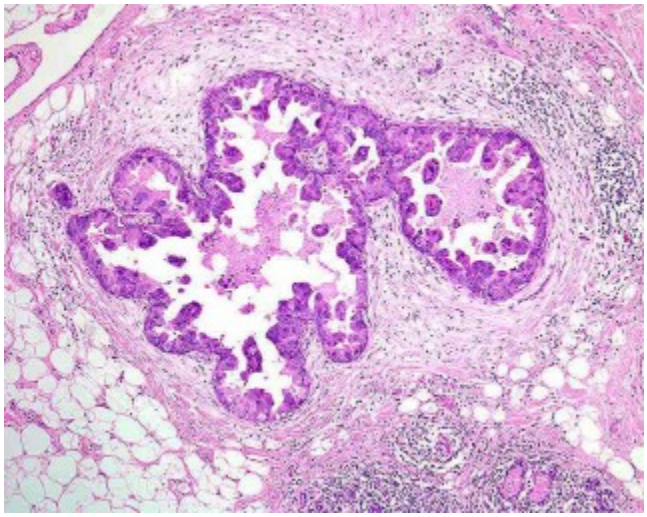
With increasing use of screening mammography, Non invasive cancers are more frequently diagnosed and now constitute 15-20% of all breast cancers. There are many methods of pathologically classifying Carcinoma Breast. Most are based on whether the tumor is invasive or noninvasive and whether it is derived from the duct system or the lobule. Most tumors arise from the ductules.

Invasive ductal carcinoma

This is the most common type of breast carcinoma. It is a stony hard tumor. Gritty on transection show tumor retraction below cut margins. Microscopically primitive glandular pattern is seen. Metastasis to axillary lymph nodes is common. Prognosis is poor.

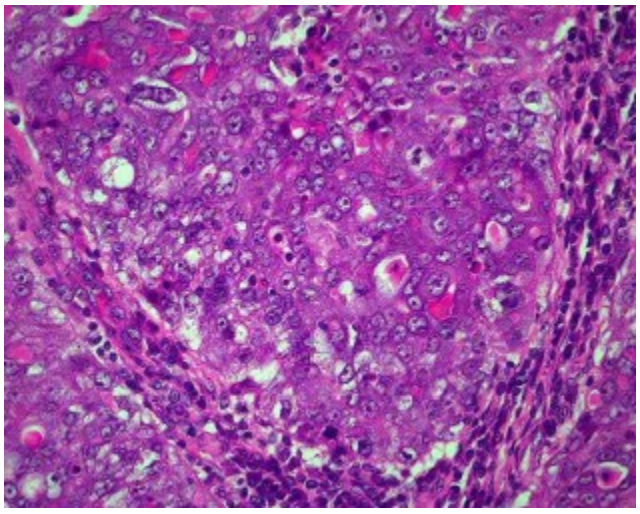


PAPILLARY CARCINOMA



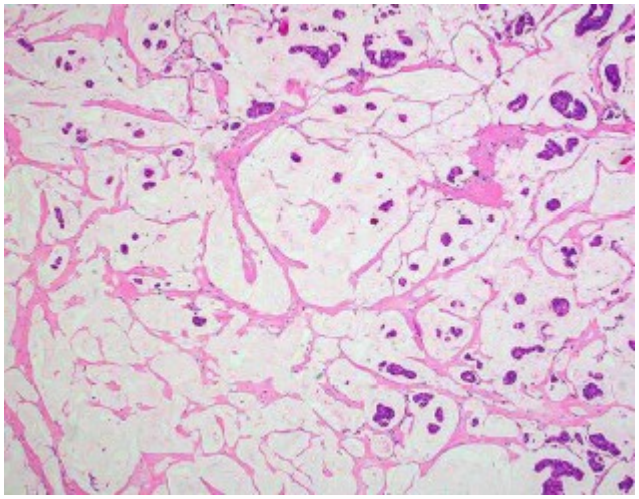
This is slow growing bulky circumscribed tumor occurring characteristically in post menopausal woman. Microscopically a vascular anaplastic growth extends along the thickened ductal wall into the surrounding tissue. The prognosis is better than invasive ductal carcinoma.

MEDULLARY CARCINOMA



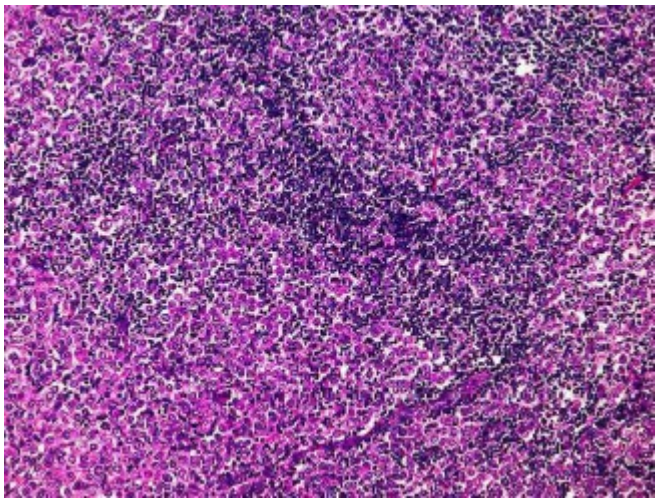
Solid syncytium like sheets of large cells with vesicular often pleomorphic nuclei. There is moderate to marked lymphocytic infiltration. 10 year survival rate is 90%.

COLLOIDAL MUCINOUS



Prognosis is good. Lymph nodal metastasis is infrequent.

LOBULAR CARCINOMA



Most common cause of bilateral carcinoma is lobular carcinoma. Prognosis is poor. Multicentric in origin.

Spread of cancer breast[xv]

Direct spread into the parenchyma occurs in a characteristic satellite pattern. Spread along the lymphatics to the regional nodes. Spread along the ducts –field cancerization. blood spread to lungs, bone, liver, adrenals and ovary.

Clinical feature

Breast lump, nipple discharge, pain, loss of weight, axillary node, breast ulcer, nipple retraction and others are common clinical features. While any portion of the breast, including the axillary tail, may be involved, breast cancer commences most frequently in the upper, outer quadrant. Most breast cancers will present as a hard lump,

which may be associated with in drawing of the nipple. As the disease advances locally there may be skin involvement with peau d'orange or frank ulceration and fixation to the chest wall. This is described as cancer-encuirasse. About *5* percent of Carcinoma Breast in the UK will present with either locally advanced disease or symptoms of metastatic disease. This figure is nearer 20 per cent in the developing world. These patients must then undergo a staging evaluation so that the full extent of their disease can be ascertained. This will include a careful clinical examination, chest X-ray, serum alkaline phosphatase and gamma glutamine transaminase (GGT), with liver ultrasound if these are abnormal, and an isotope bone scan .This is important for both prognosis and treatment — a patient with widespread visceral metastases may obtain an increased length and quality of survival from systemic hormone or chemotherapy, but she is not likely to benefit from surgery as she will die from her metastases before local disease becomes a problem. In contrast, patients with relatively small (less than *5* cm in diameter) tumours confined to the breast and ipsilateral lymph nodes rarely need staging beyond a good clinical examination as the pick-up rate for distant metastases is so low

Investigations[xvi]

Non invasive

1. MAMMOGRAM
2. ULTRA SONOGRAM
3. CT
4. MRI

Invasive

1. FINE NEEDLE ASPIRATION CYTOLOGY
2. TRUCUT BIOPSY
3. INCISION BIOPSY
4. EXCISION BIOPSY

Others

1. SERUM ESTROGEN ESTIMATION
2. SERUM CHOLESTEROL ESTIMATION
3. SEROLOGICAL MARKERS
    a. estrogen receptor immunocyte chemical assay
    b. C erb B2 (HER 2 /neu)
    c. Ps 2

Breast screening[xvii]

National breast cancer screening in UK is well established. The results of chamber lien etal 1993 are the overall acceptance rate was 71%. The breast cancer detection rate was 6.2 per thousand women. 95% of the programme achieved a recall rate of less than 10 % .these results are extremely satisfactory. The largest reduction of mortality rate was observed in 50-60 years. Among women age 40-49 there was no reduction in mortality. Un doubtfully screening tests detects tumor in earlier biological stage but

false positivity causes anxiety and necessitate further diagnostic procedures.

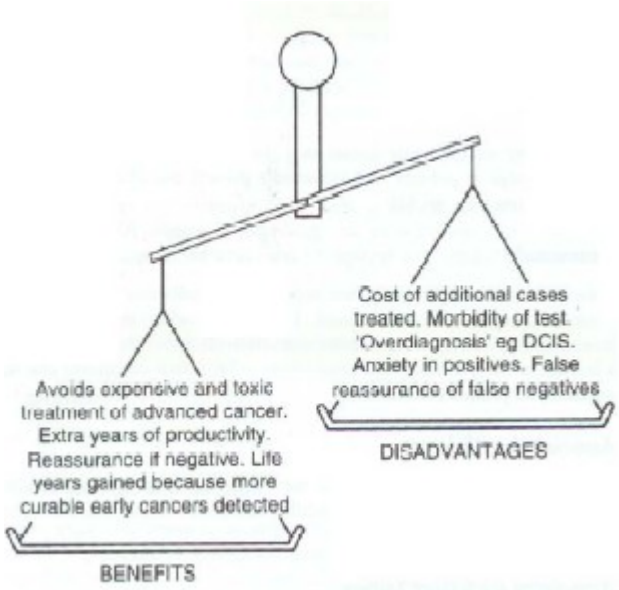


Fig. 46.40 Benefits and disadvantages of breast cancer screening.

Prognosis of breast cancer[xviii]

Patient related

Tumor related

Treatment related

Patient related

More frequent of local recurrence in younger patients.

TUMOR RELATED

Histological grade

1. Cytoarchitectural type.

There is no significant prognostic difference between ordinary invasive ductal and invasive lobular carcinoma. Morphologic variants of invasive ductal carcinoma with a more favorable prognosis are tubular carcinoma, cribriform carcinoma, medullary carcinoma (when strictly defined), pure mucinous carcinoma, papillary carcinoma, adenoid cystic carcinoma, and juvenile (secretory) carcinoma. A variant of lobular (and sometimes ductal) carcinoma associated with an extremely bad prognosis is signet ring carcinoma. The prognosis of inflammatory carcinoma is also particularly ominous.

2. Microscopic grade.

The two most widely used systems over the years for the microscopic grading of breast carcinoma have been those of Bloom and Richardson and Black, the first based mainly on architectural features (extent of tubule formation) and the second on the degree of nuclear atypia. Since both architecture and cytology have been found to correlate with prognosis, the sensible proposal has been made to use them in conjunction.

Elston has been the most vocal champion of this approach, which is usually referred to as the Nottingham modification of the Bloom-Richardson system and which also incorporates the evaluation of mitotic activity. In this scheme, the

grade is obtained by adding up the scores for tubule formation, nuclear pleomorphism, and mitotic count, each of which is given 1, 2, or 3 points. This results in a total score of 3 to 9 points, which is translated into the final grade by the following formula:

3 to 5 points - Grade I;

6 to 7 points -Grade II;

8 to 9 points -Grade III.

3. Type of margins.

Tumors with "pushing" margins have a better prognosis than tumors with infiltrating margins. This applies not only to medullary carcinoma, but also to other types of well-circumscribed neoplasm.

4. Tumor necrosis.

Tumor necrosis is associated with an increased incidence of lymph node metastases and decreased survival rates, but this feature is usually associated with tumors of high histologic grade.

5. Stromal reaction.

Surprisingly, it has been found that tumors with an absence of inflammatory reaction at the periphery have a lesser degree of nodal metastases and presumably a better prognosis. Obviously, these considerations do not apply to the specific case of medullary carcinoma.

6. Microvessel density.

The very interesting observation has been recently made that invasive breast carcinomas having a prominent vascular component in the surrounding stroma behave in a more aggressive fashion than the others. It should be added that microvessel density is a phenomenon independent from intratumoral endothelial cell proliferation, and that an increase in microvessel density has also been noted in intraductal carcinoma, particularly of the comedo type.

7. Elastosis.

It has been claimed that breast carcinomas with no associated elastosis have a lower rate of response to endocrine therapy than those with gross elastosis. In terms of survival rate, no convincing differences have been found between tumors with and without elastosis.

8. CEA staining pattern.

This immunohistochemical feature has not been found to relate to prognosis.

9. Vimentin staining pattern.

The claim has been made that Vimentin expression is associated with poor prognosis in node-negative ductal carcinomas

10. Cathepsin D.

Despite original claims to the contrary, assays for neither cathepsin D immunoreactivity in the tumor nor serum levels of this enzyme have proved to have independent prognostic value.

11. C-erbB-2 (neu/HER-2) oncogene.

As already stated, amplification of this oncogene (which encodes a transmembrane glycoprotein with tyrosine kinase activity known as p185) is seen in almost all cases of comedo-type intraductal carcinoma, in 10% to 40% of invasive ductal carcinomas and in only a few cases of invasive lobular carcinoma.

12. p53 and nm23.

Accumulation of p53 protein have been said to correlate with reduced patient survival.

13. Bcl-2.

A relationship between Bcl-2 protein expression and long-term survival in breast carcinoma has been shown. Bcl-2 is also correlated with estrogen receptor status.

14. Skin invasion.

Breast carcinomas in which invasion of the overlying skin has occurred are associated with a decreased survival rate. Invasion of dermal lymph vessels as a determinant of the "inflammatory carcinoma" picture is a particularly ominous

prognostic sign.

15. Nipple inversion.

Involvement of the nipple by carcinoma is associated with a higher incidence of axillary metastases.

16. Lymphatic tumor emboli.

The presence of tumor emboli in lymphatic vessels within the breast is associated with an increased risk of tumor recurrence. Blood vessel emboli. This finding shows a high correlation with tumor size, histologic grade, tumor type, lymph node status, development of distant metastases, and poor prognosis.

17. Paget's disease.

The presence or absence of Paget's disease in invasive ductal carcinoma is of no prognostic relevance per se.

18. Estrogen receptors.

Several authors have concluded that patients with estrogen receptor positive tumors— whether determined biochemically or immunohistochemically—have a

longer disease-free survival than the others. However, the differences in long-term prognosis are minimal and perhaps not statistically significant.

19. DNA ploidy.

20. Cell proliferation.

Determination of S-phase fraction by flow cytometry has emerged as a very important prognostic determinator. As such, it has been incorporated into the combined grading scheme espoused by Elston

21. Axillary lymph node metastases.

This is one of the most important prognostic parameters. Not only is there a sharp difference in survival rates between patients with positive and negative nodes, but the survival rate also depends on the level of axillary node involved (low, medium, or high), the absolute number (fewer than four versus four or more), the amount of metastatic tumor, the presence or absence of extra nodal spread, and the presence or absence of tumor cells in the efferent vessels. Interestingly, patients in whom the initial lymph node sections are negative but who are found to have micro metastases on serial sections have the same prognosis as patients in

whom no tumor is found. For prognostic purposes, the best grouping seems to be the following: negative nodes, one to three positive nodes, and four or more positive nodes.

22. Pattern of lymph node reaction.

It has been suggested that the microscopic appearance of the regional node (lymphoid response and/or sinus histiocytosis) is an indication of the type of host response to the tumor and that it relates to prognosis. The issue remains controversial; if there is indeed a correlation, it does not seem to be a statistically significant one.

23. Internal mammary lymph node metastases.

Survival in patients with involvement of this lymph node group is lower than in those without such involvement, especially if only patients with one to three

positive axillary nodes are evaluated.

24. Local recurrence.

This is a sign of ominous prognosis. In one series of sixty patients with ipsilateral chest wall recurrence and no detectable distant metastases, all patients eventually died of metastatic breast carcinoma.

TREATMENT RELATED

This is too complex and multifactorial an issue to be properly addressed here. Suffice to say that all available evidence suggests that the outcome in breast carcinoma depends more on the nature of the individual tumor than on the type of therapy performed. There is certainly a striking similarity in survival rates from different centers employing widely disparate therapeutic approaches. A complicating factor in evaluating therapeutic results is the marked individual variations in the natural life history of the disease, which renders imperative use of carefully randomized studies. Most of these studies have shown no significant differences in survival among the various groups.

Treatment[xix]

The therapy of breast carcinoma includes surgery, radiation therapy, hormonal therapy, and chemotherapy (the latter sometimes combined with bone marrow

transplantation), depending on the type and extent of the disease.

Surgical therapy, traditionally synonymous with Halsted's radical mastectomy, now comprises a wide variety of newer options, which include partial mastectomy (lumpectomy or segmentectomy), total (simple) mastectomy, and modified radical mastectomy.

Radiation therapy has been employed as a postoperative adjunct (especially in connection with the more limited operations), sometimes as the primary treatment, and for the control of locally recurrent disease.

When conservative surgery is employed, microscopic evaluation of the surgical margins becomes necessary. Several studies have shown that patients with positive margins are more likely to develop local recurrence as well as distant failure. Surgical margins are more difficult to evaluate for intraductal tumors, and their very utility in this circumstance has been questioned.

Breast implants used for reconstructive purposes usually develop a fibrous capsule around them .The inside surface of this capsule has a tendency to undergo *synovial metaplasia;* a process that has also been referred to as pseudoepithelization and that is microscopically very similar to "detritic synovitis. Rarely, the capsule is surrounded by benign squamous epithelium.

Systemic therapy is used for the treatment of generalized disease. Hormonal therapy, which has traditionally included the options of castration, adrenalectomy, and hypophysectomy, is now largely dependent on anti-estrogen drugs, of which tamoxifen has emerged as the most important.

Chemotherapy has had a significant impact on the survival of patients with metastatic breast carcinoma, the best results having been obtained with combination regimens. In highly selected patients, this has been combined with autologous bone marrow transplantation; it remains to be seen whether the survival benefit justifies the considerably high cost of the procedure.

In addition, chemotherapy is currently used as an adjunct following local treatment with curative intent in patients with positive axillary nodes. The decision as to whether to give chemotherapy or hormonal therapy to node-negative patients is a difficult one and is dependent upon a variety of clinical and pathologic parameters. Chemotherapy has also been used sequentially combined with conservative surgery and radiation in patients with localized large (>=3 cm) tumors in order to avoid mastectomy.

MATERIALS AND METHODS

Fifty cases of Carcinoma Breast admitted in various surgical units and surgical Oncology Unit in Kilpauk Medical College Hospital, Chennai over a period of 3 years from 2003- 2006 were taken up for this study.

A complete clinical evaluation of the cases including history, physical examination and necessary investigations were done to confirm the diagnosis, stage of disease and definitive treatment.

Investigations done were FNAC, TRUCUT biopsy, excision biopsy, plain X ray chest, and ultrasound abdomen in all cases.

For all stages of Carcinoma Breast, surgery is done for loco regional control of the disease in our institution. Modified radical mastectomy, simple mastectomy, hormone therapy radiotherapy, and chemotherapy were given. CMF (Cyclophophamide, Methotraxate, and 5-Flurouracil) or CAF (Cyclophophamide, Adriamicin, and 5-Flurouracil) regimen is used for chemotherapy. Tamoxifen and bilateral oopherectomy were used for hormone therapy.

Patients had regular follow up at regular intervals to find out morbidity, disease free survival, local recurrence, systemic metastasis and overall survival. X ray chest, ultrasound abdomen, liver function test, complete hemogram were done for every 6 months, skeletal survey in selected cases were done.

RESULTS OF THE STUDY

Fifty cases of cancer breast admitted in various surgical units in Kilpauk Medical College Hospital were studied during the period of 2003 to 2006.

Age

In our series of study the highest incidence of breast cancer has occurred in the age group between 40-50 years

The youngest patient is 24 years old female

Menstrual status

Average age of menarche is 14 years.

Earliest being 12 years of age, and delayed menstruation up to 17 years of age.

Parity

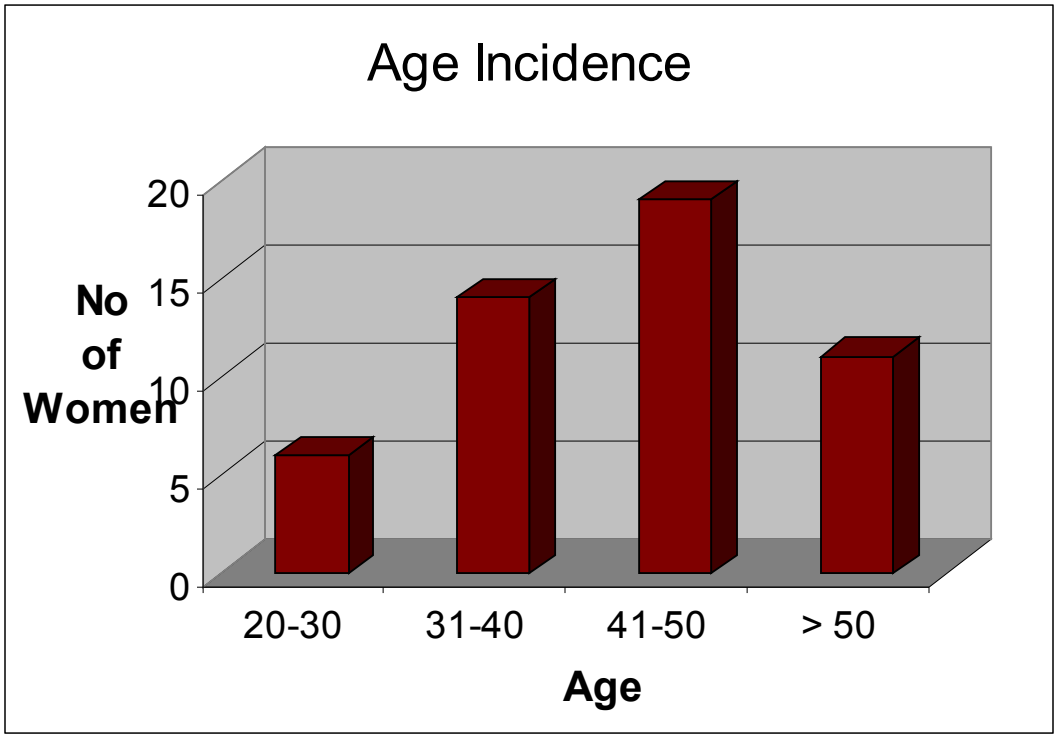
Unmarried	2
Nullipara	4
Para one	8
Para2-3	21
Para 3 – 5	10
More than 5	5

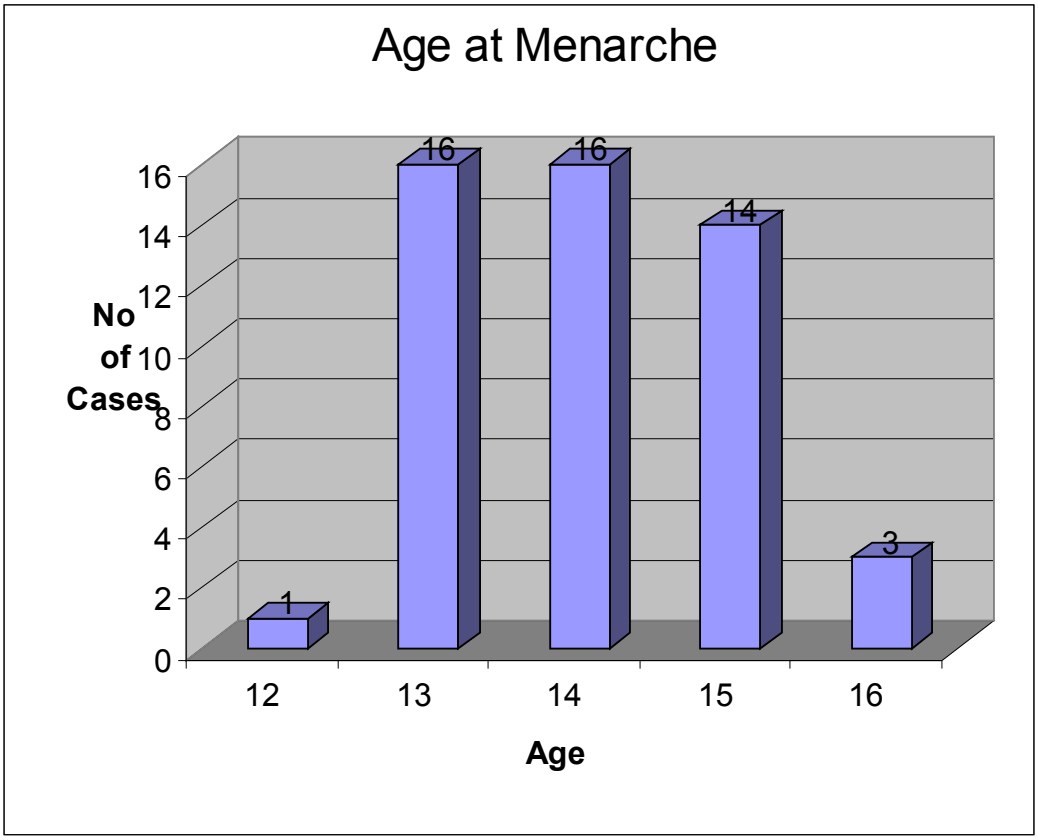
Lactational status

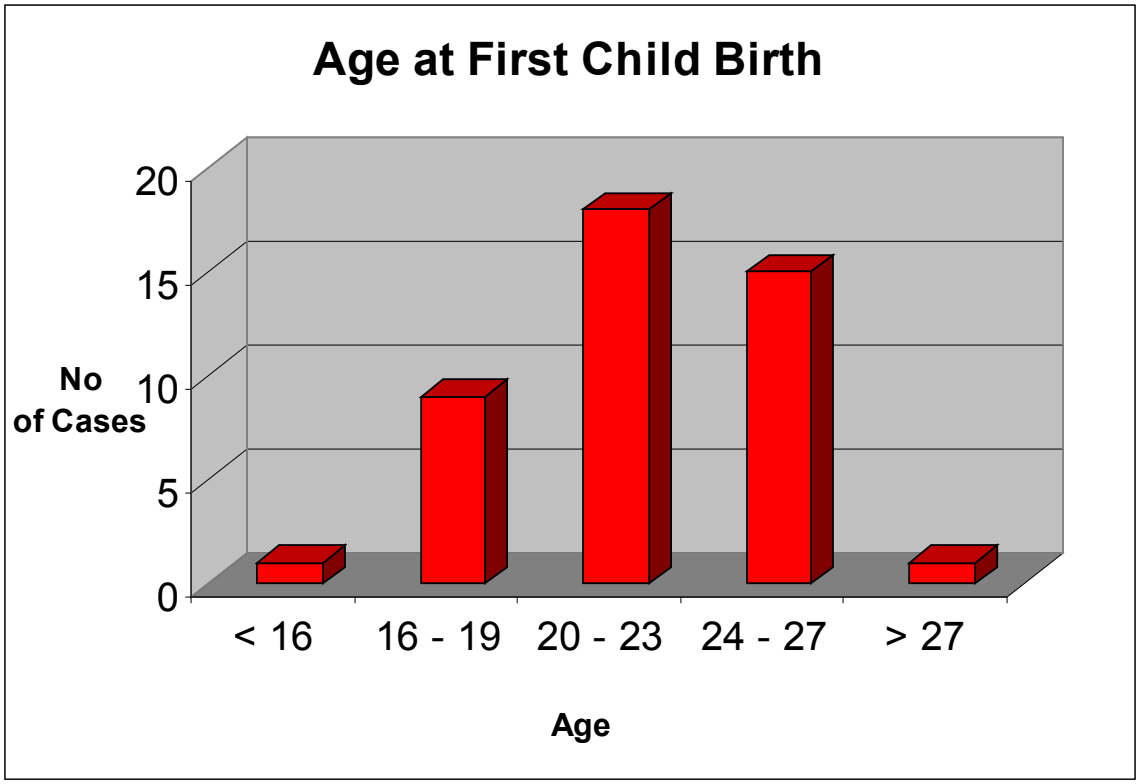
Average duration of Lactational time is more than one year in 42% cases.

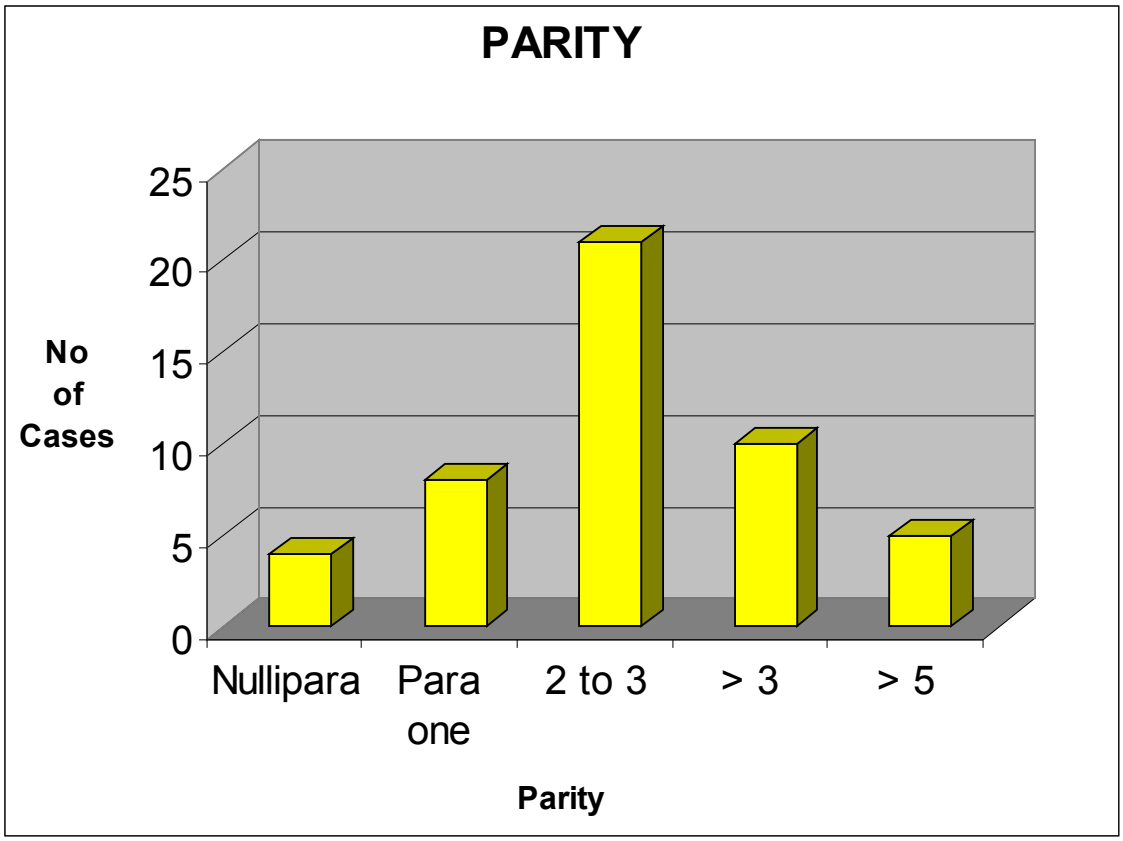
4 cases were Nullipara and two patients were unmarried.

Duration of lactation	No of cases
< 3 months	2
3-6 months	5
7-9 months	12
10-12 months	4
More than 12 months	21


Age Incidence
No of Women
20
15
10
5
0
20-30
31-40
41-50
> 50
Age


Age at Menarche
No of Cases
16
14
12
10
8
6
4
2
0
1
16
16
14
3
12
13
14
15
16
Age


Age at First Child Birth
No of Cases
20
15
10
5
0
< 16
16 - 19
20 - 23
24 - 27
> 27
Age


PARITY
No of Cases
25
20
15
10
5
0
Nullipara
Para one
2 to 3
> 3
> 5
Parity

Age at first child birth

The entire patient had their first child birth before 28 years. None of the mother had first child after 28 years. Nullipara 4 cases. Unmarried 2 cases.

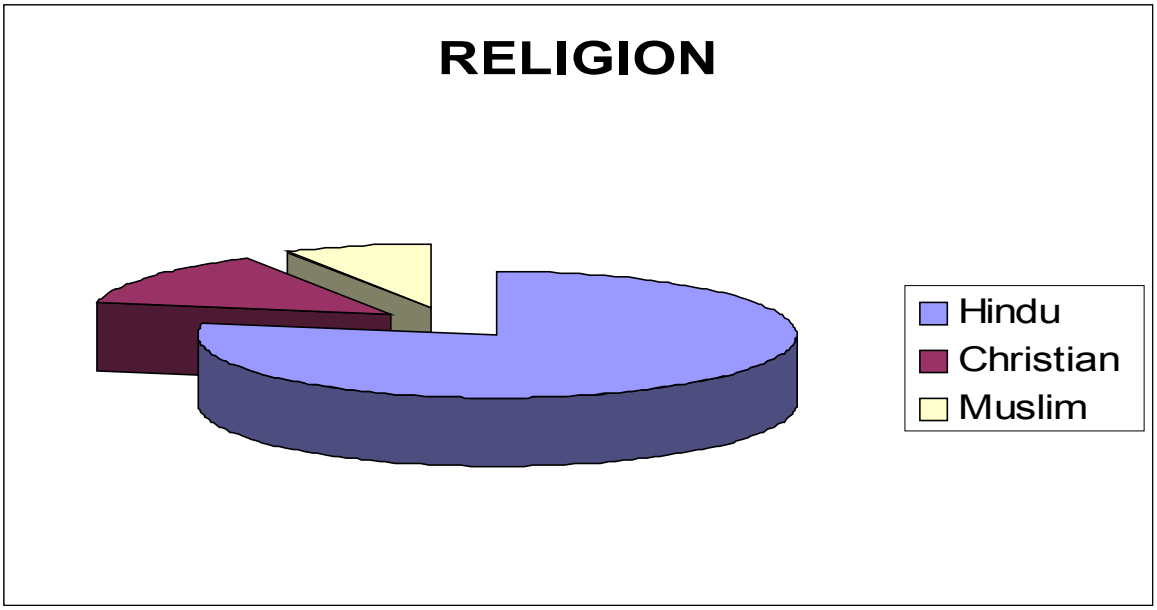
Age in years	No of cases
<16	1
16 – 19	9
20 – 23	18
24 – 27	15
> 27	1

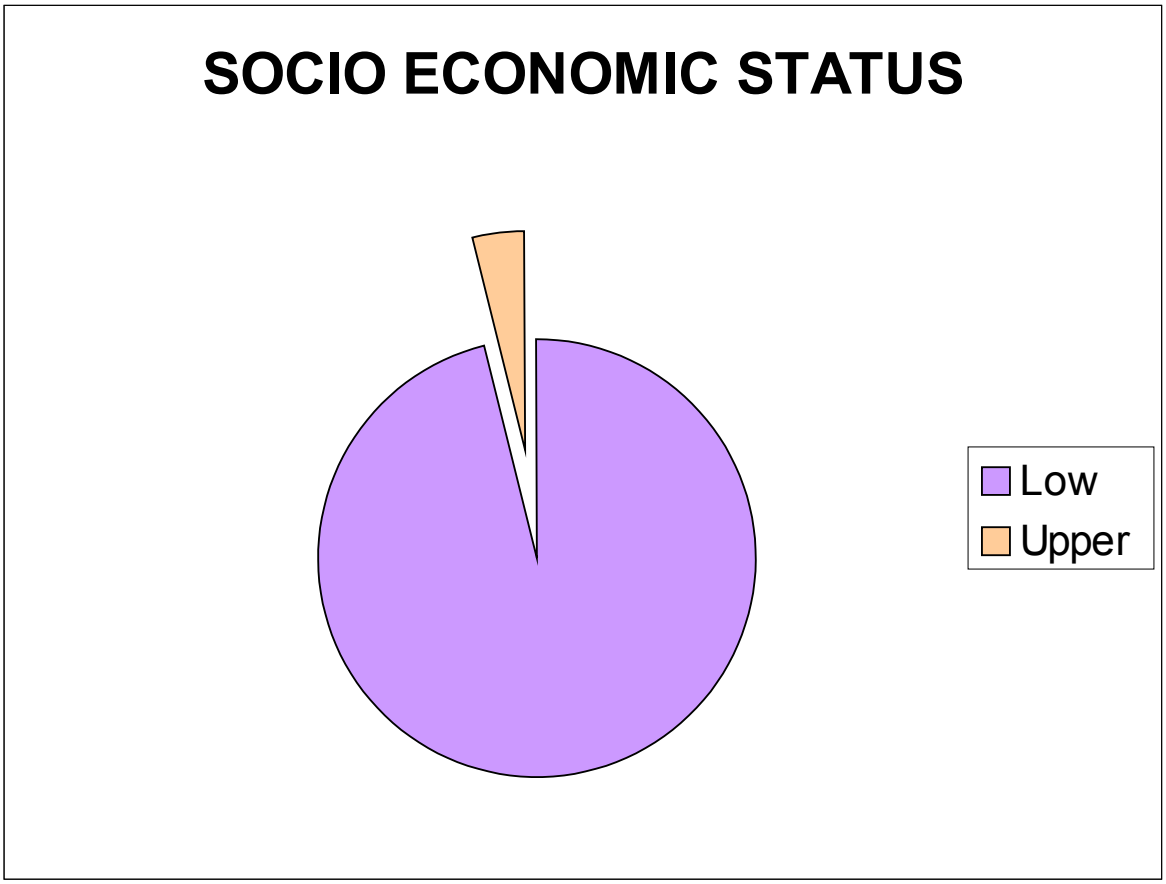
Socio economic status

Low	Upper
48	2

Religion

Hindu	39
Christian	7
Muslims	4





Geographic distribution

The cases reported were from North Tamil Nadu and Migrants from Andhra Pradesh to Tamil Nadu.

Clinical feature

All cases were presented with lump breast. In 15 patients pain was associated with lump breast. Discharge from nipple was present in 4 cases only.

Duration of lump	No of cases
< 3 months	12
4-5 months	12
6-7 moths	11
8-9 months	4
10-11 months	6
> one year	5

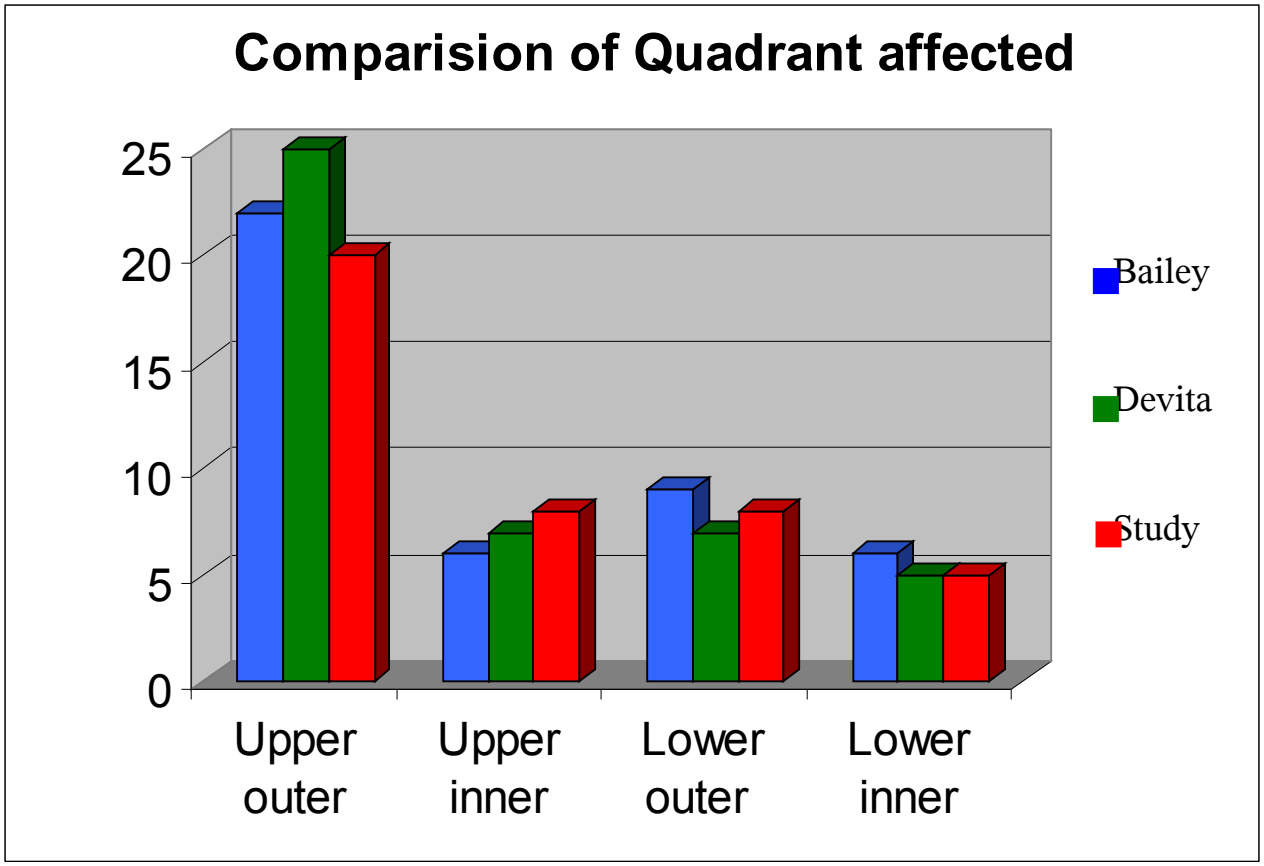
Discharge from the nipple

Less than one week	1
Less than 15 days	2
Less than one month	1

Site

Left breast is affected in 54% of cases in my series. Upper outer quadrant is more commonly involved (44%).

Upper outer	22
Upper inner	6
Lower outer	9
Lower inner	6
Central	5
Diffuse	2



TN

M staging

Staging	No of cases	Staging	No of cases
T1 N0 M0	0	T3 N1 M0	16
T1 N1 MO	0	T3 N2 M0	2
T2 N0 M0	4	T4 N1 M0	4
T2 N1 M0	11	T4 N2 M0	1
T2 N2 M0	2	T4 N3 M0	1
T2 N2 M1	0	T4 N2 M1	1
T3 N0 M0	8		

Staging

Stage	No of cases
Stage I	0
Stage II A	4
Stage II B	20

Stage III A	19
Stage III B	5
Stage IV	1

Investigation

Fine needle aspiration cytology

Positive in 45 cases

Inconclusive in 5 cases

Trucut biopsy

Positive in 4 cases

Negative in 1 case

Histopathological examination

Invasive ductal carcinoma NOS 48 cases

Lobular carcinoma 1 case

Paget's 1 case

Nodal status

Axillary node was clinically positive in 37 cases. Biopsy proved in 25 cases. Supraclavicular node was clinically positive in 1 case. Biopsy positive in 1 case

Opposite axilla positive in 1 case

Treatment

Modalities of treatment

1. Surgery

Type of surgery	No of cases
Patey's modified radical mastectomy (post menopausal women)	35
Patey's modified radical mastectomy with bilateral oopherectomy(pre menopausal women)	09
Palliative total mastectomy	4
Lumpectomy	2

2. Chemotherapy

All the cases except 5 cases treated with CAF regime 6 cycles Cyclophosphamide, doxorubicin, and fluorouracil (CAF).

CYCLOPHOSPHAMIDE

40 to 50 mg per kg of body weight in divided doses over a period of two to five days, or 10 to 15 mg per kg of body weight every seven to ten days, or 3 to 5 mg per kg of body weight two times a week, or 1.5 to 3 mg per kg of body weight a day.

ADRIAMYCINE

Intravenous, 60 to 75 mg per square meter of body surface area, repeated every

twenty-one days

5-FLUROURACIL

300 to 500 mg per square meter of body surface repeated monthly.

3. Endocrine manipulation

Tamoxifen was given to post menopausal case. (Tamoxifen 10 mg twice a day for 5 years)

Morbidity of surgery

Wound infection	3 cases
Flap necrosis	5 cases
Lympodema	8 cases
Lymph collection	15 cases
Numbness	12 cases
Frozen shoulder	2 cases

Discussion

This is a study of 50 cases of Carcinoma Breast during the period of 2003- 2006.

Causes of Carcinoma Breast are unknown. However epidemiological data indicates well defined factors that indicate the liability to breast cancer. Such factors are genetic, endocrine and environmental.

Age[xx]

Carcinoma Breast incidence is increasing with age. Carcinoma Breast is occasionally seen in late teens but there after there is a rapid age specific rise up to 40 years. Then the rate is increases slowly although overall breast cancer rate continues until old age. The cumulative risk for developing breast cancer between ages 20-40 is 0.5% .where as between 50-70 is 5 %.this accounts for the fact that majority of the breast cancer patients are over 50 years of age.

In my study the incidence of carcinoma breast in the age group of 30-40. is 28%, between 40-50 years is 38% incidence above 50 years is 22%.

As comparable to western series there is a steady increase in incidence after 30 years.

The development of second breast cancer may be a clinical manifestation of multifocal origin of breast cancer or may be an entirely new occurrence. There appears to be an overall rise 0.75-1% per year. Thus the relative risk of developing the second non synchronous primary, after 20 years of initial diagnosis of the disease is 1.5%.

Menarche [xxi]

Age of menarche and establishment of regular ovarian cycle seems to be strongly associated with breast cancer risk. Woman whose menarche occurs before the age of 12 has relative risk of 2.3 %. When the menarche is associated with delay in establishment of regular ovulatory cycles, there is 20% decrease in the breast cancer incidence and it's thought to have an additional protective effect.

In my study, only 2% of the patients menstruated at the age of 12. 30%menstruated at 13 years. 30% menstruated at 14 years. 28%menstruated at 15 years. 6% menstruated at the age of 16 years and 4% menstruated at the age of 17 years. Age at menarche has little significance and less protective in this series of study.

Family history[xxii]

Female relatives of the breast cancer may have increased risk of disease. The risk is greatest in patients with first degree relatives, especially when the patient is under the age of 50 at the time of diagnosis.

If the first degree relative has Carcinoma Breast, relative risk is 1.7 -2.5. If the second degree relative had Carcinoma Breast, risk is 1.5 %. Direct genetic factor risk is about 5%.

The *BRCAI* gene has been cloned and is located on the long arm of chromosome 17 (17q). The gene frequency in the population is approximately 0.0006. *BRCA2* is located on chromosome 13q. Women who are thought to be gene carriers may be offered breast screening (and ovarian screening in the case of *BRCA1,* which is known to impart a 50 per cent lifetime risk of ovarian cancer), usually as part of a research programme, or may be offered generic counselling and mutation analysis. Those who prove to be 'gene positive' have an 80 per cent risk of developing breast cancer, predominantly whilst premenopausal. Many will opt for prophylactic mastectomy, although this does not completely eliminate the risk.

Radiation[xxiii]

An increased risk of the breast cancer has been found in survivors of nuclear exposure, women treated for postpartum mastitis by irradiation and professionals, patients exposed to multiple radiographs

In my study there is no predisposing factor like irradiation.

Body weight[xxiv]

There is little correlation between risk of breast cancer and body weight. In my study the minor controversial risk factors like alcohol, diet, oral contraceptives, and hormonal replacement therapy are not found. Though 8% showed diabetes mellitus, in which there may be a disturbance in cholesterol metabolism and level of estrogen.

Benign breast lesion

Benign breast lesions except multiple papillomatosis are not usually recognized as a major risk factor. There are no such predisposing factors in my study, except premenstrual cyclical mastalgia in 6 patients.

Age at first child birth[xxv]

In contrast to western study the patients with first child birth before the age of 19 were 38%. In 36% of the patients the first childbirth was between 20-23 years

About 74% of our patients had their first child birth before 23 years. The protective influence of early age at first child birth is less significant. In this study.

Parity[xxvi]

Multi parity is not protective against breast cancer. Nulliparity has the risk of 1.4% compared to parous women. However this protective effect of parity is totally due to age at first child birth. In those, whose first child birth curred after the age of 30, there appeared to be no protective effect with relative risk of 0.94%. Evidence suggests that with child birth over age of 35 have increased risk of breast cancer. In my study most breast cancer occurred in multipara and is about 72%. Incidence in nullipara is 8%. 10% of cases were grand multipara.

Lactational status

Though 42% of our patients have lactated for more than one year, lactation doesn't seem to have any protective effect.

Clinical feature[xxvii]

Majority of our women in my study presenting with Carcinoma Breast had lump in the breast. Pain in the breast in 15 cases and 4 cases had nipple discharge.

Most common occurrence of breast cancer in our study is right side 46%. 54% of cases in left side. The primary site of cancer in the breast is upper outer quadrant 44%.

12% of cases in upper inner quadrant.18% of cases in lower outer and 12% of cases in lower inner quadrant.10% in central and 10% diffuse.

Our study well correlated with the western study that upper outer quadrant is common and lower inner quadrant 12%and lower outer quadrant 18%.

S. no	Quadrant	Devita	My study
1	Upper outer	48%	44%
2	Upper inner	15%	12%
3	Lower outer	11%	18%
4	Lower inner	6%	12%
5	Central	17%	10%
6	Diffuse	3%	4%

Pathological features[xxviii]

Histological assessment helps to know the patient prognosis and allows greater understanding of biology of the disease. Several pathological classifications are in use. The most commonly used are presented by WHO. It is proved that most tumors arise in the terminal duct of breast regardless of pathological type.

Pathological classification of breast cancer

Most of the breast cancers are ductal carcinoma of breast. Others are less common.

Clinical staging

In my study only 32% of cases were early cancer. All other cases were locally advanced Carcinoma at the time of admission. Most of our patients had lump breast. About 70% had lump breast for more than 3 - 7 months. About 10% of the patients reported only after 1 year. The incidence of metastasis is about 2%. Recurrent cancer occurred in 1 case.

Stage	No of cases
Stage I	0
Stage II A	4
Stage II B	20
Stage III A	19
Stage III B	5
Stage IV	1

The best indicators of the prognosis are tumor size and lymph node status. In our study clinically palpable nodes in axilla and Supraclavicular region were 74%. Among them histologically positive were only in 62% cases.

The second major site of regional metastasis for cancer breast is internal mammary nodes. Because of the non availability of the sophisticated investigation we have not evaluated its incidence.

Our study of nodal status was mainly on axillary nodal involvement. Approximately 74% have evidence of spread to axillary lymph node. But in study it was

62%. The likelihood of axillary node involvement appears to be directly related to the size of primary tumor. Detection of axillary involvement by physical examination has high false positive and false negative rate.

If the axillary nodes are palpable histological evidence of metastasis was not found in 12%. Conversely if axillary node were not detectable clinically, metastasis was detected in 15% of cases histologically. The short coming of the clinical examination is of particular importance. Because, histological involvement of axillary node has high correlation with the prognosis. In our study the false positivity rate was 12%.

Supraclavicular node and internal mammary node involvement is associated with poor prognosis.

No site is immune to the spread of tumor most commonly involved organs are bone, lungs, brain, skin, liver, Ovary and peritoneum.

Diagnosis of Carcinoma Breast

Confirmation of the clinical diagnosis is mainly by pathology

FNAC[xxix]

It has an advantage of being performed as an outpatient procedure and immediate

results are obtained. The technique we followed is, by using 23G needle, atraumatic aspiration after fixing the mass, by 3 or more pass.10 ml syringe is used to aspirate the material and it is spread on a slide and sent for histopathological examination.

Out of 50 cases we submitted, the result showed that false negative rate was 2%. Total negative cases were 5. These 5 cases submitted for trucut biopsy and 4 cases found to be positive and 1 cases true negative. So ended up in a false negative rate of 2%. Sensitivity in our study is 90%. In our study, we have not come across false positive result compared to 2% as expressed in oxford text book of surgery. The disadvantage of aspiration cytology is it cannot differentiate the insitu carcinoma from invasive carcinoma.

Evaluation of the patients with Carcinoma Breast

Once the diagnosis of the breast cancer is made out other investigations were done to evaluate the patient further. All our patients were subjected to investigations like chest X ray, hemoglobin, complete blood count, serum alkaline phosphatase. Because of the non availability of the mammography, bone scan and brain scan, our patients were not subjected to these investigations. Our patients were routinely submitted for ultrasound abdomen and pelvis for liver and ovarian metastasis.

Staging

Though there are many methods of staging, we have followed TNM staging in all our patients. Our study shows early Carcinoma Breast in 32% of cases.

Stage	No of cases
Stage I	0
Stage II A	4
Stage II B	20
Stage III A	19
Stage III B	5
Stage IV	1

Treatment of the Carcinoma Breast [xxx]

The treatment of Carcinoma Breast has changed dramatically over the past 10 years. The disease free survival rate has not been altered much between modified radical mastectomy and other limited procedure followed by radiotherapy. However, the ultimate choice of therapy is influenced by the personal values and fears of the individual patient and final choice is that of patient herself.

Since the protocol in our institution is modified radical mastectomy and bilateral oopherectomy for pre menopausal early operable breast cancer, we did the same for 9 cases. Two cases underwent lumpectomy alone. 35 post menopausal women were subjected to modified radical mastectomy. 4 cases were found to be inoperable and they under went palliative mastectomy. Completion mastectomy had been done for recurrent cases. All the cases were subjected to post operative chemotherapy and radiotherapy and endocrine manipulation.

Ovarian ablation overwhelmingly improved both the recurrence free survival and overall survival in young women but had little effect on the women more than 50 years.

Hormone therapy

Adjuvant hormonal manipulation for the treatment of the breast cancer has been simplified by tamoxifen. Tamoxifen is weak estrogen agonist and moderate estrogen antagonist. Adjuvant Tamoxifen therapy improved both the recurrence free survival and overall survival. It significantly reduces the incidence of contra lateral breast disease. Response rate are 30% in unselected patients, 50% in ER positive patients, 70-80% in both ER and PR positive patients. Regular follow up to asses the endometrial thickness is necessary if the patient is on tamoxifen. We didn't come across any endometrial carcinoma in patients on tamoxifen.

We have not subjected the patients to adrenalectomy, LHRH agonist, aminoglutethimide, megestrol acetate for hormonal manipulation.

Chemotherapy

As most of the patients were presented with advanced breast cancer we have tried combination of palliative surgery, radiotherapy, chemotherapy and hormonal manipulation. Our patient had no chance to undergo immunotherapy like BCG and

levamisole. As multi pronged approach is superior to a single agent, we have given CMF or CAF as chemotherapy for 6 cycles. Since we had followed up the cases for only 2-3 years five year survival rate was not evaluated. Among the 45 patients who had chemotherapy 10 cases received CAF regime all others were on CMF regime.

Radiotherapy

All our patients had postoperative radiotherapy.

Morbidity in surgery

Three patients had post operative infection. Flap necrosis occurred in 5 cases. 15 patients had lymph collection which was managed by needle aspiration. Lympodema is seen in 8 cases.

CONCLUSION

Fifty cases of Carcinoma Breast patients were studied and the following conclusions are arrived

1. **Social status**

   It is common in poor socio economic group.

2. **Incidence**

   The highest incidence rate is 66 % between 30-50 years age group. They were affected in their prime age of life. So mass screening program is essential to detect early breast cancer in our society.

3. **Age**

   Youngest affected female is 24 years.

4. **Hereditary**

   There is no clear evidence about the role of heredity in carcinoma breast in our society

5. **Menarche**

88 % of our cases attained menarche between 13-15 years.

6. Parity

The predominant group affected in our study is multipara-72%. Nullipara is least affected group. So multipara women are not considered to be the protective group against carcinoma breast in this study.

7. **Age of first child birth**

2% cases had their first child before the age of 16. 74% of cases had between 16-23 years. Early child birth doesn't seem to be protective in females of this study.

8. **Breast feeding**

All patient lactate their children. 42% lactated for more than one year. Long period of breast feeding doesn't seem to have any protective effect.

9. Frequency of occurrence of breast cancer is more in upper outer quadrant.

10. Left breast is most affected than Right Breast.

11. Trucut biopsy was the chief investigation of choice with 100 % true

positivity

12. Modified radical mastectomy with or without oopherectomy is the commonest surgery performed.

13. 96 % of the cases had infiltrating ductal carcinoma.

14. Only 16 cases had early breast cancer.

15. Only 90% had chemotherapy. Remaining 10% did not turn up for chemotherapy.

16. Axillary clearance helps in loco regional control rather than disease free survival.

17. Surgical oopherectomy is better in controlling the disease in pre menopausal women. Since ER and PR status could not be available in our hospital in the present setup.

The prognosis depends upon the tumor differentiation, TNM staging, axillary node involvement and behavior of the tumor . The best indicators of likely prognosis in Carcinoma Breast are still tumor size and lymph node status. However, it is realized that some large tumours will remain confined to the breast for decades whereas some very small tumors are incurable at diagnosis. Hence the prognosis of

a cancer depends not on its chronological age but on its invasive and metastatic potential. In an attempt to define which tumours will behave aggressively, and thus require early systemic treatment, a host of prognostic factors has been described. These include histological grade of the tumour, hormone receptor status

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