A STUDY ON RELATIONSHIP BETWEEN EDUCATIONAL AND SOCIO-ECONOMIC STATUS AND EARLY DIAGNOSIS OF CARCINOMA BREAST IN FEMALES

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CERTIFICATE

This is to certify that this dissertation titled **"A STUDY ON RELATIONSHIP BETWEEN EDUCATIONAL AND SOCIO-ECONOMIC STATUS AND EARLY DIAGNOSIS OF CARCINOMA BREAST IN FEMALES"** submitted by **DR.UMA.M** to the faculty of General surgery, TheTamilnaduDr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MS degree Branch I General Surgery, is a bonafide research work carried out by her under our direct supervision and guidance from January 2011 to December 2012.

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I DR.UMA.M solemnly declare that the dissertation titled "**A STUDY ON RELATIONSHIP BETWEEN EDUCATIONAL AND SOCIO-ECONOMIC STATUS AND EARLY DIAGNOSIS OF CARCINOMA BREAST IN FEMALES" has** been prepared by me . This is submitted to the **Tamilnadu Dr.M.G.R. Medical University, Chennai,** in partial fulfillment of the regulations for the award of MS degree (Branch I) General Surgery.

Place : Madurai **DR.UMA.M**

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CONTENTS

INTRODUCTION

Breast Cancer is the most common site specific cancer in women and is the leading cause of death from cancer in women age around 22-59 yrs. It accounts for 26% of all newly diagnosed cancers in females and is responsible for 15% of cancer related deaths in females**.**

The incidence of breast cancer varies in different countries in the world. Women residing in industrialized countries tend to have higher incidence than women residing in less industrialized countries.

Breast Cancer distribution differs by geography, regional lifestyle, racial or ethnic background. In general both breast cancer incidence and mortality are relatively lower among the female populations of Asia and Africa, relatively underdeveloped nations, and nations that have not changed to the westernized reproductive and dietary patterns . In contrast, European and North American women from heavily industrialized or westernized countries have a substantially higher incidence of breast cancer.

Although often related, the factors that influenced the incidence of breast cancer differ from those that affect mortality. Incidence rates are lower among populations with females who begin child bearing at young ages and who have multiple full term pregnancies and increased duration of breast feeding.

These features characterize many underdeveloped nations and also many eastern nations. Disparities in breast cancer survival are closely linked to disparities in socio economic status .Poverty rates and proportions of the population that lack health care insurance are some of the socio economic factors that create barriers to effective breast cancer screening and result in delayed breast cancer diagnosis, advanced stage distribution, inadequacies in comprehensive treatment and ultimately increased mortality rates.

Long-term survival of women with breast cancer mainly depends upon the stage of the disease at the time of presentation. Attempts to control death due to breast cancer therefore relied on promoting early detection of cancer and its treatment. A Comprehensive breast history, a thorough breast examination, and a clear record of findings and follow-up can detect cancer in early stage [9].

Early diagnosis and proper referrals, availability of female doctors, facilities to detect breast cancer earlier by mammography as a tool for screening purpose, and availabilities of facilities for proper treatment can decrease the mortality rate in CA breast [4].

EPIDEMIOLOGY OF BREAST CANCER:

Breast cancer is most common cancer found in females in Europe (180000 cases per year), The United States (130000 cases per year), Australia and many Latin American Countries. Breast Cancer is rare before age of 20 -30 years but incidence rises very steadily up to age 50 years. Mortality rate due to breast cancer in Western Europe and Northern America are of order of 15-25 per Lakh women that is 30-40 % of incidence rate [2].

The highest incidence rates has occurred in Canada, United States, Spain, Sweden(3-6 percent annually) and lowest rate found in Norway and Denmark. Breast Cancer rates differ by race and ethnicity. Though American-African women have a lower overall incidence of breast cancer compared with Caucasian women, African-American have a higher incidence of breast cancer before 35 years of age. The reasons for these disparities are not understood but the possible explanations include a) Distribution of risk factors for breast cancer b) Differential utilization of mammographic screening c) Differences in inherent genetic susceptibility d) Tumor characteristic differences e) Differential access to treatment f) Differences in prevalence of comorbidities in women diagnosed with carcinoma of breast.

The Smith surgical papyrus (3000-2500 B.C) is the first to document about and this cancer occurred in men and the author's conclusion about this cancer is that there is no treatment for breast cancer [5].

In De Medicina Celsus quoted on the importance of operations for breast cancer of earlier stage. "None of these may be removed but the cacoethes (early cancer), the rest are irriated by every method of cure. The more violent the operations are, the more aggressive they grow" [6].

Rudolf Virchow found that CA breast arise from epithelial cells and then spreads along lymphatic vessels. He is considered as the architect of new cellular theory on pathogenesis of carcinoma breast.

Le Dran noted that breast carcinoma was a local disease that spreads by lymphatic vessels to axillary lymph nodes. In nineteenth century Moore emphasized complete resection of breast with removal of axillary lymph nodes which are palpable. In 1894 both Halsted and Meyer advocated radical mastectomy as treatment of carcinoma of breast. In 1948, Patey introduced modified radical mastectomy for of treatment of operable breast cancer but advanced.

AIMS & OBJECTIVES OF THE STUDY

1) To analyze the relationship between socio economic and educational status and early diagnosis of CA Breast.
2) To emphasize the need for early detection of breast cancer.

ANATOMY OF BREAST

Breast is a tubulo alveolar type of Modified sweat gland. It is fully formed in female and Vestigial in male. It Overlies 2^{nd} to 6^{th} ribs and extends from side of the sternum to the anterior axillary line on both sides. Posteriorly breast rest on fascia of Pectoralis major, upper end of Rectus sheath, Externaloblique and serratus anterior [2].

Nipple is a conical prominence in the center of areola devoid of fat, hair or sweat glands. Composed of circularly arranged smooth muscle for lactation and erection. Areola contains sebaceous glands, sweat glands and accessory glands of montgomery for lubrication.

Retromammary space is space between investing layer of breast and pectoral fascia. It contains small amount of fat, lymphatics and small blood vessels. It allows breast some degree of movement on pectoral fascia.

Components of breasts includes Glandular apparatus, fibrous stroma and supporting structures, adipose tissue which contains arteries, veins, lymphatics, nerves and Infiltrating cells.

Glandular component of the breast consists of ducts which branches radially and spreads outward and downward from nipple areola complex. At the summit, subareolar ducts widen as lactiferous sinus.

Lactiferous ducts exit through 10-15 orifices in the nipple. At the opposite end the ducts after progressive branching end in clusters of spaces called terminal ductules/acini .These are the milk forming organs of the breast.Each acini with their efferent ductules called lobules/lobular acini. Each ductal system is functional independent [3].

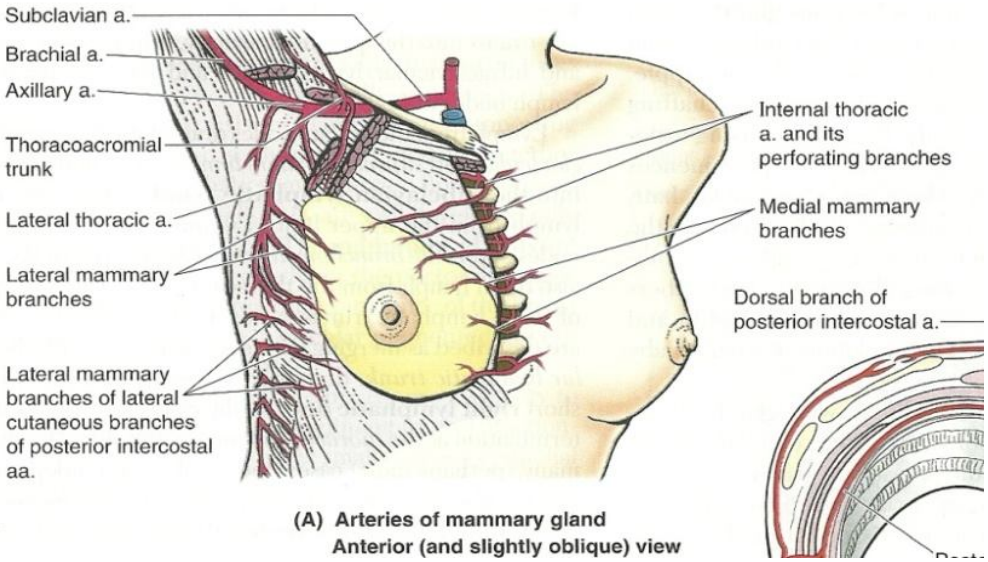
Fibrous stroma contains Cooper's ligament which is nothing but dense connective tissue coursing throughout the fat from skin to underlying deep fascia. It Provides shape to the breast and Holds breast upwards. Tethering of this ligament by scirrhous carcinoma produces dimple on the surface of breast.

Fibrous stroma also contains specialized loose connective tissue investing terminal lobule which Contain capillaries, lymphocytes, and mononuclear cell infiltrates. Fatty tissue fills the gap between glandular apparatus and produces distinguished shape of breast.

Arterial blood supply of breast

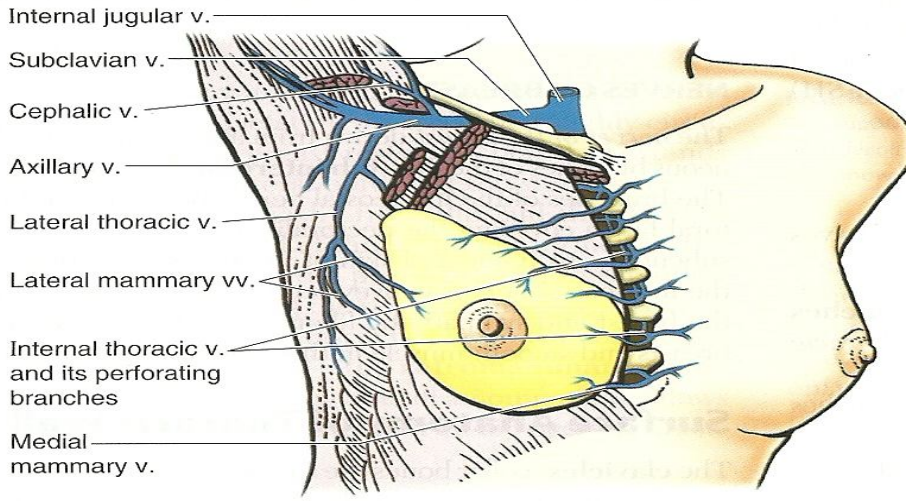
Blood supply of breast is mainly from a) Perforating branches of internal mammary artery through its perforator branches b)Lateral branches of 2-4th posterior intercostal arteries c) branches of axillary artery which includes, Lateral thoracic and pectoral branches of thoraco-acromial artery. The superomedial perforating branch of the internal mammary vessels is important and supplies 60% of total breast.

ARTERIAL BLOOD SUPPLY OF BREAST



(A) Arteries of mammary gland
Anterior (and slightly oblique) view

VENOUS DRAINAGE OF BREAST



(C) Veins of mammary gland
Anterior (and slightly oblique) view

Venous drainage

Three groups of deep veins that drain the breast are a) Posterior Intercostal veins (2^{nd} -4^{th}) through its perforator branches b) Tributaries of Axillary vein c) Perforating branches of the internal thoracic vein. Batson's venous plexus, which overlies the vertebrae and extending from skull base to the sacrum, is a route for metastastic spread of breast cancer to the vertebrae, skull, pelvis and ribs [2].

Nerve supply to the breasts

Sensory nerve supply of the breast derived from lateral cutaneous branches of the 3rd to 6th intercostal nerves. The nerves exist the intercostals spaces between slips of the muscle serratous anterior. The Sensory nerves supply of skin over the upper part of breast is by supraclavicular nerve through its anterior branches. Intercosto brachial nerve is a lateral cutaneous branch of second intercostals nerve which if resected leads to sensory loss over medial part of upperarm.

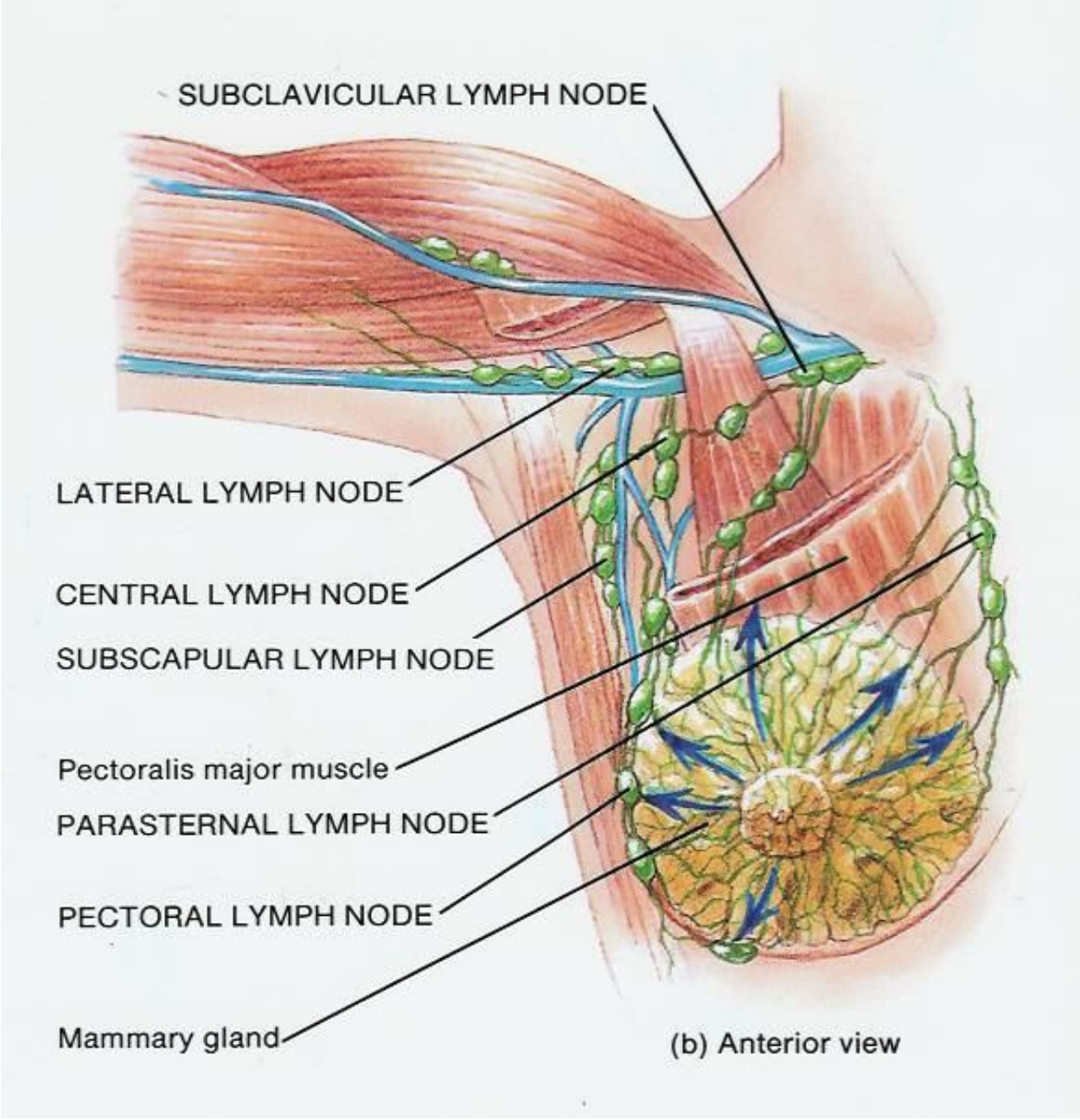
Lymphatic drainage of breast

Breast is drained by 2 set of lymphatics

a) Lymphatics of skin over breast
b) Lymphatics of the parenchyma of breast

More than 75% of lymph drains into axillary lymph nodes

FIG: LYMPHATIC DRAINAGE OF BREAST



Lymphatics of skin over the breast - drain the integuments over breasts. They do not drain areola and nipple. Upper part drains into supraclavicular nodes, Outer part drains into axillary nodes and Inner part drains into internal mammary nodes. Lymphatics of skin communicate across midline. Mammary cancer spread along lymphatics to produce nodules in skin.

Lymphatic drainage of parenchyma

Lymph from the breast drains into the following lymph nodes. The axillary lymph node which consists of six groups a) Lateral group that lie medial to the axilliary vein which receive lymph drainage from upper extremity. b) Anterior or pectoral group that lie along vessels of thoraco-lateral and receive drainage of lymph from lateral part of breast. c) Posterior or Scapular group that lie along the subscapular vessels and drains the posterior part of neck, trunk and shoulder. d) Central group that lie behind the muscle of pectoralis minor and receive lymph drainage from external mammary and scapular group of lymphnodes .e) Subclavicular or Apical group that lie posterior and superior to pectoralis minor muscle. f) The interpectoral (Rotter's Nodes) that are interposed between the pectoralis major and minor muscle.

Surgical levels of axillary lymph nodes

Level I include Anterior or Pectoral Group of axillary lymph nodes, Subscapular or posterior and lateral axillary lymph nodes.

Level II includes Central axillary lymph nodes, some apical axillary lymph nodes and Interpectoral lymph nodes (Rotter's).

Level III includes Apical or infra clavicular lymph nodes.

Anatomical significance

Lymphatic drainage of the mesenchymo epithelial components of breast is the principle route for metastasis of adenocarcinoma of breast. A thorough knowledge about the anatomy of lymphatic drainage plexus and related lymph nodes of the breast is required. It is important for knowing the principles of performing sentinel lymph node biopsy or to perform axillary dissection adequately and by safety method.

EMBRYOLOGY

Development of breast:

During 5^{th} or 6^{th} week of fetal development two vertical ectodermal thickenings (mammary ridges, milk lines) develop in embryo .Paired breast develop along the ridges which starts from the axilla to the inguinal region[3].

Nipple develops from rostral part of each bridge. The mammary glands develop from the nipples during fetal life. Breast develops as ectodermal in growth which forms a primary tissue bud in the mesenchyme.

From Primary bud 15 to 20 secondary buds develop. Major lactiferous ducts develop that ends into a mammary pit which is shallow. The pit is transformed into nipple by mesenchymal proliferation.

Breast does not fully develop till pubertal age .Then it enlarges due to hormonal action of estrogen and progesterone that leads to epithelial and connective tissue proliferation.

Breast is not completely developed till females become pregnant. Absence of breast (amastia) is rare and it is due to failure in normal development of mammary ridge which occurs at 6^{th} week of intrauterine life.

PHYSIOLOGY OF THE BREAST

Development and function of breast are regulated by various hormonal stimulus by Estrogen, Progesterone, Prolactin, Oxytocin, Cortisol, Thyroid Hormone and Growth Hormone [8].

For normal development and function of breast Estrogen, Progesterone and Prolactin are necessary. Estrogen and Progesterone are necessary for epithelial differentiation and development of lobules and ducts. Prolactin is responsible for lactogenesis in late pregnancy and postpartum period.

The regulation of release of hormones Estrogen and Progesterone from ovaries is by Gonadotropins luteinizing hormone (LH) and follicle – stimulating hormone (FSH).The realease of LH and FSH regulated by secretion of gonadotropins from the hypothalamus [2].

By negative and positive feedback effects, secretion of FSH, LH and GnRH are controlled by circulating Estrogen and Progesterone. With onset of puberty sensitivity of hypothalamic-Pituitary axis to negative feedback decreases but increases to positive feedback from Estrogen. These sequence of physiological events lead to onset of menstruation and leads to an increase in size and density of breast, engorgement of breast tissues and proliferation of epithelium.

Changes in Breast During pregnancy:

There is an increase in circulating estrogen and progesterone which causes alteration in form and substance of breast. There is proliferation of Epithelium of duct and lobules, darkening of skin of areola and prominence of Montgomery's glands. Minor duct branches during I and II trimesters and develop in III trimester leading to accumulation of fat in epithelium of alveoli and alveolar ductal spaces filled by colustrum.

After delivery of placenta the circulating level of estrogen and progesterone decreased that permits the prolactin for lactogenesis. Production of milk and its release are regulated by reflex arcs of nerve which begins in the nerve endings of nipple and areola .Oxytocin causes cells of myoepithelium to contract and compress the alveoli which causes milk to expel into lactiferous sinuses.

Menopause:

The level of estrogen and progesterone secreted by ovaries decreases and ducts and alveoli of breast involutes. Breast tissues are replaced by fibrous connective tissue and adipose tissues.

PATHOLOGY OF CARCINOMA BREAST

The cell of origin:

The cell of origin of breast cancers is very significant for its implication on etiology and treatment. Although the majority of tumor cells would consist of non stem cell progeny, only the malignant stem cells would contribute to tumor progression or recurrence. Effective treatment would need to target only this population, which to date has been difficult to define. The most likely cell type of origin for the majority of carcinomas is the *ER*-expressing luminal cell, since the majority of cancers are ER-positive and precursor lesions, such as atypical hyperplasias, are most similar to this type of cell. ER-negative carcinomas may arise from ER-negative myoepithelial cells [2].

Classification

Most breast malignancies are of adenocarcinoma type that are divided into In situ carcinomas and Invasive carcinomas. In Situ carcinomas are subdivided into DCIS (80%) and LCIS (20%) .Invasive carcinomas are subdivided into No-special-type carcinoma (ductal) (79%) , Lobular carcinoma(10%) and other types 1%.

Ductal Carcinoma In Situ (DCIS)

It consists of population of malignant clonal cells limited to ducts and lobules by the basement membrane. It is histologicaly characterized by epithelial proliferation of ducts that leads to growth of papilla within duct lamina. Earlier in the

development, the cancer cells donot exhibit nuclear atypical, mitoses or pleomorphism which makes differentiation of early DCIS from hyperplasia due to benign disease.

DCIS is classified according to grade of nucleus and presence of necrosis.There is fivefold risk in females with DCIS to develop invasive cancer. The invasive cancers that develop in DCIS are observed in same quadrant and side of the breast where DCIS was initially detected.

With advent of mammographic screening, diagnosis of DCIS has rapidly increased. Detected as a result of calcifications or periductal fibrosis. Five subtypes are solid, comedo, cribriform, papillary and micro papillary.

Lobular Carcinoma In Situ (LCIS)

LCIS orginate from terminal duct lobules and seen mainly in breast of female. LCIS is characterized by cancer cells that distend and alter the terminal duct lobules but ratio between nucleus and cytoplasm are normal. Mucoid globules of cytoplasm are important pathological feature of LCIS. About 25% of womenwith LCIS develop invasive cancer.Invasive cancer develops in any side of the breast not depending on initial focus of LCIS.The risk for development of invasive cancer is increased in LCIS.

LCIS is always an incidental biopsy finding. When both breasts are biopsied, LCIS is bilateral in 20% to 40% of cases, compared with 10% to 20% of cases of DCIS. LCIS is more common in young women, with 80% to 90% of cases occurring before menopause.

Invasive Carcinoma, No Special Type (NST; Invasive Ductal Carcinoma)

Includes majority of the carcinomas (70% to 80%). Morphology: firm too hard with irregular border. When cut or scraped, they typically produce a characteristic grating sound. There is a wide range of histologic appearances**.**

Invasive Lobular Carcinoma

Usually present as a palpable mass or a mammographic density with irregular borders. Greater incidence of bilaterality. The histologic hallmark is the presence of dyscohesive infiltrating tumor cells, often arranged in single file. Signet-ring cells containing an intracytoplasmic mucin droplet are common [2].

Atypical lobular hyperplasia, LCIS, and invasive lobular carcinoma all consist of dyscohesive cells with oval or round nuclei and small nucleoli .The cells lack the cell adhesion protein E-cadherin. Foote and Stewart originally classified the invasive breast cancer as follows 1) Paget's disease of nipple 2) Ductal carcinoma of invasive type 3) Adenocarcinoma with productive fibrosis 4) Medullary carcinoma which constitutes 4% 5)Mucinous or colloid carcinoma about 2% 6)

Papillary carcinoma 2% 7)Tubular carcinoma 2% 8) Invasive Lobular carcinoma about 10% and rare cancers like Adenoidcystic Apocrine.

Paget's disease of the Nipple is characterised by presence of chronic, Eczematous eruption of the nipple, which converts into an ulcerative and weeping lesion. It usually associated with DCIS or invasive cancer. A lump may be present or absent. Biopsy from the nipple will show features of pagetoid change .Pathognomic feature of this cancer is presence of large, pale, cells with vacuoles (Paget cell) in the epithelium of rete pegs are important pathological feature.

Disease of Paget's can be differentiated from melanoma of superficial spreading type by the presence of CEA immunostaining and presence of S-100 antigen immunostaining in melanoma. Surgery is the main treatment for this tumor which includes either removal of lump or breast or modified radical mastectomy depending on the extent involved and presence or absence of invasive cancer. Axillary lymphnode metastasis can occur in about 60 % of cases of invasive ductal carcinoma.It occurs mainly in post or perimenopausal women of age group 50 to 60 years.

Metastasis

Lobular carcinomas - different pattern of metastasis. Metastasis to the peritoneum and retroperitoneum, the leptomeninges (carcinoma meningitis), the gastrointestinal tract, and the ovaries and uterus.Metastatic lobular carcinoma

maybe mistaken for signet ring cell carcinoma of the GI tract. Common underlying molecular etiology. Characterized by the loss of E-cadherin, a cell adhesion molecule that functions as a tumor suppressor.

OtherTypes: 1)Medullarycarcinoma 2)Mucinous carcinoma 3)TubularCarcinoma 4)Invasivepapillarycarcinoma 5)InvasiveMicropapillarycarcinoma 6)Metaplastic carcinoma.

Medullary Carcinoma:

Medullary carcinoma constitutes only 4% out of all invasive cancers and belongs to BRCA1phenotypic carcinoma of breast. Most common in women in the sixth decade.It may closely mimic a benign lesion clinically and radiologically.The cancer is grossly hemorrhagic and soft.But clinically,it is deepseated within the breast and bulky..It can occur bilaterally in 20% of cases.On microscopical examination it consists mainly of lymphocytes and plasma cells within a dense lymphoreticular infiltrate,active mitosis with large pleomorphic nuclei, minimal ductal or alveolar differentiation. It is poorly differentiated, has slightly better prognosisand Lymph node metastases are infrequent.

Mucinous (Colloid) Carcinoma:

It occurs in older women and tends to grow slowly. It is characterized by aggregates of low grade cancer cells which are surrounded by extracellular mucin. It appears glistening and gelatinous macroscopically. In microscopic section cancer

cells may not be seen if there is more mucinous component. Hence multiple section analysis is needed to conform the diagnosis. It is usually diploid, well to moderately differentiated, and ER positive. Lymph node metastases are uncommon and the overall prognosis is slightly better.

Tubular carcinoma:

Tubular carcinomas are diagnosed by mammographic screening and occur mostly in perimenopausal women. On microscopical examination tubular elements are seen which are arranged haphazardly. Diploid, ER positive, and HER2/neu negative have excellent prognosis. Distant metastasis are rare in invasive cribriform, carcinoma, axillary lymphnode metastases are rare.

Papillary & Micro papillary:

Papillary Carcinoma usually occurs in older age group around 70 years.This tumor is usually small attaining 3 cm diameter rarely. This tumor is characterized by multilayered epithelium and papillae .Axillary lymphnode metastases are rare. The survival rate are similar to tubular and mucinous carcinoma. It is Invasive Papillary Carcinoma and usually ER positive. It has Favorable prognosis but Invasive micro papillary carcinoma is ER negative and HER2 positive. It has Poor prognosis.

Modes of Metastasis:

1) In contiguity spread 2) Lymphatic spread to Axillary and other lymph Nodes3) Blood Borne to Bones, Liver, Brain etc.4) Trans-coelomic spread to peritoneum.

RISK FACTORS FOR CA BREAST:

Family History:

Breast cancer is 3 to 4 times less likely to occur in females with negative family history of breast carcinoma than with positive history of breast cancer in first degree relative of their family. Risk is increased in those cases whose mother or sibling's breast cancer occurred before menopausal age group or bilateral cancer or in patients with family history positive for breast cancer where two or more first degree relatives are affected with ca breast.BRCA1 and BRCA2 gene mutation accounts for less than 10% of familial breast cancer [6].

Reproductive History:

Early onset of menstrual cycle and menopause at late age contribute to more risk of breast cancer but premenopausal oophorectomy reduces the risk. Women with no children and women with pregnancy at fullterm after 35 years have 1.5 times incidence higher of carcinoma breast than multiparous. Long period of lactation found to decrease the risk of carcinoma breast. Each full term pregnancy leads to 3% reduction in risk of breast cancer [8].

Menstrual History:

Late onset of Menstrual cycle and menopause by artificial means found to have decreased risk but increase in incidence in patients who attained menarche before 12 years or attained menopause naturally after 50 years.

Benign breast condition such as papillomatosis, or hyperplasia of atypical epithelium, and density of breast more in mammogram are more prone for increased risk of carcinoma breast.

The women who develops carcinoma in one breast has more chance of getting cancer in opposite breast.

Contralateral breast cancer occurs at rate of 1-2 percent per year in these patients. Increased intake of fatty diet can increase the incidence of breast cancer. Long term doses of estrogen in women who have attained menopause may have increased risk of developing carcinoma of breast.

Genetics:

Breast cancers of inherited type are found to be associated with mutation of gene present on chromosome 17. BRCA 1 gene mutation is found to be associated with increased risk of early onset of cancer of breast and ovary. .Of about 85% of females with BRCA 1 gene mutations can develop carcinoma of breast in their life time.BRCA1 breast cancer are associated with invasive ductal which are hormone receptor negative and poorly differentiated. Another gene BRCA 2 which is

associated with mutation of gene on chromosome 13, are found in nearly 1% of carcinoma of breast in women under 40 yrs of age. Ataxia telengectasia mutation and p53 Gene mutation is also found to be associated with breast cancer. The susceptibility to breast cancer in BRCA2 families belong to autosomal dominant trait and higher penetrance.BRCA2 gene associated breast cancer associated with invasive ductal carcinoma and usually well differentiated. Test for gene mutation is done for females who are at increased risk of breast cancer. The test that is available is gene sequence analysis. Females belonging to the high risk factors may undergo mastectomy and oophorectomy prophylactically. Tamoxifen an selective estrogen receptor modulator can be used as preventive agent which is approved by FDA [2].

Symptoms and Signs of Breast Cancer:

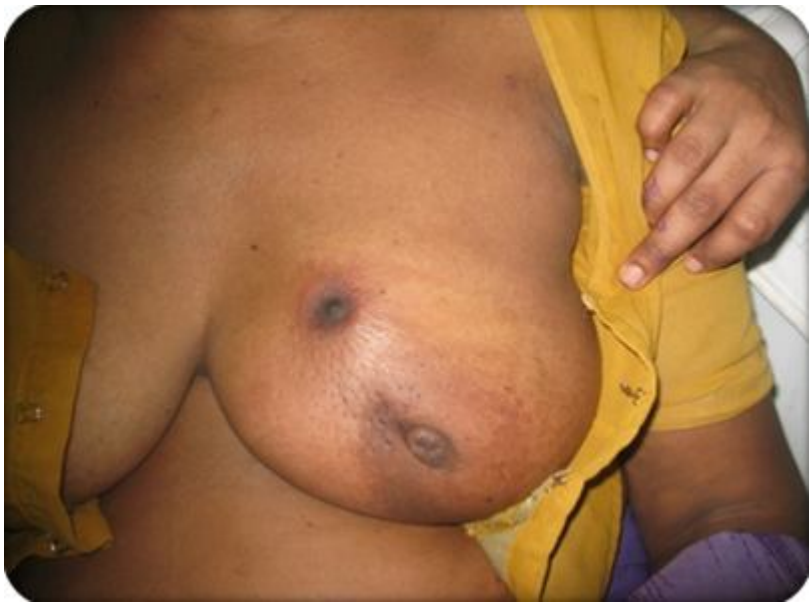
The main complaint in almost 70% of the patients with carcinoma breast is a painless lump in breast. Other symptoms noted are pain in the breast; discharge from nipple or with erosion, retraction of nipple with itching or redness. It may also present as mass in axilla or edema of the arm as the first symptom. Weight loss, jaundice, bone pain may be rarely seen on initial presentation due to systemic metastases.

For proper inspection of the breast during physical examination, patients should be instructed to sit with arms by her sides and raise the arm over head. In this position any abnormal difference in size of the breast can be made out and even mild nipple retraction or dimpling of skin may be made out clearly.

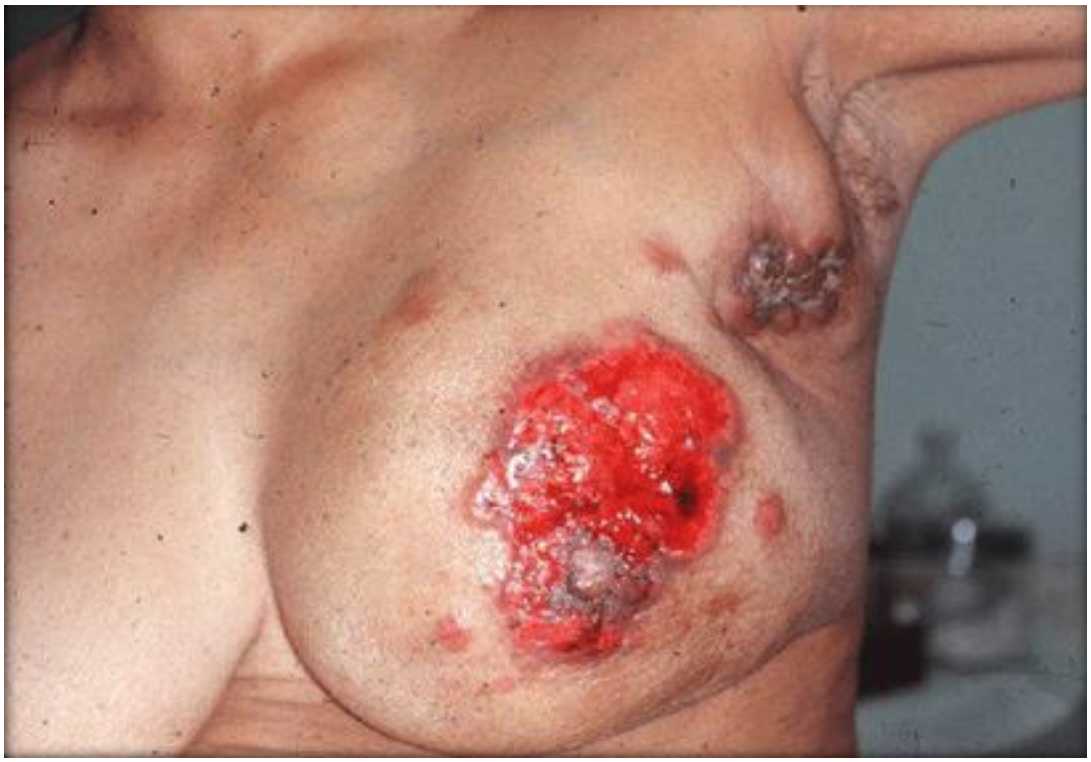
Patient can also be examined in supine or lying position.Both axilla and supraclavicular region should be examined for any enlargement of nodes in the above area.

Carcinoma breast usually present as mass with firm to hard in consistency,not tender with ill defined margins. In paget's disease nipple erosion may be the only presentation in patients. Serous or bloodstained discharge from the nipple may occur but is usually found in benign disease of breast.

PEAU-D-ORANGE APPEARANCE WITH NIPPLE RETRACTION IN CA BREAST PATIENT



CA BREAST WITH SKIN ULCERATION



INVESTIGATIONS

The Investigations are done to

1) To confirm the diagnosis.
2) To assess the extent of disease.
3) To assess the prognostic and predictive factors.
4) To assess the general condition of the patient.

Diagnostic Test:

1) FNAC:

FNAC is a method in which by using 23 gauges needle cells are aspirated for cytological examination. Cellular material obtained by FNAC is expressed on to microscopic slideand the slide is airdried or fixed using 95% ethanol. After that the slides are examined microscopically .The sensitivity and specificity are nearly 100% when a mass in the breast is evident clinically. The rate of false positive diagnosis is very low in case of FNAC.FNAC also yields a very high false negative rate.The main disadvantage of FNAC is that non invasive cancer cannot be differentiated from invasive carcinoma.

2) CORE-NEEDLE BIOPSY:

It is a method by which core of tissue is obtained by using large cutting needle or by biopsy devices like tru-cut needle. Automated device are also used to obtain core biopsy. It is done under local anesthesia. Specimens obtained are kept in

formalin and examined by paraffin blocks. Core biopsy has the advantage that tumour markers such as estrogen receptor(ER), progesterone receptor (PR) and Her-2 / neu over expression can be performed on core of tissue.

3) OPEN BIOPSY:

Open biopsy or excisional biopsy is done when tumor size more than 4 cm. It is done under local anesthesia. It should be done before a definitive treatment. Neddle biopsy or FNAC are less expense and complications are less, when compared to excisional biopsy. But when FNAC and needle biopsy are inconclusive excisional biopsy must be done. Excisional biopsy is done to remove the entire lesion, not a part of lesion [6].

4) IMAGE GUIDED BIOPSY:

It is done to diagnose non palpable lesions.

IMAGING TECHNIQUES:

1) **Mammography**

Used as Screening as well as Diagnostic purpose. Mammography which is used conventionally delivers radiation at a dose of 0.1cGy for each study. Mammography which is used for screening purpose detects breast carcinoma in patients who are asymptomatic. It is also done in high risk patients like when there is a 1) Family history positive or susceptibility to genetic mutation. Annually after 25 years or 5-10 years prior to age of youngest breast cancer stage in family 2)

Lobular crcinoma in situ or Atypical Hperplasia 3)Prior History of breast cancer 4) Women with lifetime risk >20% 5) Prior thoracic radiotherapy: Annually after 25 years or 8-10 years after RT. For Normal Risk Patients screening is done yearly for patients above 40 years of age [7]. View by Craniocaudal (CC) and the mediolateral oblique (MLO) are the two important views used for screening mammography. The MLO view is used for imaging the outer and upper quadrant and axillary tail. This view will cover the maximum volume of breast tissue. For proper visualization of breast in the medial aspect MLO view is obtained. This view allows greater compression of breast than MLO view.[10]

For abnormal findings such like mass in breast with nipple discharge diagnostic mammography are used. For exact location of the abnormality CC view is used along with 90 degree lateral view. Mammographic abnormality which is obscured by the tissues are covered above with compression device. Specific mammographic features which suggest breast carcinoma diagnosis of breast cancer are a) A Mass which is solid with presence or absence of stellate features. b) Thickening of breast tissue is not symmetrical c) Clustered micro calcifications.d) Suspicious lesion with fine stippled calcium are more in favour of breast cancer. It is an important sign of cancer in younger females who don’t have any other abnormality.

Mammography is used for early breast cancer detection which provides a true positive rate of 90%. In Xero mammography techniques image is obtained on a

Xerography plate that gives mostly positive image. Digital mammography is developed to allow observer to manipulate the degree of contrast in the image which is useful in women with dense breast and women less than 50 yrs of age. Digital and screen film mammography had similar accuracy rate [13].

Breast imaging reporting and data system (BI-RADS) was deviced to standardized mammographic terminology which facilitates outcome monitoring and reduce confusing interpretations. BI-RADS uses a standardized lexicon to facilitate the uniformity of mammographic reports from different radiology facilities .The standardized mammography report also includes an overall assessment of the probability of malignancy that is incorporated in an impression at end of every mammographic report. There are six assessment categories each associated with the management recommendation.

Only BI-RADS categories 1, 2 and 0 should be used for screening mammograms.

BI-RADS category “0” - “incomplete assessment ’’- identifies cases in which additional images is needed before a final assessment can be need. Once the additional imaging is accomplished the cases assigned one of the six “final assessment” categories .The inclusion of final assessment in the impression of every mammography report eliminates equi vocation by the interpreter .The final assessment also facilitates the follow-up and tracking of patients, because each final assessment category is associated with one specific follow-up

recommendation. Mammography, ultrasound breast and MRI are now included in BI-RADS (2003) new edition [12].

Mammography: Final assessment categories

Category 1: Assessment is negative

Description and recommendation- Routine Screening is recommended.

Category 2: Benign finding

Routine screening is recommended .This is a definitely benign finding.

Category 3: Probably benign finding

Very high probability of benignity, therefore short term followup is recommended to establish stability.

Category 4: Abnormality which looks doubtful

Malignancy probability is reasonable but not characteristic. Biopsy should be considered.

Category 5: Malignancy is highly suggested

Proper action should be taken as probability of malignancy is very high

Category 6: Known Cancer. Appropriate action should be taken.

FIG: MAMMOGRAPHY – CRANIO-CAUDAL VIEW

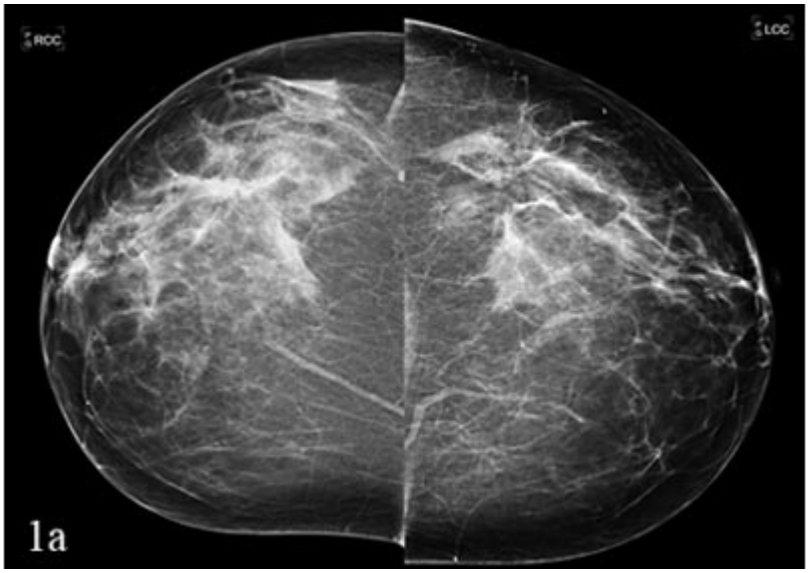
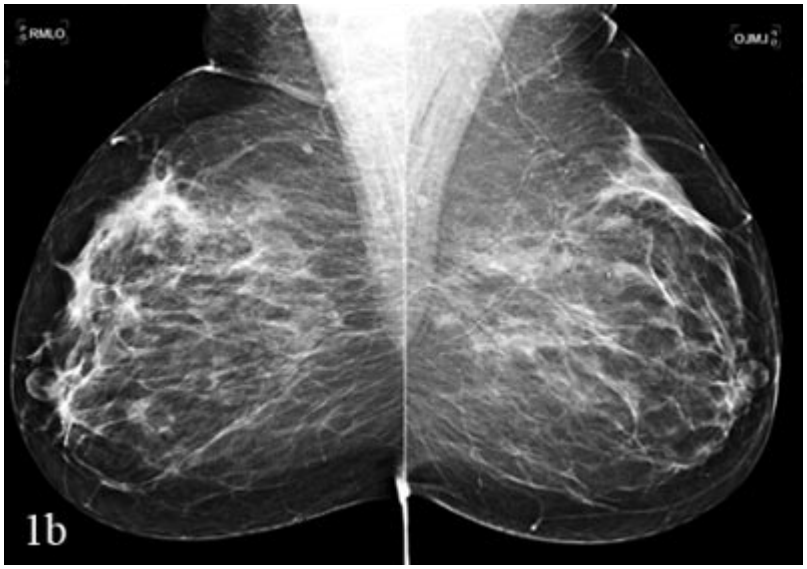


FIG: MAMMOGRAPHY MEDIOLATERAL OBLIQUE VIEW



Ductography :

Ductography are done when there is a nipple discharge which is a fluid that contains blood. Mammography is done after injecting a contrast media which is radiopaque into one of the major ducts.

Blunt cannula of small size is inserted into the nipple ampulla after the duct is gently enlarged with a dilator. CC and MLO mammographic views are obtained after injecting 0.2ml of contrast media which is dilute. Small filling defects obtained after injection of contrast media is suggestive of intraductal papillomas. Breast carcinoma may appear as multiple intra luminal filling defects or as irregular masses [2].

ULTRASOUND

It is the imaging modality of choice in young women with dense breasts. It is done to resolve equivocal mammographic findings. It defines Cyst masses and Demonstrate echogenic qualities of solid abnormalities. Benign Breast mass appears as smooth contours with oval or round shape with echoes internally and well-defined posterior and anterior margins.CA Breast has walls that are irregular but smooth margin may also be seen along with acoustic enhancement. Ultrasound does not detect lesions less than 1 cm diameter.

MAGNETIC RESONANCE IMAGING

Breast cancer when diagnosised by MRI is low in probability in conditions where there are negative findings in both mammography and physical examination.MRI is useful in Screening high risk women and contralateral breast in newly diagnosed breast cancer. It is more sensitive than mammogram to assess the response after neoadjuvant chemotherapy and plan Breast conservation surgery. It differentiates scarring from recurrence. It is useful in patients when axillary lymph node is positive for adenocarcinoma or Paget's disease present without a primary in clinical examination or other imaging [12].

METASTATIC WORKUP

- X-ray Chest
- Ultra-sound Abdomen
- CT Scan chest
- Skeletal survey/Bone scan

X-ray chest:

It is done to rule out pleural effusion, Lung involvement or erosion of Rib.

Ultra-sound Abdomen:

Ultra-sound Abdomen is done to rule out involvement of liver, presence of Ascites, Kruckenberg tumor and pleural effusion.

CT Scan chest:

It is done when there is doubtful lesion on X ray chest or when chest wall involvement suspected. CT scan can pick up internal mammary nodes, small lung, liver and brain metastasis.

Skeletal survey:

Skeletal survey includes X ray Skull AP & Lateral , X ray spine of dorsolumbar and X ray cervical spine and X ray pelvis .

Bone scan:

Indications are T3, T4 lesions, when there is bone pain and Elevated Alkaline phosphates.

INVESTIGATIONS FOR PROGNOSTIC/PREDICTIVE FACTORS:

- **Prognostic:** Sentinel lymph node biopsy
- **Predictive :** ER/PR status,Her2 neu status

Sentinel Lymph Node Biopsy:

Sentinel Lymph Node is the first node encountered by the tumour cells as they metastasize to the axilla. It is a representative of entire axillary basin. Biopsy of sentinel lymph node is indicated to know the axillary lymph node status in clinically negative lymph nodes **with** T1 or T2 primary breast cancer [20].

Technique: Vital blue dye or radio-labelled colloid injected into the parenchyma and measured with lymphoscintigraphy with gamma camera. It provides same staging information with more accuracy and less morbidity.

Indications:

It is indicated in breast cancer in early stage without palpable nodes. When a previous exicisional biopsy done. And also useful in multifocal tumours confined to one quadrant [21].

Hormone Receptor levels:

Estrogen and progesterone levels should be determined in breast carcinoma because these hormonal levels predict response to hormone therapy.Better prognosis is seen in tumors with Estrogen receptor positive tumors than tumors of negative estrogen receptor. Estrogen and progesterone receptor levels may be determined by a competitive binding assay to measure cytosol receptor levels or by immunohisto chemical assay where a monoclonal antibody binds to the receptor.

Molecular markers also play a role in determining the prognosis of the breast cancer.HER-2neu is a transmembrane protein which is involved in regulation and control of cellular growth. Over expression of HER-2neu is an independent predictor of poor prognosis in CA breast patients. It is also a predictor of favourable response to chemotherapy in node positive breast cancer patients.

The density of neovascularization and the occurrence of cathepsin D, myc, ras and p53 are also measured in specimens of breast tumors. Measurements of S phase fraction and the proliferation marker Ki-67 which is used to estimate the growth rate of malignant tumors.DNA content of tumor cells measured by flow cytometry also correlates with prognosis [16].

STAGING OF BREAST CANCER:

Staging place an integral role in the management of breast cancer .Breast cancer staging is used to determine the extent of the disease, predict survival overall and provide guidance for therapy. Epidemiologists and public health researches rely on breast cancer staging methods to evaluate trends in breast cancer incidence, screening programs, treatment outcomes and risk factors worldwide. Staging also place an integral part in advances in breast cancer research and in the application of basic science to clinical science [15].

Evolution of staging system:

Early staging systems for breast cancer were based on feasibility of operative intervention. Tumors where classified as either operable or inoperable. In 1905 German Physician Steinthal recommended three different classifications for breast cancer. This classification was based on clinical factors that were considered as important in predicting prognosis. Primary Tumor size was included in this primitive staging scheme. In 1928 Lee and Stubenbord included an index of the

rate of tumor growth in the staging scheme. This method was the first to attempt assessment of biology of individual tumors and their potential for progression. In 1940 four stage MANCHESTER classification was introduced it permitted staging based on clinical criteria, the extent of local involvement by the primary tumor, the presence of mobile axillary lymph node which is palpable and metastasis in distant organ. Disadvantage of this classification is it neither includes pathologic information nor tumor size.

Manchester System

Stage I:

The tumor is confined to the breast. Involvement of the skin may be present, provided the area is small in relation to the size of the breast

Stage II:

The tumor does not extend beyond breast and presence of lymph nodes in the axilla.

Stage III:

Tumor extension beyond the breast is demonstrated by the following:

a) Invasion, fixation or ulceration of skin of a large area in relation to the size of the breast.

b) Fixity of tumor to deeper structures like muscle, fascia and presence of mobile axillary nodes.

Stage IV:

The tumor extension beyond the breast is characterized by the following

a) Fixation or matting of the axillary nodes

b) Fixity of tumor to chest wall

c) Presence of metastasis in supraclavicular nodes or in the contralateral breast

d) Satellite nodules or distant metastases

In 1943 PORTMANN described a staging system that included clinical, pathologic and radiographic characteristic of breast cancer .This classification included skin involvement,the location and mobility of the primary tumor and extent of local and distant metastases.

Portmann Classification

Stage I:

Skin- not involved

Tumor-localized to breast, mobile

Metastases-none

Stage II:

Absence of skin involvement.

Tumor-confined to breast, mobile

Presence of Metastasis in axillary node evaluated by microscopic examination.

Stage III:

Edema of skin, brawny red induration and inflammation which is not caused by infection, extensive ulceration, multiple secondary nodules.

Diffuse infiltration of breast with tumor, fixity of tumor to chest wall, Breast edema and secondary tumors.

Metastasis in axillary lymph node which is fixed with absence of distant metastasis clinically or roentgenologically.

Stage IV:

Skin-involved or not involved

Tumor-localized or diffuse

Metastasis in both axillary and supraclavicular lymph nodes with presence of distant metastasis clinically or roentgenologic evidence of more distant metastases.

Columbia Clinical Classification :

Stage A:

Absence of involvement of skin, fixation of tumor to chest wall or non palpable axillary node.

Stage B:

Absence of either involvement of skin or fixity of tumor to chest wall with axillary node palpable not more than 2.5 cm and mobile.

Stage C:

Signs of advanced breast carcinoma which are considered as grave are:

1) Edema of skin not involving more than one third of skin overlying the breast

2) Ulceration of skin

3) Fixity of tumor to chest wall

4) Presence of involvement of axillary node more than 2.5 cm in size.

5) Axillary nodes fixed to skin or underlying structures.

Stage D:

Signs of advanced breast carcinoma includes:

1) Out of five grave signs any two signs should be present as given in stage C.

2) Involvement of skin more than one third of skin which overlies the breast.

3) Satellite skin nodules

4) Carcinoma of inflammatory type

5) Presence of supraclavicular node involvement.

6) Metastasis in internal mammary node by presence of parasternal tumour

7) Involvement of edema of arm

8) Metastases in distant organ

Columbia clinical classification:

Four stages were defined .Staging included physical examination and roentgenographic information.Tumor size and pathologic data was not included in

this staging. Based on five “grave signs “ staging was done.It includes 1)skin edema of Breast skin 2) skin overlying breast ulcerated 3)fixity of tumor to chest wall 4) fixity of node to skin or deep tissue 5)node of axillary group more than 2.5cm. Stage A and B were considered as operable cancers.Stage C were considered as locally advanced cancer.Stage D tumors were considered as inoperable tumors.

TNM SYSTEM:

Pierre Denoix introduced TNM System in 1940 which represented to classify cancer based on morphologic patterns of malignant tumors which influenced prognosis such as size of the primary tumor (T), presence and extent of regional lymph node involvement (N), and presence of distant metastases (M).

TNM System was originally conceived to be a simple system that would classify patients into various groups each with the different survival rate and prognosis.

Currently the most popular staging system is the TNM System based on AJCC sponsored by the American college of society and American college of surgeons.

Staging system currently requires confirmation by microscopy and typing of tumor by histology before doing any stage classification. Any patient with documented breast cancer may then be staged by clinical or pathological criteria (Designated by “c” prefix or “p” prefix).Diagnostic staging requires complete clinical examination

with assessment of same side or opposite side neoplastic involvement of skin, breast tissue, muscle and lymph nodes.

The microscopic diagnosis of breast cancer must be confirmed by examination of breast tissue. Routine laboratory examinations, chest X-ray and bilateral mammograms are also recommended.

Specific Stages:

T Stage (Tumor Size) :

Clinical tumors stage is the size of the tumor reported in centimeters based on physical examination and various imaging modalities. The pathologic T stage is based on tumor size on the final pathologic specimen measuring only the invasive component.

N Stage:

Staging of clinical node depends on physiological and radiological examination which includes CT and ultrasound and not including lymphoseintigraphy. Metastases to ipsilateral supraclavicular lymph node disease were considered to have prognosis similar to that for patients with distant disease.

Staging of lymph node pathologically depends on biopsy of sentinel lymph node or dissection of axillary node completely.

M Stage:

Metastasis in distant organs is M_1 disease. Supraclavicular lymph node diseases on same side is not considered as distant metastasis, but included in locally advanced disease. Metastatic disease is evidenced by physical examination and clinical history. Imaging modalities may or may not be included.

AJCC primary tumor (T) classification for breast cancer:

TX : Assessment of Primary tumor cannot be done

T0 : No evidence of primary tumor

Tis : Carcinoma in situ

Tis(DCIS): Ductal carcinoma in situ

Tis(LCIS) : Lobular carcinoma in situ

Tis(Paget's) : Paget's disease of the nipple Not associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma.Carcinomas in parenchyma of breast associated with Paget's disease are categorized based on the size and characteristics of the parenchymal disease.

T4: Direct extension of tumor to skin or chest wall. Tumor can be of any size.

Note: Skin involvement alone cannot be considered as T4.

T4a: Tumor extending to chest wall but invasion of pectoralis muscle not included.

T4b: Edema (including peau d'orange) or Ulceration of skin or satellite nodules ipsilaterally which are not the criteria for inflammatory carcinoma.

T4c: Both T4a and T4b

T4 d: Inflammatory carcinoma

TNM- Nodal Status, Clinical:

Nx: Assessment of Regional Lymph nodes cannot be done.

No: No metastasis in regional lymph node

N1: Metastases in axillary node level I and II of same side which is mobile

TNM- Nodal Status, Clinical:

N2: **N2a**: Axillary node level I and II on same side matted to each other or with adjacent structure.

N2b: Absence of axillary node involvement in presence of clinically palpable same side internal mammary node.

Nodal Status- Pathological:

pNx: Assessment of Regional lymph nodes cannot be done.(e.g.,Nodes when removed previously for pathologic study)

pN0: No regional lymph node metastasis histologically

Note: Small clusters of cells not more than 0.2 mm are known as isolated tumor cell clusters. It also includes single tumor cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or

by immunohistochemical(IHC) methods. ITCs containing nodes are not included in the total positive node count for purpose of N classification but should be included in the total number of nodes evaluated.

pN0(i-) : No regional lymph node metastasis histologically,negative IHC.

pN0(l+) : Regional lymph node contains Malignant cells in not more than 0.2 mm(detected by H&E or IHC including ITC)

pN0(mol-) : No metastases in regional lymph node

pN0 (mol +): Positive molecular findings (RT-PCR), but no metastasis in regional lymph nodes detected by histology or IHC

Classification is based on whether axillary lymph node dissection done or not

pN1: Micrometastases or metastases in 1-3 axilliary lymph nodes and /or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected

pN1mi: Micrometastases(greater than 0.2 mm and/or more than 200 cells but none greater than 2.0mm)

pN1a: Metastases in 1-3 axilliary lymph nodes, at least one metastasis greater than 2.0mm

pN1 b: Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected

pN1 c: Metastases in internal mammary lymph nodes which are detected on clinical examination in the absence of axillary lymph node or presence of metastases in axillary lymph nodes of 1-3 .

pN2: Metastases in 1-3 axillary lymph nodes or in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastases.

pN2 a: Axillary lymph node metastasis in 4-9 nodes. One tumor deposit should be more than 0.2 mm.

pN2b : Internal mammary lymph node metastasis detected clinically with absence of metastasis in axillary lymph node.

pN3 : Metastases in axillary lymph nodes in ten or more or infraclavicular (level III axillary) lymph node metastasis or same side internal mammary node detected clinically. In presence of one or more axillary lymph node involvement or more than three axillary lymph node with sentinel lymph node detected micro or macro metastasis.

pN3 a: Metastases in ten or more axillary lymph nodes (at least one tumor deposit greater than 2.0mm) or metastases to the infraclavicular (level III axillary lymph) nodes

pN3 b: Axillary lymph node metastasis in more than ten nodes. Deposit in one tumor more than 2mm or involvement of infraclavicular node.

pN3c: Supraclavicular lymph nodes metastasis on same side.

TNM-Metastasis:

Distant Metastasis (M)

M0: Distant metastases not evident by clinical or radiological.

cM0(l+): Absence of distant metastasis by clinical or radiographic evidence but tumor cells shows deposits microscopically in blood or bone marrow or involvement of nodes that are not regional lymph node and should not be more than 0.2 mm.

M1: Distant detectable metastases are determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

STAGING:

Stage 0	**Tis**	**N_0**	**M_0**
Stage IA	**T_1**	**N_0**	**M_0**
Stage IB	**T_0**	**N_1**	**M_0**
	T_1	**N_1**	**M_0**
Stage II A	**T_0**	**N_1**	**M_0**
	T_1	**N_1**	**M_0**
	T_2	**N_0**	**M_0**
Stage II B	**T_2**	**N_1**	**M_0**
	T_3	**N_0**	**M_0**
Stage III A	**T_0**	**N_2**	**M_0**
	T_1	**N_2**	**M_0**
	T_2	**N_2**	**M_0**
	T_3	**N_1**	**M_0**
	T_3	**N_2**	**M_0**
Stage III B	**T_4**	**N_0**	**M_0**
	T_4	**N_1**	**M_0**

	T_4	**N_2**	**M_0**
Stage III C	**Any T**	**N_3**	**M_0**
Stage IV	**Any T**	**Any N**	**M_1**

There are five stage grouping (0,I,II,III AND IV) in the new TNM staging system. Stage 0 refers to preinvasive cancers that are (carcinoma in situ) which means the tumor has not penetrated the basement membrane of the lobule or duct. These tumors have an excellent prognosis as there are no regional or distant metastases in this stage. Tumor belonging to Stage I are micrometastatic.

Stage II A and Stage II B include tumors with regional lymph node metastases and therefore carry a worse prognosis. Stage III A , Stage III B and Stage III C includes tumors that are locally advanced hence these tumors also have a worse prognosis. Stage IV refers to distant systemic spread of the disease which also has a worst prognosis.

Histologic Grade

GX	Assessment of Grade cannot be done.
G1	Low combined histologicgrade (favourable)
G2	Intermediate combined histologicgrade(moderate favourable)
G3	High combined histologic grade (unfavourable)

This grading is based on Nottingham combined histologic grade. The grade G of the tumor is designated based on the morphologic features of primary tumor which includes mitotic count, pleomorphism of nuclei and formation of tubule.

Overview of Breast Cancer:

Insitu Breast Cancer (Stage 0)- Both DCIS AND LCIS are indistinguishable from atypical hyperplasia or from early invasion of cancers. Mammography on both sides is done to find the extent of insitu carcinoma or a second cancer. Treatment options for LCIS are either observation, chemoprevention with tamoxifen and bilateral total mastectomy. This is for prevention or detection of the invasive cancer at an earlier stage as there is 25 to 35% risk of LCIS developing into invasive cancer.

Low grade DCIS which includes papillary, cribriform or solid which is not more than 0.5 cm in diameter can be managed by removal of lump alone, without radiation if margins resected are free of disease. DCIS that are not palpable are surgically resected under the guidance of localized needle technique.

Women with DCIS treated with mastectomy have recurrence locally and mortality rates less than 2%.When managed with removal of lump and adjuvant radio therapy recurrence rate is 9%.

Early Invasive Breast Cancer (Stage I, IIA or IIB):

Mastectomy with assessment of axillary lymph node status and breast conserving therapy are considered for patients with Stage I and II breast cancer. Axillary node dissection is considered when there is axillary lymph node shows metastatic disease. Breastconservation therapy is not indicated in multicentric disease, previous radiotherapy to either chest wall or breast, surgical margins involved and scleroderma.

Level I and II axillary nodes dissection are done in early invasive breast cancer. Sentinal lymph node dissection is done to evaluate the status of axillary lymph node in patients who have clinically negative lymph nodes.

Adjuvant chemotherapy is given for patients with node positive tumors or with patient tumor size more than one cm and patient with node negative cancer more than 0.5 cm. Tamoxifen therapy is given for patients with positive hormone

receptor cancers that are more than 1cm.Trastuzumab is the only HER/2neu targeted agent and can be used in metastatic and adjuvant setting. It is used for treatment of HER-2/neu, node positive tumor [22].

Advanced Local-Regional Breast Cancer (Stage III A or III B):

Stage III A OR III B are locally advanced breast carcinoma with absence of distant metastasis by clinical examination. Surgery is combined with radiationtherapy and chemotherapy for treatment of this tumor in order to provide local regional disease free survival. In some patient with Stage IIIA cancer downstaging of the tumor can be done by neoadjuvant chemotherapy and allow breast conserving surgery [2]. Ipsilateral breast tumor recurrence rate are more in patients with clinical N2 or N3 disease. In both Stage IIIA and III B disease surgery is followed by adjuvant radiationtherapy.

Distant Metastases (Stage IV):

Stage IV breast cancer cannot be cured by treatment but survival rate may be increased. Hormonal therapies are more preferred than cytotoxic chemotherapy because of minimal toxicity. Females with positive hormone receptor cancers are treated by hormonal therapy. Metastases to bone and soft tissue also treated by hormonal therapy.

Chemotherapy is given systemically for patients with hormone receptor negative cancers and metastatic cancer refractory to hormonal therapy.

Bisphosphonates may be given with chemo or hormonal therapy in women with bone metastases.

Local-Regional Recurrence:

Local-Regional breast cancer recurrence are divided into two groups those who have underwent mastectomy and those who underwent removal of lump. Women who have been treated previously with mastectomy undergo surgical resection of local recurrence with suitable reconstruction. Chemo and antiestrogen therapy is given if no radiotherapy is given to chest wall. Women who underwent lumpectomy should again undergo mastectomy with suitable reconstruction.

The 5 yr survival rate for patient with Stage I diseases 94%, Stage II A 85%, Stage IIB 70% ,Stage III A and IIIB 52 and 48% respectively. Stage IV tumor 18%.

Survival rate in breast cancer has significantly increased in the last two decades due to improvement in screening and local and systemic therapies.

Early detection of Breast Cancer:

A.Screening Programmes:

Screening program includes both mammographic and physical examination of female patients who are without symptoms identify about ten cancers per thousand above the age of 50 and about two cancer per thousand in females below age of

50.For maximum result in screening programs, mammographic and physical examination are necessary. Breast cancers at earlier stage can be found only by mammography in about 35-50% and by palpation another 40% can be found.

Abnormalities that are found by screening mammogram is malignant when biopsy is performed..Women aged 20-40 yrs should examine her breast regularly and routinely every 2-3 years. Annual breast examination must be done in females above 40 years [7].

The sensitivity of mammography varies from 60-90% which depends upon different factors including age of patient, tumor size, appearance and location of tumor by mammography. Mammography is more sensitive in older women than young females with dense breast and can detect malignancies up to 90 %.Tumors with absence of calcification and small in size is less likely to be detected in females with dense breast [10].

For non palpable abnormalities the rate of specificity of mammography is 30-40% for females below age 50 years and for clinically evident it is 85-90%.There is no doubt about beneficial effect in females aged 50-60 yrs who undergo screening and all clinical trials have confirmed it. The benefit of screening in women above 70 yrs is not conclusive.

B. Self-Examination:

There is no improvement in survival rate by self breast examination. The cancer society of America does not recommend monthly self breast examination at 20 yrs age. It recommends that patient should be made aware of BSE and about its benefit harm and its limits. The correct technique of performing BSE should be taught to women.

Patient who are in Premenopausal age group should do breast self examination should be done after eighth day of menstrual period. It should be done infront of a mirror with hands by side or above the head or press firmly on hips which contracts the muscle pectoralis causing dimpling or lump to become more prominent . Breast can also examined in supine position by palpation with opposite hand.

C. IMAGING:

Before a lump can be detected, Mammography is the most reliable method of detecting a breast cancer .Slow growing cancers can be detected by mammography atleast two years before reaching a size identified by palpation. Less than 0.4 cGy is delivered by flim screen mammography to midpoint of breast per view.

Digital mammography allows an easier method to maintain and review mammogram but it does not provide better images nor increased detection rates more than film mammography [7, 10].

Digital mammography are better in women with dense breast. Calcifications are more easily recognized mammographic abnormality.

Most common findings are clustered polymorphic microcalcifications which are atleast 5-8 in numbers and aggregrated in one part of the breast and differs from one another in shape and size mostly branched are VorY configuration.

Indications for mammography are a) To Screen females who are without symptoms and high risk for developing breast cancer at regular intervals b) Evaluation by Regular interval once in a year in each breast which as breast cancer that is potentially cureable. c) For evaluation of breast mass not well defined or suspicious lesion in breast d) to search in patients with axillary node metastasis in absence of primary tumor or primary not found.

e) For monitoring female with breast carcinoma treated already by radio therapy and surgery. f) For detection of opposite side breast in a postmastectomy patients.

Biopsy should be done inspite of mammography in patients with doubtful mass. Before biopsy mammography should be done so that areas which are doubtful can be identified and opposite breast can be evaluated.

Mammography is not an alternative for biopy as it does not show clinical cancer in breast which is very dense as seen in young women with fibrocystic changes and may not reveal medullary cancers.

For screening in women who are at increased risk of carcinoma of breast, MRI and Ultrasound may be used. The sensitivity of MRI is much higher than mammography but specificity is lower.MRI is useful in women with breast inplants to determine the character of a lesion present in the breast and to search for inplant rupture.

It is also helpful in patients who underwent lumpectomy and radiation. Positron Emission tomography may play a role in imaging atypical lesions but are less sensitive for early breast cancer.It is used mainly for evaluation of metastatic deposits.

MATERIALS AND METHODS

This study was carried out in 150 patients who were admitted in the department of general surgery, Government Rajaji Hospital, Madurai during the period from January 2011 to December 2012.

This Study which was undertaken was a prospective case series study and was started after getting due clearance from the institute of ethical committee, Government Rajaji Hospital, Madurai Medical College. Patients were included in this study after getting their informed written consent and they were assured that information obtained from them will be kept confidential.

Inclusion Criteria for patients in this study consist of patient of any age presenting with the lesion suspected of breast carcinoma and proved by FNAC and TRU-CUT biopsy and all relevant investigations to stage the disease like chest X-ray, ultrasound abdomen, liver function test, mammography and skeletal survey done for advanced cases to rule out metastasis.

Patients excluded where those who presented with symptoms of breast on clinical examination but on investigation there was no malignant pathology of breast and male patients with breast carcinoma excluded.

Patients data was collected in standardised proforma which included age, socio economic status, level of education, duration of symptoms, detection of lump by the patient or medical practitioner, into three class lower, middle and upper any previous visit to local doctor for this illness, any prior investigations performed and stage of tumor at time of presentation.

Socio economic status defined by kuppusamy scale was used in this study which was based on three major variables contributing to socio economic status which included education, occupation and income. Based on these three variables score given and socio economic status classified into five class.

- Score of 26-29-upper class
- Score 16-25-upper middle
- Score of 11-15 as lower middle
- Score of 5-10 as upper lower
- Less than 5- lower class.

In this study upper middle and lower middle combined as middle class and upper lower and lower combined as lower class. Hence in this study socioeconomic status classified into three class lower, middle and upper.

Literacy status classified into illiterate and educated which is further classified into primary (I-IV), secondary (High School and Higher Secondary) and higher education (Graduate and above).

People belonging to higher socio economic status or with higher education were not admitted in our hospital during the period of this study.

Definition for stage at diagnosis was based on classification for clinical staging of breast cancer outlined in American joint committee on cancer staging. Patients data collected were analyzed statistically.

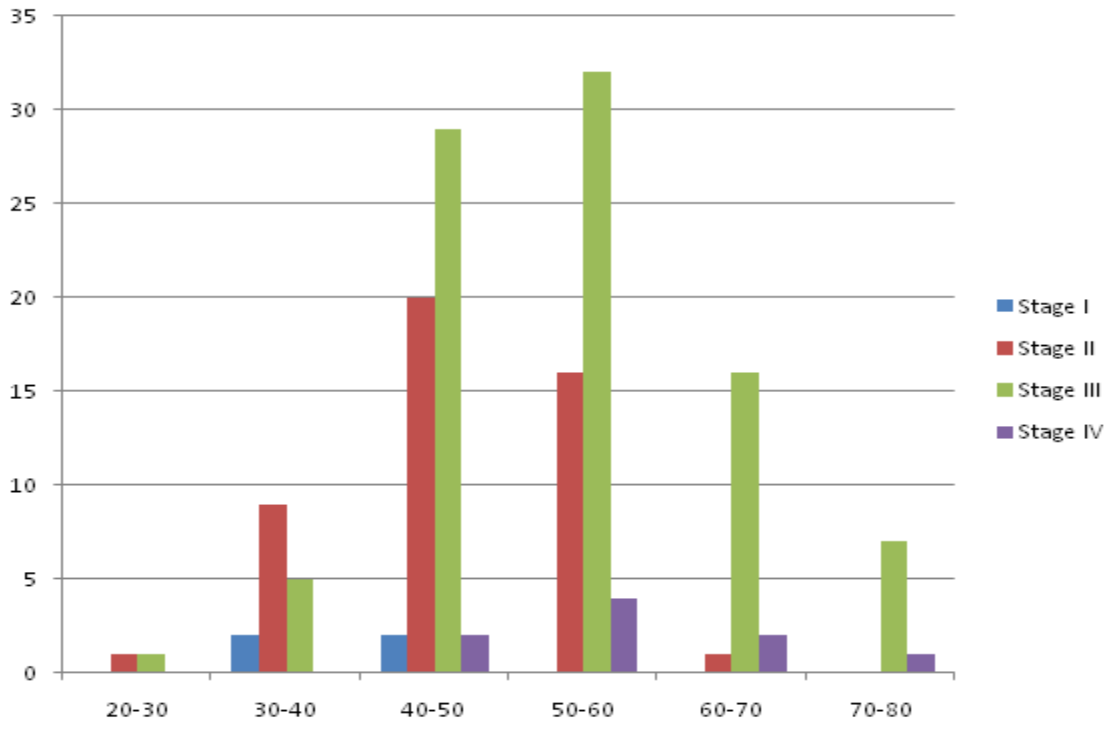
OBSERVATION AND RESULTS

The findings of the study can be tabulated as follows.

AGE DISTRIBUTION IN THE STUDY

Age in years	Stage I	Stage II	Stage III	Stage IV
20-30	**-**	**1**	**1**	**-**
30-40	**2**	**9**	**5**	**-**
40-50	**2**	**20**	**29**	**2**
50-60	**-**	**16**	**32**	**4**
60-70	**-**	**1**	**16**	**2**
70-80	**-**	**-**	**7**	**1**

AGE DISTRIBUTION IN THE STUDY



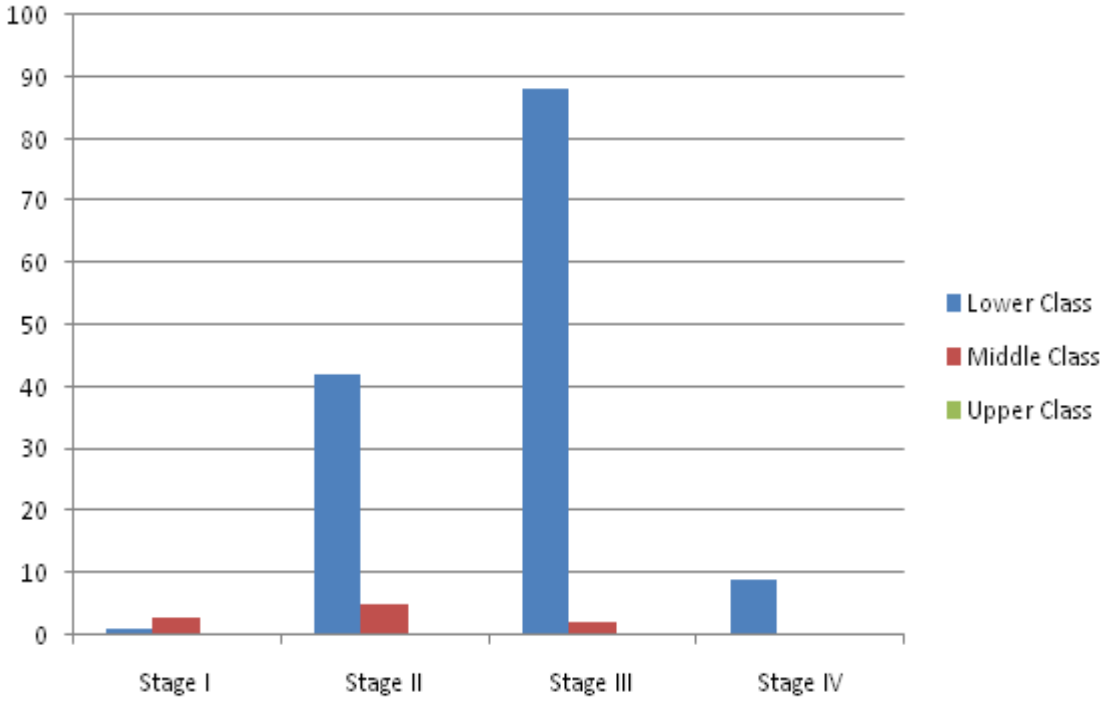
DISTRIBUTION OF STAGE OF TUMOR BASED ON SOCIO ECONOMIC STATUS OF PATIENT

Stage of the tumor	Lower Class	Middle Class	Upper Class
I	1	3	-
II	42	5	-
III	88	2	-
IV	9	-	-

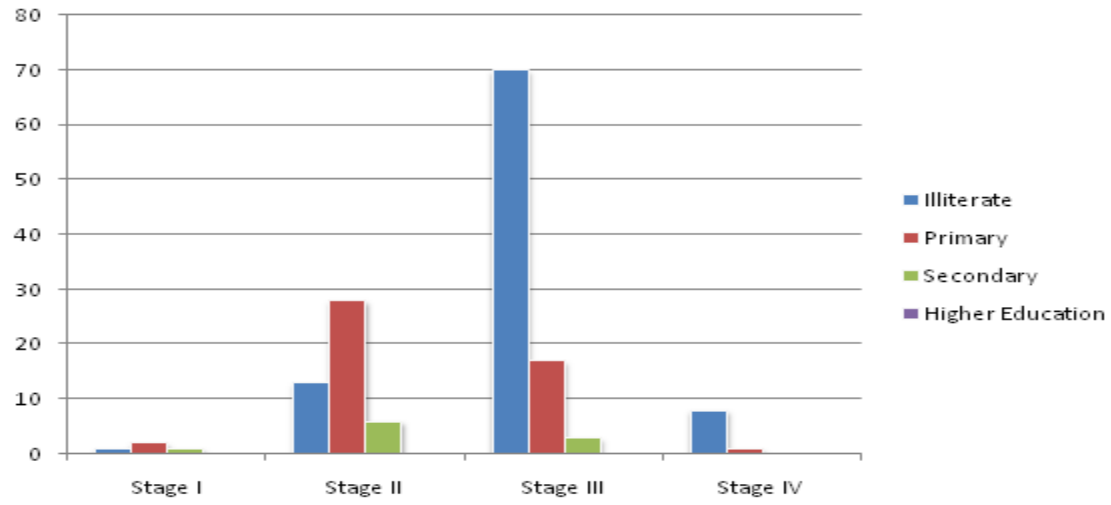
DISTRIBUTION OF STAGE OF TUMOR BASED ON LITERACY STATUS OF PATIENTS

Stage of tumor	Illiterate	Primary	Secondary	Higher Education
I	1	2	1	-
II	13	28	6	-
III	70	17	3	-
IV	8	1	-	-

DISTRIBUTION OF STAGE OF TUMOR BASED ON SOCIO ECONOMIC STATUS OF PATIENT



DISTRIBUTION OF STAGE OF TUMOR BASED ON LITERACY STATUS OF PATIENTS



DISTRIBUTION OF STAGE OF TUMOR BASED ON DURATION OF ILLNESS

Stage of tumor	< 3 mon	3-6 mon	6-12 mon	>12 mon
I	4	-	-	-
II	12	32	3	-
III	-	1	68	21
IV	-	-	3	6

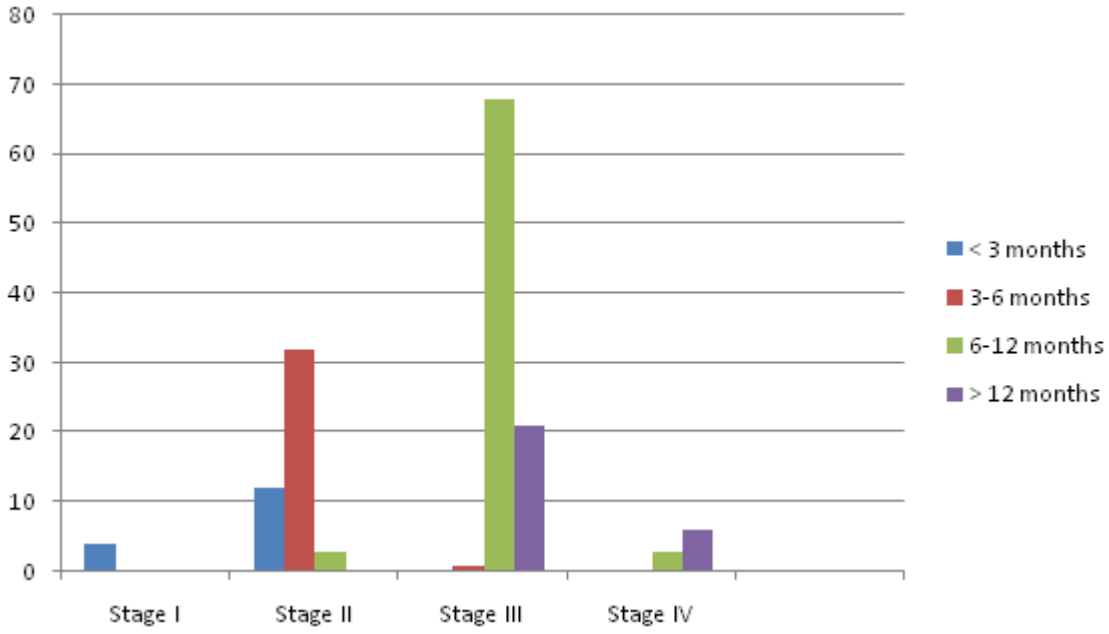
DISTRIBUTION OF DURATION OF ILLNESS ACCORDING TO LITERACY STATUS OF PATIENTS.

Literacy	< 3 mon	3-6 mon	6-12 mon	> 12 mon
Illiterate	2	12	55	23
Primary	10	20	13	5
Secondary	4	3	3	-
Higher Education	-	-	-	-

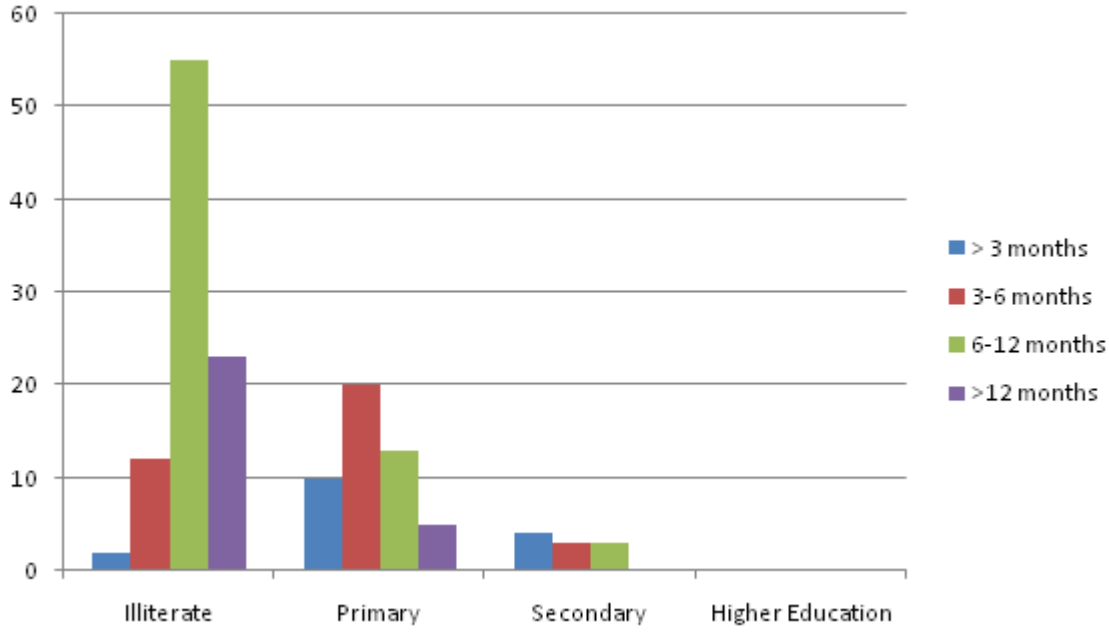
DISTRIBUTION OF DURATION OF ILLNESS ACCORDING TO SOCIO ECONOMIC STATUS OF PATIENTS.

Socio Economic Status	< 3 mon	3-6 mon	6-12 mon	>12 mon
Lower	11	30	71	28
Middle	5	4	1	-
Higher	-	-	-	-

DISTRIBUTION OF STAGE OF TUMOR BASED ON DURATION OF ILLNESS



DISTRIBUTION OF DURATION OF ILLNESS ACCORDING TO LITERACY STATUS OF PATIENTS.



DISTRIBUTION OF STAGE OF TUMOR ACCORDING TO DURATION OF SYMPTOMS IN ILLITERATE PATIENTS

Stage of tumor	< 3 mon	3-6 mon	6-12 mon	> 12 mon
I	1	-	-	-
II	1	10	2	-
III	-	2	50	18
IV	-	-	3	5

DISTRIBUTION OF STAGE OF TUMOR AND DURATION OF ILLNESS IN PATIENTS WITH PRIMARY EDUCATION

Stage of Tumor	< 3 mon	3-6 mon	6-12 mon	> 12 mon
I	2	-	-	-
II	8	20	-	-
III	-	-	13	4
IV	-	-	-	1

DISTRIBUTION OF STAGE OF TUMOR AND DURATION OF ILLNESS IN PATIENTS WITH SECONDARY EDUCATION

Stage of Tumor	< 3 mon	3-6 mon	6-12 mon	> 12 mon
I	1	-	-	-
II	3	3	-	-
III	-	-	3	-
IV	-	-	-	-

DISTRIBUTION OF STAGE OF TUMOR AND DURATION OF ILLNESS IN LOW SOCIO- ECONOMIC CLASS OF PATIENTS

Stage of Tumor	< 3 mon	3-6 mon	6-12 mon	> 12 mon
I	1	-	-	-
II	10	29	3	-
III	-	1	65	22
IV	-	-	3	6

DISTRIBUTION OF STAGE OF TUMOR AND DURATION OF SYMPTOMS IN MIDDLE CLASS PATIENTS

Stage of Tumor	< 3 mon	3-6 mon	6-12 mon	> 12 mon
I	3	-	-	-
II	2	3	-	-
III	-	1	1	-
IV	-	-	-	-

DISCUSSION

In our study 150 patients with breast cancer were studied over a period of two years from January 2011 to December 2012. Ca breast was found to be more common among females in the age group of 40-60 yrs (70%).

This compares favorably with studies done by Bibb and Sandha [46] in which maximum number of cases among African women and white women were around the age of 48yrs and 59 years respectively.

Out of 150 patients admitted, 4 patients (2.7%) presented in Stage I, 47 patients (31.3%) in Stage II, 90 patients (60 %) were in Stage III and 9 (6%) were in Stage IV. These results were not too dissimilar from a study done by Faisal Bilal Lodhi[55] where 25% of patients presented in Stages I & II. 62.7% were in Stage III and 12% were in Stage IV.

Out of 150 patients 92 patients (61.3%) were illiterate,48(32%) were educated upto primary level,10 patients(6.7%) with secondary education.Out of 150 patients ,140 patients (93.3%) belonged to low socio economic status and 10 patients(6.7%) belonged to middle class.According to educational status out of 92 illiterate patients only one patient presented in stage I,13 patients(14.1%) presented in stage II ,70 patients (76.1%) in Stage III and 8 patients(8.7%) in Stage IV. out of 48 patients who were educated upto primary level only 2 patients(4.2%) presented in Stage I and 28 patients(58.3 %) presented in Stage II,17 patients(35.4%) presented

in Stage III and 1 patient(2.1%) presented in Stage IV. This is quite different from a study done by O'malley et al [56] where 30% of women with a low education presented with late stage disease.

Out of 140 patients belonging to a lower socio economic status only one patient presented in Stage I ,42 patients(30%) in Stage II 88 patients(62.9%) in Stage III ,9 patients(6.4%) in Stage IV. Out of 10 patients who belonged to middle class, 3 patients (30%) presented in Stage I, 5 patients (50%) in Stage II, 2 patients(20%) in Stage III. These results are dissimilar from a study done by Wanq ce where 25.4% of people from a low socioeconomic status presented in Stage III and Stage IV whereas 20.4% of people from a high socioeconomic status presented in a late Stage.

Out of 150 patients only 49 patients presented to hospital for treatment before 6 months of initiation of symptoms and the remaining 101 patients came to hospital for first visit only after 6 months of appearance of initial symptoms. Among 49 patients who presented before 6 months of symptoms, 4 patients were in Stage I, 44 patients in Stage II and 1 patient in Stage I. Among illiterate group 14 patients came for 1st visit before 6 months of initiation of symptoms 12 patients were in early Stage and 3 patients in late Stage of Cancer and 78 patients presented after 6 months of initiation of symptoms out of which 2 patients were in Stage II, 68 patients in Stage III and 8 patients in Stage IV.

Among patients who were educated upto primary level 30 patients came to hospital for 1st visit before 6 months from imitation of symptoms out of which 2 patients in Stage I and 28 patients in Stage II.18 patients came after 6 months of initiation of symptoms out of which 17 patients in Stage III and 1 patient in Stage IV.

Among patients who were educated upto secondary level 7 patients came to hospital before 6 months from initiation of symptoms, Out of which 1 patient in Stage I and 6 patients in Stage II .Only 3 patients came after 6 months of initiation of symptoms and were found to be in Stage III.

Out of 140 patients belonging to lower socio economic status 41 patients(29.3%) came to hospital for 1st visit before 6 months from appearance of symptoms.Among those 41 patients ,1 patient (2.4%)was found in Stage I,39 patients(95.1%) in Stage II and 1 (2.4%)patient in stage III.99 patients (70.7%) came after 6 months from apperance of symptoms out of which 3 patients (3.1%)in Stage II,87 patients(87.9%) in Stage III and 9 patients(9.1%) in Stage IV.

The results were more or less similar to the study done by Faisal Bilal Lodhi [55] who found that 64% of patients came after 6 months of symptom and out of it 60%found to be in advanced stage and only 4% in stage II.

Among 10 patients who were belonging to middle class,8 patients presented to hospital before 6 months from initiation of symptoms out of which 3 were found in Stage I,5 patients in Stage II and 1 patient in Stage III and only 1 patient came after 6 months of initiation of symptoms and was found to be Stage III.

Among 150 patients about 5 patients came with prior investigations which included FNAC and biopsy and they all belong to middle class and were educated.

Among 150 patients lump was detected by the patient itself by 148 patients and 2 were detected by a Medical Practitioner.

Out of 150 patients 51 patients (34%) presented in early stage of cancer and 99 patients(66%) presented in late stage of cancer.14 illiterate patients (15.2%) ,30 patients (62.5%) of primary education and 7 patients(70%) of secondary education presented in early stage and remaining 99 patients(66%) presented in advanced stage of cancer and among them 78 patients(84.8%) were illiterate,18 patients of primary education and 3 patients of secondarily educated presented in late stage of cancer. In 150 patients,43 patients (37%) of low socio economic status and 8 patients of middle class presented in early stage(Stage I and II) and the remaining 97 patients(69.3%) of low socio economic status and 2 patients belonging to middle class presented in late stage of cancer(Stage III and IV) .

Out of 150 patients only 49 patients presented to hospital before 6 months from initiation of symptoms. Patients who presented before 6 months were mostly found in early stage(Stage I and II) and patients presenting after 6 months of initiation of symptom were found to be in late stage (Stage III and IV).Patients delay in presentation was more in low socio economic patient and illiterate group and majority of this group presented in late stage of cancer. Therefore patients delay in presentation plays a major role in determining the stage of the tumor.

Patients delay in presentation is more in illiterate and low socioeconomic status than in educated and middle class due to lack of awareness, negligence and financial resources. This delay in presentation adversely influence the stage of diagnosis.

Impact of social inequality in cancer is not being given adeqate attention in this country. Lower and middle income group constitutes majority of population in our country. Hence socioeconomic study of cancer is important for preventive measures and therapeutic action plans.

Many studies on socioeconomic variation in western countries observed late stage presentation of cancer and decreased survival among poor population. Reasons are mostly due to lack of health insurance, lack of access to health care and lack of information about detection of cancer and treatment.

This study clearly display the necessity of early medical attention to symptoms of breast cancer by creating awareness about detection of breast cancer at earlier stage and there by improve the survival rate of patients with breast carcinoma.

Review of other Studies:

Studies have reported that likelihood of breast cancer survival can be influenced by socio economic and demographic factors such as income status(Boyd et al,1999,Thomson et al,2001) [39] and economically deprived(Macleod et al,2000)[48].

Women of low socio economic status with breast cancer have poor out comes than high socio economic status women. (Thomson et al 2001) [39]. Socio economic factors were considered as independent prognostic factors for the stage at diagnosis (Gentile-brevet et al 2008) [50].

Survival is affected by increased duration of symptoms among breast cancer patients (ARNDT et al 2003) [33]. Detecting new breast cancers in its earliest stages increases the probability of long term survival that is why early detection of disease is of utmost importance (HARVAHAN et al 2007) [51].

Low level of female literacy is often associated with poor access to health facilities and poor health awareness (kuman et al 1997).

women with low income were more likely to wait for a longer period of time following the onset of breast cancer symptoms before seeking medical treatment due to financial problem (Rabia ali et al 2008) [54].

In another study performed in 2003 it was found that patients who residing in low income neighbourhoods were significantly more likely to present in stage III or IV in comparison to patients who lived in neighbourhoods of higher income (33% vs 24% O'malley, Legloser, Shema and Cuest) [56].

Additionally O'malley et al 2003 found that women presenting with later stage disease were more likely to lie in low education (30%) and blue-collar neighbourhoods (29%) [56].

CONCLUSION

In our study among 150 patients 34% presented in early stage and 66% presented in late stage. Among the patients who presented in early stage :

- 15.2%belonged to Illiterate
- 62.5% belonged to patients educated upto primary level
- 70% of patients educated upto secondary level.

In remaining 66% who presented in advanced stage of cancer :

- 84.8%were Illiterate,
- 37.5% were primarily educated
- 30%were secondarily educated.

In 150 patients,30.7% of low socioeconomic status and 80% of Patients belonging to middle class presented in early stage(stage I and II)and remaining 69.3% of low socioeconomic status and 20%belonging to middle class presented in late stage (stage III and IV).

Patient of about 32.7% who presented before 6 months of initiation of symptom were found in early stage I and IIand patients of about 67.3% who presented after 6 months of initiation of symptom were found in late stage(stage III and IV).

About 62.5% of patients with primary education,70% of secondary education and 13.4% of illiterate patient presented before 6 months and were found in early stage I and II. and remaining 84.7% of illiterate,37.5% of primary education and 30% of secondary education presented after 6 months and found to be in stage III and IV. Only 29.2% of low socioeconomic status but 90% of middle class presented before 6 months and were found in stage I and II. Remaining 70% of low socioeconomic status and 10% of middle class presented after 6 months of initiation of symptom were found in stage III and IV.

In Our Study Patients who were educated upto primary and secondary level with middle income presented in early stage of breast cancer than patients who were illiterate with low socioeconomic status.

Majority of the patients belonging to low socioeconomic and illiterate group presented in advanced stage of breast cancer due to patient's negligence and lack of awareness about breast cancer.

Delayed presentation of female breast cancer has a strong and significant attribution to patient delay which will definitely have a worse impact on stage of breast cancer.

RECOMMENDATION:

Lower income group does not have adequate financial access to health care delivery system and also due to fear of loss of daily wages they neglect the symptoms and present to hospital only if the disease has become detrimental to her life.

Also in our country breast is considered to be a sexual identity for female and most of female patients hesitate to disclose to their family members and feel shy or embraced to consult a doctor. In addition to socioeconomic factors sociocultural factors also play an important barrier to early diagnosis of ca breast.

Hence targeted plans to increase breast cancer screening and treatment coverage in patients with lower socio economic status could reduce much of socio economic disparity in breast cancer diagnosis and treatment.

National health care programmes should be launched for public awareness and early detection of breast cancer by screening mammography in all above age of 40 yrs, and importance of regular self breast examination which can detect the lesion earlier which will provide a better survival and reduction in mortality rates due to breast cancer.

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PROFORMA

Name of the patient:

IP no:

Age:

Sex:

Address:

Occupation of the patient or Occupation of Patient's Husband or Guardian:

Family income per month:

Literacy Status:

Socio-Economic Status:

Chief Complaints:

1. **Lump**
2. **Pain**
3. **Discharge from nipple**
4. **Retraction of nipple**

Family History:

Menstrual History:

Marital History:

Parity and Feeding History:

Duration Of Symptoms:

Time Interval Between Appearance Of Symptoms and First Visit To Hospital:

Detection Of Lump by patient or medical practioner:

Any prior visit to local hospital or prior investigations:

Stage of tumor at time of admission:

Investigations:

1. **FNAC**
2. **Biopsy**
3. **Mammogram**
4. **Chest x-ray**
5. **Ultra sound breast**
6. **Ultra sound abdomen and pelvis**

7.CT chest

8.X-ray LS spine

9.X-ray Pelvis

10.X-ray Skull

KEY TO MASTER CHART

LITERACY STATUS.

I = ILLITERATE

P = PRIMARY EDUCATION

S = SECONDARY EDUCATION

HE = HIGHER EDUCATION

SOCIO -ECONOMIC STATUS(SES)

L = LOWER CLASS

M = MIDDLE CLASS

H = HIGHER CLASS

DS= DURATION OF SYMPTOMS IN MONTHS

MASTER CHART

SL.NO	NAME	I.P. NO	AGE	LITERACY	SES	DS	TNM	STAGE GROUPING
1	SHAILIA BEGAM	001223	43	p	L	8	T3 N1 M0	III
2	AANDAL	001245	60	I	L	10	T2 N2 M0	III
3	NACHIAR	001248	46	I	L	12	T3 N2 M0	III
4	SARASWATHY	001708	38	p	L	9	T3 N1 M0	III
5	JAYARANI	0021231	56	I	L	4	T2N0M0	II
6	JEYANTHI	002761	41	p	L	8	T3N1M0	III
7	MALLIGA	004791	56	I	L	9	T3N2M0	III
8	JANAKI	005471	62	I	L	7	T3N1M0	III
9	SELVI	006472	62	I	L	6	T3N1M0	III
10	MARIAMMAL	008710	45	p	L	12	T3N2M0	III
11	SARADHADEVI	008712	58	I	L	8	T2N2MO	III
12	VIJAYALAKSMI	009408	54	I	L	12	T4N1M0	III
13	AMUDHA	009935	38	p	L	4	T3NIM0	III
14	JEYA	0012156	46	I	L	8	T3N2M0	III
15	MEENAKSHI	0012426	46	I	L	8	T3N1M0	III
16	AMUDHAVALI	0012706	31	p	L	2	T2N0M0	II
17	VELLAMMAL	0012780	26	I	L	11	T3N2M0	III
18	VEDHAMMAL	0013534	45	I	L	7	T4N0M0	III
19	KANJANADEVI	0017220	36	S	M	2	T2N0M0	II

20	VIJAYA	0018766	59	I	L	9	T4N1M0	III
21	VENI	0020937	42	P	L	6	T3N2M0	III
22	ANNAKODI	0033722	48	I	L	4	T2N0M0	III
23	SUNDARAVALLI	0033899	46	P	L	8	T3N1M0	III
24	VIJI	0033995	47	I	L	9	T3N2M0	III
25	PIDARI	0035836	55	I	L	10	T4N1M0	III
26	JEYAPONNU	0043880	35	P	L	7	T3N1M0	III
27	SEENIAMMAL	0043976	70	I	L	11	T3N1M0	III
28	NAGASUNDARI	0044214	46	I	L	5	T3NIM0	III
29	MAHESWARI	0044375	46	I	L	24	T4N3M1	IV
30	MAYILU	0054369	29	P	L	4	T2N0M0	II
31	MUTHULAKSMI	0044358	46	P	L	2	T2N0M0	II
32	UMA	0044708	54	I	L	12	T4N3M1	IV
33	VEERAMMAL	0045213	62	I	L	12	T4N1M0	III
34	GANDHIMATHI	0045684	53	I	L	12	T4N2M0	III
35	LAKSHMI	0049055	31	P	L	2	T2N0M0	II
36	CHITRA	0049207	45	I	L	6	T3N1M0	III
37	PANDIMEENA	0050964	46	P	L	12	T3N2M0	III
38	MASILAMANI	0052615	45	I	L	12	T4N0M0	III
39	SAVITHRI	0052640	46	P	L	3	T2N0M0	II
40	BAGYAVATHI	0053147	35	I	L	9	T3N1M0	III
41	SHANTHI	0054261	38	P	L	5	T2N0M0	II
42	KASTHURI	0053022	63	I	L	6	T3N1M0	III

43	MANORAMA	0046051	53	S	M	2	T2N0M0	II
44	PANDHANAM	0053261	37	I	L	10	T3N1M0	III
45	SABITHA	0054529	45	P	L	3	T2N0M0	II
46	KAVITHA	0054975	53	I	L	8	T3N2M0	III
47	DEVIKA	0055342	54	I	L	9	T3N2M0	III
48	LAKSMIRANI	0055510	46	S	L	6	T3N1M0	III
49	NAGARANI	0055761	45	P	L	2	T2N0M0	II
50	MUTHAYEE	0055741	43	I	L	12	T4N1M0	III
51	SHANTHA	0055196	49	P	M	1	T1N0M0	I
52	SARADHA	0055320	40	S	M	9	T3N1M0	III
53	ELAVARASI	0056874	51	I	L	8	T3N1M0	III
54	RANI	0056894	40	I	L	6	T3N1M0	III
55	LATHA	0056904	54	P	L	2	T2N0M0	II
56	MUTHUSELVI	0057218	35	S	M	3	T2N0M0	II
57	PANCHU	0056944	68	I	L	12	T4N1M0	III
58	CHINNATHAI	0057407	45	I	L	11	T3N2M0	III
59	SUSHEELA	0054731	53	I	L	5	T3N1M0	III
60	VARADHAMMA	0058741	69	I	L	7	T4N3M1	IV
61	SANMUGAYEE	0057870	70	I	L	12	T4N2M1	IV
62	MEENAKA	0058491	49	I	L	6	T3N1M0	III
63	KANCHARAM	0058431	62	I	L	12	T4N2M0	III
64	KAMALA	0058871	45	S	L	2	T2N0M0	II
65	PETCHIAMMAL	0059357	60	I	L	6	T3N1M0	III

66	CHITRADEVI	0059467	45	S	M	3	T2N0M0	II
67	CAUVERY	0059661	48	I	L	4	T3N1M0	III
68	GAYATHRI	0059944	51	P	L	3	T2N0M0	II
69	ALAMELU	0060186	70	I	L	5	T3N1M0	III
70	MURUGAMMAL	0060434	35	I	L	1	T1N0M0	I
71	NANDHINI	0060712	45	P	L	4	T2N0M0	II
72	ELAMMA	0060784	70	I	L	14	T4N2M0	III
73	MARY	0060434	35	P	M	1	T1N0M0	I
74	GANGA	0060812	59	I	L	7	T3N1M0	III
75	GOVINDHAMA	0060851	72	I	L	8	T3N1M0	III
76	PARVATHY	0061051	45	P	L	14	T4N1M0	III
77	KANI	0061218	45	P	L	3	T2N0M0	II
78	KAMATCHI	0061176	42	I	L	5	T3N1M0	III
79	DURGA	0061211	66	I	L	6	T3N1M0	III
80	POORNAM	0061920	45	S	M	1	T1N0M0	I
81	KANNAMMA	006193	53	I	L	12	T4N2M0	III
82	RUKMANI	00620009	48	I	L	8	T3N1M0	III
83	THILAGAM	0062114	58	P	L	12	T4N2M0	III
84	THILAGAVATHY	0062048	58	P	L	4	T2N0M0	II
85	PALANIAMMAL	0062121	45	I	L	4	T2N0M0	II
86	MEENAL	0062774	60	I	L	9	T3N1M0	III
87	SEETHA	0062567	50	P	L	2	T2N0M0	II
88	TAMILSELVI	0062891	31	P	L	3	T2N0M0	II

89	ARIYAKANI	0062567	63	I	L	7	T3N1M0	III
90	ESAKIAMMAL	0063217	66	I	L	8	T3N2M1	IV
91	VASANTHI	0063291	49	P	L	5	T2N0M0	II
92	MANIMEGALAI	0063875	55	I	L	3	T2N0M0	II
93	NILA	0063814	60	I	L	8	T3N1M0	III
94	VASANTHA	0063291	49	S	M	5	T3N1M0	III
95	RAJALAKSHMI	0063884	50	P	L	12	T4N3M1	IV
96	KALIAMMAL	0063891	60	I	L	11	T4N2M0	III
97	FATHIMA	0064213	45	P	L	5	T2N0M0	II
98	ANNAM	0064128	56	I	L	7	T3N1M0	III
99	VALLI	0064525	57	I	L	6	T3N1M0	III
100	ALIMABEEVI	0065586	42	P	L	3	T2N0M0	II
101	VIJAYARANI	0065803	52	I	L	5	T3N1M0	III
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104	SAROJA	0066160	58	I	L	3	T2N0M0	II
105	THENAMMAL	0066298	45	I	L	11	T4N2M0	III
106	PETCHI	0067508	50	I	L	12	T4N2M0	III
107	ANANTHI	0067561	35	I	L	6	T2N0M0	II
108	KANCHANA	0067606	66	I	L	7	T3N1M0	III
109	KASIRANI	0067790	65	I	L	8	T4N2M0	III
110	NISHABEGAM	0068994	49	I	L	24	T4N3M1	IV
111	SUBBAMMAL	0069768	54	P	L	6	T3N1M0	III

112	JAYALAKSMI	0070304	50	P	L	2	T2N0M0	II
113	SEEMA	0070304	46	I	L	4	T2N0M0	II
114	NAGAMMAL	0070963	64	I	L	16	T4N2M0	III
115	PRABAVATHY	0070970	42	P	L	4	T2N0M0	II
116	PREETHY	0070895	45	I	L	6	T3N1M0	III
117	DEVAGI	0071816	45	P	L	8	T3N2M0	III
118	IRULAYEE	0071188	53	I	L	6	T2N0M0	II
119	JOTHI	0071392	70	I	L	10	T4N2M0	III
120	THEDASELVAM	0072887	54	I	L	9	T4N3M1	III
121	POORNAM	0073102	50	I	L	18	T4N1M0	III
122	CHANDRA	0073130	45	S	M	3	T2N0M0	II
123	THILLAIAMMAL	0073147	51	I	L	12	T4N2M0	III
124	CHAKMADHA	0073226	53	I	L	8	T3N2M0	III
125	PAPPATHI	0073578	50	P	L	6	T2N0M0	II
126	KULANDAI	0073225	57	I	L	5	T2N0M0	II
127	MAYILAMMAL	0074060	50	I	L	12	T4N2M0	III
128	HAMEEDNISHA	0074061	56	I	L	9	T4N1M0	III
129	THANGAMMAL	0074164	70	I	L	15	T4N1M0	III
130	NALLAMMAL	0074165	55	I	L	9	T4N2M0	III
131	KAMALAM	0074939	48	P	L	5	T2N2M0	II
132	GANGAMMAL	0075282	45	I	L	11	T4N2M0	III
133	NEELA	0075155	48	P	L	4	T2N0M0	II
134	MEENAMMAL	0076197	65	I	L	4	T2N0M0	II

135	SUBBU	0076492	54	I	L	11	T4N2M0	III
136	VEERATHAI	0075012	48	I	L	8	T3N1M0	III
137	MUTHUMARI	0075512	55	P	L	2	T2N0M0	II
138	KARUPAYEE	0076281	38	I	L	3	T2N0M0	II
139	SUMATHI	0076190	52	I	L	5	T2N0M0	II
140	BINNIAMMAL	0076202	50	I	L	12	T4N2M0	III
141	OOCHAMMAL	0076234	50	P	L	5	T2N0M0	II
142	AADHAMMAL	002327	56	I	L	10	T4N1M0	III
143	PONNUPAPPA	0076512	38	I	L	2	T2N0M0	II
144	RAMAKKAL	0076197	46	P	L	4	T2N0M0	II
145	ALAGAMMAL	0077492	58	P	L	9	T4N2M0	III
146	RAHIMANISA	0077507	57	I	L	24	T4N3M1	IV
147	PUSHPAM	0077427	55	P	L	9	T4N2M0	III
148	KALI	0082583	50	P	L	5	T2N0M0	II
149	PREMA	0088967	54	I	L	12	T4N2M0	III
150	GNANATHAI	0075488	51	P	L	7	T3N1M0	III

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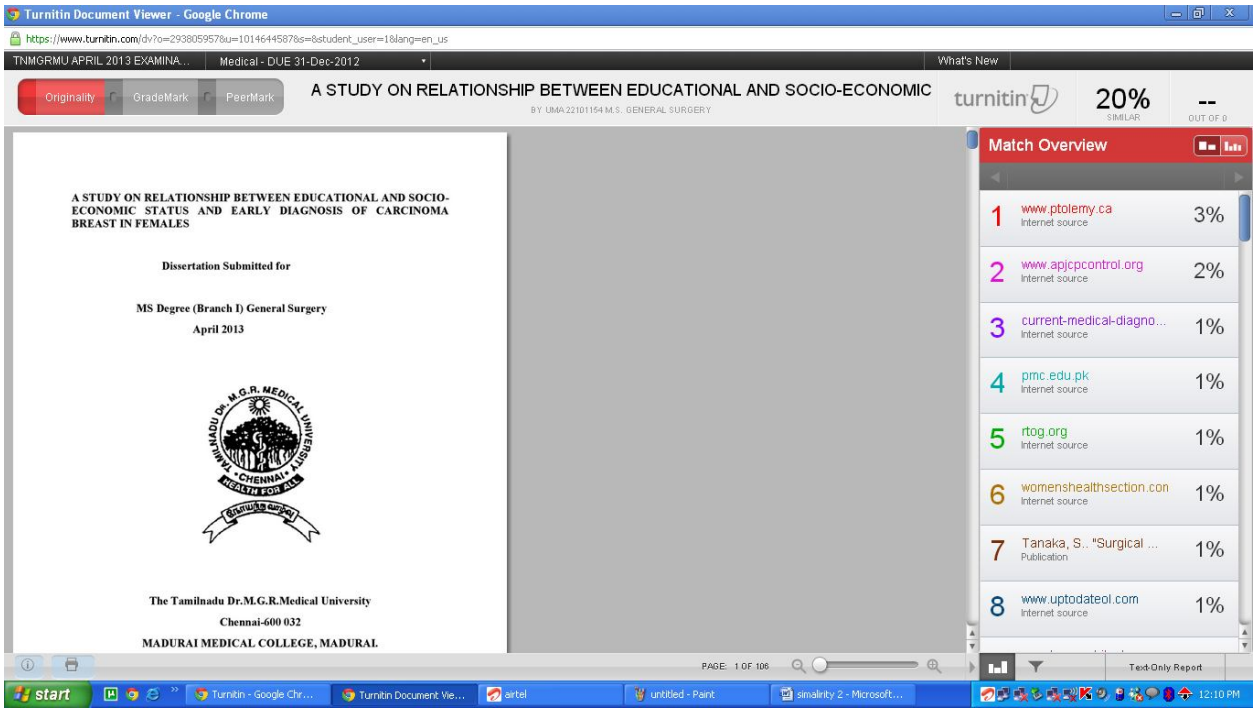
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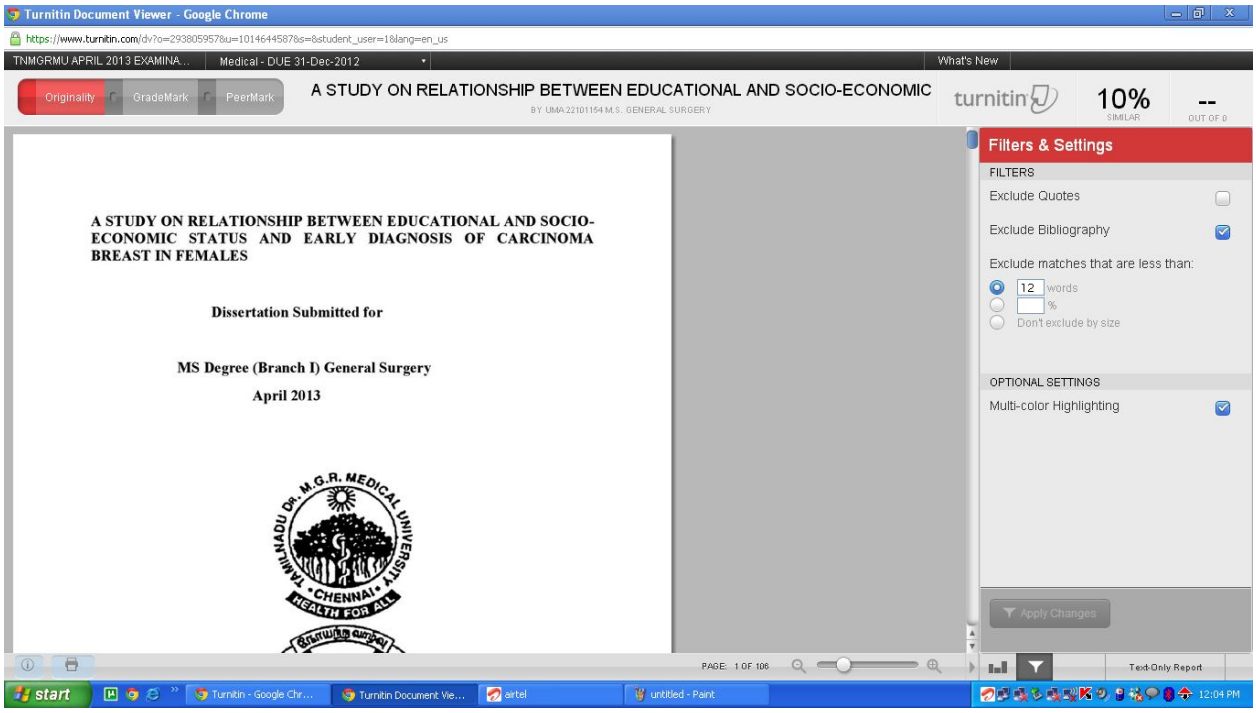
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