

**TO STUDY THE EFFECT OF ORMELOXIFENE IN THE
REGRESSION OF MASTALGIA & FIBROADENOMA**



Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment for the award of degree of

**MASTER OF SURGERY
IN
GENERAL SURGERY**

BRANCH -1

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**DEPARTEMENT OF GENERAL SURGERY
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MAY 2020

DECLARATION

I hereby declare that the dissertation entitled “**TO STUDY THE EFFECT OF ORMELOXIFENE IN THE REGRESSION OF MASTALGIA & FIBROADENOMA**”, was done by me in the Department of General surgery, Chengalpattu Medical College during the tenure of my course in M.S. General Surgery from march 2018 to march – 2019 under the guidance and supervision of **Dr. J. Selvaraj. M.S**, Professor, Department of General surgery, Chengalpattu Medical College.

This dissertation is submitted to The Tamilnadu Dr. MGR Medical University, Chennai-32 towards the partial fulfillment of the requirement for the award of M.S. Degree in General Surgery.

I have not submitted this dissertation on any previous occasion to any University for the award of any degree.

Place : Chengalpattu

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Dr. RADHLS

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This is to certify that the dissertation entitled “**TO STUDY THE EFFECT OF ORMELOXIFENE IN THE REGRESSION OF MASTALGIA & FIBROADENOMA**” is a record of bonafide work done by **Dr .S.RADHI** in the Department of General surgery, Chengalpattu Medical College, Chengalpattu during the tenure of his course in M.S. General Surgery from March – 2018 to march – 2019 under the supervision of **Dr. J. Selvaraj. M.S.**, Associate Professor, Department of General surgery and submitted in partial fulfillment of the requirements for the award of M.S. Degree in General Surgery by The Tamilnadu Dr. MGR Medical University, Chennai. This work has not previously formed the basis for the award of a degree or diploma.

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Principal Investigator : Dr.S.Radhi
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This is to certify that this dissertation work titled **“TO STUDY THE EFFECT OF ORMELOXIFENE IN THE REGRESSION OF MASTALGIA & FIBROADENOMA”** of the candidate **DR.S.RADHI** with registration Number **221711260** for the award of the degree of Master of Surgery in the branch of **M.S. GENERAL SURGERY – BRANCH I**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **3%** percentage of plagiarism in the dissertation.

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ABSTRACT

TO STUDY THE EFFECT OF ORMELOXIFENE IN THE REGRESSION OF MASTALGIA & FIBROADENOMA

Prospective Randomized control study to study the role of ormeloxifene in the regression of mastalgia and fibroadenoma, conducted in the department of General Surgery at Chengalpattu medical college, Chengalpattu.

BACKGROUND

Benign breast disease includes mastalgia, fibroadenoma, fibroadenomatous hyperplasia, fibrocystic disease, mastitis, sclerosing adenosis and breast abscess. Patients with benign breast disease often present with pain and swelling. They frequently visit the clinic for the complaints of pain and nodular swelling. Most of the benign breast disease are treated conservatively with medications and rarely surgery. There is no satisfactory treatment for these benign disease

My thesis topic is to study the effect of ormeloxifene in the regression of mastalgia & fibroadenoma. Ormeloxifene, also known as centchroman, is one of the selective estrogen receptor modulators, or SERMs, a class of medication which acts on the estrogen receptor. It is best known as a non-hormonal, nonsteroidal oral contraceptive

OBJECTIVES OF THE STUDY

1. To study the effect of Ormeloxifene in the regression of mastalgia & fibroadenoma
2. To study the time taken for the healing of benign breast diseases with the use of Ormeloxifene.

METHOD OF THE STUDY

Hundred patients in the department of General Surgery , with complaints of breast pain and lump are selected and randomly divided into two group. One group was treated with Ormeloxifene 30mg twice a wk for 12 wks and the other group with placebo such as vitamin tablets for 12 wks. The effect was assessed with pain scale , breast lump size with Lucknow –Cardiff scale and with Ultrasound breasts.

RESULTS

The patients who are treated with ormeloxifene for mastalgia and fibroadenoma shows pain relief and reduction in nodularity respectively.. 92% of mastalgia patients showed response to ormeloxifene ,whereas 80 % of nodularity reduced completely with ormeloxifene at the end of 12 weeks .

CONCLUSION

Ormeloxifene also known as centchroman , which is a selective estrogen receptor modulator was found to be effective in treating mastalgia and fibroadenoma.

INTRODUCTION

Most common benign breast disease in young females are Fibroadenoma and mastalgia . 15% palpable breast lump comes as fibroadenoma. Reproductive age group females frequently visit clinic with complaint of pain and lump in the breast. Fibroadenoma presents rarely over the age of 40-45yrs. Mastalgia may be cyclic or non-cyclic, intermittent or constant, localized or diffuse. Different pharmacological agents have been tried in the therapy of mastalgia and fibroadenoma. Ormeloxifene is a selective oestrogen receptor modulator with oestrogenic action on bones as well as antioestrogenic action on uterus and breast. Hence randomized control study conducted for the females attending Chengalpattu medical college hospital with c/o pain and lump in the breast. One group treated with Ormeloxifene 30mg twice weekly for 12 weeks, another group with vitamin tablets. Regression of symptoms of mastalgia and fibroadenoma is assessed using visual analog pain score and Lucknow Cardiff scale respectively

AIM AND OBJECTIVES

1. To assess the effect of ormeloxifene in the regression of fibroadenoma and mastalgia for those who are willing for the study.
2. To predict the time for the healing of diseases with the use of Ormeloxifene.

REVIEW OF LITERATURE

EPIDEMIOLOGY

Fibroadenoma(FA) is Benign breast diseases, due its high prevalence, fear of malignancy , it has its impacts on the quality of females life. Below 30 yrs old females, most common benign tumour is FA, It comes under Aberration in normal development and involution (ANDI). 15 % of all palpable breast lumps was FA. 20% of FA was multiple and bilateral. Etiology of fibroadenoma is endocrine abnormality, but their precise roles remains to be elucidated. FA has no modifiable risk factor.

Adult female admissions in india-8.1/1000

Surgical admissions- 6.4/1000

Total admission with bening breast disease-1.5/1000

EMBRYOLOGY OF THE BREAST

Breast is the modified sweat gland. At first on 5th or 6th weeks two ventral bands of ectoderm, form the mammary ridges / milk lines. It extend from axilla to inguinal region. Glandular tissue of the breast is formed by the epithelial / mesenchymal interactions. On 49th day, invagination of thoracic bud occurs and then involution of mammary lines takes place. 15 to 20 solid buds arises from thoracic ectodermal ingrowths , which forms lobes of alveoli and lactiferous ducts. Somatopleuric mesenchyme forms the connective tissue, vasculature , nerves and fat ¹

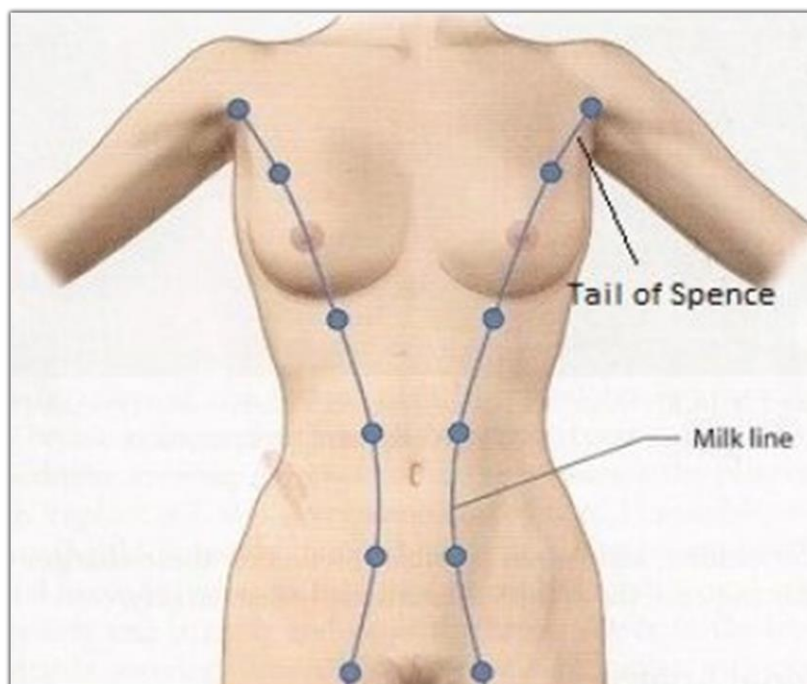
Nipple formation -56th day,

Primitive duct - 84th days,

Canalization -150th day.

During the last 2 months of gestational period, canalization of the lactiferous duct occurs. Mesenchymal proliferation forms the nipple.

The lactiferous tubules open at the small mammary pit developed by the epidermis.



CONGENITAL ANOMALY IN BREAST DEVELOPMENT

Amazia:

Nipple areola complex develops without breast tissue.

Amastia :

Absence of breast ,along with Nipple areola complex.

Athelia :

Congenital absence of nipple in single or both breast ,most commonly seen in accessory breast.

Inversion :

3% of female presents with inversion of this 85% are bilateral . Recurrent mastitis is caused by inversion of nipple.

Polymastia :

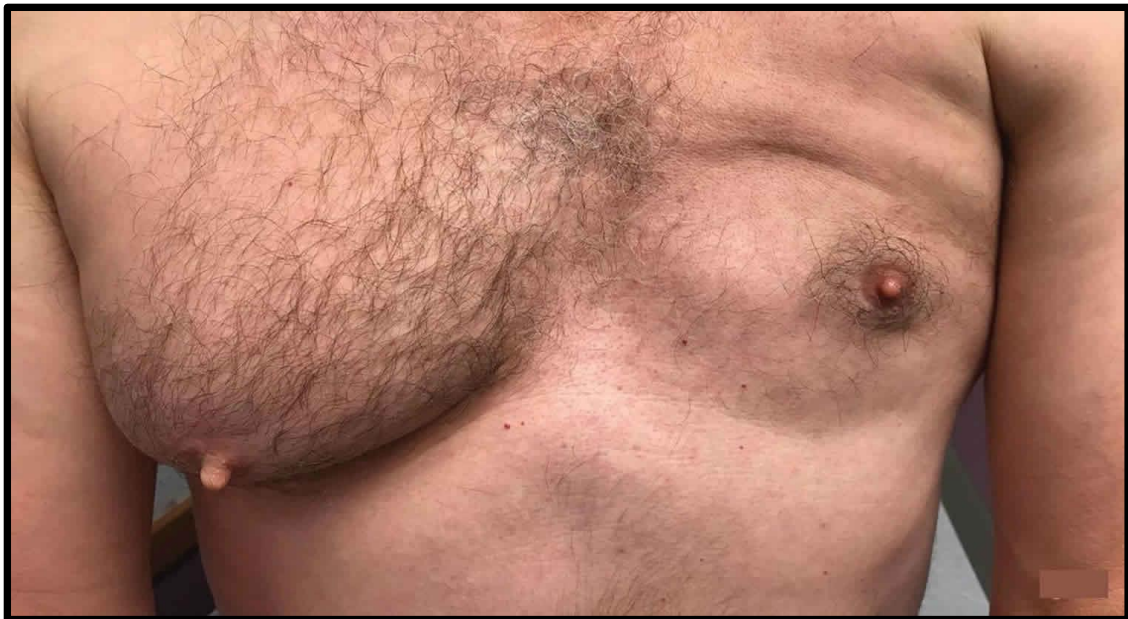
Condition of having additional breast , with or without nipples , or areola , supernumerary breast.

Polythelia :

Condition of having accessory nipples.

Poland's syndrome:

1. It is a congenital defect of the pectoralis major.
2. It is associated with various ipsilateral upper extremity anomalies
3. Homolateral breast hypoplasia .
4. Rib cage abnormalities ^{2,3}



BREAST ANATOMY

Breast lies in between subdermal layer of adipose tissue and superficial pectoral fascia.

Vertical extension- 2nd to 6th rib in the mid clavicular line.

Horizontal extension- side of sternum to mid axillary line.

Cooper's ligament – fibrous strands extends from dermis to pectoral fascia.

Pectoralis major, serratus anterior and external oblique muscles forms posterior structures. Lymphatics and vessels lies in retromammary space^{2,3}.

NIPPLE AREOLA COMPLEX:

It lacks hair and contains sweat and sebaceous glands which open directly and secrete oil from sebaceous gland, cause projections and named as Montgomery's tubercles, provides lubrication during lactation. Numerous melanocytes seen over NAC. Nipple contains numerous nerve endings, necessary for milk down reflex.

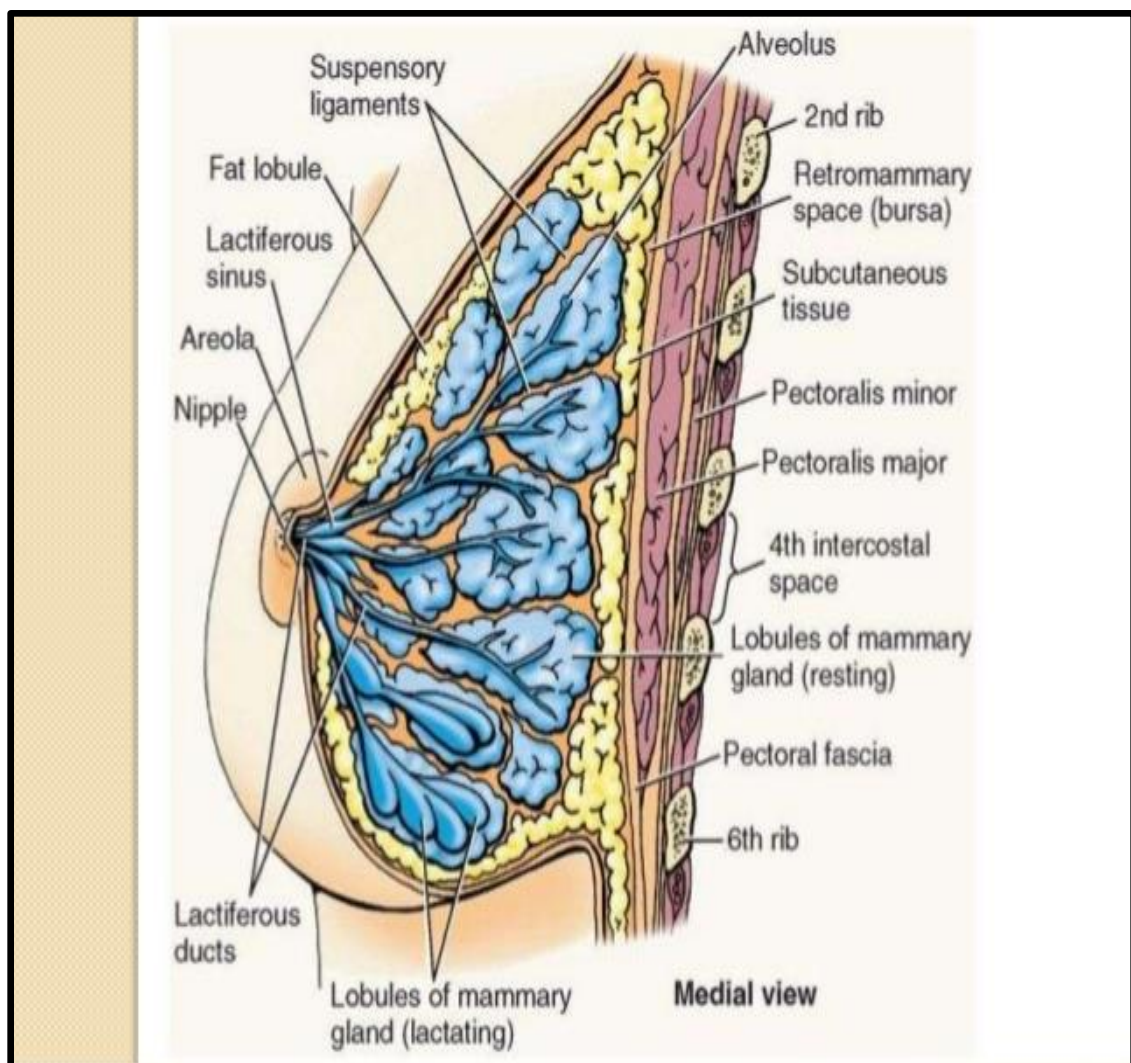
AXILLARY TAIL OF SPENCE:

Lateral extension of breast tissue through foramen of langer. Foramen of langer is a opening in a deep fascia. It crosses the anterior axillary fold.

MICROSCOPIC PICTURE:

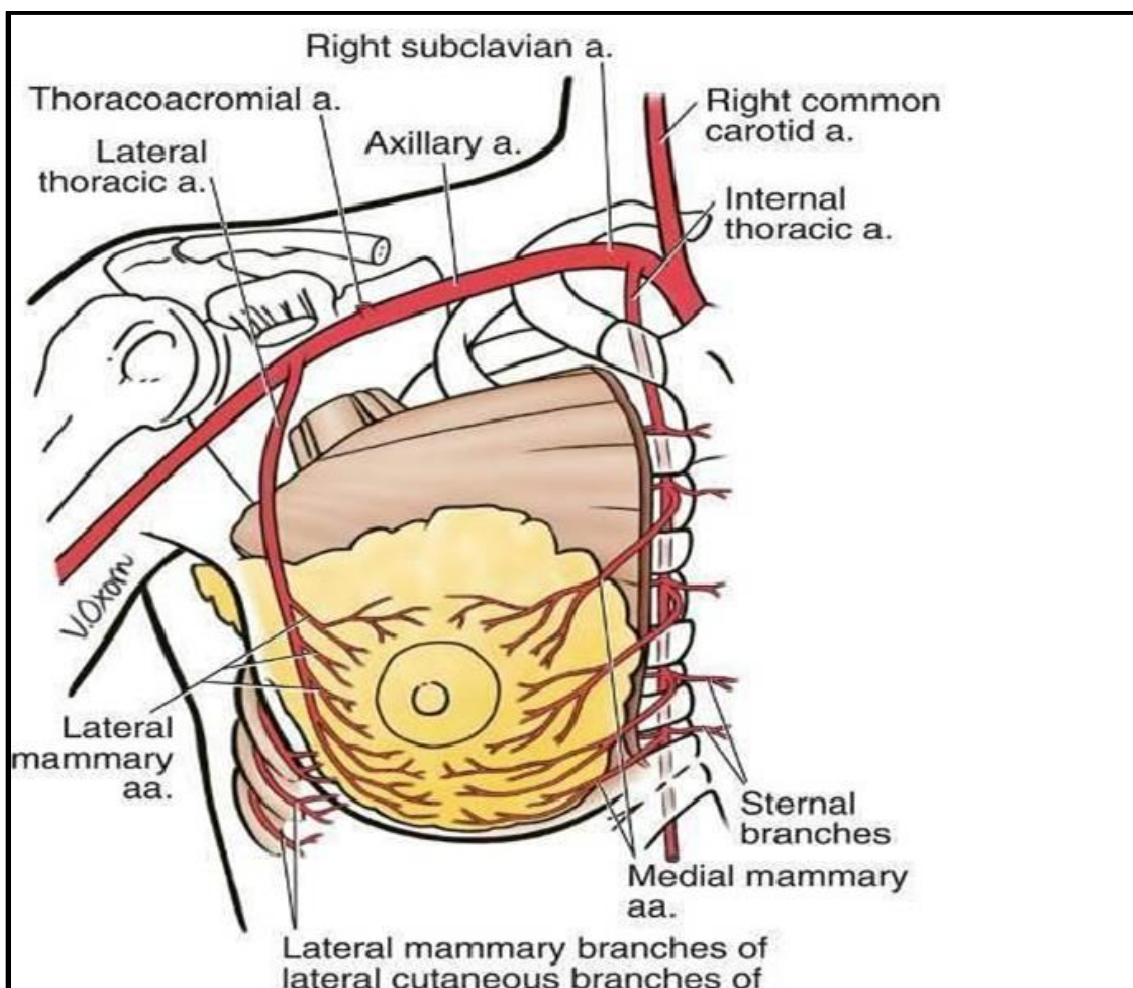
Lactiferous ducts are lined by columnar epithelium, surrounded by myoepithelial, hence the bilayered appearance. 15 to 25 orifices enters the

nipple from each lobule. Lactiferous sinus presents near the opening, where the ducts are slightly expanded. Stratified cuboidal epithelium near the opening of lactiferous ducts in the nipple is replaced by Keratinized stratified squamous epithelium¹ Intralobular terminal ductule get ramified and forms the terminal ductule lobular unit, which is the secretory units of the breast.



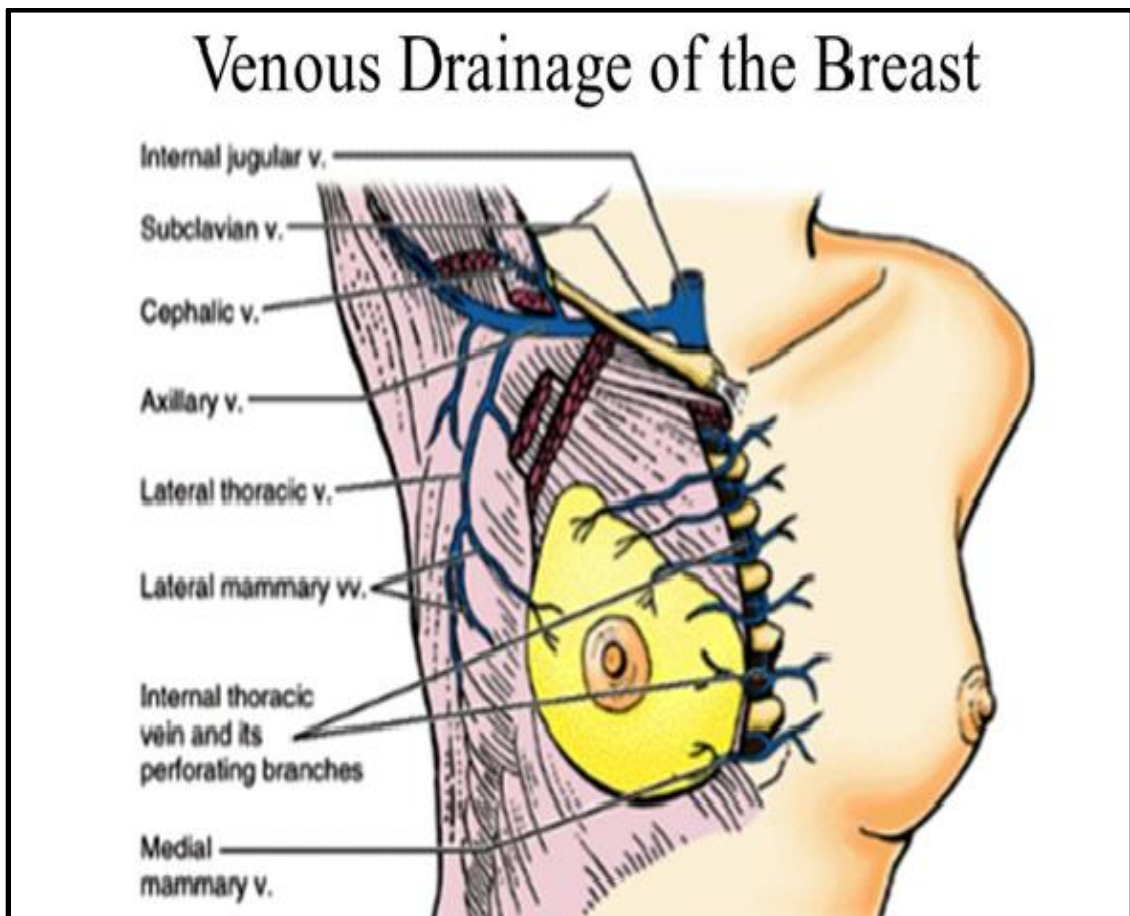
ARTERIAL SUPPLY

1. 60% by internal thoracic artery.
2. 30% by lateral thoracic artery.
3. Branches of subclavian , axillary artery , posterior intercostal artery ^{1,2,3}.



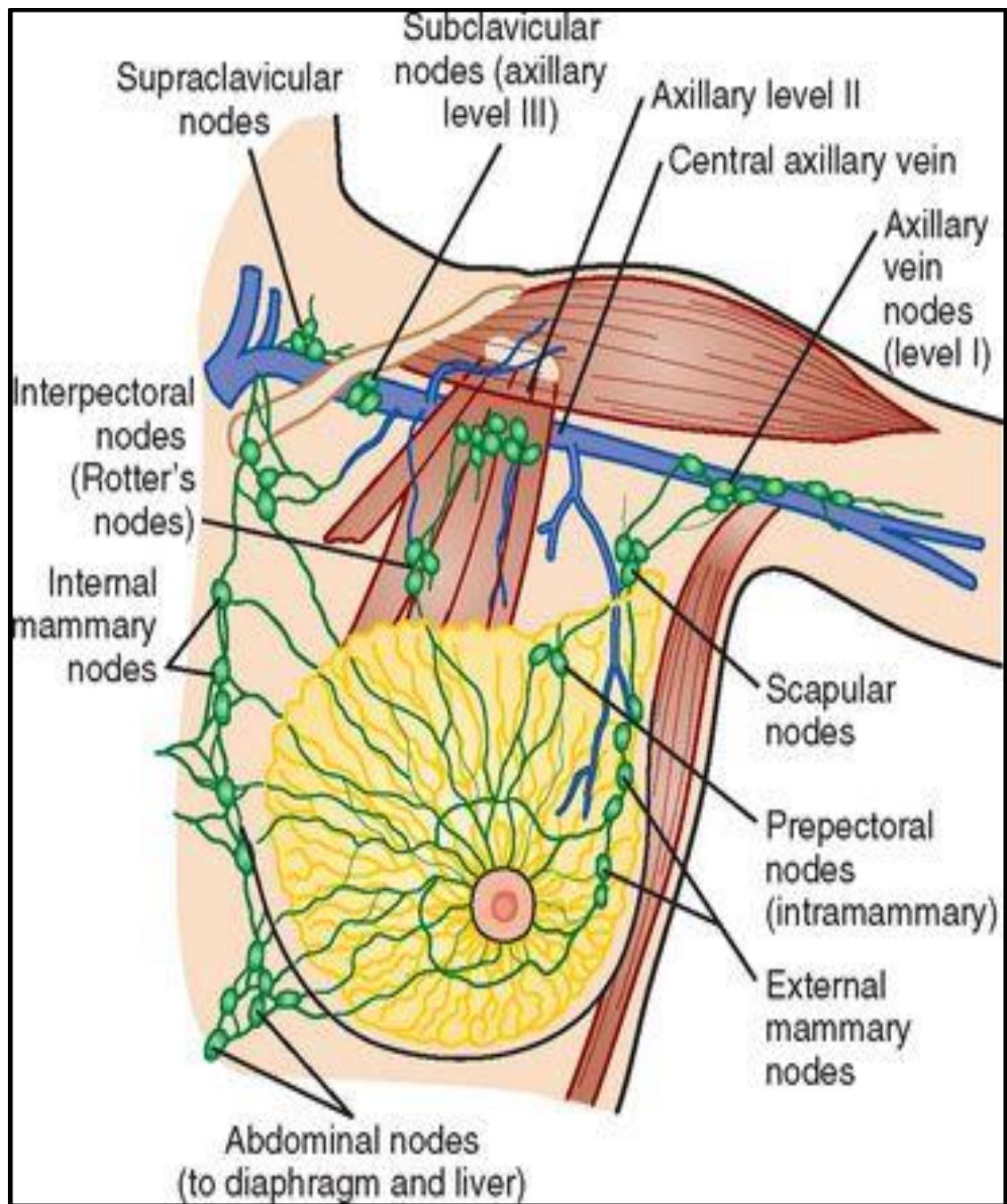
VENOUS RETURN

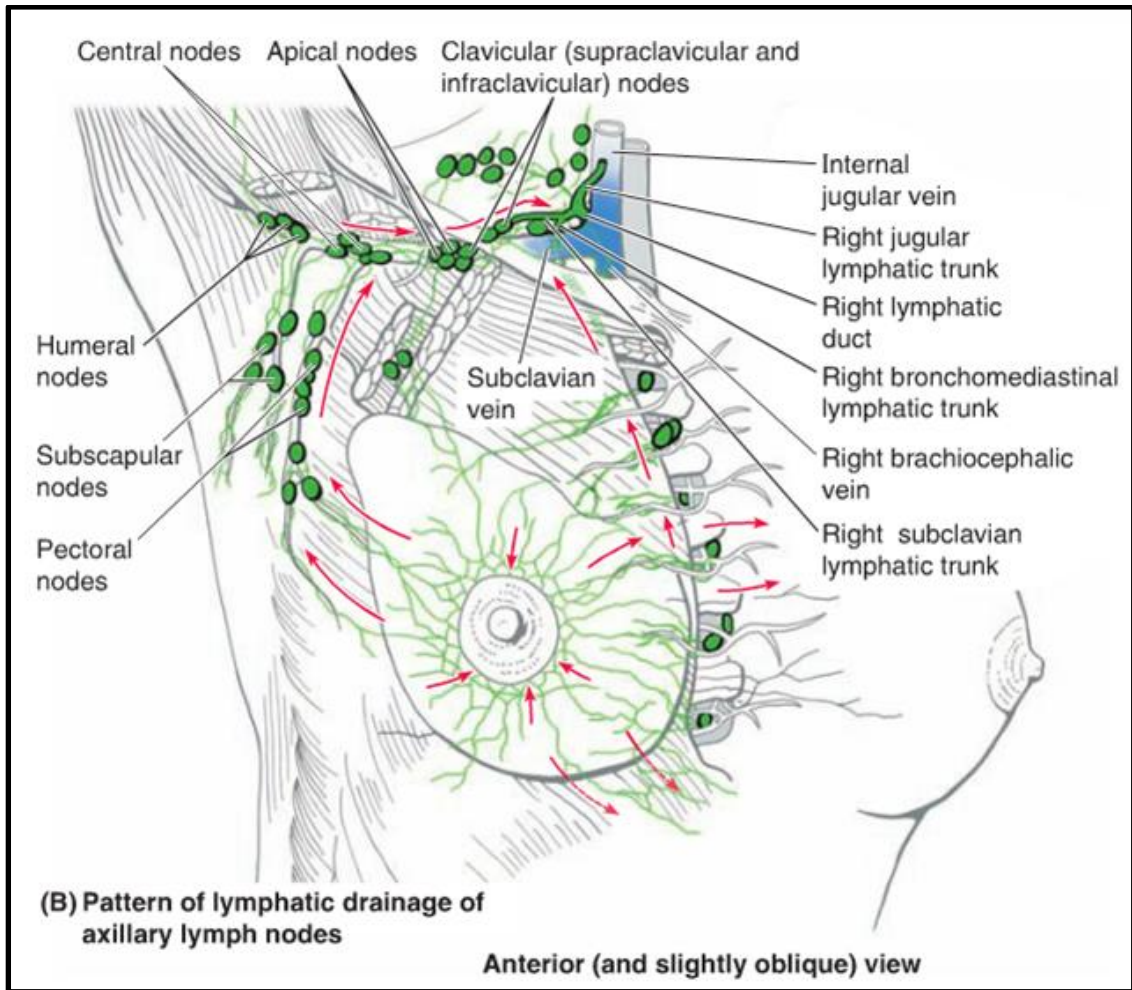
Through Batson's vertebral venous plexus, tributaries of axillary vein and internal mammary vein. Perforating branches of breast drains into internal thoracic vein and internal posterior intercostal vein.



LYMPHATIC SYSTEM:

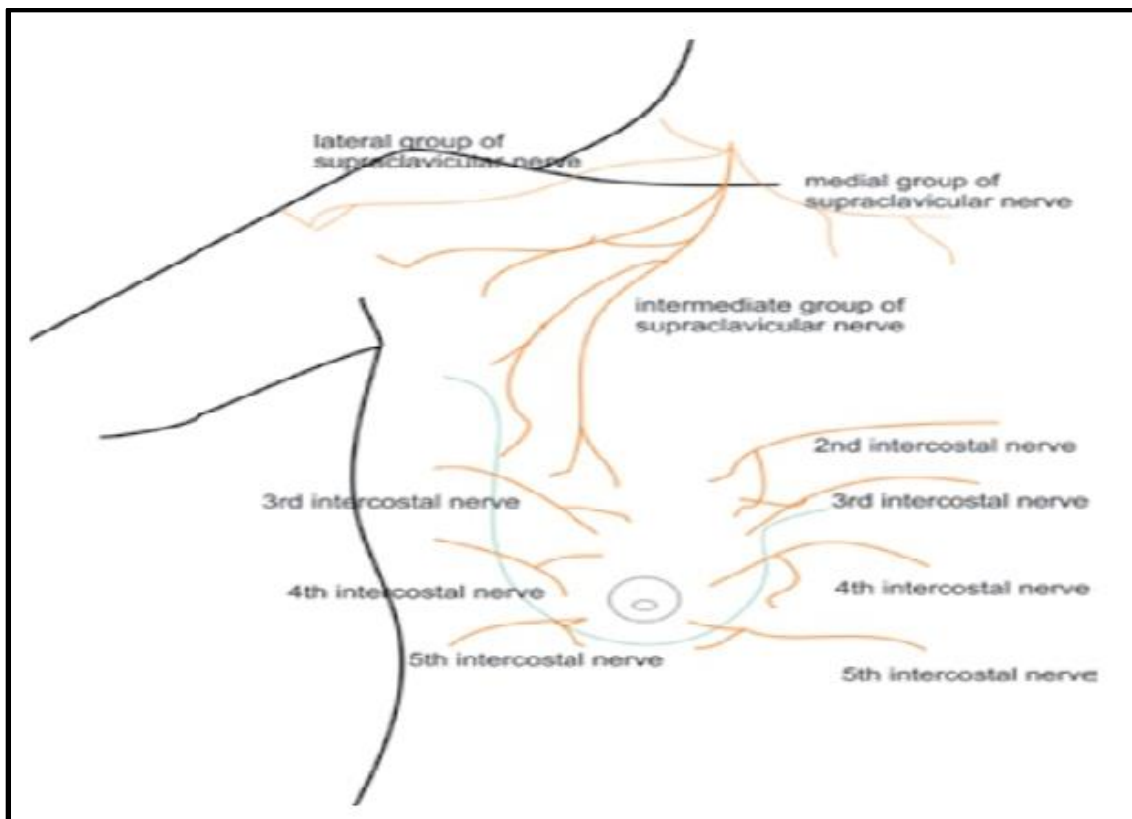
1. Superficial lymphatics drain breast skin except nipple areola complex.
2. Deep lymphatics drain breast parenchyma and nipple areola complex.
3. 75% drains into axillary group of nodes (pectoral, subscapular, central and apical groups).
4. 20% into internal mammary nodes.
5. 5% to posterior intercostal nodes.
6. Berg's level of axillary nodes:
 - a. Level I : Below and lateral to pectoralis minor {anterior ,lateral ,posterior}
 - b. Level II: behind the pectoralis minor {central}
 - c. Level III: Above and medial to pectoralis minor {apical}.
7. Drains into lateral , anterior , posterior , central , apical , interpectoral and supraclavicular group of nodes . ^{2,3,5}





NERVE SUPPLY OF BREAST:

Sensory and sympathetic nerves is the main supply , nipple has a rich sensory supply. Minor parasympathetic innervation also seen . Major part sympathetic innervation is to breast parenchyma. 3rd to 6th intercostal nerve supplies the breast .



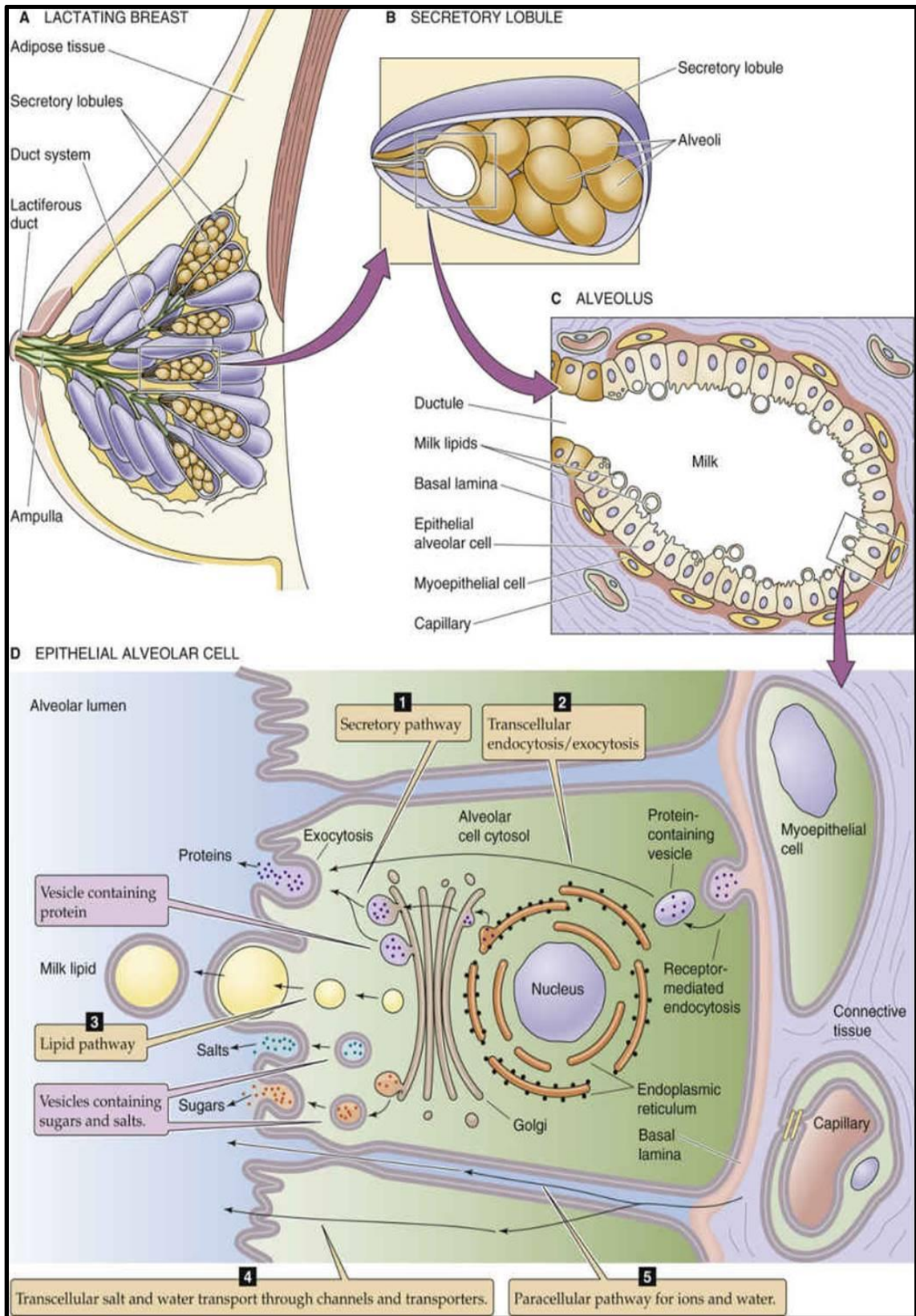
PHYSIOLOGY:

Prepuberty : Between 9-12 yrs of female child , breast development initiated by low amplitude pulses of pituitary gonadotropins. This hormone dependent maturation (thelarche) entails increased deposition of fat ,the formation of new ducts by branching and elongation. This process of growth and cell division is under the control of oestrogen , progesterone , adrenal hormones , pituitary hormones and the trophic effects of insulin and thyroid hormones.

Postpuberty : The breast epithelium and lobular stroma undergo cyclic stimulation. In early luteal phase there is hypertrophy and alteration of morphology. In late luteal phase , there is accumulation of fluid

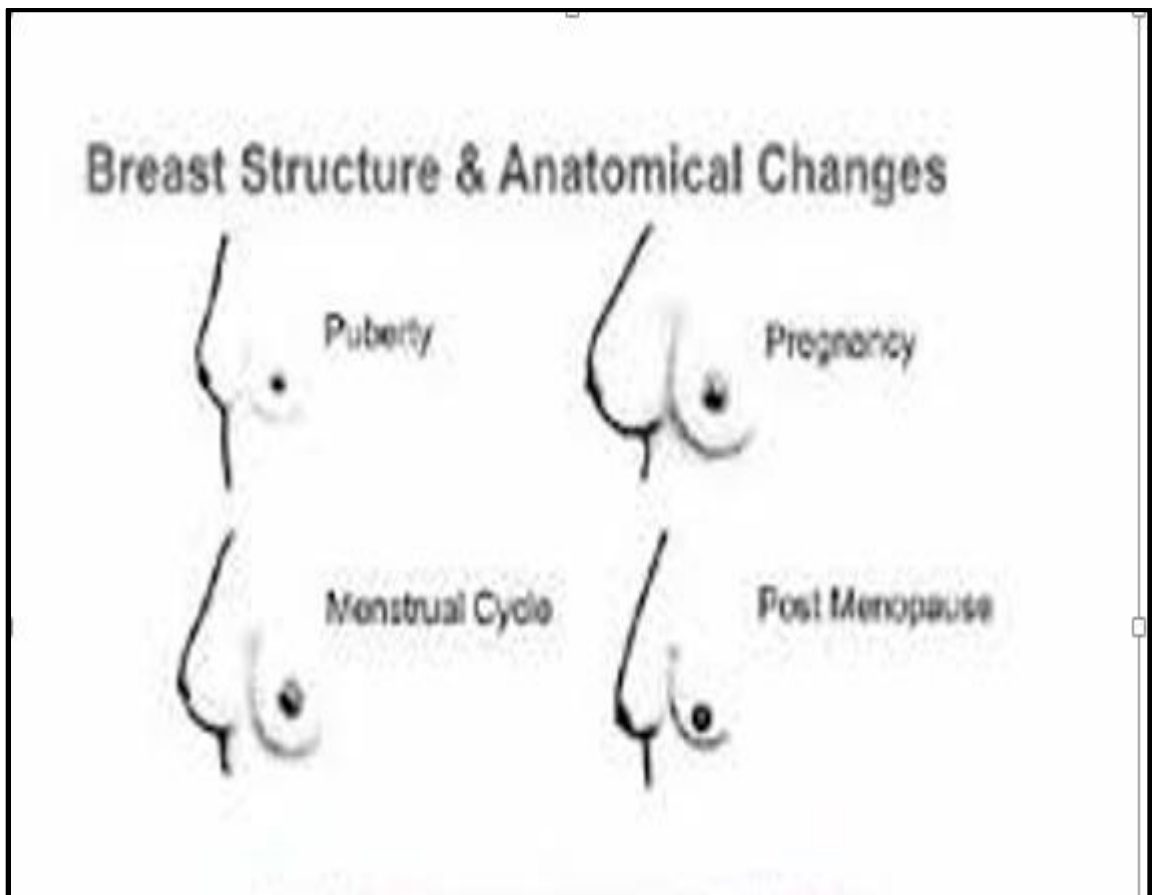
Pregnancy : During pregnancy there is lobular–alveolar growth with the development of new secretory units, this gives rise the appearance of 'adenosis of pregnancy'. Hence this secretory changes converts resting two-layer epithelium to a monolayer. As the pregnancy progress there is myoepithelial cell hypertrophy, capillary growth, vascular engorgement are apparent with Colostrum formation.

Weight of the breast increased from about 200 to 400 g, which is due to fluid accumulaton. Increased Luteal and placental sex hormones, placental lactogens, and chorionic gonadotrophins plays main role in this changes.



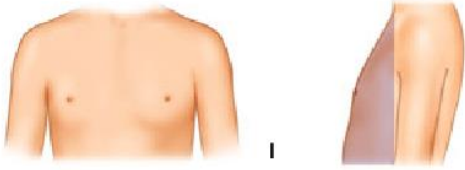


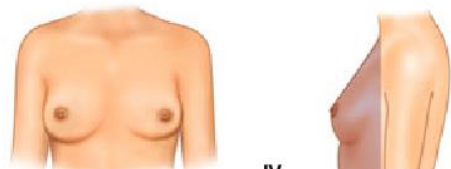
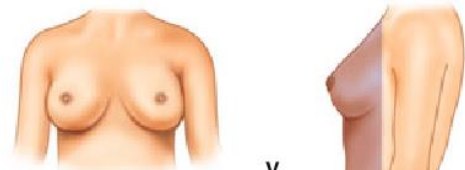
Changes at the menopause :

1. Fatty infiltration of the breast gives the low-density appearance of the parenchyma hence mammography plays the diagnostic in older woman.
2. Aberrations of this involutional change cause benign disorders .



TANNERS STAGING OF BREAST

1. Preadolescent
2. Breast bud
3. Areola diameter enlarges
4. Secondary mound, separation of contours
5. Mature female adult breast

<p>Tanner Stage 1</p>	<p>Preadolescent</p>	<p>Only papilla is elevated</p>	
<p>Tanner Stage 2</p>	<p>Breast budding</p>	<p>Enlargement and widening of the areola and mound-like elevation of the breast and papilla</p>	
<p>Tanner Stage 3</p>		<p>Further enlargement of breast and areola with NO separation of contours</p>	
<p>Tanner Stage 4</p>		<p>Projection of the areola and papilla to form secondary mound above the level of the breast and further enlargement</p>	
<p>Tanner Stage 5</p>	<p>Adult Breast</p>	<p>Projection of the papilla only, as the areola recesses to the mature contour of the breast</p>	

ANDI OF THE BREAST

Cardiff breast clinic explains the Aberrations of Normal Development and Involution, (**ANDI**) and their pathogenesis. There is a spectrum of breast condition range from normal to disorder to disease in different age groups. ANDI should be carefully examined clinically to rule out malignant conditions.

ANDI based on three phases: lobular development, cyclical hormonal modifications and involutions. The pathogenesis of the disease presents as cyst formation or fibrosis or hyperplasia or papillomatosis. The commonest presentations of ANDI is cyclical pain and nodularity.

EARLY REPRODUCTIVE AGE GROUP (15-25 YRS)

Normal females have lobular development, stromal development and nipple eversion. Disorder in this period may present as fibroadenoma, adolescent hypertrophy, and nipple inversion respectively. Severe abnormality of the above conditions present as giant fibroadenoma, gigantomastia, subareolar abscess and mammary duct fistula.

LATE REPRODUCTIVE AGE GROUP (25 TO 40 YRS)

Normal cyclical hormonal effect on stroma and on glands may present as cyclical changes of menstruation and epithelial hyperplasia of pregnancy. Disorder of this present as cyclical mastalgia, nodularity and bloody nipple discharge. Disease of this present as incapacitating mastalgia, fibroadenosis.

INVOLUTION AGE GROUP(35-55YRS)

Normally lobular involution , duct involution, dilatation, sclerosis ,epithelial turn over takes place during this period. Disorder of lobular involution present as macrocysts and sclerosing lesions. Duct ectasia, nipple retraction and epithelial hyperplasia are the disorders noted during this period. Disease are Periductal mastitis and epithelial hyperplasia with atypia ¹⁴.

GYNAECOSMASTIA:

Gynaecomastia is due to hyperoestrogenism or due to decreased androgens. Epithelial and stromal proliferation leads to hypertrophy of male breast. It may be unilateral or bilateral. It is usually bilateral in CLD, testicular tumours, Klinefelter syndrome, CRF, cryptorchidism.

Simon's classification :

Group 1: small enlargement, no skin excess

Group 2A : Moderate enlargement, no skin excess

Group 2B : Moderate enlargement, with minor skin redundancy

Group 3 : Marked enlargement with extra skin or pendulous breast

Surgical excision for those patients who need cosmetic correction, or can use tamoxifen, danazol, and also treat the cause.

MASTALGIA:

Mastalgia is tightness, tenderness or sharp pain in one or both breasts, it can be cyclical or non cyclical . It is due to hyperoestrogenism , excessive caffeine ingestion , abnormal prolactin secretion , abnormal fluid retention in breast ^{6,7}.

CYCLICAL MASTALGIA:

Cyclical breast pain is linked to the menstrual cycle and fluctuating hormone levels during the cycle. Usually starts in the second half of the menstrual cycle, increases until the period begins, then settles. It settles during pregnancy and menopause. It lacks correlation between clinical, radiological, and histological features. In mammogram ,one breast is translucent , whereas the other shows dense and nodular appearance . This is the Wolfe DY pattern (by courtesy of Dr B. Shepstone) . Can be treated with evening primrose oil, danazol, bromocriptine, tamoxifen. Evening primrose oil gives unsaturated fatty acids reverses the balance of saturated to unsaturated and helping to relieve mastalgia. ^{7,8}.

Side-effects:

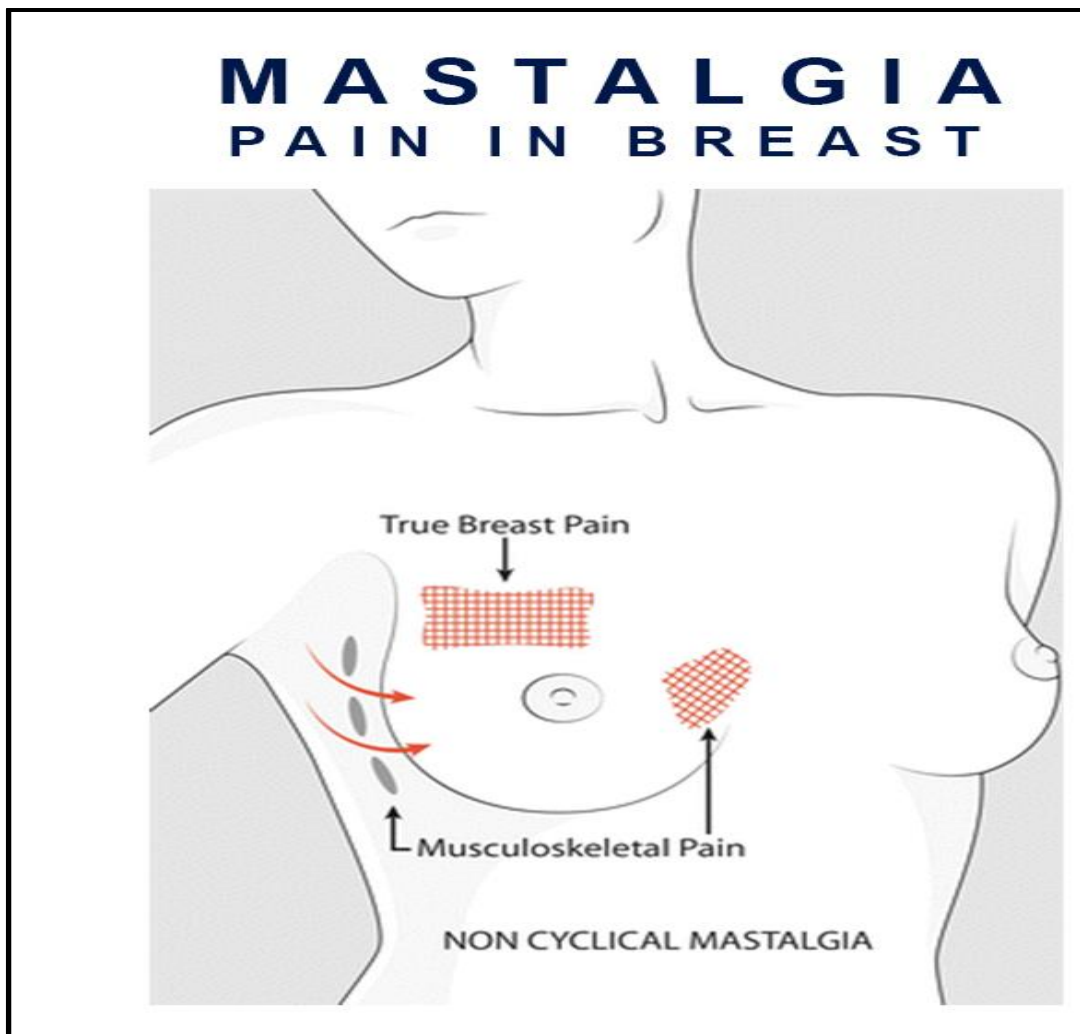
Tamoxifen: Weight gain and hot flushes , it is contraindicated in pregnancy

Danazol: weight gain, acne, amenorrhoea, masculinization with hirsutism, voice changes, and reduction of breast size.

Bromocriptine: nausea, postural hypotension, vomiting, and dizziness,

NON – CYCLICAL MASTALGIA:

It is not associated with the menstrual cycle, can be either constant or intermittent (comes and goes). Noncyclic pain may come from the breast or may come from somewhere else, such as nearby muscles or joints, and may be felt in the breast. Median age of presentation of 45 yrs. Usually present as 'burning' or 'dragging' rather than a 'heavy feeling'. It is not associated with lumpiness to the same degree as cyclical mastalgia . The mastalgia is well localized, with 'trigger spot zone' . The best example of which is duct ectasia / periductal mastitis , sclerosing adenosis .



MASTITIS:

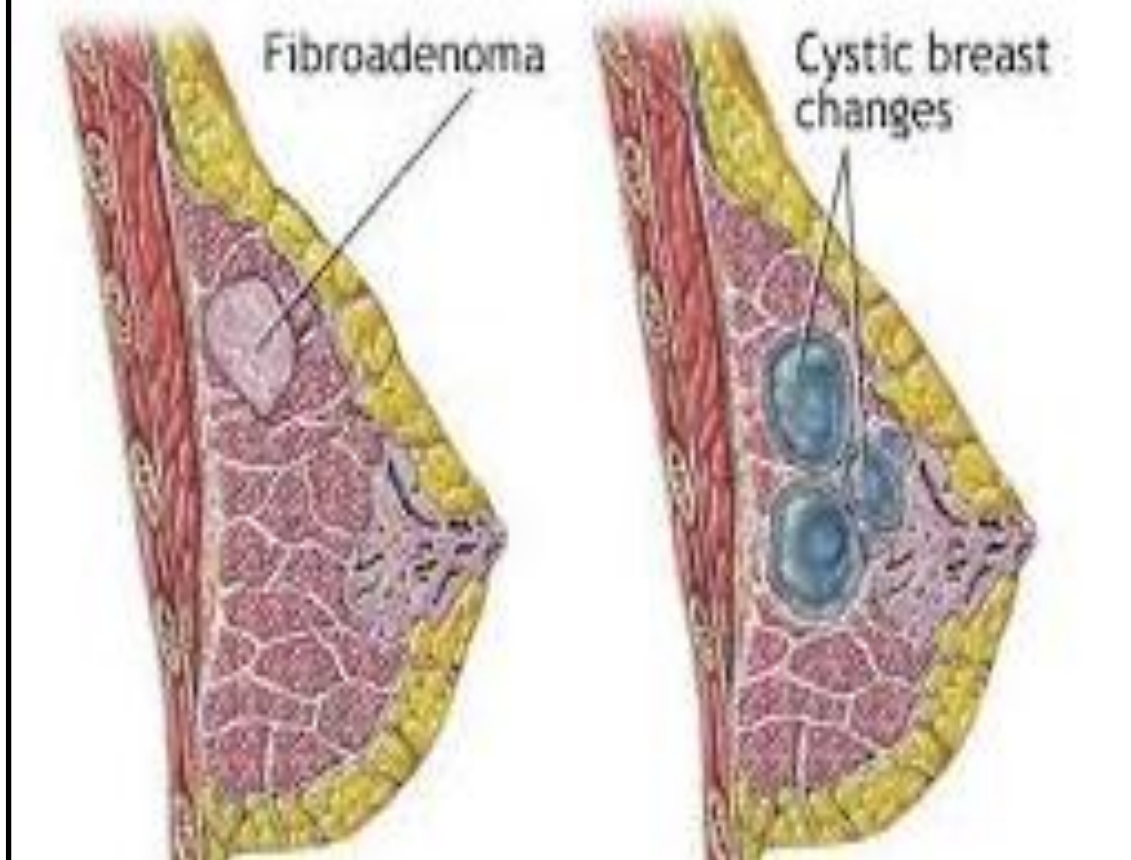
Mastitis is an inflammation of breast tissue , by infection. Mastitis most commonly affects women who are breast-feeding, it is called lactation mastitis. Inflammation results in breast pain, swelling, warmth and redness. Patient presents with lump and burning pain, sometimes with bloody discharge. Subareolar mastitis , intramammary and retromammary mastitis are the types. Mimics scirrhus carcinoma of the breast.



FIBROADENOMA

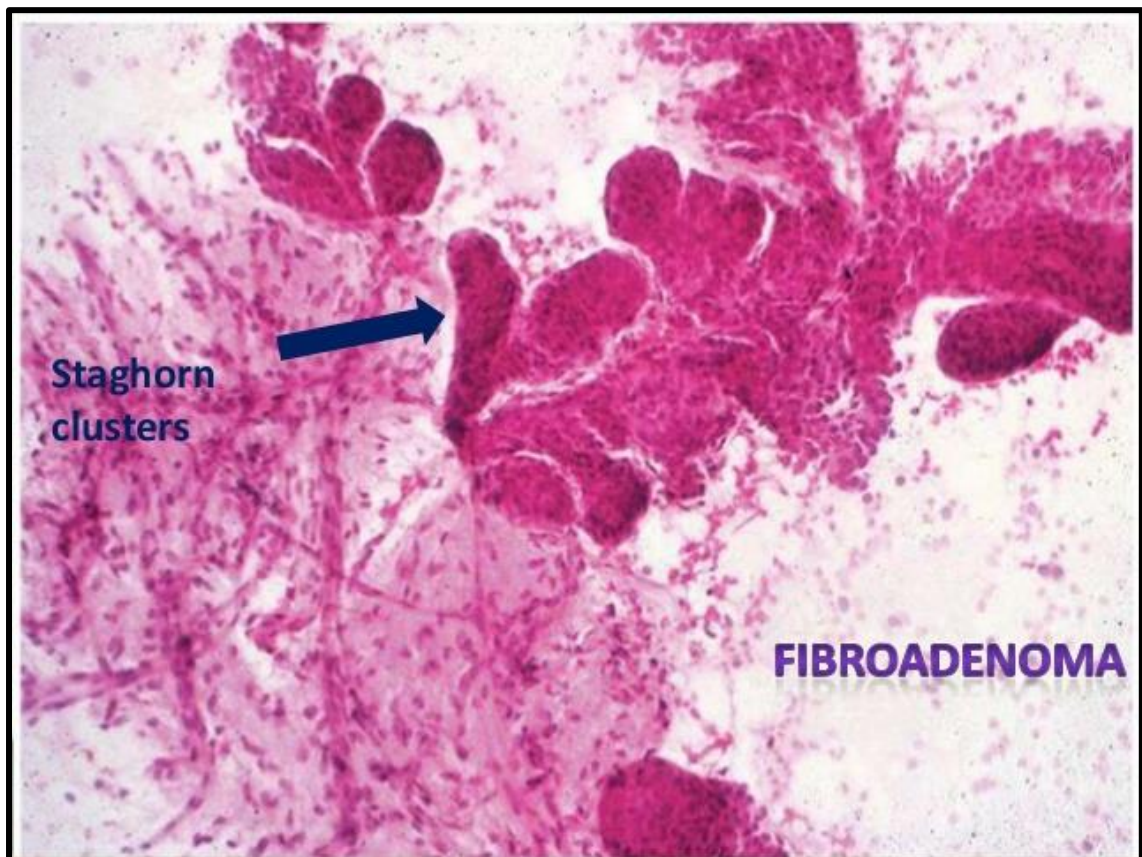
- Fibroadenomas are consist of both connective tissue and epithelial proliferation.
- Fibroadenoma incudes simple bening fibroadenoma , gaint fibroadenoma and phyllodes tumour
- .It is a common cause of discrete, firm, and mobile lump noted in breast between 15 to 25 yrs age group .
- Slow growing and remains same size for a quite long time ,usually shows 1 to 3 cm growth over a period of 5 yrs.
- On palpation the swelling is very smooth , not warm , not tender ,firm and mobile with well defined border.
- Otherwise called as breast mouse .
- Usually present as single lesion , sometimes multiple lesions can be seen unilateral or bilaterally.
- Axillary LN are usually not enlarged.
- Stroma compressed adjacent ducts forms a curved slit-like structures (intracanalicular pattern) .
- Sometimes surrounds the duct circumferentially (pericanalicular pattern). In locally invasive condition fibrous stroma with increased cellularity and atypia is noted .
- About 10 per cent of patients have multiple fibroadenomas .
- It is due to hyperresponsiveness of a lobular tissue to oestrogen. Hence Ormeloxifene can be used to suppress the proliferation of ductolobular tissue of fibroadenoma.

Common benign causes of breast lumps



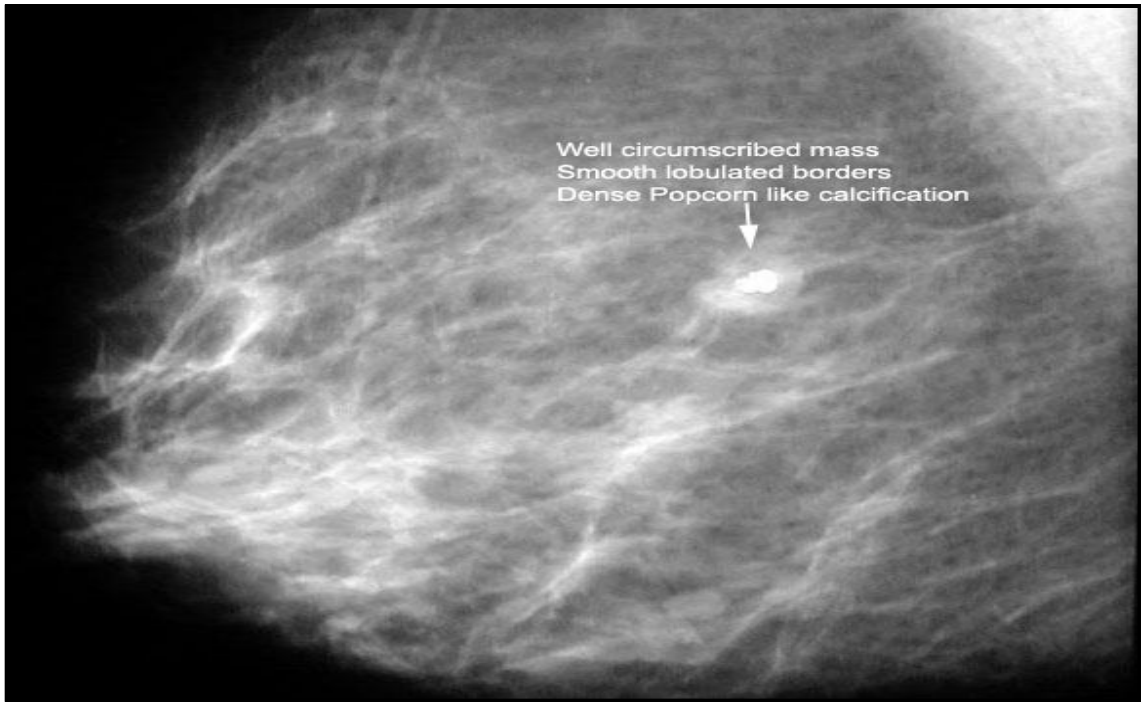
FNAC PICTURE OF FIBROADENOMA:

1. Large bland epithelial cells with branching shows staghorn appearance.
2. Cells of myxoid substance with tissue fragment.
3. There are large number of bare bipolar nuclei.
4. Fibromyxoid stroma shows fragmentation.
5. Using 8G or 11G large needle gives more tissue sample , decrease sampling error.



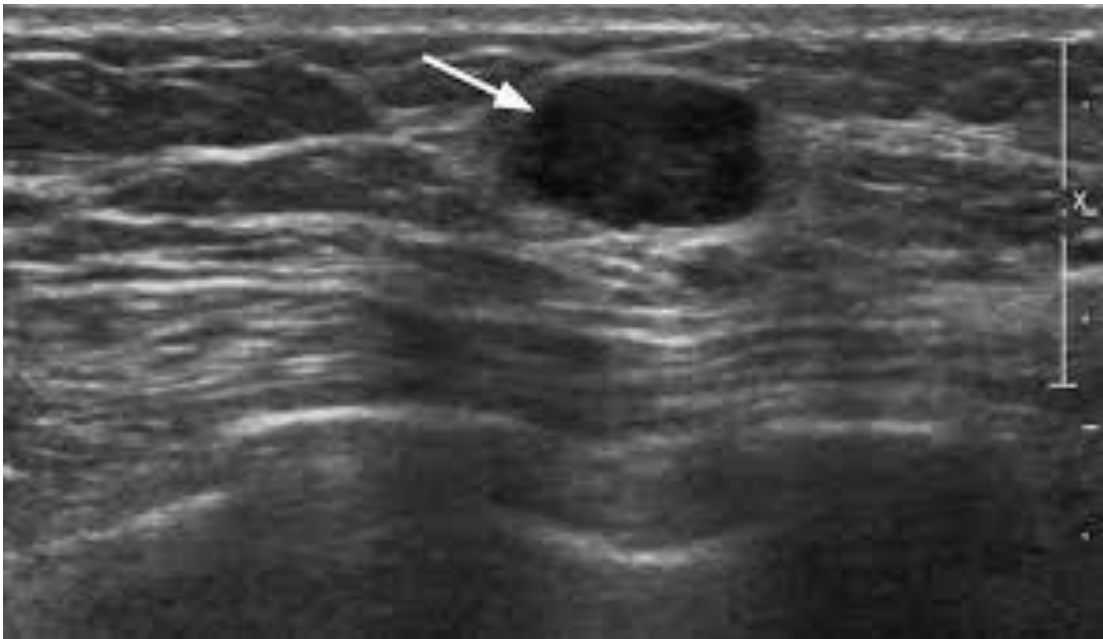
Mammography:

Round mass with smooth margin , showing central or amorphous calcification .



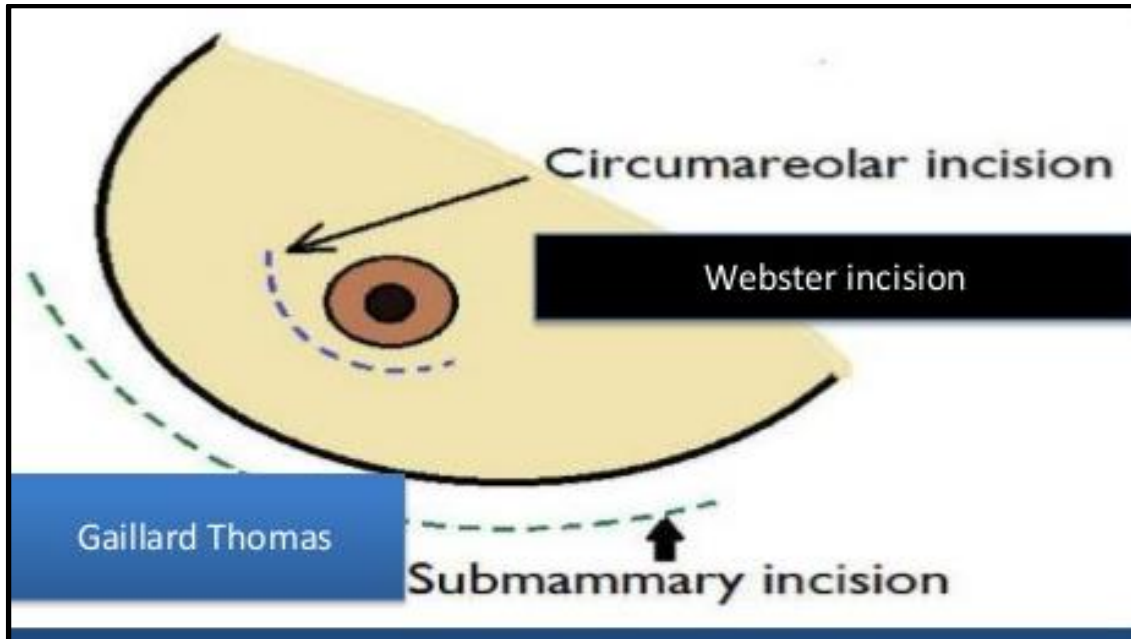
USG appearance :

1. Capsulated well defined lesion.
2. Anteroposterior diameter is shorter than the width .
3. Margins are well circumscribed .
4. Shows internal echogenicity which is homogenous . But sometimes vary from isoechoic to hypoechoic.
5. Pseudocapsule , thin capsule which is formed by compression of adjacent structures.



INCISION USED FOR EXCISION BIOPSY:

1. circumareolar incision called as webster`s incision.
2. submammary incision is Gaillard Thomas incision.

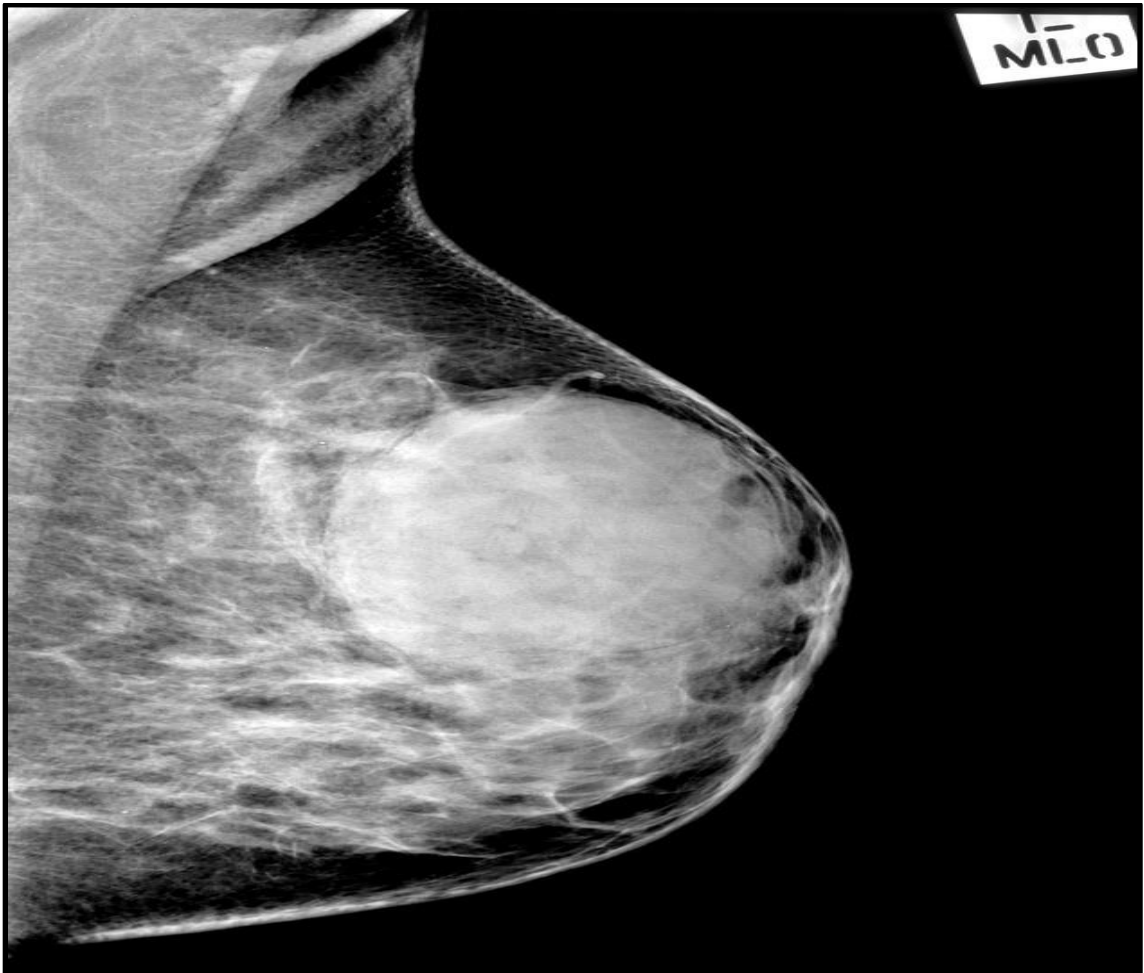


INDICATIONS FOR EXCISION:

1. Swelling size >3 cm or gaint .^{1,2,3,15,16}
2. Recurrent cyst .
3. Multiple number.
4. Cosmetic .

GIANT FIBROADENOMA:

Giant fibroadenoma has a bimodal age of presentation; Swelling size more than 5 cm comes under giant fibroadenoma . On slides it shows hypocellular stromal with variable epithelial components. Patient presents with pain and rapid increase in size of breast . On inspection there is enlarged breast with nipple displacement . Overlying skin is stretched and shiny. Enucleation is the treatment of choice by using proper cosmetic incision.



PHYLLODES TUMOUR:

Otherwise called as phyllodes sarcoma, cystosarcoma, cystosarcoma phyllodes, and benign cystosarcoma. Present as painless ,large ,mobile lump. Unilateral , rapidly progressive in nature. It has wide spectrum of activity from benign condition to a locally aggressive, and it can also metastasize . Phyllodes is characterized by irregular surface projections ,this is the predisposing cause for tumour recurrence . Macroscopic appearance of cut surface is soft, brown in colour, with areas of necrosis and haemorrhage. On histology stroma shows hypercellularity, with numerous atypia and mitoses. Usually no axillary lymphadenopathy seen, if it presents then it is aggressive. Wide local excision is the initial treatment . Lung is the most common site of metastasis .There is no role for adjuvant radiotherapy and chemotherapy.

Grading of phyllodes tumours:

Depends on their mitotic index and degree of pleomorphism.

Low-grade tumours - 5 or fewer mitoses /10 HPF;

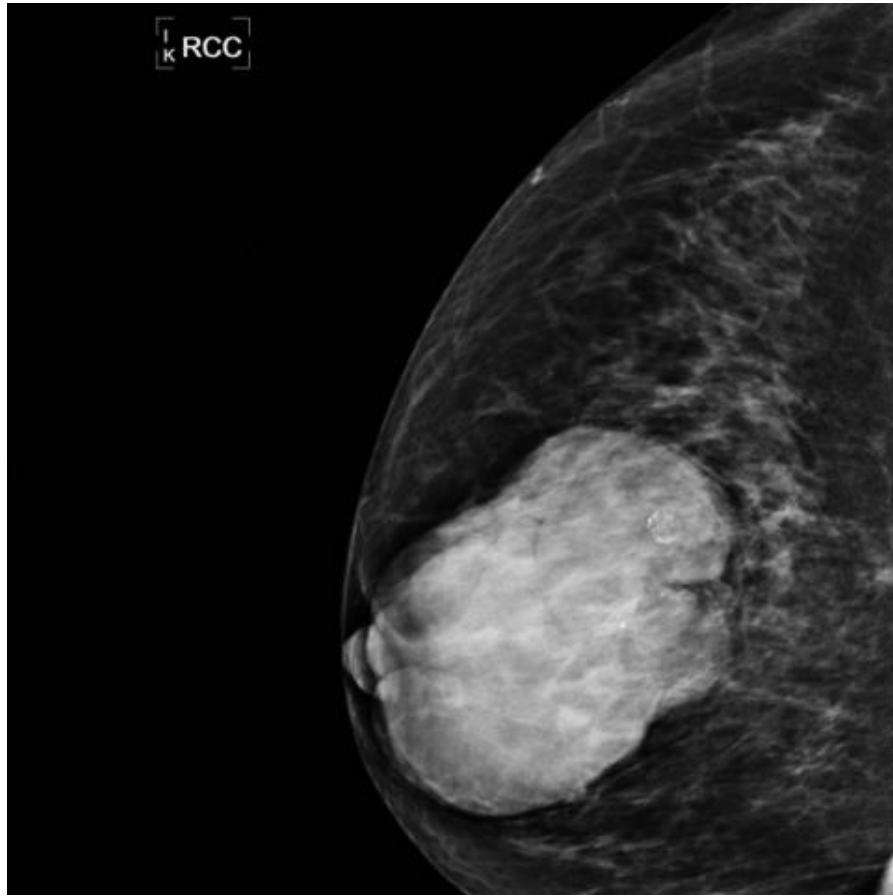
High-grade tumour - 10 mitosis or more/10 HPF;

The tendency for recurrence is high for higher-grade tumours.

On USG , tumour appears as well defined lesion with low level of internal echoes. There is solid and cystic spaces.

On mammogram ,due to pressure effect on the surrounding area there is a zone of translucency known as halo sign.

MRI : It appear as lobulated lesion with septations.

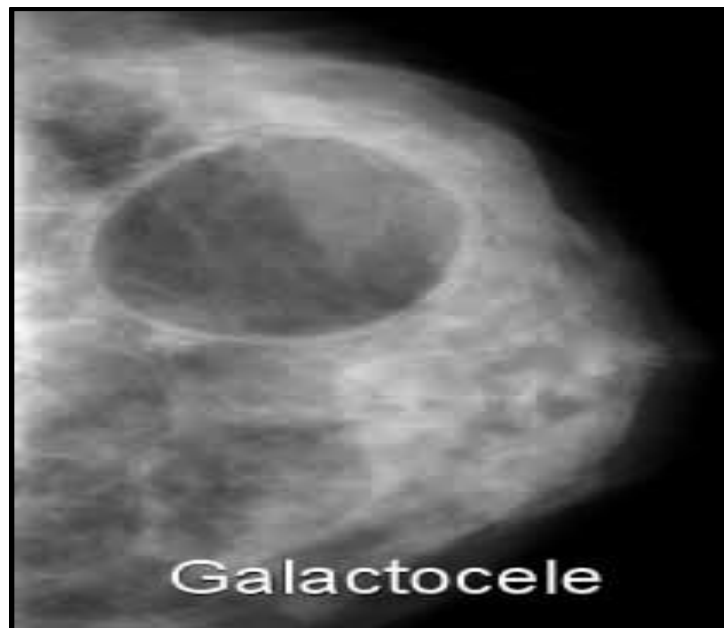


Treatment :

With clearance of one centimetre margin , excise the tumour. If it is more than 10 centimetre , prefer mastectomy^{15,16}.

GALACTOCELE:

1. Galactocele is milk collected in pre-existing simple cyst.
2. Usually seen in woman who recently stopped her breast feeding.
3. Due to obstruction of lactiferous duct.
4. On mammogram with calcification mimics carcinoma of breast.
5. Not normally infected as the milk within is sterile , get infection through cracked nipple .
6. Treatment is by aspiration of the contents or by excision of the cyst.
Antibiotics are given to prevent infection ¹¹.



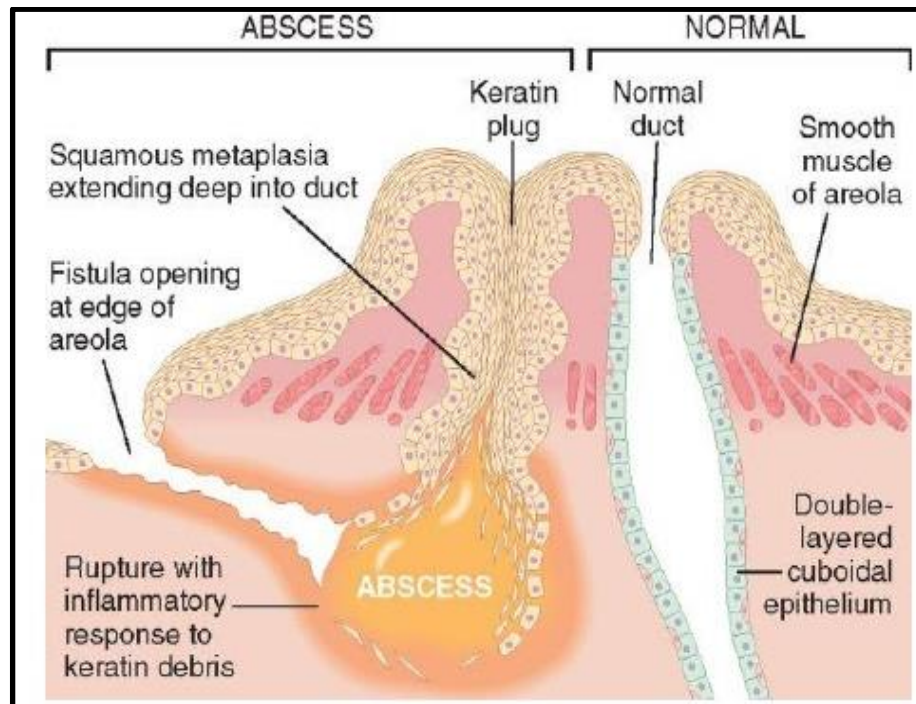
MONDOR'S DISEASE:

It is a condition characterized by thrombophlebitis of the superficial veins of breast and anterior chest wall. It is named after Henri Mondor's, a surgeon in Paris, France who first described the disease. It has abrupt onset of superficial pain, with possible swelling and redness of a limited area of their anterior chest wall or breast. Mondor's disease is self-limiting and usually benign. A cause is not identified, but when found includes trauma, surgery, or inflammation such as infection. There may be occasional cases of associated cancer. Management is with warm compresses , restriction of hand movements, and pain relievers, most commonly NSAIDS . When thrombophlebitis affects the greater veins, it can progress into the deep venous system, and may lead to pulmonary embolism .



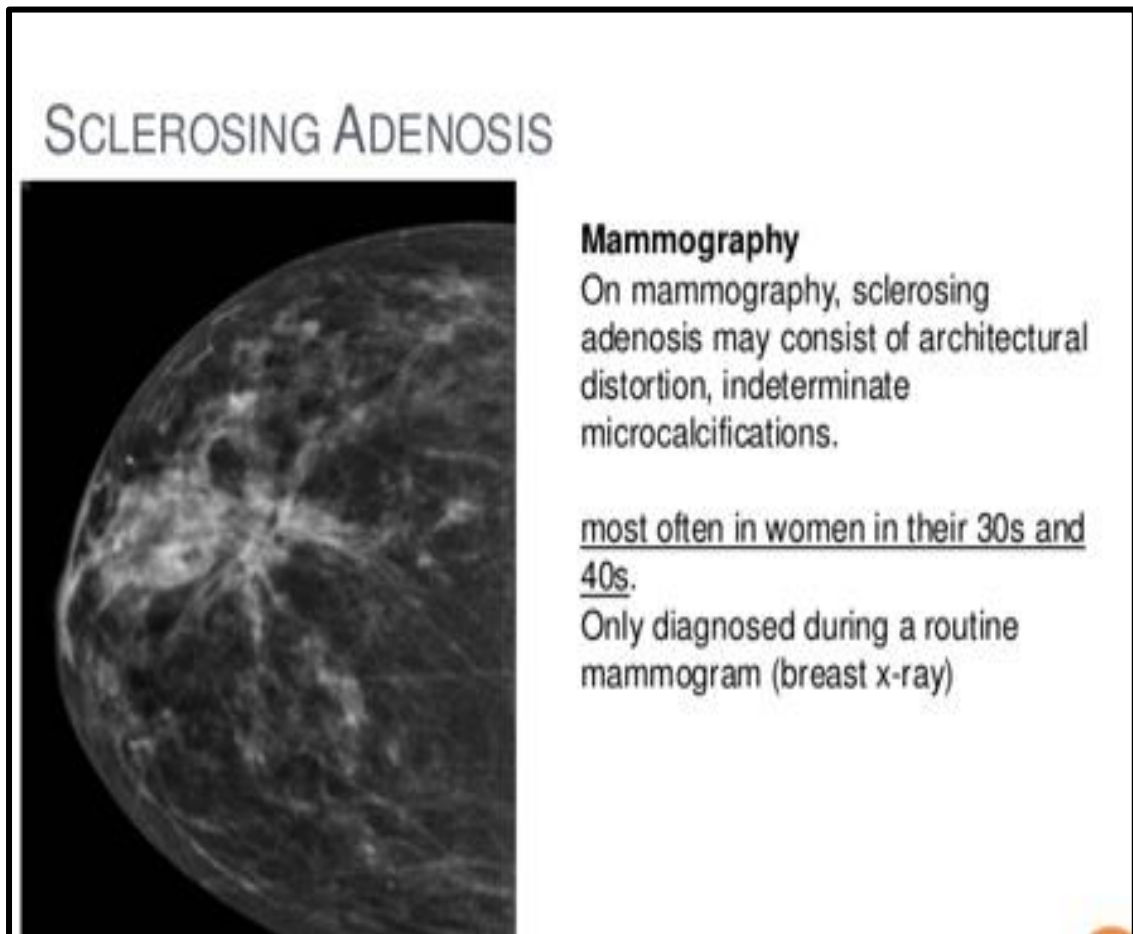
ZUSKA-ATKINS DISEASE:

Also known as “lactiferous fistula“, it is a rare and recurrent disorder characterized by draining abscesses around the nipple. Associated with vitamin deficiency A, and also in smoker. **Zuska's breast disease** can also lead to nipple retraction. It is frequently aseptic inflammation and has been associated with squamous metaplasia of lactiferous duct. Treated with antibiotic and then surgical excision.



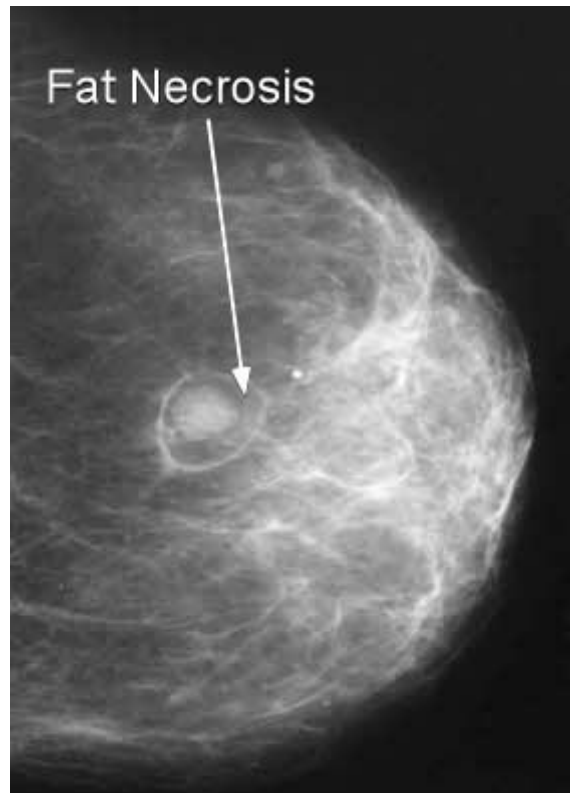
SCLEROSING ADENOSIS :

Sclerosing adenosis is a mobile mass in the 30- to 50-year. It is frequently Smooth painful mass occasionally present as mastalgia. It as an ANDI, shows fibrous stromal distortion with lobular enlargement.



FAT NECROSIS:

Patients with fat necrosis has previous history of trauma. Hard lump shows inflammatory changes, tethering and oedema. FNAC is diagnostic. Mammography features mimics cancer.



LIPOMA:

It is uncommon soft mass . Adenolipoma is a variant form of lipoma. If fibrotic component is noted then it is regarded as a hamartoma.

CHRONIC ABSCESS:

Inflammatory breast conditions with increasing use of antibiotics results in a chronic, sterile abscess. Aspiration or by open drainage with excision of the wall is the treatment of choice .

DUCT ECTASIA/PERIDUCTAL MASTITIS:

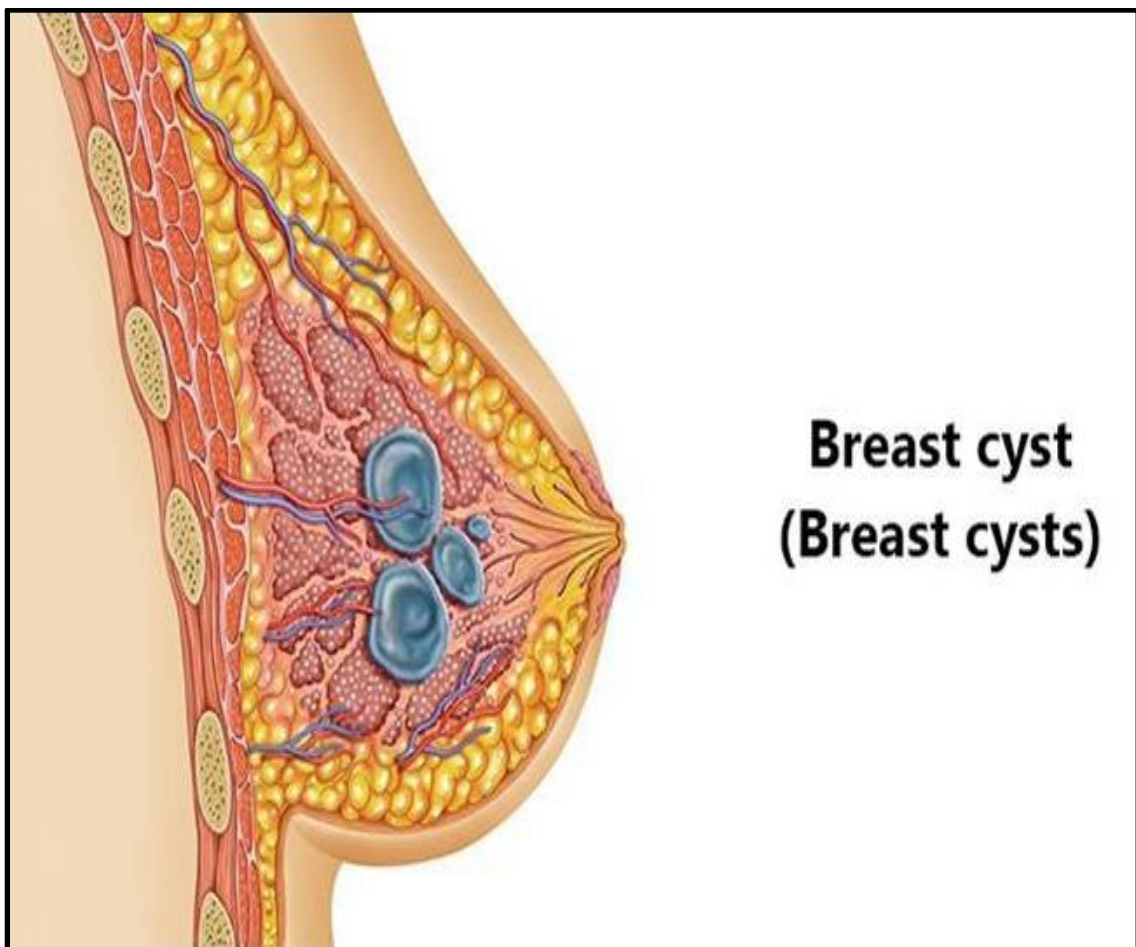
Pathogenesis in duct ectasia/periductal mastitis was simple dilatation of duct. Otherwise called as plasma cell mastitis, mastitis obliterans. Dilated ducts fill with a stagnant, thick, green or creamy secretion (grumous) associated with ulceration in epithelial lining, leads to further inflammation. Present as painful periareolar mass with nipple bloody discharge . Slit like nipple retraction can occur .Cone excision of the duct, Hadfield surgery.

CYCLICAL NODULARITY:

Many patients present with mass rather than pain. Elliciting history its size varies with the menstrual cycle. On examination it is a diffuse, and nodular swelling that may be somewhat tender.

BREAST CYST:

It is aberration of normal lobular development, due to hyperoestrogenism. Macrocysts formed by coalesce of microcyst. Occurs in perimenopausal period , smooth and tense on palpation . Diagnosed by aspiration of cystic fluid . If the aspirate is bloody then surgical excision should be done to rule out malignancy
2,13 .



Two types :

1. **Simple cyst:** In this lining epithelium is cuboidal, sodium potassium ratio is >3 , pH is <7.4 , low recurrence ,not associated with malignancy.
2. **Apocrine cyst:** Lining epithelium is apocrine , sodium potassium ratio is <3 , pH is >7.4 , moderate recurrence ,chances of malignancy is there.

On USG :

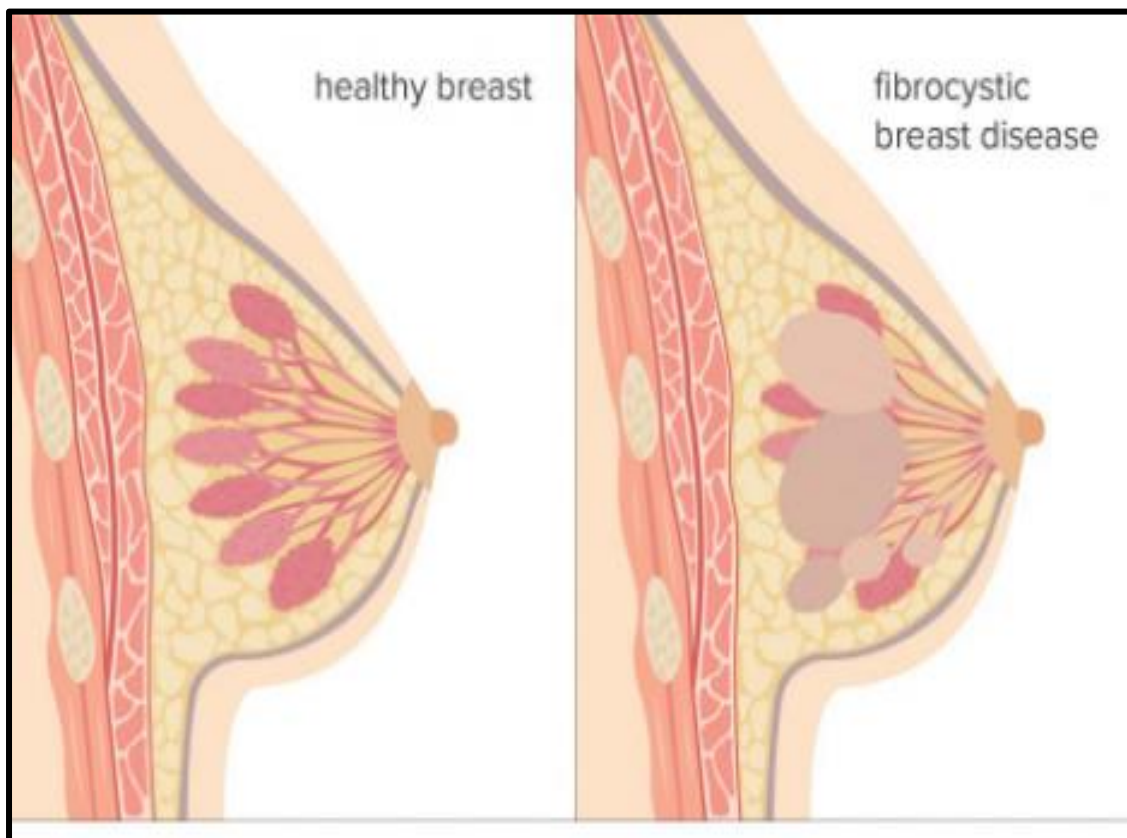
Anechoic with posterior enhancement. Relative mobility in the surrounding tissue. Cyst with above finding includes in BIRAD-2 Round or oval shape.

USG has 98% accuracy for diagnosis simple cyst.



FIBROCYSTIC DISEASE OF THE BREAST:

Breast lumps that fluctuate in size with the menstrual cycle comes under ANDI. Fluid-filled round or oval sacs (cysts) A prominence of scar-like fibrous tissue (fibrosis) . Overgrowth of cells (hyperplasia) lining the milk ducts or milk-producing tissues (lobules) of the breast with Enlarged breast lobules (adenosis) . Fluctuating oestrogen levels during your menstrual cycle can cause breast discomfort and areas of lumpy breast tissue that feel tender, sore and swollen. It is usually seen in upper outer quadrant , it is multiple in schimmelbush's disease .One cyst enlarges and which is palpable it is bluedome cyst of bloodgood. stromal proliferation , adenosis , and cyst formation are the sequential events seen in fibrocystic disease. Diagnosed by USG , FNAC and mammography.



Classified as

1. Non proliferative with moderate hyperplasia
2. Severe hyperplasia without atypia
3. Atypical hyperplasia with atypia

Treatment:

Indications for excision

1. Intractable pain,
2. Bloody discharge,
3. Bluedome cyst,
4. Atypical hyperplasia on histology.

BREAST TUBERCULOSIS (Tb):

1. Breast is resistant to Tb bacillus, hence tuberculosis of breast is rare.
2. Seen in association with pulmonary Tb.
3. Can spread by blood, or lymphatics.
4. Nipple areola complex not involved in tuberculosis breast.
5. Clinical features : Ill defined lump, irregular surface, multiple discharging sinus, matted nodes.
6. Can mimic Carcinoma breast
7. ATT is the treatment of choice, if there is any cold abscess it needs drainage.

SELF BREAST EXAMINATION

Step 1: Lying down

1. Lie down on your back with a pillow under shoulder .
2. Use the pad of three middle fingers on your right hand for palpating your left breast.
3. Palpate by light , medium , firm pressure in a circular motion with out taking fingers.
4. Follow an up and down pattern .
5. While showering repeat this steps .

Step 2: In front of mirror

1. Look for any changes in breast in following position.
2. Arms by the side ,above your head ,on your hips and bending forward with your hands on hip.

1. Examine your breasts in the shower.



2. Examine your breasts in the mirror with your arms down, up, and on your hips.



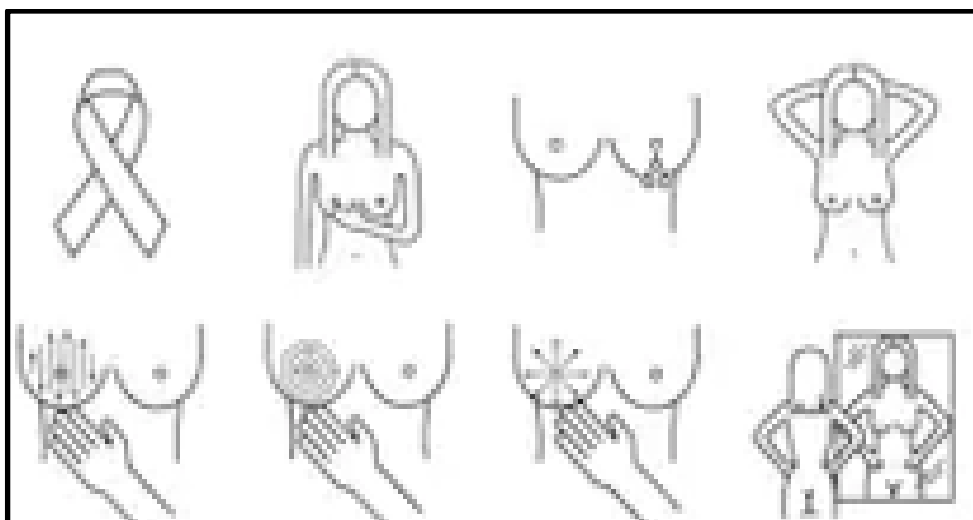
3. Stand and press your fingers on your breast, working around the breast in a circular direction.



4. Lie down and repeat step 3.



5. Squeeze your nipples to check for discharge. Check under the nipple last.



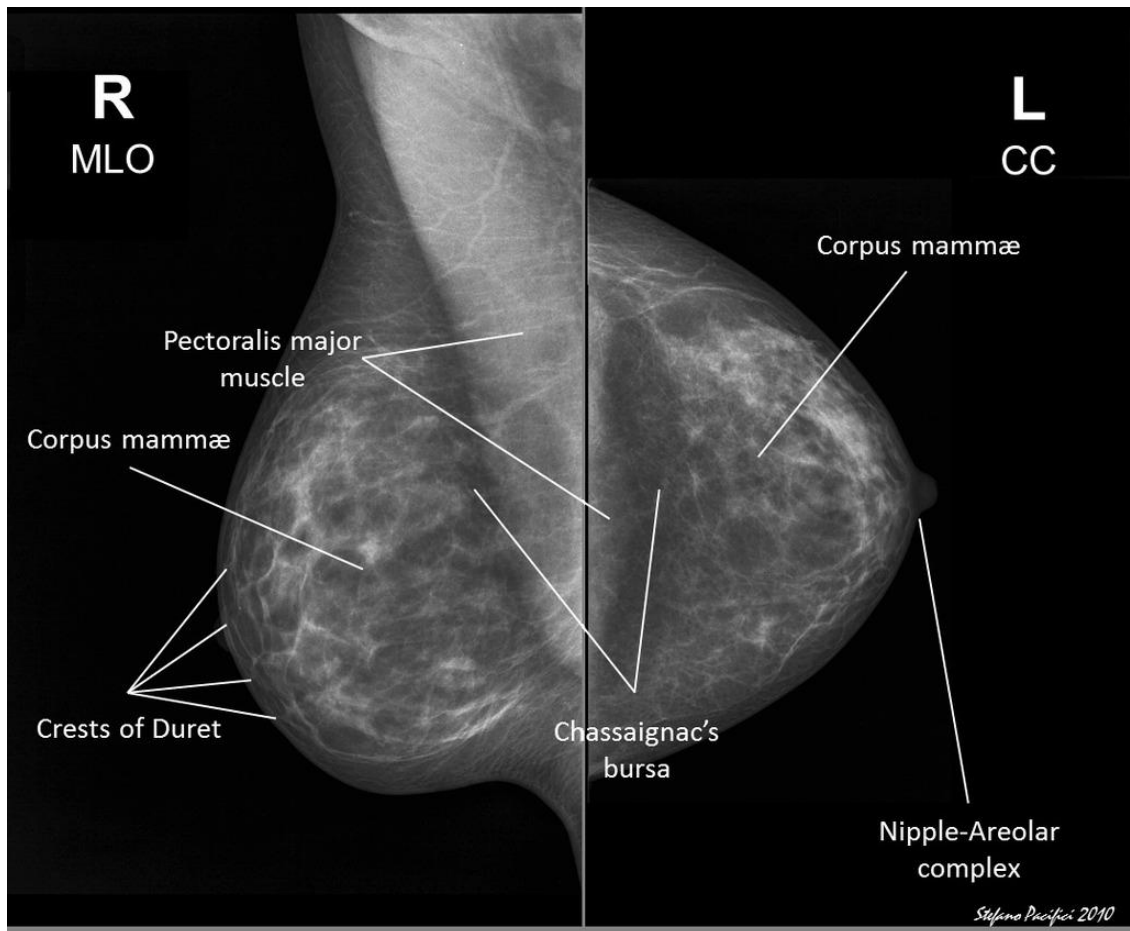
ULTRASONOGRAM (USG)

- USG uses high frequency sound waves between 3to7 MHz.
- Now we are using 20 MHz, it measures millimeter lesions.
- It differentiate solid or cystic lesion.
- It also useful for discriminating lesions in young females with dense breast.
- USG is the initial investigation, which is quick ,cheap ,non invasive technique.
- Specificity of the lesion increased by experienced sonologist.
- Not used as screening procedure.

MAMMOGRAM :

Mammogram is an x-ray picture of the breast. mammograms use doses of ionizing radiation.

Uses low voltage high ampearage x rays . 0.1 gy is used. It can be taken in two views craniocaudal and mediolateral view.



Indications:

- In post menopausal women
- As screening procedure
- Evaluate patients with nipple discharge, lump.
- In obese patient
- MRI guided biopsy taking.
- For those who under going breast conservative surgery.

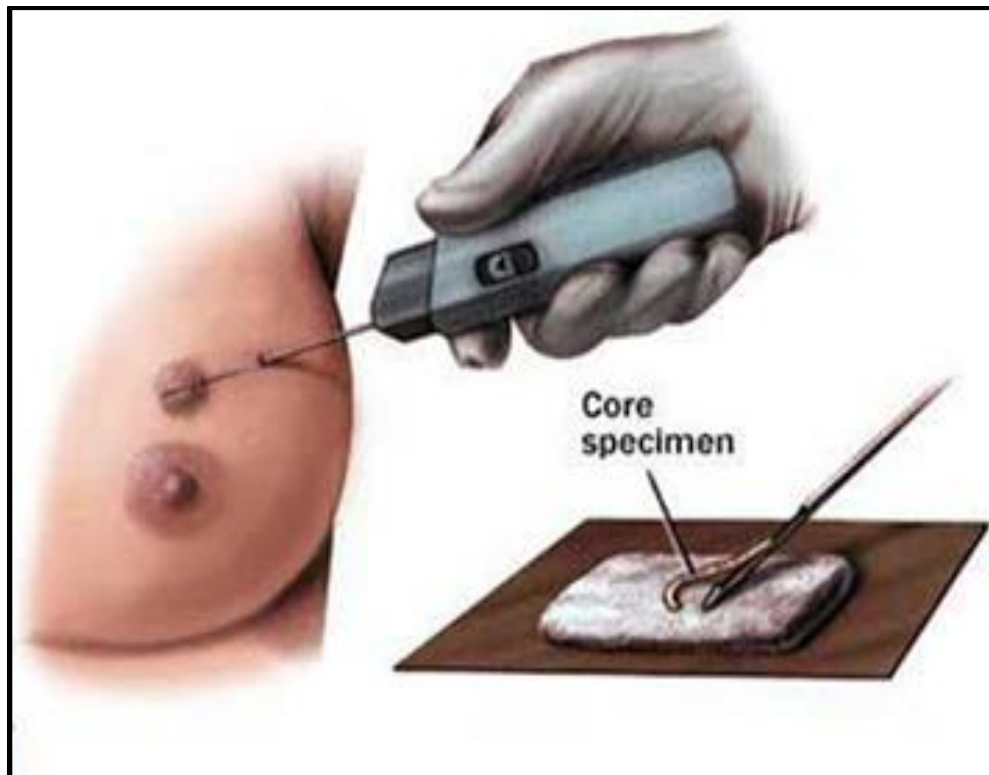
BI-RADS CLASSIFICATIONS		
BI-RADS	FINDINGS	FURTHER MANAGEMENT
0	Incomplete assessment	Need of additional imaging or prior examination
1	Negative	Routine Screening
2	Benign	Routine Screening
3	Probable benign - risk of malignancy is lower than 2%	Ultrasound imaging is necessary or a control mammography imaging and examination within 6 months
4	Suspicious - Risk of malignancy is 2-94%	Further cytology or pathohistology investigation is necessary
5	Highly Suspicious - Risk of malignancy is higher than 94%	Referral to a surgeon is necessary

FINE NEEDLE ASPIRATION CYTOLOGY (FNAC):

- Done with 22 gauge needle.
- Needle is repeatedly inserted into the mass with negative pressure, after releasing the suction needle is withdrawn.
- Scanty fluid with cellular material is stained for cytology.
- Advantages of FNAC is easy, least invasive and rapid .
- Very deeply located and difficult to hold and palpate is biopsied by USG guided FNAC.

TRUCUT BIOPSY:

Under LA ,by using 14-18 G needle large sample of tissue taken to find the receptor status .and also helps to differentiate the insitu from invasive carcinoma



Excision biopsy:

In tumour with size <4cm . incision should be planned in such way that it could be included in feature mastectomy incision.

Edge biopsy :

Taken in ulcerative and fungating lesion.

Discharge from nipple:

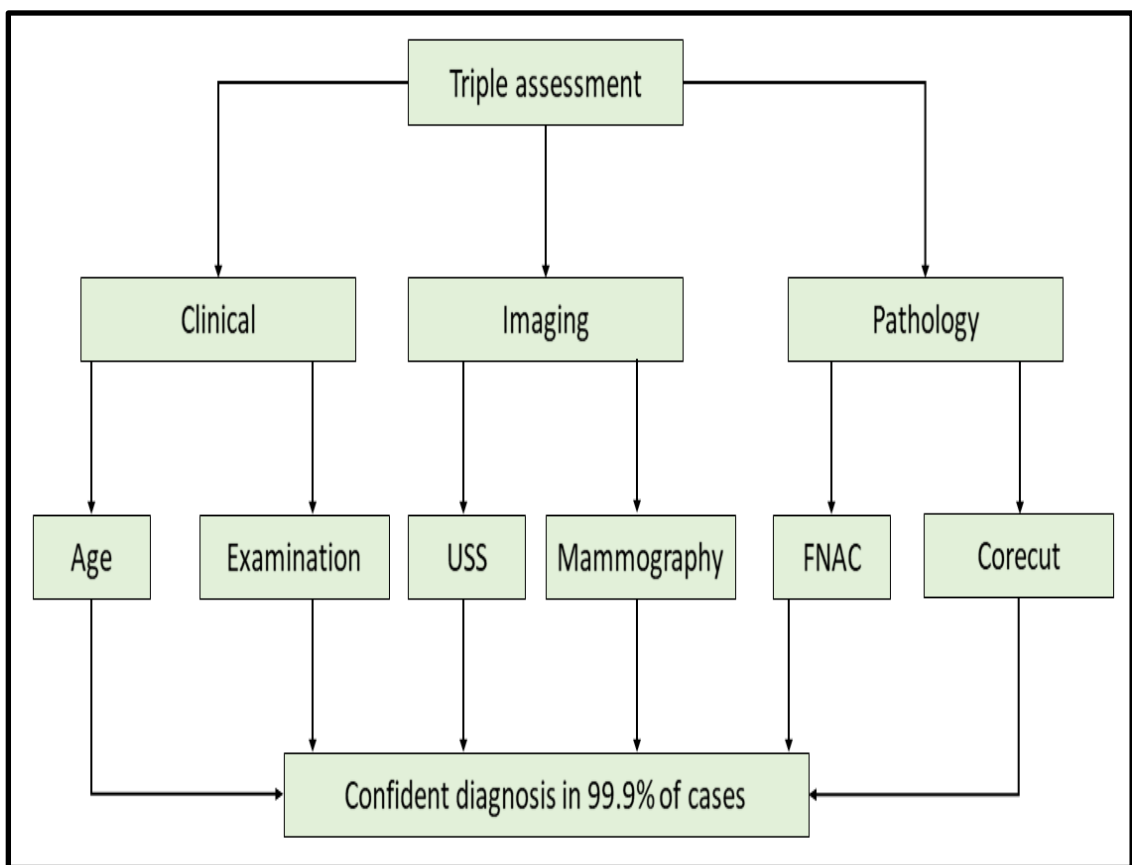
Ductal lavage could be done and fluid taken for cytology

MAGNETIC RESONANCE IMAGING :

1. Previously diagnosed with breast cancer and to determine the extent of the cancer
2. Suspected leak or rupture of a breast implant
3. Family history and other risk factors,
4. Very dense breast tissue, and mammograms didn't detect a prior breast cancer
5. History of precancerous breast changes eg., atypical hyperplasia or lobular carcinoma in situ
6. To differentiate scar tissue from recurrence.
7. Used in pregnant woman

TRIPLE ASSESSMENT:

Combination of three tests, i.e. clinical examination, radiological imaging (mammography, ultrasonography) and pathology called as triple assessment test is used to accurately diagnose all palpable breast lumps. Together they give sensitivity of 99%



OESTROGEN:

- Oestrogen secreted in the corpus luteum, graafian follicle of the ovary and placenta .
- In the liver oestradiol is oxidized to oestrone and then hydroxylated to estriol.
- Highly potent one in circulating hormone is oestradiol.
- From adipose tissue stroma , circulating oestrogen produces during postmenopausal period .
- Dehydroepiandrosterone gives oestrone , which is synthesized by adrenal gland .
- Oral potency is increased by Ethinyl substitutions at C17 position.
- By this it bypass 1st pass metabolism in liver. .
- 17β estradiol followed by estrone and estriol contains a phenolic A ring with a hydroxyl group at carbon 3 and a β -OH or ketone in position 17 of ring having oestrogen receptors ($ER\alpha, ER\beta$) .

ORMELOXIFENE:

- Also known as centchroman, is one of the selective estrogen receptor modulators, or SERMs, a class of medication which acts on the estrogen receptor.
- Ormeloxifene is a non-steroidal, non- hormonal oral contraceptive which was taken once in a wk. In India, Ormeloxifene has been used as a contraception since the early 1990s.
- It has high affinity interaction with ER, antagonizing the effect of estrogen on uterine and breast tissue and stimulating effect on vagina, bone, CVS and CNS.
- Ormeloxifene not only preferred as oral contraceptive, but also useful for management of dysfunctional uterine bleeding as it has antioestrogenic action on uterus.
- It may delay menstrual cycle. It doesnot show common side effects like nausea ,vomiting ,weight gain and abnormal liver function.
- It is taken orally. 26% of unchanged product excrete in feces ,remaining get metabolished by demethylation.
- Ormeloxifene has been given for benign breast disease like mastalgia and fibroadenoma as a dose of 30 mg twice a week for twelve week^{9,10, 11}

MATERIAL AND METHODS

TYPE OF STUDY:

Prospective Randomized control study conducted in the department of General Surgery at Chengalpattu Medical College

ETHICAL CLEARANCE:

The study protocol was received by the institutional ethical committee and is approved by the committee

METHOD OF STUDY

- 100 patients attending the department of General Surgery both inpatients and outpatients with complaints of breast pain and lump are selected and randomly divided into two group
- One group was treated with Ormeloxifene 30mg twice a week for twelve weeks and the other group was treated with placebo such as vitamin tablets for twelve weeks. The response was assessed with pain scale and breast lump size assessed with Lucknow –Cardiff scale as well as Ultrasound breasts

INCLUSION CRITERIA:

- Age group 20-50 years
- With mastalgia and breast swelling or nodularity

EXCLUSION CRITERIA:

- Patients with breast carcinoma
- Patient with uterine hyperplasia
- Lactating mothers
- Pregnancy
- Patients taking oral contraceptive pills

Study group is divided into two groups with 50 numbers in each group

Group A : Treated with Ormeloxifene

Group B : Treated with Placebo

After getting consent from the patient group A is treated with Ormenloxifene 30mg twice a week for 12 weeks and group B is treated with Placebo(Vitamin Tablets) twice a week for 12 weeks .Both the group Patient's followed for 6 months .

Mastalgia patient's are analysed with visual analog pain scale ranges from 0 to 10

- Scale 0 – No Pain
- Scale 1 –Mild Pain
- Scale 5 –Moderate Pain
- Scale 10 – Severe Pain

Fibroadenoma patient's nodularity was assessed by Lucknow Cardiff Scaling and Ultrasonogram. Nodularity scaling ranges from 0 to 4.

- Scale 0 – Extreme extent of normalcy
- Scale 1 –Moderate Nodularity
- Scale 4 – Maximum Nodularity ¹²

RESULTS AND OBSERVATIONS

Table 1 : Mean Age Of Study	
Group	MEAN \pm SD
Ormeloxifene	26.3 \pm 5.89
Placebo	25.96 \pm 5.82

Table 2 : Age Category of the study				
Age in Years	Ormeloxefine		Placebo	
	No	%	No	%
16-20	11	22%	10	20%
21-25	15	30%	14	28%
26-30	9	18%	12	24%
31-35	15	30%	14	28%

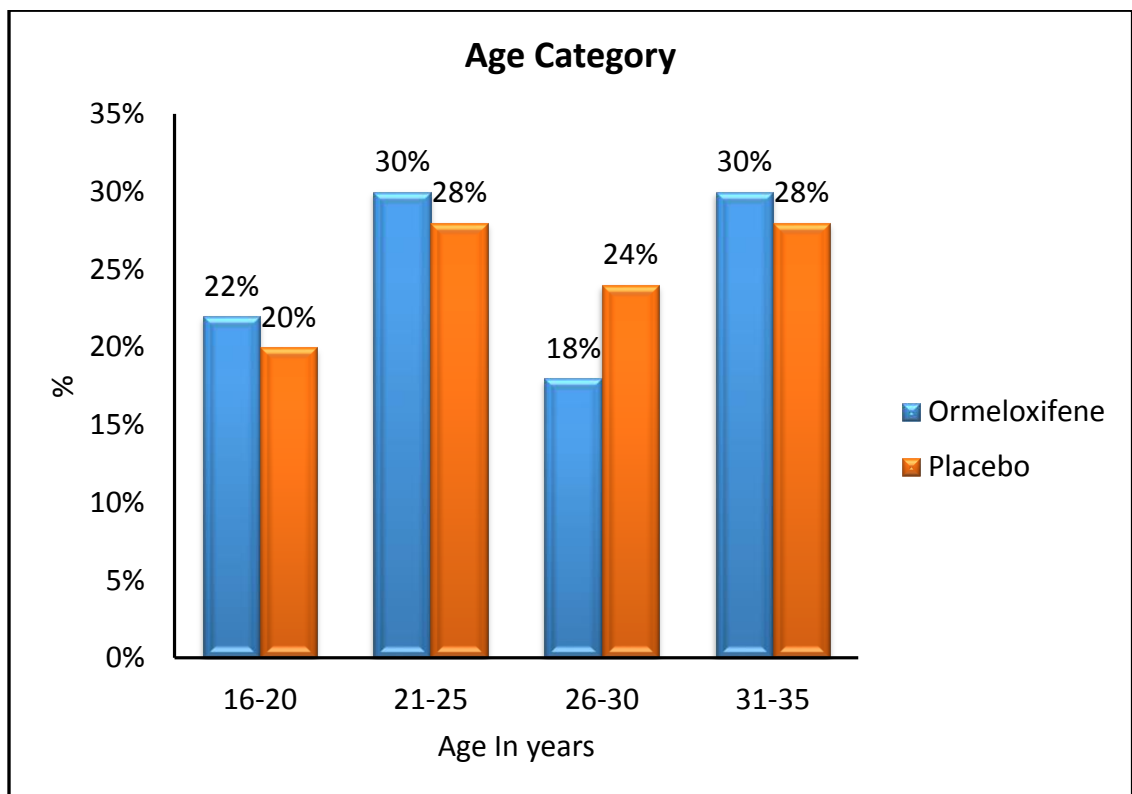


Table 3 : Mastalgia in the Study				
Group	Mastalgia			
	Positive		Negative	
	No	%	No	%
Ormeloxifene	20	40%	30	60%
Placebo	24	48%	26	52%

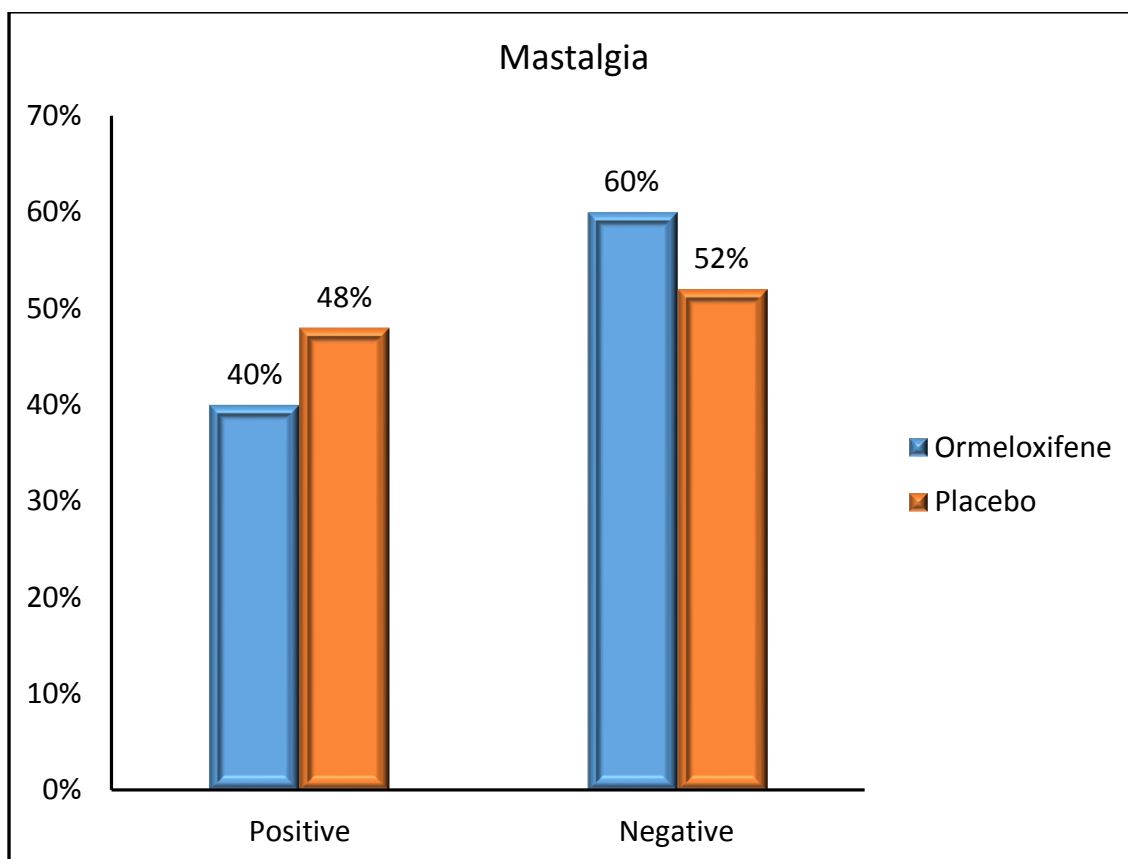


Table 4 : Fibroadenoma in the Study				
Group	Fibroadenoma			
	Positive		Negative	
	No	%	No	%
Ormeloxifene	32	64%	18	36%
Placebo	28	56%	22	44%

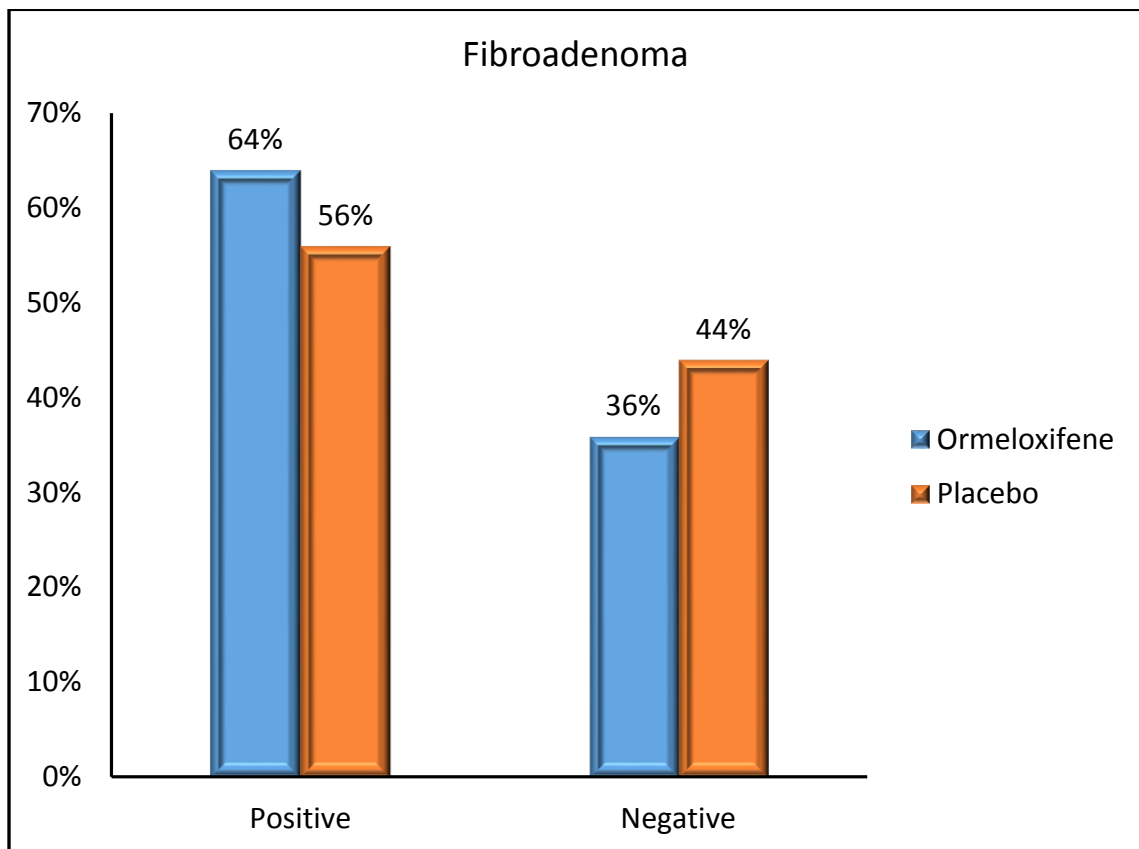


Table 5 : Pain Relief (VAS) in the Study				
Group	Pain Relief (VAS)			
	0	1	5	10
Ormeloxifene	46(92%)	0(0%)	4(8%)	0(0%)
Placebo	26(52%)	2(4%)	18(36%)	4(8%)

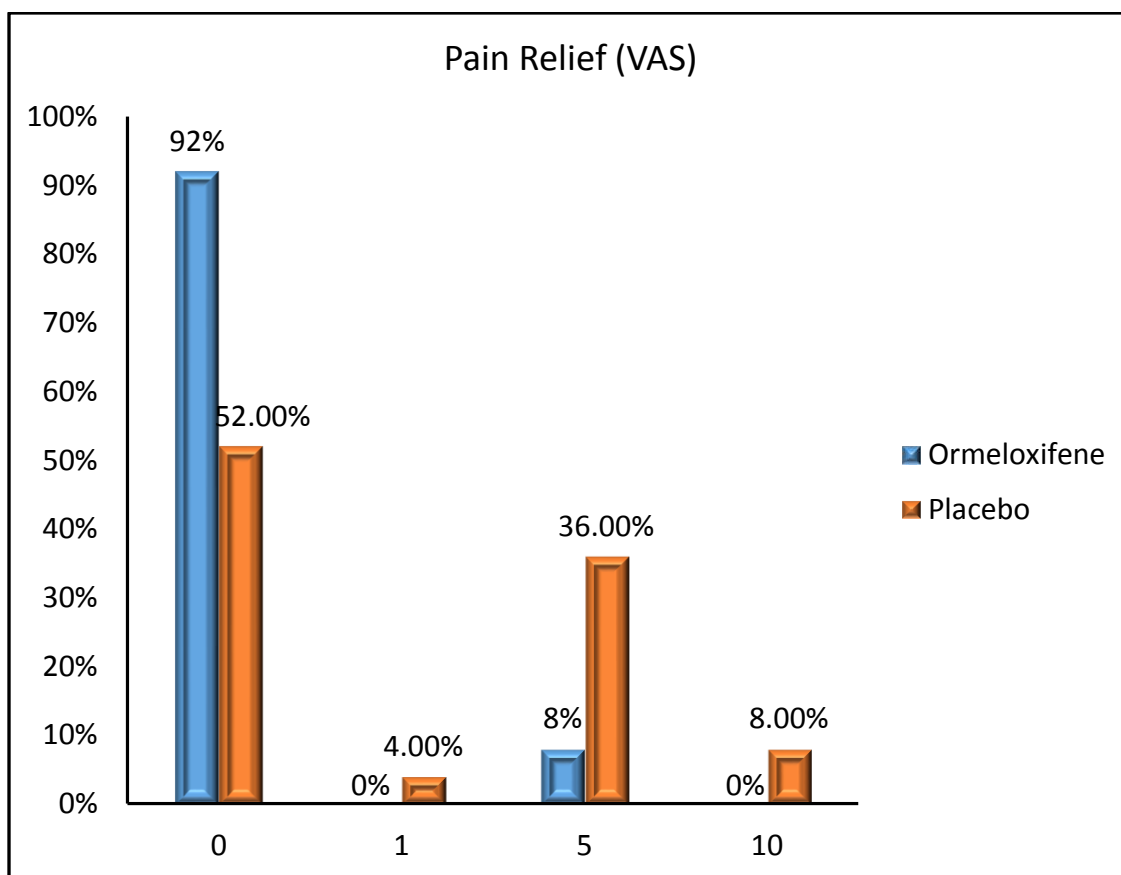


Table 6 : Association of Ormeloxifene with VAS in the study					
Ormeloxifene	VAS				Total
	0	1	5	10	
Not Given	26	2	18	4	50
Given	46	0	4	0	50
Total	72	2	22	4	100
Chi - Square Tests					
	Value	df	Asymp.Sig (2-sided)		
Pearson Chi Square	20.465*	3	0		
Likelihood Ratio	23.583	3	0		
Linear by-Linear association	17.225	1	0		
No of Valid cases	100				
* - 4 cells (50.0%) have expected count less than 5 . The minimum expected count is 1.00					

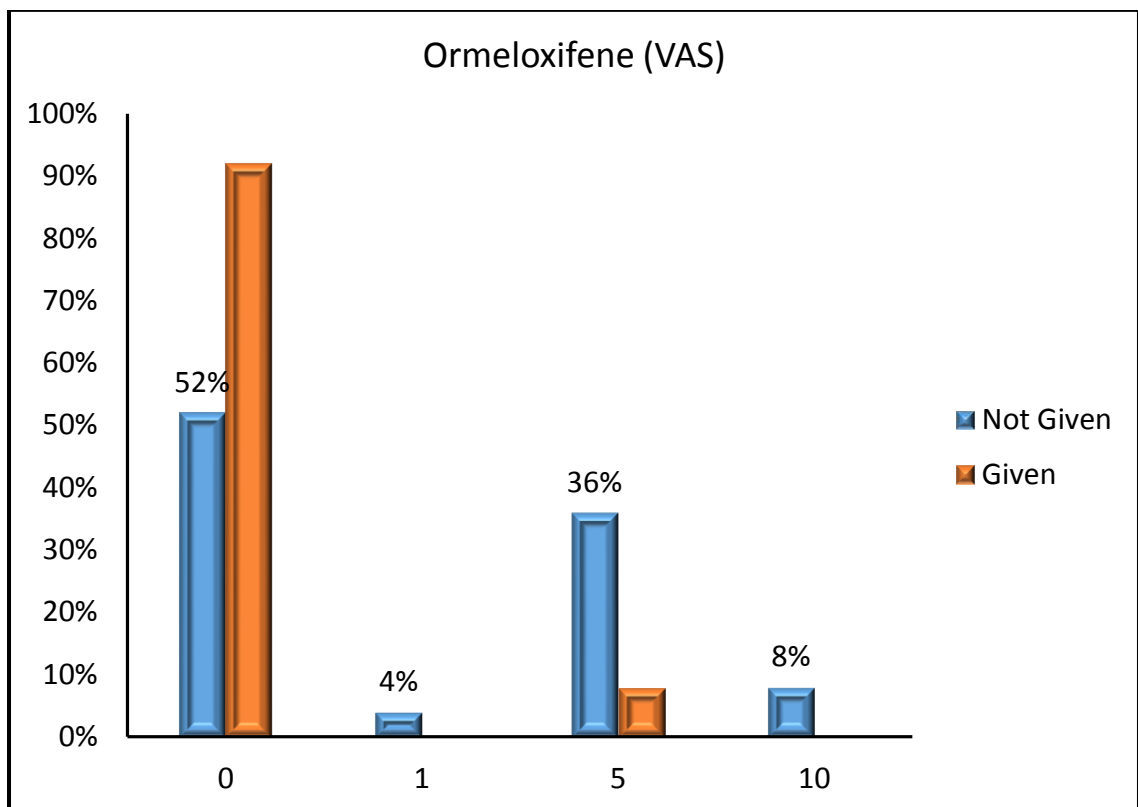


Table 7 : Association of Placebo with VAS in the study					
Placebo	VAS				Total
	0	1	5	10	
Not Given	46	0	4	0	50
Given	26	2	18	4	50
Total	72	2	22	4	100
Chi - Square Tests					
	Value	df	Asymp.Sig (2-sided)		
Pearson Chi Square	20.465*	3	0		
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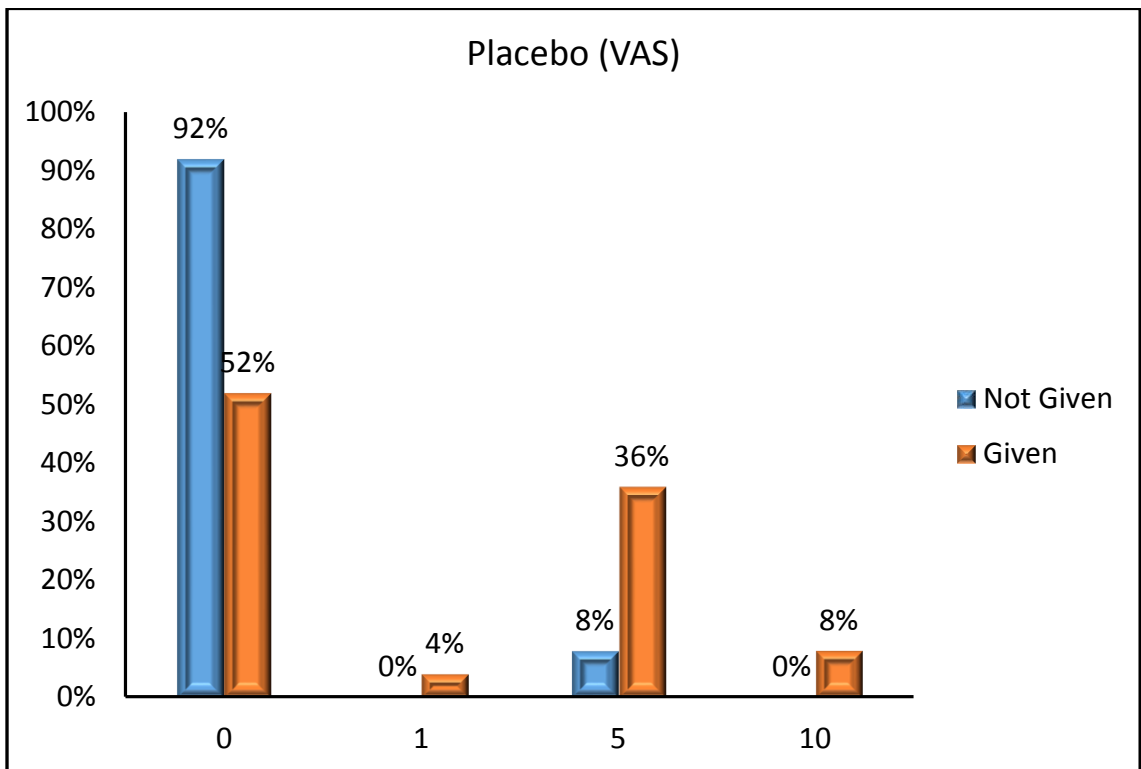


Table 8 : Association of Ormeloxifene with Nodularity(Cardiff scaling) in the study				
Ormeloxifene	Nodularity(Cardiff scaling)			Total
	0	1	4	
Not Given	21	1	28	50
Given	40	7	3	50
Total	61	8	31	100

Chi - Square Tests			
	Value	df	Asymp.Sig (2-sided)
Pearson Chi Square	30.579*	2	0
Likelihood Ratio	34.343	2	0
Linear by-Linear association	26.527	1	0
No of Valid cases	100		
* - 2 cells (33.3%) have expected count less than 5 . The minimum expected count is 4.00			

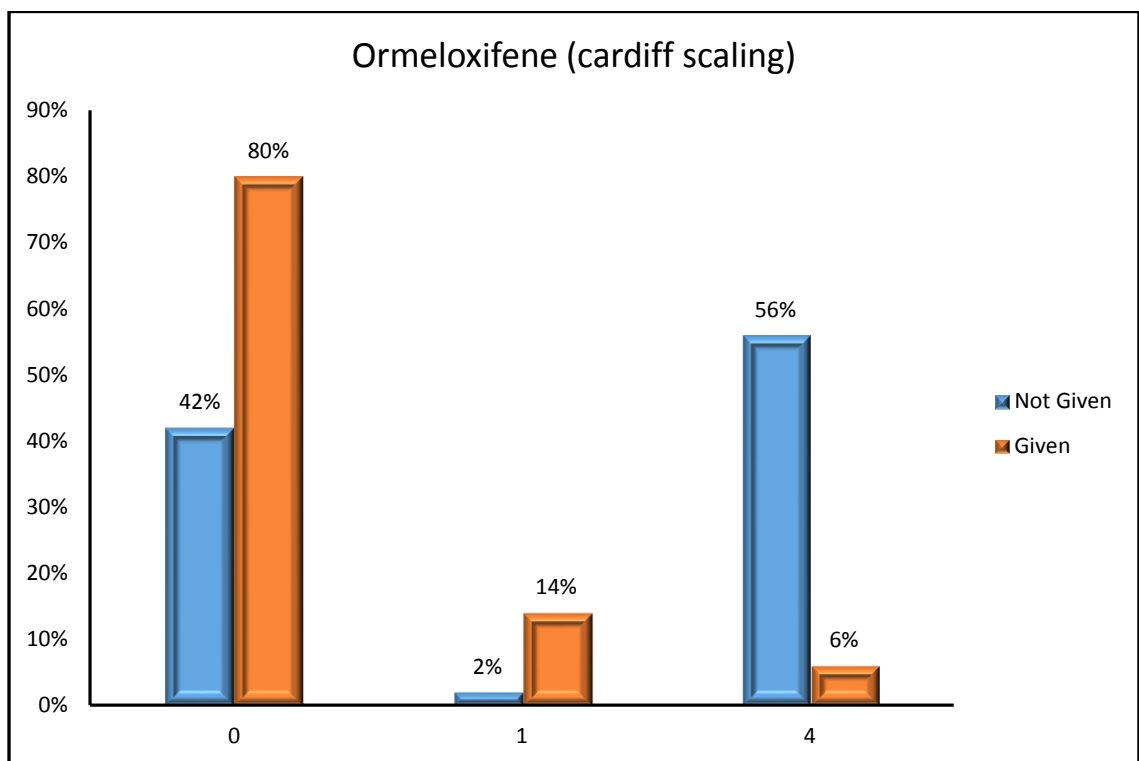


Table 9 : Association of Placebo with Nodularity(Cardiff scaling) in the study				
Placebo	Nodularity(Cardiff scaling)			Total
	0	1	4	
Not Given	40	7	3	50
Given	21	1	28	50
Total	61	8	31	100

Chi - Square Tests			
	Value	Df	Asymp.Sig (2-sided)
Pearson Chi Square	30.579*	2	0
Likelihood Ratio	34.343	2	0
Linear by-Linear association	26.527	1	0
No of Valid cases	100		

* - 2 cells (33.3%) have expected count less than 5 . The minimum expected count is 4.00

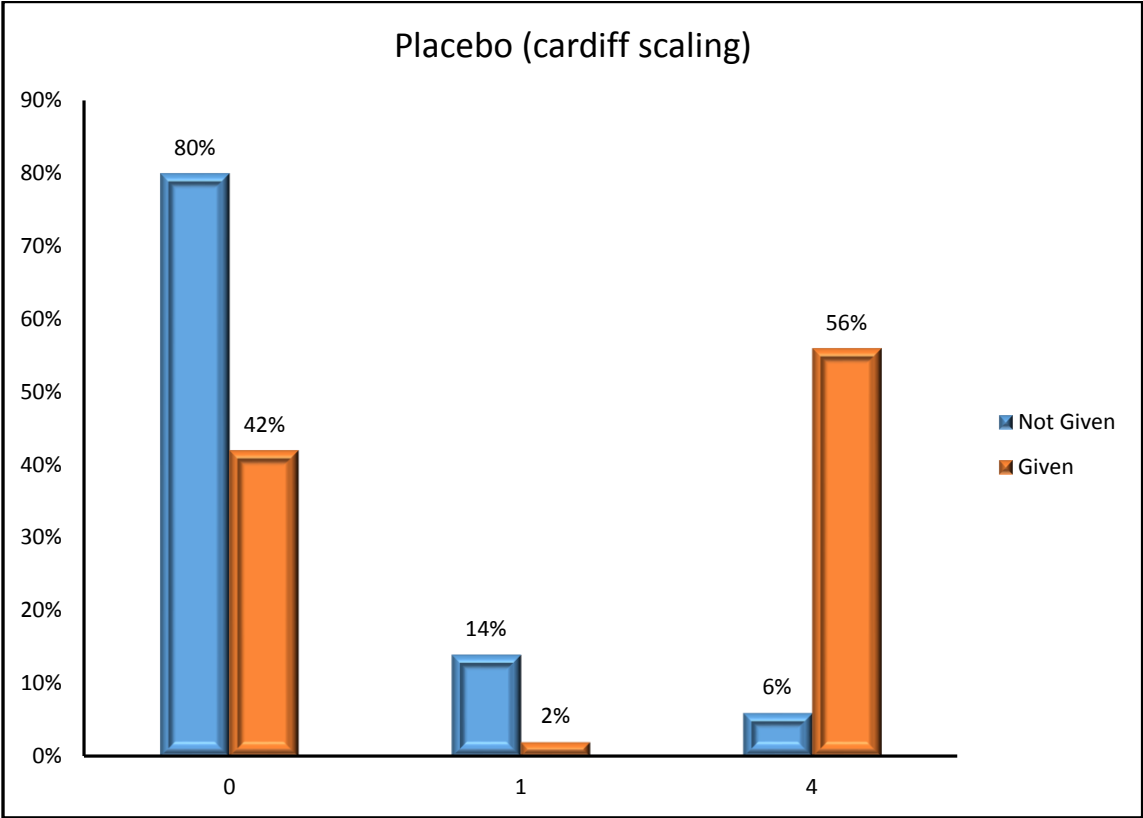
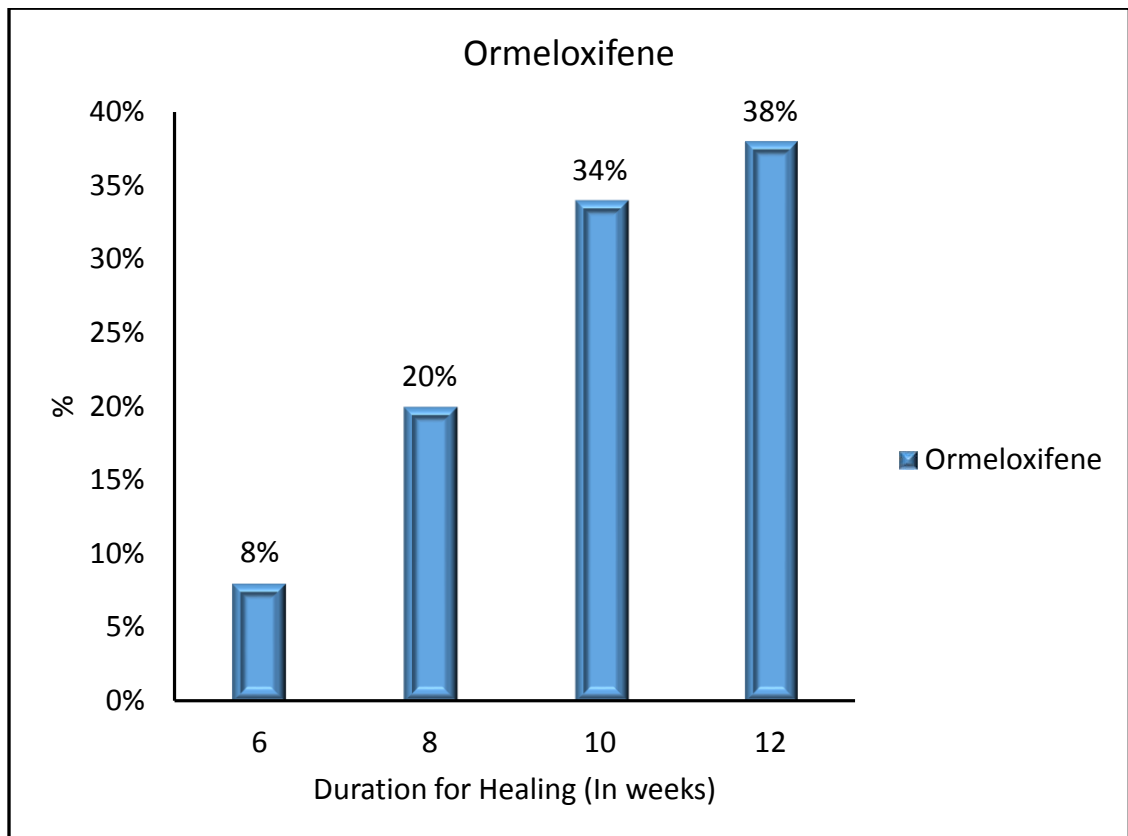


Table 10 : Duration for healing in the study				
Group	Duration for healing(In weeks)			
	6	8	10	12
Ormeloxifene	4	10	17	19



DISCUSSION

Fibroadenoma is the most common benign tumour of females less than 30 yrs old and 2nd most common neoplasm of females , 20 % of the patient shows bilateral and 20 % shows multiple fibroadenoma . There was lot of medical management but there is no proof and standard treatment for these benign breast disease conditions like fibroadenoma and mastalgia . surgical treatment also not satisfactory as it leads to lot of mental stress, hence I decided to do this study instead of simple observation in patients who is willing for treatment ,as 15 % of fibroadenoma will regress spontaneously over 1 – 6 yrs observation.

There are lot of studies going on to find the effectiveness of tamoxifene ,danazol, for regression of fibroadenoma and mastalgia. But above this drugs has reported some side effects . With ormeloxifene , only minimal studies was conducted and also found to be effective in treating fibroadenoma and mastalgia with minimal side effects.

Hence, I have conducted a prospective randomised control study in Chengalpattu medical college ,of about hundred patients coming to hospital with the complaints of pain in the breast and lumpiness in the breast . The patients are selected according to the inclusion and exclusion criteria. In the age group of 15-35 yrs and those with mastalgia and breast swelling or nodularity are included in the study. The patients with breast carcinoma, and those with uterine hyperplasia and lactating mothers are excluded in the study.

Patients with benign breast disease includes mastalgia, fibroadenoma, fibroadenomatous hyperplasia, fibrocystic disease, mastitis, sclerosing adenosis and breast abscess. Patients with benign breast disease often present with pain and swelling. They frequently visit the clinic for the complaints of pain and nodular swelling. Most of the benign breast diseases are treated conservatively with medications and rarely surgery. There is no satisfactory treatment for this benign disease. After getting the informed consent from the patient, they are divided into two groups with 50 in each.

One group was treated with Ormeloxifene 30mg twice a week for twelve weeks and the other group was treated with placebo such as vitamin tablets for twelve weeks. Then for fibroadenoma patient subjected to fine needle aspiration cytology to rule out malignancy ,and also ultrasonogram of the breast .The response was assessed with pain scale and breast lump size assessed with Lucknow –Cardiff scale as well as Ultrasound breasts. The patients are followed for 6 months.

Mean age of study patients treated with ormeloxifene is 26.3years and those treated with placebo is 25.96 years .Of these 44 patients has mastalgia ,among them 20 (40%) was treated ormeloxifene and the remaining 24(48%) was treated with placebo. simillarly of total 60 patients of fibroadenoma, 32 (64%) patients with ormeloxifene and the remaining 28 (56%) with placebo . 56 mastalgia and 40 fibroadenoma patients in control group is again divided into two, one group is treated with ormeloxifene and the other with placebo.

Using visual analog pain scale, the above mastalgia patient is assessed, 92% of the mastalgia has score 0, 0% of patients has score 1 ,then 8% patients has score 5% and 0% of patient had score 10. Thus 92 % of patients fully cured with ormeloxifene and also only 8 % has moderate pain

By using Lucknow Cardiff scaling for assessing nodularity , 80% had score 0 , 14 % had score 1, only 6 % shows score 4 .And hence 80 % of patients completely cured with ormeloxifene ,14 % has decreased size in nodularity and size . Only 6% doesnot show any response to treatment with ormeloxifene. And also mean time for healing is 10 weeks. Hence the calculated p value for ormeloxifene is 0.000 which is statistically significant. The patients treated with ormeloxifene has no adverse effect, with good patients compliance. The study data is based on 6 months follow-up only. Long term results of ormeloxifene on recurrence and further decrease in size require further studies in future.

CONCLUSION

Patients with mastalgia and fibroadenoma attend the clinic for the fear of malignancy. Reassurance is enough after the thorough investigation. But pain affects the day to day activities. These patients treated with ormeloxifene 30mg twice a wk, which is selective estrogen receptor modulator with antioestrogenic action on breast, had good compliance with the no side effects.

Ormeloxifene therapy in fibroadenoma patients showed statistically significant regression of nodularity and also decrease the pain in mastalgia patients in a period of twelve weeks.

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PATIENT CONSENT FORM

STUDY DETAIL:

TO STUDY THE EFFECT OF ORMELOXIFENE IN THE REGRESSION OF MASTALGIA, FIBROADENOMA AND FIBROADENOMATOUS HYPERPLASIA IN CHENGALPATTU MEDICAL COLLEGE

STUDY CENTER:

CHENGALPATTU MEDICAL COLLEGE & HOSPITAL, CHENGALPATTU

PATIENT NAME:

PATIENT AGE:

IDENTIFICATION NUMBER:

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

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reasons, without my legal rights being affected. I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if withdraw from the study, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperative with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms.

I hereby give consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic test.

Signature/Thumb impression:

Place:

Date:

Patient name and address:

Signature of the investigator:

Place:

Date:

Study investigator's name:

INFORMED CONSENT FORM

Title of the Study : **TO STUDY THE EFFECT OF ORMELOXIFENE IN THE REGRESSION OF MASTALGIA, FIBROADENOMA AND FIBROADENOMATOUS HYPERPLASIA**

Name of the Participant :

_____.

Name of the Principal (Co-Investigator) :

_____.

Name of the Institution : Government Chengalpattu medical college and Hospital

Name and address of the sponsor / agency(ies) (If any) : _____

Documentation of the informed consent :

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in : **TO STUDY THE EFFECT OF ORMELOXIFENE IN THE REGRESSION OF MASTALGIA, FIBROADENOMA AND FIBROADENOMATOUS HYPERPLASIA**

(title of the study).

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____ months including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.*
7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.*
8. I have not participated in any research study within the past _____month(s).*
9. I have not donated blood within the past _____months----add if the study involves extensive blood sampling.*
10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.*
11. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.
12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.
13. I have understand that my identity will be kept confidential if my data are publicly presented .
14. I have had my questions answered to my satisfaction.
15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

சுயஒப்புதல்படிவம்

ஆய்வுசெய்யப்படும் தலைப்பு :

**TO STUDY THE EFFECT OF ORMELOXIFENE IN THE
REGRESSION OF MASTALGIA, FIBROADENOMA AND FIBROADENOMATOUS
HYPERPLASIA IN CHENGALPATTU MEDICALCOLLEGE**

ஆய்வுசெய்யப்படும் இடம்:

பங்குபெறுபவரின் பெயர்:

பங்குபெறுபவரின் வயது:

பங்குபெறுபவரின் எண் :

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டுள்ளது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கின்றேன். எந்தகாரணத்தினாலோ, எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக்கொள்ளலாம் என்றும் அறிந்துகொண்டேன்.

இந்த ஆய்வுசம்பந்தமாகவோ, இதைசார்ந்து மேலும் ஆய்வுமேற்கொள்ளும்போதும் இந்த ஆய்வில்பங்கு பெறும் மருத்துவர், என்னுடைய மருத்துவஅறிக்கைகளைபார்ப்பதற்கு என் அனுமதி தேவைஇல்லை என அறிந்துகொள்கிறேன். இந்த ஆய்வின் மூலம்கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்க மாட்டேன். இந்த ஆய்வில் பங்குகொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம்:

சாட்சியாளரின் கையொப்பம்:

இடம்:

இடம்:

தேதி:

தேதி :

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்

ஆய்வாளரின் கையொப்பம்:

இடம்:

தேதி:

PROFORMA

- 1. NAME:**
- 2. AGE:**
- 3. OP/IP NO:**
- 4. HISTORY:**
- 5. COMORBIDITIES:**
- 6. MARITAL STATUS:**
- 7. VITALS:**
- 8. GENERAL EXAMINATION:**
- 9. SYSTEMIC EXAMINATION:**
- 10. EXAMINATION OF BREAST:**
- 11. BLOOD INVESTIGATION:**
- 12. ULTRASOUND OF BREAST:**
- 13. FINE NEEDLE ASPIRATION CYTOLOGY REPORT:**

MASTER CHART

S No	Name	Age	Mastalgia	Fibroadenoma	Ormeloxifene	Placebo	VAS	Lucknow cardiff scaling	Time in weeks
1	Mahalakshmi	19	0	1	1	0	0	0	10
2	Viji	26	1	0	0	1	5	0	*
3	Suganthi	19	0	1	1	0	0	0	12
4	Nandhini	21	0	1	0	1	0	4	*
5	Pavithra	19	0	1	1	0	0	0	10
6	Ponniyammal	34	1	1	0	1	5	4	*
7	Kamali	35	1	0	1	0	0	0	6
8	Sasikala	30	0	1	0	1	0	4	*
9	Divya	17	0	1	1	0	0	0	10
10	Geetha	26	0	1	0	1	1	4	*
11	Keerthana	18	0	1	1	0	0	0	12
12	Amsa	21	0	1	0	1	0	4	*
13	Indra	35	1	0	1	0	5	0	6
14	Mahalakshmi	22	0	1	0	1	0	4	*
15	Gothavari	32	0	1	1	0	0	1	12
16	Krishnaveni	29	0	1	0	1	0	4	*
17	Lakshmi	23	1	0	1	0	0	0	8
18	Rukku	27	1	0	0	1	5	0	*
19	Banu priya	19	0	1	1	0	0	4	12
20	shobana	21	0	1	0	1	0	4	*
21	Surekha	24	0	1	1	0	0	0	10
22	Akila	18	0	1	0	1	0	4	*
23	Yamini	29	1	0	1	0	0	0	8
24	Murugammal	34	1	0	0	1	10	0	*
25	Mageshwari	23	0	1	1	0	0	0	12
26	Tamilselvi	33	0	1	0	1	0	4	*
27	Snegha	21	0	1	1	0	0	1	12
28	Aarthi	22	1	0	0	1	5	0	*

S No	Name	Age	Mastalgia	Fibroadenoma	Ormeloxifene	Placebo	VAS	Lucknow cardiff scaling	Time in weeks
29	Valarmathi	26	1	0	1	0	0	0	8
30	Vani	31	1	0	0	1	5	0	*
31	Sugumari	29	0	1	1	0	0	4	10
32	Bargavi	20	0	1	0	1	0	4	*
33	Revathi	19	0	1	1	0	0	0	12
34	Saroja	33	1	0	0	1	10	0	*
35	Yazhalini	20	0	1	1	0	0	0	10
36	Renuka	22	0	1	0	1	0	4	*
37	Mary	35	1	0	1	0	0	0	10
38	Fathima	32	1	0	0	1	5	0	*
39	Sudha	19	0	1	1	0	0	0	12
40	Vennila	26	1	0	0	1	5	0	*
41	Amutha	29	1	0	1	0	0	0	8
42	Rajalakshmi	28	0	1	0	1	0	4	*
43	Samundeeswari	30	0	1	1	0	0	0	8
44	Abiramalatha	17	0	1	0	1	0	1	*
45	Suganya	29	1	0	1	0	0	0	6
46	Priya	25	0	1	0	1	0	4	*
47	Pannimalar	33	1	0	1	0	5	0	10
48	Harini	22	1	0	0	1	5	0	*
49	Hemalatha	27	0	1	1	0	0	0	12
50	Bharani	19	0	1	0	1	0	4	*
51	Manju	34	1	0	1	0	5	0	12
52	Piyadharshini	18	0	1	0	1	0	4	*
53	Bhavatharani	23	0	1	1	0	0	0	10
54	Saghana bee	34	1	0	0	1	1	0	*
55	Arokiya mary	35	1	0	1	0	5	0	12
56	Gandhimathi	20	0	1	0	1	0	4	*
57	Santhosini	32	1	0	1	0	0	0	10
58	Sindhusree	22	0	1	0	1	0	4	*
59	Rathidevi	25	0	1	1	0	0	0	10
60	Dhanalakshmi	20	0	1	0	1	0	4	*
61	chithra	34	1	0	1	0	0	0	8

S No	Name	Age	Mastalgia	Fibroadenoma	Ormeloxifene	Placebo	VAS	Lucknow cardiff scaling	Time in weeks
62	Neelavani	35	1	0	0	1	5	0	*
63	Vanmathi	32	0	1	1	0	0	0	12
64	Kasthuri	24	0	1	0	1	0	4	*
65	Santha	35	0	1	1	0	0	4	12
66	Kokila	22	1	0	0	1	5	0	*
67	Andal	33	0	1	1	0	0	0	10
68	Kanchana	34	1	0	0	1	5	0	*
69	Gowri	23	0	1	1	0	0	0	10
70	Yamini	34	1	0	0	1	10	0	*
71	Radha	23	1	0	1	0	0	0	8
72	Salini	19	1	0	0	1	5	0	*
73	Poonguzhali	22	0	1	1	0	0	1	12
74	Shreeja	29	1	0	0	1	5	0	*
75	Dhirsha	23	1	1	1	0	0	1	12
76	Nagaeshwari	21	0	1	0	1	0	4	*
77	Rupa	29	1	0	1	0	0	0	8
78	Annapoorani	27	1	0	0	1	0	0	*
79	Shylaja	21	0	1	1	0	0	1	12
80	Noorjagan	35	1	0	0	1	5	0	*
81	Swathi	20	0	1	1	0	0	0	10
82	Durga	18	0	1	0	1	0	4	*
83	Ramya	34	1	0	1	0	0	0	10
84	Kamala	19	0	1	0	1	0	4	*
85	Poornima	29	1	1	1	0	0	0	8
86	Devaki rani	27	1	0	0	1	5	4	*
87	Rajeshwari	21	0	1	1	0	0	1	12
88	Sasi	35	1	0	0	1	5	0	*
89	Susila	20	0	1	1	0	0	0	10
90	Anchigashree	21	0	1	0	1	0	4	*
91	Kajol	35	1	0	1	0	0	0	6
92	Kaveri	22	0	1	0	1	0	4	*
93	Yamuna	32	0	1	1	0	0	1	12
94	Anu	29	0	1	0	1	0	4	*

S No	Name	Age	Mastalgia	Fibroadenoma	Ormeloxifene	Placebo	VAS	Lucknow cardiff scaling	Time in weeks
95	Kavitha	23	1	0	1	0	0	0	8
96	Shanthi	27	1	0	0	1	5	0	*
97	Jayashree	23	0	1	1	0	0	0	10
98	Malathi	35	1	0	0	1	10	0	*
99	Aadhilakshmi	25	0	1	1	0	0	0	12
100	Geetha	32	1	1	0	1	5	4	*