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Diagnostic Approach to Palpable Breast Lump - A Quadruple Assessment

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Abstract: ***The vast majority of the lesions that occur in the breast are benign. Much concern is given to malignant lesions of the breast because breast cancer is the most common malignancy in women in Western countries; however, benign lesions of the breast are far more frequent than malignant ones. With the use of mammography, ultrasound, and magnetic resonance imaging of the breast and the extensive use of needle biopsies, the diagnosis of a benign breast disease can be accomplished without surgery in the majority of patients. Because the majority of benign lesions are not associated with an increased risk for subsequent breast cancer, unnecessary surgical procedures should be avoided. It is important for pathologists, radiologists, and oncologists to recognize benign lesions, both to distinguish them from in situ and invasive breast cancer and to assess a patient's risk of developing breast cancer, so that the most appropriate treatment modality for each case can be established.***

Keywords: Breast Lump, USG Beast, FNAC, Assessment, Mammography

1. Introduction

The first step in evaluation of breast lump is the clinical assessment. Although many a times clinician can confidently make the diagnosis of benign or malignant lesion, the possibility of mistake is always there even in experienced hands.

The triple test for breast diseases involve,

1) Clinical assessment
2) Imaging modality – Mammography
3) Fine needle aspiration biopsy/cytology

In modified triple test ultra sonogram is used instead of mammography.

Clinical diagnosis of breast cancer is of higher sensitivity than specificity and has high diagnostic error. Mammography and FNAC respectively have lower sensitivity than specificity but have high positive predictive values.

When combined in the triple assessment, a definitive diagnosis can be made when the diagnoses concur, suggesting that the triple assessment has a high sensitivity, specificity, positive predictive value and negative predictive value with minimal error and excellent Kappa statistic.

The output of the triple assessment in reproducible, making it a valid and reliable diagnostic approach to diagnosis of breast cancer.

Mammography is the proven and preferred method for breast cancer screening. But when mammography reveals a non-palpable breast lesion further imaging studies are often required to more precisely identifying the characteristics and location of the mass.

The first attempts to use radiography for the diagnosis of breast abnormalities were made in the late 1920's, but mammography, as we understand it nowadays, using dedicated X-ray units, was developed in the 1960s.

During the past 2 decades a number of additional methods for assessing breast lesions have been investigated. These include Thermography, Radioisotope scanning, ultrasound, computed tomography, and magnetic resonance imaging.

Ultrasonographic examination of the breast is an extremely effective diagnostic tool when used in conjunction with physical and mammographic examination. It is painless, requires no roentgenographic exposure, and with proper training it can be easily performed in a timely, convenient manner.

2. Need for the Study

Breast lump is the clinical presentation of numerous breast diseases ranging from innocent benign cysts to malignant lesions. Distinction of benign from malignant is of paramount importance for patient care and proper management[1].

Breast cancer is the most common site specific cancer in women and is the leading cause of death from cancer for women of age 40 to 44 year[2, 3]. It accounts for 33% of all female cancers and is responsible for 20% of the cancer related deaths in women[3].

Presently a wide range of diagnostic modalities is available for the evaluation of breast lump. Conventional open biopsy, considered to be the gold standard for confirming diagnosis, has significant morbidity, is costly and time consuming. To overcome these issues, various biopsy techniques like, Tru-cut needle biopsy, later, core-needle version vaccum assisted biopsy (VAB) devices such as mammotome, image guided advanced breast biopsy instrumentation (ABBI) and minimally invasive breast biopsy evolved. Notwithstanding their cost and limited availability, all cause significant trauma to the patient and are not patient friendly.

Mis-diagnosed breast cancer accounts for the greatest number of malpractice claims for errors in diagnosis. Litigation often involves younger women whose physical examination and mammography may be misleading[3].

Two techniques that are currently available with excellent patient tolerability are mammography and fine needle aspiration cytology. However if employed alone the reliability of mammography and FNAC is only around 82% and 78% respectively[1].
There are numerous reports that if the results of clinical assessment, mammography and FNAC are all combined, the accuracy of diagnosis reaches 100%[4]. Furthermore these techniques provide information on tumor size, number, extent and grade pre-operatively[5].

Thus there is a dire need for evolving a method for establishing the diagnosis pre-operatively, which is cost effective, least invasive and least disturbing the patient, with accuracy comparable to open biopsy.

3. Aim and Objectives

- To correlate between clinical diagnosis, ultrasonography, mammography and FNAC.
- To compare diagnostic accuracy of ultrasonography in palpable breast lump in correlation with triple assessment.

4. Review of Literature

Donegan [6] stated that most breast cancers appear as palpable masses, usually found by patients. However not all palpable abnormalities represent discrete masses. This is especially true in women younger than 40 years of age, in whom normal glandular nodularity may be mistaken for dominant masses.

Imaging evaluation of the breast is established as an essential part of modern multidisciplinary approach for effective investigation and management of breast lump. This includes ultrasound and Doppler scanning, conventional digital mammography and recently MRI and contrast enhanced ultrasound[7].

Diagnostic mammography is the first imaging study employed to evaluate breast abnormalities and as opposed to screening mammography, it is performed when a breast abnormality is already present[8]. It is a more comprehensive examination and consists of multiple specialized images.

To promote uniformity and standardization of mammographic interpretation, American college of Radiography (ACR) and other international organizations, with mutual consensus, have adopted and recommended universal implementation of breast imaging reporting and data system (BIRADS) [9].

FNAC is easily performed and sensitivity ranges from 80-95%[10] and false positive aspirates are seen in less than 1% of cases. False negative results are seen in 4-10% and are most common in fibrotic or well differentiated tumors [10].

Ultrasonography is an important method of resolving equivocal mammography findings defining cystic lesions and demonstrating the echogenic qualities of specific solid abnormalities[2, 11]. Incorporation of ultrasound in the triple assessment of palpable breast masses can result in a reduction of total costs for the diagnosis and treatment of breast cancer [12].

False negative rate of mammography has been reported to be as high as 16.5%. Multiple studies have shown that the false negative rate for a combined mammographic and sonographic evaluation varies from 0-2.6% and together these imaging modalities can be reassuring if follow up is planned when clinical assessment is not highly suspicious[13].

Thus the triple test with incorporated ultra sonogram is quiet, least invasive and cost effective[14] in terms of money and time. Furthermore it can be applied as a single stage diagnostic approach, decreasing the deleterious psychological effects on the patients from delay in diagnosis[15].

5. Mammography

Mammography has been used in North America since the 1960s and the techniques used continue to be modified and improved to enhance image quality. Conventional mammography delivers a radiation dose of 0.1 centigray (cGy) per study. By comparison, a chest x-ray delivers 25% of this dose. However, there is no increased breast cancer risk associated with the radiation dose delivered with screening mammography. Screening mammography is used to detect unexpected breast cancer in asymptomatic women. In this regard, it supplements history and physical examination.

With screening mammography, two views of the breast are obtained, the cranio-caudal (CC) view and the medio-lateral oblique (MLO) view. The MLO view images the greatest volume of breast tissue, including the upper outer quadrant and the axillary tail of Spence. Compared with the MLO view, the CC view provides better visualization of the medial aspect of the breast and permits greater breast compression.

Diagnostic mammography is used to evaluate women with abnormal findings such as a breast mass or nipple discharge. In addition to the MLO and CC views, a diagnostic examination may use views that better define the nature of any abnormalities, such as the 90-degree lateral and spot compression views. The 90-degree lateral view is used along with the CC view to triangulate the exact location of an abnormality.

Spot compression may be done in any projection by using a small compression device, which is placed directly over a mammography abnormality that is obscured by overlying tissues. The compression device minimizes motion artifact, improves definition, separates overlying tissues, and decreases the radiation dose needed to penetrate the breast. Magnification techniques (x1.5) often are combined with spot compression to better resolve calcifications and the margins of masses.

Radiological Anatomy of the Breast[16]

Schematically, the radiological examination may show the

following normal anatomical structures:

- Skin
- Nipple and areola
- Fatty tissue
- Breast proper, or corpus mammae
- Blood vessels

Skin

The skin appears as a thin, continuous, radiopaque rim, homogeneous in density, approximately 1 mm thick and readily visible against the radiolucency of the underlying subcutaneous premammary fatty tissue. If the breast is very dense, because of the higher density of the underlying parenchymal structure, however, the skin may occasionally not show up clearly even on a correctly exposed mammogram.

Nipple and areola

The skin surrounding the nipple - the areola - can be upto 3-5 mm thick, with a central opacity, roughly cylindrical in shape and of variable size and density, corresponding to the nipple. Posteriorly there it a generally triangular, heterogeneous trabecular area, the retroareolar region, which is of particular interest on account of the difficulty of detecting any focal abnormalities, that may be there. Under normal conditions the lactiferous ducts and sinuses are not seen. If they are enlarged they resemble ribbon-like opacities of varying thickness, running in parallel or divergent lines.

Fatty tissue

Varying amounts of fatty tissue may be present, forming anything from a thin subcutaneous layer to "islets" of various sizes that may occupy the whole breast, depending on the characteristics and age of the individual woman.

The parenchymal cone is surrounded by fatty tissue which constitutes the premammary fat anteriorly and the retromammary fat posteriorly. Anteriorly, subcutaneous fat appears as a radiolucent layer of variable thickness, traversed by planar sheets of fibrous tissue, the Islets of Duret, which accommodate Cooper's ligaments.

The superficial extensions of Cooper's ligaments come to peaks attached to the skin, which anchor the body of the breast to the subcutaneous tissue, known as retiticula cutis. Posteriorly, adipose tissue outlines the retromammary space (the bursa of Chassaignac) which separates the breast from the prepectoral fascia overlying the pectoralis major muscle.

Breast tissue proper or corpus mammae

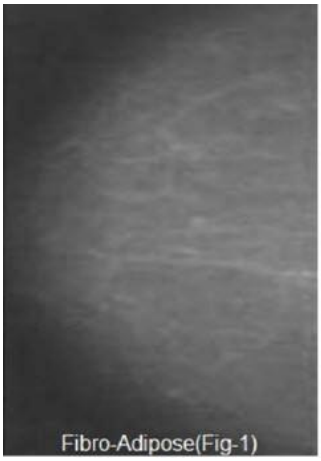
The body of the mammary gland is roughly cone-shaped, with the floor resting on the chest wall and the tip projecting towards the nipple. The shape and density of breast structures vary from individual to individual, and are influenced by specific sensitivity to hormonal stimuli, which affect the relation between the various tissue components and hence the morphology of the breast.

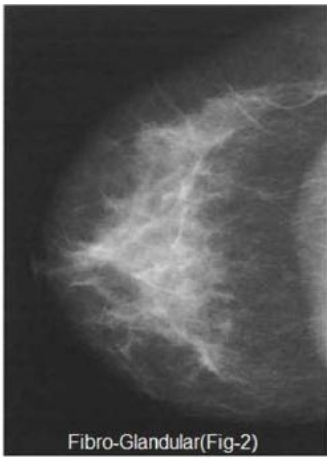
The concept of mammographic density as being strictly related to advancing age is obsolete, so adipose tissue is not synonymous with a senile breast and, similarly, the so-called "dense breast" is not necessarily a young breast. Nor is it possible to establish a link, in terms of pathogenesis and symptoms, between breasts that are patchy and dense at mammography and coalitions such as dysplasia or fibrocystic breast disease.

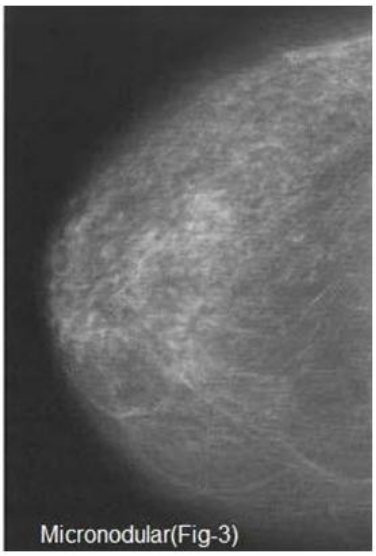
These terms have given rise to much confusion among clinicians and radiologists; not only are they well and truly outdated but they are in fact inappropriate with modern radiology, since they belong to the realm of pathology.

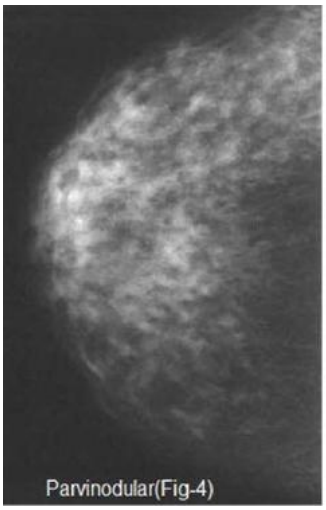
The variety in the mammographic appearance of the "individual" types of mammary structures is in all likelihood related to differences in the normal processes of development and involution, more than to pathological conditions. For teaching purposes it may be useful to classify mammographic structures into six main groups reflecting the most frequently encountered breast tissue patterns.

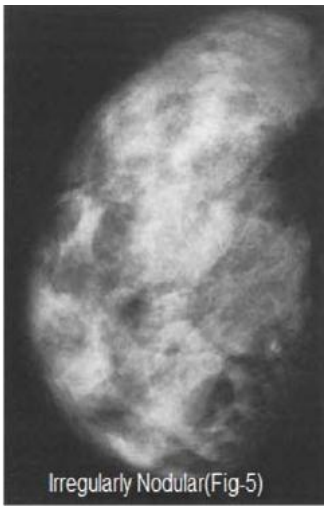
1) Fibro-adipose – total absence of fibro-glandular tissue. Only traces of stromal network may remain(Fig-1)
2) Fibro-Glandular – typical triangular fibro-glandular configuration, typically showing the tip of triangle in the retroareolar region and the peri-mammary spaces. The parenchymal component is planar in appearance or slightly nodular. The texture of the stroma is readily recognized, with the crests of Duret outlining the adipose areas between the retinacula cutis. (Fig-2)
3) Micronodular structure - Less adipose tissue is seen. The fibro-glandular component is abundant, most of it forming a "cobblestone" effect made of small radiopaque nodular opacities measuring up to 3mm diameter. (Fig-3)
4) Parvinodular structure - similar to micronodular structure, but the elementary radiopaque nodules are larger, some reaching 6-7mm in diameter(Fig-4)
5) Irregularly nodular structure - The fibro-glandular component is heterogeneous, featuring nodules of various sizes, either solitary or clustered in "patches". The stroma may be more or less marked. (Fig-5)
6) Dense structure - Virtually o fatty tissue is present. The mammogram shows an intensely and uniformly radiopaque glandular and stromal "block" n which the structures of the breast cannot be distinguished. (Fig-6)

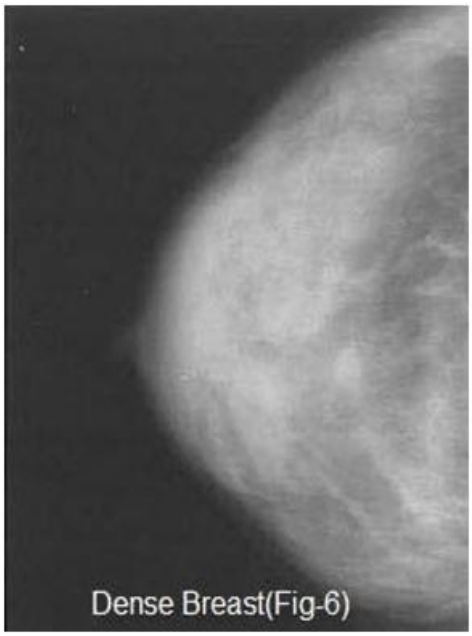

Fibro-Adipose(Fig-1)


Fibro-Glandular(Fig-2)


Micronodular(Fig-3)


Parvinodular(Fig-4)


Irregularly Nodular(Fig-5)


Dense Breast(Fig-6)

Pectoralis muscle

The pectoralis muscle is homogeneously radiopaque; it is located in front of the chest wall and is shaped like an upside-down triangle in the lateral and mediolateral oblique views. In the craniocaudal view it is crescent shaped and variably visible depending on the anatomy of the chest and the position and compression of the breast.

In a very small proportion of cases (1%) one can see medially a small triangular or flame-shaped portion of muscle adjacent to the sternum, which must not be misinterpreted as a mass.

Generally, a correctly executed mediolateral oblique projection shows the lower margin of the pectoralis muscle following an imaginary line that runs an-teriorly through the nipple.

Blood vessels

Vessels are more readily visible in breasts that contain plentiful fatty tissue, and appear as thin ribbon-like opacities that may be more or less tortuous; vessel walls may be calcified, in which case they have typical "railway-line" images. In the early stages of calcification, only scattered elongated "casts" are seen, in a linear pattern, reflecting partial, fragmentary calcification of the vascular wall.

The detection and identification of elementary mammographic signs form the basis for correctly interpreting breast pathologies and describing them accurately in the mammographic report.

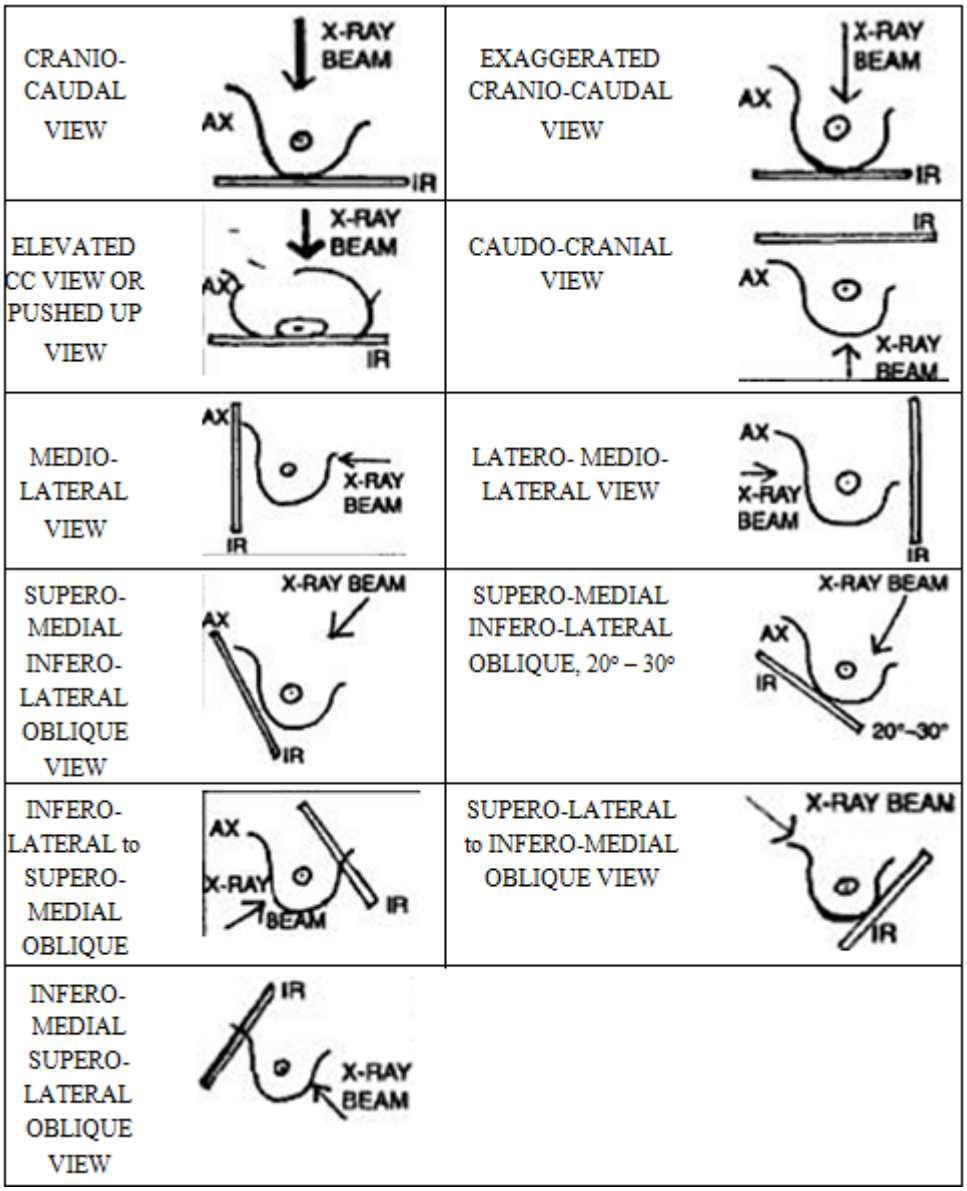
The specific features are the basis for classifying the lesions as benign or malignant. These features define the positive predictive value i.e., the odds that a mammographic sign is associated with or actually shows a cancerous lesion.

Mammographic signs can be described in terms of:

- Opacity (mass)
- Architectural distortion
- Calcification
- Radiolucency
- Asymmetry
- Focal Asymmetry
- Skin thickening and retraction
- Edema and trabecular thickening
- Asymmetrically dilated ducts

Views in Mammography[17]

Screening or diagnostic mammography consists of at least two standard views: Craniocaudal and mediolateral oblique. These views demonstrate the fibroglandular breast tissue. Right and left views are examined side by side so that asymmetries can be observed. Schematic representation of the standard views and special views is shown in Fig-7.



Other special views used in mammography are

- Implant Displacement
- Tangential View
- Axilla View
- Post-Mastectomy View
- Cleavage View
- Rolled Lateral View
- Rolled Medial View
- Nipple in Profile View
- Spot Compression View.

Disadvantages of Mammogram

- Harder to detect a mass in dense breast, as the sensitivity is dependent on density, plus the age and hormone status of the patient
- Tends to understate the multifocality of a lesion
- Positioning is very important, as cancer can be missed because of poor positioning.
- Static examination technique

- Poor soft-tissue discrimination
- Superimposition of fibro-glandular tissues
- Ionizing radiation

Figure 8: Mammographic View of Fibroadenoma

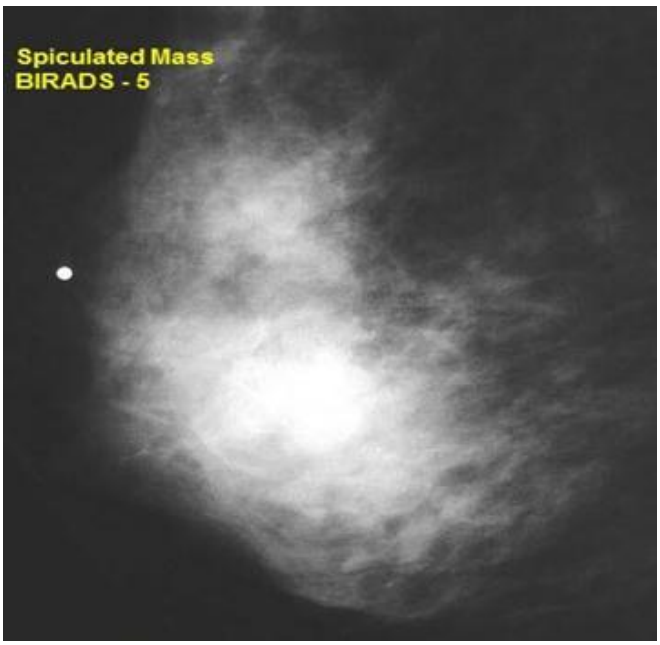


Figure 9: Mammographic View of Carcinoma

Ultrasonogram

Wild and Neal first described the use of ultrasound to examine the breast in 1951. However, clinical application of breast sonography was limited by the relatively poor quality of the available ultrasound equipment. At that time, ultrasound could only visualize gross lesions, huge cysts, and massive carcinomas. In recent years, however, advances in ultrasound technology, including the development of hand-held transducers and improvements in imaging quality, have rekindled interest in ultrasound of the breast. The appeal of ultrasound has been further bolstered by concerns about the radiation exposure associated with mammography and the fact that ultrasound is less cumbersome to the patient.

The primary use of Ultrasonography in the evaluation of breast disease is to distinguish between solid and cystic breast lesions. This includes non palpable lesions detected with mammography as well as vaguely palpable lesions. Ultrasound is extremely accurate in determining the fluid-filled nature of most simple cysts (Basic aspect of ultrasound and Diagnostic features on ultrasound).[19]

Ultrasound can be particularly useful when mammography is contraindicated or produces nonspecific results. In pregnant women, because of the need to avoid radiation exposure and the tendency to have increased breast density, ultrasound is the modality of choice for evaluating masses. Even palpable masses may not be visible on radiography in a dense breast.

Normal fibro-glandular tissue may partly or completely obscure masses on mammography. Ultrasound, however, can determine if these masses are cystic or solid. Peripheral masses in thin women may be difficult to visualize on mammography. In these cases, ultrasound is indicated for evaluation.

[1]Ultrasound can further help in the controversial area of evaluating a palpable mass in a woman under the age of 30. Since the breasts of these women are more sensitive to radiation than are those of older women, radiologic procedures such as mammography are not routinely recommended.

Ultrasound, however, is an ideal first-line test for evaluating a symptomatic breast. For example, a galactocele, which usually presents as a palpable doughy mass, is commonly found in lactating or pregnant women. On Ultrasonography, a cystic or hypoechoic oval or rounded structure can be seen, with multiple floating internal echoes.[18]

Chronic or acute breast abscesses occur most often in younger women, especially those who are lactating. They are generally found in the subareolar region.

Ultrasound is the initial procedure of choice in the evaluation of a possible breast abscess. It is particularly effective in detecting a breast abscess that may be causing an acute mastitis. The abscess usually presents as a hypoechoic lesion with multiple internal echoes and increased through-transmission. Debris within the abscess may layer out in a dependent fashion, forming a fluid/debris level.

Ultrasound is excellent in determining the presence of an implant leak or rupture and is more comfortable and cheaper than magnetic resonance imaging.[18]

Normal Ultrasonographic Breast Anatomy

For adequate interpretation of breast ultrasound, the normal breast Ultrasonographic anatomy must be clearly understood. The skin of the breast, usually 1 to 3mm thick, is imaged as 2 hyper echoic lines with a very thin hypo echoic zone between them. These lines correspond to the interface between the transducer and the skin and between the skin and the subcutaneous tissue.

Immediately beneath the skin are prominent round or oval fat lobules, which appear as relatively homogenous hypoechoic structures. These are interrupted by echogenic Cooper's ligaments that extend to the chest wall and insert on the undersurface of the dermis. The breast parenchyma varies widely in its echogenicity with thin curvilinear bands of connective tissue extending through it. The juvenile breast is composed mainly of dense glandular tissue with very little fat and therefore appears as diffusely hyper echoic parenchyma.

The postmenopausal, partly involuted, breast has slightly increased subcutaneous fat with fat lobules distributed throughout the breast parenchyma. The postmenopausal breast has very little parenchyma with prominent Cooper's ligaments.

During pregnancy and lactation the appearance is similar to that of the juvenile breast. Beneath the breast parenchyma is a zone of hypo echoic retro mammary fat, posterior to which are hypo echoic sheets of pectoral muscle fibers.

As the examiner moves the transducer, several structures will become readily apparent. Medially, the costal cartilages can be seen as curvilinear hypoechoic bands or well-defined oval structures, depending on the orientation of the transducer. As you move laterally, the ribs can be imaged.

The ribs appear as semilunar hyperreflective structures with strong posterior shadowing. In the retroareolar region, branching ducts can occasionally be seen as areas that vary from hypo echoic to anechoic.

Usually, these are not visible when of normal caliber, but they can be seen even when minimally dilated.

Ultrasonographic Breast Pathology

Ultrasound of the breast is used predominately to differentiate cysts from solid masses. Cystic lesions are overwhelmingly benign in nature. Ultrasound has been found to be extremely accurate in differentiating between cystic and solid lesions, whether the masses were found by palpation or mammography.

Because almost 25% of all palpable masses are cysts, the ability to recognize when a mass is cystic is an important feature. The diagnosis of an ultrasound-visualized mass can be based on several characteristics including margins, echogenicity, internal echo pattern, retrotumoral phenomenon, compressibility, and the lateral/anteroposterior dimension ratio.

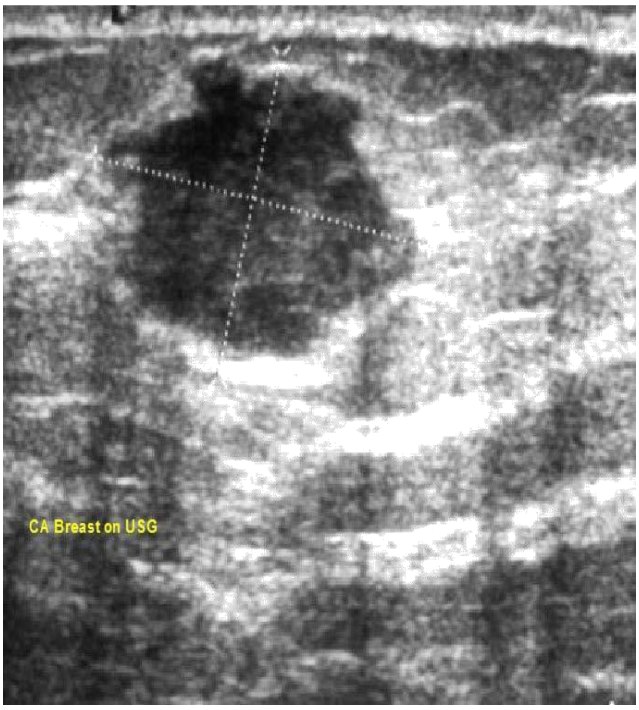


Figure 10: Ultrasonographic View of Carcinoma Breast

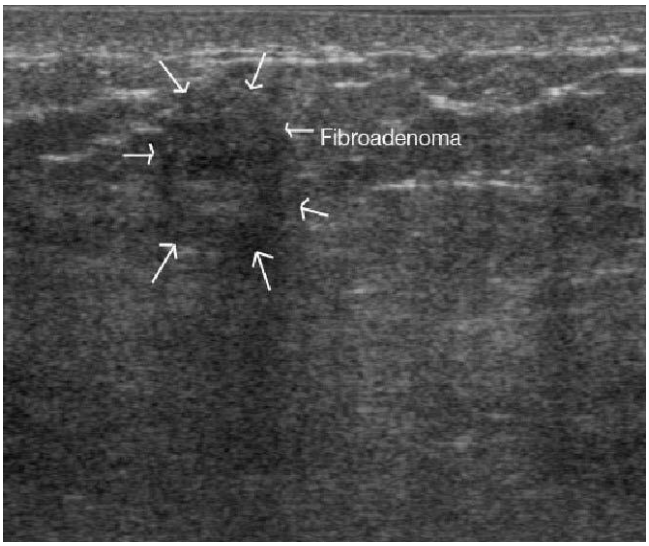


Figure 11: Ultrasonographic View of Fibroadenoma Breast

6. Materials and Methods

Source of Data

All patients with lump in the breast, attending OPD / admitted to Krishna Hospital, during the period from December 2012 to June 2014.

Method of Collection of Data

In out patient department detailed history and thorough physical examination of patients having palpable breast lump was carried out and entered in proforma. Patients were informed about mammography, ultrasonography and informed consent was obtained from the patient before subjecting to the fine needle aspiration cytology of the breast lump.

Sample size: 50 patients

Sampling method: Simple random sampling

Inclusion Criteria: All women above age of 30years presenting with Palpable breast lumps.

Exclusion Criteria: Patients with
1) Patient with acute and tender breast lump.
2) Patient with ulcerated breast lump.
3) Recurrent breast lump of previously operated case of confirmed malignancy.

Investigations
1) Mammography of both breasts
2) Ultra-sonogram of both breasts
3) Fine needle aspiration cytology of breast lesion, direct or image guided
4) Histopathological examination

Clinical examination
Can be considered under following heads

Patient position: Patient Examined in sitting position with hands by side and hands above head, supine position, recumbent position and leaning forward position.

Breast boundaries: The rectangular area bordered by the clavicle superiorly, midsternum medially, the mid axillary line laterally and the inframamarry or 'bra line' inferiorly.

Examination pattern: Palpation begins in the axilla in a straight line down the midaxillary line to the bra line. Fingers then move medially and palpation continues up the chest in a straight line to clavicle. Entire breast is covered in this manner going up and down.

Fingers: The three middle fingers with metacarpophalangeal joint slightly flexed are used and the pads of these fingers are the palpating area.

Duration: About 3 minutes are to be spent on each breast.

Other issues: Palpation of supra clavicular and axillary regions to detect adenopathy is a standard part of clinical breast examination.[19]

Mammography and / or Ultra sound was done for patients before FNAC. The results were analyzed and categorized according to BIRADS (Breast Imaging Reporting and Data System) score. Both cranio-caudal and medio-lateral views are taken and the image was assessed and scored using the BIRADS

Breast Imaging Reporting and Database System (BI-RADS®)

CATEGORY	ASSESSMENT
0	Needs further evaluation
1	Negative
2	Benign Finding
3	Probably Benign
4	Probably Malignant
5	Malignant
6	Proven Malignancy

Figure 12: BIRADS Scoring System

FNAC

Materials
Needles - 23/22 gauge 30-50 mm needle are recommended for the breast

Syringes - 5-10ml, good quality plastic disposable syringes that provide good negative suction.
Slides thoroughly cleaned dry glass slides free of grease to be used. The aspirate can be smeared between two standard microscope slides.

Fixative - 90% ethanol.
FNAC diagnoses were respectively scored as:
Insufficient sample - C1
Benign - C2
Probably Benign - C3
Suspicious of malignancy - C4
Malignant - C5

Patient preparation
Procedure must be explained and patient must be placed in a comfortable position. For breast lumps simple spirit swab provides disinfection and local anesthesia is not usually required except in apprehensive patients.

Technique
The needle connected to a syringe is introduced into the lesion. A vertical approach is less painful and gives better perception of depth. Negative suction is applied and multiple passes are made within the lesion. Negative suction is released before the needle is withdrawn.

Processing the sample
The sample is expelled onto a slide. Aspirate can be 'dry' (numerous cells in small amounts of tissue fluids) or 'wet' (small number of cells suspended in fluid or blood). A dry aspirate is smeared with the flat of a microscopy slide.

A wet aspirate is smeared in two steps, first move the smearing slide from one end of the specimen slide holding it at a blunt angle and second smear cellular component with the flat of the slide. Smear is fixed with alcohol and subjected to Pap/H&E staining.[20]

7. Observations and Results

The patients attending surgery OPD with complaint of

breast lump and who expressed consent for the study were involved and investigations were done as outlined in method of study. 50 patients entered the study and all patients were subjected to all investigations. The results of the study are shown in the following tables.

The sensitivity, specificity, positive and negative predictive values of each investigation was calculated individually.

Table 1: Age distribution in breast neoplasm

Age groups	No. of cases	% of cases
31-40yrs	1	2
41-50 yrs	14	28
51-60 yrs	18	36
61-70 yrs	16	32
71-80v	1	2
Total	50	100

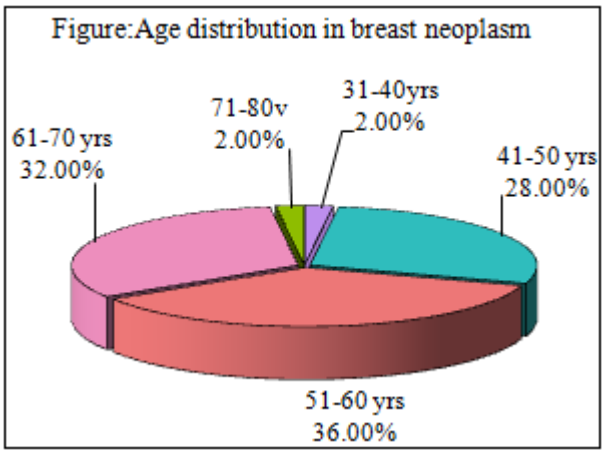


Table 2: Distribution of breast neoplasms according to the side of involved breast

Side	No. of cases	% of cases
Right breast	27	54
Left breast	23	46
Bilateral	0	0
Total	50	100

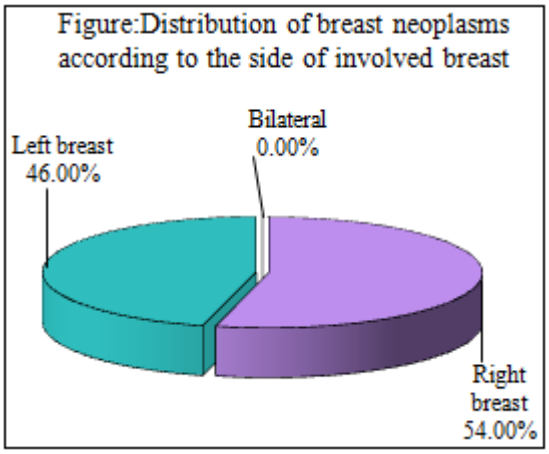


Table 3: Distribution of benign and malignant lesions diagnosed clinically.

Lesions	No. of cases	% of cases
Benign	27	54
Malignant	23	46
Total	50	100

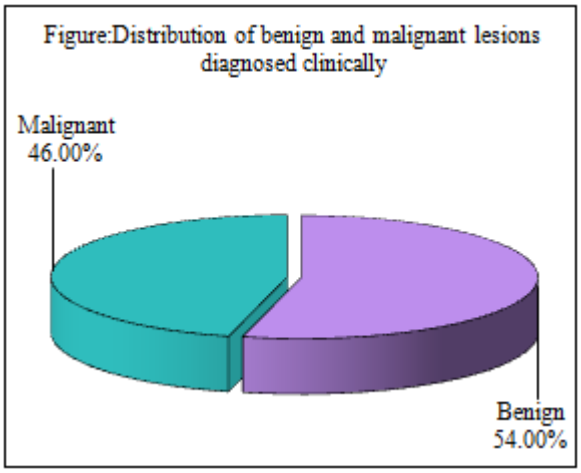


Table 4: Distribution of benign and malignant cases on mammography

Lesions	No. of cases	% of cases
Benign	24	48
Malignant	23	46
? Malignant	2	4
Inconclusive	1	2
Total	50	100

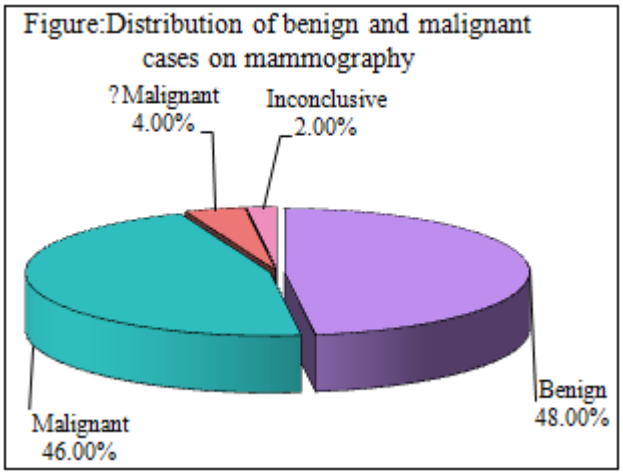


Table 5: Distribution of benign and malignant cases in FNAC

Lesions	No. of cases	% of cases
Benign	20	40
Malignant	30	60
Total	50	100

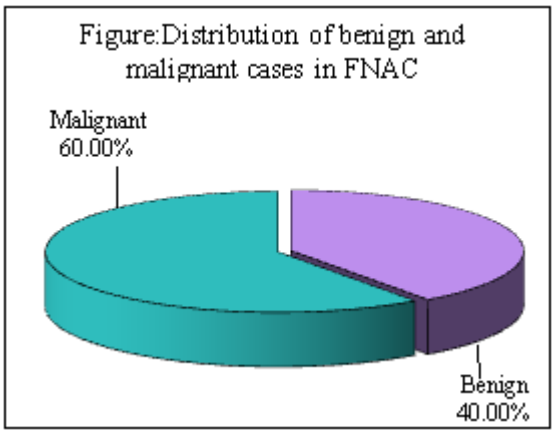


Table 6: Distribution of benign and malignant cases on USG

Lesions	No. of cases	% of cases
Benign	23	46
Malignant	26	52
? Malignant	1	2
Total	50	100

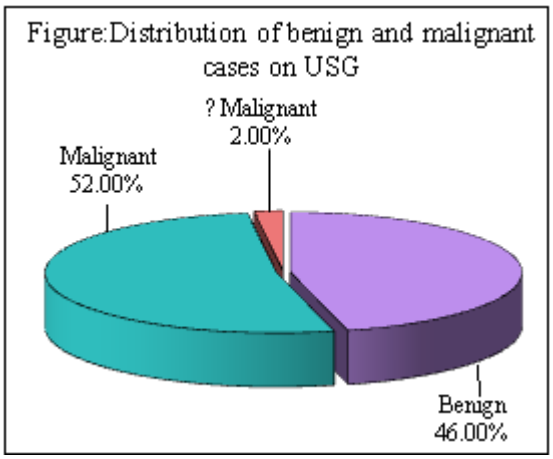


Table 7: Distribution of benign and malignant lesions on Histopathology

Lesions	No. of cases	% of cases
Benign	19	38
Malignant	31	62
Total	50	100

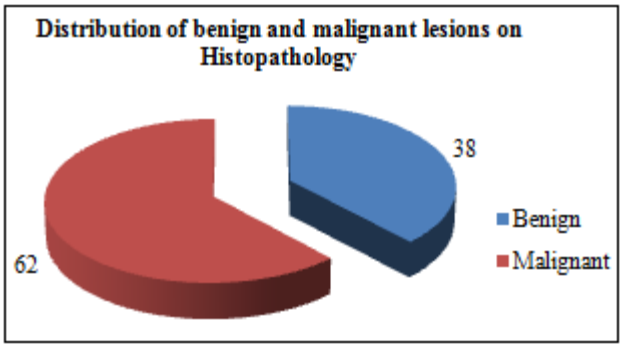


Table 8: Comparison of Diagnostic modalities with Histopathology

Diagnostic modalities	Benign	Malignant	Inconclusive	? Malignant	Total
Clinical examination	27	23	0	0	50
Mammography	24	23	1	2	50
FNAC	20	30	0	0	50
USG	23	26	1	0	50
Histopatholgy	19	31	0	0	50

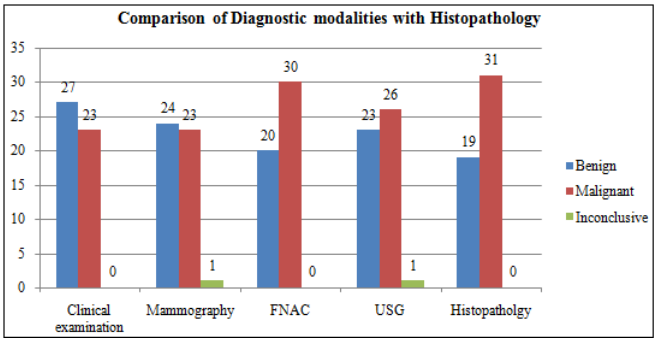
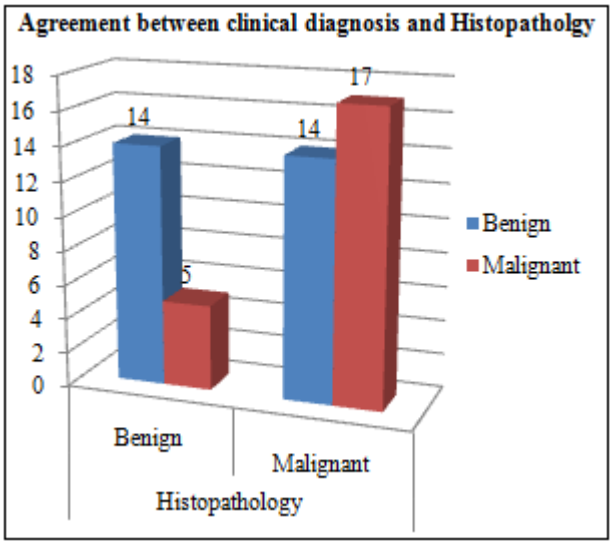


Table 9: Agreement between clinical diagnosis and Histopatholgy

Clinical diagnosis	Histopathology			
	Benign	Malignant	Total	%
Benign	14	14	28	56.00
Malignant	5	17	22	44.00
Total	19	31	50	
%	38.00	62.00		



Kappa statistic

Agreement	Expected Agreement	Kappa	Std. Err.	Z-value	p-value
62.00%	48.56%	0.2613	0.1325	1.9700	0.0243*

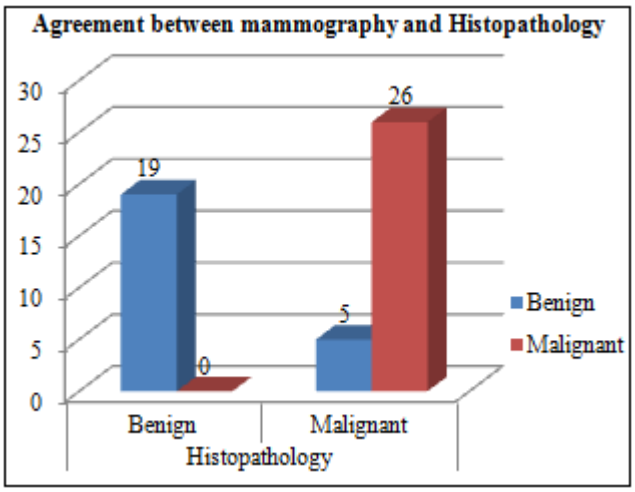
*p<0.05

Table: Sensitivity and specificity

Sensitivity	a/a+b	73.68
Specificity	d/c+d	54.84
Positive predictive value	a/a+c	50.00
Negative predictive value	d/(b+d)	77.27
Disease prevalence	(a+b)/(a+b+c+d)	38.00

Table 10: Agreement between mammography and Histopathology

Mammography	Histopathology			
	Benign	Malignant	Total	%
Benign	19	5	24	48.00
Malignant	0	26	26	52.00
Total	19	31	50	
%	38.00	62.00		



Kappa statistic

Agreement	Expected Agreement	Kappa	Std. Err.	Z-value	p-value
90.00%	50.48%	0.7981	0.1385	5.7600	0.00001*

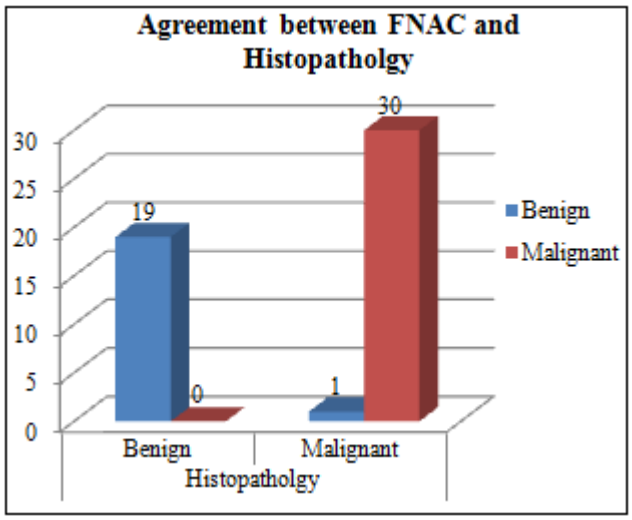
*p<0.05

Table: Sensitivity and specificity

Sensitivity	a/a+b	100.00
Specificity	d/c+d	83.87
Positive predictive value	a/a+c	79.17
Negative predictive value	d/(b+d)	100.00
Disease prevalence	(a+b)/(a+b+c+d)	38.00

Table 11: Agreement between FNAC and Histopatholgy.

FNAC	Histopatholgy			
	Benign	Malignant	Total	%
Benign	19	1	20	40.00
Malignant	0	30	30	60.00
Total	19	31	50	
%	38.00	62.00		



Kappa statistic

Agreement	Expected Agreement	Kappa	Std. Err.	Z-value	p-value
98.00%	52.40%	0.9580	0.1413	6.7800	0.00001*

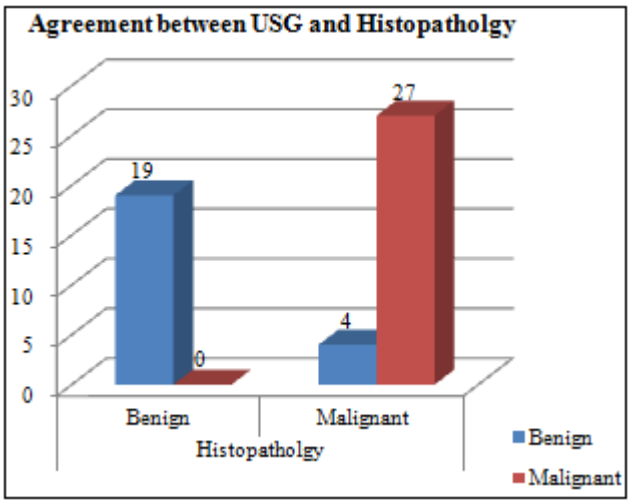
*p<0.05

Table: Sensitivity and specificity

Sensitivity	a/a+b	100.00
Specificity	d/c+d	96.77
Positive predictive value	a/a+c	95.00
Negative predictive value	d/(b+d)	100.00
Disease prevalence	(a+b)/(a+b+c+d)	38.00

Table 12: Agreement between USG and Histopatholgy.

USG	Histopatholgy			
	Benign	Malignant	Total	%
Benign	19	4	23	46.00
Malignant	0	27	27	54.00
Total	19	31	50	
%	38.00	62.00		



Kappa statistic

Agreement	Expected Agreement	Kappa	Std. Err.	Z-value	p-value
92.00%	50.96%	0.8369	0.1395	6.0000	0.00001*

*p<0.05

Table: Sensitivity and specificity

Sensitivity	a/a+b	100.00
Specificity	d/c+d	87.10
Positive predictive value	a/a+c	82.61
Negative predictive value	d/(b+d)	100.00
Disease prevalence	(a+b)/(a+b+c+d)	38.00

8. Discussion

In this present study 50 patients with age more than 30 years who presented with breast lump in OPD were evaluated using the component of triple assessment (clinical examination, mammography, FNAC) and Utrasound of breast. The results from each investigation were compared with gold standard- Histopatholgical report.

Table 13: Parameters of all investigations

Investigations	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Clinical examination	73.68	54.84	50.00	77.27
USG	100	87.10	82.61	100
Mammography	100	83.87	79.17	100
FNAC	100	96.77	95	100

Out of 50 patients 36% patients belonged to age group 51-60 years. Patients with palpable breast lump were involved in study. Patients with nipple discharge, induration, redness and history of previous breast carcinoma surgery were excluded.

The lesion involved right breast (54%) more commonly.

The sensitivity, specificity, positive and negative predictive value of each investigation was calculated individually. FNAC had highest sensitivity (100%), specificity (96.77%) and positive predictive value(95.00) for all palpable lesions.

Incorporation of mammogram just adds up to diagnosis when patient has lump that is clinically palpable and to rule out multi centric and multi focal disease. Yet mammogram becomes important tool when there is no lump palpable cinically.

Incorporating sonography in this study proved to be very useful as the agreement between sonography and histopathology was 92%. Ultrasound becomes very important tool when a situation arises where a mammogram could not differentiate solid tumor from cyst.

Ultrasonography can replace mammogram (Modified triple test) as the improved techniques approaches the specificity (100%) and positive predictive value by 82.61% in the present study.

As shown in Table 1 neoplasms are more common in elder age group i.e.51-60 years (36%) . There is only 1(2%) case in age group of 31-40years and 1(2%)case in age group of 71-80years.

The clinical presentation of most common side for breast lump is right i.e. 27 cases (54%) which is slightly more than left side i.e. 23 cases (46%).

1) Clinical examination

The clinical impressions of benign lesion were in 27(54%) cases and 23(46%) cases were diagnosed as malignant.

2) Mammography

As shown in table 4, 24(48%) cases out of 50 were diagnosed as benign , 23(46%) were malignant ,2(4%) were ?malignant and 1(2%) was inconclusive.

3) FNAC

On cytology 20(40%) patients with palpable breast lump were diagnosed as benign while 30(60%) cases were proved as malignant. There is no inconclusive OR ?malignant cases detected on cytology.

4) Ultrasonography

23(46%) cases out of 50 were diagnosed as benign and 26(52%) were diagnosed as malignant ultrasonographically. Only 1(2%) case remained as? malignant. While out of 26(52%) cases of malignant lesions on sonography, clinically 3 cases were diagnosed wrongly as benign which were malignant on USG. And out of 26(52%) malignant cases on USG 3 cases were diagnosed as 2(4%)? malignant and 1(2%) as inconclusive on mammography.

After discussion of distribution of benign, malignant, ?malignant and inconclusive results on triple assessment and USG, individual test of triple assessment with USG were compared with histopatholgy.

Agreement percentage of clinical diagnosis and histopathology was 62.00% and sensitivity and positive predictive value were 73.68% and 50.00% respectively.

On comparison of mammography and histopatholgy , agreement percentage was 90%.

Agreement percentage of FNAC and histopatholgy was 98% and sensitivity and specificity were 100% and 96.77% respectively. Amongst all comparisons in this study this combination has yielded highest percentages of sensitivity (100%), specificity (96.77%) and positive predictive value (95.00%).

Agreement of USG with histopatholgy was 92% and sensitivity, specificity and positive predictive value were 100%, 87.10% and 82.61% respectively.

Similar studies evaluating the components of triple assessment are taken and the results of the present study compared with those studies. Studies involving use of Ultrasound as one of the component (modified triple test) or as individual investigation are also analyzed.

Table 14: Comparison of FNAC results with other study.

Study	Al-Muhim et al[10]	Philip j et al[21]	Present study
Sensitivity	91.7%	79.1%	100%
Specificity	100%	97%	96.77%
Positive predictive value	100%	-	95%

Table 15: Comparison of Mammogram results with other study.

Study	Al-Muhim et al[10]	Philip j et al[21]	Present study
Sensitivity	87.5%	87.6%	100%
Specificity	97.3%	86.4%	83.87%
Positive Predictive value	87.5%	-	79.17%

Table 16: Comparison of clinical examination results with other study

Study	Al-Muhim et al[10]	Philip j et al[21]	Present study
Sensitivity	82.6%	84%	73.68%
Specificity	97.3%	83.1%	54.84%
Positive predictive value	88.4%	-	50%

Table 17: Comparison of USG results with other study

Study	Ashley et al[22]	Ghazala et al[23]	Present study
Sensitivity	65%	67%	100%
Specificity	95%	92.4%	87.10%
Positive		-	82.61%

predictive value			

In a study done by Ahmed I et al[24], the TT was concordant in 19 cases (54.28 %) i.e. all the benign cases detected by the triple test were benign on final biopsy (100 % specificity and NPV), all the malignant lesions detected by TT turned out to be malignant on final biopsy (100 % sensitivity and PPV). They concluded as: The study shows that when TT is concordant, final treatment may be ensued without open biopsy. In non-concordant cases, FNAC stands as single most important investigation. However due to its false negative results, other components of triple test need to be employed to enhance its efficacy and diagnostic yield.

Reinikainen et al[25] had a series of 84 patients where they compared Mammogram, USG, FNAC, HPE by a scoring system. 81 were detected to have lumps of which 53 were malignant. They have found sensitivity and specificity of FNAC to be 92 % and 83 % respectively where as in the present study they are 100% and 96.77 %.

In a study done by Philip J Drew et al[21] to compare the sensitivity and specificity of the traditional triple assessment of symptomatic breast lesions with contrast-enhanced dynamic magnetic resonance imaging, they found the sensitivity of each modality: clinical examination 84%, mammography 87.6%, fine-needle aspiration cytology 79.1%, and specificity : clinical examination 83.1%, ultrasound 88.9%, mammography 86.4%, fine-needle aspiration cytology 97%. The results of this study were compared with results of present study.

Al-Muhim et al [10], in a study to assess accuracy of the "triple test" in the diagnosis of palpable breast masses in Saudi females, found that Physical examination showed 82.6% sensitivity, 97.3% specificity and 86.4% positive predictive value. Mammography showed 87.5% sensitivity, 97.3% specificity and 87.5% positive predictive value and fine-needle aspiration cytology (FNAC) showed 91.7% sensitivity, 100% specificity and 100% positive predictive value in concordant cases (elements had either all malignant or all benign results). They concluded that the triple test was 100% accurate in the diagnosis of palpable breast lesions when all three elements were concordant.

A palpable mass in a women's breast represents potentially serious lesion and requires evaluation by history taking and physical examination.

A solid lesion requires a firm diagnosis and this usually calls for removing the lesion for histopathological examination. A positive result on cytology after aspiration is sufficiently accurate to justify one stage diagnosis and treatment.

A negative or suspicious finding on FNAC is inconclusive and a radiological investigation is required. Although in some instances the probability of malignancy may be exceedingly small, it is never zero. If biopsy is not recommended, the probability of malignancy in that patient should be estimated so as to decide whether the level of risk is acceptable for that particular patient. In such instances methods like "Triple test" OR "Modified triple test" can increase the accuracy of diagnosis, at least from an unnecessary surgical intervention.

9. Summary

The vast majority of lesions that occur in the breast are malignant and that is why much concern is given to malignant lesions of breast because breast cancer is the most common malignancy in women in Western countries. As the benign lesions are not associated with an increased risk for subsequent breast cancer, unnecessary surgical procedures should be avoided.

In this study patients with breast lump complaints were evaluated with clinical examination, FNAC, Mammogram and Ultrasonogram. The sensitivity, specificity, positive and negative predictive values were calculated for each of the modalities and compared.

50 patients were included in the study with age more than 30 years. Malignant diseases were more common than benign in this study.

The sensitivity, specificity, positive and negative predictive values of Clinical examination is 73.68%, 54.84%, 50%, 77.27%, USG is 100%, 87.10%, 82.61%, 100%, Mammogram is 100%, 83.87%, 79.17%, 100%, and FNAC is 100%, 96.77%, 95%, 100%.

Quadruple test is very useful tool in evaluating the breast diseases. In patients with definite breast lump, Clinical examination FNAC and USG may be sufficient to rule out malignancy and this may be cost effective by avoiding a Mammogram. Mammogram is needed in patients with no clinically palpable lump and to rule out multi centric and muli focal disease.

10. Conclusion

Quadruple test is a very useful tool in evaluating the breast diseases.

In patients with definite lump, Clinical examination (by experienced hands), FNAC and USG may be sufficient to rule out malignancy and this may be cost effective by avoiding a mammogram.

Mammogram is needed in patients with no clinically palpable lump and to rule out multi centric and multi focal disease.

Ultrasound is not only useful in detecting malignancy, not visible or not suspected on the mammogram but can reduce the suspicion of malignancy in some patients.

Adding USG to the triple test did not add up to the negative predictive value of Triple test, but USG may be used instead of mammogram to avoid the radiation due to mammogram. USG can also be used at the remote places where mammogram facility is not available.

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Proforma for Evaluation of Breast diseases by Quadruple test

Name:

Age: Sex:

OP Number: IP Number:

Presenting Complaint: Duration of Complaint:

Lump

Pain

Nipple Discharge

Nipple Retraction

Others

History of Present Illness:

Past History:

1. Similar history:
2. Medical illness:
3. Surgical illness:
4. Drug history:

Personal History:

1. Diet:
2. Sleep:
3. Appetite:
4. Bowel:
5. Bladder:
6. Addiction:

Menstrual History:

Obstetrical History:

Family History:

Detailed family history of breast carcinoma in siblings and cousins, in parents, aunts and uncles, and in grandparents.

General Examination:
Temperature:
Pulse:
Blood pressure:
Pallor:
Icterus:
Clubbing:
Oedema:
Lymhadenopathy:

Level 1:- Anterior: Lateral: Posterior:
Level 2:- Central:
Level 3:- Apical:

Systemic Examination:

Cardiovascular system:
Respiratory system:
Abdomen:
Central nervous system:

Local Examination:

Inspection (Examination of affected breast in comparison with normal breast):
1. Size and position of breast:
2. Nipple/areola complex:
3. Skin over the breast:

Scar-
Engorged veins-
Redness-
Peau d' Orange-

4. Swelling:-
Position-
Size-
Skin over the swelling-

Palpation:
1. Normal breast:
2. Affected breast:

Temperature-
Tenderness-
Swelling-

Consistency:-
Fixity o skin:-
Fixity to breast tissue:-
Fixity to pectoralis major:-
Fixity to chest wall:-

Investigations:-
1) Mammogram
2) Ultrasonogram
3) FNAC
4) Histo-Pathology

Final Diagnosis:

Comments: