ORIGINAL RESEARCH

Mammography in correlation to ultrasound in patients having nipple pathologies and its clinicopathological correlation

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Abstract

Background: The nipple-areola complex is a region of the breast that has unique characteristics. Due to its special structural features, the lesion of nipple is major part of breast disease and disease treatment. Most patients with nipple pathologies present with the associated symptoms upon clinical examination like nipple discharge, nipple retraction, nipple inversion and changes in nipple skin, shape, volume, and symmetry. There are many different benign, malignant and congenital lesions in the nipple. Malignant lesion includes Paget's disease, invasive ductal carcinoma and benign lesion includes adenoma, Leiomyoma, papilloma, abscess, warts, inflammation etc.

Objectives: The aim of this study was to study the USG & mammographic findings in patients presenting with nipple pathologies and to elicit the sensitivity, specificity and diagnostic efficacy of mammography and ultrasonography in the presence or absence of nipple lesion in patients with nipple pathologies like pathological nipple discharge, nipple retraction, nipple inversion, skin changes.

Methods: 100 patients who presented with nipple pathologies & associated clinical symptoms like nipple discharge were included in the study. Patients had undergone mammography and ultrasound and their imaging features were analysed as per ACR BI-RADS lexicon 5th edition. The lesions were classified as benign or malignant based on histopathology.

Results: In our study38% of the total patients were found malignant; who were having nipple pathologies like nipple discharge, nipple retraction ; and 62% of the total patients were found benign. Involvement of nipple areola complex among malignant lesions was seen in 20% cases on mammogram and 29% cases on USG. USG is more sensitive than mammography for detection of involvement of NAC. Breast masses having spiculated margins, angular margins and micro lobulations indicated a malignant pathology on both mammogram and USG. The negative predictive value of USG in detecting malignancy amongst patients with nipple discharge, nipple retraction and nipple inversion was slightly higher than mammography (100% vs. 88.24%) and associated with higher sensitivity of USG (100% vs. 94.74%) but less specific as compared with mammography (66.18%vs. 54.55%).

Conclusion: Ultrasound has high sensitivity and specificity in the diagnosing nipple lesions, it is the first-line imaging examination to characterize and identify nipple lesions, to distinguish benign and malignant lesions, and to guide the management of nipple pathology

by facilitating US-guided percutaneous biopsy or planning the surgical excision of the lesion. Mammography has a limited role in evaluating the nipple; it is more sensitive to identify microcalcifications, in some malignant lesions, and to reveal the retro areolar mass.

Introduction

The nipple is the central region of breast, and is the most important part of the breast structure and function [1]. The nipple-areola complex is a region of the breast that has unique characteristics. Due to its special structural features, the lesion of nipple is major part of breast disease and disease treatment [2]. Most patients with nipple pathologies present with the associated symptoms upon clinical examination [3]. Nipple discharge , nipple retraction, nipple inversion and changes in nipple skin, shape, volume, and symmetry. Characteristically, a bilateral or long-standing nipple retraction is benign, while the presence of an acquired unilateral nipple inversion implies an underlying malignancy [4]. A benign process is indicated by a central, slit-like nipple retraction, while malignancy typically produces whole nipple inversion associated with areola distortion. Skin changes include erythema, ulceration, edema or satellite skin nodules. [5].

A wide variety of abnormal conditions can affect the nipple- areola complex, including developmental abnormalities, benign processes (e.g., inflammation, infection, tumours), and invasive and non-invasive .There are many different benign, malignant and congenital lesions in the nipple. Malignant lesion includes Paget's disease, invasive ductal carcinoma and benign lesion includes adenoma, Leiomyoma, papilloma, abscess, warts, inflammation etc. For malignant disease Paget's disease is rare and incidence is 1%-3% is noted among in all breast cancer patients [6].Plasma cell mastitis is a type of nonpuerperal benign mastitis with an incidence of 1.1% to 75% and has high clinical misdiagnosis rate [7].For congenital nipple lesions, the incidence of polythelia in the general population ranges from 0.22% to 5.6%, depending on factors such as genetics and race [8].

Commonly used breast examination methods include x-ray mammography, magnetic resonance imaging (MRI) and ultrasound (US). The advantage of x-ray mammography is that it is more sensitive to identify microcalcifications in some malignant lesions, but the structure of the nipple cannot be clearly depicted and it is to reveal the retro areolar mass. MRI has a better resolution for the relationship between the mammary ducts and the range of the malignant lesions [9].Breast ultrasound has a high sensitivity and specificity in the diagnosis of nipple lesions ,it is used to identify and characterize nipple lesions, distinguish between benign and malignant lesions, and guide the management of nipple pathology by facilitating US-guided percutaneous biopsy or planning the surgical excision of the lesion[10].In clinical presentations, erosion and discharge of the nipple are more predictive of a malignant process ($P < 0.05$). Paget's disease and nipple adenoma may have similar clinical manifestations, such as bloody discharge, erosion, and pain [11].

Leiomyoma of the nipple could be asymptomatic for long periods or present as a mass or with specific recurrent spontaneous severe pain when applying pressure or after exposure to the cold. Plasma cell mastitis may present with nipple discharge and nipple retraction, characterized by swollen breasts and redness, although some of the patients do not show these signs of inflammation. Nipple warts are soft and painless skin tags. Periductal mastitis also known as Duct ectasia most common in the 40 to 49 years old group who are not in the lactation period. Most of the diseases occur in multiparas around menopause and post-pregnancy women [12].Plasma cell mastitis, also known as Periductal mastitis, is a benign inflammatory disease of the breast. Plasma cell mastitis may be secondary to benign duct ectasia in a patient with pain behind the nipple and the retro areolar region [13].The clinical manifestations are complex and varied, such as nipple retraction, pain, nipple discharge, palpable mass below NAC, areola abscess, and nipple fistula. Invasive ductal carcinoma is

the most common malignant tumour of the breast, generally presents as an ill-defined retroareolar mass .Occasionally, it can be located immediately behind the nipple or it can originate in another location and extend to the nipple, nearly 10% arise in the central ducts less than 2 cm from the nipple [14].

In cases involving the nipple-areolar complex, the most common clinical manifestation is unilateral nipple retraction and distortion of the areola. It is important to differentiate between inversion and retraction of the nipple. Inversion refers to the complete invagination of the nipple, which is mostly symmetrical and physiological. Retraction refers to focal inversion of the nipple-areolar complex and is asymmetrical and acquired. Both inversion and retraction can have benign or malignant causes; the time course and the presence of underlying disease are important [15].

Materials and methods

The prospective observational study has been carried out in between, Dec 1, 2021 to Nov 30, 2022, on patients who presented with pathological nipple lesion & clinical symptoms like nipple discharge, nipple retraction, nipple inversion, skin thickening in Radiology Department, Government Medical College & Associated Group of Hospitals, Kota.100 Cases who fulfilled the selection criteria during the study period were included. Selection of the cases was based on convenience sampling.

Patient selection

1. All female patients in the age group between 30-70 years of age presented with nipple pathologies and clinical symptoms were included.
2. Complete clinical details after providing them detailed information about the protocol and informed consent was obtained.
3. Symptoms with proper history of patients were recorded into the data base for study analysis and physical examination.
4. Radiological evaluation including the mammography and ultrasound of these 100 patients was done. All 100 patients had their ultrasound data collected on the same day of the mammography. Patient questionnaires were completed during each screening visit.

Radiological evaluation

Mammography and ultrasound were done for all the 100 patients having nipple pathologies and clinical symptoms based on inclusion and exclusion criteria.

Bilateral mammography was done by using **AMULET Digital mammography system by FUJIFILM** machine. Both cranio- caudal (CC) and medio- lateral oblique (MLO) views and any additional views were analyzed as per ACR- BIRADS lexicon 5th edition. Symmetry, mass characteristic, LN presence and then BI-RADS score were reported for each case.

Bilateral breast US was performed by using **ALPINION ECUBE 15 equipment**. In supine position, breast, nipple areola complex and axilla were scanned with a high-resolution linear probe (7-12 MHZ). B- Mode scanning was done in both radial and anti- radial directions. Doppler was used whenever needed. Multiple images in different planes were obtained on gray scale US; dilated ducts site, calibre and presence and characteristics of intraductal mass were assessed.

Observations

Case 1: A patient came with the complaints of nipple retraction and lump in right breast
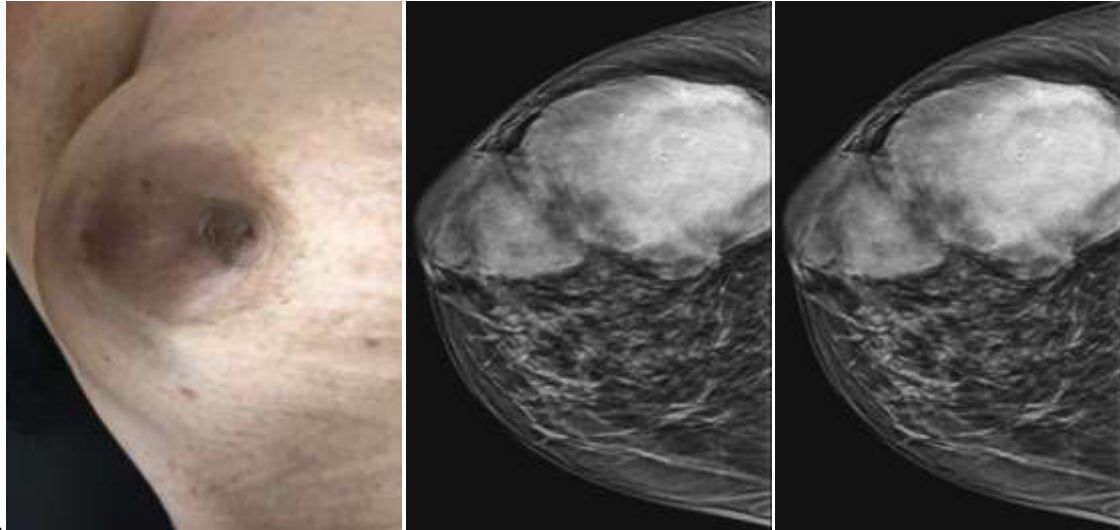

DBT showing large high density oval shaped lesion with well circumscribed and few microlobulated margins and few internal rod like calcifications, in upper outer quadrant with involvement of nipple areola complex. Histopathology revealed Ductal carcinoma in situ.
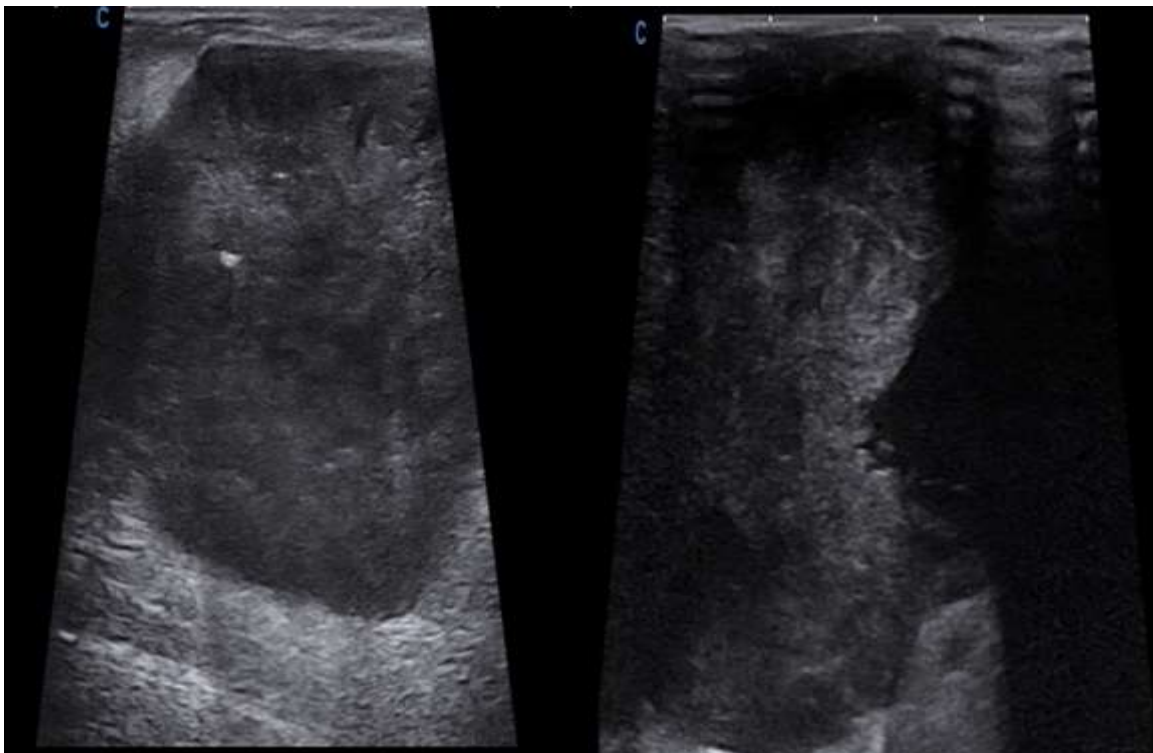

USG images are showing large well circumscribed solid mass in right breast with microlobulated margins , and few internal calcific foci with involvement of NAC.

Case 2 – A patient came with the complaints of nipple retraction and lump in left breast.
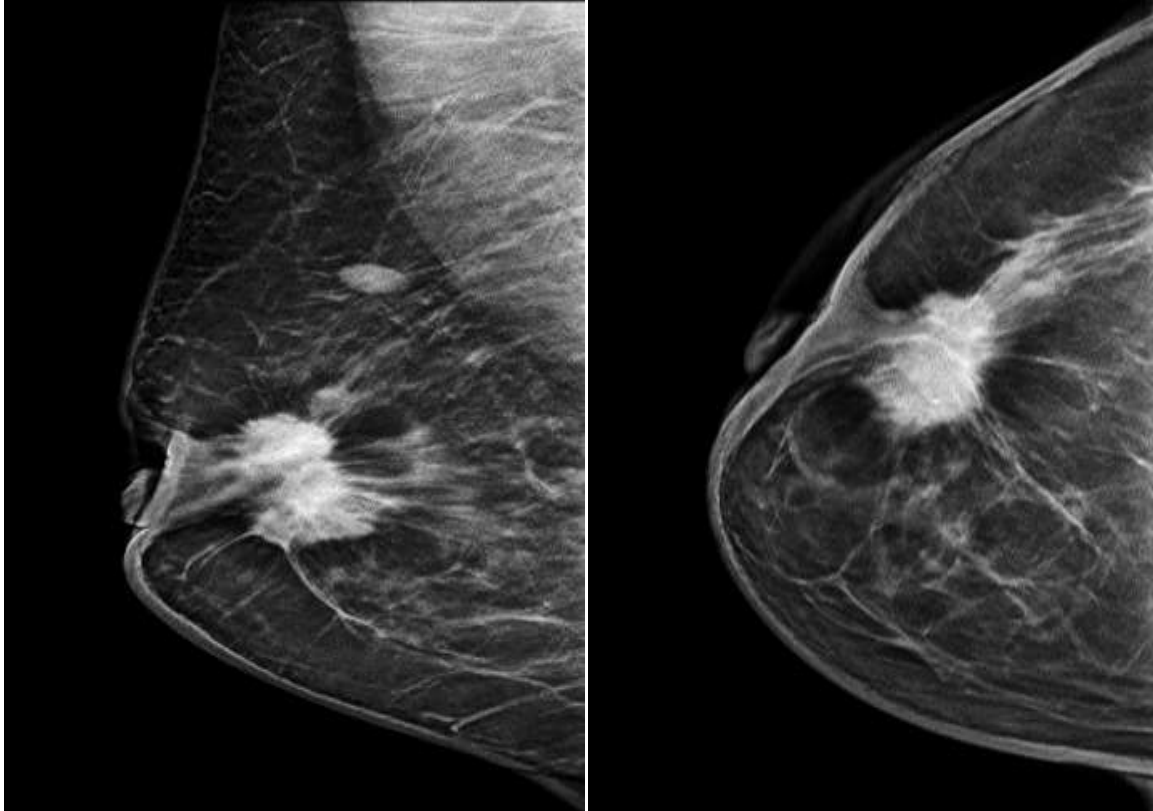

Mammograms (MLO & CC View) revealed an ill-defined, high-density retro-areolar lesion with spiculated margins. A tiny irregular high density satellite lesion is also noted in MLO view. Nipple retraction and skin thickening were also noted. The lesion was confirmed as Ductal Carcinoma on histopathology.
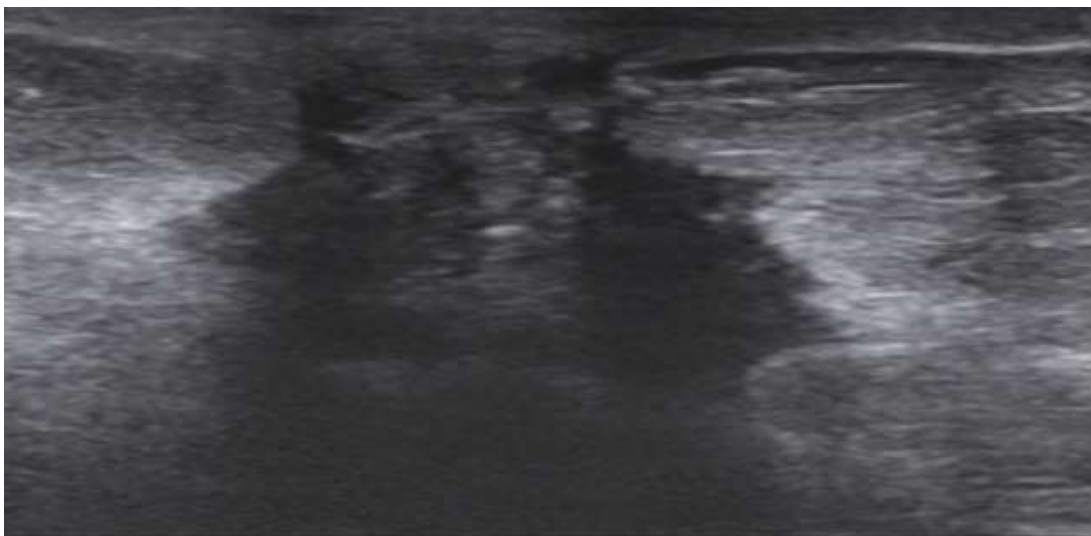
USG image showing ill defined heterogenous lesion with spiculated margins with multiple calcific foci in retroareolar region.

Case 3 – A patient came with the complaints of brownish coloured nipple discharge from right breast which was consistent with blood.
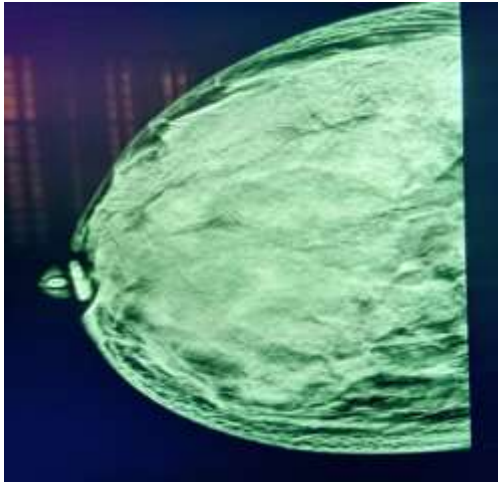
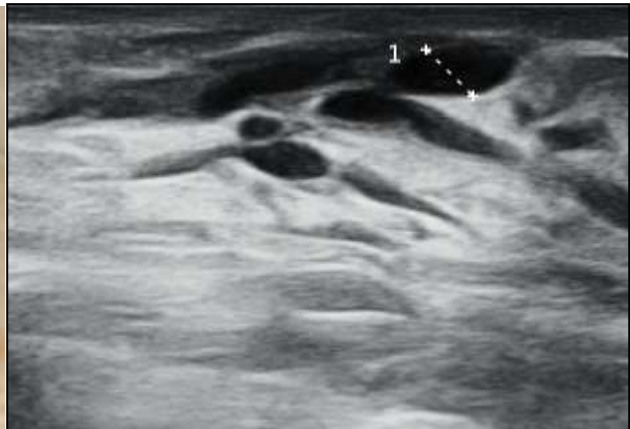| DBT showing heterogeneously dense fibroglandular tissue in right breast.	USG image showing intraductal echogenic lesion – consistent with intraductal papilloma

Case 4-A 39 year old female came with the complaints of red coloured nipple discharge from left breast which was consistent with blood.

Image showing expressible brownish bloody nipple discharge from right breast	USG image showing multiple, dilated, anechoic, tubular structures- consistent with Duct ectasia.

Results

In our study, maximum number of patients were in the age group of 40-49 years (30%).Maximum proportion of the study subjects had Breast Density type B (48%).Most of the patients had complaint of pathological nipple discharge (66%) followed by breast lump

(48%) and nipple retraction (31%).Nipple areola complex was seen involved in 20% of the patients on mammogram. Lump was appreciated in 51% of the total patients on mammogram. On USG, dilated ducts were found in 55% of the total patients, among whom single duct was dilated in 35% patients and multiple ducts were dilated in 20% of the total patients. Intraductal Lesion on was seen in 28% of the total patients on sonography. 38% of the total patients were found malignant; who were having nipple pathologies like nipple discharge, nipple retraction; and 62% of the total patients were found benign. Involvement of nipple areola complex among malignant lesions was seen in 20% cases on mammogram and 29% cases on USG. USG is more sensitive than mammography for detection of involvement of NAC. Breast masses having spiculated margins, angular margins and micro lobulations indicated a malignant pathology on both mammogram and USG. The negative predictive value of USG in detecting malignancy amongst patients with nipple discharge, nipple retraction and nipple inversion was slightly higher than mammography (100% vs. 88.24%) and associated with higher sensitivity of USG (100% vs. 94.74%) but less specific as compared with mammography (66.18%vs. 54.55%).

Table 1- Distribution of the study subjects according to type of calcifications seen on mammogram

Type of calcification	Frequency	Percent
Benign rounded calcification	1	1
Benign vascular calcification	3	3
Coarse	2	2
Microcalcification	3	3
Fine linear	6	6
Fine Pleomorphic	13	13
No calcification	72	72
Total	100	100

Table 2- Distribution of the study subjects according to nipple areola complex (NAC) involvement on mammogram

NAC involvement	Frequency	Percent
Absent	80	80
Present	20	20

Table 3- Distribution of the study subjects according to nipple areola complex (NAC) involvement on ultrasonography

NAC Involvement	Frequency	Percent
Absent	68	68
Present	32	32
Total	100	100

Table 4- Distribution of the study subjects according to dilatation of duct on ultrasonography

Duct dilatation	Frequency	Percent
Multiple	20	20
Single	35	35
No lesion	45	45
Total	100	100

Table 5- Distribution of the study subjects according to birads staging

BIRADS Category	Frequency	Percent
I	11	11
II	23	23
III	14	14
IV A	11	11
IV B	3	3
IV C	10	10
V	21	21
VI	7	7
Total	100	100

Table 6–Diagnostic efficacy of mammography

BIRADS Category	Histopathological Malignancy		Total	Diagnostic Value
	Yes	No		
BIRADS (IV, V, VI)	36	7	43	Sensitivity- 94.74%, Speficity-68.18%, PPV- 83.72%, NPV- 88.24%
BIRADS (II, III)	2	15	17	
Total	38	22	60	

Table 7–Diagnostic efficacy of breast ultrasonography

BIRADS Category	Histopathological Malignancy		Total	Diagnostic Value
	Yes	No		
BIRADS (IV, V, VI)	38	10	48	Sensitivity- 100%, Speficity- 54.55%, PPV- 79.17%, NPV- 100%
BIRADS (II, III)	0	12	12	
Total	38	22	60	

Discussion

Radiology is an important step in the work up of nipple pathologies; it can provide a clue to the underlying pathology and prompt the right management. All the patients we have shown came with the complaints of nipple discharge, nipple retraction, nipple inversion, skin and patients came with the complaints of additional breast lump.Mammographic BI-RADS assessment was reliably able to distinguish between benign and malignant lesions in our study. The 66% of the females were having pathological nipple discharge in my study, out of which 21 patients (31.8%) were found malignant on histopathology. So Pathological nipple discharge is an alarming symptom for breast malignancy .The nipple retraction was found in 31% of the cases and nipple inversion was found in 6% of the cases; both inversion and retraction can have benign or malignant causes .Breast having extremely dense fibroglandular tissue may miss a mass or other intraductal pathologies on mammogram; but on USG, 28% of the dilated ducts show intraductal lesion, which was not appreciated on mammography.

Involvement of nipple areola complex among malignant lesions was seen in 20 % cases on mammogram and 29% cases on USG. USG is more sensitive than mammography for detection of involvement of NAC. The breast mass having spiculated margins; angular margins and microlobulations indicate a malignant pathology on mammogram and USG, so diagnosis and management can be done at its earliest .In our study; 13% of the breast masses show fine pleomorphic or 6 % linear calcification on mammogram; which also indicates malignancy. This pattern of calcification can't be detected on USG. The diagnostic efficacy of Mammography is as follows- Sensitivity is 94.74%, Specificity is 68.18%, PPV- 83.72% &NPV- 88.24%. The diagnostic efficacy of Breast Ultrasonography is as follows- Sensitivity- 100%, Specificity-54.55%, PPV- 79.17% & NPV- 100%. Therefore, US is more sensitive than mammography but less specific than mammography. In our study, out of 100 patients, 38 patients had histologically proven malignancy; amongst them maximum have DCIS/Ductal carcinoma followed by infiltrating ductal carcinoma. Maximum patients had history of pathological nipple discharge and nipple retraction.

Conclusion

Ultrasound and mammography are used for evaluation of nipple. Ultrasound have high sensitivity in the diagnosis of nipple lesions, it is the first-line imaging examination to characterize and identify nipple lesions, distinguish benign and malignant lesions, and guide the management of nipple pathology by facilitating US-guided percutaneous biopsy or planning the surgical excision of the lesion.A routine mammography has a limited role in evaluating the nipple; it is more sensitive to identify microcalcifications. In some malignant lesions, and to reveal the retro areolar mass.USG is more sensitive in our study because mammogram was normal in patients having ductal ectasia; breast US enables the visualization of dilated ducts and intraductal causes of pathologic nipple discharge. Being familiar with the various US techniques that assist in the detailed visualization of subareolar ductal structures is helpful for accurately detecting and diagnosing lesions. This would rule out the possibility of neoplastic changes and provide clues for non-neoplastic etiology that guide the management, assure the patient and reduce repeated unnecessary consultations.

This study suggests

1. Pathological nipple discharge, nipple retraction/nipple inversion can be an early sign for DCIS and should be given due attention for early diagnosis and treatment.
2. USG is found to be more sensitive and more specific imaging modality than mammography as it can better characterize and identify nipple lesions, distinguish benign and malignant lesions, ductal ectasia and pathologies related to dilated ducts,
3. USG also guide the management of nipple pathology by facilitating US-guided percutaneous biopsy or planning the surgical excision of the lesion.

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