Original Research Paper

STUDY OF TRIPLE ASSESSMENT MODALITIES IN EVALUATION OF PALPABLE BREAST LUMPS.

Authors:
Sur Aparajita[1], Tambekar Manisha[2], Athavale Akshay[3*], Doshi Riddhi[4], Dalvi Almas [5]
[1]*Senior resident, Department of Pathology, MGM Medical College, Navi Mumbai.*
[2]*Associate Professor, Department of Pathology, MGM Medical College, Navi Mumbai.*
[3]*Resident, Department of Pathology, MGM Medical College, Navi Mumbai.*
[4]*Resident, Department of Pathology, MGM Medical College, Navi Mumbai.*
[5]*Senior resident, Department of Pathology, MGM Medical College, Navi Mumbai.*
Corresponding Author:
Dr Akshay Athavale
MGM Medical College, Navi Mumbai.
Department of Pathology, MGM Medical College Navi Mumbai.

ABSTRACT:
Detection of lump in the breast causes lot of anxiety and fear of a cancer diagnosis in females. It is crucial that a careful evaluation is performed so that correct and appropriate management can be organized in a timely and efficient way. The triple assessment of breast plays a valuable tool in preoperative assessment of breast masses which will be more accurate with high sensitivity and specificity. The aim of the study was to study the significance of triple assessment in evaluation of palpable breast lumps and to determine the sensitivity, specificity, predictive values and accuracy of triple assessment in evaluating palpable breast lumps. A retrospective and prospective study of 100 cases, conducted over a period of 4 years (July 2017 to June 2021) in females with palpable breast lumps and undergoing clinical breast examination (CBE), sonomammography, FNAC and histopathological examination. Out of 100 cases, the benign lesions were seen in age group 31-40 years (26%) and malignant lesions in the age group 41-50 years (12%). The most common benign breast lesion was fibroadenoma and most common malignant lesion was Infiltrating Duct carcinoma. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of all three parameters of triple assessment when compared with histopathology was 100 %, 98.57%, 96.66%, 100% and 98% respectively with a significant P-value (0.00001). The triple assessment is a very useful tool to evaluate the palpable breast lumps and is easily available, cost-effective, least invasive and a rapid patient friendly diagnostic tool for the diagnosis of breast lumps thus decreasing the rate of morbidity and mortality.

KEYWORDS: Clinical breast examination (CBE), Fine needle aspiration cytology (FNAC), Palpable breast lump, Sonomammography, Triple Assessment.

INTRODUCTION:

Breast cancer is the most common and leading cause of cancer deaths in women. Due to the globalization and adoption of western culture, increased life expectancy and diagnosis in late stages, the incidence of breast cancer in females has increased in the developing countries [1]. In a study conducted in Indian females in 2017, carcinoma of breast was rated number one cancer with age with incidence rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women [2]. According to the National Institute of Clinical Health and excellence (NICE) and the Association of Breast Surgeons guidelines, patients with symptoms that could be caused by breast cancer, the diagnosis is done by Triple assessment (clinical breast examination, mammography and/ or USG imaging and FNAC and/or Core biopsy) [1,3]. Triple assessment saves time as it helps in diagnosing breast cancer at an early stage so that it can be treated with the modern therapy and are therefore potentially curable. Clinical breast examination (CBE) is examination of breast masses and skin changes done by health professional [4]. CBE is an important step in the diagnosis and monitoring of various breast lesions and can be used as an alternative screening method [5]. CBE alone is not adequate for definitive diagnosis of breast cancer and so in such situations X-ray, mammography or Sonomammography can demonstrate such lesions, which can then be subjected to fine needle aspiration cytology (FNAC) for

pathological confirmation [6]. Sonomammography (USG) has become a very important tool in breast imaging and is very fruitful in detecting small size breast carcinomas that are not detected on mammography [7]. FNAC plays an important role in early diagnosis of palpable breast lump(s). When compared with a single adopted diagnostic procedure, these three modalities are more accurate, reliable, and acceptable in diagnosing breast lesions [8]. Triple assessment helps in differentiating benign from malignant lesions. The patients who are diagnosed with benign lesions can be followed up and the patients who are diagnosed as malignant are subjected to surgery thereby reducing the rates of unnecessary surgery.

MATERIALS AND METHODS:
A retrospective and prospective study conducted over a period of 4 years (July 2017 to June 2021)

Sample size: 100 cases

Study design: A retrospective and prospective study.

Place of study: Department of Pathology, MGM Medical College and Hospital, Kamothe, Navi Mumbai.

Inclusion criteria
1. Females presenting with palpable breast lump(s) undergoing clinical breast examination (CBE), sonomammography (USG), FNAC and histopathological examination.

Exclusion criteria
1. Males presenting with palpable breast lump.
2. Patients previously operated for breast cancer.
3. Pregnant and lactating mothers.
4. Patients who are not willing to give consent for FNAC.
5. FNAC yielding inadequate material.

Procedure: The data was gathered and reviewed from the medical records of the institution and the requisition form accompanying the specimens. Detailed clinical history including age, gender, menstrual history, past history was taken followed by the triple assessment of breast: clinical breast examination (CBE), sonomammography (USG) and fine- needle aspiration cytology (FNAC) keeping histopathology as gold (reference) standard.

Clinical Breast Examination: All the patients were subjected to CBE and both the axillae were palpated for lymphadenopathy. The CBE findings were categorized into benign and malignant lesions.

Sonomammography: All female patients underwent sonomammography of both breasts including bilateral axillae. The radiologist analyzed and categorized the radiological findings by using the BIRADS system (Breast Imaging Reporting and Data System) created by American College of Radiology. BI-RADS 1-3 were grouped together as benign lesions and BI-RADS 4-6 were grouped together as malignant lesions. The USG findings were categorized into benign and malignant lesions.

FNAC: A total of 100 patients were subjected to FNAC after obtaining informed consent. In cystic lesions fluid was aspirated, centrifuged and smears were prepared from the sediment. After aspiration, if the cyst disappears, if re-examination revealed any solid areas, re-aspiration was performed. Direct smears prepared were fixed in 95% ethyl alcohol for at least 30 minutes or overnight and fixed smears were stained using PAP and H&E stain while air dried smears were stained with May Grunwald Giemsa (MGG) stain. The cytology smears were categorized into diagnostic categories (C1- C5) proposed by National Cancer Institute (NCI) in 1996.[9] Final cytology diagnosis was categorized into benign (category C2 and C3) and malignant (category C4 and C5) lesions.

Histopathological Examination: All the histopathological specimens were received in 10% formalin and then 3 - 5 microns thick sections were cut and stained with hematoxylin and eosin stain. The final histopathological diagnosis was categorized into benign and malignant lesions and was considered as reference gold standard.

Statistical analysis: The collected data was stored and analysed using in Microsoft Excel and by using SPSS test of significance 'p' value was calculated. P <0.05 was considered statistically significant. The specificity, sensitivity, PPV, NPV and diagnostic accuracy were calculated.
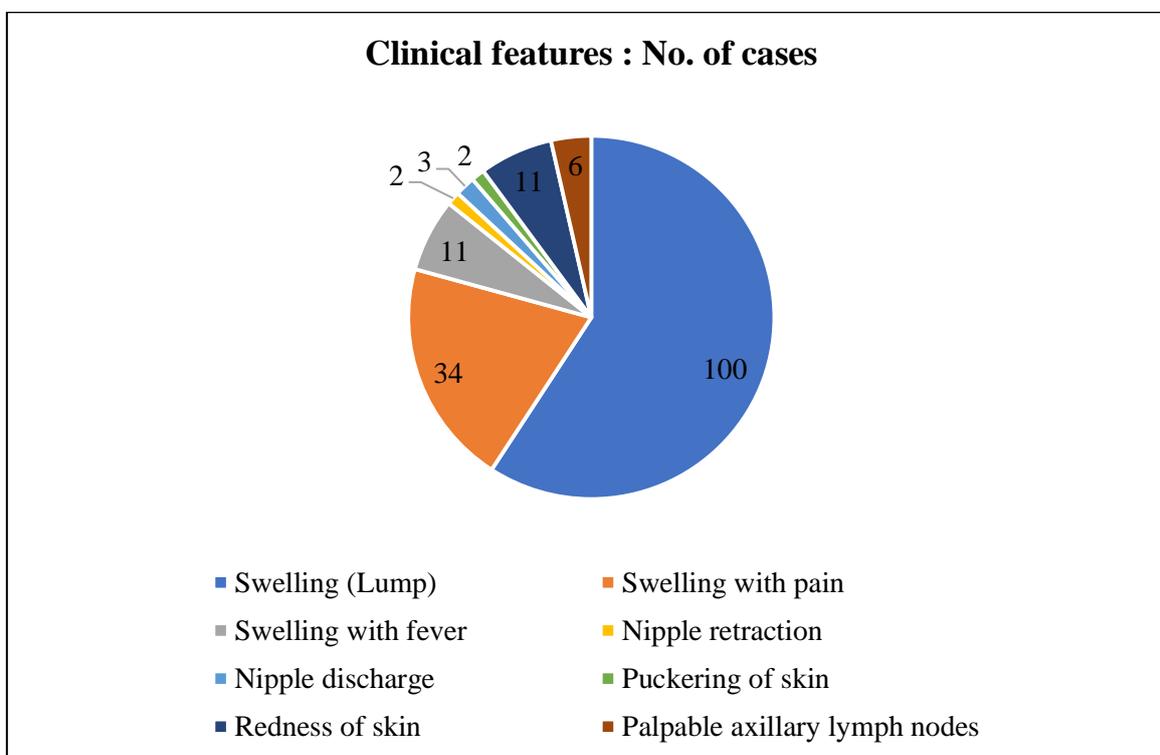
RESULTS:
Age distribution: The study comprised of 100 cases of females with breast lump(s) with age ranging from 14 to 84 years with a mean age of 36.27 years. The maximum number of cases were in the age group of 31-40 years followed by 41-50 years. On FNAC, benign lesions were commonly seen in age-group of 31-40 years (26%) and malignant lesions in 41-50 years (12%) of age-group (Table 1).

Table 1: Age-wise distribution of benign and malignant breast lesions on FNAC.

Age group (Years)	FNAC		
	Benign	Malignant	Total
11-20	14	0	14
21-30	18	1	19
31-40	26	8	34
41-50	11	12	23
51-60	2	2	04
61-70	0	3	03
71-80	0	2	02
>80	0	1	01
Total	71	29	100

Clinical presentation: The most common clinical feature was lump in breast (100 cases) and 34 cases were associated with pain (Figure 1).

Clinical features : No. of cases

- Swelling (Lump)
- Swelling with pain
- Swelling with fever
- Nipple retraction
- Nipple discharge
- Puckering of skin
- Redness of skin
- Palpable axillary lymph nodes

Figure 1: Clinical features of patients

Duration of lump: Maximum cases were of duration ≤5 Months (59 cases).

Site of breast lump: The right breast (49 cases) was slightly more involved than the left breast (48 cases) and bilateral involvement was seen in 3 cases.

Quadrant: The lump was commonly noted in the upper outer quadrant (64 cases) of breast followed by upper inner quadrant (15 cases), lower outer quadrant (10 cases), lower inner quadrant (7 cases) and central (11 cases).

Size of breast lump: 84 cases had size of < 5 cms, wherein, benign lumps were 62% and malignant lumps were 22.8%. 8 cases each of benign and malignant lumps were of size ≥5cms.

Clinical breast examination: 28 cases were diagnosed as malignant and 72 cases as benign (Figure 2).
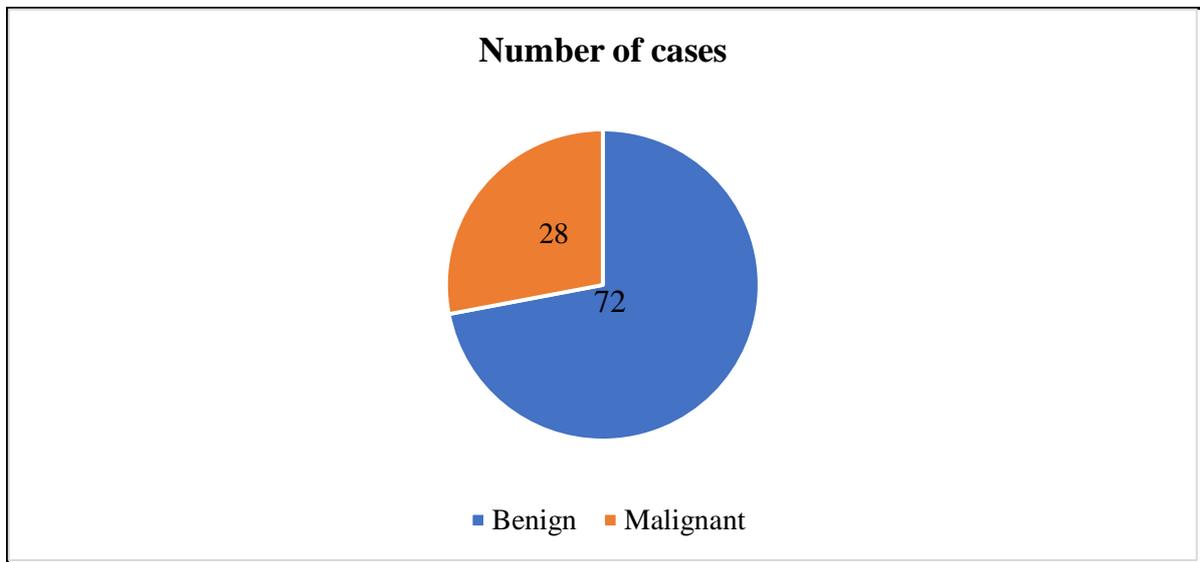
Figure 2: Categorization of breast lesions on clinical breast examination

Sonomammography: The maximum number of cases (43 cases) were seen of BI-RADS 2 followed by BI-RADS 3 (19 cases), BI-RADS 4 (18 cases), BI-RADS 5 (11 cases) and BI-RADS 1 (9 cases). 29 cases were diagnosed as malignant and 71 cases as benign (Table 2).

Table 2: Number of benign and malignant lesions on sonomammography/ ultrasonography

Sonomammographic Diagnosis (BIRADS Score)		Number of cases
Benign (n=71)	BIRADS score 1	9
	BIRADS score 2	43
	BIRADS score 3	19
Malignant (n=29)	BIRADS score 4	18
	BIRADS score 5	11
	BIRADS score 6	0
Total		**100**

Cyto-histopathological correlation: On correlation, 99 cases were in concordance and 1 case was discordant. The most common benign breast lesion was fibroadenoma (57 cases) and malignant lesion was infiltrating duct carcinoma (25 cases) on HPE (Table 3).

Table 3. Cyto-histopathological correlation of various breast lesions.

IAC Category	FNAC Diagnosis	Number of cases	Histopathology Diagnosis (Gold Standard)
C2	Breast Abscess	2	Breast Abscess (n=2)
	Acute mastitis	3	Acute mastitis (n=3)
	Granulomatous Mastitis	2	Granulomatous Mastitis (n=2)
	Galactocele	1	Galactocele (n=1)
	Fibroadenoma	53	Fibroadenoma (n=46) Giant Fibroadenoma (n=1) Complex Fibroadenoma(n=1) Fibroadenoma with fibrocystic change (n=4) Phyllodes (n=1)

	Fibroadenoma with fibrocystic change	2	Fibroadenoma with fibrocystic change (n=2)	
	Fibrocystic Disease	2	Fibrocystic Disease (n=1) Sclerosing adenosis (n=1)	
	Benign proliferative breast lesion	4	Fibroadenoma (n=3) Fibrocystic disease (n=1)	
	Lipoma	1	Lipoma (n=1)	
C3	Proliferative Breast lesion with atypia	1	IDC (n=1)	
C4	Atypical Ductal Hyperplasia	2	IDC (n=1) Atypical Ductal Hyperplasia (n=1)	
	Suspicious of malignancy	8	IDC (n=5) IDC with fibrocystic change(n=1) DCIS (n=1) Infiltrating lobular carcinoma (n=1)	
C5	Epithelial Malignancy	17	IDC (n=16) IDC with DCIS (n=1)	
	Malignant spindle cell lesion	2	Leiomyosarcoma -intermediate grade (n=1) Malignant Phyllodes Tumour (n=1)	

Triple Test: 69 cases were diagnosed as benign, and 25 cases were diagnosed as malignant by all the three modalities. 99 cases showed concordance while one case which was diagnosed as malignant on triple test was benign on HPE (Table 4).

Table 4: Findings of different modalities of triple assessment

CBE	Sonomammography	FNAC	Triple Test (Benign/ Malignant)	HPE	
				Benign	Malignant
B	B	B	B- 69	69	0
B	B	M	M-2	0	2
B	M	B	B-0	0	0
B	M	M	M-1	0	1
M	M	M	M-25	0	25
M	B	M	M-1	0	1
M	B	B	B-0	0	0
M	M	B	M-2	1	1

On comparison of modality of triple assessment (CBE, USG and FNAC) with histopathology, showed statistically significant correlation with p value of <0.00001 (Table 5).

Table 5: Distribution of cases on Clinical Breast Examination, Sonomammography and FNAC

| Modality of triple assessment		No. of cases	Histopathology		P- Value
			Malignant	Benign	
Clinical Breast Examination	Malignant	28	27	1	
	Benign	72	3	69	
Sonomammography	Malignant	29	28	1	
	Benign	71	2	69	
FNAC	Malignant	29	29	0	<0.00001
	Benign	71	1	70	
Triple assessment test	Malignant	30	29	1	
	Benign	70	0	70	

The triple assessment test showed high sensitivity when compared to each modality of triple test. (Table 6).

Table 6: Diagnostic efficacy of triple test according to histopathological diagnosis (Gold standard)

Modality of triple assessment	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
Clinical Breast Examination	90.00	98.57	96.42	95.83	96
Sonomammography	93.33	98.57	96.55	97.18	97.97
FNAC	96.66	100	100	98.59	99
Triple assessment test	100	98.57	96.66	100	98
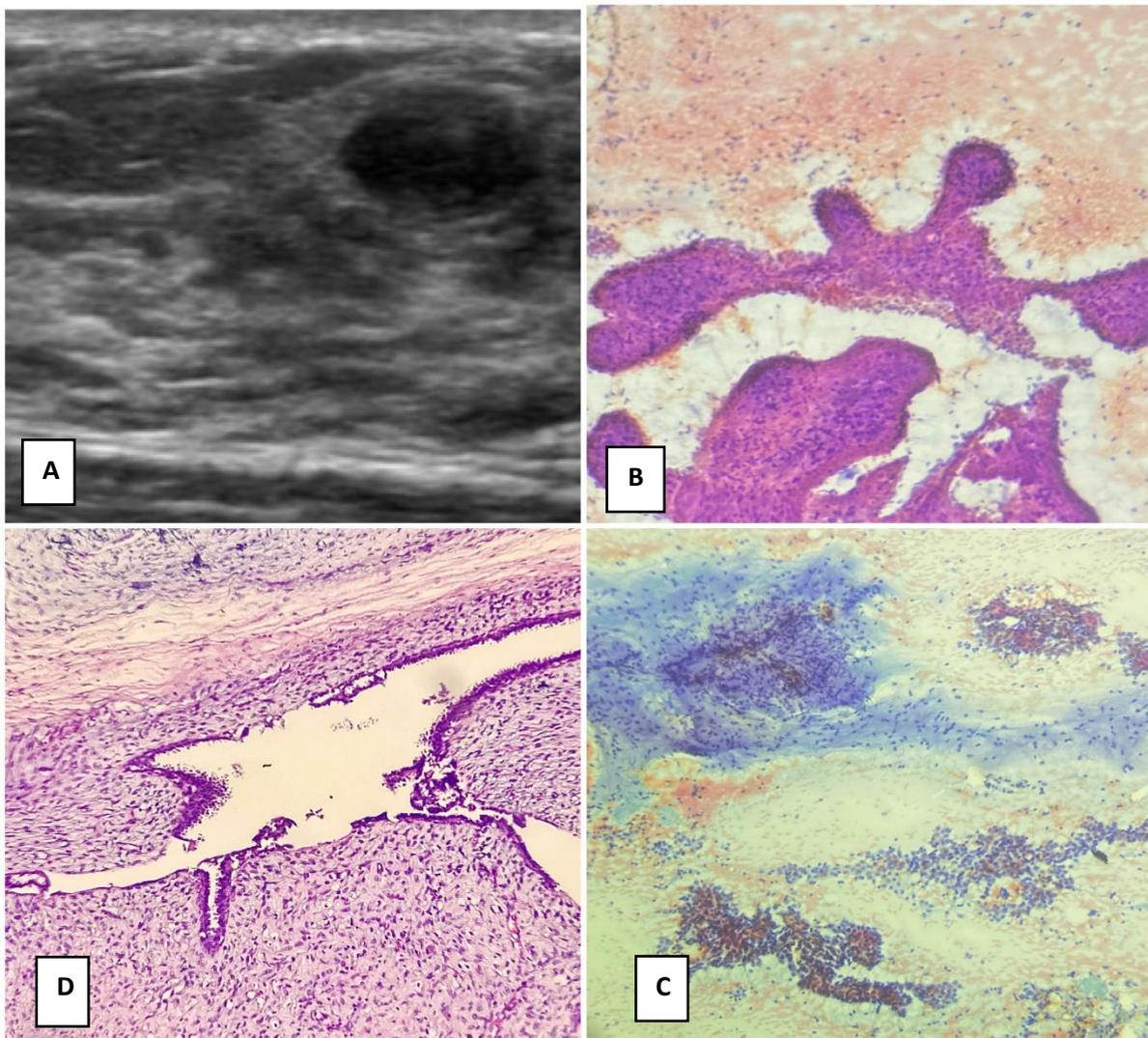
Figure 3: BIRADS II- An oval wider than taller, heterogeneously hypoechoic lesion with well-defined smooth margins and large punctate calcifications; B & C - Cellular smears with branching fragments of duct epithelium with stromal fragment and numerous single bipolar nuclei in the background. (PAP, x4) and branching fragments of duct epithelium with bipolar nuclei and haemorrhage in the background (PAP, x10); D - Low & High power view of Infiltrating duct carcinoma of breast. (H&E)
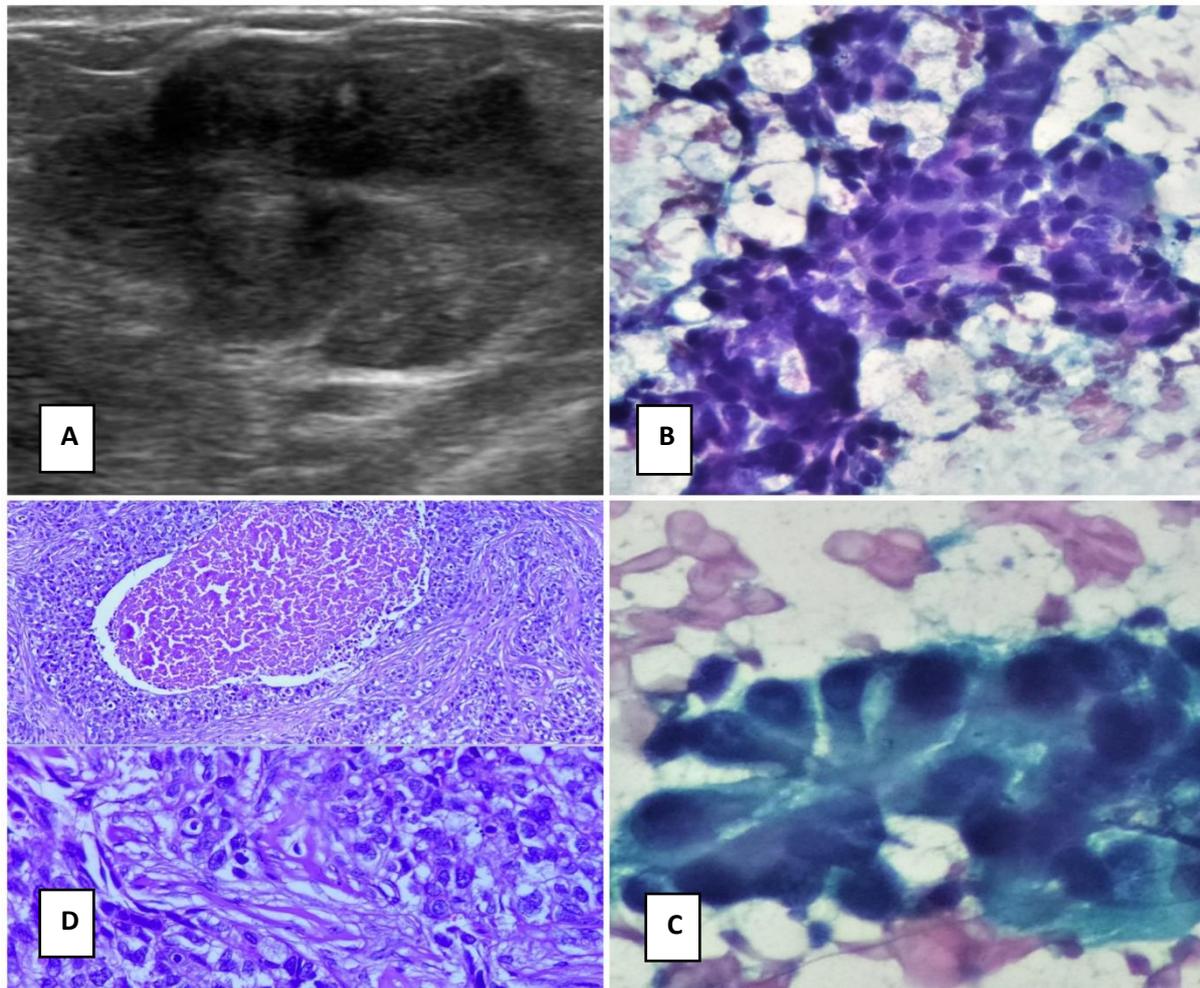
Figure 4: A - BIRADS V- A Large heterogeneous, predominantly hypoechoic, irregular mass lesion with preferential growth and showing invasion of nipple areola complex and underlying chest wall; B and C - Infiltrating Duct carcinoma showing nuclear pleomorphism, hyperchromasia, irregular nuclear membrane on a hemorrhagic background. (PAP, x10 & x40). D - Low & High-power view of Infiltrating duct carcinoma of breast. (H&E)

DISCUSSION:

The present study included 100 females who presented with lump in breast. The age range was 14-84 years and the mean age was 36.27 years. The maximum number of cases were seen in the age group of 31-40 years (34%) followed by 41-50 years (23%) (Table 1), these findings were consistent with the findings of Rana et al.[10] Pain was present in 34% of cases, and fever in 11 % cases which was similar to the findings of Singh et al.[11] We observed maximum cases (n=59) having duration of lump less than 6 months wherein, 37 were benign and 22 were malignant cases. Clinical Breast Examination: Palpation of breast is very essential in detecting masses and can help to find out whether the mass in breast is benign or malignant. In the present study, right side of the breast (49%) was slightly more involved than the left side (48%). These findings were consistent with findings observed by Bhadani et al.[12] In this study, the most common quadrant involved by benign and malignant lump was upper outer quadrant (Benign- 43% & Malignant-21%). Saispandana et al.[13] observed 46% of malignant lumps in the right upper outer quadrant (46%) as compared to benign lump (38.3%). In the present study, 76 lump were firm, 20 were hard and 4 were cystic to soft in consistency. Vishnuteja et al.[14] also found more lumps with firm consistency (81.3%) followed by hard consistency (10 %) and cystic to soft consistency (8.6%) In our study, we observed 3% cases of nipple discharge which is similar to the

findings observed by Solanki et al.[15] (4%). On CBE, 72 cases were benign, and 28 cases were malignant (Figure 2). When compared with histopathological examination, it showed concordance of 96% which is similar to the observations made by Nigam et al.[16] and Saispandana et al.[13] (97.3% and 94% respectively). It is considered as the primary method and best modality for screening breast cancer.

USG: In the present study, ultrasound results were analysed and categorized according to BI-RADS score (43 cases) which is similar to the findings of Vishnuteja et al.[14] In our study, 71 cases were diagnosed as benign, and 29 cases were diagnosed as malignant on ultrasonography. When compared with histopathology, out of 71 benign cases, concordance was seen in 69 cases and 2 cases were favouring diagnosis of malignancy. Out of the 29 cases diagnosed as malignant, 28 cases showed concordance and one case showed discordance. The overall concordance rate of sonomammography in our study was 96% which is similar to the concordance rate observed by Jan et al.[17] and Nigam et al.[16]

FNAC: In this study, out of 100 cases, 71 cases were diagnosed as benign and 29 cases as malignant. Among the benign lesions, fibroadenoma was the commonest lesion whereas, IDC was commonest among the malignant lesions which is similar to the observations made by Vishnuteja et al.[14] and Jan et al.[17]

On correlation of the triple assessment modalities with histopathology, 69 cases showed all three triple test modalities to be benign and were in concordance with histopathological diagnosis and 25 cases showed all three modalities to be malignant which were confirmed on histopathology (Table 4). In the present study, Triple assessment showed high sensitivity of 100 %, specificity 98.57%, PPV 96.66%, NPV 100%, with 'P' value (0.00001) which was statistically significant (Table 6). Studies done by Jan et al.,[17] Nigam et al.[16] and Solanki et al.[15] showed similar statistically significant 'P' values. When we compared the triple assessment results with the histopathology, we found high diagnostic accuracy of 98%, which is similar to the findings observed by Saispandana et al.[13] and Sinha et al.[18] All of them showed a diagnostic accuracy of 98%, 98% and 98.9% respectively.

CONCLUSION:

The triple assessment will be an essential and helpful tool in evaluating palpable breast lump(s) leading to early diagnosis of various breast lesions and thus, decreasing the rate of morbidity and mortality. When all the three components of triple assessment are concordant with each other, the surgeon can initiate definitive therapy without the need of an open biopsy.

REFERENCES:

1. Sharma P, Tewari V, Sharma AK. Triple Test: A 'One Stop' Diagnostic Test in Evaluation of Breast Lesions and its Correlation with Histopathology. Sch. J. App. Med. Sci.2016;4(8D):3002-3008

2. Malvia S, Bagadi SA, Uma SD, Saxena S. Epidemiology of breast cancer in Indian women. Asia Pac J Clin Oncol.2017;13(4):289-295.

3. Khoda L, Kapa B, Singh KG, Gojendra T, Singh LR, Sharma KL. Evaluation of modified triple test (clinical breast examination, ultrasonography, and fine-needle aspiration cytology) in the diagnosis of palpable breast lumps. J Medical Society.2015 ;29(1):26-30.

4. Niaz MI, Tirmazi FH, Farooq O. Triple assessment- efficacy in diagnosis of malignant breast lump. Professional Med J.2012;19(5):620-624.

5. Mittra I, Mishra GA, Dikshit RP, Gupta S, Kulkarni VY, Shaikh HKA, Shastri SS, Hawaldar R, Gupta S, Pramesh CS, Badwe RA. Effect of screening by clinical breast examination on breast cancer incidence and mortality after 20 years: prospective, cluster randomised controlled trial in Mumbai. BMJ. 2021; 24;372: n256. PMID:33627312.

6. Kachewar SS, Dongre SD. Role of triple test score in the evaluation of palpable breast lump. Indian J Med Paediatr Oncol.2015;36:123-7.

7. Gokhale S. Ultrasound characterization of breast masses. Indian J Radiol Imaging.2009;19(3):242–247.

8. Bukhari MH, Arshad M, Jamal S, Niazi S, Bashir S, Bakhshi IM, Shaharyar. Use of Fine in the Evaluation of Breast Lumps. Patholog Res Int.2011;2011:689521.

9. Dayal S, Krishna M, Kannaujia SK, Singh S. Gray Lesions of the Breast and its Diagnostic Significance: A Retrospective Study from Rural India. J Microsc Ultrastruct. 2021;9(3):119-124.

10. Rana ML, Sharma SC. To correlate the Modified Triple Test (MTT) for palpable breast mass with histopathology. International Journal of Scientific Research. 2018;7(9):78-80.

11. Singh K, Azad T, Gupta GD. The Accuracy of Ultrasound in Diagnosis of Palpable Breast Lumps. JK Science. 2008;10(4):186-88.

12. Bhadani PP, Smita S, Jamal I, Sinha R, Majumdar S. Reliabilty of fine needle aspiration cytology in the evaluation of palpable breast lumps – An institutional based study. Archives of Cytology and Histopathology Research. 2017;2(2):50-54.

13. Saispandana D, C S Harsha, S V S Rao. Triple assessment in evaluation of breast lump. JMCR. 2020;8(1):653-657.

14. Vishnuteja M, Rout SS, Sahoo PK. A prospective study of triple assessment in evaluation of breast lump. Int. J. Adv. Res.2021;9(03):65-71.

15. Solanki PV, Juneja IA, Chaudhari ND. Modified triple assessment in the diagnosis of breast lump in Saurashtra region of Gujarat. Int Surg J. 2020;7:3289-93.

16. Nigam M, Nigam B, Triple Assessment of Breast – Gold Standard in Mass Screening for Breast Cancer Diagnosis. IOSR-JDMS. 2013;7(3):1-7.

17. Jan M, Mattoo JA, Salroo NA, Ahangar S. Triple assessment in diagnosis of breast cancer in Kashmir. Indian J Surg.2010; 72:97-103.

18. Sinha NK, Kumari N. A study to evaluate the relevance and validity of triple assessment in diagnosing carcinoma breast. J. Evolution Med. Dent. Sci. 2020;9(16):1386-1389.