

EVALUATION OF BREAST DISEASES BY TRIPLE TEST WITH USG AS 4TH COMPONENT

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ABSTRACT:

OBJECTIVE

- To assess the effectiveness of Triple test (TT) in evaluation of breast diseases.
- To compare Triple Test (as a combined diagnostic modality) to each of its components.
- To find whether addition of Ultrasound to Triple Test, provides any benefit to the diagnosis

STUDY DESIGN

Prospective study

SETTING

Krishna Hospital and Research Centre , Karad

SUBJECTS AND METHODS

All patients fulfilling inclusion criteria with Breast disease who visited surgery OPD in Krishna Hospital & Medical Research Centre, Karad within the duration of December 2020 to July 2022, were assessed based on the guidelines of triple test for breast diseases along with USG of affected breast. The final result was obtained and the accuracy of all the tests were compared.

RESULTS

The data analysis encompassed the detailed information of patients attending surgical OPD with the breast lump, above 15 years of age. Total of 40 patients were selected as per the criteria as discussed earlier. Each patient in concern with various data and their study results with respect to Modified Triple Test were analysed in detailed. Clinical examination has a sensitivity of 90.9% which means that around 9.1% of the breast cancer cases are missed clinically. Ultrasound breast has high sensitivity and negative predictive value of 93.33%. Hence Modified triple test can be used as a reliable and fairly accurate means of diagnosis of breast carcinoma

Further studies with larger sample sizes are required to reach the conclusion if USG breast can be used as frequently as mammography as USG provides better results in women with dense breast tissue and has lesser radiation exposure

CONCLUSION

- From the study it can be concluded that modified triple test can be a very useful tool in evaluating the breast disease.
- Mammogram and USG are needed in patients where no clinically palpable lump is present and to rule out multi focal disease.
- Though ultrasonogram is an operator dependant investigation but it plays an important role in detecting breast lump where mammography is inconclusive specially in young females with dense breast tissue and also reducing the exposure to radiation during screening over the years.

INTRODUCTION:

One of the commonest presentation of women in surgical OPD is with finding of “BREAST LUMP”. According to the available literature and findings over the years suggest that benign lumps are more common but in spite of this fact malignancy needs to be ruled out in every female presenting with breast lump.

In India, Breast carcinoma hold the position of the 2nd most common malignancy in women. Incidence of breast carcinoma shows increasing trend with every year which falls into the range of approximately 19-33%. According to recent studies, phenomenon of “AGE SHIFT” has also been observed in the incidence of breast carcinoma over the past twenty to twenty-five years in India which means that the incidence of breast carcinoma has shown an increase from 7 to 15% predominantly among the age group of 30-40 years.

Since the majority of the lesions get the diagnosis of benign lump but ruling out of malignancy of breast lump hold more importance and is of more concern as malignant lesions can be life threatening if not attended in appropriate window of time and breast cancer is also the most common malignancy found in women residing in Western countries; but benign lesions of the breast are far more frequently seen than malignant ones.

The availability of various radiological modalities like mammography, ultrasound, and magnetic resonance imaging of the breast and the extensive use of needle biopsies to obtain the histopathological status, arriving to the diagnosis of a benign breast disease can be accomplished without surgery in most of the patients. As the majority of lesions are benign in nature and generally don't show association with an increased risk for developing breast cancer, unrequired surgical procedures should be avoided. It is of great importance that pathologists, radiologists, and oncologists successfully recognize benign lesions, and are able to distinguish them from in situ and invasive breast cancer and to evaluate an individual patient's risk of subsequently developing breast cancer, so the most adequate plan of treatment modality for each individual case can be planned. The first step in evaluation of breast lump and first patient-doctor interaction for the said concern is the clinical assessment. Several clinicians with the help of only clinical examination in a number of cases can confidently make the diagnosis of benign or malignant lesion, but it always holds the risk of missing out malignancy even in highly experienced hands.

The triple test for breast diseases involves,

1. Clinical assessment
2. Radiological modality – Mammography has been used traditionally used
3. Pathological modality - Fine needle aspiration cytology (FNAC)

In modified triple test ultrasonogram is used along with mammography. Clinical diagnosis of breast cancer possesses higher sensitivity compared to its specificity and also has high diagnostic error, on the other hand mammography and FNAC respectively showed to have lower sensitivity than specificity but comparatively have high positive predictive values. On combining all the above said investigations in the triple assessment, the outcome is we can reach a definitive diagnosis more accurately, which suggests that the triple assessment has a high sensitivity, specificity, positive predictive value and negative predictive value which makes it an ideal assessment modality to plan further treatment of patients presenting with complaints of breast lump/diseases.

Along with above established results of triple assessment the added benefit is that the results obtained from triple assessment is reproducible and hence making it a reliable diagnostic

modality to approach and plan the treatment of breast cancer. Mammography over the years due its accessibility and not being operator dependant has proven itself as the preferred method for screening for breast cancer among females. But in cases where mammography reveals a non-palpable breast lesion or gives an inconclusive report , further imaging studies are often needed to diagnose more precisely and identify the characteristics and location of the lump to as much accurately as possible.

One of the ventures to utilize radiography to arrive at the conclusion the of breast abnormalities were attempted in the late 1920's, but mammography, as a developed screening method known to us now , making use of committed X-ray units, was established in the 1960s. In the past two decades numerous additional methods has been developed to assess breast lesions which a number of methods like Thermography, Radioisotope scanning, ultrasound, computed tomography, and magnetic resonance imaging. Ultrasonography of the breast is an exceedingly productive diagnostic modality when it is used along with clinical and pathological examination. Ultrasonography has added advantages of being painless, no exposure radiation, and along with proper and skill full training it can be easily executed in a timely, regular manner and can become one of the essential modalities for screening of breast lumps . As our study aims to evaluate breast disease with triple assessment test with the use of USG as the fourth component , we will try to establish the accuracy and utility of USG in regular screening and diagnosis of breast diseases

MATERIALS AND METHODS

Above is a prospective study. All patients fulfilling the above stated inclusion criteria presenting with complaints of breast diseases in Krishna Hospital & Medical Research Centre, Karad were included in the study

☐ INCLUSION CRITERIA:

- Females between 15 - 60 years presenting with
 1. Breast lumps which are clinically palpable.
 2. Any complaints associated with breast .

☐ EXCLUSION CRITERIA:

Patients with

- A. Fungating breast lump.
- B. Open biopsy and HPE performed prior to presentation to our hospital.
- C. Patients who did not continue treatment / lost follow up / underwent non- surgical treatment (chemotherapy/radiotherapy).

SAMPLE SIZE:

Minimum number of breast lump cases required to enroll is determined using appropriate formula which was estimated to be 40

PERIOD OF STUDY

the study which was conducted from December 2020 to July 2022 including data collection , compilation and analysis .

STUDY DESIGN

All patients fulfilling inclusion criteria with Breast disease who visited surgery OPD in Krishna Hospital & Medical Research Centre, Karad within the duration of December 2020 to July 2022,

were assessed based on the guidelines of triple test for breast diseases along with USG of affected breast. The final result was obtained and the accuracy of all the tests were compared.

RESULTS

All the data collected will be analysed under this section including the detailed information of patients who attended the surgical OPD with the breast lump, above 15 years of age and maxima of 60 years of age. A total of 40 patients were included in accordance to the criteria that is discussed earlier in this study. Each and every patient included with various data and their individual study results with criteria of Modified Triple Test were analysed in detailed description.

Distribution of age:

Among the included study population, age group as the basis, 15 years old patients being the youngest among the study group and 60 years is being the oldest, it was found that the most commonly affected age group were present among the age group of 30-39 years.

Table 1. Comparison of Age Distribution of Patients and Breast Lump

Sr no	Age group	Total no of patients (%)
A	15 - 30 years	04 (10%)
B	30 -39 years	17 (42.5%)
C	40 - 49 years	12 (30%)
D	50 - 60 years	07 (17.5%)

Hence with the help of Table 1 we can conclude that among this study group, patients presenting with breast lump are most common among the group of 30-39 years old patient. According to the literature, it has been recorded that the incidence of breast cancer has shown age shifts over past twenty years in India which means incidence of breast cancer has increased from 7 to 16% among the age group of 30-39 years.

Parity:

Parity	Number of patients		
	Benign	Malignant	total
Nulliparous	04 (40%)	06 (60%)	10 (100%)
Multiparous	25 (80%)	05 (20%)	30 (100%)
Total	29 (70%)	11 (30%)	40 (100%)

Table 2. Comparing Parity with percentage of Benign and Malignant Breast Disease.

The above table shows that in our study group, malignant breast lump showed predominance among the nulliparous group of women

Menstrual Age:

Menstrual status of women was used as a basis to categorise the study group into the categories of

- a) premenopausal,
- b) perimenopausal and,
- c) postmenopausal

the obtained results were by this division is demonstrated in Table 3.

On exemplifying the Table 3 we inferred that benign lump was most common

Among all three categorists. However, the comparison also suggests that among the premenopausal group of women ,findings of benign lump is more prevalent, whereas on evaluating the perimenopausal and postmenopausal group of women malignant tumour is comparatively more common.

Menstrual status	Total number of patients (%)		
	Benign	Malignant	Total
Pre-menopausal	21 (91.30%)	02 (9.7%)	23 (100%)
Peri-menopausal	04 (44.44%)	05 (55.55%)	09 (100%)
Post-menopausal	04 (50%)	04 (50%)	08 (100%)
Total	29	11	40

Table 3. Comparing menstrual status of women with percentage of benign and malignant breast Disease

Frequency of side of breast lump:

Among the study group, breast lump appeared to be more common on left side account for about overall 54% age. The bilateral tumors are least common shown in Table 4.

Tumour side	Percentage of patients
Right side	40%
Left side	54%
Bilateral	6%

Table 4: Frequency of occurrence of breast lump in accordance to side of diseased breast

Location of tumour in the affected breast:

Amongst all the females included in the study group, the location of most lump and its prevalence to the quadrant was also assessed. Based on the findings, most of the patients presenting with breast lump were found to be located in the upper outer quadrant of the diseased breast and minimum number of patients were seen to have the lower inner quadrant of the breast involved with lump. This finding can be attributed to the fact that estrogen receptors are more prevalent in the upper outer quadrant of breasts.

Quadrant of diseased breast showing lump	Percentage age of patients
Upper outer (U/O)	61%
Upper Inner (U/I)	14%
Lower Outer (L/O)	12%
Lower Inner (L/I)	04%
Central	09%

Table 5. Distribution of Breast lump according to involved quadrant of diseased breast with percentage of cases.

Histopathological Report:

According to existing literature fibroadenoma is the most common benign tumour which is similar to the results obtained in our study. Next common benign tumour among the study group was found to be fibrocystic disease of breast. One of our study patients received the diagnosis of ductal carcinoma in situ (DCIS) . Out of the malignant cases, ductal carcinoma is the commonest which corresponds to the previous study results found in existing literature.

Final histopathological report of specimen	Number of patients
Fibroadenoma	19
Fibro cystic disease	08
Cystosarcoma phylloides	02
Proliferative without atypia	02
Ductal carcinoma in situ	01
Ductal carcinoma	04
Lobular carcinoma	01
Mucoid carcinoma	03

Table 6. Final histopathological report of Specimen

Results of clinical examination:

Clinical examination	Histopathological report		total
	Malignant	Benign	
Malignant	10	01	11
Benign	01	28	29

Table7. Comparison of findings of clinical examination against final histopathological Reports of specimen

From the data available in Table 7. the following results were obtained and the results are listed below:

- Sensitivity – 90.90%
- Specificity – 96.55%
- Positive predictive value – 90.90%
- Negative predictive value – 96.55%

It is concluded from the above study that clinical examination has a sensitivity of 90.9% which means that around 9.1% of the breast carcinoma cases are missed clinically. In spite of this, clinical examination is a reliable method to assess the breast lump as it possesses fairly high specificity and it demonstrates high negative predictive value hence establishing itself as effective method for initial judgement of the breast lump.

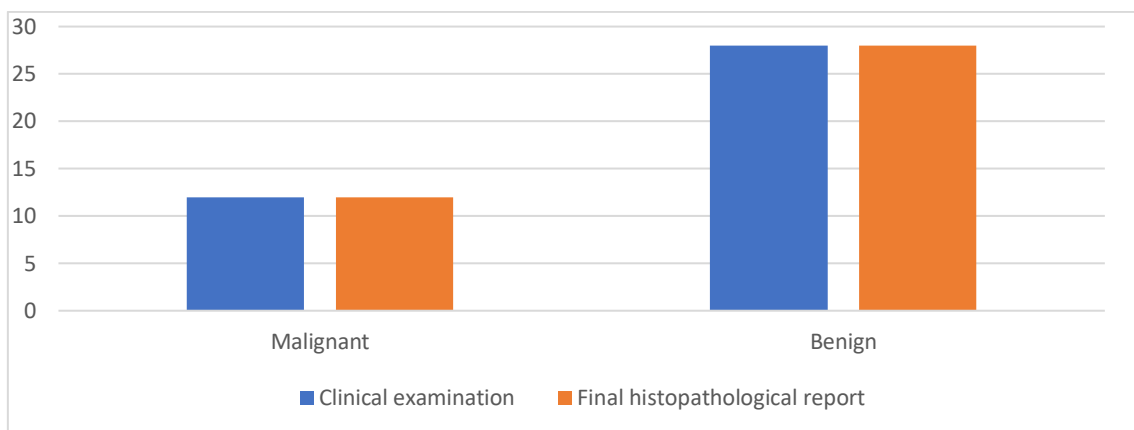


Chart 01: Bar diagram demonstrating the comparison between the results of clinical examination against results of final histopathological report

Table 8. Comparison between Ultrasound Results against Final histopathological Report

Ultrasonography	Histopathological report		Total
	Malignant	Benign	
Malignant	09	02	11
Benign	02	27	29

Results of USG:

- Sensitivity – 81.81%
- Specificity – 96.55%
- Positive predictive value – 81.81%
- Negative predictive value – 96.55%

Results of ultrasound breast are highly operator dependent. The results of the study show that if the radiologists are experienced and skilled enough ultrasonography of breast shows relatively high sensitivity and negative predictive value of 96.55%

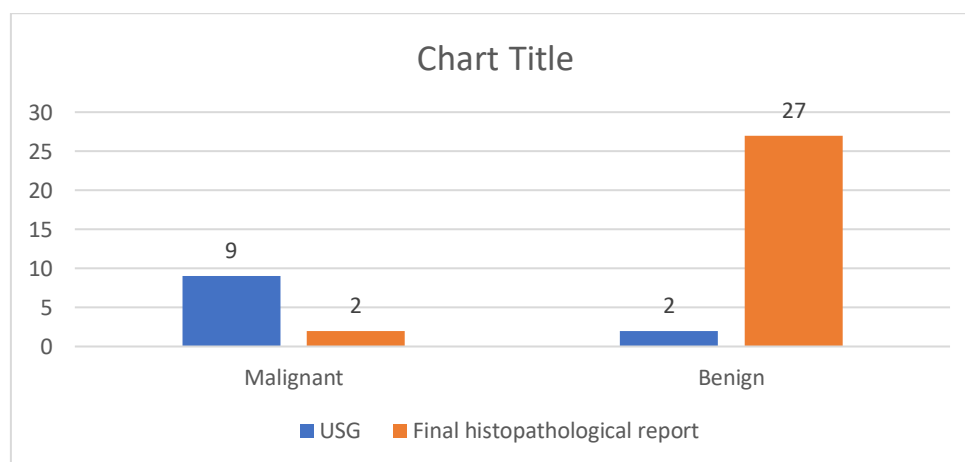


Chart 02: Bar diagram demonstrating results of USG against the results of final histopathological report

Table 9. Comparing results obtained between .FNAC and Final histopathological Report of specimen:

FNAC	Histopathological report		Total
	Malignant	Benign	
Malignant	10	04	14
Benign	02	24	26

Results of FNAC:

- Sensitivity – 83.33%
- Specificity – 85.71%
- Positive predictive value -71.42%
- Negative predictive value – 92.30%

On analysing the above results, it can be inferred that even though FNAC has a sensitivity of 83.33%, it possesses positive predictive value of 92.30%. So those who are diagnosed to be positive for malignancy can be candidates for planning definitive surgical management.

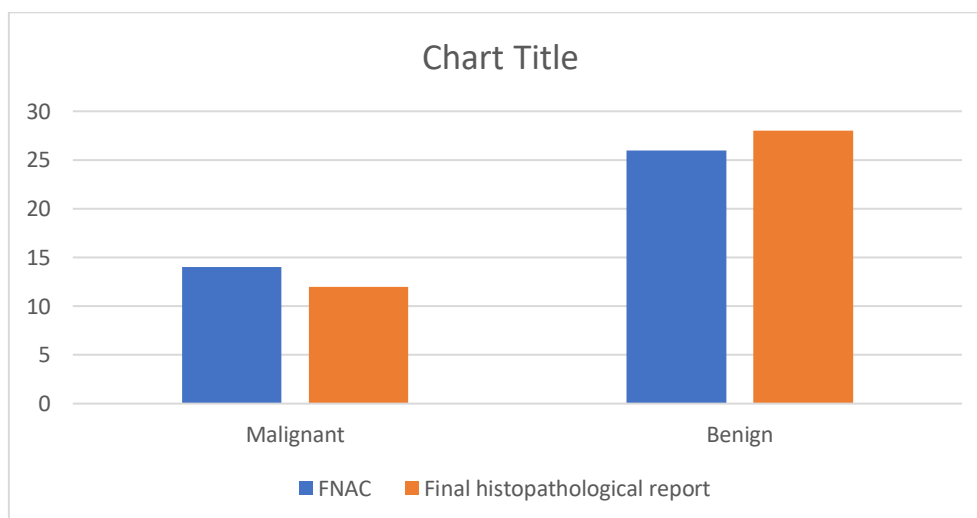


Chart 03: Bar diagram showing comparison between the results obtained by FNAC against final histopathological report of specimen.

Table 10: Comparison between results of mammogram and final histopathological report of specimen:

Mammogram	Histopathological report		Total
	Malignant	Benign	
Malignant	10	04	14
Benign	02	24	26

Sensitivity :83.33%

Specificity: 85.71%

Positive Predictive Value: 71.42

Negative Predictive Value: 92.30%

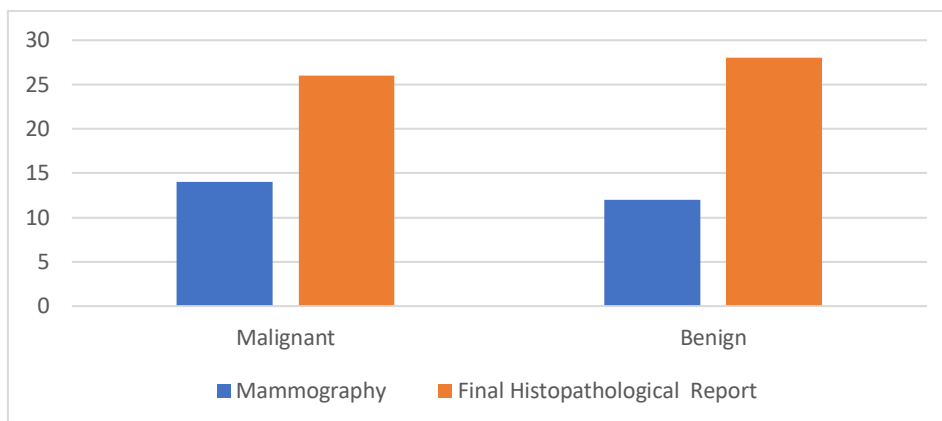


Table 11. Comparison between .combined results of modified triple test against final histopathological report

	Histopathological Report		Total
	Malignant	Benign	
Malignant	9	2	11
Benign	2	27	29

Results of modified triple test:

- Sensitivity – 81.81%
- Specificity – 93.10%
- Positive predictive value – 81.8%
- Negative predictive value – 93.10%

The above study demonstrates that the combined results of Modified Triple Test are almost similar to the findings of the final histopathological report of specimen. Hence it can be stated that modified triple test can be used as a reliable and fairly accurate modality to arrive at the diagnosis of diagnosis of breast carcinoma and help in planning necessary treatment for the patients.

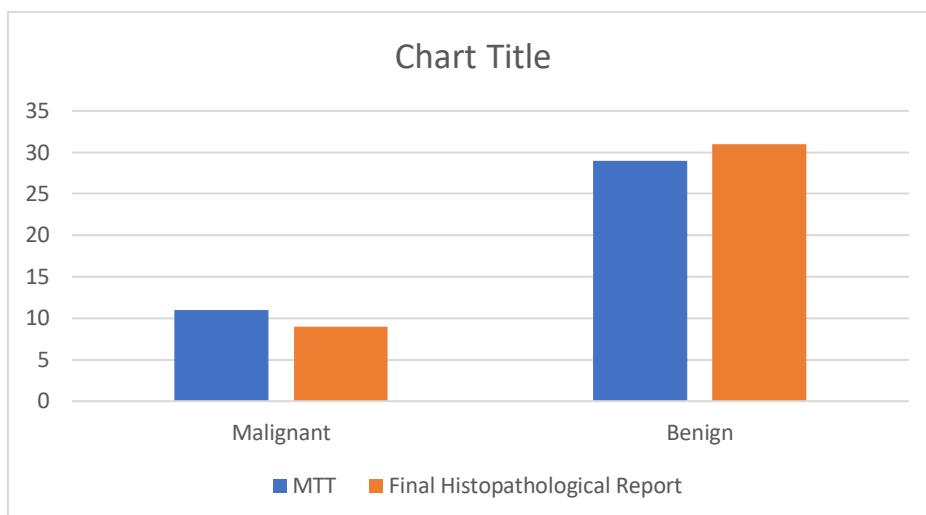


Chart 04: Bar diagram illustrating the results of MTT against final histopathological report of specimen

Table 12. comparison of each Individual component of Modified Triple Test (MTT) and Combined Results of Modified Triple Test(MTT) :

	Clinical examination	USG	FNAC	Mammogram	MTT
Sensitivity	90.90%	81.81%	83.33%	83.33%	81.81%
Specificity	96.55%	96.55%	85.71%	85.71%	93.10%
Positive predictive value	90.90%	81.81%	71.75%	71.42%	81.8%
Negative predictive value	96.55%	96.55%	92.30%	92.30%	93.10%

After analysing the results of all the individual and combined components of modified triple test we can infer the following:

- Clinical examination alone demonstrated sensitivity of 90.9%, while USG showed sensitivity of 81.81%, FNAC showed sensitivity of 83.33%, mammography showed sensitivity of 83.33% and modified triple test showed sensitivity of 81.81% hence clinical examination can be a very good modality to predict and establish the need of further investigations.
- Ultrasound examination has a high sensitivity of 81.81% but since it is operator dependant and given the operator is skilful USG is a reliable method that can be used for screening of breast lump.
- Among the three components fine needle aspiration cytology has high negative predictive value of 92.30% hence plays a very important role in ruling out malignancy.

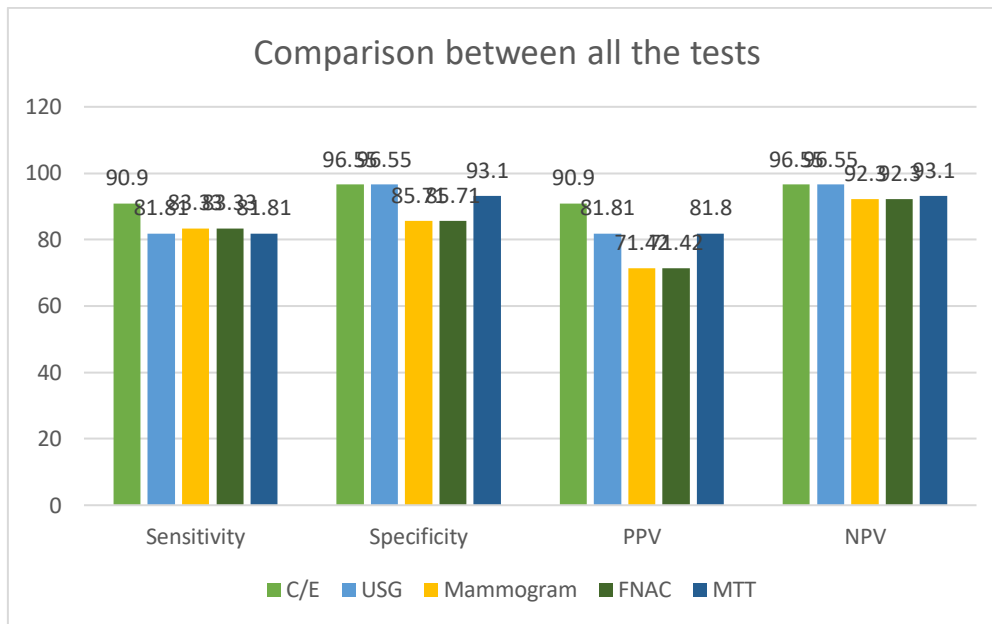


Chart 05: Bar diagram represents the individual. component and combined results of Modified Triple test

DISCUSSION:

Triple test includes clinical examination, radiological examination and histopathological examination to diagnose the cases of breast malignancy. In this study the triple test was conducted along with ultrasonogram to see the efficacy of the investigation and the combined results obtained with USG as 4th component can be termed as Modified Triple Test for the purpose of this study

The current study includes a total of 40 patients. It was found from that in most of the population were found to be in 30-39 years age group with total 17 (42.5%) patients. This was followed by patients in the age group 40-49 years with 12 patients(30%) 7 cases(17.5%) in the 50-60- year age group and 4 patients (10%)in 15-30 years.

In a similar study by Christina Wai et al ,the study included total 320 patient whose age ranged from 19-91 years. This feature was slightly dissimilar to our study where the age group maxima is limited to 60 years only. Whereas the study population of the present study is relatively less therefore the accuracy of our study could be slightly less compared to that of studies of larger sample size.

Another study by P. Kameshwari prasad observed that, out of total 40 patients who were included in the study, the age range was from 15 to 60 years. In this study it was found that majority of the patients were in the age group of 51-60 (30%) and minimum cases of breast neoplasm were below age group of 20 years.

Parity of the study population was assessed in the present study, and it was divided into groups, nulli parous and multi parous. It was observed total 10 patients out of 40 were nulli parous and 30 patients were multi parous. It was observed that there was relatively higher percentage of malignancy among the nulli parous women. Also, it was observed that total 29 patients of benign nature were present, and 11 malignancies were found.

In the present study patients were also assessed based on their menstrual status. They were grouped into 3 groups. Premenopausal, perimenopausal and post-menopausal. It was observed

that majority of the premenopausal patients, 23 patients, 20 patients were found to have benign tumor (86.95%) and in the other groups such as perimenopausal and postmenopausal groups there were relatively less patients. In the study population as well, maximum patients were in the premenopausal group with total 23 patients out of 40.

Laterality of the tumours was assessed during examination. It was observed that 54% of tumours were on the left side among the study population whereas 40% were found in the right sided breast. 6% of the tumours were present bilaterally.

Location of the tumor in the breast was assessed. It was observed that majority of the tumor were present in the upper outer quadrant, 61%, which was followed by upper inner with 14%, lower outer 12% and lower inner quadrant only 4% of the tumours were found while central location of the tumour was found to be 9%.

On histopathological examination fibroadenoma was found to be most common tumour among the study population with dominance of 19 cases which was followed by

- 8 cases of fibro cystic disease,
- 2 cases of cystosarcoma phylloides,
- 2 cases of proliferative without atypia,
- 1 case of ductal carcinoma in situ was observed,
- 4 cases of ductal carcinoma where found,
- 1 cases of lobular carcinoma and,
- 3 cases of mucinous carcinoma.

In P kameshwari prasad study based on clinical diagnosis it was observed that the most common tumour was fibroadenoma with total 37.5%, 12.5% of fibrocystic disease, 7.5% phyllodes tumour and 42.5% of the study population was found to have carcinoma.

On clinical examination it was found that the malignant cases were 11 (27.5%) in total out 40 whereas 29 (72.5%) cases of benign lesion were found on the clinical examination. On comparing with final histopathological report as well it was observed that total 11 (27.5%) malignant cases were present, and 29 (72.5%) cases of benign lesion were found. On comparison of these results with the results of clinical examination sensitivity was found to be 90.90%, specificity was 96.55%, positive predictive value was 90.90% and negative predictive value found calculated as 96.55%. from this it can be inferred that clinical examination has sensitivity of 90.9% which shows that around 9.1% of the breast carcinoma is missed clinically. But due to its high specificity of 96.55% clinical examination remains a reliable method of breast examination.

Final histopathological reports were compared with the ultrasonogram reports. It was observed that on the USG 11 cases of malignant were present (27.5%) and 29 cases of benign lesion were present (72.5%).

Application of contingency table showed that the USG had sensitivity 81%, specificity 96.55% and negative predictive value was 96%. From this it can be inferred that if the radiologists are highly experienced and skilled enough then the diagnosis of the breast lesion becomes very accurate.

FNAC investigation showed that the total malignant cases were found to be 14 cases whereas benign cases were 26 . When compared with the biopsy results it was observed that the sensitivity of FNAC was relatively less 83.33%, but specificity was found to be 85.71%. It can be inferred from the analysis that FNAC has sensitivity of 83.33% but positive predictive value of 71.42 % and negative predictive value of 92.30 % This is indicative that FNAC plays an important role in ruling out malignancy

On comparing the final histopathological report of the excised mass with mammogram ,14 cases (%) out of 40 were suspected to have malignancy while 26(%) cases were suspected to have benign lesions according to the mammogram results giving us the inference that mammogram showed sensitivity of 83.33%, specificity of 85.71%, positive predictive value of 71.42% and negative predictive value of 92.30% hence playing a better role of ruling out malignancy During triple test investigation malignant cases were found to be 11 (27.5%) and benign cases total 29 (72.5%). The comparison of MTT with biopsy showed that the sensitivity of MTT was relatively less 81.81%, specificity 93.10% and positive predictive value of 81.8% and negative predictive value of 93.10%. it can be inferred from the findings that these results comparable to histopathological findings. And it is a reliable and fairly accurate test for diagnosing breast carcinoma.

Following table shows the comparison of the accuracy of all the tests:

	Clinical examination	USG	FNAC	Mammogram	MTT
Sensitivity	90.90%	81.81%	83.33%	83.33%	81.81%
Specificity	96.55%	96.55%	85.71%	85.71%	93.10%
Positive predictive value	90.90%	81.81%	71.75%	71.42%	81.8%
Negative predictive value	96.55%	96.55%	92.30%	92.30%	93.10%

In Kameshwari Prasad study, clinical examination was compared with histopathological findings. The specificity of clinical examination was found to be 92%, sensitivity 100%, positive predictive value 88.2% and negative predictive value was 100%.

When mammography was compared with histopathological findings, sensitivity of mammography was 86.67%, specificity was 92%, positive predictive value 86% and negative predictive value was 92%.

USG comparison with histopathological findings showed the observer dependence on the sonography. The sensitivity was found to be very low compared to other techniques with only 66.67%, specificity was 100%, positive predictive value 100% and negative predictive value of 83%.

Comparison of FNAC with histopathological findings showed the sensitivity 86.67%, specificity 100%, positive predictive value 100% and negative predictive value of 92%.

These findings were found to be similar to the present study, it can be inferred from this that, USG has significant sensitivity due to which it can add to the diagnosis, it becomes an important technique where mammogram cannot differentiate the tumours from the cyst.

Study by Christina J.Wai et al	Study by P. Kameshwari prasad	Current study
Sample size: 320 Age group:19-91 years of age	Sample size:40 Age group:15 years-60 years	Sample size:40 Age group :15 years -60 years

AIM: to modify the conventionally used triple test with addition of USG and core biopsy	AIM: to assess the effectiveness of triple test in evaluating breast diseases and to find out the advantages of USG	AIM: to evaluate breast diseases by triple test with USG as 4 th component
CONCLUSION: USG and core biopsy added some diagnostic value and is not necessary to be done in all routine cases however their addition helped in establishing the diagnosis in low suspicion cases	CONCLUSION: triple test is an effective and useful tool specially in cases of breast diseases with non-palpable lumps USG helps in cases of inconclusive mammography results	CONCLUSION: USG proves to be useful in cases with clinically non palpable lump and inconclusive mammography reports while giving the advantage of lower radiation exposure over the years in case for screening purpose

CONCLUSION:

- From the study it can be concluded that modified triple test can be a very useful tool in evaluating the breast disease.
- Mammogram and USG are needed in patients where no clinically palpable lump is present and to rule out multi focal disease.
- Though ultrasonogram is an operator dependant investigation but it plays an important role in detecting breast lump where mammography is inconclusive specially in young females with dense breast tissue and also reducing the exposure to radiation during screening over the years.