

**A Study on Early Detection of Breast Carcinoma by Quadruple Assessment in a Tertiary Care Teaching Hospital**P. Aruneswari<sup>1</sup>, S. Senthil Kumar<sup>2</sup>, Prasanth M. M<sup>3</sup><sup>1</sup>Assistant Professor, Department of General Surgery, Government Medical College, Krishnagiri<sup>2</sup>Assistant Professor, Department of General Surgery, Government Medical College, Krishnagiri<sup>3</sup>Senior Resident, Department of General Surgery, Government Medical College, Krishnagiri

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**Abstract:**

**Introduction:** Breast lumps are one of the common problems encountered in women. These lumps are frequently seen in younger to middle aged women and often they go undetected for various reasons. Early recognition of malignancy plays a vital role for improving survival. The need of the hour is a system to detect malignancy earlier and minimize the time needed for the detection of malignant lumps. This study was done to determine the clinical characteristics of palpable breast lumps and with the objective of detecting malignancy earlier in patients presenting with palpable breast lumps using a quadruple assessment.

**Materials and Methods:** This is a Prospective observational study done in 50 patients was included in this study after application of inclusion and exclusion criteria. Each patient underwent a quadruple assessment comprising of a detailed Clinical examination, Ultrasonography of breast, mammogram and Fine Needle aspiration. All the patients finally underwent surgery for their condition and the results of the quadruple assessment were analyzed individually and collectively and were compared to histopathological diagnosis.

**Results and Discussion:** In our study breast, lumps were commonly seen in the age group of 31 to 40 years. Pain over the lump was an important symptom in our study the upper outer quadrant was commonly involved with tumor. When the clinical examination findings were examined as a whole clinical examination had sensitivity of 70 % and specificity of 87% for the detection of malignancy. Mammogram had a sensitivity of 95% for malignancy detection and ultrasound was found to have a sensitivity of 90% in detecting malignancy. In our study, sensitivity and specificity of FNAC to detect malignancy were 95% and 100% respectively. The sensitivity of quadruple assessment for the detection of malignancy was 65% and the specificity for the detection of malignancy was 100%.

**Conclusion:** Breast cancer is the foremost cause of cancer related death in young females; hence early detection of breast cancer carries much importance it has been shown that Ultrasound is as accurate as mammography in detection and differentiation of palpable breast lumps and it can also aid in guiding the site for FNAC and biopsy. Four components of the quadruple test complemented each other and when done with experienced clinicians and Radiologists can reduce the time lag for the detection of malignancy and help us to institute early definitive treatment.

**Keywords:** Breast Lump, FNAC, Mammogram, USG.

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**Introduction**

Breast masses are localized swellings that feel different from the surrounding breast tissue. It is a symptom/sign for a variety of conditions. As approximately 10% of breast masses ultimately lead to a diagnosis of breast cancer, it is important for women with a breast lump to receive appropriate evaluation. [1,2] In the last decades there is little increasing of knowledge and development of breast cancer management, which resulted in little decrease of mortality rates from breast cancer. [3,4]. In India, Breast carcinoma is the 2nd most common malignancy in women. Incidence increasing every

year, which ranges approximately 19- 33%. Incidence of cancer breast shows "AGE SHIFT" over the past twenty years in India that is incidence increased from 7 to 15% in the age group of 30-40 years. [5] Advanced breast cancer stage is associated with high morbidity and mortality. Hence, early-stage disease should be promptly differentiated from benign disease for proper management at the earliest with proper assessment. Early detection and treatment is a key to preventing breast cancer from spreading. A confident diagnosis can be made in 95% of the cases through a combination of clinical

examination, imaging (including mammogram and/or sonomammogram) and fine needle aspiration cytology (FNAC). Breast lump assessment should be an ordered one. So, sequential evaluation named "triple test" was formalized. This was introduced with an aim to avoid expensive potentially morbid negative biopsy and to let the clinician to proceed directly for definitive management without further investigations. Triple test proved to be a gold standard diagnostic modality in lump breast.

Clinical assessment should be the initial investigation but it is not very certain to make a clear-cut diagnosis. Hence to proceed with next diagnostic test, the Imaging study- Mammogram. In 1950, Robert Egan at the Texas University introduced Mammogram. In 1966 Philip Strax introduced mammogram as a screening procedure.

Mammography and USG breast are the standard imaging techniques for detection and evaluation of breast disease. Mammography has been the "gold standard" in breast cancer screening and detection for more than 40 years. However, mammography is known to have a certain false-negative rates. According to data from the Breast Cancer Detection Demonstration Project, the false-negative rate of mammography is about 8-10%. Possible causes for missed breast cancers include dense parenchyma obscuring a lesion, poor positioning or technique, perception error, incorrect interpretation of a suspicious finding, subtle features of malignancy, and slow growth of a lesion. [6]

USG breast is non-invasive easily available, cheaper and accurate tool in diagnosing breast masses. It is very helpful in pre surgical assessment of tumor size of even 2mm. [7] It is the method of choice for differentiating solid from the cystic lesions, for further characterizing mammographic findings and better appreciating palpable breast lesions.

With invent of FNAC entire outlook in the evaluation and management of breast lump changed, it serves as an effective tool in confirming the diagnosis. FNAC being safe, minimally invasive, painless and technically each procedure that can be carried out for assessing the entire patient with palpable breast lumps.

FNAC has a high diagnostic accuracy rate (97%) in the hands of experiencedcytopathologists.8 It helps to confirm the clinical diagnosis without open biopsy. FNAC should be practiced as a routine procedure as there is high degree of correlation with histopathologic findings.

The present study was carried out in an effort to evaluate the usefulness of quadruple assessment in early diagnosis of breast cancer including both USG and mammogram into the fold.

## Material and Methodology

This study was done as a prospective observational study at Department of General Surgery, Government Medical College Hospital, Krishnagiri for a period of one and half year. 50 consecutive patients presenting to the outpatient and Inpatient department of the Department of General surgery with complaints of a palpable breast mass willing for lump excision were included in this study. Patients with advanced disease which makes the diagnosis obvious and not willing for lump excision were excluded

The study was conducted after obtaining permission from the Institutional Ethics Committee. The patients were clearly explained about the nature of study and its implications and an informed written consent was obtained from the patients after explaining the procedure in their vernacular language.

A detailed History regarding the complaints, the mode of presentation, site of lump and associated symptoms was obtained, a complete physical examination and examination of the breast and the mass was made. Each patient underwent a modified triple test, which included a complete clinical examination, next was the ultrasound examination of the breast mass and finally Fine Needle aspiration of the breast lump was made.

Breast Examination included examination of the breast, the axilla on both sides, both supraclavicular fossa and all lymph node areas were examined to rule out generalized lymphadenopathy. Ultrasound examination of both breasts, axillary region and supraclavicular lymph nodes was also done. Mammography is a high-resolution X-ray imaging of the breast obtained by compression of the breast tissue. FNAC was done by a pathologist. All the patients had some form of surgery based on the result of the modified triple test, patients with benign lesions had excision biopsy and malignant lesions had Modified Radical Mastectomy, the surgical specimens were examined in the pathology department and the results were classified as benign or malignant.

The particulars in the pro forma were tabulated in Microsoft excel program and statistical analysis was done using SPSS software system and appropriate statistical tests were used as necessary and various parameters were analyzed and result of the modified triple test were analyzed individually and collectively, finally the result was compared to Histopathological diagnosis.

## Results

In our study of 50 patients, most common age group involved was 31-40 years, followed by 41-50 years. Coming to duration of symptoms 50 % of patients had symptom for 3-6 months, followed by

34% of patients having symptoms for less than 3 months, rest 6% of patient had symptoms for more than 6 months. There was not much difference in side affected with 27 patients had right side affected and 23 had left side affected. Pain over lump was present in 19 patients. Most common quadrant involved was upper outer quadrant in 24 patients followed by lower inner quadrant in 12 patients. Lower outer quadrant was involved in nine patients and upper inner quadrant was involved in five patients.

In our study 21 patients had maximum lump size of 2 cm, 19 patients had maximum size of 3 cm while rest had maximum size up to 5 cm. The lump was

firm in 29 patients, hard in 20 patients and cystic in one patient. Axillary node was involved in 18 patients in our study. On mammogram in our study, it was BIRADS 3 commonly seen in 24 patients followed by BIRADS 5 in 15 patients and BIRADS 4 in four patients, BIRADS 1 was seen in 1 patient and BIRADS 2 in 6 patients.

Next, we did different method of examination and investigation to identify type of lesion. On clinical examination, 32 were benign and 18 were malignant. On USG breast 29 were benign 18 were malignant and rest 3 were inconclusive. On FNAC 31 were benign and 19 were malignant. On mammogram, 31 were benign and 19 were malignant.

**Table 1: Quadruple Assessment**

Clinical Examination	No of Patients	Percentage
Benign	32	64.00%
Malignant	18	36.00%
USG Finding	No Of Patients	Percentage
Benign	29	58.00%
Malignant	18	36.00%
Inconclusive	3	6.00%
Fnac	No Of Patients	Percentage
Benign	31	62.00%
Malignant	19	38.00%
Mammogram	No Of Patients	Percentage
Benign	31	62.00%
Malignant	19	38.00%
Quadruple Assessment	No of Patients	Percentage
Benign	37	74.00%
Malignant	13	26.00%

The most common surgical method done was excision in 31 patients followed by Modified radical mastectomy in 18 patients and Incision and drainage in one patient. All specimens were sent for histopathology. Among our study group 30 were benign and 20 were malignant lesions. Among 20 malignant cases, six had pain over lump. Fourteen

patients had axillary node involvement. Coming to final diagnosis, among malignant lesion 17 were infra ductal carcinoma, two were intrapapillary carcinoma and one was ductal carcinoma in situ. Among benign Fibroadenoma was more common followed by benign phylloides and fibrocystic disease.

**Table 2: Type of lesion**

Malignant	Number	% Age (N = 50)	% Age (N = 20)
Infra Ductal Ca	17	34.00%	85.00%
Ductal Ca In Situ	1	2.00%	5.00%
Intra Papillary Ca	2	4.00%	10.00%
Benign(N=30)	Number	% Age (N = 50)	%Age (N = 30)
Fibroadenoma	17	34.00%	56.00%
Breast Abcess	1	2.00%	6.00%
Benign Phylloides	7	14.00%	22.00%
Fibrocystic Disease	3	6.00%	10.00%
Lactating Adenoma	1	2.00%	3.00%
Lipoma	1	2.00%	3.00%

Among 20 patients with malignant findings on HPE, when we compared with clinical examination it was positive finding only in 14 patients. 18 patients among 20 malignant had positive findings in USG. 19 patients among 20 malignant had positive findings in FNAC. 19 patients among 20 malignant had positive findings in mammogram. As a whole based on quadruple assessment 13 had positive findings among 20 malignant patients. Based on above results sensitivity and specificity was derived as in below table 3.

**Table 3: Comparison of all methods**

	C/E	USG	FNAC	Mammogram	Quadruple
Sensitivity	70.00%	90.00%	95.00%	95.00%	65.00%
Specificity	87%	100%	100%	100%	100%
Positive Predictive Value	78%	100%	100%	100%	100%
Negative Predictive Value	81.25%	93.75%	96.77%	96.77%	81.08%
Accuracy	80%	96%	98%	98%	86%

### Discussion

Breast lumps are one of the commonest findings in women attending surgical clinics, presence of a lump invokes a sense of fear and insecurity among these women and all the lumps are believed to be malignant, since breast malignancy is very much amenable to curative treatment when detected early, so it becomes essential that malignancy is detected at earlier stages to allay fear and institute early treatment. Multimodal investigations are therefore used for the preoperative detection of malignancy. [9]

Of these tests the Quadruple assessment consisting of Clinical examination, USG, Mammography and Fine needle aspiration cytology has been used with fairly accurate results and has been evaluated in our study. The primary aim of this quadruple assessment is to make an accurate preoperative diagnosis, thereby avoiding unnecessary surgeries in case of a benign breast lump.

Our study tries to evaluate the efficiency of the quadruple assessment (i.e. Clinical Breast examination, Ultrasound of breast, Mammogram and FNAC) as isolated tests and as a combination for the detection of malignancy, in this study Histopathological examination of the breast lump was used as the reference standard for comparison.

In a retrospective study done by Gobler et al 207 patients with palpable breast masses were examined and it was concluded that if the result of combined evaluation consisting of a triple test of clinical examination, mammography and cytology were concordant, a diagnostic accuracy was 100 % and with discordant results 75% of masses were malignant. Gobler arrived at a conclusion that preliminary surgical biopsy and frozen section of the lesion may not be all that necessary when the triple test unequivocally identifies malignancy. [10]

In a systematic review of 15 studies in which the triple test was used for the diagnosis of palpable breast lumps, a combination of the three tests is consistently more sensitive than a single test, and the capability of identifying malignancy approaches 95 to 100 % when at least one component of the triple test is positive. When all the components of the triple test are in agreement, the probability that the diagnosis is right is approximately 99% whether it is positive or negative diagnosis. [11] Jin Young Kwak, et al in a 2006 study investigated the appli-

cation of the Breast Imaging Reporting and Data System Final Assessment System in Sonography of Palpable Breast Lesions and Reconsideration of the Modified Triple Test in this study they followed up 160 palpable breast lesions and subjected the lesions to palpation-guided FNAC, targeted sonography, and then histopathologic confirmation was done. It was shown in this study that Ultrasonography of breast was as accurate as palpation guided Fine needle aspiration for not missing the diagnosis of malignancy.[12]

A large multicenter study supported by the Avon Foundation and the National Institutes of Health was created through the American College of Radiology Imaging Network. In this project, a protocol to assess the efficacy of screening breast ultrasound was implemented in 14 imaging centers to better define the role of US in breast cancer screening. The study reported higher cancer detection in high-risk women that underwent annual ultrasound screening in addition to mammography compared to those that underwent mammography alone. [13]

In the light of the above information, we discuss the results of our study, our study was an observational study and 50 patients were subjected to the study. In our study breast lumps were commonly seen in the age group of 31 to 40 years (62%) and least commonly seen after the age of 60 years, this is similar to the distribution seen in other studies. Younger aged women have more education standards and awareness that lead them to present earlier in the course of disease. About 50% of all the patients had symptoms for 4 to 6 months which was similar to that seen in few studies but some studies reported shorter duration of symptoms of mean of 3 months (Afsar A Bhatti et al 2010). [14]

The maximum lump size in our study was most commonly 2 cm (42%) followed by 3 cm (38%) and 29 had firm consistence while 20 had hard consistency suspecting malignancy. In our study 31 patients underwent excision, 18 underwent modified radical mastectomy and one patient of breast abscess required incision and drainage. Histopathological examination confirmed 20 to be malignant and 30 to be benign, among malignant infraductal carcinoma was commonest presentation (34%) while in benign fibroadenoma was most common (n=17) followed by benign phylloides (14%), 3 patients had fibrocystic disease. Pain over the lump was an important symptom and 31% of patients

with painless lumps had malignancy on histopathological examination (30 out of 50) in contrast to 15 % of the patients with painful breast lumps (6 out of 19). Similar findings were also seen in a study conducted by Kaire innos et al (BMC public health 2013) and the usual mode of presentation of malignancy was a painless palpable lump. [15]

In our study the upper outer quadrant was commonly involved with tumor (45.6%) this was also consistent with the findings with a study done by Khemka et al., Hussain et al., and Khoda et al (JMS 2015). It has been demonstrated that the upper outer quadrant of the breast has more amount of epithelial tissue compared to other quadrants leading to more incidence of tumors. [16-18]

Axillary lymph node involvement was seen in 36 % (18 out of 50) of patients presenting with breast lumps and out of the patients who had axillary nodes 77%(14 out of 18) had biopsy proven malignancy, so axillary node involvement is a strong predictor that the tumor is malignant, this has also been recorded by Voss M et al. It has been concluded in the study that patients with stage 3 breast cancer have a higher incidence of axillary metastasis and well differentiated tumors tend to metastasize slowly. So axillary involvement may be a pointer towards advanced or fast-growing malignancy and should prompt immediate attention. [19]

When the clinical examination findings were examined as a whole clinical examination had sensitivity of 70% and specificity of 87% for the detection of malignancy. Positive predictive value of Clinical examination was 78% and Negative predictive value was 81.25%.

On analysis of various studies, it has been shown that sensitivity of the Clinical breast examination ranges from 21% to as high as 100% and the specificity ranges from 50% to 97.8%. In the present study, the high sensitivity could be because only patients with confirmed palpable lumps were included for the study. Our results are in concordance with many studies. [14]

### **Mammogram**

In our study BIRADS was evaluated and BIRADS 3(48%) was most common followed by BIADS 5 (30%), 3 cases were benign and 19 were suspected for malignancy. The quadruple assessment used mammography as one of its components and mammogram had a sensitivity of 95% for malignancy detection. Crystal et al (2003), Susan k et al (2005), Corsetti et al (2006) and Sahiner et al (2007) had supported the use of mammogram in young patients with dense breast tissues and it was found to have a sensitivity of 89% in detecting symptomatic and palpable breast abnormalities. [20-23] Though relatively a fresh modality mam-

mogram has gained widespread popularity due to easy availability of the equipment, it is less expensive and is non-invasive and can provide accurate information in tumors more than 2mm. Both USG and mammography have their inherent advantages and disadvantages that have been discussed in literature.

In our study 19 out of 50 patients had ultrasound findings suggestive of malignancy; out of them all had biopsy proven malignancy. Mammogram had a sensitivity of 95% and specificity of 100% for the detection of malignancy, Positive predictive value for detection of malignancy was 100%, Negative predictive value to rule out malignancy was 96.77%.

These findings when compared to available literature shows good correlation and, in a study, done by Khoda et al, mammogram sensitivity was 91.6%, specificity was 100%, positive predictive value was 100%, negative predictive value was 97.3%. [18]

### **Ultrasonography of Breast**

In our study 18 out of 50 patients had ultrasound findings suggestive of malignancy; out of them all had biopsy proven malignancy. Mammogram had a sensitivity of 90% and specificity of 100% for the detection of malignancy, Positive predictive value for detection of malignancy was 100%, Negative predictive value to rule out malignancy was 93.75%. Similarly in a study done by Pande et al sensitivity, specificity, positive predictive value and negative predictive value for ultrasonography were 95%, 94.1%, 95.5%, and 93.7%, respectively. Another study by Jan et al also yielded similar results. [24]

A sensitivity of 90 % means 10 malignant lesions would be missed out of 100 malignant lesions, so the diagnosis of a benign lump always does not mean that it is benign and it would need a combination of tests to confirm it, but nonetheless USG of the breast is a valuable and easy tool for the detection of malignancy.

### **Fine Needle Aspiration Cytology**

In our study Fine Needle aspiration classified, 31 patients out of 50 (62%) as having benign breast disease, whereas 19 patients (38%) were diagnosed to have malignant disease. All patients with FNAC report suggestive of malignancy were biopsy proven to have carcinoma. But 1 out of 60 patients (1.6%) who were reported to have benign disease had malignant disease.

Sensitivity and specificity of Fine Needle Aspiration Cytology to detect malignancy were 95% and 100% respectively. Positive predictive value was 100% and Negative predictive value was 96.77%.

**Table 4: FNAC Results in Various Studies [25-29]**

Study	Sensitivity %	Specificity%	PPV	NPV
Our study	95	100	100	96.77
Sankaya & Dongre	88.37	96.42	97.43	84.37
Choi et al	77.70	99.20	97.43	84.37
Mohammed et al	90.62	100	100	95.08
Kim et al	94.59	87.91	79.54	97.03
Park and Ham	76.90	91.60	-	-

It is shown that the results of our study are comparable to various studies and the values closely resemble the results seen by Mohamed et al. So the results indicate that FNAC as an independent variable has adequate diagnostic power and this is further enhanced by combination with other 2 tests.

### The Quadrapule Assessment

Using quadruple assessment 13 patients (26%) had features suggestive of malignant disease and 37 patients (74%) were suspected to have benign

breast disease. All of the 13 patients suspected to have malignancy on Quadrapule assessment were biopsy proven to have malignant breast disease, whereas 7 out of 37 patients assigned to have benign disease on quadruple assessment turned out to be malignant. The sensitivity of quadruple assessment for the detection of malignancy was 65% and the specificity for the detection of malignancy was 100%. The positive predictive value of the Modified triple test was 100% and the Negative predictive value was 81.08%.

**Table 5: Comparison of Studies Using quadruple assessment**

Study	Sensitivity %	Specificity%	PPV	NPV
Our study	65	100	100	81.08
Shreastha et al [30]	73.7	96.3	95	78.9

This comparison shows that our results were comparable to the results seen in many studies and it has shown that the quadruple assessment can be used as a valuable clinical test for the detection of malignant lumps and it helps us to plan the surgical treatment earlier, accurately and helps us save time needed for a definitive diagnosis.

### Conclusion

Breast cancer is the foremost cause of cancer related death in young females; hence early detection of breast cancer carries much importance. The quadruple assessment in our study was an accurate predictor of malignancy, all of the patients who were suspected to have malignancy by our assessment had malignancy on histological analysis and specificity was 100%, that proved it as a best initial test for diagnosis of malignancy preoperatively. Of the four components of the FNAC, mammogram and Ultrasound of breast had 100% specificity for the diagnosis of malignant lumps. So it is a suitable diagnostic modality for breast lumps in young women of childbearing age. It has been shown that Ultrasound is as accurate as mammography in detection and differentiation of palpable breast lumps and it can also aid in guiding the site for FNAC and biopsy

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