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Assessment of the Modified Triple Test for Palpable Breast Masses: The Value of Ultrasound and Core Needle Biopsy

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Abstract: Background: Breast cancer is the most frequent cause of cancer death among women worldwide.. Early detection is very important with great impact on outcome. Newly developed modifications have been done to the original triple test (FNAC, Mammography & clinical assessment) to include ultrasound (US) and core biopsy to determine their role in evaluating palpable breast masses. **Methods**: A prospective study done on fifty female patients aged between 18 and 55 years old complaining of clinically palpable breast lump selected from Al Menoufia University Hospital Surgery Clinic and subjected to both the triple score test using FNAC and modified triple score (mTTS) using core biopsy according to the protocol of work up. **Results**: All pathological results for all patients who underwent operations were identical to that obtained from the core biopsy confirming its accuracy and sensetivity. As regard the comparison between FNAC and final post-operative pathology there was no significance but the most important is that there are four cases proved to be carcinoma in situ however FNAC showed that they were atypical cells. **Conclusions:** We found that the Core Needle biopsy is superior to FNAC with identical results to the postoperative excisional biopsy pathological results Nevertheless, FNBC still a very useful, cheap, rapid, effective diagnostic tool that cannot be neglected or condoned especially in straightforward cases and in experienced hands. MTTS proved to be useful and comparable and even superior to the conventional TTS without hazard of radiation, in diagnosing breast masses.

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Keywords: breast, cancer, modified triple test, original triple test, core biopsy, and mammogram.

1. Introduction:

Breast cancer is the second leading cause of cancer deaths among women. [(1)]. Breast cancer has a complicated etiology that includes genetic, biological, behavioral, environmental and social factors. Factors known to increase a woman's chance of developing it include age , family history, previous radiotherapy to the chest wall, certain breast conditions (such as lobular neoplasia and multiple papillomatosis), early menarche, late menopause, later age at first full-term pregnancy and nulliparity. [(2)].

Since the first mastectomy which was carried out by Halsted in 1882, surgeons have faced several problems such as skin flaps necrosis, wound breakdown, seroma, infection, nerve injuries, lymphedema, phantom breast syndrome and hematoma.(3).

From the total female cancer cases in Egypt, breast cancer represented 35.1%.The primary site of lymphatic drainage of the breast is the axillary lymph nodes that involved in regional metastatic disease in breast cancer. Axillary lymph node dissection is the standard treatment of axillary lymph node.(4).

Women can reduce their risk of breast cancer by maintaining a healthy weight, reducing alcohol use, increasing physical activity, and breast-feeding [(5)] High levels of physical activity reduce the risk of breast cancer by about 14% [(5)].

Breast cancer is often first detected as an abnormality on a mammogram before it is felt by the patient or healthcare provider. Mammographic features suggestive of malignancy include asymmetry, micro-calcifications, and a mass or architectural distortion. If any of these features are identified, diagnostic mammography along with breast ultrasonography should be performed before a biopsy is obtained. In certain cases, breast magnetic resonance imaging (MRI) may be warranted. [(6)]. Breast cancer evaluation should be an ordered inquiry that begins with symptoms and a general clinical history. This is followed by a sequence that has become formalized as triple assessment, which includes the following components: clinical examination, imaging (usually mammography, ultrasonography, or both) and needle biopsy [(7)]. Breast cancers are classified by several grading systems. The

original triple test score (TTS) clinical examination, mammogram, and fine-needle aspiration (FNA) biopsy has long been used to evaluate palpable breast masses. Another modification has been done to the original TTS to include ultrasound (US) and core biopsy to determine their role in evaluating palpable breast masses. [8]

Each of these influences the prognosis and can affect treatment response. [9]. The aim of the study is to assess the result of the modified triple test for palpable breast masses that aiming at adding the value of ultrasound and core needle biopsy compared to the original triple test, which includes clinical examination, mammogram, and fine needle aspiration biopsy for early detection and management of breast cancer.

2. Patients and methods:

This prospective study made on fifty patient aged between 18 and 55 years old complaining of a suspected breast lump during the period from May 2014 till December 2019 . Patients selected from Al Menoufia University Hospital Surgery Clinic. The regular sheet filled for all the patients. After fulfilling the medical history and clinical examinations of both breasts and axillae to exclude any hidden medical problems for any breast lesions include (mass, size, site, tenderness, indurations, discharge, redness, or any other abnormalities). Then the patients were subjected to the protocol of work up where all the 50 patients were subjected to original triple test (clinical assessment, mammography and FNAC) group A and the same 50 patients subjected to the modified triple test by adding the ultrasound and core needle biopsy group B after taking their consent and approval of the institutional ethical committee. Then the results of comparison were tabulated.

Excluding patients with a diagnosed breast cancer, females with inflammatory conditions of breast and females with a previous history of operation on the same side of breast.

Statistical analysis:

Data were collected, coded, revised and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The data were presented as number and percentages for the qualitative data, mean, standard deviations and ranges for the quantitative data with parametric distribution and median with inter quartile range (IQR) for the quantitative data with non-parametric distribution. Chi-square test was used in the comparison between two groups with qualitative data and Fisher exact test was used instead of the Chi-square test when the expected count in any cell found less than 5.Independent t-test was used in the comparison between two groups with quantitative data and parametric distribution and Mann-Whitney test was used in the comparison between two groups with quantitative data and non-parametric distribution.

3. Results:

The total number of the patients is 50 after clinical examinations all of them were subjected to mammography and FNAC then to core needle biopsy and ultrasound in order to compare results accurately so we divided them to category A (FNAC & Mammogram) & B (core biopsy & US) with 50 patients each.

As regard to demographic data, our study showed that 42% were between 36 to 50 years and 22% were between 51 to 65 years **(Table 1)**.

Table (1): Distribution of age groups in studied patients

Age (year)	No. of patients (No.=50)	(%)
≤20	3	6.0%
21-35	5	10.0%
36-50	21	42.0%
51-65	11	22.0%
> 65	10	20.0%

The most common period for breast cancer was between 36-50 years (table 1)

Table (2): Descriptive data of patient comorbidities

Co morbidities	No. of patients (No.=50)	(%)
Normal	31	62%
Diabetes mellitus	13	26.0%
Hypertension	14	28.0%
Ischemic heart disease	5	10.0%

According to the most co morbidities help in developing breast lump, (Table 2) showed that 62% were normal, 28% were hypertensive, 26% were diabetic and 10% were with ischemic heart disease.

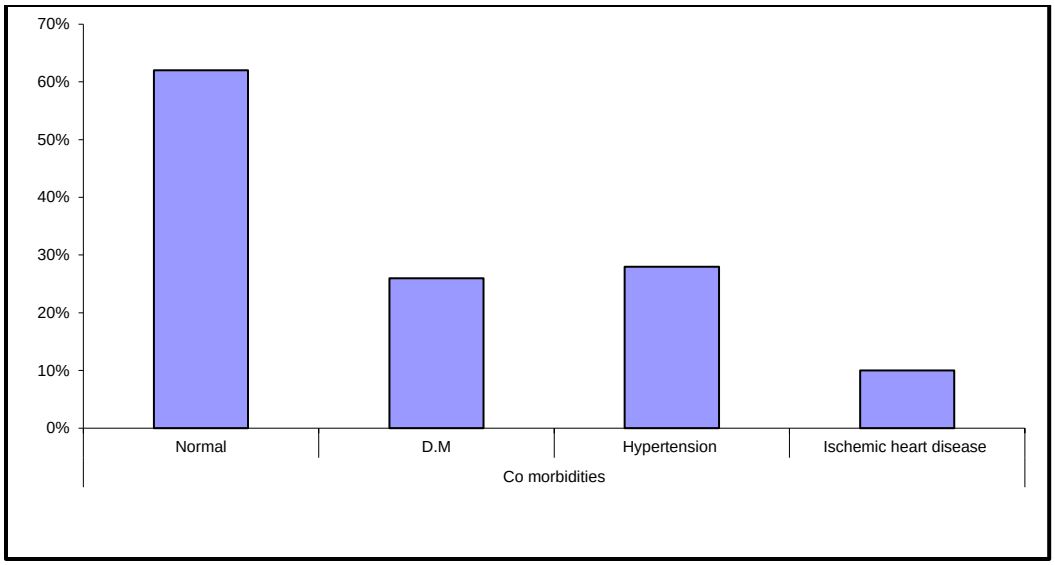

Figure (1): Co-morbidities

Table (3): Descriptive data of side and site of complaint

		No. of patients(No.=50)	(%)
Side of complaint	**Left side**	24	48.0%
	Right side	23	46.0%
	Screening without specific side	3	6.0%
Site of complaint	**LIQ**	11	22.0%
	UOQ	36	72.0%
	UIQ	0	0
	LOQ	0	0
	Screening without specific side	3	6.0%

As regard to the site and size of complaint, upper outer quadrant in the left side is the commonest as seen in (Table 3)

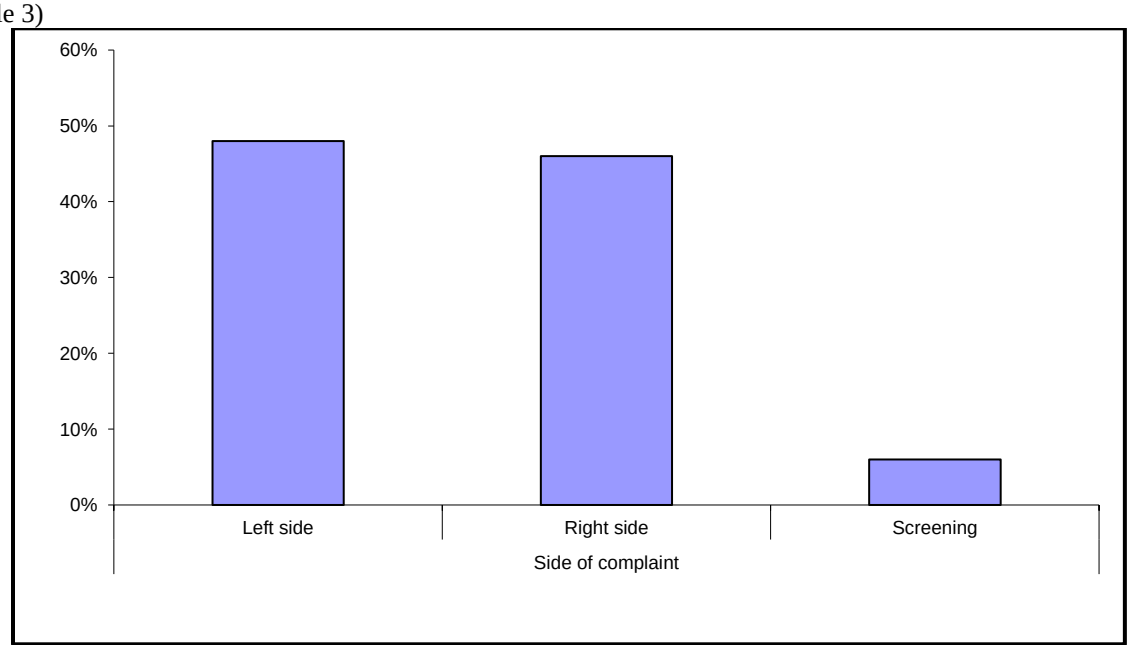

Figure (2): Side compliant

Table (4): Descriptive data of radiological assessment

Radiological assessment		**No**	**%**
Mammography results	**Benign**	15	30.0%
	Calcification (macro)	7	14.0%
	Small lesion	3	6.0%
	Speculation	25	50.0%
Micro Calcification	**No**	37	74.0%
	Yes	13	26.0%

In mammography, 50% which are the highest percentage showed speculation and 74% with no micro-calcifications as shown in (Table 4)

Table (5**):** Descriptive data of ultrasound

		No	**%**
Ultrasound	**Nonspecific L.N**	24	48.0%
	N0	11	22.0%
	N1	11	22.0%
	N2	1	2.0%
	NAD	3	6.0%

In ultrasound , 48 % showed no specific lymph node as seen in (table 6)

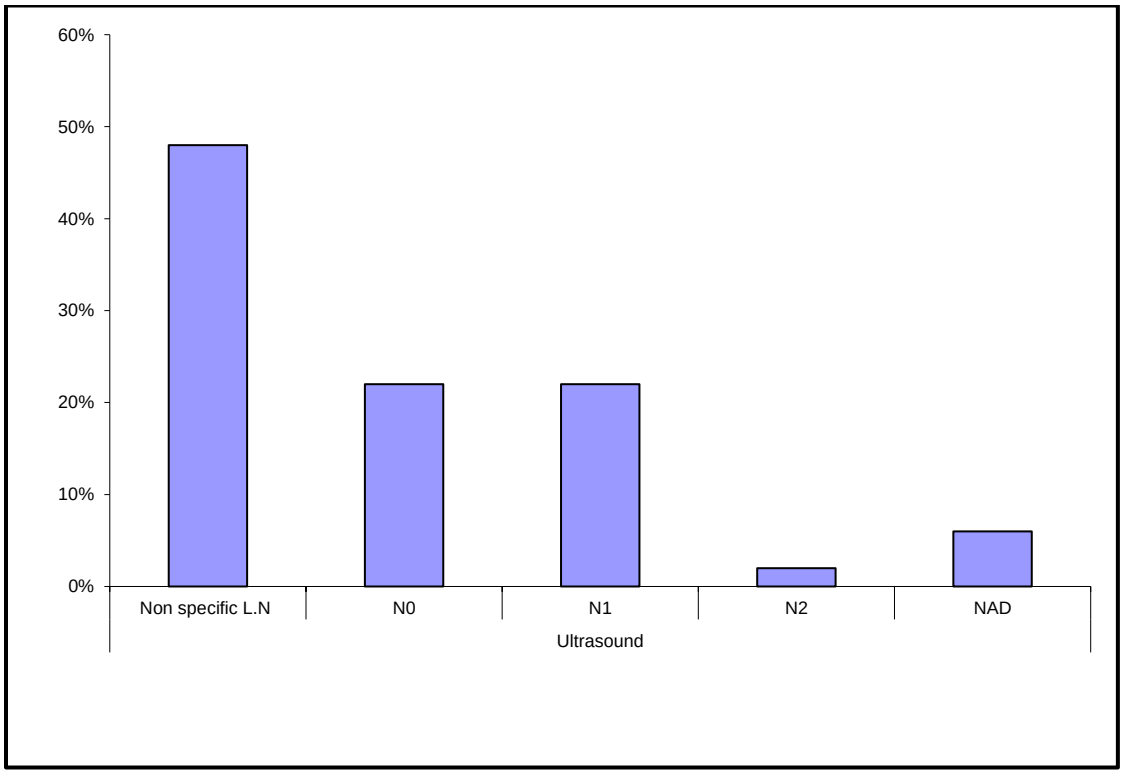

Figure (3): Ultrasound

Table (6): Comparison between care biopsy and FNAC

	Core biopsy (No.50)		**FNAC(No.50)**		**Chi square test**	
	No	**%**	**No**	**%**	**X^2**	**P value**
FA (Fibro-adenoma)	15	30.0%	15	30.0%	0.000	1.000
IDC (Invasive ductal carcinoma)	31	62.0%	31	62.0%	0.000	1.000
DCIS (Ductal carcinoma in situ)	3	6.0%	0	0.0%	3.093	0.078
LCIS (Lobular carcinoma in situ)	1	2.0%	0	0.0%	1.01	0.314
Atypical cells	0	0.0%	4	8.0%	4.167	0.041**(S)**

As regard to the comparison between core biopsy and FNAC, there was statistically significant increase in atypical cells. This show that the core biopsy had reached a confirmed final diagnosis at the time where the FNABC was still non conclusive.

Table (7): comparison between core biopsy and final postoperative biopsy as regard pathology:

	Core biopsy (No.50)		Final post operative biopsy (No.37)		Chi square test	
	No	%	No	%	X^2	P value
Fibro-adenoma (FA) (with operation done)	2	30.0%	2	5.4%	0.00	1.000
Fibro-adenoma FA (with no operation done follow up only)	13	26%	0	00.0%	14.943	0.001
Invasive ductal carcinoma (IDC)	31	62.0%	31	62.0%	0.000	1.000
Ductal carcinoma in situ (DCIS)	3	6.0%	3	6.0%	0.000	1.000
LCIS (Lobular carcinoma in situ)	1	2.0%	1	2.0%	0.000	1.000

This table shows that all pathological results for all patients who underwent operations were identical to that obtained from the core biopsy confirming its accuracy and sensitivity.

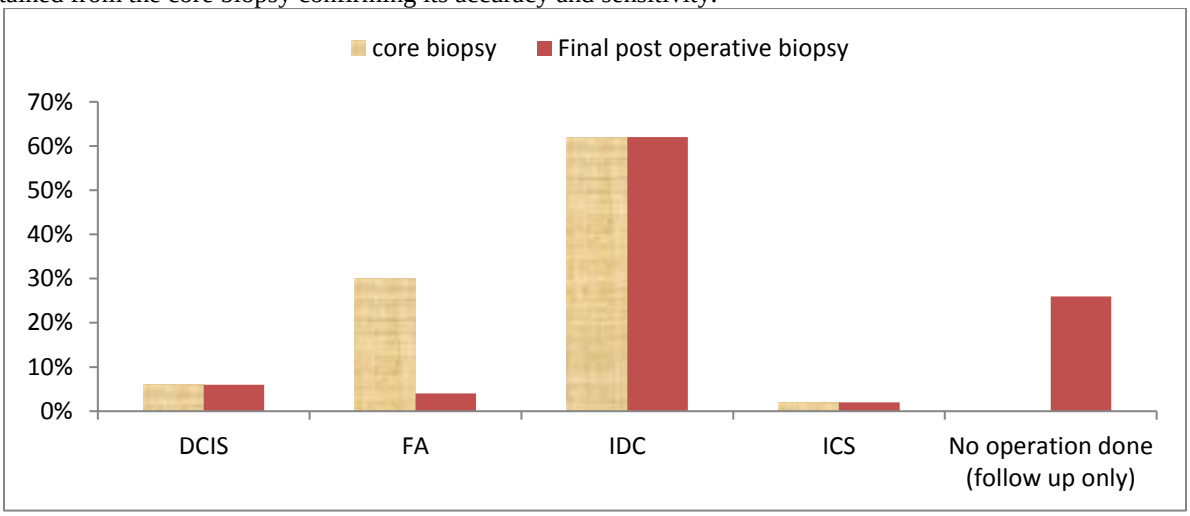

Figure (6): Comparison between core biopsy and final post operation biopsy

Table (8): Comparison between FNAC and final post operation biopsy

	FNAC(No.50)		Final post operative biopsy (No.37)		Chi square test	
	No	%	No	%	X^2	P value
Fibroadenoma FA (with operation done)	2	30.0%	2	5.4%	0.00	1.000
FA (with no operation done follow up only)	13	26%	0	00.0%	14.943	0.001
Invasive ductal carcinoma (IDC)	31	62.0%	31	62.0%	0.000	1.000
Ductal carcinoma in situ (DCIS)	0	0.0%	3	6.0%	3.093	0.078
LCIS (Lobular carcinoma in situ)	0	0.0%	1	2.0%	1.01	0.314
Atypical cells	4	8.0%	0	0.0%	4.167	0.041**(S)**

As regard the comparison between FNAC and final post-operative pathology there was no significance but the most important is that there are four cases proved to be carcinoma in situ however FNAC didn't prove that apart from atypical cells while the core biopsy proved that the 4 patients (8% of cases) pathology was carcinoma in situ which elevates the degree of accuracy of core biopsy over FNAC

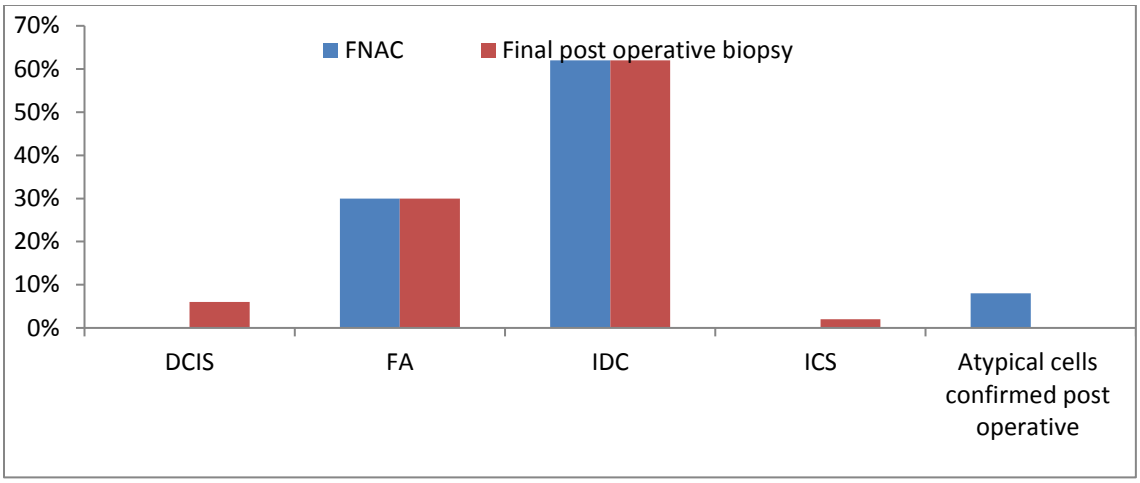

Figure (6): Comparison between core biopsy and final post operation biopsy.

4. Discussion:

The breast cancer has a high incidence and mortality rate worldwide [(16).] The employment of multimodality tests preoperatively for diagnosis helps in differentiating benign from malignant lesions. The primary goal of the triple test is to make the correct preoperative diagnosis, avoiding open biopsy in case of a benign breast lump.[(9)]. A single-modality test is not accurate enough to make the correct diagnosis for a breast lesion. However, the accuracy of the diagnosis can be increased by employing multimodality tests. A number of modalities together are more accurate and reliable compared to a single-modality test, despite having their own technical limitations.[(9)]

In comparison with other studies as **Wai et al[(8)]** who concluded that US and/or core biopsy added little to the accuracy or predictive value of the original TTS and **Kerlikowske et al [(9)]** who concluded that Women whose screening mammography results are interpreted as "suspicious abnormality" or "highly suggestive of malignancy" have a high risk for breast cancer and should undergo core-needle biopsy or needle localization with surgical biopsy. **Graf et al[(7)]** who concluded that the data strongly suggest that palpable noncalcified solid breast masses with benign morphology at mammography and US can be managed similarly to non-palpable BI-RADS category 3 lesions, with short-term follow-up (6-month intervals for 2 years)..Our study showed that the modified triple test is of agreat value in screening of breast cancer in early diagnosis and screening proved by detection of carcinoma in situ which couldn't be detected by usual FNAC incorporated in the original test. In addition to the value of detection of early changes developed to an old benign lesion by ultrasound through BIRAD classification rather than mammography signs that appear later at the sequel of the disease progression that may affect the proper time in early detection of the disease.

As regard age, our study revealed that the most common age of breast cancer was between (36-50) years that represented 42% followed by the group between (51-65) years that represented 22%. In accordance with our study, **Bhatta et al [(10)]** study revealed that carcinoma was most commonly diagnosed in the age group of 40-49 years in female patients (40%) followed by in the group of 30-39 and 50-59 years (21.5% each). In a study by **Thapa et al [(11)]** out of the 944 female breast cancer patients, 263 (27.9%) were <40 years6. The mean age was 34.6 ± 5.0 years among younger patients compared to 54.1 ± 9.9 for those ≥ 40 years which is in line with our study results.

28% of patients were hypertensive, 26% were diabetic and 62% were normal. Being the same patients there was no statistically significant difference in co-morbidities regarding studied group. For site and side of complaint, this study showed that 48% were left side, 6% were screening, 22% were LIQ and 72% were UOQ.

There was statistically significant increase in the number of lesions in comparison to with site of complaint (UOQ) but there was no statistically significant difference in side of compliant. Similar observations were made by **Khemka et al. [(1)]** and **Hussain et al. [(12)],** in their studies the majority of breast lumps were found in the upper outer quadrant. The relative higher occurrence of breast lump in the upper outer quadrant of breast compared to the other quadrants is because much of the epithelial tissue of breast is present in this quadrant

Bhatta et al [(10)] in his study showed that the most common site for breast mass was upper outer quadrant like our study results.

Aljarrah et al [(13)] in his study stated that breast

cancer occurs almost equally in the right and left breast nearly like our results where we found it in left side in 48% and right side in 46% and bilateral for screening in 6% and he documented also that the most commonly affected the upper outer quadrant (UOQ) telling that among all 65 patients in his study, 42 patients i.e. 64.6% presented with breast mass in upper outer quadrant of the breast followed by retroareolar area (12.3%) that matched our study. **Deen et al** (14) in their study had found that 46.12% of patients in whom upper outer quadrant was involved in breast cancer. The larger mass of breast tissue in the upper outer quadrant is responsible for the commonest occurrence at this location.

As regard as radiological assessment, 30% were benign, 50% were speculation and 26% were calcification .There was statistically significant increase in group A (FNAC & Mammogram) in comparison to group B (core biopsy&US) with mammography (speculation) but there was no statistically significant difference in calcification.

In our study, we found that post operation pathology 6% were DCIS, 4% were FA and 62.0% were IDC. There was statistically significant increase in group A in comparison to group B with radiological ultrasound.

Excision biopsy is considered to be the gold standard for the diagnosis of breast lump. Emphasis has been placed now-a-days on improving method for establishing a definitive diagnosis of breast mass prior to surgery. This study reflects the comparability between Fine Needle Aspiration Cytology and Core Needle Biopsy in the diagnosis of breast carcinoma considering the histological diagnosis from excision specimen being gold standard. In our study, total 50 patients were included. We found that the Core Needle biopsy is superior to FNAC with identical results to the postoperative excisional **biopsy** pathological results. We found that whereas FNAC failed to reach final conclusion to 8% of cases describing them as atypical cells the core needle biopsy reached final diagnosis as 6% DCIS and 2% LCIS with complete identical match to the post-operative excisional biopsy pathological result. This show that the core biopsy had reached a confirmed final diagnosis at the time the FNABC was still non conclusive. Unlike our results few studies like **Koccay et al** [16] and **Tothova et al** [16] showed that the diagnosis of ductal carcinoma in situ (DCIS) is difficult with core biopsies. Whereas most of the studies that have been conducted to compare the role of FNAC and other histological investigations like Core Needle reached conclusions very compatible with our results. For example, **Pieter et al** [17] study first published April 2001 which include 286 breast lesions (cysts and micro-calcifications without a soft tissue mass excluded), both ultrasound-guided FNAC and CNB were performed in the same session by the same operator. Histologic follow-up was collected, and for those lesions that were not excised the results of the most recent mammography was used. A combination of the findings of both FNAC and CNB were evaluated. For the lesions selected in this study, FNAC and CNB are comparable for most parameters, but CNB has a higher specificity and lower suspicious rate. Also **Karol et al** [18] study published in 2012 including 4326 mammotomic biopsies performed at their institution in 2000–2006, ADH (atypical ductal hyperplasia) was diagnosed in 134 patients (3.1%) which done by core biopsy that could not be clarified by FNAC like our study with emphasis that all histo-pathological blocks were reviewed by the same pathologist then patients underwent surgery to remove the suspected lesion.

Kocaay et al., [15] recorded his Data that were collected from 123 women who have suspicious palpable breast masses from 2007 to 2010 and concluded that Sensitivity and specificity showed that in the case of true histopathologic classification, core biopsy is superior to FNAC. Nevertheless, he concluded also that FNAC's role as a fast, simple and cheap diagnosis cannot be ignored. It is an effective diagnostic tool in most patients, in comparison to the correct and specific typing of core biopsies in benign lesions which protect patients from the open biopsy and this was in line with our study results and our point of view. Whereas **Ibikunle et al** [19] documented that breast FNACs compare very well with excisional biopsies histology and are extremely useful in managing breast lumps conditioned by doing it by experienced hands. He concluded that FNAC is a reliable breast lump diagnostic tool and advise that clinicians should continue to promote this diagnostic approach in the surgical management of breast lumps as a fast and cheap diagnostic tool, as highlighted by previous studies.

Conclusion:

We found that the Core Needle biopsy is superior to FNAC with identical results to the postoperative excisional biopsy pathological results Nevertheless, FNBC still a very useful, cheap, rapid, effective diagnostic tool that cannot be neglected or condoned especially in straightforward cases and in experienced hands. Also both core biopsy and FNAC provides safe noninvasive reliable tools protecting the patients from open biopsy especially the core biopsy mainly in doubtful cases with results nearly identical to the open biopsy.

MTTS proved to be useful and comparable and even superior to the conventional TTS without hazard of radiation, in diagnosing breast masses.

Recommendation: conduct the study on a large

sample size to get more confirmation about the accuracy of triple test.

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