The Value of Triple Assessment of Breast Masses in Comparison to Histopathological Diagnosis in a Sample of Female Patients in Wasit Provinc

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ABSTRACT:

BACKGROUND:

One of the most prevalent presentations in outpatient clinics is a breast lump. A palpable mass in a woman's breast could be benign or cancerous, and it needs to be evaluated very well. The triple evaluation approach, which combines clinical examination, radiological imaging, and fine needle aspiration cytology, was used to diagnose the nature of a breast mass. The gold standard for confirming a diagnosis is still an open biopsy.

OBJECTIVE:

To evaluate the role of the triple assessment (a combination of clinical examination, ultrasonic examination, and Fine needle aspiration cytology) in the diagnosis of breast lumps and its correlation with histopathological diagnosis.

MATERIALS AND METHODS:

A Cross-sectional study including 60 females patients was collected from Al-Karama Teaching hospital and private histopathology laboratory in Wasit Province to include cases referred from 1st January 2019-1st April 2021. The results of fine needle aspiration cytology, clinical examination, and ultrasound were compared to those of histopathology to assess the diagnostic accuracy of them.

RESULTS:

This study included 60 women with breast lesions. The results of this study shows that 36 (60%) of cases were approved as having breast cancer and 24 cases (40%) were approved as benign breast lesions. Twenty five women (41.7%) were aged 40-49 years. There were 22(36.7%) women presented with regular mobile soft mass, 12(20%) women with irregular immobile hard mass. Forty six percent of all women (28 cases) were presented with breast lesion located at upper outer quadrant.

The validity of clinical diagnosis according to the gold standard histopathology in diagnosing breast masses found to be 68.3%, the sensitivity and specificity of clinical diagnosis for detecting breast masses according to the gold standard histopathology were52.8%, 91.7%respectively.

Validity of Ultrasound test according to the gold standard histopathology in diagnosing breast masses found to be 86.7%, 80.6% sensitivity, 95.8% specificity.

Validity of FNAC according to the gold standard histopathology found to be 93.3%.

91.7% sensitivity, 95.8% specificity, only 3 cases was false negative.

Validity of triple assessment according to the gold standard histopathology found to be 97.4%, 94.1% sensitivity, 100% specificity.

CONCLUSION:

The most accurate of the three components of the triple test (clinical assessment, ultrasonography examination, and fine needle aspiration cytology) is fine needle aspiration cytology. The triple modalities are more accurate when used together than when used separately.

KEYWORDS: clinical examination, ultrasound, Fine needle aspiration cytology, Histopathology, breast masses.

INTRODUCTION:

One of the most prevalent presentations in outpatient clinics is a breast mass[1]. It's possible that a palpable tumor in a woman's breast either benign or malignant, and it requires thorough examination[2]. Breast carcinoma is the most common cancer in women around the world, and it is also the main cause of cancer death among

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women [3]. The nature of a breast lump was determined using the triple evaluation process, which includes clinical examination, radiological imaging, and fine needle aspiration cytology, for the conclusive diagnosis of a breast lumps, histological diagnosis remains the gold standard procedure [4]. Breast lumps with well-defined margins, soft, spherical and movable, and associated with pain and nipple secretion are the most typical clinical presentation of benign breast disorders. Breast cancer is characterized by a painless lump that is firm, fixed, and irregularly shaped, as well as dimpling of the breast surface, nipple retraction and bloody nipple discharge, and enlarged axillary lymph nodes[5]. Breast ultrasonography is a valuable examination tool that is mostly used in younger women under 40 years old, Mammography is advised for women over the age of 40 years who have a less dense breast [6]. FNAC is frequently used to assess palpable breast tumors, cysts, and even non-palpable mammographic abnormalities. When compared to histopathology diagnosis from core needle or open biopsy tissues, it is far less invasive, easier, faster, and less expensive[7]. Hence, our aim is to evaluate the role of the triple assessment (a combination of clinical examination, ultrasonic examination, and Fine needle aspiration cytology) in the diagnosis of breast lumps and its correlation with histopathological diagnosis.

SUBJECTS AND METHODS:

A Cross-sectional retrospective study was collected from January 2021 to January 2022 which includes 60 female patients and was collected from Al-Karama Teaching hospital and private histopathology labs in Wassit Province to include cases referred from 1st January 2019 - 1st April 2021.

Inclusion criteria

All breast lesions in female patients of different age group.

Exclusion criteria

1. Bleeding diathesis.
2. Pregnant women.
3. Patients who made fine needle aspiration cytology, but they didn't do histopathology.

FNA Sampling:

Fixation of the mass by left hand and holding syringe with attached needle gauge (21-23) by right hand. Insert it and do negative pressures then move the needle (back and forth cutting motions of the needle and in rotatory way). Then release the negative pressure slowly while the needle still inside. Pull the needle out, material obtained directly spread over the slides (number of slides will vary from case to case) and put in the fixative material (95% ethanol) for 20 to 30 minutes. Cytology Reports were interpreted as unsatisfactory, benign, malignant, and suspicious pathology.

- If it was impalpable breast mass, then the patient is advised for US guided aspiration, US performed by radiologist.

Statistical analysis

For both data entry and statistical analysis, the Statistical Package for Social Sciences (SPSS) version 24 was utilized.

The formula for sesiyivity is TP/(TP + FN).

- The formula for specificity is TN/(TN + FP).

TP/(TP + FP) is used to compute the positive predictive value (PPV).

TN/(TN + FN) is used to compute the negative predictive value (NPV).

TP+TN/Grand Total equals Accuracy.

Measurement of agreement (inter-rater reliability) by Kappa statistic was calculated for each test (CD, US, FNAC, and triple assessment) against gold standard histopathological examination (HPE) and its statistical significance by chi square test. The results were compared with those of histopathology as a gold standard. Kappa=0-0.20 no agreement, kappa=0.21-0.39 minimal agreement, kappa=0.40-0.59 weak agreement, kappa=0.60-0.79 moderate agreement, kappa=0.80-0.90 strong agreement, and kappa above 0.90 almost perfect agreement. P value <0.05 was considered as statistically significant.

RESULTS:

According to Age, presentation and site: This study included 60 women with breast disease. There were 14 (23.3%) women below 40 years, 25 (41.7%) aged 40-49 years, and 21 (35.0%) women aged 50 years or more. There were 22 (36.7%) women presented with regular mobile soft mass; 12 (20%) women with irregular immobile, hard mass; 7 (11.7%) women with lymphadenopathy; 20 (33.3%) women with pain; 10 (16.7%) women with nipple retraction; 11 (18.3%) with bloody nipple discharge; 6 (10%) with yellowish nipple discharge; and 4 (6.7%) women with changes to the skin's texture.

Women presented with breast lesion located at upper outer quadrant were 46.7%, while 30% of women presented with breast lesion located at periareolar/subareolar region. (table 1).

Histopathological diagnosis

The results of this study show that 36 (60%) of studied women were approved as malignant cases and 24 (40%) were approved as benign cases according to histopathology(figure 1).

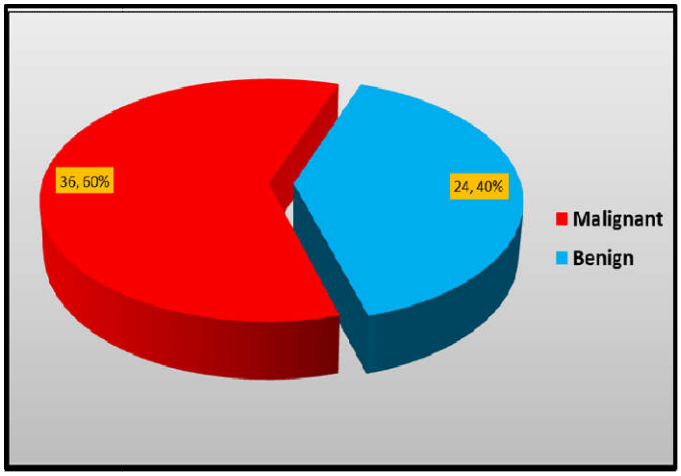

Figure 1: Distribution of studied cases according to the gold standard histopathology test.

Table 1: Types of breast lesion according to histopathology.

Breast lesion	Frequency	%
Usual Ductal hyperplasia	2	3.3
Duct ectasia	2	3.3
Mastitis	6	10.0
Fibroadenoma	10	16.7
Non proliferative breast lesion	2	3.3
Fat necrosis	2	3.3
Invasive ductal carcinoma NST	29	48.3
invasive lobular carcinoma	5	8.3
In Situ ductal carcinoma	2	3.3
Total	60	100.0

Validity of clinical examination: This test detected 19 cases of true positive (TP), and it labeled 22 cases as true negative cases, 91.7% specificity (Sp), 52.8% sensitivity (Sn), positive predictive value (PPV) was 90.5%, and negative predictive value (NPV) was 56.4%. Accuracy found to be 68.3%. The measure of agreement (Kappa Statistic) was calculated and was 0.403 (week agreement). P value was less than 0.001 which is highly significant. (Table 2).

Table 2: Validity of Clinical diagnosis according to the gold standard histopathology in diagnosing breast cancer.

Clinical diagnosis	Histopathology		Total	P†	Kappa*
	Positive (Malignant)	Negative (Benign)			
Positive(Malignant)	19	2	21	<0.001	0.403
Negative (Benign)	17	22	39		
Total	36	24	60		

† χ^2 test where P was significant at ≤ 0.05
* Kappa Measure of Agreement

Validity of Ultrasound test: This test detected 29 cases of true positive (TP), and it labeled 23 cases as true negative cases TN, 80.6% sensitivity Sn, and 95.8% specificity Sp, positive predictive value (PPV) was 96.7%, and negative predictive value (NPV) was 76.7%. Accuracy was 86.7%.The measurement of agreement (Kappa Statistic) was calculated and found to be 0.733 (moderate agreement). P value was less than 0.001 which is highly significant.(table 3).

Table 3 Validity of US according to the gold standard histopathology in diagnosing breast cancer.

US	Histopathology		Total	P†	Kappa*
	Positive (Malignant)	Negative (Benign)			
Positive(Malignant)	29	1	30	<0.001	0.733
Negative (Benign)	7	23	30		
Total	36	24	60		

† χ^2 t-test where P was significant at ≤ 0.05
* Kappa Measure of Agreement

Validity of FNAC: This test detected 33 cases of true positive (TP) (figure 4,5) . Twenty three cases as true negative cases (figure 3). The sensitivity Sn91.7%, 95.8% specificity Sp, positive predictive value (PPV) was 97.1% and negative predictive value (NPV) was 88.5%. Accuracy was 93.3%.The measurement of agreement (Kappa Statistic) was calculated and found to be 0.863 (strong agreement). P value was less than 0.001 which is highly significant.(table 4).

Table 4:Validity of FNAC test to the gold standard histopathology in diagnosing breast cancer.

FNAC	Histopathology		Total	P†	Kappa*
	Positive (Malignant)	Negative (Benign)			
Positive (Malignant)	33	1	34	<0.001	0.863
Negative (Benign)	3	23	26		
Total	36	24	60		

† χ^2 t-test where P was significant at ≤ 0.05
*Measure of Agreement

Validity of triple assessment

Out of 60 cases, the triple test was concordant (all three tests were either benign or malignant); 16 cases were malignant and 22 cases were benign. (Figure 2)

This test detected 16 cases of true positive (TP), and it labeled 21 cases as true negative cases, has a sensitivity (Sn) of 94.1 % and a specificity (Sp) of 100 % , The positive predictive value (PPV) was 100 % and the negative predictive value (NPV) was 91.9 % in this study. The accuracy was determined to be 97.4 %. The measurement of agreement (Kappa Statistic) was calculated and found to be 0.946 (perfect agreement). (Table 5)

Table 5: Validity of concordant triple assessment in the diagnosis of breast cancer using the gold standard histopathology; (n=38).

Triple assessment	Histopathology		Total	P†	Kappa*
	Positive (Malignant)	Negative (Benign)			
Positive (Malignant)	16	0	16	<0.001	0.946
Negative (Benign)	1	21	22		
Total	17	21	38		

† χ^2 t-test where P was significant at ≤ 0.05
* Kappa Measurement of Agreement

Triple test was non concordant

Among 22 cases; there were 3 cases found to be benign and 19 cases found to be malignant on histopathological analysis, in non-concordant circumstances, FNAC was found to be the most accurate (2 false negative and 1 false positive). (Table 6)

Table 6: Non concordant triple assessment according to the gold standard histopathology in diagnosing breast cancer, (n=22)

Test		Histopathology		Total
		Malignant	Benign	
Clinical Diagnosis	Malignant	3	2	5
	Benign	16	1	17
	Total	19	3	22
US	Malignant	13	1	14
	Benign	6	2	8
	Total	19	3	22
FNAC	Malignant	17	1	18
	Benign	2	2	4
	Total	19	3	22

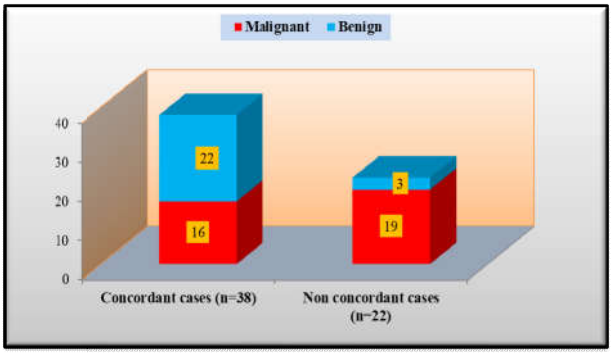

Figure 2: Triple assessment (concordant and non-concordant) according to the gold standard histopathology in diagnosing breast cancer.

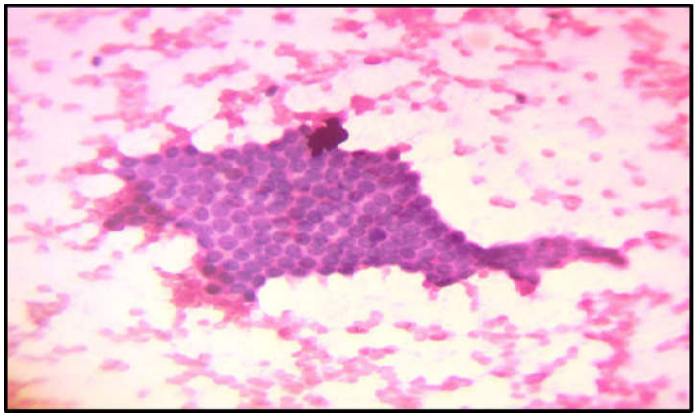

Figure 3: Fibroadenoma, tightly cohesive cluster of bland looking epithelial cells is an important clue for avoiding an over-diagnosis of malignancy (H&E,10x).

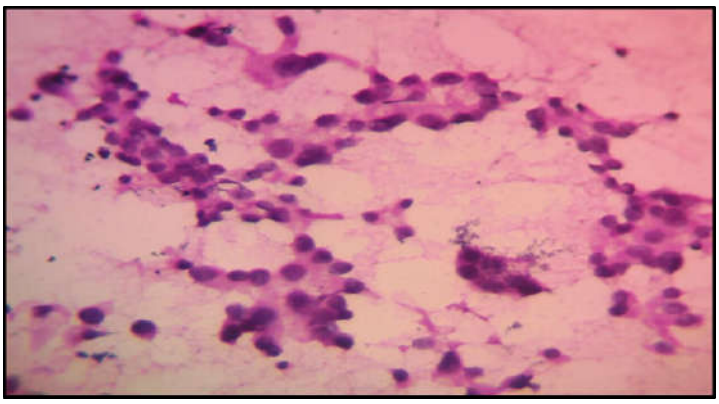

Figure 4: Breast carcinoma, the cells are dispersed both as isolated cells and as loosely cohesive clusters (H&E, 20x).

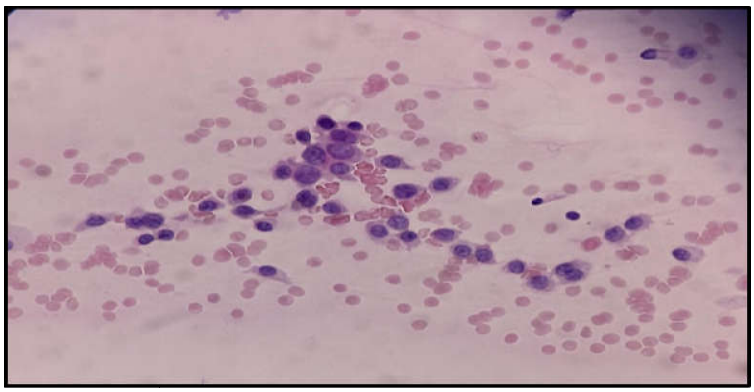

Figure5: invasive lobular carcinoma of breast, individual cells with eccentric nuclei (H&E, 20x).

DISCUSSION:

The study recruited 60 females, the sample was mainly in the age group 40-49 years, the largest percent, the highest frequency (36.7%) of women presented with regular mobile soft breast mass; the least percent presented with change in skin texture (6.7%). About half of those women presented with breast lesion located at upper outer quadrant. These figures are in agreement with a preliminary analysis of the database findings of 855 females with breast disease in Iraq in 2016 by Alwan NA. which showed that 35% of them were diagnosed in the (45-54) years of age with palpable breast masses 94%.[8]In the present study, (60%) of studied women were diagnosed as malignant cases and (40%) were benign cases according to histopathology reports, (48.3%) patients had invasive ductal carcinoma, (8.3%) patients had invasive lobular carcinoma, and only 2 patients diagnosed to have ductal cancer in situ which represents 3.3%. This was in agreement with the Iraqi preliminary database analytic study, which found that 46% of the studied sample were diagnosed with breast cancer. The most frequent pathology was infiltrative ductal carcinoma (67 percent) [8] . Patients who have cancer in our study represent 60% of cases which is in agreement to study done by Talib et al in 2017 in Wasit province in Iraq. A total of 73 female patients with palpable breast mass were included in this study, in 41 patients, the breast lumps were malignant while in 32 patients the breast lumps were diagnosed as benign [9].

Regarding Validity of clinical examination in the present study, it was found that clinical examination had detected 19 cases of true positive cases, and 22 cases were labeled as true negative cases, so the accuracy of the clinical examination alone in diagnosing breast cancer is found to be

68.3% with a significant weak agreement with histopathology (0.403). This disagrees with results of a study by Khoda L et al in India 2015 that the accuracy was 91.6% , with high sensitivity 90% and specificity 95 %.[10]

Regarding validity of ultrasound test in this study, the test detected 29 of true positive cases, and 23 cases as true negative cases, Accuracy of 86.7%. With significant moderate agreement with histopathology .These findings are consistent with a study that performed in 2018 by Hiba Mohammed et al in which sonography had detected benign lesions in 30cases (42.8%) of cases, Malignant characteristics were seen in 15 (22.4%) of the patients, which were later confirmed as malignant by FNA and biopsy. That was also in agreement with the result reported by (Sperber et al) in 2003[11, 12].

Regarding validity of FNAC in comparison to the gold standard (histopathology): This study found that it was of 91.7% sensitivity, 95.8% specificity, positive predictive value was 97.1%, and negative predictive value was 88.5%, and accuracy found to be 93.3%, with strong significant agreement. This is also had been found by Talib et al in 2017 when they studied the accuracy of FNAC in comparison with histopathology in diagnosis of breast lesion in Wasit Province the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAC were 90.24%, 100%, 100%, 88.88%, and 94.52% respectively[9].

Regarding validity of triple assessment in comparison to histopathology, this test had, 94.1% sensitivity, 100 percent specificity, positive predictive value was 100 percent, and negative predictive value was 91.9 percent. Accuracy found to be 97.4 percent. With a significant perfect agreement, the findings are in agreement with a study by Ghafouri et al in Iran 2006. Also comparable to the triple assessment approach by Bishop et al in Nigeria 2004. [4, 13]

CONCLUSION:

The most accurate of the three components of the triple test is Fine needle aspiration cytology. The triple modalities of clinical examination, radiological examination, and fine-needle aspiration cytology (FNAC) are more accurate when used together than when used separately. Ultrasound has been shown to be a valuable and complementary technique in the evaluation of breast lesions with a bigger rule in dense breasts. The most prevalent presenting age for breast lesions was 40-49 years old, with the most common symptom being a lump in the upper outer quadrant.

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