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Shna A. Mustafa [(1)]
Nazar Jawhar [(2)]
Jalal Ali Jalal [(3)]
Dlovan S. Khoshnaw [(4)]

(1) Department of Histopathology, Rizgary Teaching Hospital, Erbil. Iraq

(2) Department of Pathology, College of Medicine, University of Nineveh. Iraq

(3) Department of Basic Sciences/Pathology, College of Medicine, HMU, Erbil. Iraq

(4) Department of Radiology, Rizgary Teaching Hospital, Erbil. Iraq

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BIRADS, Cytopathology and Histopathological Approach for Diagnosis of Breast masses in Erbil, A comparative Study

ABSTRACT

Background: Breast masses are the most common surgical problems among females; that is why their management requires an efficient and accurate evaluation using the least invasive and most accurate methods with a minimal patient's discomfort.

Objectives: To determine the reliability and application of sonographic BIRADS lexicon in comparison with Fine needle aspiration cytology and Core needle biopsy results in order to differentiate benign from malignant breast masses. Also to determine the accuracy of FNAC and CNB in diagnosis of breast masses, including the sensitivity, specificity, positive and negative predictive values of both techniques in Erbil city and to compare the results of this study with those of others.

Materials and Methods: This is a crosssectional study that was conducted on 132 female patients with breast masses who attended the breast cancer unit in Erbil at Rizgari Teaching Hospital, Maternity Teaching Hospital and some private clinics in a period spanning from 15 th July 2012 to 15th February 2013. After being detected sonographically, sonographic guided fine needle aspiration cytology (FNAC) and core needle biopsy (CNB) of breast masses were performed. Masses were classified according to the sonographic BIRADS lexicon, FNAC and CNB. Pathological results were compared with sonographic features.

Results:

Hypoechoic breast mass with axillary lymph nodes had shown highest presentation on BIRADS classification (30 samples of FNAC) in which most of them (70%) were malignant C5, while on CNB irregular hypoechoic mass had the highest presentation 29 samples were (79.3%) malignant B5. BIRADS, FNAC comparison had a high sensitivity of (97.5%) and negative predictive value of (92.8%). However, this study revealed a lower FNAC specificity (62.2%) and positive predictive value (73.6%). In the same line, CNB sensitivity and negative predictive value were high 95.5% and 92.6% respectively while the specificity and positive predictive value were low (59.5% and 71.7%).

Conclusions: The BIRADS classification revealed that the highest frequencies of breast masses were among U5 (highly suspicious of malignancy) and U4 (suspicious of malignancy). Ultrasonic morphologic grading revealed that less than 30% of irregular outline masses of breast masses with axillary lymph nodes were benign masses and the reverse is true for those with well-defined masses or parenchymal changes.

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**Corresponding author E mail :* nazar3nhn@yahoo.com

Introduction:

Breast remains the leading site of the cancer in women (Jaykar *et al* 2013, Alwan 2010)). The diagnostic assessment of patients with breast symptoms is based on the Multidisciplinary, Triple Diagnostic Methods: **A**. Clinical assessment. **B.** Imaging assessment: ultrasound and mammography. **C.**FNAC and CNB (Brancato *et al* 2011). The breast imaging facilities should include x-ray mammography and high frequency ultrasound with probes suitable for breast imaging (12 MHz or more) (Willett *et al* 2012). A lexicon of sonographic descriptors of breast masses with attendant assessment categories has been developed by the American College of Radiology (ACR) in 2003 (Costantini *et al* 2006). The clinical and imaging work up should be completed before FNAC or CNB is performed. Breast needle biopsies should be performed under imaging guidance in order to achieve greatest accuracy and reduce the need for repeated procedures (Brancato *et al*2011 and Willett *et al* 2012).

Advantages of CNB over FNAC are obvious as well: even though FNAC is faster, cheaper, less prone to complications and provides an almost immediate diagnosis, CNB allows a more complete characterization of the lesion, including differentiation between invasive, in situ disease, grade and hormone receptor status, as well as CNB has repeatedly, but not invariably, been shown to yield more conclusive diagnoses than FNAC in both malignant and benign masses, (Helena 2008 and Kooistra *et al* 2010).

Patients and methods

This is a prospective study conducted during seven months from 15th July 2012 to 15th February 2013, a total of 132 women with breast mass(es) were examined. Cases were taken from Erbil breast cancer unit in Maternity Hospital, Rizgari Teaching Hospital and private ultrasound and histopathology clinics and labs in Erbil city.

All cases were examined by trained

radiologists using ultrasound (GElogic P5 linear probe 12Mhz; Siemens Acuson X300 linear probe 10Mhz) and classified according to BIRADS classification (Costantini etal2006), patient with BIRADS grade 3 and above were selected and underwent ultrasound guided (FNAC and or CNB) as an out-patient procedure. Of these, 48 patients underwent FNAC (under ultrasound guide) using a G21 needle, six slide smears were made and fixed in alcohol 95%, and stained by H&E. Cytological results were then classified in to (C1-C5) accordingly (Brancato etal 2011). Then Fifty-nine patients underwent histologic sampling using CNB from both the breast mass and axillary LNs. Histological results were scored in to (B1-B5) according to the pathology results (Brancato etal 2011). After taking a True cut biopsy by a needle gauge 14 or 18, the tissue was fixed in 10% buffered formalin, tissue processing done then 4 micron thick sections were cut by microtome, then staining with routine H& E done. In 25 patients both FNAC and CNB were done at the same time.

Exclusion Criteria: 1. previous breast carcinoma. 2. Big ulcerating breast masses.

Statistical Analysis

Data were analyzed using the statistical package for social sciences (SPSS version 19). Fisher`s exact test (rather than Chi square test) was used to compare between proportions because the expected count of more than 20% of the cells of tables was less than 5.

P-value of less than or equal to 0.05 was considered as statistically significant.

Results

This study included 132 females with an age range between 21-80 years and a mean age of 45.9 years.The peak age was in the fifth decade, accounted for 34.8% of cases. Sixty seven (51%) cases had right breast masses, 58 (44%) cases had left breast masses. The remaining 5% had bilateral breast masses. The upper outer quadrant 38 (28.8%) cases was the commonest quadrant involved followed by the lower inner quadrant

31 (23.5%) lesions, then each lower outer quadrant and upper inner quadrant 28 (21.2%) cases,while the retro-areolar (central) 7 (5.3%) cases was the lowest site.

By Ultrasound, & in regards to the border of the mass, the most common was a well-defined hypoechoic mass (in 48 cases (36.4%)) followed by irregular outline hypoechoic mass (in 34 cases (25.8%)). There were combined hypoechoic breast mass and axillary lymph node enlargement in 32 (24.2%) cases. While the reminders composed of complex cystic & solid 6 (4.5%) cases and parenchymal changes 12 (9.1%) cases.

Seven cases had multiple &bilateral masses, so the total number of lesions detected by ultrasound was 139, each was individually scored & sampled. The BIRADS classifications revealed highest frequency among U4 and U5 42 (30.2%) cases & 48 (34.5%) cases respectively followed by U3 33 (23.7%) cases, U2 15 (10.8%) cases, while U6 have the least frequency in only one (0.72%) case.

Of the 139 lesions, 77 FNA & 87 CNB were done (a total of 164 samples). Twenty-five cases had both FNA & CNB. See table 1 & 2hown in Table 1 and Table 2 for correlation of results of FNAC and CNB.

Table 1: FNA and CNB Scores.

FNA Score	N0. (%)	Core Scores	N0. (%)
C1	4 (5.2)	B1	0
C2	27 (35.1)	B2	42 (48.3)
C3	6 (7.8)	B3	0
C4	3 (3.9)	B4	0
C5	37 (48.1)	B5	45 (51.7)
Total	77 (100)	Total	87 (100)

Table 2: Correlation of results of FNAC and CNB.

FNAC grade	N0. of FNAC	N0. of CNB	Benign	Malignant
C1	2	2	2	0
C2	1	1	1	0
C3	2	2	2	0
C4	3	3	0	3
C5	17	17	0	17

Of the 77 samples of FNAC cases, the ultrasound grading revealed that the majority of breast masses with axillary lymph nodes were malignant.In contrast,those lesions with complex masses or parenchymal changes were benign; and the difference was statistically significant (p= 0.001) as shown in Table 3.

Table 3 :Correlation of breast mass border by US with FNAC Results.

Border	FNAC grade N0. (%)					Total N0. (%)	P-Value
	C1	C2	C3	C4	C5		
Well-defined hypoechoic mass	2(8.3)	13(54.2)	1(4.2)	0(0)	8(33.3)	24(100)	**0.001***
Irregular outline hypoechoic mass	0(0)	0(0)	1(9.1)	2(18.2)	8(72.7)	11(100)	
Hypoechoic breast	1(3.3)	6(20)	2(6.6)	0(0)	21(70)	30(100)	
Complex mass (cystic & solid)	1(20)	3(60.0)	0(0)	1(20)	0(0)	5(100)	
Parenchymal Changes	0(0)	5(71.4)	2(28.6)	0(0)	0(0)	7(100)	
Total	4(5.2)	27(35.1)	6(7.8)	3(3.9)	37(48.1)	77(100)	

In 87 cases of CNB,ultrasonic morphologic grading revealed that more than70% of

irregular outline breast masses with axillary lymph nodes were malignant masses while most of the well-defined masses or parenchymal changes turned out to be benign, and the difference was highly significant (p value < 0.001) as shown in Table 4.

Table 4: Correlation between breast mass border by US with CNB Results.

Border	CNB grade		Total N0. (%)	P-Value
	Benign mass B2 N0. (%)	Malignant B5 N0. (%)		
Well-defined hypoechoic mass	23(74.2)	8(25.8)	31(100)	<0.001*
Irregular outline hypoechoic mass	6(20.7)	23(79.3)	29(100)	
Hypoechoic breast mass + axillary LN	5(27.8)	13(72.2)	18(100)	
Complex mass (cystic & solid)	3(100.0)	0(0)	3(100)	
Parenchymal changes	4(66.7)	2(33.3)	6(100)	
Total	41(47.1)	46(52.9)	87(100)	

Out of 139 masses, 164 samples taken between FNAC (77) and CNB (87) and for each sample a BIRADS score was given even if it is the same for both tests, as shown in tables 5, 6, and 7.

Table 5: Correlation of BIRADS with FNAC grade.

BI-RADS	FNAC grade					Total N0. (%)	P-Value
	Inadequate C1	Benign C2	Atypia C3	Suspicious of Malignancy	Malignant C5		
Benign (U2)	1(90)	9 (90)	0 (0)	0 (0)	0 (0)	10 (100)	<0.001
Indeterminate/probably benign (U3)	2 (14.2)	10 (71.4)	1 (7.14)	1 (7.14)	0 (0)	14 (100)	

BI-RADS	FNAC grade					Total N0. (%)	P-Value
	Inadequate C1	Benign C2	Atypia C3	Suspicious of Malignancy	Malignant C5		
Suspicious of malignancy (U4)	0 (0)	8 (42.1)	5 (26.3)	0 (0)	6 (31.5)	19 (100)	
Highly suspicious of malignancy (U	1 (3)	0 (0)	0 (0)	2 (6)	31 (91)	34 (100)	
Total	4 (5.2)	27 (35)	6(7.9)	3 (3.9)	37 (48)	77 (100)	

Table 6: Correlation of BIRADS with CNB grade.

BI-RADS	CNB grade		Total N0. (%)	P-Value
	Benign lesion (B2) N0. (%)	Malignant (B5) N0. (%)		
Benign (U2)	5 (83.3)	1 (16.7)	6 (100)	<0.001
Indeterminate/ probablybenign (U3)	20 (95.2)	1 (4.8)	21 (100)	
Suspicious of malignancy(U4)	14 (48.3)	15 (51.7)	29 (100)	
Highly suspicious of malignancy (U5)	3 (9.7)	28 (90.3)	31 (100)	
Total	42 (48.3)	45 (56.7)	87 (100)	

Table 7: PPV and NPV for BIRADS: Pathology (FNA +Core biopsy)

BIRADS	Pathology		Total
	Malignant	Benign	
Malignant	82	31	113
Benign	3	48	51
Total	85	79	164

Sensitivity = x100 = 96.4%
Specificity = x100 = 60.8%
PPV = x100 = 72.6%
NPV = x100 = 94.1%

Out of eighty seven cases, results have shown forty five malignant cases with different histopathological types, the most common one was the ductal type as shown in Table 8.

Table 8: Histopathological type with BIRADS

BIRADS	Invasive Ductal carcinoma	Invasive Lobular Carcinoma	Carcinoma Insitu	Secondary Lesion	Total
U3	0 (0)	0(0)	0(0)	1 (100)	1 (100)
U4	9(81.8)	1(9.1)	1(9.1)	0(0)	11(100)
U5	28(87.5)	3(9.4)	1(3.1)	0(0)	32(100)
U6	1 (100)	0(0)	0(0)	0(0)	1(100)
Total	38 (84.4)	4 (8.9)	2(4.4)	1(2.2)	45 (100)

Discussion

Breast cancer is a major cause of morbidity & mortality among female, and according to International Agency for Research on Cancer by World health organization (IARC) study, the highest figures of breast carcinoma are mainly seen in post-menopausal women (IARC 2008).

The current research showed that the mean age was 45.9 (mean a range 40-49 years), a finding similar to that described by other studies (Yalda 2013, Al-Janabi 2003, Omar et *al* 2003

and Elkum *et al,* 2007). Such finding is of great importance because tumors at middle age or younger behave more aggressively compared to that of elderly patients (Jaykar *et al* 2013).

The lesions were slightly more in the ri ght breast (51%) than the left (44%). Within the breast, the upper outer quadrant zone was most commonly affected (28.8%). A comparable findings were described by many prior studies (Nigam and Nigam 2013, Awad *et al* 2012,Alhelfy 2010 and Lubab 2008). Radiologically, in comparisone to the breast fat, the majority of the lumps (86.4%) showed hypoechoic BIRADS echogenicity. Again, this result coincide with what was demonstrated by other works (Taj-Aldean and Hassan 2009, Costantini *et al,* 2006 and Hong *et al,*2008).

In the current study, we relied on descriptor assessment sonographic IRADS categories for determination of mass shape, orientation, margins, echopattern, posterior acoustic features & microcalcifications. Fourty eight lesions had well- defined margins; of these, 33.3% and 25.8% turned to be malignant on FNAC and CNB, respectively. Whereas 34 cases had irregular margins of which,72.7% and 79.3% turned out to be malignant on FNAC and CNB,respectively. In other words,the majority of well-defined masses were benign and those with irregular margins were malignant. Although similar results reported by other(Costantini *et al*, 2006, Hong *et al*, 2008 and Panda *et al*,2003), nontheless, margin configuration on sonography could not be used independently to predict the tumor behavior.

As far as FNAC results are concerned, the number of benign masses on FNAC(C2) formed 35.1% of cases, the bulk of breast FNAC diagnoses as benign ranging from 24–77.5% of cases in several other studies (Ishikawa *et al*, 2007,Day *et al*, 2008 and Rosa *et al*, 2011),which supports our findings.

In this study, the equivocal diagnostic cytologic categories (C3and C4)

comprised 11.7% of cases. Other researchers demonstrated equivocal cytologic from (14-17.7%) (Kanhoush *et al,*2004;Nguansangiam *et,al* 2009; Chaiwun *et al, 2005*,Lim *et al 2004* and Chaiwun *et al* 2002). This indicate that this category was neither underused or over used in this study.

Regarding those cases having both FNACand CNB; as far as the C3 category,both cases proved to be benign on CNB (B2), while all the 3 cases in the diagnostic category of C4;proved to be malignant on CNB (B5). These results are in concordance with the reported literature values where majorit y of the C3 cases proved to be benign, while most of C4 cases proved to be malignant on subsequent histopathological examination (Kanhoush *et al,* 2004 and Deb *et al,* 2001).

The presence of axillary lymph node en largement with breast mass was observed in less than ¼ th of patients. Although a relatively high prevalence of malignancy was demonstrated on both FNAC (70%) andCNB (72.2%) ,presence of axillary lymph node enlargement does not always indicate malignancy and vice versa that is absence of detectable axillary lymphnodes by clinico-sonographic means does not exclude malignancy.

In our study ,we depended on FNAC and/or CNB for final diagnosis and we correlated,these findings with BIRADS grading. Overall, 48 lesions(24.5%) wer e considered as benign on sonography (BIRADS II and III) and 91(65.5%) malignant (IV,V and VI).On the other hand, FNAC and CNB revealed that48.1% and 47.1%, respectively,were benign and 52% and 52.9% respectively, were malignant.In comparison with BIRADS, Combined FNAC and CNB resulted in high sensitivity (96.4%) and negative predictive value (94.11%) whereas the specificity and positive predictive value were low (60.8% and 72.6% respectively). These results are nearly similar to those obser ved by others (Costantini *et al* 2006,

Hong *etal*, 2008 and Baker *et al*, 1999).

The relatively low values of specificity and positive predictive value of both FNAC and CNB might be due to the sub categorization of BIRADS findings and the inclusion of a large number of false positive findings within the category “IV and V”.

Concerning invasive malignancy, all cases were considered as BIRADS categories IV and Vwith no categorization into IDC and ILC. In FNAC and CNB, apart from 2 insitu carcinoma cases and one metastatic carcinoma , all were infiltrative breast carcinoma (84.4%IDC and8.8%ILC). These results are similar to that of (Alhelfy 2010).

Conclusions

1. All IV and V BIRADS categories are malignant on tissue sampling.

2. Ultrasound morphologic grading revealed that more that 70% of lesions with irregular outline or breast masses with suspicious axillary lymph nodes were malignant,while majority of masses with well defined out lines revealed a benign nature on histopathology and cytology.

3. Sensitivity and specificity for FNAC and CNB were 100%.

4. BIRADS,

Combined FNAC and CNB resulted in high sensitivity (96.4%) and negative predictive value (94.11%) whereas the specificity and positive predictive value were low (60.8% and 72.6% respectively).

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