

ORIGINAL ARTICLE

Fine needle aspiration cytology in breast lump - its cytological spectrum and statistical correlation with histopathology

Ghosh A¹, Ghartimagar D², Sathian B³, Narasimhan R⁴, Talwar OP⁵

¹Associate Professor, ²Assistant Professor, ⁴Professor, ⁵Professor and Head, Department of Pathology

³Assistant Professor, Department of Community Medicine, Manipal College of Medical Sciences, Pokhara, Nepal.

Abstract	Introduction	Methods	Result	Conclusion	References	Citation
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Article Cycle

Address for Correspondence: Arnab Ghosh, Associate Professor, Department of Pathology, Manipal Teaching Hospital, Manipal College of Medical Sciences, Pokhara, Nepal
E Mail ID: drghosharnab@yahoo.com

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Abstract

Introduction: FNAC is a well-recognized method of investigation in breast lump and has high sensitivity and specificity. In this study we analyze the spectrum and efficacy of FNAC diagnoses in breast lump. **Material and method:** It was a hospital based retrospective study conducted from the data retrieved in the Pathology department. All FNAC breast cases reported between July 2008 to Dec 2009 except "inadequate aspirate" cases were included in the study. Corresponding biopsy were correlated where available. Diagnostic tests with ROC curve were used to find out the efficacy of FNAC. **Result:** A total of 196 FNAC cases were reported including 152 as benign, 7 as suspicious for carcinoma and 37 as carcinoma. Majorities were premenopausal females and commonest age group was 31-40 years. 88% of lumps were less than 5 cm. In reliability analysis, we got an excellent agreement of FNAC and Biopsy with kappa value as 0.882 [88.2%] ($p=0.0001$). Sensitivity and specificity were 90.2% and 100% respectively. 95.1% of the area was under the ROC curve with p -value=0.0001. Positive predictive value is 100% but the Negative predictive value varies according to the age and size. **Conclusion:** FNAC in experienced hands is a very useful tool with very high specificity and rare false positive result. Sensitivity can be further improved with clinical correlation.

Key Words

FNAC; Breast; Carcinoma; Sensitivity; Specificity; NPV; PPV; LR

Introduction

Breast lumps are common in women. About 10% women visiting health organization clinics present with breast lumps as the chief complaint. 80-85% of breast lumps are benign and rest are malignant. (1,2,3) Breast carcinoma is the leading cause of cancer incidence and death in women.(4) An estimated 1.38 million new cancer cases

diagnosed in 2008 (23% of all cancers). It is now the most common cancer both in developed and developing regions.(4) Early detection is the mainstay in management of breast carcinoma. FNAC is a routine procedure in clinical evaluation and initial diagnosis in breast lump worldwide. FNAC is safe and produces minimal tissue trauma and discomfort to the patient and is carried out as an outpatient procedure. Furthermore, FNAC

is known to have high specificity [99%] and more than 80% sensitivity in the diagnosis of breast lumps thus helping in further plan in management of these cases.(1,5-9)

Aims & Objectives

Objective of the present study is to find out the spectrum of benign and malignant lesions in all the FNAC performed and reported in cases presented with breast lump. The FNAC diagnoses have also been correlated with histopathology diagnoses in all those cases where tissue biopsies were available.

Methods

Study design and setting: It was a hospital based retrospective study carried out from the data retrieved from the Dept of Pathology of Manipal College of Medical Sciences, Nepal in a period from July 2008 to Dec 2009. All cases of female breast lump which were undergone FNAC in the above period were retrieved.

Inclusion criteria: Among these FNAC cases, all available histopathology have been included to correlate with corresponding cytology diagnosis. In histopathology, all types of tissue biopsy viz. core biopsy, incisional biopsy, excisional biopsy, lumpectomy and mastectomy were included.

Exclusion criteria: Those cases which were reported as "inadequate" on FNAC have been excluded from this study.

Clinical Methods: FNAC were performed with 23 gz needle and 10 cc syringe. Aspiration slides were routinely stained with MGG and PAP stain. In histopathology, tissues were fixed in 10% formalin, processed routinely and stained in H&E stain. All the FNAC cases have been analyzed according to the age of the patient, size of the lump, frequency and percentage of different types of cytology

diagnosis as well as were correlated with available tissue diagnoses.

Dependent Variable: Dependent variables were FNAC and Biopsy.

Independent Variable: Independent variables were age[16-20, 21-30, 31-40, 41-50, 51-60, 61-70 and 71-80], size of the lump [<2 cm, 2-5, 5 – 10, and >10, menopausal status[Premenopausal age group (<45), Postmenopausal age group (>45)].

Ethical Clearance: Ethical committee approval was taken before the study.

Sample size calculation: In a pilot study of 10 patients showed Sensitivity (P) =90%, Q= 100-P = 100-90 =10%, Precision, (E) = 10%. Sample size required for the study is 43 cases with both FNAC and Biopsy done.(10)

Data management and statistical analysis The data collected was analyzed using Excel 2003, Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and EPI Info 3.5.1 Windows Version. Diagnostic test and ROC curve used to find out the efficacy. Kappa coefficient used to find out the reliability. $p < 0.05$ was considered as statistically significant.(11)

Result

The total number of FNAC cases was 196 in the present study. Among these, 69 cases also had histopathology diagnoses to compare with the FNAC diagnosis. The age range found to be 16 to 72 years and the mean age being 35.2 years. In our study left sided lesions (103 cases) were slightly more than right sided lesions (93 cases) in a ratio of 1.1 : 1. All cases were grouped into 3 categories viz., benign, suspicious of malignancy and malignant as per FNAC diagnosis and [Table 1](#) show their age wise distribution. Maximum number of FNAC have been performed in the age range of 31-40

years (69 cases, 35%) followed by 21-30 (42 cases, 21%) and 41-50 year group (39 cases, 20%). Furthermore, 71% of cases were of premenopausal age group (<45 years).

Considering the size at presentation, majority of the patients (88%) had lump below 5 cm in size ([Table 1](#)). However 23 cases (13%) were reported as “suspicious” or “malignant” among 172 cases of lumps smaller than 5 cm, in contrast to 21 malignant cases (88%) out of 24 cases larger than 5 cms in size. ([Table 1](#))

All the different FNAC diagnoses, their respective frequencies and available corresponding histopathology have been shown in [Table 2](#). Majority of the cases, 152 cases (78%) were found to be benign in contrast to 44 cases (22%) reported either as suspicious of malignancy or as malignant. Among benign conditions, commonest cytology diagnosis was “proliferative breast disease without atypia” (86 cases) followed by fibroadenoma (34 cases). Among 196 total FNAC cases, 69 cases had undergone subsequent biopsy and follow up histopathology were available. Among 152 benign cases, 26 cases had histopathology correlation. In contrast, biopsy was available in all 37 cases which were reported as “carcinoma” and in 6 out of 7 cases which were reported as “suspicious of malignancy” on FNAC. Though biopsy was advised in all “suspicious” cases reported on FNAC, 1 patient was lost to follow up.

[Table 3](#) show comparison between FNAC and histopathology diagnoses. All 26 benign and 37 malignant cases on FNAC showed similar number of benign and malignant conditions on histopathology ([Table 3](#)). Among 6 cases reported as “suspicious” on FNAC, 4 cases showed ductal carcinoma while 2 showed atypical ductal hyperplasia on histopathology ([Table 3](#)). Among malignant cases commonest

type was ductal carcinoma, both on FNAC and histopathology

We have analyzed all 69 cases which have both FNAC and histopathology diagnoses for finding the efficacy of FNAC using reliability and validity ([Table 4](#)).

Reliability: It is the ability of FNAC to give consistent result on repeated applications. We got reliability kappa value of the FNAC as 0.882 [88.2%] ($p=0.0001$). Kappa score greater than 75% indicates a very strong or excellent agreement of FNAC and Histopathology diagnosis.

Validity: Positive predictive value of FNAC is 100% in all the cases, so the ability of FNAC to detect a malignant case is 100%. But the Negative predictive value which is the ability of FNAC to detect a non-malignant case varies according to the age and size. It was decreasing while age of the patient increases. It was also less in size of the lump between 2-5 cm. In the total cases, Negative likelihood ratio test is showing that a false negative result on FNAC is 9.8 times more likely to occur in a malignant case as compared to non-malignant case and it increases with age. In patients with age less than 40 years and in lumps of size less than 2 cm, FNAC has 100% efficacy.

[Graph 1](#) shows the ROC curve with Area under the curve 0.951 [95.1%] and p -value=0.0001 (significant).

Discussion

FNAC is an invaluable tool for preoperative diagnosis and also postoperative follow up of breast lump. Pathologists being trained in and aware of both microscopic and macroscopic features, are in ideal position to perform FNAC on palpable lesions and to give accurate diagnosis.

Age and size distribution: In the current study, among 196 patients presented with breast lump, age range was found to be 16 – 72 years and the mean age was 35.2 years. Our findings corroborate well with other studies with mean age 33, 35.1 and 33.7 years respectively.(12-14) However in a series by Dennison G et al the mean age of presentation was much higher (59.3 years).(3) In present study majority (71%) patients were in premenopausal age and the commonest age group was 31-40 years (35 %). In the study by Harirchi et al most of the lumps were more than 5 cm which is in contrast to our data.(15) In our study there is marked increase in percentage of malignancy in lumps more than 5 cm (88% versus 13%)

FNAC - Cytological Diagnosis: Benign lesions were much more common comprising 78% cases in contrast to 22% cases diagnosed as malignancy or suspicious of malignancy. Similarly, as in our study, Dennison G et al also found that out of 143 cases, 73.4% were benign compared to 26.6% malignant cases.(3) In current data, among 139 cases in the reproductive age group, only 14% were diagnosed as malignant while among the postmenopausal group, 42% cases (24/57) were malignant. This correlates well with other studies done by Harirchi I, Brathwaite A, Medina Franco H, and Place R, where more number of breast carcinoma were found in postmenopausal age group.2, (15-17)

On FNAC, the main features of benign aspirate include cohesive clusters of ductal epithelial cells, presence of myoepithelial cells and minimal anisonucleosis. On the other hand atypia is suggested when the epithelial clusters are more discohesive, there are less number of myoepithelial cells and cells show presence of anisonucleosis with occasional prominent nucleoli. Frank carcinoma cases show cellular smears with cells showing marked anisonucleosis and frequent large prominent nucleoli.

Among the 152 **benign lesions**, the most common diagnosis reported was “proliferative breast disease without atypia” (86 cases, 52%) followed by fibroadenoma (34 cases, 22%). In all cases diagnosed as fibroadenoma, smears were cellular and showed characteristic monolayered clusters of cells with minimal atypia, bare nuclei and fragments of fibromyxoidstroma. However, it is possible that, some of the cases reported as “proliferative breast disease without atypia” were actually fibroadenoma with low cellular yield lacking the characteristic cytological picture of fibroadenoma. Thus the number of “proliferative breast disease without atypia” may appear high and the number of fibroadenoma may appear low in our study. We however did not have any histopathology of “proliferative breast disease without atypia” group as these patients were subjected to follow up only. We had reported 18 cases of fibrocystic disease which showed benign epithelial cells and foamy macrophages. Inflammatory lesions were found only in 14 cases. All inflammatory cases were of acute inflammatory etiology with necrotic and proteinaceous background. In 2 inflammatory cases, associated lactational changes were also noted. Benign lesions including fibroadenoma, fibrocystic diseases and inflammatory conditions comprised more than 90% of cases in studies done by Dutta S K, Devitt J E, and Otu AA.(18-20)

We had 6 cases which were initially reported as “suspicious” or “with atypia” on FNAC and later biopsy were performed as advised. On FNAC they showed discohesive cell clusters with occasional nuclear atypia (Figure 1). On histopathology, 4 of them showed ductal carcinoma while 2 showed atypical ductal hyperplasia (Figure 2). Retrospectively on reviewing the 4 cases, the major cause of not detecting the carcinoma was hemorrhagic aspirate with low cellular yield.

Ductal carcinoma is the commonest type of breast carcinoma seen world wide¹In our study, as well, 37 of 41 (90.2%) **malignant** cases are of ductal subtype which corroborates with other data.^(1,14,15) All these cases on FNAC showed malignant cells with obvious nuclear atypia ([Figure 3](#) & [Figure 4](#)) and on histopathology showed prominent desmoplasia ([Figure 5](#)) We also had 2 cases each of lobular and medullary carcinoma which are cytologically different from ductal carcinoma.

FNAC - Statistical significance: Sensitivity and specificity of diagnosing breast carcinoma on FNAC is high and in expert hands false positive and false negative cases are very rare.^(1, 21) In the current study the specificity was 100% and overall sensitivity 90.2%. This corroborates well with other studies.^(21,22) There was no false positive case in the current study. However in studies by Young and Homesh, false positive cases were 1.1% and 1.5% respectively.^(14,22)

Conclusion

FNAC is well recognised for its high accuracy and efficacy rate in investigation of breast lump. False results especially false positive results are very rare which can be further minimised with proper clinical correlation. In suspicious or doubtful cases, histopathology is confirmatory.

Competing Interests The authors do not have any conflict of interest arising from the study.

What this study adds: We have done detailed statistical analysis regarding efficacy in FNAC breast lump using reliability and validity tests using ROC curve. This study corroborates with international studies in higher centres reconfirming the utility of FNAC.

Recommendation

Future Scope of the study Multi-centric study should be done to assess the spectrum of FNAC diagnosis and its utility in the whole country.

Authors Contribution

AG designed the study, interpreted the data, drafted the manuscript, and revised it. DGM envisages the study with AG, acquired the data, interpreted the data, and revised the manuscript. RN and OPT revised the manuscript; BS participated in statistical analysis, interpreted the data, and revised the manuscript. All authors approved the final manuscript.

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Tables

TABLE 1: DISTRIBUTION OF ALL CASES (N=196) ACCORDING TO AGE GROUPS

Age range	Number of cases, %	Benign	Suspicious	Malignant
16-20	6 , 0.3%	6		0
21-30	42 , 21%	37	1	4
31-40	69 , 35%	60	2	7
41-50	39 , 20%	26	1	12
51-60	28, 14%	16	2	10
61-70	9 , 0.5%	5	1	3
71-80	3 , 0.2%	2		1
Premenopausal age group (<45)	139 , 71%	119	4	16
Postmenopausal age group (>45)	57 , 29%	33	3	21
Size of lump				
Upto 2 cm	64 , 33%	60	2	2
>2-5	108 , 55%	89	5	14
>5 – 10	21 ,11%	3		18
>10	3 , 0.2%	0		3
Total	196	152	7	37

TABLE 2: FNAC DIAGNOSES IN ALL CASES (N=196) AND CORRESPONDING AVAILABLE HISTOPATHOLOGY

Diagnosis on FNAC		Number of FNAC cases	Number of Histopathology cases
Benign	Fibroadenoma	34	11

N= 152	Fibrocystic change	18	8
	Inflammatory lesion	14	4
	Proliferative breast disease without atypia	86	3
Suspicious N= 7	Proliferative breast disease with atypia / Suspicious for carcinoma	7	6
Malignant N= 37	Carcinoma , Ductal	33	33
	Carcinoma , lobular	2	2
	Carcinoma , Medullary	2	2
Total		196	69

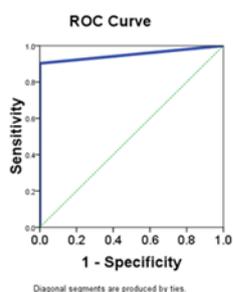
TABLE 3: CORRELATION HISTOPATHOLOGY AMONG 69 CASES

FNAC diagnosis	Histopathology diagnosis								Total FNAC cases which had histopathology
	Fibroadenoma	Fibrocystic change	Inflammatory lesion	Fibroadenosis	Atypical Ductal Hyperplasia	Ductal Carcinoma	Lobular Carcinoma	Medullary Carcinoma	
Fibroadenoma	11								11
Fibrocystic change		8							8
Inflammatory lesion			4						4
Proliferative breast disease without atypia	1			2					3
Suspicious for carcinoma					2	4			6
Carcinoma , Ductal						33			33
Carcinoma , lobular							2		2
Carcinoma , Medullary								2	2
Total Histopathology cases	12	8	4	4		37	2	2	69
						Histopathology diagnosis n=69			
						Nonmalignant n=28		Malignant n=41	
						Benign	Atypia		
FNAC diagnosis n=69				Nonmalignant n=32		Benign	26	0	0
						Suspicious	0	2	4
				Malignant , n=37		0	0	37	

TABLE 4: SENSITIVITY AND SPECIFICITY ANALYSIS OF FNAC

Variable	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Likelihood Ratio (Positive)	Likelihood Ratio (Negative)
Total cases	90.2	100	100	87.5	-	0.098
Age groups						
21-30	100	100	100	100	-	0
31-40	100	100	100	100	-	0
41-50	92.3	100	100	85.7	-	0.077
51-60	83.3	100	100	85.7	-	0.167
61-70	75	100	100	83.3	-	0.25
71-80	100	100	100	100	-	0
Size						
<2 cm	100	100	100	100	-	0
2-5 cm	78.8	100	100	82.6	-	0.212
5 – 10 cm	100	100	100	100	-	0
>10 cm	100	-	100	-	-	

Graph

GRAPH 1 ROC CURVE FOR THE FNAC TEST

Figures

FIGURE 1: FNAC SHOWING EPITHELIAL CELL CLUSTERS WITH PRESENCE OF MYOEPIHELIAL CELLS BUT SEVERAL CELLS SHOW PROMINENT NUCLEOLI – DIAGNOSED AS “WITH ATYPIA”, MGG STAIN, 400X

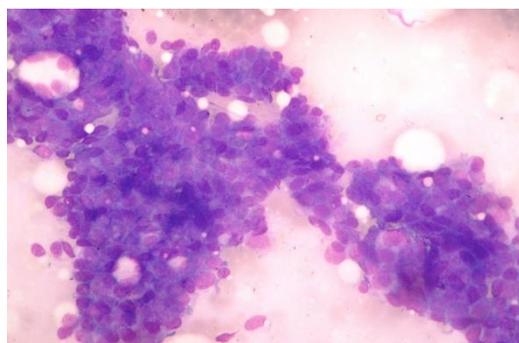


FIGURE 2: HISTOPATHOLOGY SHOWING EPITHELIAL PROLIFERATION AND SEVERAL CELLS SHOW PROMINENT NUCLEOLI – DIAGNOSED AS ATYPICAL DUCTAL HYPERPLASIA. H & E STAIN, 400X

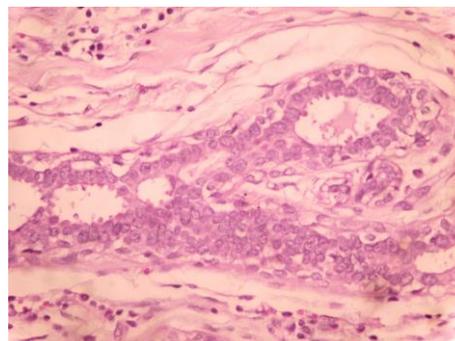


FIGURE 3. FNAC SHOWING SHEETS OF EPITHELIAL CELLS WITH PROMINENT ANINUCLEOSIS AND PROMINENT NUCLEOLI – DIAGNOSED AS “CARCINOMA”, MGG STAIN, 400X

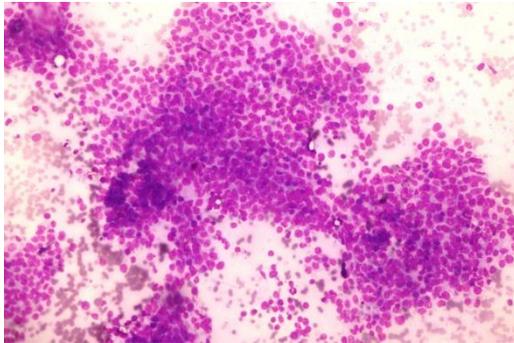


FIGURE 4: FNAC SHOWING CLUSTERS OF MALIGNANT CELLS WITH PROMINENT ANINUCLEOSIS AND PROMINENT NUCLEOLI – DIAGNOSED AS “CARCINOMA”, MGG STAIN, 1000X

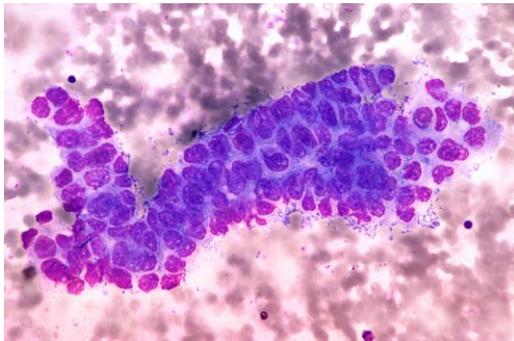


FIGURE 5: HISTOPATHOLOGY SHOWING INFILTRATING DUCTAL CARCINOMA WITH IN-SITU AREAS. H & E STAIN, 100X

