

CYTOHISTOLOGICAL CORRELATIVE STUDY OF BREAST LESIONSKanchana P. V. N¹, P. V. B. Ramalaxmi², K. Prasada Reddy³, D. Raiza⁴**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: BACKGROUND: Breast lump is fairly common complaint in females for which patient seeks medical advice and becomes anxious about the diagnosis. Quick diagnosis by Fine needle aspiration cytology (FNAC) relieves patient's anxiety and assists in their pre-operative management and overall treatment. **AIMS:** To study the cytological spectrum of breast lesions in correlation with histological appearances to evaluate the utility of FNAC in the diagnosis of palpable breast lesions. **MATERIALS AND METHODS:** Total of 180 cases were studied by FNAC of which 42 cases specimen was received for histopathology examination (HPE). Diagnostic accuracy was studied by statistical analysis. **RESULTS:** In this study of 42 cases of correlation, maximum cases were obtained for fibroadenoma followed by malignancy. FNAC diagnosis was consistent with HPE in 41 cases and inconsistent in one case. **CONCLUSION:** FNAC can reliably distinguish between benign and malignant conditions, neoplastic and non-neoplastic conditions. The result compared with other studies substantiate the findings of the series that FNAC of breast is a sensitive and specific modality that assist in diagnosis and management of breast lesions.

KEYWORDS: FNAC; breast lesions; HPE.

INTRODUCTION: Lump breast is a fairly common complaint for which patient seeks medical advice and becomes anxious about the diagnosis. FNAC is an important diagnostic procedure used to evaluate breast lesions and to assist in their pre-operative management and overall therapy. In addition to the initial diagnosis, FNAC is of value in staging the disease, documenting recurrence and identifying tumor transformation. It has acquired a very important role in the diagnosis of palpable breast lesions and has largely replaced open biopsy, especially frozen sections. It is a simple, inexpensive, minimally invasive method and relatively painless. It provides the diagnosis in a short time and has low risk of complications. There are no contraindications to FNAC of breast lumps.

This study aims at correlating the cytological diagnosis and HPE to evaluate sensitivity, specificity and diagnostic accuracy thereby its role in preoperative diagnosis of palpable breast lump and planning proper management.

MATERIALS AND METHODS: The present study includes aspiration smears of all cases with breast lump. These cases were referred to the cytology lab in the department of pathology. The total number of aspiration smears done were 180 cases. In 42 cases we obtained specimens.

After taking consent and relevant history, FNAC was done after local examination. Smears were stained with Haematoxylin and Eosin. Histopathology specimens were examined, sections were given from representative area, processed and stained with Haematoxylin and Eosin.

RESULTS: The present study includes 180 cases of FNACs of breast lesions received at the Cytopathology laboratory, during the period January 2010 – June 2012. Breast lesions constituted 11.05% of the total FNACs done during this period.

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The clinical data as per the proforma and cytological interpretation were received from all cases and histopathological correlation done wherever possible. The following observations were documented. Out of 180 cases HPE was available for 42 cases. In 41 cases histopathological findings correlated with cytological diagnosis. It varied and uncorrelated in 1 case. In this case, diagnosed as benign in cytology but was malignant histopathologically. Hence a total of 42 cases out of 180 were ultimately subjected for comparison. This study was done retrospectively and prospectively, the data was tabulated methodically and analysed statistically. The extent of correlation between FNAC and histopathology was noted.

Out of 180 cases, 2 cases with bilateral lesions of different diagnosis on each side were excluded from the study for statistic purpose. So a total of 178 cases are included in this study.

In the present study the youngest patient was a 13 years and oldest was a 65 years. Maximum number of patients 102 cases (57.3%) were noticed between 21-40 years, (Table-1). Of 180 cases, 7 cases (3.9%) Were male and 173 cases (96.1%) were female.

Out of the total 178 FNACs, 148 cases were diagnosed as nonmalignant based on cytological findings. Majority of the lesions were diagnosed as fibroadenoma (64 cases) comprising of 43.24% followed by fibroadenosis of 36 cases and fibrocystic disease of 23 cases comprising of 24.32% and 15.54% respectively. (Table 2)

On cytology majority of malignant breast lesions were diagnosed as duct cell carcinoma, 26 cases (86.66%) followed by medullary carcinoma 2 cases (6.66%). (Table 3)

Of 178 cytologically positive breast lesions 42 cases were processed for histopathological examination, correlation revealed 7 cases of true positivity and 34 cases of true negativity, no case of false postivity and 1 case of false negativity. Hence the sensitivity of 87.5% and specificity of 100% was obtained. There were no false positive cases reported cytologically, resulting in a positive predictive value of 100%. One false negative case was reported cytologically as ductal epitheliosis and histopathologically proved malignant resulting in the negative predictive value of 97.14%. The overall diagnostic accuracy was 97.62% which was statistically significant. (Table 4). In this study of 42 cases of correlation, maximum cases were obtained for fibroadenoma – 26 cases, followed by malignancy – 7 cases. FNAC diagnosis was consistent with histopathological examination in 41 cases and inconsistent in one case (Table 5).

DISCUSSION: Now-a-days fine needle aspiration cytology is a widely used simple and best diagnostic method in breast lesions and in selection of patients for surgical treatment. The present study of FNAC of breast lesions is found to be quite reliable.

From a total of 180 cases of breast lesions 178 cases are included in this study. Most of the lesions were seen between 21-40 years of age group.

Out of 178 cases of cytologically diagnosed FNACs 148 cases (83.15%) were non-malignant and 30 cases (16.85%) were malignant. Out of all non-malignant lesions fibroadenoma constitutes the dominating lesion 64 cases (43.24%). This is also true in the study of Mansoor I¹ and another study by Adesunkanmi AR et al.²

The present study was found to be quite effective and reliable diagnostic test. Majority of the cytological diagnosis are consistent with histological diagnosis and is depicted in percentage in table No. 6 In this study 8 cases were diagnosed as breast abscess in the age range between 19-60 years. Smears showed benign ductal epithelial cells against background of acute inflammatory cells. Only two cases returned for histopathological examination and were proved so.

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There was a case of plasma cell mastitis in a 55year lady with subareolar mass. The smear showed few degenerating ductal epithelial cells, plenty of plasma cells, few macrophages and lymphocytes. It has to be differentiated from periductal mastitis which in addition has plenty of squamous cells. It correlated with histopathology.

A 25 years lady presented with history of bilateral nipple discharge intermittent for the past 7 years. On examination both nipples inverted, healed scar in the periareolar area on the left side and had thick whitish nipple discharge bilaterally and no palpable mass in either breasts. The smears from nipple discharge from both sides showed:

Plenty of benign squamous epithelial cells, anuclear squames, few bland ductal epithelial cells and acute inflammatory cells. Acid Fast Bacilli and Grams stain both were negative. The diagnosis was Periductal mastitis. (Figure 1)

Out of 148 non-malignant FNACs 64(43.24%) cases were diagnosed as fibroadenoma. Maximum incidence was seen between 20-30 years age. Mansoor I and Adensunkanmi found fibroadenoma to be the most common benign breast lesion similar to our study.^{1,2} It was bilateral in 5 cases and multiple in 3 cases. Out of 64 cases histopathological correlation was obtained in 26 cases. Out of 26 cases, all 26 cases were correlated with cytological findings. (Figure 2, 3)³ Thirty six cases were diagnosed as fibroadenosis which comprised 24.32%. Bilateral in 3 cases. Smear pattern was that of fibroadenoma but of less cellular yield. Out of 36 cases of cytologically diagnosed fibroadenosis one case specimen was received and it correlated with FNAC.

In the current study 1 case was diagnosed as benign phyllodes on cytological examination in a patient aged 45years. She underwent simple mastectomy. Histopathology features were consistent with benign phyllodes and correlated with the cytological diagnosis.⁴

Of 178 FNACs 23 cases were diagnosed as fibrocystic disease. Most of the patients were between 31-40 years. Fibrocystic disease comprised of 15.54% (23 cases) of total benign lesions. Bilaterality was noticed in 13.04% (3 cases). In a study by Kumar R the average age of presentation for fibrocystic change was 33 years similar to our study.⁵ Out of 23 Cases specimens were received for histopathological correlation in one case and correlated with FNAC.

Gynaecomastia is a common lesion encountered in male breast. It constituted about 4.73% (7 cases) of all benign lesions. For the 7 cases the age range was 18-58 years, 2 cases were diagnosed in 2nd decade indicating hormonal pubertal changes.⁶ It was bilateral in one case. In the current study 1 specimen was received for correlation and it correlated with cytological diagnosis.

In this study malignant lesions comprised of 16.85% (30 Cases) of 178 smears. The age range was 25-65 years with maximum cases in the 51-60year age group. The youngest patient to have carcinoma was 25 year aged lady in this study. In a study by Murray H S the youngest patient to have carcinoma was 27years.⁷

Of the 30 cases, 25 cases were diagnosed as duct cell carcinoma. For statistical convenience no attempt was made to differentiate insitu carcinoma and invasive carcinoma. Two cases were diagnosed as medullary, another two cases as metaplastic carcinoma of squamous type and one as papillary type.

Out of 30 cases diagnosed as malignant from a total FNACs of 178 cases, 7 cases were obtained for histological correlation. Out of 7 cases, 4 cases correlated with cytological diagnosis as duct cell carcinoma, one case diagnosed as duct cell carcinoma was IDC with squamous differentiation, one case was medullary carcinoma, correlated so and another case cytologically IDC

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(Figure 4) was intracystic ductal papilloma with foci of carcinoma. Thus all the 7 cases cytologically diagnosed as malignancy correlated so histopathologically too.

One case reported cytologically as ductal epitheliosis was histopathologically IDC schirrous type with DCIS. False negative result can be due to sampling and not to interpretive difficulties.⁸ This is especially true for schirrous type.^{9,10}

The most common malignant pattern noticed is a cellular smear with single as well as small clusters of atypical epithelial cells with decreased cohesiveness, scanty cytoplasm with hyperchromatic nuclei against necrotic and granular chromatin background.

Among all the above ductal carcinomas, in one case a 65 year old lady presented with Right side subareolar mobile mass of 5x3 cms, healed ulcer in the nipple areolar region with destruction of the nipple. FNAC of the smear from the mass showed features of IDC and no lymphnodes were palpable in the right axilla. She underwent modified radical mastectomy for Right breast. Histopathology of areolar region showed characteristic Paget's cells in clusters in basal epidermis and in single's in upper epidermis. (Figure 5) These cells stained positively with PAS (Periodic Acid Schiff) stain.¹¹ Sections from larger mass showed IDC with predominantly squamous differentiations and foci of ductal carcinoma in situ comedo type (Figure 6).

Other two masses showed DCIS comedo type with calcification. All the 7 lymphnodes were negative for malignancy and showed the features of dermatopathic lymphadenitis. This is a case of Paget's disease which is a rare manifestation of breast cancer (1-4% of cases) presented with infiltrating duct cell carcinoma with squamous differentiation another rarity (Seen in 3.7% of cases).¹² and had multiple foci (Another rare feature) of DCIS with comedo pattern. Prognosis of the Paget's disease is as that of underlying carcinoma.¹³

In the current study a 55 year aged woman presented with a mass of 8years duration in the right breast that grew rapidly since 1 year. On examination nipple was retracted, a few ulcers over skin, serosanguinous nipple discharge and a large mass both cystic and solid occupying whole of the breast measuring 10x10 cms was noted. Clinically axillary lymphnodes were not palpable.

Nipple discharge showed blood cellular elements and FNAC of the mass showed clusters of atypical cells with pleomorphic and hyperchromatic nuclei. It was diagnosed as IDC.

Histopathology revealed features of ductal papilloma with foci of carcinoma. 8 Lymphnodes showed reactive lymphadenitis.

In this case aspiration was done from multiple sites due to large size of the mass which led to detection of carcinoma by FNAC, otherwise histopathology is a must to rule out focal carcinoma in a ductal papilloma.

In the present study incidence of medullary carcinoma was 6.66%. Features potentially helpful in the cytologic differential diagnosis of a carcinoma with prominent lymphoplasmacytic background are nucleolar size (4 microm in MC, vs. 1.5 and 2 microm in IDC and AMC, respectively) and the degree of nuclear atypia.¹⁴ 1 case was received for correlative study and was proved correct on histopathological examination.

The statistical analysis was carried out in proved cases with cytohistological correlation. Study of 42 cases revealed the sensitivity of 87.5%, specificity of 100% and an overall diagnostic accuracy of 97.62% (Table 7) which is comparable with other studies.

The present study shows sensitivity of 87.5% approximately equivalent to Aziz M et al and highest sensitivity was reported by Nggada et al.

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In regard to specificity the current study showed 100% which is equal to that reported by Kamphausen et al, Aziz M et al and is the highest value reported.

The positive predictive value in the present study is 100% which is equal to that reported by Kamphausen et al, Aziz M et al and is the highest value reported.

The negative predictive value in the present study is 97.14% which is almost equal to Collaco et al.

The overall diagnostic accuracy in the present study is 97.62% which is almost equal to Nggada et al.

The present study confirms the view that FNAC has high ability to detect benign and malignant lesions with high efficacy and accuracy. Thus fine needle aspiration cytological study can be a safe, simple and effective tool for defining and diagnosing breast lesions.

Thus FNAC of breast is a sensitive and specific modality in diagnosing breast lesion and in management of the breast lesions.

CONCLUSION: A total of 178 cases are included in this study. The maximum numbers of patients were between 21-40 years of age, 4% males and 96% females. Histopathological correlation was obtained in 42 cases which showed true negative of 34 cases, true positive of 7 cases, false positive nil case and one false negative case.

The current study revealed a sensitivity of 87.5%, specificity of 100%, positive predictive value of 100%, negative predictive value of 97.14%, false positive ratio of 0%, false negative ratio of 12.5% with an overall diagnostic accuracy of 97.62%.

FNAC can reliably distinguish between benign and malignant conditions, neoplastic and nonneoplastic conditions. The result compared with other studies, substantiate the findings of the series, that FNAC of breast is a sensitive and specific modality that assist in diagnosis and management of breast lesions. FNAC has been found to be a most valuable economic, simple and safe diagnostic procedure in the work up of breast lesions providing enough clinical information of underlying pathological condition especially in experienced hands.

Age	Inflammatory	Non Inflammatory Non - Neoplastic	Benign	Malignant	Total	Percentage (%)
11-20	2	7	18	-	27	15.17%
21-30	2	20	29	3	54	30.33%
31-40	2	25	13	8	48	26.97%
41-50	3	13	8	6	30	16.85%
51-60	2	3	-	11	16	8.99%
61-70	-	1	-	2	3	1.69%
Total	11	69	68	30	178	100.00%

TABLE NO. 1: AGE DISTRIBUTION

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Lesion	No. of case	Percentage
Inflammatory	11	7.43%
Fibroadenoma	64	43.24%
Fibrocystic Disease	23	15.54%
Fibroadenosis	36	24.32%
Benign Phyllodes	1	0.68%
Ductal epitheliosis	3	2.03%
Lipoma	1	0.68%
Gynaecomastia	7	4.73%
Duct papilloma	2	1.35%
TOTAL	148	100%

TABLE NO. 2: DISTRIBUTION OF NON MALIGNANT BREAST LESIONS

Lesion	No. of case	Percentage (%)
Duct cell carcinoma	26	86.66%
Duct cell carcinoma – medullary	2	6.66%
Duct cell carcinoma – papillary type	1	3.33%
Metaplastic squamous cell carcinoma –	1	3.33%
TOTAL	30	100%

TABLE NO. 3: DISTRIBUTION OF MALIGNANT BREAST LESIONS

Sl. No.	Statistical Index	Result
1	Sensitivity	87.5%
2	Specificity	100%
3	Positive Predictive Value	100%
4	Negative Predictive Value	97.14%
5	False Positive ratio	0%
6	False Negative Ratio	12.5%
7	Accuracy	97.62%

TABLE NO. 4: STATISTICAL VALUES

		Histopathological	Examination
	With Biopsy	Consistent	Inconsistent
Cytology			
Breast abscess	2	2	-
Plasma cell mastitis	1	1	-
Fibroadenoma	26	26	-
Fibrocystic change	1	1	-
Fibrodenosis	1	1	-

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Benign phyllodes	1	1	-
Duct epitheliosis	1	-	1
Gynaecomastia	1	1	-
Duct papilloma	1	1	-
Malignancy	7	7	-

TABLE NO. 5: CYTOHISTOLOGICAL CORRELATION

Diagnosis	No. of Cases diagnosed in FNAC	No. of Cases consistent with HPE	No. of cases inconsistent with HPE	% of consistency
Inflammatory	3	3	00	100%
Fibro adenoma	26	26	00	100%
Fibrocystic disease	01	01	00	100%
Fibroadenosis	01	01	00	100%
Benign phyllodes	01	01	00	100%
Gynaecomastia	01	01	00	100%
Duct papilloma	01	01	00	100%
Malignancy	07	07	00	100%
TOTAL	41	41	00	100%

TABLE NO. 6

No.	Study	Sensitivity	Specificity	Positive Predictive value	Negative predictive value	Accuracy
1	Langmuir et al ¹⁵	90	94	-	-	-
2	Park et al ¹⁶	76.9	91.6	-	-	-
3	Nggada et al ¹⁷	95.7	98.7	-	-	97.7
4	Aziz M et al ¹⁸	85.29	100	100	98.79	82.02
5	Feichter et al ¹⁹	89.9	99.3	----	----	88.5
6	Mehmood et al ²⁰	94.1	96	----	----	95.5
7	Callaco et al ²¹	92.1	98.6	99.4	98.1	----
8	Kamphausen et al ²²	90	100	100	90	----
9	Current Study	87.5	100	100	97.14	97.62

TABLE NO. 7: CORRELATION WITH OTHER STUDIES

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Figure 1: FNAC of periductal mastitis: smear shows plenty of anucleate squames.

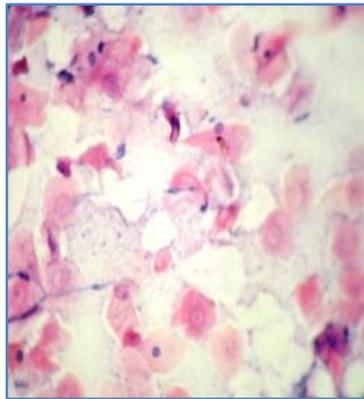


Fig. 1

Figure 2: FNAC Fibroadenoma Branching monolayered bland ductal epithelial cells with bare nuclei in the background.

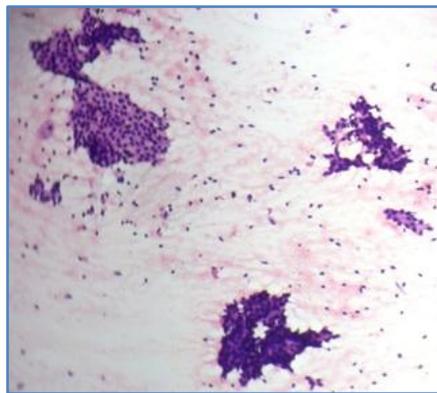


Fig. 2

Figure 3: HPE fibroadenoma - patent and compressed ducts surrounded by stromal tissue.



Fig. 3

Figure 4: FNA Papillary carcinoma diagnosed as IDC.

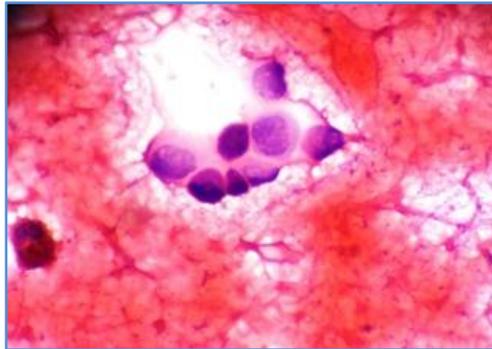


Fig. 4

Figure 5: Paget's cells in the epidermis- large cells in cluster and singles with clear cytoplasm and hyperchromatic nuclei.



Fig. 5

Figure 6: Comedocarcinoma with squamous differentiation.

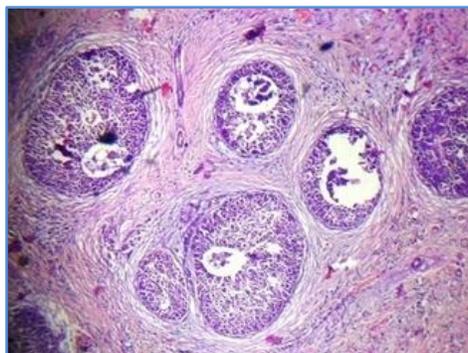


Fig. 6

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