

PROSPECTIVE STUDY OF CYTO HISTOPATHOLOGICAL CORRELATION OF BREAST LESIONS

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ABSTRACT: INTRODUCTION: Cancer of breast is the second most common cause of cancer in women. In the present era, late marriage, late child birth, shorter period of breast feeding and nulliparity or low parity have contributed to increase in the number of cases. Fine needle aspiration cytology (FNAC) is a useful method for initial evaluation and diagnosis of breast cancers and it has the ability of providing necessary prognostic predictive information. **AIMS AND OBJECTIVES:** The aim of the present study is to evaluate the accuracy of FNAC of breast lesions with histopathological correlation. To study the cytomorphological features of palpable breast lumps. To study the various cytological patterns in aspirates from breast lesions and to classify them into non-neoplastic, benign and malignant lesions. To correlate the cytology findings with subsequent histopathological diagnosis wherever possible. To establish accuracy and efficacy of aspiration cytology as an early and preoperative diagnostic aid. To compare the statistical analysis of present study with other contemporary studies. **MATERIALS AND METHODS:** The present study includes the study of aspiration smears of all cases referred to the Department of Pathology, Andhra medical college, Visakhapatnam from various outpatient departments from King George Hospital, with a palpable breast lesion. True cut Biopsy and Mastectomy specimens for Histopathological correlation **RESULTS:** Out of 952 analyzed cases benign lesions were 691(72.58%), malignant lesions were 146(15.33%), non-neoplastic lesions were common in the age group of 21-30 years, benign lesions in 21-30 years, and malignant lesions were common in the age group of 41-50 years. Majority of the patients were female with 913(95.90%) and male patients are 39(4.09%). The results of sensitivity (97.18%), specificity (98.74%), positive predictive value (97.18%) and negative predictive value (98.74%) with diagnostic accuracy of 98.26%. **CONCLUSION:** FNAC has been found to be a most valuable, cost effective and safe diagnostic procedure in the work up of breast lesions providing more direct information of underlying pathological condition. The present study support the view that FNAC of breast should be the initial diagnostic procedure in the evaluation of breast lesions to reduce the number of patients subjected to unnecessary surgical intervention.

KEYWORDS: Fine needle aspiration cytology, Histopathology, Infiltrative duct cell carcinoma.

INTRODUCTION: Cancer of breast is the second most common cause of cancer in women. In the present era, late marriage, late child birth, shorter period of breast feeding and nulliparity or low parity have contributed to increase in the number of cases. Clinically the diseases of breast present with lump in breast or nipple discharge. Palpable breast lump is a common diagnostic problem and a constant source of anxiety for the patients as well as the surgeons, because of the risk of cancer and the cosmetic disfigurement following surgery.

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Fine Needle Aspiration Cytology is an important part of triple assessment¹ (clinical examination, imaging and FNAC) of palpable breast lumps although histopathological diagnosis is a universally accepted confirmatory mode of diagnosis and follow up. Most cases of breast lumps are benign. FNAC is quick, simple, cost effective and less traumatic as well as highly sensitive and specific method for assessment of breast lump.

FNAC is the least invasive technique of obtaining a cell diagnosis and very accurate if both the surgeon and cytologist are experts. Excisional Biopsy was an accepted practice in the past, but a preoperative diagnosis by FNAC offers several advantages.^{2,3} FNAC is the first line of investigation for all breast lesions and also useful in the diagnosis of inoperable or recurrent breast cancer and even as a treatment for benign cystic lesions.

AIMS AND OBJECTIVES: The aim of the present study is to evaluate the accuracy of FNAC of breast lesions with histopathological correlation. To know the incidence of different breast lesions over a period of 22 months from December 2012 to September 2014. To undertake prospective study of various breast lesions in relation to age and sex distribution. To study the cytomorphological features of palpable breast lumps.

To study the various cytological patterns in aspirates from breast lesions' and to classify them into non-neoplastic, benign and malignant lesions. To correlate the cytology findings with subsequent histopathological diagnosis wherever possible. To establish accuracy and efficacy of aspiration cytology as an early and preoperative diagnostic aid. To compare the statistical analysis of present study with other contemporary studies.

MATERIALS AND METHODS: The present study includes the study of aspiration smears of all cases referred to the Department of Pathology, Andhra medical college, Visakhapatnam from various outpatient departments from King George Hospital, with a palpable breast lesion. The period of study is from December 2012 to September 2014. The total number of breast lesion aspirations done was 1012 and we obtained specimens of various types' viz., true cut biopsy and mastectomy for histopathological correlation in 230 cases.

Proper clinical history was taken and cytology aspirations of breast lumps done under aseptic conditions were fixed for 15-30 minutes with isopropyl alcohol and stained with Haematoxylin & Eosin.

The specimens received were fixed in 10% formalin for 24 hours, routinely processed and stained with haematoxylin and eosin.

RESULTS: In the present study 1012 cases with breast lesions were analyzed, for a period of twenty two months from December 2012 to September 2014 at the department of pathology, Andhra medical college Visakhapatnam.

Cytological diagnosis of these cases are divided into non neoplastic, benign, and malignant. Cytological diagnosis of the cases are divided into non neoplastic, benign, and malignant. Out of 952 analyzed cases benign lesions are 691(72.58%), malignant lesions are 146(15.33%).

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In the present study non-neoplastic lesions are common in the age group of 21-30 years, benign lesions in 21-30 years, and malignant lesions are common in the age group of 41-50 years.

In the present study majority of the patients are female with 913(95.90%) and male patients are 39(4.09%).

In the present study in cytology non-neoplastic lesions include Inflammatory lesions which have abscess, nonspecific mastitis, and granulomatous mastitis. Other lesions of non-neoplastic lesions include benign cystic lesions, galactocele and fat necrosis. Majority of the lesions are Inflammatory lesions with 55.62%.

In the present study Benign lesions include fibroadenoma, fibroadenosis, fibrocystic change, phylloides tumor, duct papilloma, gynaecomastia and epithelial hyperplasia. Fibroadenoma has 49.92% followed by fibroadenosis and fibrocystic change.

In the present study Duct cell carcinoma 141 cases, medullary 4 cases and one mucinous carcinoma are diagnosed in cytology.

In the present study in Histopathology majority of the lesions are fibroadenoma 45.28% followed in incidence by Infiltrative ductal carcinoma NOS, Other carcinomas, Fibrocystic change, Usual Ductal hyperplasia and Gynaecomastia.

In the present study Malignant lesions in Histopathology are Infiltrative duct cell carcinoma with 86.4% followed by Medullary carcinoma, Malignant phylloides, Neuroendocrine carcinoma, Mucinous carcinoma, Infiltrating secretary carcinoma and the total number of malignancies are 125.

In the present study in epithelial lesions Invasive ductal carcinoma NOS 108(72%), followed by other carcinomas 17(11.33%) Usual Ductal hyperplasia, fibroadenosis follows. In the present study in histopathology of Fibro epithelial tumors Fibroadenoma 168(86.15%) is followed by Fibrocystic change and Phylloides tumor. (Fig. 6, 7)

Histopathological correlation was possible in 230 cases which showed Two cases of fibroadenoma deferred in histopathology to fibrocystic change and fibro adenosis respectively as both the conditions are benign these two cases are neither false positives nor false negatives. But deferred within benign lesions. So the number of cases deferred is six. (Table 3)

Two cases of atypical ductal hyperplasia deferred to fibroadenoma with apocrine change and fibroadenoma. One case each of epithelial hyperplasia and benign breast lesion deferred to infiltrative ductal carcinoma, two cases of fibroadenoma deferred to fibro cystic change and fibro adenosis

The results of sensitivity (97.18%), specificity (98.74%), positive predictive value (97.18%) and negative predictive value (98.74%). Importantly diagnostic accuracy in present study of 98.26% proves the worth of FNAC as diagnostic modality and hence its utility.

DISCUSSION: A 22 month study was done to evaluate the diagnostic utility of fine needle aspiration cytology of breast lesions. Age of patient varied from 9-90 yrs. Most of the benign cases were in 21-30 yrs age group and malignant cases were in 41-50 yrs. age group. Out of total 1012 cases, male patients were 39(4.09%) and females were 973 (95.90%).

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Out of 1012 cytology cases inadequate 60(5.92%), non-neoplastic 115(12.07%), benign 691(72.58%), and malignant 146(15.33%). Smears were reported as inadequate 60(5.92%) because of scant cellularity and hemorrhagic aspirate. (Table 1) Out of remaining 952 cases, 230 cases were received for histopathological correlation. Out of 1012 cases, right side 587 (58.1%) was commonly involved than the left side 390(38.6%). In malignant cases, lump was commoner on left side 89(61.3%) than on right side 56(38.7%). Upper outer quadrant 515(50.9%) commonly involved than upper inner quadrant 173(17.1%).

We have encountered an interesting case of 30 years old female previously diagnosed as mucinous carcinoma left breast now presented with right breast lump and growth in the scar area of the left breast which showed mucinous carcinoma. (Fig. 3, 4, 5). Usually mucinous carcinoma occurs in the age group of 50-60 years and better prognosis, but in this case age of occurrence was 30 years and bilateral involvement of breast was seen with poor prognosis.

We have also encountered another case of 48 years old female, breast mastectomy specimen, cut section showing 6x4 cm grey white firm to hard area, microscopically showing squamoid nature of tumor cells diagnosed as Metaplastic carcinoma breast. (Fig. 8, 9).

In cytology Fibroadenoma 345(49.92%) was commonest followed by fibroadenosis 155(22.43%), and fibrocystic change 128(18.52%) in benign conditions. Amongst malignancies, commonest lesion was IDC-NOS 141(96.57%) (Fig 1, 2), followed by medullary carcinoma 3(2.73%).

One case of infiltrating duct cell carcinoma falsely reported as benign breast lesion in cytology. One case of infiltrating duct cell carcinoma reported as epithelial hyperplasia without atypical in cytology. Two cases of atypical ductal hyperplasia in cytology diagnosed as fibroadenoma with apocrine change and fibroadenoma consecutively in histopathology. Two cases of fibroadenoma reported as fibrocystic change, and fibro adenosis. (Table 3) Positive cytohistopathological correlation was seen in 224 cases of 230. (Table 2)

Age wise distribution of cases showed that maximum number of patients with breast lump attending cytology OPD were from 21-40 yrs. age group. Similar results were obtained by Tiwari et al⁴ (2007). Ariga et al⁵ (2002) also showed maximum patients in 21-40 yrs. age group.

The distribution of benign and malignant cases showed that benign cases were most common in 21-30yrs (36.17%) age group, followed by 31-40 yrs. (31.98%) and 11-20 yrs. (17.65%) and malignancy was common in 41-50 yrs. (29.45%) age group followed by 31-40 yrs. (26.02%) and 51-60 yrs. (26.02%) age group. Our findings were well correlated with Tiwari *et al*,⁴(2007), Sunita Saxena *et al*,⁶ (2005), Ariga *et al*,⁵ (2002) and Sandhya P Iyer *et al*,⁷(2008) Nilay Chakrabarti *et al*(2009).

The commonest presenting symptom was lump in breast seen in 98.8% followed by pain in breast 25.4%, nipple discharge 12.6%, inversion 6.6% and ulcer 1.2%. The other miscellaneous complaints were menstrual irregularities, malaise, and anorexia and weight loss especially in malignant cases.

Lumps were commoner on right side in 588 cases (58.1%) than on left side in 391 cases (38.6%). Lump in the bilateral breast were found in 33 cases (3.3%). In malignancies, lumps were commoner on left side (61.3%) than on right side (38.7%) as in literature (Sainsbury *et al*,⁸ 2008; Patrikar *et al*,³ 2008; Amrikachi *et al*,⁹ 2001). The upper outer quadrant was most commonly involved in both benign (50.3%) as well as malignant (52.5%) cases.

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Most of the mobile lesions were benign (98.4%) except a case of breast abscess and three cases of granulomatous mastitis which were immobile. Amongst the malignancies, most were immobile except fifteen cases of IDC-NOS diagnosed which were mobile. Thus early carcinomas could be mobile and produce erroneous clinical impression.

Most of the benign cases were firm on palpation. On the other hand most of the malignant cases were hard usually stony hard on palpation.

In our study out of total 146 malignant cases, 30(21.3%) showed metastatic deposits in the lymph node.

Thin straw colored aspirate in 16 cases of fibrocystic disease and 4 cases of fibroadenoma. Most of the fibroadenomas (73.4%) yielded whitish aspirate along with 7 cases of gynaecomastia and 5(6.3%) cases of malignancy. Most of the malignant cases (83.8%) yielded hemorrhagic aspirate while hemorrhagic aspirate with granularity was seen in 7(8.8%) malignant cases. One case of malignancy showed creamish aspirate. Purulent aspirate was seen in abscess and granulomatous lesion.

Out of 691(72.58%) benign cases, fibroadenoma (49.92%) was most frequent followed by fibroadenosis (22.43%), and fibrocystic disease (18.52%) and. Least common lesions were simple cyst (0.3%), lipoma (0.3%). Sandhya P Iyer et al⁷ (2008) also reported fibroadenoma (35%) most common benign breast lesion.

The results of previous studies show values of sensitivities ranging from 84% to 97.1%, specificities from 96% to 100%, positive predictive values ranging from 79.3% to 100%, negative predictive values from 89.36% to 98.79%. (Table 4)

The present study the sensitivity was 97.18% approximately equivalent to Zhang Qin et al,¹⁰ the highest sensitivity was reported by Zhang Qin et al.¹⁰

Regarding specificity in the present study showed 98.74% specificity which is almost equal to Jan et al.²

The positive predictive value in the present study is 97.18% Negative predictive value is 98.74%. The overall diagnostic accuracy in the present study is 98.26% which is almost equal to Zhang Qin et al.¹⁰

The present study confirms the view that FNAC has potential ability to detect both benign and malignant lesions with high accuracy. Thus FNAC can be effective and safe diagnostic method for defining breast lesions and most useful tool in the diagnosis of breast lesions.

CONCLUSION: Fine-needle aspiration cytology is a patient friendly, easy, reliable, repeatable and simple diagnostic test. It is a quick and safe OPD procedure to diagnose breast lesions and can be employed at the bed side. When performed by an expert pathologist, the diagnostic accuracy of FNAC is very high. A high sensitivity and a high positive predictive value proved that a positive FNAC in the breast means a definite diagnosis of the concerned pathology when compared with the final histology report.

The high specificity and a high negative predictive value for malignancy illustrated the high accuracy of FNAC in the diagnosis of malignancy in the breast. Aspiration cytology differentiates between benign and malignant condition preoperatively, so reduces patient's anxiety and also helps the surgeon to plan the surgery. FNAC also gives cytological grade of

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malignant lesion which correlates well with histopathological grade, which is also one of the prognostic criteria. FNAC has reduced the rate of open biopsies and hence the surgical workload.

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OBSERVATIONS	NO. OF CASES	PERCENTAGE
Inadequate aspirations	60	5.92%
Total number of cases analyzed	952	94.07%
Non neoplastic lesions	115	12.07%
Benign lesions	691	72.58%
Malignant lesions	146	15.33%
Total number of breast aspirations	1012	

Table 1: Cytological Observations

Lesions	No. of cases	Percentage
Fibroadenoma	130	58.03%
Infiltrative duct cell carcinoma	69	30.8%
Fibrocystic change	08	3.57%
Phylloides	05	2.23%
Gynaecomastia	04	1.78%
Abscess	04	1.78%
Miscellaneous	04	1.78%
Total	224	100%

Table 2: Cytohistopathological positively correlated cases (n=224)

Cytology diagnosis	No. of cases	Histopathological diagnosis
Atypical ductal hyperplasia	2	Fibroadenoma & fibroadenoma with apocrine change
Fibroadenoma	2	Fibro cystic change & fibro adenosis
Benign breast lesion	1	Infiltrative duct cell carcinoma NOS
Epithelial hyperplasia	1	Infiltrative duct cell carcinoma NOS
Total no. of cases	6	

Table 3: Deferred cases in cytology and histopathology (n=6)

Sl. No.	Study	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
01	Colloco et al ¹¹ (1999)	92.1	98.1	99.4	98.1	-
02	Feichter et al ¹² (1997)	89.9	99.3	-	-	88.5
03	Jan et al ² (2002)	92.6	98.48	.	-	-

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04	Mehmood et al ¹³ (2003)	94.1	96.0	-	-	95.5
05	Dennison et al ¹⁴ (2004)	90	-	-	.	-
06	Bangash et al ¹⁵ (1994)	87.81	-	-	-	-
07	Zhang Qin et al ¹⁰ (2004)	97.1	97.3	-	-	97.2
08	Present Study (2015)	97.18	98.74	97.18	98.74	98.26

Table 4: Correlation with other studies

Figure 1: Photo micrograph showing discretely arranged atypical pleomorphic cells with hyperchromatic nuclei in duct cell carcinoma. (H & E 40x)

Figure 2: Photo micrograph showing Infiltrating duct cell carcinoma, with comedo type of necrosis. (H & E 100x)

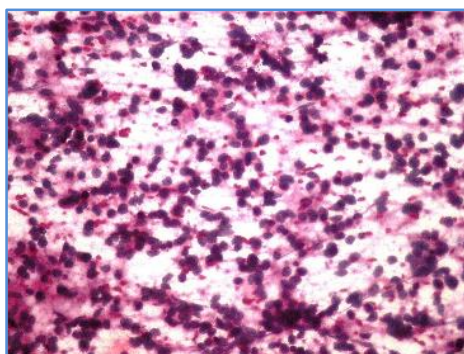


Figure 1

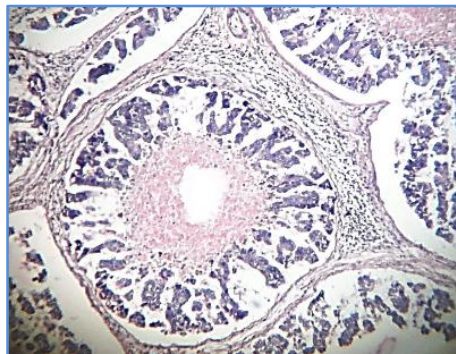


Figure 2

Figure 3: Clinical photograph showing; 30 year female with operated left breast & now presented with right breast lump.

Figure 4: Photo Gross specimen, Cut section showing growth of 5x4cms, grey white with axillary pad of fat showing lymph nodes.



Figure 3



Figure 4

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Figure 5: Photo micrograph showing Clusters of atypical ductal epithelial cells floating in pools of mucin. (H&E, 100x)

Figure 6: Photo gross specimen, Cut section showing grey white tumor with lobulated appearance.

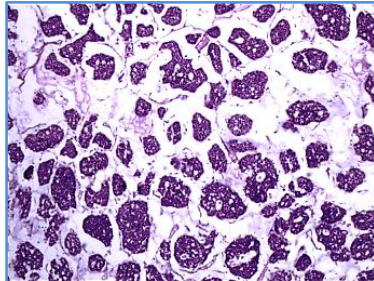


Figure 5



Figure 6

Figure 7: Photo micrograph showing spindle shaped cells in phylloides tumor. (H & E 100x)

Figure 8: Photo Gross specimen Cut section showing grey white irregular growth measuring 6x4 cm.

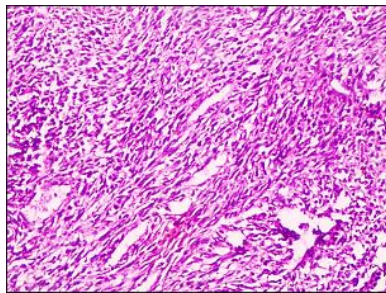


Figure 7



Figure 8

Figure 9; Photo micrograph showing sheets of Ductal epithelial cells with squamoid change showing abundant eosinophilic cytoplasm, nucleus with prominent nucleoli and keratin material (H & E; 100x).

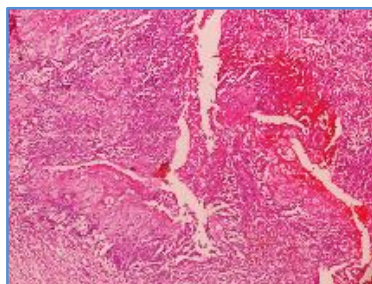


Figure 9

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