

## Cytological study of palpable breast lumps with their histological correlation

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### ABSTRACT

**Background:** FNAC is an inexpensive and highly accurate means of diagnosing both benign and malignant breast lesions. The procedure provides a rapid and non-morbid diagnosis before the operation which enables the patient and the surgeon to discuss and plan therapeutic alternatives in a rational atmosphere.

**Objectives:** To evaluate role of fine needle aspiration cytology in the diagnosis of breast lesions and to compare the cytological findings with the histopathology wherever possible. In addition the sensitivity, specificity and accuracy of FNAC in breast lesions are carried out.

**Material and Methods:** The present study was carried out on 200 patients who presented with palpable lump in the breast in the Department of Pathology, Government Medical College, Patiala over a period of 2 years. Cytological Diagnosis was correlated with histological findings wherever possible.

**Results:** Cytologically, the lesions were categorized into 4 major categories, benign 143 (71.5%), malignant 37 (18.5%), suspicious or atypical 10 (5%) and unsatisfactory 10 (5%). Out of these 200 cases, 85 cases (42.5%) were available for histopathological examination. The most common benign lesion in this study was fibroadenoma 23/52 (44.2%) and the most common malignant lesion was infiltrating ductal carcinoma (28/33) Diagnostic accuracy of FNAC for benign lesion was 94.2% while for malignant lesion, it was 96.7%. The sensitivity, specificity and overall diagnostic accuracy of FNAC came out to be 93.7%, 98.1% and 96.4% respectively.

**Conclusion:** FNAC is a simple and reliable method for diagnosis of both benign and malignant lesions quite accurately thus reducing unnecessary surgeries. The present study proved that the procedure has high sensitivity, specificity and diagnostic accuracy. Though it cannot categorize the lesion in some cases but it can rule out malignancy in most of the cases. Considering its low cost and quick results, it can be a potential tool for screening of breast cancers.

**Key words:** Breast lump, FNAC, mastectomy, malignancy

### Introduction

Fine needle aspiration cytology (FNAC) is an inexpensive and highly accurate means of diagnosing both benign and malignant breast lesions and it can replace frozen section diagnosis if supplemented with ancillary techniques like flow-cytometry and cell block preparation. In fact it has the advantage of providing a rapid and non-morbid diagnosis before the operation. This situation enables the patient and the surgeon to discuss and

plan therapeutic alternatives in a rational atmosphere. As with any other technique, experience of the aspirator and diagnostician minimizes false positive and false negative rates. [1] The management of breast disease needs a well planned, coordinated strategy not only in treatment but also in diagnostic interventions. The use of preoperative diagnostic techniques like FNAC allows better use of resources, including operating time and reduces patient's

anxiety.<sup>[2]</sup> FNAC is a valuable technique which has gained a lot of popularity. This is quite a simple procedure and early results are available. But in inexperienced hands sufficient cells may not be obtained in every patient. There are large numbers of false positive and false negative cases, and a combination of FNAC with some simple procedures like intraoperative imprint cytology helps to reach 100% accuracy.<sup>[3]</sup>

The present study has been conducted to evaluate the role of FNAC in the diagnosis of palpable breast lesions in terms of sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the procedure using the standard statistical formulas. Thus the efficiency of this procedure to detect benign and malignant lesion and to clearly rule out malignant lesion will be checked. The results of our study will be compared with similar studies conducted in India and abroad. The study will also be used to find out frequency of various benign and malignant lesions of breast along with their age and quadrant-wise distribution as most of the breast lesions are benign in nature and thus pre-operative cytological diagnosis can reduced unwanted surgeries thus reducing the morbidity.

### Material and Methods

The present study was carried out on 200 patients who presented with palpable lump in the breast in the department of Pathology, Government Medical College, Patiala over a period of 2 years. FNAC was done with a franzen's handle with a 10 ml syringe attached. The material aspirated was routinely stained with May Grunwald Giemsa stain (MGG). Some slides were kept for other stains wherever needed. The histological sections of the

mastectomy and lumpectomy specimens were stained with haematoxylin and eosin stain. The cytological diagnoses were compared with histopathology wherever possible. The positive predictive values and diagnostic accuracy were calculated using standard formulas.

The following statistical methods were used in the study conducted.<sup>[4]</sup>

True positive: These were the patients with malignant disease, positive cytological results confirmed on histopathology

True Negative: These were the patients without malignant disease, negative cytological results confirmed on histopathology

False positive: These were the patients diagnosed positive on cytology but on histopathology the results turned out to be negative for malignancy.

False Negative: These were the patients diagnosed negative on cytology but on histopathology the results turned out to be positive for malignancy.

Sensitivity: It is calculated as

$$\frac{\text{True positive}}{\text{True Positive} + \text{False Negative}} \times 100$$

Specificity: It is calculated as

$$\frac{\text{True negative}}{\text{True negative} + \text{False Positive}} \times 100$$

Diagnostic accuracy: It is the proportion of correct results in relation to all the cases studied. It is calculated as

$$\frac{\text{True Positive} + \text{True negative}}{\text{True positive} + \text{false negative} + \text{true negative} + \text{false positive}} \times 100$$

### Results

Cytological diagnoses were broadly classified into 4 categories; benign, malignant, suspicious and unsatisfactory. For all practical proposes suspicious cases

were considered as malignant and lumpectomy was strongly advised in all the suspicious cases. Of the 200 cases examined cytologically, 143 cases i.e. 71.5 % were categorized as having benign cytology, thirty 37 cases i.e. 18.5 % were categorized as malignant, 10 cases i.e. 5% were categorized as suspicious and 10

cases i.e. 5% were categorized as inadequate. Out of eighty five cases available for histopathological examination thirty three (33) came out to be malignant while fifty two (52) came out to be benign by histopathological examination.(Table1)

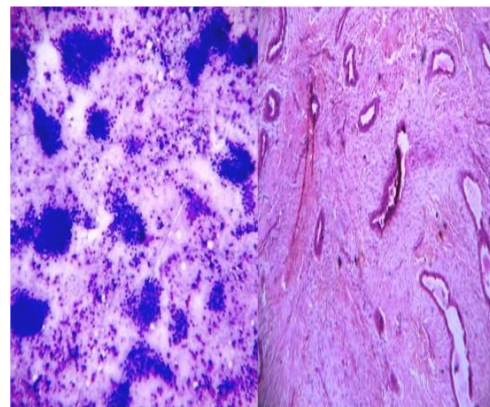
**Table 1: Cytohisto-correlation in 85 follow up cases**

Sr No	Cytological Diagnosis	No.of cases	HPE available in	HP diagnosis		False positive	False Negative
				Benign	Malignant		
1	Benign	143	52	49	03	-	03
2	Malignant	37	24	01	23	01	-
3	Suspicious/Atypical	10	07	00	07	-	-
4	Unsatisfactory	10	02	02	00	-	-
<b>Total</b>		<b>200</b>	<b>85</b>	<b>52</b>	<b>33</b>	<b>01</b>	<b>03</b>

In the present study the most common benign lesion was fibroadenoma with 23 cases out of total 52 cases i.e. 44.23%. The lesion was characterized by large branching sheets of bland epithelial cells and fragments of fibromyxoid stroma in the background of benign bipolar nuclei. (Fig. 1)

There were 19/52 i.e. 36.53 % cases of fibrocystic disease which is characterized by sheets of ductal epithelial cells of apocrine type and scattered single bipolar nuclei in the background of variable amount of cyst fluid and macrophages. Four cases (7.69%) of breast abscess showed both acute and chronic inflammatory cells along with ductal

epithelial cells showing regenerative atypia. 2 cases (3.84%) of Gynaecomastia were diagnosed.



**Fig. 1** Cytology of fibroadenoma showing typical antral horn pattern and myoepithelial cell in the background and corresponding histology showing hyperplasia of ducts & stroma

There was presence of epithelial fragments along with single bipolar nuclei. Moderate nuclear variation and atypia was also seen in the epithelial cells. One case of intraductal papilloma was diagnosed. The smear showed multiple fingers like fragments of ductal epithelial cells with fibro vascular core. The background showed variable amount of benign bipolar nuclei and macrophages. One case of cystosarcoma phylloides was diagnosed. Cytologically the lesion was characterized predominantly by fragments of myxoid stroma and groups of ductal epithelial cells in the background of numerous fibroblast types of bare bipolar nuclei. One case of fibroadenosis was diagnosed which showed groups of ductal epithelial cells showing acinar pattern at places in the background of bare bipolar nuclei.

One case of breast abscess was proved to be plasma cell mastitis on histology. There was intense chronic inflammatory infiltrate along with many plasma cells which leads this diagnosis.

In the present study the most common malignant lesion was infiltrating ductal carcinoma having 28/33 cases i.e. 84.8%. (Table 2) The smear was highly cellular with tumor cell showing loss cohesion, nucleomegaly, increased nucleo-cytoplasmic ratio and marked nuclear pleomorphism. There were no bare bipolar nuclei or the myoepithelial cells. (Fig. 2) The background consists of necrotic debris and blood.

One case of combined malignancy (IDC+ILC) was diagnosed which showed

both ductal lobular epithelial cells. The lobular component was characterized by round uniform looking cells with hyperchromatic nuclei and scanty cytoplasm. There was typical Indian file arrangement of tumor cells at places. One of the suspicious cases turned out to be infiltrating lobular carcinoma on histology. The smear showed scanty cellularity but the cells were definitely malignant but the exact nature of the tumor cells was not identified. One case of medullary carcinoma was diagnosed. The smear showed highly anaplastic cells with lymphocytes around the tumor cells. The possibility of medullary carcinoma was considered which was proved on histology.

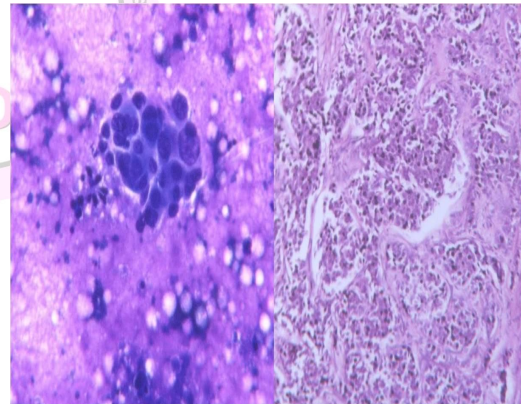


Fig.2 Cytology of IDC showing malignant ductal epithelial cells & subsequent histopathology of the same case

Another suspicious case turned out to be ductal carcinoma in situ. The cells were showing atypical nuclei but the loss of polarity was not as much as in infiltrating ductal carcinoma. One case of cystosarcoma phylloides was proved to be malignant fibrous histiocytoma (MFH) on histology. The smear showed scanty

cellularity with most of the tumor cells showing spindle shaped nuclei.

So the sensitivity of the FNAC in our study comes out to be 93.7% while specificity of the procedure is 98.1%.

There is 96.7% value for a positive test while 96.2% value for a negative test. The overall accuracy of the procedure comes out to be 96.4%

**Table 2: Malignant lesions confirmed on histopathology (n=33)**

	<i>Diagnosis on HP</i>	<i>No. of cases</i>	<i>Percentage</i>
<b>1</b>	Infiltrating ductal carcinoma (IDC)	28	84.8
<b>2</b>	Infiltrating ductal carcinoma + Infiltrating lobular carcinoma (IDC +ILC)	01	3.0
<b>3</b>	Infiltrating lobular carcinoma (ILC)	01	3.0
<b>4</b>	Medullary carcinoma (MC)	01	3.0
<b>5</b>	Ductal carcinoma in situ (DCIS)	01	3.0
<b>6</b>	Malignant Fibrous Histiocytoma (MFH)	01	3.0
	<b>Total</b>	<b>33</b>	<b>100</b>

For fibroadenoma the maximum patients were between age group 21-30 (11/23 i.e. 47.8%) followed by age groups 31-40 (8/23 i.e. 34.7%). There were three (03) cases i.e. 13.0% in the age group (11-20 years) one patient was 42 years old. For fibrocystic disease the maximum patients were between 31-40 years (11/19 i.e. 57.8%) followed by the age 21-30 years (03/19 i.e. 15.7%). There were two (02) cases i.e. 10.5 % each in the age groups 41-50 and 51-60 years and one of the patients was 65 year old. Infiltrating ductal carcinoma was found maximum in fifth decade (41-50) having 09/28 i.e. 32.14% cases followed by 08/28 cases i.e. 28.57% in the age group (31-40) years. There were 05/28 i.e. 17.85% cases in 51-

60 age group and 03/28 i.e. 10.71% cases in 61-70 age group. One patient of IDC was 75 years old female.

For fibroadenoma maximum number of cases (15/23 i.e. 65.21%) were seen in the upper outer quadrant followed by 03/23 cases i.e. 23.80% in the central quadrant. There were 02/23 cases i.e. 11.90% in both upper inner and lower inner quadrant. There was one case in the lower outer quadrant. For fibrocystic disease maximum number of cases (05/19 i.e.26.31%) was seen in the upper outer and central quadrant followed 03/19 cases i.e. 15.78% each in the upper inner, lower outer and lower inner quadrant. For IDC maximum number of patients were seen in the upper outer quadrant (14/28

i.e. 50%) followed by 5/28 cases i.e. 17.85% in the central quadrant. There were 4/28 cases i.e. 14.28% in the upper inner quadrant, 03 cases i.e. 10.71% in the lower outer and 02 cases i.e. 7.14% in the lower inner quadrant.

For fibroadenoma, out of twenty two (22) cytologically diagnosed cases, eighteen (18) turned out to be same on histopathology while four (04) cases were diagnosed to be fibrocystic disease. So the accuracy in diagnosing fibroadenoma by FNAC came out to be 81.8 % in this study. For fibrocystic disease, out of seventeen (17) cytologically diagnosed cases, twelve (12) came out to be same on histopathology, two (02) cases were diagnosed as fibroadenoma, two (02) cases were diagnosed as infiltrating ductal carcinoma and one (01) case was diagnosed as fibroadenosis. So the accuracy in diagnosing fibrocystic disease by FNAC came out to be 70.5 % in this study.

For twenty two (22) cases of infiltrating ductal carcinoma on cytology, twenty one (01) was proved to be same while one case was proved to be fibrocystic disease on histopathology. So the accuracy in diagnosing infiltrating ductal carcinoma by FNAC came out to be 95.4% in this study.

## Discussion

“Fine-needle aspiration (FNA) biopsy is an established and highly accurate method for diagnosing breast lesions.” The use of core biopsy (CB) is being increasingly advertised but its procedure is more cumbersome, expensive and time consuming as compared to FNA procedure.<sup>[5-7]</sup>

“Although fine-needle aspiration (FNA) biopsy of the breast has been

shown to be a safe and accurate technique, many surgeons question whether it is reliable enough to replace excisional biopsy. If FNA biopsy is followed by an excisional biopsy for confirmation, it would seem that the cost of diagnostic workup would be increased, but it has been seen that FNA biopsy is cost effective even when followed by an excisional or frozen section biopsy for confirmation. It is considered safe and reasonable to expand its use to smaller hospitals where the personnel may be initially less experienced with the technique”.<sup>[8,9]</sup>

The present study was conducted at Department of Pathology, Government Medical College Patiala to find out the cytological patterns of various palpable breast lesions and to correlate the cytological diagnosis with histopathology wherever possible so as to find out the false positive rate, false negative rate, positive predictive values and diagnostic accuracy of the procedure.

In the present study the most common benign lesion was fibroadenoma having 23 cases (44.23%) out of 52 histologically confirmed benign cases. Park & Ham and Choi et al found similar incidence of fibroadenoma in their studies having 50% and 55.6% cases respectively.<sup>[10,11]</sup> Fibroadenoma are easy to diagnose in most of the cases because of typical antral horn type clusters and bipolar population of cells however if the size of the mass is large and cells shows atypia, a cautious approach is needed and excision biopsy should be advised. (Fig 1) Most of the cases of fibroadenoma occur in young patients and many patients give history of pain during menstruation.

There were 28 (84.84%) confirmed cases of infiltrating ductal carcinoma (IDC)

out of 33 histologically confirmed malignant cases. Most of the smears of IDC were highly cellular with cells showing frank malignant changes like nuclear hyperchromasia, high nucleocytoplasmic ratio and irregular nuclear margins. (Fig 2) Silverman et al found similar incidence of infiltrating ductal carcinoma (94.44%).<sup>[13]</sup> Infiltrating ductal carcinoma shows different types of variation like mucinous change, squamous metaplasia and malignant squamous component.

In the present study, there were 143 cases diagnosed under the benign category from which 52 cases were available for histological follow up. Out of these 52 confirmed cases, 49 cases were found to be benign while three cases were found to be malignant (false negative cases). Of these 3 cases, two were infiltrating ductal carcinoma (IDC) while one case was turned to be malignant fibrous histiocytoma (MFH).

Out of 37 cytologically diagnosed malignant cases, 24 were available for histology. Of these histological confirmed cases, 23 were proved to be malignant while one case was proved to be benign (false positive case).

Out of 10 cases of suspicious or atypical category, 7 were available for histology. All the 7 cases proved to be malignant with 5 cases diagnosed as IDC, one case as ILC and one case as DCIS.

In the present study there was one false positive case (1.9%). This case was diagnosed as infiltrating ductal carcinoma breast but on subsequent histology, it proved to be fibrocystic disease with marked atypia of the lining epithelium. Various studies have shown many cases of fibroadenoma and fibrocystic disease which turned out to be malignant on cytology.

There were 3 false negative cases in the present study (9.09%). 2 cases were diagnosed as fibrocystic disease on cytology which were proved to be infiltrating ductal carcinoma while one case which was diagnosed as cystosarcoma phylloides turned out to be a case of malignant fibrous histiocytoma (MFH) on histology. Choi et al suggested many cause of false negative diagnosis, the most common being interpretive error followed by cystic change, needle out of focus, bloody aspiration and scanty cellularity.<sup>[11]</sup> In the present, study there were two causes of false negative results. In first case which was falsely reported as fibrocystic disease on cytology turned out to be IDC on histology, the cause was missing of malignant focus and hitting the area which was showing features of fibrocystic disease. In case of malignant fibrous histiocytoma, it was the scanty cellularity as well as the interpretive error which leads to false negative error. So the present study is comparable to studies conducted by Choi et al.<sup>[11]</sup>

In the present study, sensitivity was 93%, specificity 98%, positive predictive value 96.7%, negative predictive value 96% and diagnostic accuracy 96%. Various authors like Hammond et al, Watson et al and Nicosia et al have given different values viz. sensitivity ranging from 77.9% to 94%, specificity ranging from 98% to 99.5%, PPV ranging from 96.7% to 99.62%, NPV ranging from 94% to 99.62% and diagnostic accuracy ranging from 95 to 96%.<sup>[12-14]</sup>

So the results of present study is comparable to the studies conducted by other authors (Table 3)

**Table 3: Comparative analysis of various statistical values**

Author	Total No of cases	Sensitivity	Specificity	Positive Predictive value	Negative Predictive value	Diagnostic Accuracy
Hammond et al	678	94.0%	98.0%	98.0%	94.0%	96.0%
Watson et al	350	77.9%	99.5%	97.8%	93.8%	95.0%
Nicosia et al	1875	93.2%	99.5%	99.6%	99.6%	95.6%
Present study	200	93.0%	98.0%	96.7%	96.0%	96.0%

FNAC of breast is one of the most important and cost effective modality for the diagnosis of breast lumps. The major advantages of this procedure are that it is easy to perform, very cost effective and can be done at OPD basis without giving any types of anaesthesia. With a high sensitivity, specificity and diagnostic accuracy, it is a boon for developing countries like India, where it can be used as a screening tool for diagnosis of potentially malignant lesions.

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