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DIAGNOSTIC UTILITY OF ASPIRATION BIOPSY OF THE BREAST LESIONS

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ABSTRACT

Fine needle aspiration biopsy of breast lump is an accepted and established method to determine the nature of lump and it may play an important role when it is difficult to determine the nature of the breast lump by clinical examination. It has been shown that FNAB can reduce number of open breast biopsies. Study was done to assess utility of FNAC as the initial diagnostic tool in patients with breast lump, to define diagnostic criterion, to subcategorize lesions into specific entities, evaluate false negatives and false positives, to cytological grade infiltrating duct carcinoma – not otherwise specified (IDC-NOS) on the Robinson's cytological criteria and correlate with histological grading based on Elston's modified Blooms and Richardson method. Evaluating the efficacy of FNAB in surgical management and statistics. Prospective 2 year study of 334 patients was at a tertiary care hospital. A proforma was made for careful clinical examination of the breast lump. Patient was explained the procedure. FNA was done with 20-22G needle and 5-10cc syringe. Smears were fixed in 90% ethanol and stained H&E, PAP and Giemsa. Age of the patients was 11-90 years. Fibroadenoma was the most common benign lesion whereas IDC-NOS was the most common malignant lesion found. Cyto-histopathological correlation was found in 181 cases.

Key Words: *Breast Fnac, Fibroadenoma, Idc-Nos, Cytohistopathology Correlation*

INTRODUCTION

Breast is one of the most frequently aspirated organs in fine needle aspiration cytology. Cancer of the breast is the second most common cause of malignancy in women. Increase in cases of breast cancer is related to late marriage, birth of child in later age, shorter period of breast feeding and nulliparity or low parity. It is estimated that in 2001 there were approximately 80,000 new breast cancer cases in India. The population based cancer registry data from the various parts of the country has revealed breast cancer as the commonest cancer amongst women in Delhi, Mumbai, Ahmedabad, Calcutta and Trivandrum. Fine needle aspiration biopsy of breast lump is an important part of triple assessment (clinical examination, imaging and FNAC) of palpable lump (Tiwari, 2007). It is an accepted and established method to determine the nature of lump. It has been shown that FNAB can reduce number of open breast biopsies. The demand of FNAC's has swelled over last few decades and pathologist is under increasing pressure to provide correct diagnosis. There is no doubt that expertise comes with experience.

Aims & Objectives

- 1) To assess utility of FNAC as the initial diagnostic tool in patients with breast lump.
- 2) To define diagnostic criterion in interpretation of each breast lesion.
- 3) To subcategorize FNAC breast smears into specific entities.
- 4) To discuss circumstances and conditions in which false negative and false positive diagnosis might occur.
- 5) To cytologically grade infiltrating duct carcinoma – not otherwise specified (IDC-NOS) on the Robinson's cytological criteria and correlate with histological grading based on Elston's modified Blooms and Richardson method.
- 6) To demonstrate impact of FNAB diagnosis on further surgical management of breast masses.
- 7) To compare statistical data in terms of sensitivity, specificity, positive and negative predictive values and diagnostic accuracy with available literature.

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MATERIALS AND METHODS

A total of 2980 patients visited to cytology OPD over a two year period. Out of 334 cases, 183 cases were received for histopathological correlation. Statistical values were calculated and compared with similar studies. After careful clinical examination of the breast mass for its presence, consistency and any signs suspicious of malignancy, patient was placed in comfortable position for FNAC and explained the procedure. Taking complete aseptic precautions, aspiration of the mass was done by 20-22G needle. The aspiration sample was placed on the glass slide and smears were made by inverting a second glass slide over the drop and as it spreads, pulling the slides apart horizontally or vertically. This produces monolayer of cells and small micro biopsies with good cellular detail while still preserving some intercellular orientation and even occasional stromal and epithelial cell relationships. Smears were allowed to either air dry or were fixed immediately while the surface is still wet, with 70-90% ethyl alcohol. Routinely at least 2 fixed smears were subjected to H & E and remaining smears to Pap staining. The air dried smears were stained with Giemsa.

Performa included- Name; Age; Reg. No.; Case No.

Clinical features- 1.Lump in the breast; 2.Diffuse nodularity; 3.Breast pain; 4.Nipple discharge; 5.Inversion; 6.Fungating growth; 7.Miscellaneous; Examination of breast (Sainsbury, 2008).

Inspection - Nipple: Position, retraction, ulceration, discharge.

Areola: Crack, fissure, ulcer, eczema, discharge.

Skin over breast: Inflamed, dimpling, retraction, peau d'orange, fungation, nodules.

Palpation; Unilateral/Bilateral; Site-Quadrant; Size; Mobility; Tenderness; Consistency; Fixity

Lymph Nodes: Number; Size; Consistency; Mobility

Staining Wet fixed : H&E, PAP

 Air dried : Giemsa

 Any other : Gram's, AFB

Reporting

Final report

Histopathological diagnosis

Reporting

1. Duct and acinar cells

2. Myoepithelial cells

3. Apocrine cells

4. Foam cells

5. Fat cells

6. Fibrocytes

7. Giant cells

8. Atypia: Mild/Moderate/Severe.

9. Tumor cells: Number - scarce/moderate/abundant, arrangement, nuclear size, nuclear shape, cytoplasm, mitosis, grading.

Background: Mucus, secretion, debris, RBC, polymorphs.

Broad categorisation

- Unsatisfactory

- Benign

- Atypical

- Suspicious of malignancy

- Malignancy

Final subtyping of pathological entity

Histopathology (whenever available)

Statistical indices

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RESULTS AND DISCUSSION

A two year study was done to evaluate the diagnostic utility of fine needle aspiration cytology of breast lesions. Age of patient varied from 11-90 yrs. Most of the benign cases were in 21-30 yrs age group and malignant cases were in 41-50 yrs age group. 364 cases were categorized as inadequate 30 (8.2%), benign 249(68.4%), atypical 5(1.4%), suspicious 7 (2%) and malignant 73(20%). Out of 334 cases, right side (58.1%) was commonly involved than the left side (38.6%). In malignant cases, lump was commoner on left side (61.3%) than on right side (38.7%). Upper outer quadrant (50.9%) commonly involved than upper inner quadrant (17.1%). Fibroadenoma (38.3%) was commonest benign lesion followed by fibrocystic change (6.9%) and abscess (6.3%). Amongst malignancies, commonest lesion was IDC-NOS (75%), followed by lobular carcinoma (6.3%). One case of IDC-NOS was falsely reported as breast abscess as the aspirate was mainly from central necrotic portion of tumor. All the cases reported as atypical turned out to be fibroadenomas. One case out of seven cases reported as suspicious for malignancy turned out to be fibroadenoma on histopathological examination. This was false positive diagnosis. Positive cytohistopathological correlation was seen in 181 cases. A single false positive and false negative were reported. Cytological grading was comparable with histopathological grading in all cases of IDC-NOS. IDC-NOS grade II was the most common grade on cytology as well as on histopathology.

Out of total 334 cases, male patients were 11(3.3%) and females were 323(96.7%). We categorized cases as inadequate 30(8.2%), benign 249(68.4%), atypical 5(1.4%), suspicious 7 (2%) and malignant 73(20%). Smears were reported as inadequate (8.2%) because of scant cellularity and hemorrhagic aspirate. Out of remaining 334 cases, 183(54.7%) cases were received for histopathological correlation. Age wise distribution of cases showed that maximum number of patients with breast lump attending cytology OPD were from 31-40 yrs age group. Similar results were obtained by Tiwari *et al.*, (2007). Ariga (2002) also showed maximum patients in 31-40 yrs age group. The distribution of benign and malignant cases showed that benign cases were most common in 21-30yrs (32.3%) age group, followed by 31-40 yrs (24%) and 11-20 yrs (22.8%) and malignancy was common in 41-50 yrs (36.3%) age group followed by 31-40 yrs (22.5%) and 51-60 yrs (17.5%) age group. Our findings were well correlated with Tiwari *et al.*, (2007), Sunita Saxena *et al.*, (2005), Ariga *et al.*, (2002) and Sandhya P Iyer (2008), Nilay Chakrabarti (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 (58.1%) than on left side (38.6%). Lump in the bilateral breast were found in (3.3%). In malignancies, lumps were commoner on left side (61.3%) than on right side (38.7%) as in literature (Sainsbury, 2008; Patrikar *et al.*, 2008; Lilleng *et al.*, 1995; Amrikachi *et al.*, 2001). The upper outer quadrant was most commonly involved in both benign (50.3%) as well as malignant (52.5%) cases. Most of the mobile lesions were benign (98.4%) except a case of breast abscess and three cases of tuberculous mastitis which were immobile. Amongst the malignancies, most were immobile except five cases of IDC-NOS (Grade-I) and sixteen cases of IDC-NOS (Grade-II) 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 80 malignant cases, 17 (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 tuberculous lesion as well as in a case of filariasis. Out of 249 (68.4%) benign cases, fibroadenoma (38.3%) was most frequent followed by fibrocystic disease (6.9%) and abscess (6.3%). Least common lesions were simple cyst (0.3%), lipoma(0.3%) and filarial breast disease(0.3%). Sandhya P Iyer (2008) also reported fibroadenoma (35%)

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as most common benign breast lesion followed by fibrocystic change (28.3%). Out of total 128 fibroadenomas reported on cytology we obtained 100 cases for histopathological correlation. 100% correlation was obtained. The classical fibroadenoma revealed biphasic pattern consisting of epithelial and fibromyxoid stromal fragments. The monolayered sheet of cells showed typical antler horn pattern and presence of myoepithelial cells within these sheets. The background comprised of numerous bare nuclei which were typically bipolar or spindle in shape. Histopathology showed intracanalicular, pericanalicular or mixed pattern. Two cases of juvenile fibroadenoma were encountered showing marked epithelial cellularity. There was 100 % correlation in 23 cases of fibrocystic disease with histopathology. Out of 21 cases of breast abscess diagnosed by FNA, 4 cases were received for histopathological correlation. Of these, a case of IDC-NOS (Grade –II) was falsely diagnosed as abscess i.e. false negative case (due to extensive necrosis of central portion of tumor). All the 19 cases of fat necrosis showing foamy macrophages against plasmaceous background correlated with histology.

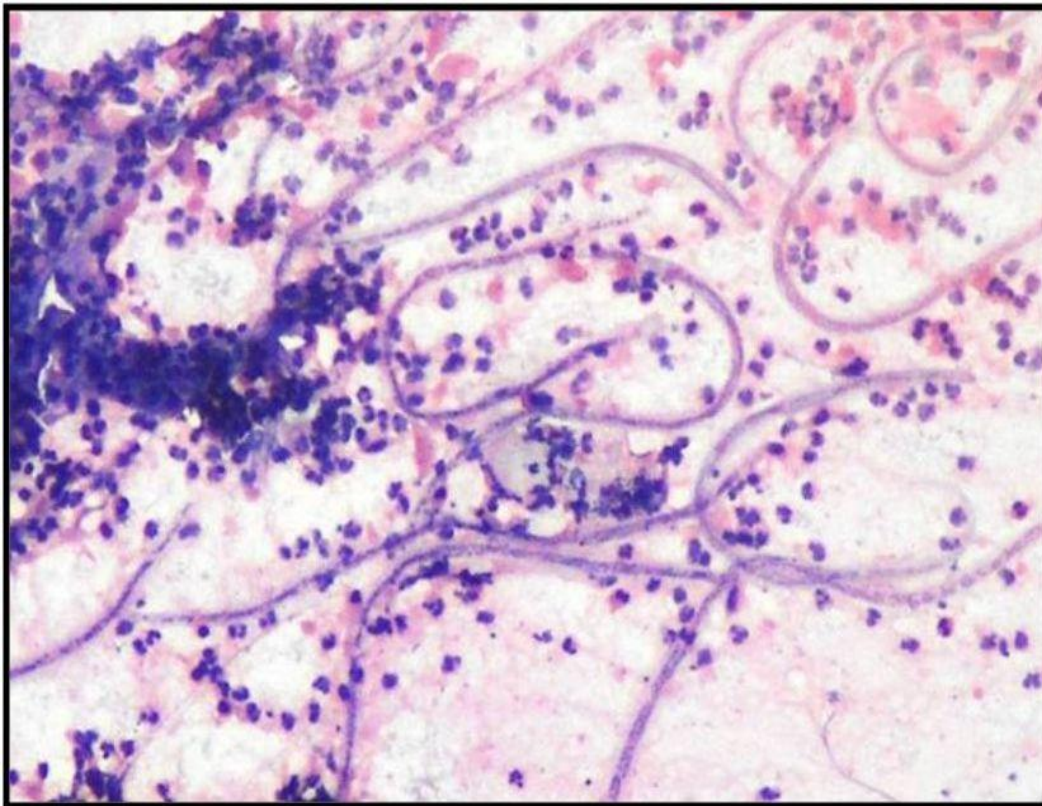


Figure 1: Breast filariasis: Numerous microfilarial parasite of *W. Bancrofti* with inflammatory cells and degenerated ductal epithelial cells in the background. (HE X 200)

4 of total 18 cases of granulomatous mastitis of tuberculous etiology were received for histopathology confirming the diagnosis. Out of four cases of duct ectasia we obtained only one case for histopathological examination, which was confirmed as duct ectasia. In our study, we reported a case of 24 year old female with filarial breast disease. Aspirate was purulent and smear showed numerous microfilariae which were identified as those of *Wuchereria bancrofti* by the presence of hyaline sheath, length of cephalic space and presence of somatic cells (nuclei) [Figure 1]. Somatic cells appeared as granules that extends from head to tail. The tail tip was free of nuclei. *W. bancrofti* is the most common cause of filarial breast disease as per literature (Patrikar *et al.*, 2008). Out of 19 cases of lactating adenoma reported on cytology we got 9 cases for histopathological correlation and were confirmed as lactating adenoma. Total 11 male patients visited cytology OPD with complains of breast lump. Out 11

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cases, 10 were reported as gynaecomastia which is the most common male breast lesion as per literature too (Lilleng *et al.*, 1995; Amrikachi *et al.*, 2001). Remaining one case was reported as IDC-NOS which is 1.2% of total malignant cases in our study. Incidence of male breast cancer is less than 1%. Our incidence rate is slightly higher. One case reported as lipoma on cytology was confirmed on histopathological examination. Two cases each of benign phylloides and intracystic papilloma on FNAC were confirmed by histopathology. Out of 5 cases in atypical category, 4 cases were received for histopathology and diagnosed as fibroadenoma. Of 80 cases of malignancy, 60(75%) were IDC-NOS, followed by lobular carcinoma (6.3%), papillary carcinoma (3.8%), mucinous carcinoma (2.5%) [Figure 4,5], medullary carcinoma (2.5%)[Figure 2], malignant phylloides (1.2%) (Figure 3). 7 (8.7%) cases were reported as suspicious for malignancy.

These findings were comparable with other studies (Tiwari, 2007; Saxena *et al.*, 2005; Ariga *et al.*, 2002; Khemka *et al.*, 2009). Out of seven cases reported in suspicious category, we received six cases for histopathological correlation. Out of six, five cases were confirmed as IDC-NOS. Remaining case was diagnosed as fibroadenoma with myxoid stroma reported as suspicious of mucinous carcinoma on cytology. This was the only false positive diagnosis. The differentiation of myxoid fibroadenoma from mucinous carcinoma is difficult because myxoid stromal degeneration in fibroadenoma mimics extracellular mucinous material in mucinous carcinoma. These entities are known diagnostic pitfalls in the literature (Orell and Karin, 2005; Progačnik and Us-Krasovec, 2004; Malburger *et al.*, 1997).

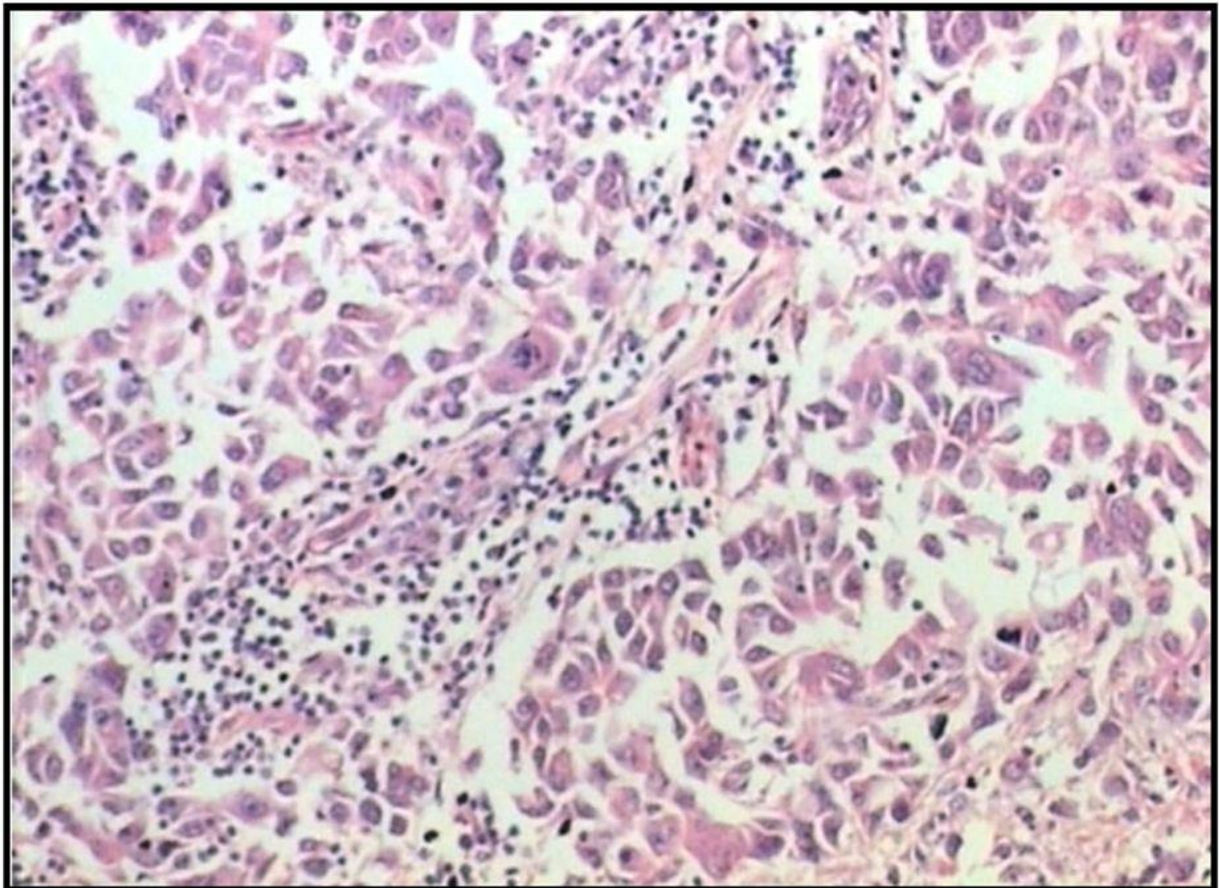


Figure 2: Medullary Carcinoma: Malignant cells with large pleomorphic nuclei and lymphocytic infiltration. (HE X200)

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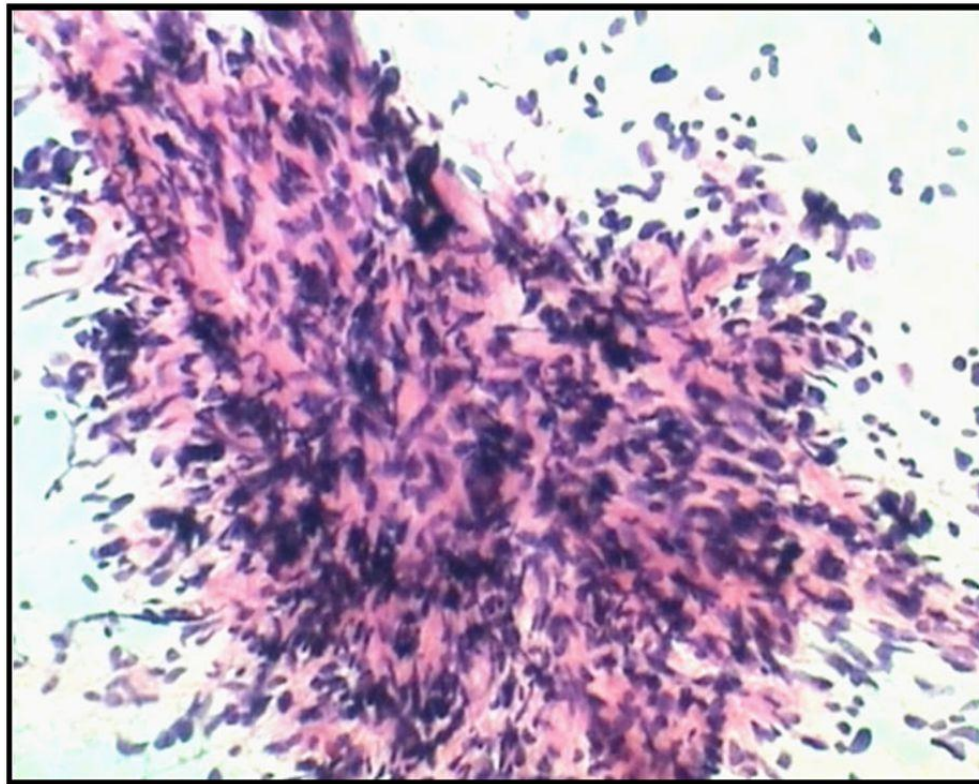


Figure 3: Malignant Phyllodes: Spindle cells with hyperchromatic and pleomorphic nuclei surrounded by benign ductal epithelial cells. (HE X200)

Progačnik *et al.*, (2004) also reported similar false positive case. 27 (45%) cases received for histopathology out of 60 cases of IDC-NOS diagnosed on cytology showed 100% correlation. All the cases diagnosed as IDC-NOS on cytology were graded from I to III based on the Robinsons cytological grading criteria (Robinson *et al.*, 1994) which includes dissociation of cells, cell size as compared to RBC size, uniformity of the cells, presence or absence of nucleoli, nuclear margin and chromatin pattern. Each of these features given score from 1 to 3 and sum total of all the six features put together is calculated.

Score 6 to 11 : Grade I

Score 12 to 14 : Grade II

Score 15 to 18 : Grade III

In our study all the 60 cases IDC-NOS cases were graded on cytology. Majority 29 (48.3%) cases of them were grade II, 22 cases (36.7%) were grade I and followed by 9 cases (15%) were grade III. As compared to Robinson *et al.*, (1994) studies showed 34% grade I, 44% grade II and 22% grade III carcinoma. In 27 cases received for histopathological examination, cytological grade compared with well established Elston modification of Richardson and Bloom classification. It was seen that 75% cytological grade I carcinomas were histological grade I while remaining 25% of cytological grade I were histological grade II. 93.3% of cytological grade II were correlated with histological grading and 75 % of grade III were consistent with histological grade III. The Mc. Nemar's test of changes and Cohen's Kappa (Leopold, 2005). were carried out on our data. This showed that the change above between the two results i.e. cytological and histopathological grading were not significant and the results of the two tests are indeed comparable.

Out of five cases reported as infiltrating lobular carcinoma on cytology, we received two cases for histopathological correlation with 100% correlation. Both the cases of medullary carcinoma diagnosed on cytology were confirmed on histological examination. Of the three cases reported as papillary carcinoma on FNAC, two cases were received for histopathological examination and confirmed as papillary

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carcinoma. One case was reported as malignant phylloides on FNAC and was confirmed on histopathological examination. Finally the results of sensitivity (97.6%), specificity (99.3%), positive predictive value (97.6%) and negative predictive value (99.3%) [Table 1] were comparable with studies by Ariga *et al.*, (2002). , Tiwari *et al.*, (2007). and Nilay Chakraborti *et al.*, (2007) Importantly diagnostic accuracy in our study of 98.9% proves the worth of FNAC as diagnostic modality and hence its utility.

Table 1: Statistics showing cytohistopathological correlation

Cytological diagnosis	Histopathological diagnosis		Total
	Benign	Malignant	
Benign	141 (T.N.)	1 (F.N.)	142
Malignant	1 (F.P.)	40 (T.P.)	41
T.P - True Positive		T.P - True Negative	
F.P - False Positive		F.N - False Negative	

To conclude, 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 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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