



Diagnostic Utility of Fine Needle Aspiration Cytology in Evaluation of Breast Lesions

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Abstract

A palpable breast lump is a common diagnostic problem to both surgeons and general practitioners. Fine needle aspiration cytology (FNAC) is a simple, safe, rapid, minimally invasive, cost effective method for diagnosing breast lesions with minimal or no morbidity. The main purpose of FNAC is preoperative diagnosis or determination of clinically suspected breast cancers and to avoid unnecessary surgery in specific benign conditions. With the triple test assessment, of which, FNAC is an important component, majority of the breast lesions can be diagnosed confidently. As FNAC is an outpatient based procedure, the rapid diagnosis provided by FNAC relieves patient's anxiety, allows the definite treatment decisions to be made immediately and thus saves time. This study was carried out on 200 patients presenting with breast lump. The cyto-histopathological correlation was obtained in 84 cases. Out of 200 cases, 143 (71.5%) cases were diagnosed as benign and 47 cases (23.5%) as malignant and 10 (5%) as suspicious of malignancy. The most common benign lesion was fibroadenoma and the most common malignant lesion was infiltrating ductal carcinoma. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy was found to be 100%, 98.46%, 95%, 100% and 98.8% respectively. There is a good correlation between FNAC and histopathology. As FNAC is highly accurate for palpable lesions, it delivers good results and serves as a reliable tool for the diagnosis of palpable breast lesions so that management of the patients can be done effectively.

Keywords: FNAC, breast lump, breast carcinoma, fibroadenoma, triple test.

Introduction

Breast cancer is the most common cancer in women in India and accounts for 27% of all cancers in women^[1]. It is difficult to determine whether a breast lump is benign or malignant simply by clinical examination. Preoperative evaluation of breast lump is an essential part of management of

breast lesions^[2]. FNAC has become a widely accepted and established tool for diagnosis of breast lesions as it is rapid, safe, simple and cost effective method which can be used to evaluate all palpable and radiologically evident non palpable breast lesions^[3]. The application of FNAC for the diagnosis of palpable breast masses was introduced by Martin & Ellis in 1930^[4]. FNAC is an important

component of triple test which in addition to FNAC, includes clinical examination and mammography and is a standard approach to the investigation of palpable breast lumps^[5]. Histopathological examination is an universally accepted method of diagnosis and follow up; FNAC can reduce the number of open biopsies which are cumbersome, expensive and time consuming^[6] and can provide a diagnosis with only 10-30% of the cost of surgical biopsy^[7]. If the smears are satisfactory & adequate and cytological criteria are fulfilled, most of the cases can be diagnosed confidently. The definitive treatment can be offered based on cytological diagnosis without the need of histopathological examination unless there is either suspicion or disagreement^[8]. The aim of the study was to evaluate FNAC in various breast lesions and to compare the results with histopathological findings in available cases and to assess the accuracy of FNAC.

Materials and Methods

This retrospective study was carried out from January 2016 to June 2017 on 200 patients presenting with breast lumps. Out of 200 cases, cyto-histopathological correlation was obtained in 84 cases.

In all the cases, detailed history was obtained and clinical examination was carried out. After explaining the procedure in detail, consent was taken from every patient. Aspiration was done using 23-gauge needle and 10ml plastic syringe. In each case, few alcohol fixed smears and one dry smear were prepared; alcohol fixed smears were stained with Hematoxylin & Eosin stain and Papanicolaou stain while dry smears were stained with Leishman stain. One smear was kept unstained for any further evaluation. Smears were stained with Ziehl-Neelsen stain and Gram stain whenever required.

The surgical specimens received after cytology reporting of breast lesions included trucut biopsy, lumpectomy and Modified Radical Mastectomy specimens. The specimens were evaluated grossly, and trimming was done according to the standard protocol. The bits were taken from representative

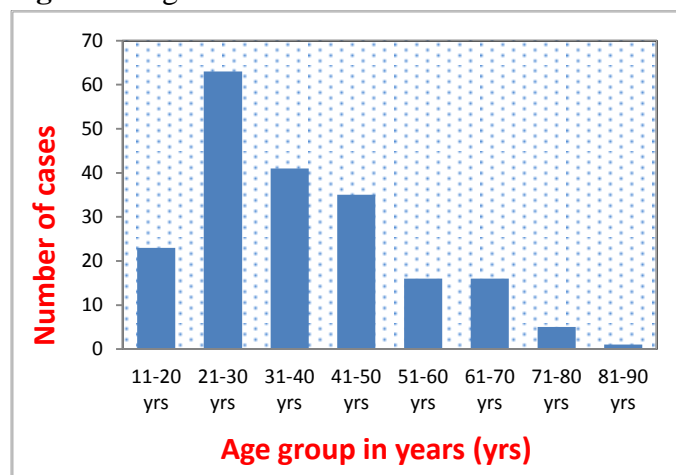
areas. The tissue was fixed in 10% buffered formalin and then processed by the routine paraffin embedding techniques. The sections were cut at 4-5 microns thickness and stained with hematoxylin and eosin.

The various cytomorphological features of breast lesions were studied, analysed and histopathological correlation was done. The sensitivity, specificity, positive predictive value, negative predictive value, accuracy rate, false positive rate and false negative rate were calculated.

Results

Fine needle aspiration was performed on 200 patients, out of them 198 (99%) were females and 2 (1%) were males with female to male ratio of 1: 0.01. The mean age was 37 year with a range of 13-90 year. Majority of the patients were in the age group of 21-30 year (Figure 1).

Figure 1: Age distribution of cases



In the present study, the oldest case was a 90 year old lady diagnosed as infiltrating ductal carcinoma-No special type (IDC-NST) and the youngest case was a 13 year old girl with a diagnosis of fibroadenoma. Out of 200 cases subjected to FNAC, 143 were reported as benign breast lesions, 47 as malignant lesions and 10 as suspicious of malignancy and their distribution according to the age is given in Table-1.

Table 1: Cytological diagnosis of breast lesions according to Age

Age group (year)	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	Total
Benign lesions									
FA	4	33	17	8	4				66
BBL	2	15	5	6	5				33
FCC		2	2	4	3				11
ANM		6	5						11
GM		3	3						6
Galactocele		4							4
PT		1	1	1					3
Lact change	1	1	1						3
MH		1		1					2
Gynecomastia		1	1						2
Fat necrosis				1					1
E cyst				1					1
									143
Malignant lesions									
IDC-NST		1	2	9	13	14	4	1	44
IDC with mucinous differentiation				1					1
IDC with neuroendocrine differentiation							1		1
Adenocarcinoma		1							1
									47
Suspicious of malignancy			4	2	2	2			10

FA-fibroadenoma ; BBL-benign breast lesion; FCC- fibrocystic change; ANM- acute nonspecific mastitis; GM- granulomatous mastitis; PT-phyllodes tumour; Lact change-lactational change; MH-Mammary hamartoma; E cyst-epidermal cyst; IDC-NST -Infiltrating ductal carcinoma (No special type)

Among 143 benign breast lesions, fibroadenoma accounted for 66 (46.15%) cases, benign breast lesions without a specific diagnosis in 33 (23.07%) cases, fibrocystic change in 11 (7.69%) cases, acute nonspecific mastitis in 11 (7.69%) cases, granulomatous mastitis in 6 (4.19%) cases, galactocele in 4 (2.80%) cases, phyllodestumour in 3 (2.10%) cases, lactational change in 3 (2.10%) cases,

Table 2: Cyto-histological correlation of benign breast lesions

Cytological diagnosis	Histological diagnosis									
	Fibro-adenoma	Mam-maryham ar-toma	Phyll-odes tumour	Ab-cess	Granul-omatous mastitis	Tubular adenoma	Lactating adenoma	Galacto-cele	Epid-ermal cyst	Total
Fibroadenoma	32	3	2			1				38
Benign breast lesion	13	1					1			15
Fibrocystic change		1						1		2
Acute nonspecific mastitis				2	1					3
Granulomatous mastitis					1					1
Phyllodes tumour			2							2
Mammary hamartoma		2								2
Epidermal cyst									1	1
Total	45	7	4	2	2	1	1	1	1	64

mammary hamartoma in 2 (1.40%) cases and gynecomastia in 2(1.40%) cases. A case of fat necrosis (0.70%) and an epidermal cyst (0.70%) were also observed.

Among 47 malignant breast lesions, IDC-NST accounted for the majority of cases i.e. 44 cases (93.61%). In two cases, variants of IDC viz. IDC with mucinous differentiation (2.13%) and IDC with neuroendocrine differentiation (2.13%) were diagnosed. A case of adenocarcinoma without any specific type (2.13%) was reported. In 10 cases, cytological diagnosis was suspicious of malignancy. Out of total 200 cases, histopathological examination was done in 84 cases. The histopathological follow up was obtained in 64 out of 143 benign lesions, 15 out of 47 malignant lesions and in 5 out of 10 cases diagnosed as suspicious of malignancy on FNAC.

The cyto-histological correlation of various breast lesions is depicted in table 2,3 and 4.

Out of 38 cases of cytologically diagnosed fibroadenoma, 32 cases were confirmed on histology (fig 2 and 3). Two cases of phyllodes tumour (fig4,5) and a case of granulomatous mastitis (fig6,7) reported on cytology were proved to be correct on histology.

There were 12 cases with cytological diagnosis of IDC-NST all of which showed invasive carcinoma on histology. (fig 8 and 9)

A case of adenocarcinoma without any specification on cytology showed evidence of metastasis from rectal adenocarcinoma on histology. (fig 10,11 and 12)

Table 3: Cyto-histological correlation of malignant breast lesions

Cytological Diagnosis	Histological Diagnosis				Total
	IDC-NST	Encapsulated papillary Ca with adjacent invasive Ca	Invasive micro-papillary	Adenocarcinoma (Metastasis from rectal adenocarcinoma)	
IDC-NST	11	1			12
IDC with mucinous differentiation	1				1
IDC with neuroendocrine differentiation			1		1
Adenocarcinoma				1	1
Total	12	1	1	1	15

Out of 10 cases diagnosed as suspicious of malignancy on FNAC, 5 underwent excisional biopsy. Out of these 5 cases, 1 case was diagnosed as multiple duct papilloma (False positive result) (fig 13 and 14) and rest 4 cases were proved to be invasive carcinoma on histopathology.

Table 4: Cyto-histological correlation of all breast lesions

Cytological Diagnosis	Histological Diagnosis		Total
	Benign breast lesions	Malignant breast lesions	
Benign breast lesions	64	0	64
Malignant breast lesions	0	15	15
Suspicious of malignancy	1	4	5
Total	65	19	84

Thus in the present study, majority of the cases showed good correlation between FNAC and histopathology. The cytological diagnosis was consistent with histopathology in 83 out of 84 cases (98.81%) and inconsistent in 1 case (1.19%).

All the cases diagnosed as suspicious of malignancy on FNAC were included as malignant in calculations.

Table 5 Analysis of results

True Positives (TP)	19
False Positives (FP)	01
True Negatives (TN)	64
False Negatives (FN)	0

The statistical analysis showed high sensitivity (100%) and specificity (98.46%) of FNAC in breast lesions, with positive predictive value (PPV) and the negative predictive value (NPV) being 95% and 100% respectively. The diagnostic accuracy was found to be 98.80%.

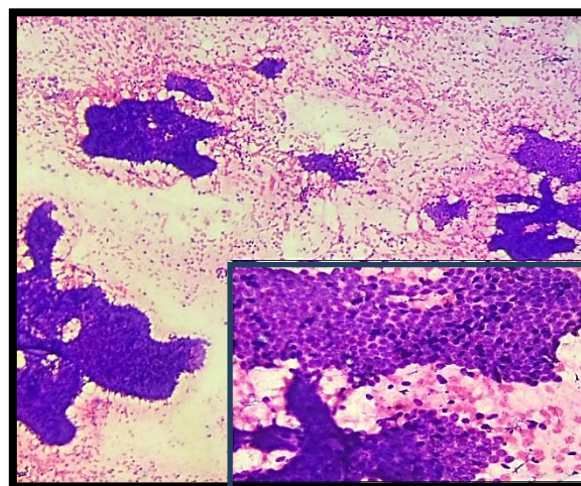


Fig. 2. Photomicrograph of fibroadenoma on cytology showing tightly cohesive clusters of ductal epithelial cells arranged in antler horn pattern. H & E X40; Inset shows high power view of ductal epithelial cells on the background of bare nuclei. H & E X 400

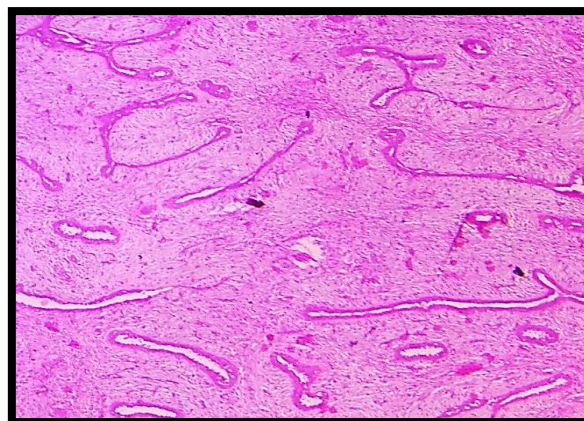


Fig 3 Photomicrograph of fibroadenoma on histology showing proliferating ducts and stroma arranged in intracanalicular and pericanalicular pattern. H & E X 40

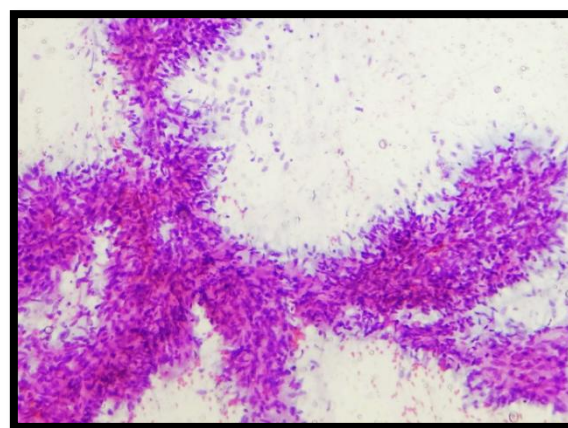


Fig 4 Photomicrograph of phyllodes tumour on cytology showing hypercellular stromal fragments. PAP Stain X100



Fig 5 Photomicrograph of phyllodes tumour showing stromal overgrowth and stromal hyperplasia with a dilated duct. H & E X100

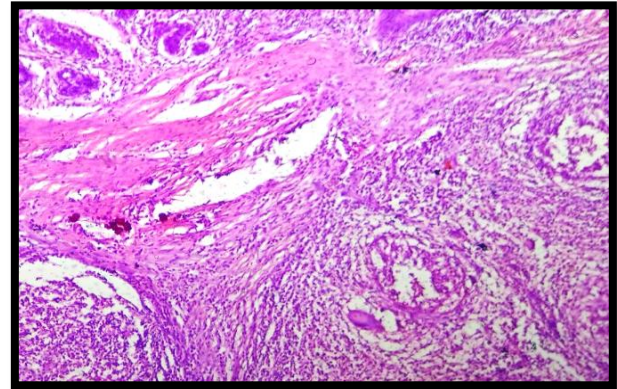


Fig. 7 – Photomicrograph of granulomatous mastitis on histology showing granulomas H & E Stain X 40

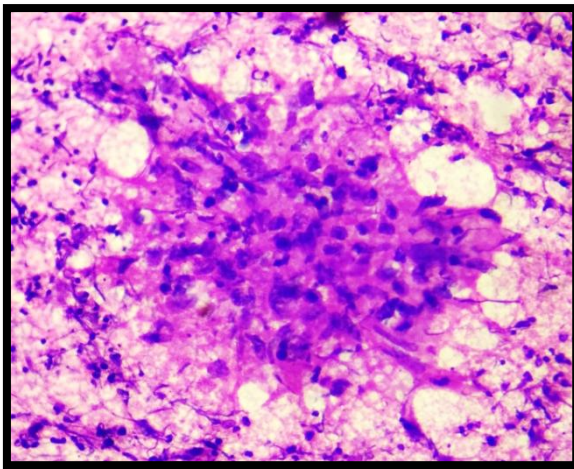


Fig. 6a Photomicrograph of granulomatous mastitis on cytology showing granuloma composed of epithelioid cells and histiocytes on the background of viable and degenerated polymorphs. H & E Stain X 40

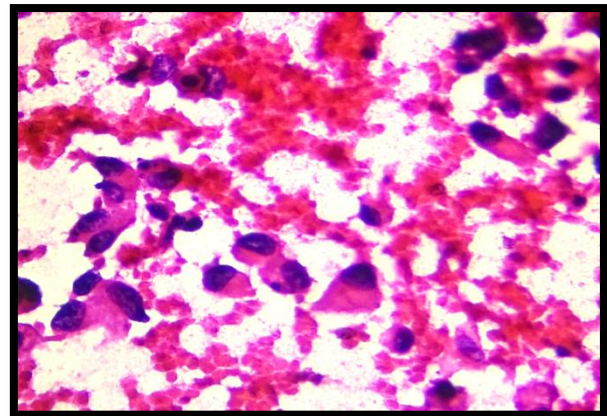


Fig 8 Photomicrograph of IDC on cytology showing round to oval cells having pleomorphic hyperchromatic nuclei and eosinophilic cytoplasm H & E X400

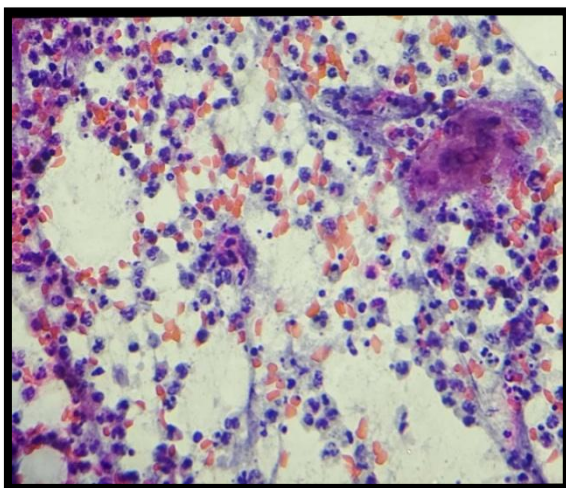


Fig. 6b – Photomicrograph of granulomatous mastitis on cytology showing multinucleated giant cell on the background of viable and degenerated polymorphs. PAP Stain X 40

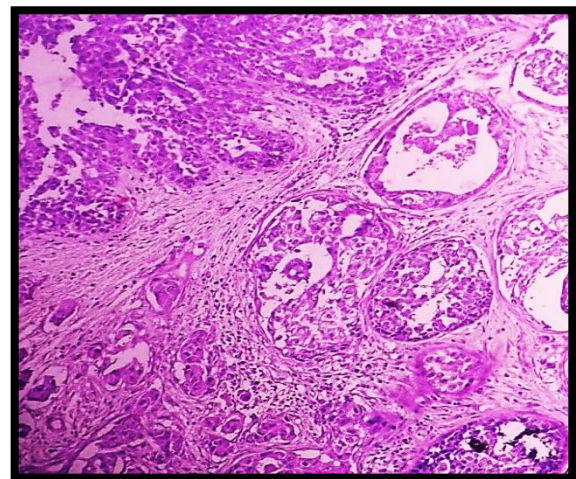


Fig 9 Photomicrograph of IDC on histology showing round to oval cells having pleomorphic hyperchromatic nuclei and eosinophilic cytoplasm arranged in sheets and tubules with foci of DCIS. H & E X 100

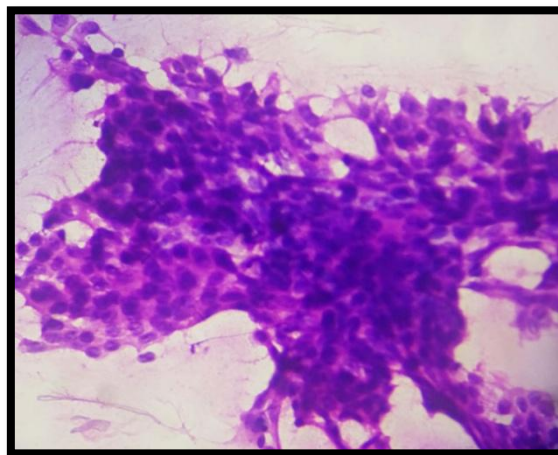
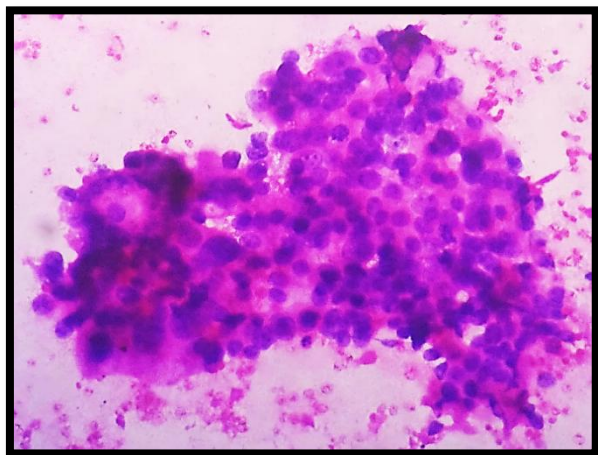


Fig 10 Photomicrograph of adenocarcinoma on cytology showing round to oval cells having pleomorphic vesicular nuclei and eosinophilic cytoplasm arranged in acinar pattern H & E X400

Fig 13 Photomicrograph of multiple duct papilloma on cytology showing cohesive clusters of ductal epithelial cells with nuclear crowding, overlapping and hyperchromasia. H & E X400

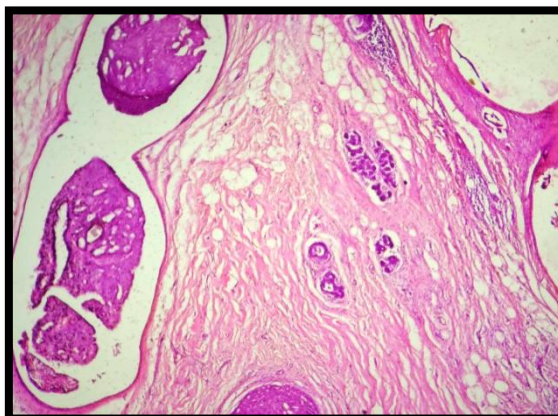
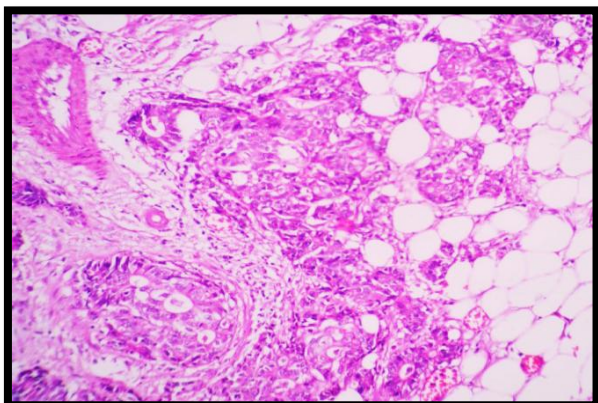


Fig 11. Photomicrograph of metastatic adenocarcinoma on histology showing round to oval cells having pleomorphic vesicular nuclei and eosinophilic cytoplasm arranged in glandular pattern. H & E X100

Fig 14. Photomicrograph of multiple duct papilloma on histology showing multiple intraductal papillomas with florid ductal epithelial hyperplasia. H & E X100

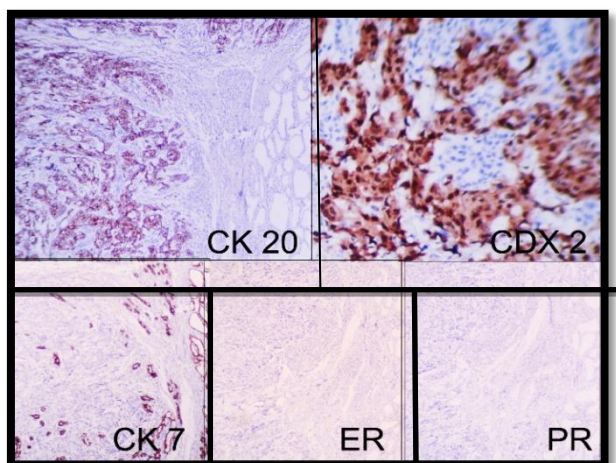


Fig 12. Photomicrograph of immunohistochemistry of metastatic adenocarcinoma of breast showing positivity for CK20 and CDX2 and negativity for CK7, ER and PR.

Discussion

Currently, FNAC is widely adopted for pathological assessment because of its many advantages. FNAC acts as a guide to clinical management. If malignancy is confirmed, additional imaging studies like bone scan, liver scan etc can be done preoperatively to determine the stage and thus a definite treatment plan can be prepared for the patient.

In the present study, benign breast lesions were the most common lesions in young females, among which fibroadenoma was the most common. The malignant lesions were common in fourth and fifth decades of life, among which infiltrating ductal carcinoma was the most common type.

The most common age group affected was 21-30 years which correlated with the studies done by Gupta R, Thakkar B and Veenakumari L. [8],[9],[10]. Fibroadenoma (n=66, 46.15 %) was the most common benign lesion and infiltrating ductal carcinoma was the most common malignant lesion encountered in this study which was also observed by Gupta R, Thakkar B, Khageshan AP, Patel A and Veenakumari L [8],[9],[10],[11],[12].

Among benign lesions, in majority of the cases, a specific typing of lesion was offered on FNAC. However, few cases could not be subtyped correctly. Two cases of fibroadenoma reported on cytology were diagnosed on histopathology as benign phyllodes tumour. The cytological findings considered to be diagnostic of fibroadenoma are cohesive sheets of epithelial cells with antler horn like appearance containing recognisable myoepithelial cell nuclei, many naked bipolar cell nuclei in background and variable number of stromal fragments. The cytological diagnosis of phyllodes tumour is usually suggested by the presence of cellular smears showing increased number of stromal fragments, some of which are large and hypercellular and are composed of numerous plump spindle cells with mild pleomorphism. Occasional sheet of benign ductal epithelium may be seen along with stromal fragments. Thus, the presence and cellularity of stromal fragments is helpful in distinguishing phyllodes tumour from fibroadenoma. However, these characteristic features may be absent in benign/low grade phyllodes tumour and hypercellular stromal fragments can be seen in cellular fibroadenoma as well^[13]. In most cases, FNAC can accurately diagnose malignant phyllodes tumour. But in cases of benign/borderline phyllodes tumour, diagnosis on FNAC becomes difficult because of overlapping cytological features of fibroadenoma and phyllodes tumour. Phyllodes tumour with marked epithelial hyperplasia may obscure stromal elements and can lead to misdiagnosis of fibroadenoma. Sometimes it is difficult to diagnose benign phyllodes tumour on cytology because of sampling problems as hypo and

hypercellular areas tend to alternate within phyllodes tumour^[13]. Thus, the differentiation between cellular fibroadenoma and benign/low grade phyllodes tumour depends entirely on the histology and the distinction may be impossible on cytology^[14].

There were 7 cases diagnosed as mammary hamartoma on histopathological examination out of which 2 cases were correctly diagnosed on cytology and 3 cases were reported as fibroadenoma, 1 case as benign breast lesion and 1 case as fibrocystic change. On histology, the mammary hamartoma is characterised by varying amounts of admixture of breast parenchyma and adipose tissue. However, it may show various changes like cyst formation, adenosis, apocrine metaplasia, pseudoangiomatous stromal hyperplasia and uncommonly epithelial hyperplasia which lead to nonspecific cytological features making FNAC diagnosis difficult.

A case of acute nonspecific mastitis reported on cytology was diagnosed as nonspecific granulomatous mastitis on histopathology. The granulomatous mastitis can be nonspecific or specific like in tuberculosis, fungal infections, sarcoidosis etc. The nonspecific granulomatous mastitis is also known as granulomatous lobular mastitis which may mimic malignancy both clinically and radiologically. It is histologically characterised by lobulocentric inflammation along with non-necrotising granulomas often accompanied by suppuration which may lead to microabscess formation. The common cytological features seen in these cases are epithelioid histiocytes, giant cells, granulomas and predominantly neutrophilic infiltrate in the background. Granulomas may or may not be present on cytology and aspirate may show only neutrophilic infiltrate. In cases where the granulomas are not seen on cytology, the definitive diagnosis relies on histopathology.

There is a gray zone area in breast cytology because of overlap of cytological features of benign and malignant lesions, justifying the need for histopathology. In our study, there were five cases reported as suspicious of malignancy on FNAC, out of which four cases were confirmed as positive

on histopathology. However, in one case, the histopathology revealed benign lesion viz. multiple duct papilloma.

A 40 year old female presented with lump in left breast who underwent USG guided FNAC. The cytological smears showed tightly cohesive clusters and monolayered sheets of ductal epithelial cells and few of the clusters showed nuclear crowding, overlapping as well as hyperchromasia and was reported as "Suspicious of malignancy".(fig 13) Excisional biopsy was advised for definitive diagnosis. On histopathology, it was diagnosed as multiple duct papilloma.(fig 14) The reason behind such cyto-histological discrepancy is that the papillary lesions show variable degrees of cytological atypia. If dual population of clusters is seen i.e clusters of benign ductal epithelial cells along with clusters showing nuclear atypia, one may express it as suspicious of malignancy. As worrying cytological atypia can occur in several benign conditions like cellular fibroadenoma, fibrocystic change with epithelial hyperplasia and various papillary lesions of breast, a definitive cytological diagnosis of malignancy should not be made in such cases but left to histology.

In the present study, all the malignant lesions were diagnosed correctly on cytology. However, there was slight discrepancy in the diagnosis of variants of infiltrating ductal carcinoma. The majority of tumours in the breast are primary. Metastatic disease in the breast is an unusual event, and even more so is metastasis of the rectum to the breast. Metastatic spread to the breast has an incidence of 0.5 to 3% from extramammary sites^[14]. A case of cytologic diagnosis of adenocarcinoma was diagnosed as metastasis in breast from primary in rectum. In this case, a young lactating lady presented with breast lump and axillary swelling mimicking malignancy in breast. FNAC from both the lesions was reported as positive for malignancy suggestive of adenocarcinoma. Patient underwent Modified Radical Mastectomy. Gross examination showed a tumour measuring 7x5x4 cm and axillary mass measuring 5.5x4x3 cm. Histologically, the tumour was composed of malignant glands of

varying size and shape. The morphology was the reminiscent of colorectal carcinoma. The patient had history of abdominal perineal resection for carcinoma rectum a year ago. In order to see whether the tumour is primary or metastatic adenocarcinoma, immunohistochemistry was performed. The tumour was CK20 and CDX2 positive and CK7, ER/PR negative, confirming the diagnosis of metastasis from the rectum. Metastasis to the breast from colorectal adenocarcinoma is very rare. It can mimic primary breast cancer and thus must be considered in the differential diagnosis of suspicious breast mass, especially if the patient has prior history of cancer. Proper diagnosis of such metastatic carcinoma requires a detailed clinical history, high index of suspicion and proper immunohistochemical workup.

Comparative analyses of cytological diagnoses of benign and malignant breast lesions in the present study with studies done by other authors are tabulated in Table 6.

Table 6 Comparative Analysis of cytological diagnosis of breast lesions by different authors

Study	No. of FNAC	Sensitivity	Specificity	PPV	NPV	Accuracy
Y D Choi (2004) ¹⁵	1297	77.7	99.2	98.4	88	91.1
Gupta R (2017) ⁸	175	85%	95.8%	89%	93.8 %	-
Patel (2018) ¹²	382	97.46	100	100	100	99.05
Present study	200	100	98.46	95	100	98.8

Thus, FNAC enables us to differentiate benign from malignant lesions with high sensitivity, specificity and diagnostic accuracy. When smears are obviously benign, patients should be reassured and can be prevented from undergoing radical surgery. In cases of clearly malignant smears, surgery or other treatments should be started without delay. While for gray zone lesions like suspicious smears, biopsy should be advised. Early diagnosis can significantly reduce morbidity and mortality.

Conclusion

The present study concludes that FNAC of breast is a highly reliable and valuable diagnostic tool when combined with clinical and imaging findings. It

should be used as a preliminary test for the diagnosis of malignancy so that definite management decisions can be made immediately.

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