Volume : 5 | Issue : 3 | March 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Diagnostic Evaluation of Breast Lumps and Its Cyto-Histological Correlation

Medical Science

KEYWORDS : Breast lumps, Fine needle aspiration cytology (FNAC), Carcinoma of breast, Fibroadenoma, Infiltrating duct carcinoma, Mastectomy.

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ABSTRACT

Background & Objectives: Breast lumps have varied pathology, and there are different techniques to prove its diagnosis. In India a large number of patients have been suffering from breast cancer and with each passing year, the number is increasing. Fine needle aspiration cytology (FNAC) is a noninvasive, inexpensive, simple, safe and highly accurate technique of diagnosing both benign and malignant breast lesions. It has high sensitivity and specificity. The procedure provides a rapid and non-morbid diagnosis before the operation thus enabling the patient and the surgeon to discuss and plan the treatment modalities rationally.

The aim of the present study is to find out the common causes of breast lesions, their risk categorization for development of cancer and to analyze the role of fine needle aspiration cytology (FNAC) of the breast lesions and to correlate the cytological findings of breast lumps with their histomorphological diagnosis on excision at our centre. In addition the sensitivity, specificity, positive & negative predictive value of FNAC in breast lesions are carried out.

Methods: This comparative study was conducted in the Department of Pathology, AGMC & GBP Hospital, Agartala, Tripura, India from December, 2013 to June, 2015. Four hundred and sixty eight (468) patients came to the Department of Surgery, AGMC & GBP Hospital, Agartala, Tripura, India in two years who had a clinically palpable breast lump and was referred and subjected to fine needle aspiration cytology (FNAC). The smears were stained with Papanicolaou, H&E, May-Grunewald Giemsa stain and special stains like ZN & PAS wherever necessary and were examined under light microscope and categorized as inadequate/unsatisfactory sample, benign inflammatory, benign proliferative, atypical/suspicious and malignant. FNAC diagnosis was compared with histological diagnosis to see the accuracy of fine needle aspiration cytology for neoplastic lesions.

Results: Four hundred sixty eight patients who presented with a breast lump in the outpatient department (OPD) of Department of Surgery at AGMC & GBP Hospital were referred to the Pathology department for FNAC. Out of 468 cases, 11 were inadequate aspirations (adequacy 97.6%). Invasive ductal carcinoma was the most commonly reported lesion with maximum incidence in the 4th, 5th and 6th decades followed by invasive lobular carcinoma and other malignant lesions.

Out of 457 breast aspiration (adequate), 301 cases showed non-neoplastic pathology. Out of which 109 smears were inflammatory and the most commonly encountered inflammatory lesions were acute mastitis or abscess (35.8%), All these cases were further confirmed by special stains (PAS, Zn) and cell block preparations and thus excluded from histopathological study.192 smears were reported as benign proliferative lesions , 44 as suspicious for malignant and 112 cases were reported as malignant lesions. Histopathological studies of all these cases were performed out of which 191 cases were benign while 1 case turned out to be malignant phyllodes tumor of the breast (false negative).Out of 44 suspicious for malignancy cases, 5 cases turned out to be benign lesion on histopathology (false positive). All the 112 cases which were diagnosed as malignant lesion on FNAC proved to be malignant on histopathology. Fibroadenoma was the commonest benign lesion noted in the age group 21-30 years and infiltrating duct carcinoma was the most common malignant lesion.

The sensitivity, specificity, accuracy, negative predictive value and the positive predictive value of FNAC was 99.3%, 97.4%, 98.2%, 99.5% and 96.8% respectively. Our results were correlated with previous studies.

Conclusion: Breast cytology is an effective and rapid method of diagnosis of breast diseases. It helps in deciding which patient needs an early open biopsy. FNAC serves as an economical and reliable tool for the diagnosis of palpable breast lesions because the cytopathological examination of these lesions before operation or treatment serves as an important diagnostic modality. FNAC of non-neoplastic lesions enjoyed utmost sensitivity & specificity and turned out to be cost effective procedure for diagnosis. Cytology helped in avoiding unnecessary surgery in 45% cases. The FNAC of breast is cheap, safe and highly accurate preoperative method for diagnosis of breast lesions. Preoperative categorization of breast lesions is of utmost importance for the management of the patient.

INTRODUCTION

Breast cancer is the leading cause of morbidity and mortality. [1, 2] In India, cancer of breast is a second most common cancer in the women [3]. Breast disorders/lumps are a fairly common presenting feature in our outpatient department. They are mostly benign and of no serious consequences but malignancy contributed a significant percentage of breast lumps. [4, 5] Breast lump is most common presentation in the most of the breast disease. It is sometimes difficult to determine whether a suspicious lump is benign or malignant simply from clinical assessment.[6] Therefore a method of definitive diagnosis of patient who present with breast lumps at the outpatient clinic is needed in order to reassure the patient and to offer the best possible treatment. A confident diagnosis can be made in 95% of the cases through a combination of clinical examination, imaging and FNAC.[7] Histopathological diagnosis is a universally accepted confirmatory mode of diagnosis & follow up, FNAC of breast lump is an important part of triple assessment(clinical examination, imaging and FNAC) of palpable breast lumps .It has been postulated that inflammatory breast disease and non-proliferative breast disease do not increase the risk of cancer. Proliferative breast disease without atypia and with atypia confers mild and moderate risk respectively, whereas carcinoma in situ is associated with substantial risk if untreated.[8] Triple assessment of breast mass had decreased the false negative rate to less than 1% [9].But FNAC can be done as an outpatient procedure and helps in rapid diagnosis. The limitations of FNAC include difficulty to differentiate ductal carcinoma in situ (DCIS), atypical ductal hyperplasia from low grade DCIS and fibroadenoma from phyllodes tumor [10, 11]. Core biopsy is an effective means

to diagnose breast lumps, but it is expensive, time consuming and associated with complication like hematomas and rarely pneumothorax [12, 13]. But in many developing countries and in some European countries, FNAC is still routinely performed for diagnosing breast lesions [14]. FNAC is a rapid, less invasive and less traumatic procedure but needs an experienced pathologist for better results. "As fine needle aspiration (FNA) has become a critical component in the investigation of palpable breast masses; false negative diagnoses have become a major concern prompting re-evaluation of the definition of specimen adequacy. Although cytopathologist agree that a number of parameters relate to the adequacy of an FNA specimen, there is no consensus on the role of epithelial cell quantitation in the determination of an adequate FNA. To better understand the significance of epithelial cellularity, false-negative FNA samples from palpable breast lesions were reviewed [15].

The aim of this study was to evaluate role of FNAC in the diagnosis of breast lesions, their risk categorization for development of cancer & to compare the cytological findings with the histopathology thus sensitivity and specificity of FNAC of breast lump in our institute.

MATERIAL & METHODS

The present study was carried out in department of Pathology of Agartala Govt. Medical College & GB Pant Hospital, Agartala, Tripura, India from December, 2013 to June, 2015 after taking permission from ethical committee of the institution. This study has been performed as a part of the Network programmme on cancer in women for NE India sponsored by the Department of Bio-Technology, Govt. of India, named as Breast Cancer awareness & screening using BSE, CBE & clinical follow up in women (30-64 years).

We have performed sensitization & awareness of women at our institution as well as screening of all palpable lumps for early detection of malignancy and onsite diagnostic program for all referral cases waiting for surgery and treatment. The patients with palpable breast lump referred from general surgery department of our institution for FNAC were involved in this study.

Study Duration:

The study was conducted for 19 months from December 2013 to June, 2015.

Sample size:

A total of 468 patients were included in this study.

Patients Protocol: A designed proforma was used to collect the consent and data of patients. History of lactation and pregnancy was included in the proforma. The case history of the patient was recorded, including history of pain, nipple discharge, ulceration of nipple and duration of lesion. The examination of breast lump was done with recording of size and site of lump, consistency and fixation to skin and underline tissue, retraction of nipple along with regional lymph node involvement. Consent was taken after due explanation of the procedure and its benefit to the patients.

All the lesions were followed for biopsy except inflammatory and inadequate samples. The inadequate lesions were advised a repeat FNAC. Both benign and malignant tumors were followed up. Patients were divided into groups, and their mean age was calculated.

Sample Selection:

Inclusion criteria

All female with unknown primary diagnosis of breast mass / lumps were subjected to FNAC followed by excision biopsy / lumpectomies or mastectomy.

Exclusion criteria

1. Patients with recurrent malignancy.
2. Patients who underwent FNAC but did not undergo subsequent histopathological diagnosis.
3. Patients undergoing past/current chemotherapeutic or prevention treatment.
4. Patients in whom FNAC was either acellular or non-diagnostic or inflammatory.
5. Male patients with breast cancer and gynecomastia.

Sampling technique:

Non-probability convenient sampling

Procedure for FNAC

A written consent was taken before performing the FNAC. FNA was done using 10ml/20ml disposable syringe each prick and for each patient. No local anesthetic was used. The needle was inserted into the palpable lesions, either once or twice depending upon the size of the nodule. Cellular material was aspirated into a syringe and expelled onto slides. Two to eight slides were prepared for each patient. One of the smears was wet fixed in 95% methanol and stained with Hematoxylin and Eosin (H&E) and Papanicolaou stains. The air dried smears were stained with Giemsa stain. The procedure was done within one hour, and the reports were signed out within 1-2 days.

Criteria For Adequacy:

There should be at least six clusters of ductal cells on each smear comprising 10 cells per cluster. At least two to three passes are made from the lump from all aspects. Cytology reporting was based on the following NHS guidelines [16].

Four Groups were defined for the FNAC Diagnosis

1. Inadequate
2. Non-neoplastic benign inflammatory/ proliferative lesions
3. Suspicious of malignancy
4. Positive for malignancy

NB: Groups 3-4 were malignant (in calculation)

Criteria for malignancy:

The morphological characteristics that were used to distinguish benign from malignant cells are as follows:

1. Abnormal grouping of cells
2. Decreased mutual adhesiveness
3. Presence of foreign cells
4. Changes in the nucleus
5. Increased/abnormal mitoses
6. Variation in size and shape of cells
7. Abnormal cytoplasmic inclusions.

Procedure for Histopathology:

The biopsy specimens were fixed in 10% formalin for 24 hours. Then gross examination was done in the Department of Pathology by consultant histopathologist. The gross and cut section findings were noted. Several bits were taken from appropriate sites for processing and paraffin embedding. From each block, sections were cut at 4-5 microns thickness and stained with H&E.

Inflammatory (109) and Inadequate (11) smears were not followed for their biopsies. Remaining 348 (benign smears, suspicious, and malignant) smears were followed for biopsies (81 mastectomies and 267 lumpectomies).

Statistical Analysis:

Data was computerized with window SPSS version16.

Specificity, sensitivity, accuracy, and predictive values were calculated, P values were also calculated, while correlation was

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seen by Pearson's correlation curve.

RESULTS

In a period of one and half years, 468 patients underwent FNAC of the primary breast lumps in the Department of Pathology.

There were 109 inflammatory lesions and 11 smears were inadequate thus inconclusive.

Cytologically inflammatory smears were not considered for biopsy and histopathological examination and thus were excluded. Remaining 348 (benign smears, suspicious, and malignant) smears were followed for biopsies (81 mastectomies and 267 lumpectomies). There were total of 301/468 (64.3%) benign lesions comprising of 109 (23.3%) inflammatory aspirates and 192(41%) benign proliferative lesions. Cytological diagnoses of other aspirations were reviewed, and lesions were classified into four diagnostic classes revealing 192 benign proliferative lesions, 112 malignant, 44 suspicious, and 11 inadequate smears (Table 1).

There were maximum lesions during the reproductive age groups, and most of these were benign. Maximum malignant lesions were seen in older age groups. This relationship was statistically significant when compared by Pearson's correlation curve. A positive correlation was observed between benign and malignant lesions **(r =0.95, P < .0001)** (Table 1, Figure 4). The age of the patients ranged between 16 to <70 years. The youngest patient diagnosed as invasive ductal carcinoma (IDC) was seen at 19 years of age. In our study, most of the benign lesions were reported (24.5% & 45.3%) in 3rd and 4th decades of life, while maximum numbers of malignant lesions (24.1and 31.2%) were reported in 5th and 6th decades (Table 1).

There were 22.0%, 35.8%, 19.3%, 11.9%, 5.5%, 0.9% and 4.6% lesions of acute suppurative mastitis, acute mastitis, non-tuberculous mastitis, chronic non specific mastitis, duct ectasia, tuberculous mastitis, and fat necrosis, respectively. The diagnosis of these lesions was made by cytology and histology of cell blocks (Table 2).

In benign proliferative breast lesions, we were very conscious about over-diagnosis, therefore our reporting style was as "smear negative for malignant lesions", and for further analysis we advised an excision biopsy for definite diagnosis to fibroadenoma, fibrocystic disease, benign proliferative disease, and phyllodes tumors. For uncertain categories we only reported "benign proliferative lesions". This class of diseases constituted the largest group of lesions with maximum incidence in the 3rd, 4th and 5th decades of life (Tables 1 and 3).

Invasive ductal carcinoma was the most common malignant lesion reported in our study with a maximum incidence in the 4th, 5th, and 6th decades, followed by invasive lobular carcinoma and other malignant lesions (Table 4). Following histopathologic correlation with FNA, we calculated the sensitivity, specificity and positive predictive values.

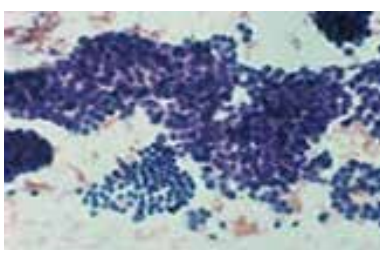
There were 5 false positive cases and 1 false negative case in this study. False positives were observed in the suspicious lesions and one false negative was observed in benign proliferative lesion.

False positives noted mainly in the interpretation of suspicious smears or with atypical features, were due to uniformly enlarged nuclei with prominent nucleoli, occasional marked nuclear enlargement, and moderate pleomorphism seen in fibrocystic disease or fibroadenoma. Regarding benign proliferative and malignant lesions no false positivity was seen. Therefore, in the this study, the sensitivity was 99.3% specificity 97.4%, efficiency 98.27%, negative predictive value 99.5%, and the positive predictive value was 96.8% (Table 5,6).

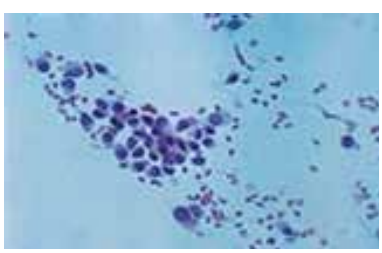
All the FNAC smears are compared with histopathology and the details given in Figures 1, 2, 3, 4.

DISCUSSION

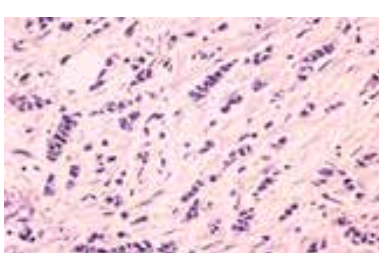
FNAC was first described by Martin and Ellis in 1930 for sampling cervical lymph nodes [17]. FNAC is a simple rapid technique performed as an outpatient procedure with less chance of complications unlike core biopsy which has risk of bleeding and occasionally rare complications like pneumothorax. It does not require any anesthesia or hospitalization and is cost effective. Experience and expertise in sampling and interpretation of specimen decide the effectiveness of FNAC. The other limitation of FNAC is it cannot differentiate few lesions like fibroadenoma from phyllodes, phyllodes from metaplastic carcinoma breast, papilloma from papillary carcinoma, and atypical ductal hyperplasia from ductal carcinoma in situ. Though a triple assessment is advocated for all palpable breast lumps, it is not feasible in developing countries like India, where affordability and availability are an issue at all centers



Invasive ductal carcinoma

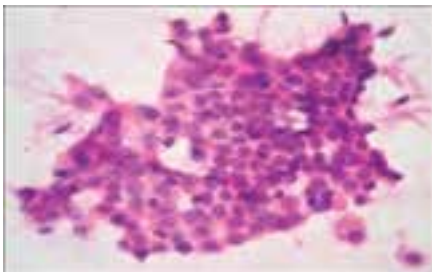


Invasive ductal carcinoma

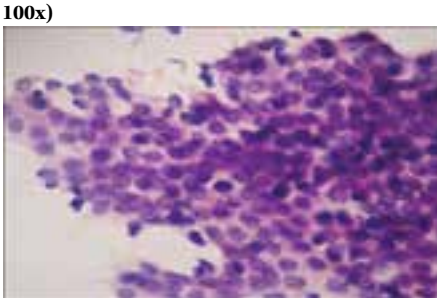


Invasive lobular carcinoma

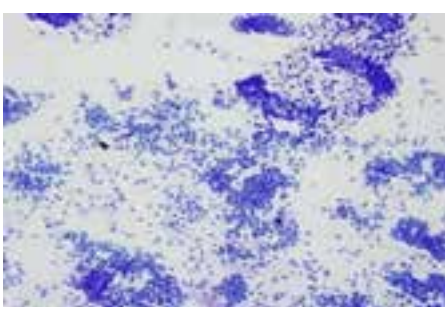
Benign phyllodes tumour showing monolayered sheets of epithelial cells in clusters and fair number of bare uclei in the background, and a stromal fragment with low cellularity (PAP,100x)



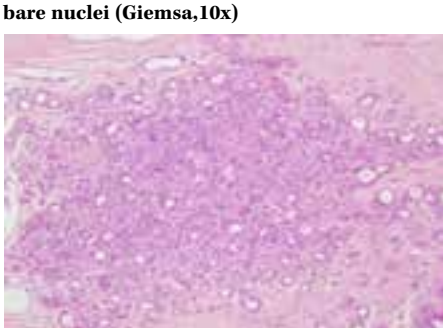
Microphotograph of fibrocystic disease showing benign ductal epithelial cells and cyst macrophages. (H and E, 100x)



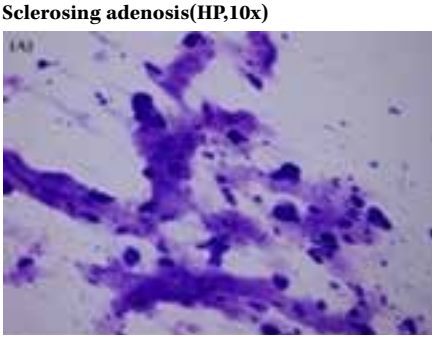
Microphotograph of ductal hyperplasia showing ductal epithelial cells in sheets show mild atypia (H & E,100x)



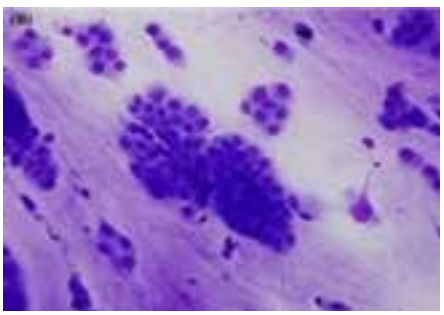
Fibroadenoma showing uniform epithelial cell groups with bare nuclei (Giemsa,10x)



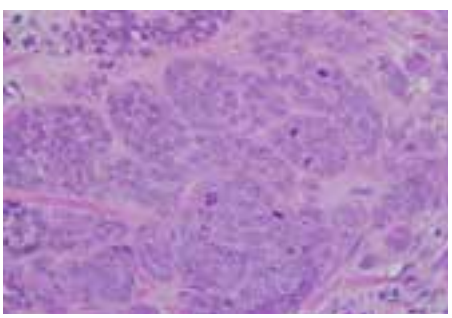
Sclerosing adenosis(HP,10x)



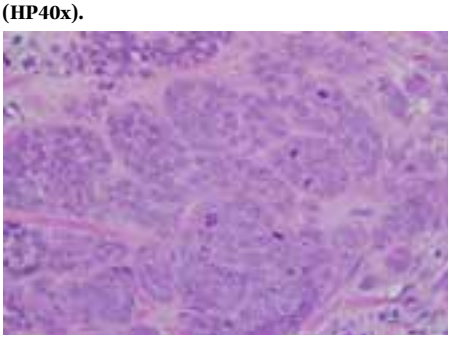
FNA smear shows clusters of tumor cells in a rich mucinous background (40x)



FNAC showing abortive micropapillae (Giemsa,100x)



High-grade invasive ductal carcinoma, with minimal tubule formation, marked pleomorphism and prominent mitoses (HP40x).



FNA breast showing epitheloid cell granuloma with caseation necrosis and ductal epithelial cells in background (Leishman, 5x)

and clinical decision takes a major role. It is an excellent, safe, and cost eective diagnostic procedure. One can get onsite immediate report with minimal cost using inexpensive equipments and a simple technique. The most significant advantage of FNAC is the high degree of accuracy, rapid results and a less invasive procedure than a tissue biopsy. FNAC of the breast can reduce the number of open breast biopsies [18–21].

Breast carcinoma is common cancer among females in India preceded by cervical cancer. [22, 23] Different studies have shown that the most common lesions are benign and needs only reassurance.[23, 24] Early screening and diagnosis of breast lesions and categorization into different groups of breast pathology is important. This can be helpful in prevention of cancer and in accurate management of the patients. Early diagnosis helps to prevent patients discomfort and anxiety. [25, 26] Fibroadenoma (table 3) is the commonest lesion in the category of proliferative breast disease without atypia that has minimal risk for cancer development. Ferguson also reported that most common breast lesion as fibroadenoma occurring before the age of 25 years of age [27]. Invasive ductal carcinoma is the commonest breast malignancy and found in the age group of 41-60 years of age [28]. The present study shows similar findings, the ductal carcinoma

Volume : 5 | Issue : 3 | March 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

being the most common breast malignancy in the age group of 41-60 year of age (table 4). In this study 2.6 % cases were unsatisfactory. Sudarat et al. [29] found 4.2% of unsatisfactory smear which needs further repeat aspiration or needs core/ incisional biopsy for analysis. Unsatisfactory sample can be due to the either lack of technical experience in performing FNA, preparation, and fixation of smears or due to FNA of illdefined, poorly localised masses or lesions with hyalinization and deeply located lumps may also be contributed to the inconclusive diagnosis [30, 31].Unsatisfactory sample can be due to insufficient experience of the pathologist, radiologist or clinician who is performing FNA or due to nature of lesion itself. FNA sampling technique is equally important as sample interpretation in reaching the correct diagnosis. Provision of adequate sample and experienced pathologist can prove FNAC as highly reliable diagnostic tool [1].

Many inflammatory breast lesions create confusion as these are presented as a palpable mass. "Mammographic, sonographic, and magnetic resonance imaging findings may not always distinguish some of the benign lesions like duct ectasia, fat necrosis from a malignant lesion." Fine needle aspiration (FNA) is a well-accepted diagnostic modality and procedure for the diagnosis of inflammatory swellings of breasts. Fine needle aspiration is the most accurate diagnostic modality for these lesions and cell blocks accentuate the reliability of the diagnosis in these benign inflammatory and curable lesions without requirement of excision biopsy or other second line investigations. In this study, these were reported as benign inflammatory diseases and their histopathologies were followed and were further categorized into different lesions. Cell blocks were prepared after making the required smears and were processed for histopathology [32– 34].

Table 1: Age of the patients presenting with lump breast.

Age in years (n = 468)	Inadequate	Benign lesion		Suspicious for malignancy	Malignant
		Inflammatory	Benign proliferative lesion		
A 16-20 (n = 25)	2	5 (4.6%)	14 (7.3%)	3 (6.8%)	1 (0.9%)
B 21-30 (n = 84)	2	14 (13%)	47 (24.5%)	7 (15.9%)	14 (12.5%)
C 31-40 (n = 183)	3	65 (60.2%)	87 (45.3%)	9 (20.5%)	19 (17%)
D 41-50 (n = 94)	2	16 (14.8%)	37 (19.2%)	12 (27.3%)	27 (14.1%)
E 51-60 (n =58)	1	7 (6.5%)	7 (3.7%)	8 (18.2%)	35 (31.2%)
F 61-70 (n = 18)	1	2 (1.8%)	0	2 (4.5%)	13 (11.6%)
G < 70 years (n = 6)	0	0	0	3 (6.8%)	3 (2.7%)
Total	11	109(23.3%)	192 (41%)	44 (9.4%)	112 (23.9%)

Table 2: Comparison of distribution of inflammatory lesions

Inflammatory lesions (n=109)	Cytology	Histopathology
Acute Mastitis	39 (35.8%)	All these cases were not considered for HPE thus excluded.
Acute suppurative mastitis	24 (22%)	
Chronic nonspecific mastitis	13 (11.9%)	
Granulomatous mastitis (non tuberculous)	21 (19.3%)	
Duct ectasia	6 (5.5%)	
Tuberculosis	1 (0.9%)	
Fat necrosis	5 (4.6%)	

Fig No. 1: Age distribution of breast lumps

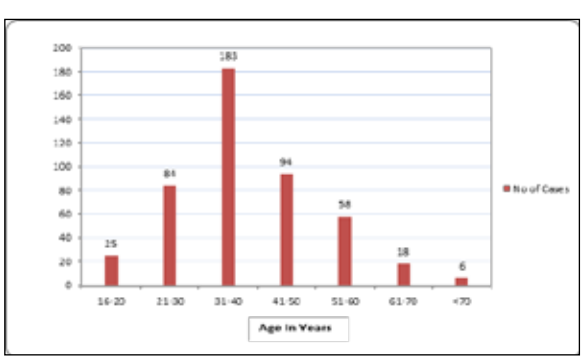


Fig.2 Age Distribution of patients with Malignancy

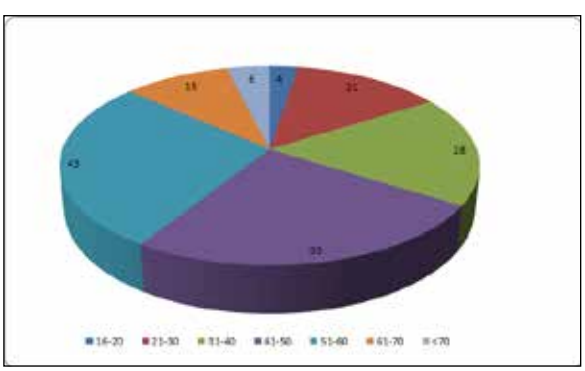


Table 3: Comparison of distribution of benign proliferative lesions

Cytologically benign lesions (n=192)	Cytology	Histopathology						
		FCD	FA	FAD	EpH	AEH	BPh	Malignant
Fibro adenoma	99 (51.5%)	10	76	7	3	1	2	0
Fibrocystic disease	78 (40.6%)	53	14	7	2	2	0	0
Benign proliferative Ds.	12 (6.3%)	0	0	7	4	0	1	0
Benign Phylloides	3 (1.6%)	0	1	0	0	0	1	1
Total	192	63	91	21	9	3	4	1

FCD: fibrocystic DS, FA: fibroadenoma, FAD: fibroadenosis, EpH: epithelial hyperplasia, AEH: atypical epithelial hyperplasia, BPh: benign phylloides

Table 4: Diagnosis of cytological suspicious & malignant smears on Histopathology

Cytology	Histopathology									
	Malignant							Benign		
	DCIS	IDC	LCIS	ILC	MC	MDC	MPh	FAD	FA	ScA
Suspicious for malignancy (n=44:9.4%)	17	12	5	5	0	0	0	2	2	1
Malignant lesions (n=112:23.9%)	4	89	2	12	2	1	2	0	0	0

DCIS: ductal carcinoma in situ, IDC: infiltrating duct carcinoma, LCIS: lobular carcinoma in situ, ILC: invasive lobular carcinoma, MC: mucinous carcinoma, MDC: medullary carcinoma, MPh: malignant phylloides, FAD: fibroadenosis, FA: fibroadenoma, ScA: sclerosing adenosis.

Table 5: Comparison of Cyto-Histological diagnosis

Cytological Diagnosis	No. of Cases	Histopathology Diagnosis		
		Consistent	Inconsistent	Total
Inflammatory	109	Excluded	Excluded	109
Benign	192	191(99.5%)	1(0.5%)	192
Malignant	112	112(100%)	0(00%)	112
Suspicious of Malignancy	44	39(88.6%)	5(11.4%)	44
Total	457	342(98.3%)	6(1.7%)	457

Fig 3: Comparison of cyto-histological diagnosis

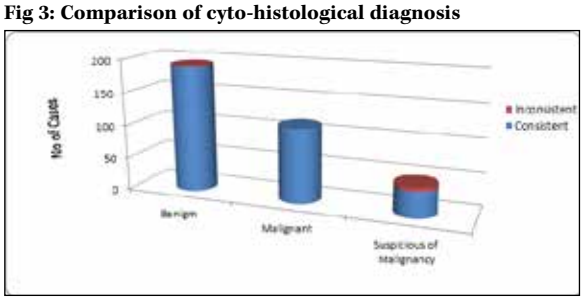
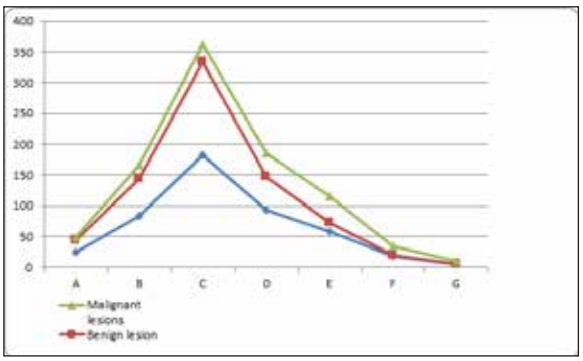


Fig 4: Correlation between Benign and Malignant lesions in different Age groups of patients presented with lump Breast.



Note: A positive correlation was observed between Benign and malignant lesions (r = 0.95, P < .0001).

Table 6 : Statistical analysis

CYTOLOGY / HISTOPATH	Positive	Negative
Positive	151	01
Negative	05	191

True positive cases (TP) = 151 False positive cases (FP) = 05
True negative cases(TN) = 191 False negative cases (FN) = 01

$$\text{Sensitivity} = \frac{TP}{TP + FN} \times 100 = \frac{151}{151 + 1} \times 100 = 99.3\ \%$$

$$\text{Specificity} = \frac{TN}{TN + FP} \times 100 = \frac{191}{191 + 5} \times 100 = 97.4\ \%$$

$$\text{Positive predictive value} = \frac{TP}{TP + FP} \times 100 = \frac{151}{151 + 5} \times 100 = 96.79\%$$

$$\text{Negative predictive value} = \frac{TN}{TN + FN} \times 100 = \frac{191}{191 + 1} \times 100 = 99.5\ \%$$

$$\text{Efficiency} = \frac{TP + TN}{TP + FP + FN + TN} \times 100 = \frac{151 + 191}{151 + 5 + 1 + 191} \times 100 = 98.27\ \%$$

Table no 7: Comparison of accuracy of FNAC

Author	Sensitivity	Specificity	Positive predictive value	Efficiency	Negative
Kline TS et al(1979)	89.5%	92.5%	85.33%	91.63%	-
Francisco D et al(1995)	93.49%	95.73%	93.49%	98.75%	95.73%
Feichter et al(1997)	86%	99.3%	99.3%	93%	85%
Premila De SR et al(1997)	93.8%	98.21%	92.70%	97.40%	-
Zhang Qin(2004)	97.1%	97.3%	-	9.2%	-
Arjun Singh et al (2011)	84.6%	100%	-	92.3%	-
Khemka A et al(2011)	96%	100%	100%	-	95.12%
Bukhari et al(2011)	98%	100%	97%	98%	100%
Present study	96.66%	98.66%	96.77%	98.11%	98.66%

Volume : 5 | Issue : 3 | March 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Table no 8 : Comparison of cytological diagnosis with other studies.

Author	Malignant	Suspicious for malignancy	Benign	Inadequate smear	Other	Total
Debra et al (1983)	131(7.79%)	300(8.92%)	1019(60.65%)	230(13.69%)	0	1680
Feither G et al(1995)	181(12.3%)	49(3.3%)	1003(68.1%)	239(26.6%)	0	1472
Premila De SR et al (1997)	92(15.33%)	15(2.50%)	486(81.0%)	7(1.16%)	0	600
Kuldeep Singh(2001)	35(14.58%)	5(2.08%)	200(83.33%)	0	0	240
Quasim et al(2009)	32(27.58%)	0	68(58.62%)	16(13.79%)	0	116
Sajid(2010)	58(47.5%)	0	64(52.5%)	0	0	122
Bukhari et al(2010)	120(28.23%)	32(7.52%)	271(63.76%)	0	2(0.47 %)	425
Shreshta et al(2011)	152(10.83%)	175(12.47%)	618(11.97%)	27(1.92%)	431(30.7%)	1403
Tohuiddin (2011)	72(13.74%)	17(3.24%)	431(82.25%)	3(0.57%)	4(0.76%)	524
Present study	112(23.9%)	44(9.4%)	301(64.3%)	11(2.3%)	0	468

There were 109 (23.3%) cases of benign inflammatory lesions, and the majority of these were of acute and chronic mastitis. "Granulomatous mastitis is a rare chronic inflammatory breast lesion that mimics carcinoma clinically and radiologically" [34–36]. There were 1 (0.9%) cases of tuberculosis; definitive diagnosis of the tuberculous mastitis was based on identification of typical cytological features under microscopy and detection of tubercle bacilli on Ziehl-Neelsen stain.

FNAC has some pitfalls in the diagnosis of Fibrocystic disease (FCD), adenosis, epithelial hyperplasia with or without atypia, apocrine metaplasia, radial scar, and papilloma [37]. Fibroadenoma and these benign lesions are more common in our setup. "Various types of adenosis have also been described, of which sclerosing adenosis and micro-glandular adenosis merit detailed description and most of these lesions mimic malignant lesions" [38].

In this study, 348 FNAC were correlated with histopathology to evaluate the diagnostic sensitivity, specificity and accuracy of this diagnostic modality. Among these lesions 192 (41%) were benign proliferative lesions. In our study, we further categorized these lesions into six main groups; namely fibroadenoma, fibrocystic disease, fibroadenosis, epithelial hyperplasia, atypical epithelial hyperplasia and benign phyllodes tumors. The spindle cell lesions were diagnosed as benign phyllodes on cytology reports. These results were confirmed by histopathology from the cellblocks and true cut biopsies. In our study, only one malignancy was seen while few discrepancies were seen in making final categories. Out of 99 FNAC diagnosed as FA, there were 76, 10, 7, 3, 2, 1 nd 1 cases of FA, FCD (when there were mixture of cysts, fibrosis, and proliferating ductal epithelium), FAD (overgrowth of both fibrous stroma, and of epithelial elements, i.e., ducts and lobules, in differing proportions), epithelial hyperplasia, benign phyllodes and Atypical epithelial hyperplasia respectively on histopathology. From 78 FCD, there were 53, 14, 7, 2 and 2 cases of FCD, FA, FAD, epithelial hyperplasia, and atypical epithelial hyperplasia respectively on histopa-thology.

In our experience, FNAC results are more reliable regarding malignant lesions; however the category of "Suspicious for Malignant Lesions" needs histopathological evaluation before performing surgical measures. Self-assessment, mammography, and true-cut biopsy may help in the accuracy of these lesions [39].

In comparative analysis of FNAC and histopathology diagnosis, we observed 6 cases of cytologically interpreted errors which were 5 false positive cases and 1 false negative case. The only false negative case diagnosed was a case of benign proliferative breast disease (benign phyllodes tumor) with moderate epithelial hyperplasia with atypia which turned out to be malignant (malignant phyllodes tumor). Out of 5 false positive cases, 4 cases were benign proliferative breast disease (2 cases each of fibroadenoma and fibroadenosis) with moderate epithelial hyperplasia by histology which was diagnosed as suspicious malignant lesion (IDC) whereas 1 false positive case was actually sclerosing adenosis, which was diagnosed as ductal carcinoma by cytology. Rest of 39 cases diagnosed as suspicious for malignancy in FNA were confirmed as malignant by histopathological examination. FNAC of breast lesions is sensitive, specific, and highly accurate as the initial investigation of palpable breast lesions in tertiary hospital. [40] Thus the FNAC smears have very high accuracy in diagnosis of breast lump.[41,42].

This study was undertaken to assess the use of FNAC as primary method for diagnosis of breast lumps. Fine Needle Aspiration Cytology has been proved to be highly efficacious method in diagnosis of palpable breast lesion in this study. The sensitivity of 99.3 % and specificity of 97.4 % obtained in our study were in accordance to sensitivity of 77-99% and specificity of 92-100% reported in various studies [43-50] as shown below by the table 7 and table 8.

CONCLUSION

The cytological examination of breast lesions prior to surgical treatment serves as a safe, rapid, economical, highly accurate method and valuable diagnostic tool to avoid undue surgery and inconvenience during biopsy. Adhering to the principle of "Triple test" and acquisition of technical, observational, and interpretative skills will further enhance the diagnostic accuracy of proliferative conditions with atypia or suspicious lesions of breast. Also the same aspiration can also be used for ancillary molecular testing. It helps to take the decision for mode of surgery. 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. The present study proved that the procedure has high sensitivity, specificity and diagnostic accuracy. It can be concluded that diagnosis of breast lesion based on FNAC should be practiced as a routine procedure as there is high degree of correlation with histopathologic findings. FNAC is also an ideal method for patients follow up if there is recurrence of breast lump. In the presence of budget constraints and personnel shortage, hospitals are required to demonstrate even great cost effectiveness in the diagnosis of breast lesions. FNAC should be used as a routine diagnostic procedure due to its cost effectiveness, thus maximizing the availability of health care to patients with breast lesions. Unsatisfactory samples should not be neglected and should be considered for excisional biopsy in presence of clinical suspicion.

Recommendations:
Proper training and skilled courses should be arranged for the technical staff because it increases the reliability and accuracy of the test.

No overemphasis should be made in the reporting of FNA and reporting of FNA and very careful strict criteria should be adapted like advised repeat FNAC, cellblock preparation, biopsy or correlation with clinical findings and so forth. Three tier systems should be used instead of 5 classes of the breast cytology, for example, benign, suspicious, and malignant. FNAC should be repeated when inadequate and improper smears are prepared.

When the results are obviously benign, patients should be reassured and can be prevented from undergoing unnecessary surgery while in the case of a clearly malignant smears, surgery and other treatment should be started without any delay.

For the gray areas, for example, suspicious and inadequate smears, either repetition of the FNA or a surgical biopsy should be recommended.

Conflict of Interests:
There is no conflict of interests.

List of Abbreviations
FNAC: Fine needle aspiration cytology
DCIS: Ductal carcinoma in situ
PAP: Papanicolaou
MGG: May-Grunwald Giemsa stain.

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