Cytolo-histological correlation of breast lump - as a part of internal quality control

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Abstract

Introduction: Fine Needle Aspiration Cytology (FNAC) has gained increasing importance in the diagnosis of breast lumps especially it is an easy, non-invasive, simple procedure which can be done on OPD basis. The pre–operative diagnosis of breast lesions by FNAC is highly relied upon. However, there can be some cytological pitfalls in the diagnosis, especially when all the characteristic component of a lesion are not obtained in the aspirate, or when there is an overlap in the cytological features.
Hence a review was undertaken with the following objectives.

1. To correlate cytologic and histopathologic diagnosis of breast lesions as a part of internal quality control.
2. To know the incidence of false positive and false negative cases.
3. To find out the sensitivity and specificity of FNACof breast lesions.

Methods: This study was conducted for a period of 3 years (April 2009 to March 2012) and 200 cases of fine needle aspirates of breast lumps studied. Out of which 126 cases were followed by histopathological correlation at pathology department; the cases are collected from Mahatma Gandhi Medical College & Research Institute, Sri Balaji Vidhyapeeth University; Pondicherry.

Results: Out of 200 cases studied by FNAC, histopathological correlation was available for 126 cases. Cytological diagnosis in general was divided into four categories, benign (76.19%), malignant (15.08%), suspicious (5.56%), and unsatisfactory (3.17%).

Maximum patients were in age group of 21 to 30 years. There were 119 female patients and 7 male patients.

Fibroadenoma (69.79%) was most common benign neoplasm. There were 5 cases (5.21%) reported by FNAC as gynecomastia.

After correlation with histopathology, there was 82.26% of correct diagnosis in all benign lesions.

There were 16 cases (84.21%) diagnosed cytologically as malignant and 3 cases (15.79%) as invasive duct carcinoma. Histopathologically all were confirmed as invasive duct carcinoma. Out of that one was reported in male breast.

The incidence of false positive case was zero, false negative case was (1.59%). The diagnostic accuracy after histopathological correlation in malignant cases was 98.36%, sensitivity was 92.86% and specificity was 100%.

Conclusion: To conclude, fine needle aspiration cytology is a fairly safe procedure in trained hands, and it gives reasonably accurate results, thereby helping the clinicians to plan the best line of treatment. Also with invention of imaging guided aspiration, FNAC went one step ahead in diagnosis of non-palpable lesion of breast. Thus a triple modality of clinical, mammographic and cytological correlation is required and for internal quality control FNAC is correlated with histopathology.

Key Words: FNAC; Breast lumps; Breast neoplasm

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Introduction

A palpable breast lump is a common diagnostic problem both to the general practitioner and to the surgeon[1].

Fine needle aspiration cytology is widely accepted diagnostic tool nowadays. It has become a routine clinical approach in many hospitals and clinics, often replacing pre-operative biopsy.

The breast is a surface organ, easily palpated and aspirated. Pathologic changes of its glandular and stromal components are extremely common. In addition to enormous reservoir of benign pathology, cancer of the breast is the most frequent malignancy and leading cause of cancer deaths in women. Traditional management of breast tumors has been surgical biopsy. As the number of biopsies of suspicious lesions has increased, the cost of screening for breast cancer is also increased. The need for cost containment has led to interest in alternative methods to open biopsy that could provide definitive diagnosis of breast cancer. Fine needle aspiration represents such an alternative technique.

In many cases of carcinoma breast, radical surgery is unnecessary. This made the need for preoperative definitive diagnosis even more necessary. Clinical examination in conjunction with fine needle aspiration cytology and mammography, also known as “triple-approach” which can divide almost all breast lesions preoperatively into benign and malignant categories. This “triple diagnostic technique”, which determine the diagnosis and assess the need for open biopsy, it was also suggested by Kreuzer and Boquoi (1976)[2] and Hermansen et al (1987)[3]. In elderly patients, breast lumps are more often malignant, and aspiration cytodiagnosis provides the least traumatic method of

diagnosis and may be the only comfortable procedure necessary in patients only is treated with hormone therapy.

Many worker like Patra et al[4], Zajdela at el[5], Bell et al[6] and Kline et al[7] have demonstrate the accuracy of fine needle aspiration cytology in the diagnosis of breast masses.

The trend towards more conservative surgery and individualized treatment has increased the importance of close correlation of radiological, cytological and histological findings.

Histopathological correlation of cytological material is also to understand the lesion more clearly and also one of the objective criteria used for Internal Quality Control.

An attempt has been made in the present study to know the utility of fine needle aspiration cytology in diagnosis of breast lesions with histopathological correlation.

Although FNAC has certain limitations.

1. Sampling error, which can give false negative results.
2. ''Suspicious'' category is the 'grey zone' for many cytopathologists
3. Inadequate smears can pose a source of difficulty in diagnosis.
4. Interpretive errors can also create problems for accurate diagnosis.[8]

Objectives of the study

1. To correlate cytologic and histopathologic diagnosis of breast lesions as a part of internal quality control.
2. To know the incidence of false positive and false negative cases.
3. To find out the sensitivity and specificity of FNACof breast lesions.

Materials and Methods

The study was a retrospective study, undertaken to study the cytologic and histopathologic correlation of brest lesions as a part of internal quality control and to determine the diagnostic accuracy of FNAC.

All the cases of breast specimens received in the Pathology Department of Mahatma Gandhi Medical College And Research Institute, Sri Balaji Vidhyapeeth University during the period between April 2009 to March 2012 were analysed.

The available specimens, tissue blocks and slides were reviewed. Wherever necessary and relevant, fresh sections were taken from the preserved tissue blocks, stained with the standard Haematoxylin and Eosin stain and some of the archived slides were restained and reviewed.

For all cases the respective cytological smears were traced and reviewed. The cytological smears were stained by the standard Haematoxylin and Eosin (H&E) stain, May-Grunwald-Giemsa (MGG) stain and Papanicolau (Pap) stain. Wherever necessary and relevant, the smears were restained and cytological evaluation was done.

200 cases of fine needle aspirates of breast lumps studied. Out of which 126 cases were followed by histopathological correlation.

The cytological diagnosis was correlated with the histopathological diagnosis and the efficacy and diagnostic accuracy of FNAC was calculated. Descriptive statistics were done to evaluate our results.

Results

A retrospective study of cyto-histopathological correlation of breast lesion was carried out at the Department of Pathology, Mahatma Gandhi medical college and research institute.

Present study was carried out during the period of April 2009 to march 2012. During this period of 3 years, 126 specimens; out of 150 cases of fine needle aspiration of breast lesions were studied and followed by the histopathological examination.

Table 1: Age incidence of breast lesions (of 126 cases)

Age range	No. of cases	Percentage
0-10	0	0 %
11-20	32	25.40%
21-30	44	34.92%
31-40	29	23.02%
41-50	09	7.14%
51-60	11	8.73%
61-70	01	0.79%
Total	126	

During the study the incidence as maximum in the range of 21 to 30 years of age, that was 44 (34.92%). There were 32 cases (25.40%) in the age group of 11 to 20 years, 29 cases (23.01%) in the 31 to 40 age group and 9 cases (7.14%) were in the age group 41 to 50 years. In the group 51 to 60 years, there were 11 cases (8.73%). In the 61 to 70 years, there was only 1 case (0.79%) reported and not a single case was reported in the 0 to 10 years age group during present study.

Table 2: Sex incidence

Sex	Total no. of cases	Percentage
Female	119	94.44%
Male	07	5.56%
Total	126	

The present study of 126 cases, 119 cases (94.44%) were the lesions from female breast; while 07 cases (5.56%) were the lesions from male breast.

Table 3: Cytological findings in breast FNA smears in general

Cytological diagnosis	No. of cases	Percentage
Benign	96	76.19%
Malignant	19	15.08%
Suspicious	07	5.56%
Unsatisfactory	04	3.17%
Total	126	

Out of total 126 cases studied by fine needle aspiration cytology, 96 cases (76.19%) revealed benign features, 19 cases (15.08%) revealed malignant features, 7 cases (5.56%) were reported as suspicious of malignancy and in 4 cases (3.17%) cytological reporting was not possible due to unsatisfactory smears.

Table 4: Cytological and histopathological correlation of benign breast lesions

Breast lesions	Cytological diagnosis		Histopathological diagnosis	
	No.	%	No.	%
1. Inflammatory lesions				
• Chronic mastitis	03	3.13%	02	2.04%
• Granulomatous mastitis	02	2.08%	03	3.06%
2. Benign proiferative disorders				
• Fibro cystic change	11	11.46%	11	11.22%
• Mammary dysplasia	-		02	2.04%
• Sclerosing adenosis	-		03	3.06%
3. Epithelial hyperplasia	2	2.08%	-	-
4. Benign neoplasms				
• Fibroadenoma	67	69.79%	66	67.34%
• Phyllodes tumour	06	6.25%	05	5.10%
• Lactating adenoma	-		01	1.02%
5. Miscellaneous				
• Gynecomastia	05	5.21%	05	5.10%
Total	96		98	

Cytologically there were 5 cases (5.20%) which were diagnosed as inflammatory lesions cytologically. Out of which 3 cases (3.13%) of chronic mastitis and 2 cases (2.08%) of granulomatous mastitis. Histopathologically there were total 5 cases (5.10%) of inflammatory lesions out of which there were 2 cases (2.04%) diagnosed as chronic mastitis and 3 cases (3.06%) were confirmed as granulomatous mastitis.

Cytologically there were 11 cases (11.46%) of benign proliferative disorders; out of which 10 cases (90.91%) were confirmed as fibrocystic change and one case diagnosed as mammary dysplasia histopathologically. Histopathologically there were 16 cases (16.33%) of benign proliferative disorders, out of which 11 cases (11.22%) of fibrocystic change**(Fig. 2),** 2 cases (2.04%) of mammary dysplasia and 3 cases (3.06%) of sclerosing adenosis were diagnosed. Cytologically 2 cases (2.08%) was diagnosed as epithelial hyperplasia with atypia. Histolopathologically diagnosed as malignant lesion Cytologically there were 67 cases (69.79%) of fibroadenoma. Out of which histopathologically 65 cases (97.01%) of fibroadenoma were confirmed and 2 cases diagnosed as fibrocystic change.(3.28%). Cytologically Phyllodes tumour was diagnosed in 6 cases (6.25%) **(Fig. 3)**. Out of which, 5 case (5.21%) correlated well histopathologically and one case (1.04%) diagnosed as fibroadenoma histopathologically making total fibroadenoma of 66 cases (67.34%) histopathologically.

There was 1 case (1.02%) of lactating adenoma diagnosed only by histopathologically; diagnosed as benign neoplasm. Aspirate of which was unsatisfactory cytologically. There was 5 cases (5.10%) of gynecomastia, which was diagnosed cytologically and correlated histopathologically.

Histogram

Showing percentage of correct diagnosis & over diagnosis in benign breast lesions

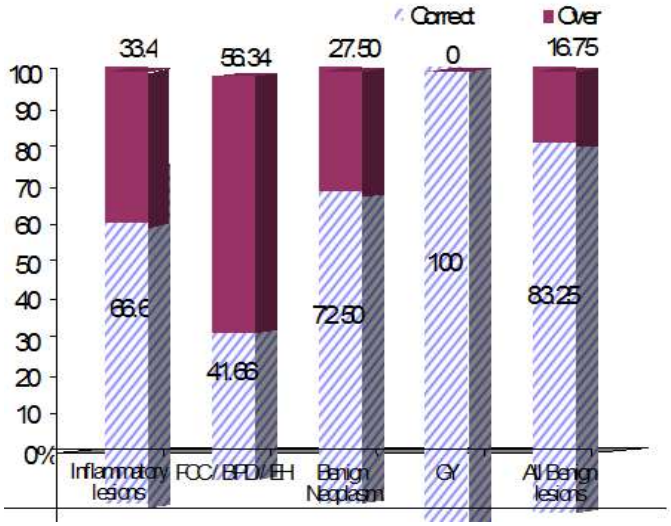

Fig. 1

Table 5: Cytological and histopathological correlation in malignant breast lesions

Lesions	Cytological diagnosis		Histopathological diagnosis	
	No.	**%**	**No.**	**%**
Malignant	16	84.21%		
Invasive duct carcinoma	3	15.79%	26	92.86%
Invasive lobular carcinoma	-		02	7.14%
Total	1**9**		28	

Cytologically 16 cases(84.21%) were diagnosed as malignant breast lesion which could not be further subtyped, while all these cases were subtyped histopathologically as invasive duct carcinoma.

Cytologically there was 3 (15.79%) case reported as invasive duct carcinoma and confirmed histopathologically.

Out of 7 cases (5.56%) diagnosed suspicious cytologically, 5 cases were diagnosed as invasive duct carcinoma, making total of 26 cases (92.86%) histopathologically as invasive duct carcinoma.**(Fig. 4)** And two cases cytologically diagnosed as suspicious; cytology smears was showing scanty cellularity, small cells in small groups and few scattered single cells with monotonously uniform size and shape and nuclei showing mild hyperchromasia, with a thin rim of cytoplasm around it, histopathologically it was diagnosed as invasive lobular carcinoma.(7.14%)

Cytologically, two cases was diagnosed epithelial hyperplasia with aytpia histopathologically it was diagnosed as invasive duct carcinoma.

Table 6: Cytohistopathological correlation of all cases (126 cases)

Cytological Diagnosis & No. of cases	**Histopathological diagnosis and No. of cases**										
	Chr. M.	**GM**	**FCC**	**MDS**	**SA**	**FA**	**PT**	**LA**	**GY**	**IDC**	**ILC**
Chronic mastitis–3	2	1									
Granulomatous mastitis–2		2									
Fibrocystic change–11			10	1							
Epithelial hyperplasia–2										2	
Fibroadenoma–67			2			65					
Phyllodes Tumour–6						1	5				
Gynecomastia–5									5		
Malignancy–16										16	

Invasive duct Carcinoma–3										3	
Suspicious-7										5	2
Unsatisfactory-4					3			1			
Total	2	3	12	1	3	66	5	1	5	26	2

Out of 3 cases (3.13%) diagnosed cytologically as chronic mastitis 2 cases was diagnosed histopathologically as chronic mastitis and 1 case as granulomatous mastitis. So there was only 66.66 **% correct diagnosis** in cases of chronic mastitis.

There were 2 cases (2.08%) during the present study which was diagnosed as granulomatous mastitis cytologically, which was correctly diagnosed histopathologically. So there was **100% correct diagnosis** in the cases of granulomatous mastitis.

There were 11cases (11.46%) diagnosed as fibrocystic disease cytologolically out of which 10 were confirmed histopathologically and 1 case was diagnosed as mammary dysplasia histopathologically. So, there was **90.90% of correct diagnosis** in cases of fibrocystic disease.

Cytologically 2 cases (2.08%) was diagnosed as epithelial hyperplasia with atypia, histopathologically it was diagnosed invasive duct carcinoma. This case was **false negative** which was misdiagnosed cytologically because failure to perceive some singly lying malignant cells having clear malignant features.

Cytologically there were 67 cases (69.79%) diagnosed as fibroadenoma. Histopathologically 65 cases were confirmed as fibroadenoma and 2 cases were diagnosed as fibrocystic change. So, **correct diagnosis in case of fibroadenoma is 97.01%.**

Cytologically 6 cases (6.25%) diagnosed as phyllodes. Hisopathologically 5 cases was confirmed as phyllodes and 1 case was diagnosed as fibroadenoma histopathologically making total cases of 66 (67.34%). So, **correct diagnosis of benign neoplasm is 72.5 %.**

There was 5 cases (5.21%) diagnosed as gynecomastia and it was correlated well with histopathological findings**.** So, **correct diagnosis was 100%.**

During the present study 16 cases (84.21%) were diagnosed cytologically as malignant breast lesions; histpathologically confirmed as invasive duct carcinoma. Also 3 cases (15.79%) diagnosed as invasive duct carcinoma cytologically which was confirmed histopathologically invasive duct carcinoma.

Out of 7 cases (5.56%) diagnosed as suspicious of malignancy, 5 cases were diagnosed as invasive duct carcinoma and 2 cases were of invasive lobular carcinoma diagnosed histopathologically.

There were 4 cases (3.17%) unsatisfactory smears cytologically, out of which 3 cases diagnosed as sclerosing adenosis histopathologically and 1 case diagnosed as lactating adenoma histopathologically.

Table 7: Cytological and histopathological correlation in general of all breast lesions (126 cases)

Cytological diagnosis	No.	%	Histopathological diagnosis	No.	%
Malignant	19	15.08	Benign Malignant	- 19	 15.08
Benign	96	76.19	Benign Malignant	94 2	74.60 1.59
Suspicious	7	5.56	Benign Malignant	- 7	- 5.56
Unsatisfactory	4	3.17	Benign Malignant	4 -	3.17 -

There were 19 cases (15.08%) diagnosed as malignant lesions, all confirmed histopathologically.

There were 96 cases (76.19%) diagnosed as benign lesions, out of which 94 cases (74.60%) were confirmed histopathologically and 2 cases (1.59%) was diagnosed as malignant lesion, making the **False negative rate of 1.59% .**

There were 7 cases (5.56%) diagnosed as suspicious for malignancy and all were confirmed histopathologically as malignant and included in true positive cases.

There were 4 cases (3.17%) of unsatisfactory smears; all cases were diagnosed as benign histopathologically.

From above observations, sensitivity, specificity and accuracy of fine needle aspiration cytology in the diagnosis of malignancy was counted applying standard statistical formula as follows:-

Table 8: Summary of statistical value

FNAC	Histopathology	
	Benign	**Malignant**
Benign/ (Atypical) (96)	94 (TN)	2 (FN)
Suspicious/ Malignancy (26)	0 (FP)	26(TP)

Benign and atypical cases combined together; suspicious and malignancy cases were combined together and the histopathological results compared.

Sensitivity = True Positive × 100 = **92.86%**
True Positive + False negative

Specificity = True negative × 100 = **100%**
True Negative + False Positive

Accuracy =
True Positive + True Negative × 100 = **98.36%** True Positive + False Positive + True Negative + False Negative

Positive Predictive Value =
True Positive × 100 = **100%**
True Positive + False Positive

Negative Predictive Value =
True Negative × 100 = **97.92%**
True Negative + False Negative

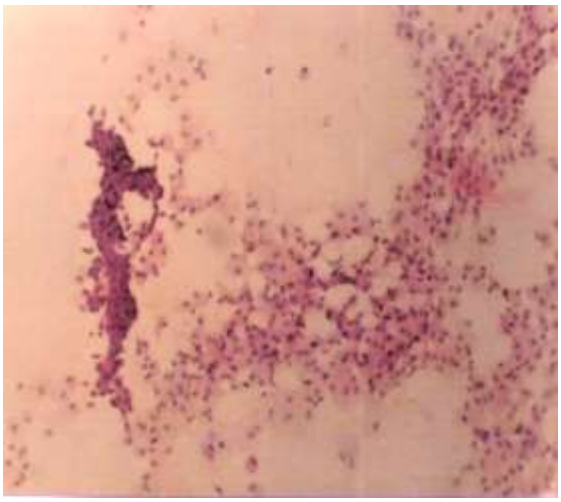

Fig. 2: Breast aspirate fibrocystic disease (10X, H&E)

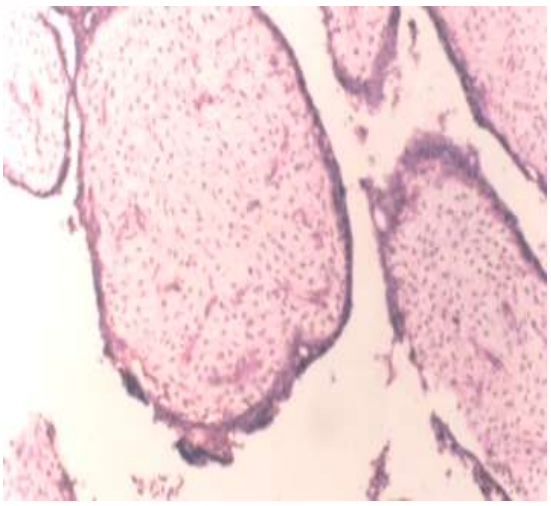

Fig. 3: Phyllodes tumor of breast (10X, H&E)

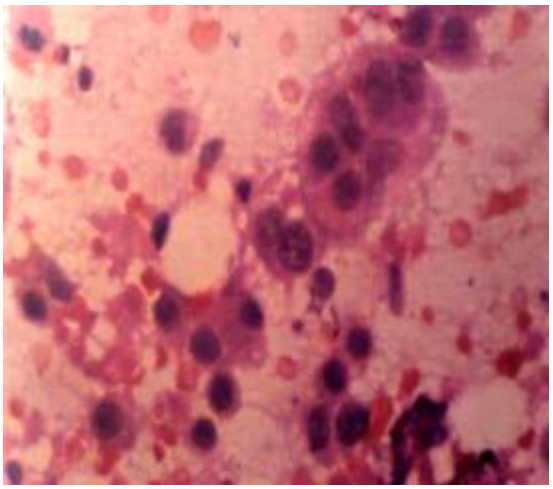

Fig. 4: Breast aspirate shows invasive ductal carcinoma (40X, H&E)

Discussion

FNAC of breast lump is an accepted and established method to determine the nature of breast lump with high degree of accuracy. The application of FNA for the diagnosis of palpable breast masses was first introduced by Martin and Ellis in 1930,[9] and since then, it has been established as an important tool in the evaluation of breast lesions. Kline et al[10] stated that the method is rapid, accurate and essentially complication free.

Obtaining a pre-operative diagnosis is desirable when dealing with breast cancer as it gives the patient a chance prior to come to terms with a diagnosis of cancer prior to surgery and allows discussion of treatment options in order to progress to a therapeutic rather than a diagnostic operation. Also reduces the benign surgical biopsy rate avoiding unnecessary surgery in women with benign lesions.

Out of total 200 cases studied cytologically during the period from April, 2004 to March 2009, of present

study 126 cases were available for histopathological correlation.

Table 9: Comparative findings of fine needle aspiration cytology with histopathological results of present study with other studies

FNAC total Patients (No)	Present Study 126	Abele et al[11] 92	Pandit et al[12] 264	Clive et al[13] 100	Kline et al[14] 2151	Norton et al[15] 49	Wanebo et al[16] 247
Results Malignant %	15.08%	30.00%	28%	44%	10%	16%	38%
Benign	76.19%	64.00%	67%	27%	36%	20%	42%
Suspicious	5.56%	5.00%	5%	20%	7%	27%	12%
Inadequate	3.80%	0.00%	-	9%	47%	37%	9%
Histologic results total Malignant	28	32	100	69	349	20	129
Total Benign	98	60	164	31	1802	29	118
False-negative							
No.	2.00	1.00	15	4	35	1	1
%	1.59%	3.00%	15%	6%	10%	5%	1%
False-positive							
No.	0	0	0	0	0	0	0
%	0	0	0	0	0	0	0
True-positive							
No.	26	28	74	44	221	8	93
%	92.85%	88.00%	74%	64%	63%	40%	72%
True-negative							
No.	94	58	154	23	735	9	102
%	95.91%	97.00%	87%	74%	41%	31%	86%
Sensitivity %	92.86%	97.00%	83%	92%	86%	89%	99%
Specificity %	100.00%	100.00%	100%	100%	100%	100%	100%
Positive predictive Value	100.00%	100.00%	100%	100%	100%	100%	100%
Negative predictive Value	97.92%	98.00%	91%	85%	95%	90%	99%
Accuracy %	98.36%	99.00%	91%	94%	96%	94%	99%

Regarding the number of cases, there were marked variations in different studies earlier. In present study the number of cases not correlated with any studies.

During the present study, carried out with 126 breast lumps, there was preponderance of benign breast lesions 98 cases (77.78%). Malignant cases are 28 (22.22%) only. Pandit et al[17], also commented that benign breast lesions are more than malignant cases.

The lower incidence of malignant lesions as compared to benign lesions in the studies of Indian worker may be due early marriage, repeated pregnancy and usual practice of breast feeding in our country.

Carcinoma arising in the male breast is a rare occurrence and FNAC of male breast also shows excellent cytohistological correlation[18]. We reported one case of malignancy on cytology; histopathology showed invasive duct carcinoma.

During present study, we had suspected a case of lobular carcinoma, histopathology confirmed the diagnosis of invasive lobular carcinoma. Lobular carcinoma is the diagnostic challenge on FNAC.

In this study, sensitivity is 92.86 %, specificity is 100% in diagnosing malignant lesions, with accuracy of 98.36 %. Positive predictive value is 100% and Negative predictive value is 97.92%; findings are correlated with other studies.

During present study, false positive case was zero; correlating well with other studies. False negative were 1.59%. Other studies show false negative in the range of 1% to 15%. False negative diagnosis can be due to sampling errors or interpretation problems.

During present study, 2 case (2.08%) cytologically diagnosed as epithelial hyperplasia with atypia, histopathologically it was reported as invasive duct carcinoma. This case was misdiagnosed, the reason may be due to sampling error.

Zajdella et al[5] found that false negative were due to size, differentiation and fibrotic elements of malignancy and whether they are adjacent to benign cyst.

During present study, we have misdiagnosed one case of fibroadenoma as phyllodes tumour cytologically and there were 4 cases diagnosed as unsatisfactory. Out of 4 cases, 3 cases were diagnosed as sclerosing adenosis and 1 case was diagnosed as lactating adenoma histopathologically.

Scopa et al[19] identified the source and nature of inaccuracies related to FNAC breast. They found that the problems were related to sampling errors and interpretation. The nature of breast lesion was the most common cause of inadequate sampling followed by experience of aspirator.

FNAC should be used with the idea of 'complimenting', not competing with routine histopathologic biopsy. To reduce the false negative and false positive diagnosis, expertise is required in correct process of performing the needle aspiration as well as in the interpretation of cytological smears.

Conclusion

To conclude, fine needle aspiration cytology is a fairly safe procedure in trained hands, and it gives reasonably accurate results, thereby helping the clinicians to plan the best line of treatment. Also with invention of imaging guided aspiration, FNAC went one step ahead in diagnosis of non-palpable lesion of breast. It should however be emphasized that aspiration cytology is one of the diagnostic methods and negative results does not always exclude the pathology. The result should always be correlated with the clinical findings and if required a repeat aspiration may be done or other means of confirmation adopted. Thus a triple modality of clinical, mammographic and cytological correlation is required and for internal quality control FNAC is correlated with histopathology.

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