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Cytomorphological study of breast lesions with histopathological correlation

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ABSTRACT

Background : Lump in the breast is the common presentation to surgical OPD. The breast lesions are spectrum of diseases ranging from non- neoplastic to neoplastic lesions. Fine Needle Aspiration Cytology(FNAC) is an important tool in the diagnosis of breast lesions.

Objectives of study :

The purpose of the present study was to study the cytological patterns of breast lesions and to test the diagnostic utility of FNAC of breast lesions by correlation with histopathology.

Methods : The present study included smears from 50 cases presenting with breast lump. All 50 cases were correlated with histopathology. Sensitivity, specificity, positive predictive value, negative predictive value, false positive rate and false negative rate were used to calculate the diagnostic accuracy of FNAC to detect malignancy in 47 cases, 2 cases were of unsatisfactory cell yield and 1 case was suspicious for malignancy, were excluded.

Results : In the present study, the results of diagnostic accuracy of FNAC to detect malignancy was sensitivity – 96.15%, specificity – 100%, positive predictive value – 100% and negative predictive value – 95.45%, false positive rate - 0% and false negative rate - 3.84%.

Conclusion : Fine needle aspiration cytology is a safe, rapid and minimally invasive procedure for the diagnosis of breast lesions. It has high sensitivity and specificity. It is effective replacement for open biopsy.

KEYWORDS | Breast lump; biopsy; Fine Needle Aspiration Cytology.

INTRODUCTION

A palpable breast lump is a common diagnostic problem. It is important not only to diagnose breast lesion as benign or malignant, but also to assay the prognosis of both. In the past, excision biopsy was advised but now FNAC is an important diagnostic tool which lessens economic burden and time consumed by doing open tissue biopsy.[1,2] FNAC is cheaper, less traumatic, requires no local anaesthesia, can generate rapid diagnosis. It plays major role in the diagnosis of small lesion, lesions located just under the skin, close to the chest wall or in periclavicular area and multiple lesions.[3]

MATERIALS AND METHODS

The present study emphasizes the role of fine needle aspiration cytology in the diagnosis of palpable breast lesions. FNAC was done in 50 patients with palpable breast lesions. This is astudy undertaken in Department of Pathology, Sri DevarajUrs Medical College, Kolar, during the period of 01-12-2008 to 30-11-2009.

Inclusion Criteria

All cases of FNAC of clinically palpable breast lesions along with its histopathology done

at Sri R. L. Jalappa hospital and Research Centre attached to Sri DevarajUrs Medical college, Tamaka, Kolar .

Exclusion Criteria

Radiologically detected breast lesions but clinically impalpable.

FNAC was performed using 22-23 gauge needle fitted to a 10 millilitre syringe. Naked eye examination of the aspirate was made and recorded, smears were stained by Papanicolaou stain and Hematoxylin and Eosin (HE), Giemsa stain. ZN (Ziehl-Neelson) stain was done whenever necessary for demonstration of acid fast bacilli (AFB).FNAC results were compared with histopathological finding of the surgically resected specimen. These specimens were subjected to gross examination and fixed in 10% formalin for 24-48 hours. Paraffin blocks were prepared from representative areas and 5 microns thickness were cut and stained with H and E. Special stains like ZN and PAS were used wherever required. Histopathological study was done separately and then results of cytological and histopathological study were correlated to evaluate the efficacy of the procedure.

INTERPRETATION OF ASPIRATE WAS DONE AS FOLLOWS

- Assess the adequacy of material in the smear.
- Cytomorphological features like cell pattern, cell population, individual cell morphology, background was studied and diagnosis was arrived.
- Breast lesions were categorized into –

Benign – satisfactory sample with no evidence of malignancy

Atypical – highly abnormal cellular findings probably reflecting malignancy

Suspicious – small number of cells suggesting malignancy

Malignant – irrefutable evidence of malignancy

Unsatisfactory – scanty cellularity, air drying, distortion artefact or obscuring blood or inflammation.[4]

Using Statistical Package for Social Sciences, version 16 statistical analysis was done in all 50 cases where FNAC diagnosis was correlated with histopathological diagnosis. Chi-square test was used to calculate test of significance and p value < 0.05 was taken as statistically significant. For diagnostic accuracy of test- sensitivity, specificity and positive predictive value, negative predictive value, false positive rate and false negative rate were calculated.

RESULTS

FNAC was done in 50 patients who had breast lump. The age of patients varied from 18 years to 72 years. Mean age of presentation was 44 years. The maximum number of cases (30%) were seen in the age group of 30-40 years (table 1). 45 were females and 5 were males.

AGE GROUP	NO OF CASES	PERCENT
10-20	1	2.0
20-30	8	16.0
30-40	15	30.0
40-50	11	22.0
50-60	11	22.0
60-70	2	4.0
70-80	2	4.0
TOTAL	50	100.0

TABLE 1 – DISTRIBUTION OF CASES IN DIFFERENT AGE GROUPS

The presenting complaint in all 50 (100%) patients was lump in the breast and 15 (30%) had pain.Out of 45 female patients 4 patients attained menarche at 10 years of age, 16 patients at 11 years of age, 15 patients at 12 years of age, 8 patients at 13 years of age and 2 patients at 14 years of age. 15 patients had attained menopause within 55 years.39 were parous and 6 females were nulliparous. The most common lesion in nulliparous females was fibroadenoma (4 cases) followed by Ductal carcinoma (2 Cases).Family history was present in only 1 case out of 50 cases. The patient was 65 year female with cytological diagnosis of Ductal carcinoma NOS. There was history of patient's sister with breast carcinoma.

Out of 50 cases, 31 cases presented with lump in right breast, 14 cases in left breast and 5 cases involved both breasts. Upper outer quadrant (14 cases) was the most commonly involved among malignant lesions and upper inner and lower outer quadrant (7 cases each) in benign lesions. 1 malignant case showed diffuse involvement of breast. Sub-areolar involvement was seen in 1 malignant case (table 2).

QUADRANT	BENIGN	MALIGNANT	TOTAL
DIFFUSE	3	1	4
LOWER INNER	3	4	7
LOWER OUTER	7	0	7
SUB-AREOLAR	0	1	1
UPPER INNER	7	7	14
UPPER OUTER	3	14	17
TOTAL	23	27	50

$\chi 2$ = 16.04, degree of freedom = 5, P value - 0.07 (p value was not significant)

TABLE 2 – DISTRIBUTION OF LESIONS IN DIFFERENT QUADRANTS OF BREAST

Most of the lesions (70%) were 2 to 5 centimetres in size. (table 3).

In 58% the lesions were firm in consistency and most of them were fibroadenoma. Hard consistency was seen in 17% of cases and most of them were malignant lesions. Soft consistency was seen in fibrocystic disease, fibroadenoma and TB mastitis. Most (18 of 27 cases) malignant lesions had ill-defined borders and most benign lesions (16 of 23 cases) had well-defined borders.

Grey white aspirate was obtained in 52% cases. Hemorrhagic aspirate was obtained in 46% of cases and most of them were malignant. 1 case of TB mastitis had purulent aspirate. Various patterns of arrangement seen in present study were – antlerhorn, clusters, monolayered sheets, acinar, tubular, Indian file and singles. Arrangement of cells in clusters and singles was most common pattern of arrangement (20%). Antler horn pattern was seen in most of fibroadenomas (table 3).

PATTERN OF ARRANGEMENT	NO OF CASES	PERCENT
ANTLER HORN,CLUSTERS	4	8.0
ANTLER HORN,MONOLAYER, CLUSTERS	8	16.0
ANTLER HORN,MONOLAYER, CLUSTERS,SINGLES	1	2.0
CLUSTERS,SINGLES	10	20.0
MONOLAYER,CLUSTERS	7	14.0
CLUSTERS,ACINAR,SINGLES	2	4.0
MONOLAYER,CLUSTERS,ACINAR	3	6.0
MONOLAYER,CLUSTERS,TUBULAR	1	2.0
MONOLAYER,CLUSTERS,SINGLES	7	14.0
MONOLAYER,CLUSTERS,SINGLES, INDIAN FILE	1	2.0
MONOLAYER,CLUSTERS,SINGLES, ACINAR	5	10.0
MONOLAYER,CLUSTERS,SINGLES, CRIBRIFORM	1	2.0
TOTAL	50	100.0

TABLE 3– DISTRIBUTION OF PATTERNS OF ARRANGEMENT

The cytologic diagnosis correlated well with histopathology (figure 1-12). Ductal carcinoma NOS (20 cases) was most common lesion among which 1 case had chemotherapy induced changes and 2 cases had ipsilateral axillary lymph node metastasis. Other cases were fibroadenoma (16 cases), fibrocystic disease (2 cases), gynaecomastia (3 cases), lobular carcinoma (1 case), TB mastitis (1 case), tubular carcinoma (1 case), pleomorphicliposarcoma with myxoid change (1 case), metaplastic carcinoma (1 case) and medullary carcinoma (1 case). Because of inadequate cell yield, 2 cases were put under unsatisfactory category and in 1 case only few cells showed features of malignancy so was diagnosed as suspicious for malignancy. 21 cases out of 23 benign cases were diagnosed as benign FNAC and 25 out of 27 malignant cases were diagnosed as malignant on FNAC (table 4).

CYTOLOGIC CATEGORIES	HISTOPATHOLOGIC CATEGORIES		
	BENIGN	MALIGNANT	TOTAL
BENIGN	21	1	22
MALIGNANT	0	25	25
SUSPICIOUS	0	1	1
UNSATISFACTORY	2	0	2
TOTAL	23	27	50

TABLE 4 - CORELATION OF CYTOLOGIC AND HISTOPATHOLOGIC CATEGORIES

2 unsatisfactory cases on FNAC turned out to be fibroadenoma on histopathology. 1 suspicious for malignancy case on FNAC was diagnosed as ductal carcinoma on histopathology. 2 cases of fibrocystic disease were misinterpreted as fibroadenoma on FNAC and 1 case of mixed ductal and lobular carcinoma was misinterpreted as lobular carcinoma on FNAC. One case of ductal carcinoma was wrongly diagnosed as fibroadenoma (table 5).

CYTO_DIAGNOSIS	DUCTAL CA	DUCTAL CA WITH CHEMO INDUCED CHANGES	DUCTAL CA WITH LN METS	FIBROADENOMA	FIBROCYSTIC DISEASE	GYNAECOMASTIA	MEDULLARY CA	METAPLASTIC CA	MIXED DUCTAL AND LOBULAR CARCINOMA	PLEOMORPHIC LIPOSARCOMA WITH MYXOID CHANGE	TB GRANULOMATOUS MASTITIS	TUBULAR CA	TOTAL
UNSATISFACTORY	-	-	-	2	-	-	-	-	-	-	-	-	2
DUCTAL CA	17	-	-	-	-	-	-	-	-	-	-	-	17
DUCTAL CA WITH CHEMO INDUCED CHANGES	-	1	-	-	-	-	-	-	-	-	-	-	1
DUCTAL CA WITH LN METS	-	-	2	-	-	-	-	-	-	-	-	-	2
FIBROADENOMA	1	-	-	13	2	-	-	-	-	-	-	-	16
FIBROCYSTIC DISEASE	-	-	-	-	2	-	-	-	-	-	-	-	2
GYNAECOMASTIA	-	-	-	-	-	3	-	-	-	-	-	-	3
LOBULAR CARCINOMA	-	-	-	-	-	-	-	-	1	-	-	-	1
MEDULLARY CA	-	-	-	-	-	-	1	-	-	-	-	-	1
METAPLASTIC CA	-	-	-	-	-	-	-	1	-	-	-	-	1
PLEOMORPHIC LIPOSARCOMA WITH MYXOID CHANGE	-	-	-	-	-	-	-	-	-	1	-	-	1
SUSPICIOUS FOR MALIGNANCY	1	-	-	-	-	-	-	-	-	-	-	-	1
TB GRANULOMATOUS MASTITIS	-	-	-	-	-	-	-	-	-	-	1	-	1
TUBULAR CA	-	-	-	-	-	-	-	-	-	-	-	1	1
TOTAL	19	1	2	15	4	3	1	1	1	1	1	1	50

TABLE 5 – CORELATION OF FNAC AND HISTOPATHOLOGY DIAGNOSIS

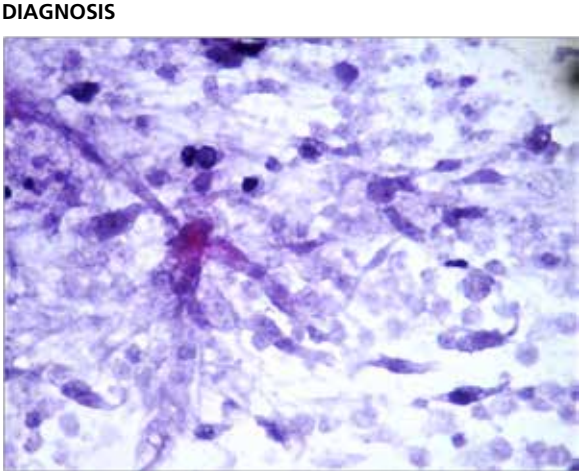

FIG 1 – FNAC of tuberculous mastitis showing cluster of epithelioid cells, few lymphocytes and necrosis. HE X 400
Inset shows acid fast bacilli. ZN X 1000

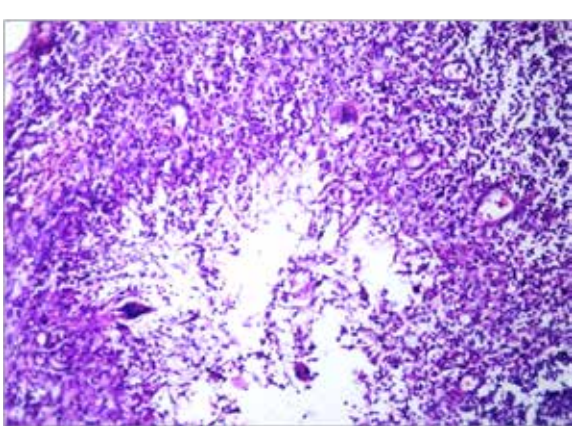

FIG 2 – HP of tuberculous mastitis showing granulomas consisting epithelioid cells, langhans giant cell and lymphocytes. HE X 100

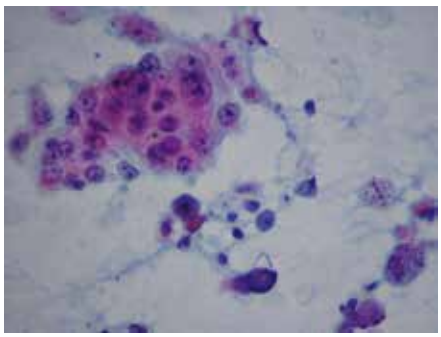

FIG 3 – FNAC of medullary carcinoma showing cells in clusters, marked anisonucleosis, stippled chromatin, prominent nucleoli and lymphocytes. PAP X 400

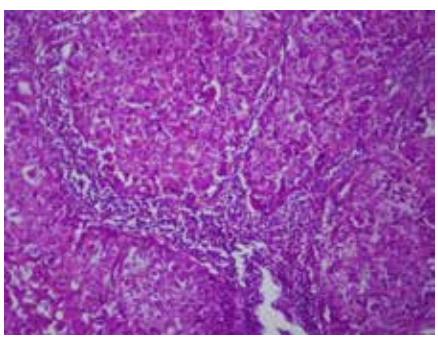

FIG 4 – HP of medullary carcinoma showing pushing borders, pleomorphic cells in sheets and lymphoplasmacytic infiltrate. HE X 100

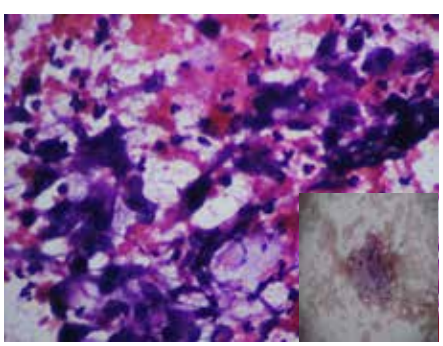

FIG 5 – FNAC of metaplastic carcinoma showing tumour cells in loosely cohesive clusters with hyperchromatic pleomorphic nuclei. HE X 400
Inset shows osteoid matrix. MGG X 400

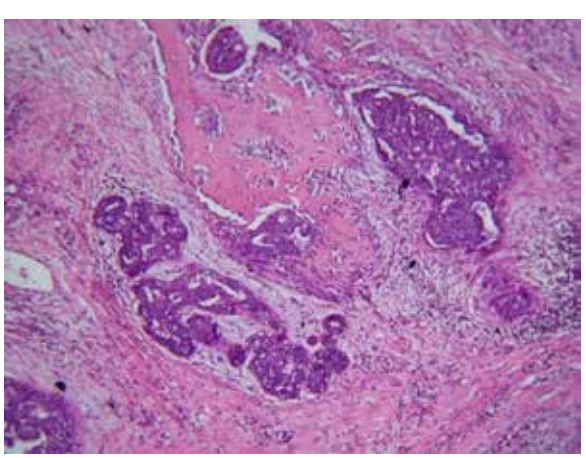

FIG 6 – HP of metaplastic carcinoma showing pleomorphic cells in glandular pattern, sheets, clusters with osteoid matrix. HE X 10

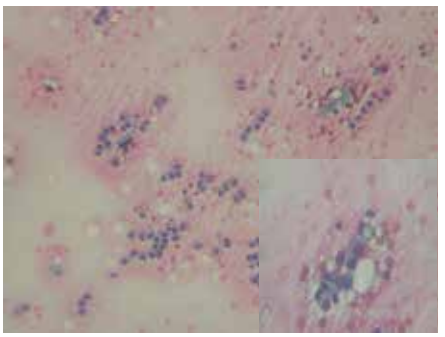

FIG 7 – FNAC of lobular carcinoma with small, uniform cell in "indian file" pattern. PAP X 100
Inset shows intracytoplasmiclumina. PAP X 100

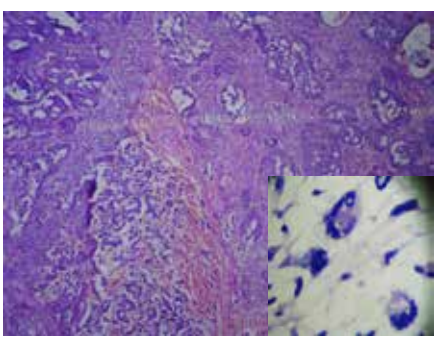

FIG 8 – HP of mixed ductal and lobular carcinoma with uniform lobular carcinoma cells on right and pleomorphic ductal carcinoma cells on left. HE X 100

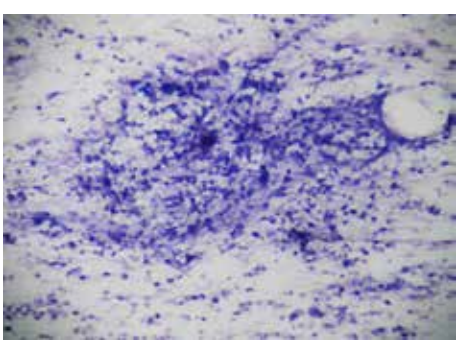

FIG 9 – FNAC of pleomorphic liposarcoma with myxoid change showing cells with abundant clear cytoplasm with peripherally pushed pleomorphic nucleus, myxoid background and necrotic debris. MGG X 100
Inset shows lipoblast. HE X 400

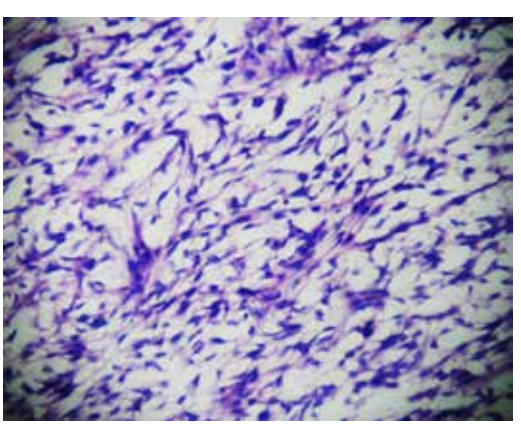

FIG 10 – HP of pleomorphic liposarcoma with myxoid change showing cells with abundant clear cytoplasm with peripherally pushed pleomorphic nucleus. HE X 100

STATISTICAL ANALYSIS

The statistical tests used in the interpretation of the results obtained in our study were the determination of sensitivity, specificity, positive predictive value, negative predictive value, false positive rate and false negative rate of FNAC as a diagnostic procedure in detecting malignancy.All 50 cases in the present study had histopathological correlation but to calculate the below mentioned parameters 47 cases were included. 3 cases (2 unsatisfactory and 1 suspicious for malignancy) were excluded from statistical assessment.

Out of 47 patients, the FNAC report of 43 patients matched with the final histopathology report. Out of the 4 patients, in which FNAC did not match, 3 showed fibroadenoma and 1 showed lobular carcinoma on FNAC. The histopathology of 2 cases of fibroadenoma on FNAC turned out to be fibrocystic disease, 1 case of fibroadenoma on cytology turned out to be ductal carcinoma and 1 case of lobular carcinoma on FNAC turned out to be mixed lobular and ductal carcinoma (table 6).

CYTOLOGY	HISTOPATHOLOGY		TOTAL
	MALIGNANT	BENIGN	
MALIGNANT	25	-	25
BENIGN	1	21	22
TOTAL	26	21	47

TABLE 6 -CYTOHISTOPATHOLOGICAL CORRELATION FOR MALIGNANT LESIONS

The results of diagnostic accuracy of FNAC to detect malignancy was sensitivity – 96.15%,specificity – 100%,positive predictive value – 100%,negative predictive value – 95.45%,false positive rate – 0%,false negative rate – 3.84%.

DISCUSSION

FNAC is one of the routinely used diagnostic procedures in patients presenting with breast lump.In our study 50 patients were subjected to FNAC of palpable breast lesions. The duration of study was 1 year. Cytology results were compared with histopathology in all 50 cases.

In the present study the age of patients varied from 18 years to 72 years. Usually breast lesions occur during reproductive period and thereafter. Our study is in accordance with various other studies described in literature by Kim A et al[5],Omoniyi-Esan G et al[6],Ballo MS et al[7].Male breast lesions are rare as compared to female breast.[8]Like the female breast, the male breast is subject to hormonal influences.[9] In the present study out of 50 patients, 5 were males and 45 were females with a male to female ratio of 1:9, showing a distinctly high incidence of breast lesions in females.The male to female ratio in different studies varied from 1:12.68 to 1:72.04.[8,10,11] In present study out of 50 lesions, most common location was upper outer region of breast (17 cases) followed by upper inner region (14 cases). Kim A et al[5] also observed similar results. In their study out of 246 cases majority were located in upper outer quadrant (135) followed by upper inner quadrant (58 cases).In the present study cytological diagnosis of benign lesions was made on 44% cases, suspicious for malignancy on 2% cases, malignancy on 50% cases and unsatisfactory on 4% cases. The smears were considered unsatisfactory in 4% cases because of scanty cellularity.

2 unsatisfactory cases on FNAC turned out to be fibroadenoma on histopathology. 1 suspicious for malignancy case on FNAC was diagnosed as ductal carcinoma on histopathology. 2 cases of fibrocystic disease were misinterpreted as fibroadenoma on FNAC and 1 case of mixed lobular and ductal carcinoma was misinterpreted as lobular carcinoma on FNAC. This limitation could be explained by sampling error i.e. the site the needle hits the lesion. 1 case of ductal carcinoma was wrongly diagnosed as fibroadenoma. This was due to interpretative error of lesion on cytology. In the study conducted by Park A et al[12] there was failure to recognize malignancy because of failure to aspirate the representative cells from the lesion rather than incorrect interpretation. Categorization of lesions on FNAC in other studies is shown in the following table.[5,12,13,14]

Kim A et al[6]concluded that higher proportion of unsatisfactory samples in their study was due to difficulty in cytologic diagnosis of large and diffuse tumours due to the presence of haemorrhage, necrosis or fibrosis in these tumours. They also stated that malignant cases can be misinterpreted as unsatisfactory, atypical or suspicious because of poor fixation of specimen. Scopa et al[15] defined satisfactory specimens as "those containing epithelial cells on more than one slide and a minimum of 10 clusters composed of at least 10 cells: the background should be non-inflammatory and/or non-necrotic". Sneige et al[16] stated that unsatisfactory specimens were "those containing less than four to six well-visualized cell groups and/or specimens distorted or obscured by blood". Hammond et al[17] stated that insufficient material was due to problem of technique and the diagnosis of atypical cells or cells suspected of being malignant may depend upon the expertise of the pathologist. Kim A et al[5] indicated that there are few limitations in breast cytopathology. To distinguish high-risk, premalignant lesions from malignant lesions the definitive diagnostic criteria are not available due to overlapping features. In study conducted by Kim A et al[5], atypical and suspicious category was derived partly due to author's lack of experience. But they stated that these categories along with suggested differential diagnosis are safer than misleading diagnosis (table 7).

STUDIES	BENIGN	ATYPICAL	SUSPICIOUS	MALIGNANT	UNSATISFACTORY	TOTAL
Kim A et al[5]	114	35	13	61	23	246
Park IA et al[12]	384	24	7	85	169	669
Takei H et al[13]	150	26	15	78	44	313
Choi YD et al[14]	981	-	38	182	96	1,297
Present study	22	-	1	25	2	50

TABLE 7 – COMPARISON OF CATEGORISATION OF LESIONS ON FNAC WITH OTHER STUDIES

STATISTICAL VALUES

In the present study the results of diagnostic accuracy of FNAC to detect malignancy was sensitivity – 96.15%, specificity – 100%, positive predictive value – 100% and negative predictive value – 95.45%, false positive rate - 0% and false negative rate - 3.84%. The results were comparable with other studies (table 8).[18]

Park SM et al[19] concluded that the cause of false negative result was due to sampling error in all FNAC samples. Park IA[12] arrived at a conclusion that "inadequate" cytologic diagnosis category offered to certain lesions even though they were discrete, obviously malignant masses clinically caused the higher than expected false negative rate in their study.

In the study done by Choi et al[14] interpretive error was the most common cause of high rate of false negative result.In our study also interpretive error was the cause for false negative result.

STUDIES	NO OF CASES	SENSITIVITY(%)	SPECIFICITY(%)	POSITIVE PREDICTIVE VALUE(%)	NEGATIVE PREDICTIVE VALUE(%)	FALSE POSITIVE RATE(%)	FALSE NEGATIVE RATE(%)
Atamdede et al	100	97.0	95.4	94.2	97.6	5.8	2.4
Barrows et al	1,283	92.2	86.0	91.1	87.5	8.9	12.5
Ciatto et al	534	97.4	99.3	98.6	98.7	1.4	1.3
Collaco et al	276	92.1	98.6	99.4	82.1	0.6	17.9
Gelabert et al	107	96.7	100	100	80.0	0.0	20.0
Kline et al	3,545	90.3	98.1	84.5	98.8	15.5	1.2
Lanin et al	100	92.8	100	100	96.9	0.0	3.1
Zajdela et al	2,772	96.1	95.3	97.2	93.5	2.8	6.5
Present study	47	96.15	100	100	95.45	0.0	3.84

TABLE 8 – COMPARISON OF STATISTICAL VALUES WITH OTHER STUDIES[18]

CONCLUSION

FNAC diagnosis will help to confirm or exclude the differential diagnosis made by the clinician. The rapid diagnosis made by FNAC relieves the anxiety of patient and helps to plan the treatment. In the present study cytologic diagnosis correlated well with histopathology and was a sensitive and specific tool.

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