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CORRELATIVE STUDY OF FINE NEEDLE ASPIRATION CYTOLOGY AND HISTOPATHOLOGY IN BREAST LESIONS: A 2 YEAR STUDY

Pathology

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ABSTRACT

Background and objectives: Fine needle aspiration cytology is an effective modality for diagnosis of breast lesions. It has high sensitivity and specificity. The aim of the study was to categorize breast lesions, correlate the FNAC diagnosis with histopathological findings and finding the accuracy.

Methods : 2 year study was conducted in our institution and in that 130 patients underwent FNAC of the palpable breast lumps after thorough physical examination. The cytological diagnosis was classified as benign, suspicious of malignancy, malignant and others. After this reporting all the patients were subjected to excision biopsy or mastectomy and its histopathological confirmation. Later diagnostic accuracy of cytology reporting was compared with that of histopathology.

Results : Out of 130 cases, 85 were benign, 32 were malignant, 5 suspicious and 8 were other non neoplastic smears. Cytological and histological correlation was found in 127 cases (97.69%) out of 130 cases. Fibroadenoma was the commonest benign lesion noted in age group of 21-30 years and infiltrating duct carcinoma was the most common malignant lesion. Accuracy of the present study was sensitivity 100%, specificity 97.89%, positive predictive value 94.59%, negative predictive value 100% and efficiency of 98.46%.

Conclusion : FNAC of breast lesions serves rapid, economical and reliable tool for diagnosis of palpable breast lesions and the cytopathological examination of these lesions before operation or treatment serves as an important modality.

KEYWORDS

Fine needle aspiration cytology, breast lumps, carcinoma of breast, fibroadenoma, infiltrating duct carcinoma.

INTRODUCTION

Carcinoma of breast is the most common non skin malignancy in women and is second only to lung cancer as a cause of cancer deaths.[1] It is the most common cause of death in females from cancer in United states, incidence is lowest in Japan and is the second commonest malignancy in our country.[2]

Surgical intervention in the form of incisional or excisional biopsy involves preoperative preparation of the patient, hospitalization and anaesthesia. It is followed by scarring, fibrosis of connective tissue altering the consistency and optical density of breast interfering with the radiological follow up of the case. To overcome these difficulties and to fill the gap in the diagnostic evaluation of the breast lesions, fine needle aspiration cytology was introduced. Fine needle aspiration cytology (FNAC) is not new technique; it was described and practiced by Martin and Ellis in 1930 at New York. This technique provides a representative sample for microscopic examination without interfering with radiological appearance of breast.[3] FNAC has now become a popular investigation to assess the nature of palpable lesions. The main purpose of FNAC is to confirm cancer preoperatively and to avoid unnecessary surgery in specific benign conditions.[4]

FNAC does not require elaborate tissue processing and is therefore the least expensive method of diagnosis. It does not require anaesthesia or hospitalisation and it takes only a few minutes to perform.[5]

It is sometimes difficult to determine whether a suspicious lump is benign or malignant simply from clinical assessment.Therefore a method of definitive diagnosis of patients who present with breast lumps at the outpatient clinic is needed in order to reassure the patients and to offer the best possible treatment.[6]

FNAC is a relatively simple, reliable, atraumatic, economical and complication free technique for the evaluation of mass lesions. It can be easily repeated if an adequate aspirate is not obtained.[6]

FNAC has superceded the use of frozen section examination in the diagnosis and management of patients with breast cancer.[7,8]

A rapid diagnosis of a malignant tumor may also allow the patient to participate in choice of therapies, some of which lead to preservation of breast (local/ segmental resection lumpectomy) followed by radiotherapy and chemotherapy. In many instances these treatments replace mastectomy, with equivalent results. Thus FNAC may save anxiety, trauma, time and money.[9]

Fine needle aspiration cytology is an effective modality for diagnosis of breast lesions. Lower rates of false positive and false negative diagnosis can be achieved if cytopathologist has personally performed the FNAC, prepared the smears and performed microscopic interpretation. Cytology diagnosis is correlated with histopathology, then one can do statistical analysis i.e. sensitivity, specificity, positive predictive value and efficiency of the procedure.[9]

Although the vast majority of male breast lesions are benign, breast cancer does occur in men and usually presents as a mass clinically indistinguishable from gynaecomastia. The routine use of FNA biopsies in male breast lesions has reduced the number of unnecessary surgical excisions.[10]

FNAC helps in early diagnosis of the malignant breast lesions.Clinicians can think for surgery, definitive management and in non malignant conditions, follow up of the case and specific treatment is advised. So it helps in reducing morbidity and mortality of the cases. This study is an attempt to correlate cytological and histopathological appearance of breast lesions. The observations in this study will be compared with similar studies.

MATERIALS AND METHODS

The present study was carried out in Department of Pathology of ESIPGIMSR and Model Hospital, Mumbai from September 2013 to August 2015 after taking permission from ethical committee of institution. This study includes a total number of 130 cases of FNAC in which histopathology examination was also done and correlated. Inclusion criteria includes clinically suspected lesions in females and males. Exclusion criteria includes specimens of lumpectomy or mastectomy without previous FNAC and smears of FNAC which are not followed by lumpectomy or mastectomy.The patients having palpable breast lump referred from Surgery department in the institution for FNAC were involved in the study. The case history of the patient was recorded, includes details of pain, nipple discharge, ulceration of nipple and duration of complaints. Examination of breast lump was done with recording of size and site of lump, consistency, and fixation to skin and underlined tissue, retraction of nipple along

with regional lymph node involvement. Consent was taken after due explanation of the procedure and its benefits to the patients.

The skin over the breast was wiped with antiseptic solution and spirit, suspected lesion was held with one hand in a position favourable to fine needle aspiration. Procedure is done by using 22 gauze needle fitted on 10ml disposable syringe. When needle had entered the lump area, the piston of the syringe was retracted thus creating a vacuum with the needle in a position to move back and fro, three or more times in a different direction of the lump. Throughout the procedure negative pressure was maintained in a syringe then before removing needle from the lump negative pressure is resolved. The needle is withdrawn and air is filled in the syringe reconnected to the needle and material is smeared on glass slide with the help of cover glass gently. The wet smear fixed with ethyl alcohol mixture stained with Papanicolaou stain. The air dried smear fixed in methyl alcohol stained with May Grunnwald Geimsa stain. The smears were screened under low and high magnification and diagnosis was made as:

Benign
Suspicious of malignancy
Malignant
Other inflammatory conditions

Cases were further followed up for histopathology. Surgical specimens obtained by either incisional biopsy, total excisional biopsy, lumpectomy, simple mastectomy or modified radical mastectomy. Paraffin sections of specimens received were stained by haematoxylin & eosin stains.

Histopathological slides are examined under low and high power magnification and classified according to WHO classification of breast tumors.

RESULTS

All 130 patients underwent a diagnostic FNAC in our Pathology department following which all underwent a definitive excisional surgical procedure after admission to hospital. All excised specimens obtained were subjected to histopathology. The cytological findings were correlated with the final histopathology report and statistical tests were used to interpret the results.

The observations and results of this study are shown below:

Table no. 1: Age and sex distribution (n=130)

Age in years	Male cases	Male %	Female cases	Female %
11-20	1	25	15	11.9
21-30	0	0	47	37.3
31-40	0	0	26	20.6
41-50	2	50	15	11.9
51-60	1	25	11	8.7
61-70	0	0	10	7.9
71-80	0	0	02	1.58
Total	**4**	**100**	**126**	**100.0**

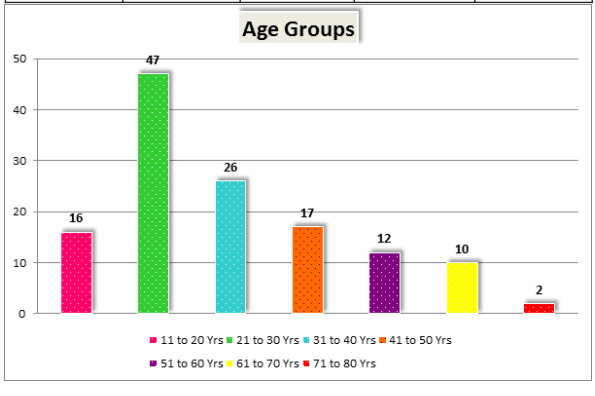

Figure 1: Age distribution of breast lumps

In this study, males contribute 4 cases(3.1%) and females contribute 126 cases (96.9%). Male to female ratio in the study is 1:31.5. In the present study maximum number of cases were females.

Amongst female, maximum cases were noted in 3rd decade i.e. 47 cases(37.3%) and they were in reproductive age group.

Table no. 2: Cytological diagnosis

Sr. no.	Cytological diagnosis	No. of cases	Percentage (%)
1.	Benign	85	65.38
2.	Malignant	32	24.6
3.	Suspicious of malignancy	5	3.8
4.	Other (non neoplastic)		
	Fibrocystic	3	2.3
	Galactocele	1	0.8
	Gynecomastia	3	2.3
	Non specific inflammation	1	0.8
	Total	**130**	**100.0**

Amongst all the cases, 85 cases were benign (65.38%), malignancy was noted in 32 cases (24.6%), suspicious of malignancy in 5 cases (3.8%) and other non-neoplastic lesion seen in 8 cases. Fibroadenoma was the commonest in all benign lesions.

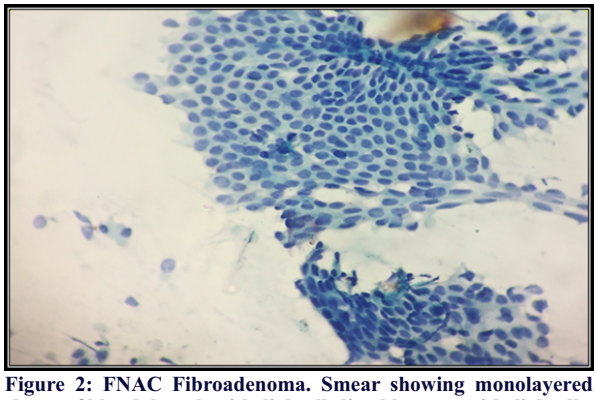

Figure 2: FNAC Fibroadenoma. Smear showing monolayered sheets of bland ductal epithelial cells lined by myoepithelial cells, bare bipolar nuclei also seen(Pap 40X)

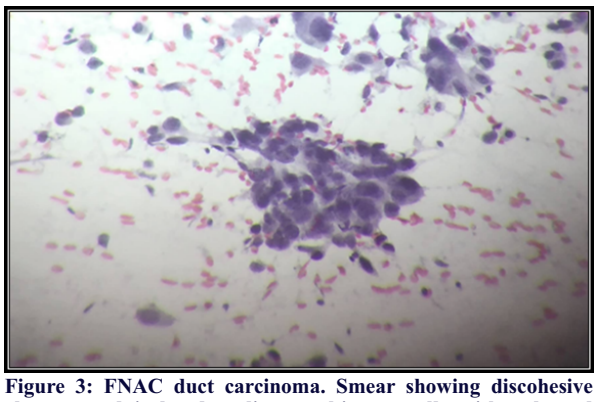

Figure 3: FNAC duct carcinoma. Smear showing discohesive clusters and isolated malignant, bizarre cells with enlarged hyperchromatic and pleomorphic nuclei. (Pap stain, 40X)

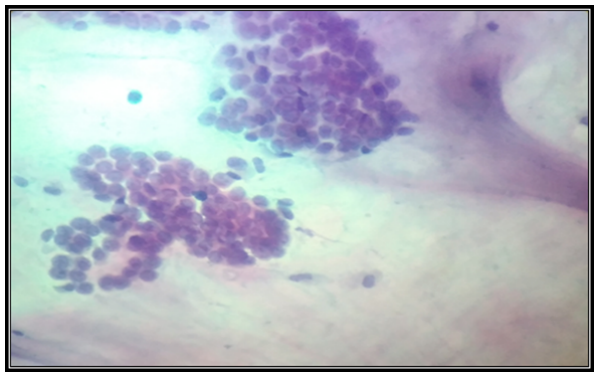

Figure 4: FNAC Mucinous carcinoma. Smear showing epithelial cells and moderate nuclear enlargement and atypia, suspended in mucin. (Pap stain, 40X)

Table no.3 : Cytological and histological correlation :

		Cytological Diagnosis							
		Benign	Malignant	Suspicious	Fibrocystic	Galactocele	Gynecomastia	Non specific in flammation	Total
Histopathological Diagnosis	Benign phyllodes Tumour	7	0	0	0	0	0	0	7
	Chronic non-specific Inflammation	1	0	0	0	0	0	0	1
	Fibroadenoma	72	0	0	0	0	0	0	72
	Fibrocystic Disease	3	0	0	3	0	0	0	6
	Galactocele	0	0	0	0	1	0	0	1
	Granulomatous mastitis	1	0	0	0	0	0	1	2
	Gynecomastia	0	0	0	0	0	3	0	3
	Infiltrating ductal carcinoma	0	25	1	0	0	0	0	26
	Intraductal carcinoma(DCIS)	0	1	2	0	0	0	0	3
	Infiltrating lobular carcinoma	0	1	0	0	0	0	0	1
	Invasive papillary Carcinoma	0	3	0	0	0	0	0	3
	Lactating adenoma	1	0	0	0	0	0	0	1
	Malignant phyllodes tumour	0	1	0	0	0	0	0	1
	Mucinous carcinoma	0	1	0	0	0	0	0	1
	Sclerosing adenosis	0	0	2	0	0	0	0	2
Total		85	32	5	3	1	3	1	130

In the present study out of 85 smears diagnosed as benign on cytology showed 72 as fibroadenoma, 7 as benign phyllodes tumor, 3 as fibrocystic disease, 1 as lactating adenoma, 1 as chronic non specific inflammatory tissue and 1 as granulomatous mastitis.

32 cases were diagnosed as malignant on cytology which on histology showed infiltrating duct carcinoma in 25 cases, invasive papillary carcinoma in 3 cases,1 as infiltrating lobular carcinoma,1 as mucinous carcinoma, 1 as intraductal carcinoma(DCIS) and 1 case as malignant phyllodes tumor.

Suspicious for malignancy was made in 5 smears of which 1 was diagnosed as infiltrating duct carcinoma, 2 as ductal carcinoma in situ(DCIS) and 2 cases as sclerosing adenosis.

In remaining cases, gynecomastia was diagnosed in 3 cases on cytology and were confirmed on histology.

Galactocele diagnosed on cytology was confirmed on histology. Three cases diagnosed as fibrocystic on cytology was diagnosed on histopathology. One case diagnosed as non specific inflammatory smear on cytology was diagnosed as granulomatous mastitis on further histology.

Table no. 4: Comparison of cyto-histological diagnosis :

Cytology diagnosis	No of cases	Histopathology diagnosis		
		Consistent	Inconsistent	Total
Benign	85	85 (100%)	0 (00%)	85
Malignant	32	32 (100%)	0 (00%)	32
Suspicious of malignancy	5	3 (60%)	2 (40%)	5
Others	8	7(87.5%)	1 (12.5%)	8
Total	130	127 (97.69%)	3 (2.31%)	130

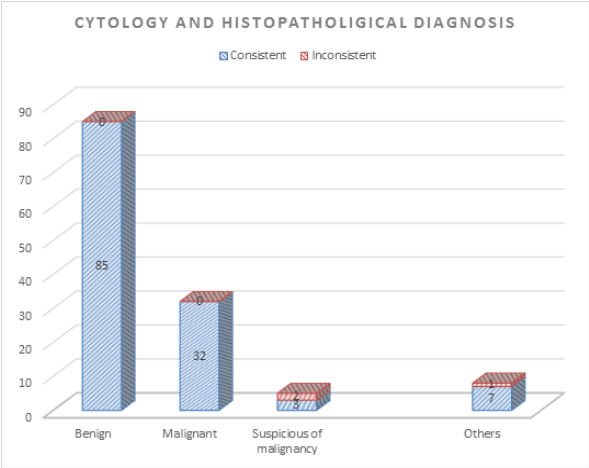

Figure 5: Comparison between cytological and histopathological diagnosis

Amongst benign and malignant lesions cytological diagnosis and histopathological diagnosis were consistent in 100% of the cases.

The lesions, which were diagnosed as suspicious for malignancy in 5 cases on cytology were found malignant in 3 (60.0%) cases and benign in 2 (40.0%) case.

In remaining non neoplastic cases, consistency was found in 87.50%.

Thus in the present study, cytological findings were consistent with histopathological findings in 127 out of 130 cases (97.69%) and inconsistent in 3 (2.31%) cases.

Table 5: Correlation of cytological and histological diagnosis Fisher's Exact test-

	Histopathological Diagnosis			Total
Cytological Diagnosis		Non Malignant	Malignant	
	Non Malignant	93	0	93
	Malignant	2	35	37
	Total	95	35	130

Chi square = 119.5 p Value <0.000001

The association is significant between cytological and histopathological diagnosis.

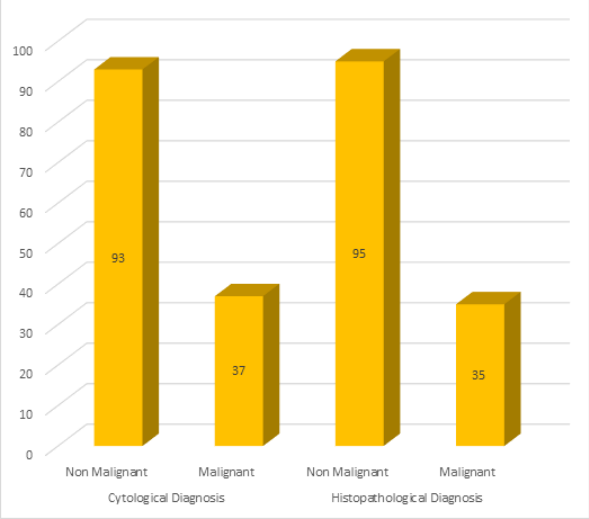

Figure 6: Correlation of cytological and histopathological diagnosis Statistical analysis:

True positive or malignant = 35
True negative or non malignant = 93
False positive = 2
False negative = 0

Sensitivity = TPX100/(TP+FN) = 100%
Specificity = TNX100/(TN+FP) = 97.89%
Positive predictive value = TPX100/(TP+FP) = 94.59%
Negative predictive value = TNX100/(TN+FN) = 100%
Efficiency = (TP+TN)X100/(TP+FP+FN+TN) = 98.46%

Table no. 6: Accuracy of FNAC

Statistics	Value
Sensitivity	100%
Specificity	97.89%
Positive predictive value	94.59%
Negative predictive value	100%
Efficiency	98.46%

DISCUSSION

The FNAC of breast lump is worldwide accepted and established method of choice to determine the nature of breast lump. Fibroadenoma was the commonest benign lesion in our study which was concurrent with findings of Debra et al(1995)[11] and invasive duct carcinoma was the commonest malignant lesion which was similar to findings of study done by Quasim (2009) et al.[12]

Table no. 7: Comparison of cytological diagnosis with other studies:

Author	Malignant	Suspicious forMalignancy	Benign	Inadequate smear	Other	Total
Debra B et al (1983)	131	300	1019	230	0	1680
	7.80%	17.86%	60.65%	13.69%	0.00%	100.00%
Feichter G et al (1997)	181	49	1003	239	0	1472
	12.30%	3.33%	68.14%	16.24%	0.00%	100.00%
Premila De SR et al(1997)	92	15	486	7	0	600
	15.33%	2.50%	81.00%	1.17%	0.00%	100.00%
Kuldeep Singh et al (2001)	35	5	200	0	0	240
	14.58%	2.08%	83.33%	0.00%	0.00%	100.00%
Qasim et al (2009)	32	0	68	16	0	116
	27.59%	0.00%	58.62%	13.79%	0.00%	100.00%
Sajid H et al (2010)	58	0	64	0	0	122
	47.54%	0.00%	52.46%	0.00%	0.00%	100.00%
Bukhari et al(2011)	120	32	271	0	2	425
	28.24%	7.53%	63.76%	0.00%	0.47%	100.00%
Shrestha et al(2011)	152	175	618	27	431	1403
	10.83%	12.47%	44.05%	1.92%	30.72%	100.00%
TouhidUddin et al(2011)	72	17	431	3	4	527
	13.66%	3.23%	81.78%	0.57%	0.76%	100.00%
Present Study	32	5	85	0	8	130
	24.62%	3.85%	65.38%	0.00%	6.15%	100.00%

In the present study percentage of malignant cases was 24.62% on cytology, this was more or less similar findings to Bukhari et al (2011)[7] and Qasim et al(2009)[12].

This percentage was more than Debra et al (1983)[11], Premila De SR (1997)[9], Feichter G et al (1997)[13], Kuldeep Singh et al (2001)[14], Shrestha et al (2011)[15] and Touhid Uddin et al (2011)[16] and was less than Sajid H et al(2010)[17].

On cytology percentage of benign, in the present study was 65.38% (85 cases). This was similar to Bukhari et al (2011)[7]. The percentage was more as compared to Debra et al (1983)[11], Shrestha et al (2011)[15], Qasim et al (2009)[12] and Sajid H et al (2010)[17]. The percentage was less as compared to Premila De SR et al(1997)[9], Feichter et al (1997)[13], Kuldeep Singh et al (2001)[14] and Touhid Uddin et al (2011)[16].

Amongst other non neoplastic lesions 8 (6.15%) cases were observed in the present study. The findings were less than Shrestha et al (2011)[15]. M Amrikachi et al (2001)[10] has found 10 cases of gynecomastia on FNAC. Anuradha Joshi et al (1999)[18] has noted 70 cases of carcinoma and 295 cases of benign breast lesions amongst males.

In the present study 3 cases were diagnosed as gynecomastia and 1 case as malignant invasive papillary carcinoma among males. Diagnostic accuracy for gynecomastia and malignancy in males was 100%.

Park I A et al (1997)[19] has observed that, the success of cytodiagnosis was varied according to histologic subtypes. FNAC tend to be inadequate and false negative in case of duct carcinoma of schirrous subtype. The main cause for inadequate smears may be due to lack of technical experience in performing FNA, preparation. Bukhari et al (2011)[7] noted that FNA of ill defined masses like lesion or lesions with hyalinization and deeply situated lumps may also be contributed to the inconclusive diagnosis.

False positive diagnosis are always interpretation errors. They are highly undesirable, but in large volume institutions, they will occur from time to time in the process of evaluation of rare lesion, diagnostic pitfalls and look alike such as epithelial atypia in some fibroadenomas, complex sclerosing lesions and sclerosing adenosis.

False positive diagnosis should be avoided because mastectomy or other treatments may in certain centres be performed based entirely on FNA cytologic findings.

In the present study we found 2 false positive cases. It was diagnosed as suspicious for malignancy on cytology which further underwent lumpectomy and histopathologically was diagnosed as sclerosing adenosis. Sclerosing adenosis cannot be clearly distinguished cytologically. Epithelial aggregates in smears may show an obvious microacinar pattern giving rise to differential diagnostic problem, particularly with tubular carcinoma. Apocrine metaplasia occurring in areas of adenosis can look extremely worrying and may be the cause of false positive diagnosis.

Table no. 8: Comparison of cytohistological correlation in various studies:

Authors	Cytohistopathological correlation	
	Consistent	**Inconsistent**
Kline TS et al (1979)	96.4	3.75
Kuldeep Singh et al (2001)	97.91	2.08
Sajid H et al (2010)	95.08	4.90
Present study	97.69	2.31

Kline T S et al (1979)[20] has observed consistency of cytological findings in 2435 cases out of 2530 cases (96.24%) and inconsistency in 95 cases out of 2530 cases (3.75%).

Singh Kuldeep et al (2001)[14] has observed that cytological diagnosis of breast cases was consistent in 235 cases out of 240 cases (97.91%) and inconsistent in 5 cases out of 240 cases (2.08%).

Sajid H Alhelfy et al (2010)[17] has noticed that cytodiagnosis of the cases were consistent with histopathological diagnosis in 116 cases out of 122 cases (95.08%) and inconsistent in 6 cases out of 122 cases (4.9%).

Thus in the present study, cytological findings were consistent with histopathological findings in 127 out of 130 cases (97.69%) and inconsistent in 3 (2.31%) cases considering benign, malignant, suspicious of malignancy and other cases categories in cytology diagnosis.

Table no. 9: Comparison of accuracy of FNAC in various studies:

Author	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Efficiency
Kline TS et al (1979)	89.50%	92.50%	85.33%	-	91.63%
Francisco D et al (1997)	93.49%	95.73%	93.49%	95.73%	98.75%
Feichter et al (1997)	86.00%	99.30%	85.00%	-	93.0%
Premila De SR et al (1997)	93.80%	98.21%	92.70%	-	97.40%
Zhang Qin (2004)	97.10%	97.30%	-	-	92.0%
Arjun Singh et al (2011)	84.60%	100.00%	-	-	92.3%
Khemka A et al (2011)	96.00%	100.00%	100.00%	95.12%	-

Bukhari et al (2011)	98.00%	100.00%	97.00%	100.00%	98%
Present Study	100.00%	97.89%	94.59%	100.00%	98.46%

In the present study sensitivity was high as compared to Kline TS et al (1979)[20], Feichter et al (1997)[13], Premila De SR (1997)[9], Zhang Qin (2004)[21], Arjun Singh et al (2011)[22], Khemka A et al (2011)[23] and Franscisco D et al (1997).[24]

Specificity in present study was similar to Premila De SR (1997)[9] and Zhang Qin (2004).[21] The positive predictive value of present study was similar study to Franscisco D et al (1997).[24] The negative predictive value was similar to Bukhari et al (2011)[7] and efficiency is similar to Franscisco et al (1997)[24] and Bukhari et al (2011).[7]

Thus in the present given study the sensitivity, specificity, positive predictive value, negative predictive value and efficiency of FNAC is 100.00%, 97.89%, 94,59%, 100.00% and 98.46% respectively.

CONCLUSION:

The FNAC of breast is safe, easy, reliable, rapid, economical and highly accurate method for diagnosis of breast lump preoperatively. FNAC of breast lump should be used as preliminary investigationin outdoor patient department. High specificity and a high negative predictive value for malignancy suggests that FNAC differentiates between benign and malignant lesions very well preoperatively, so reduce patient's anxiety and also helps surgeon to plan the surgical management.

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