

Spectrum of breast lesions and cyto- histopathological correlation - A retrospective study in a teaching institution in North Malabar

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Abstract

Introduction: Breast carcinoma is the most common malignancy in women. Fine needle aspiration Cytology (FNAC) is an important component of triple approach for diagnosing breast lesions and is highly sensitive, specific, rapid and easy to perform. FNAC has an important role in the preoperative evaluation of breast lesions and deciding treatment.

Materials and Methods: The present study was carried out among 350 patients who presented to a tertiary care hospital in North Malabar during a 4 year period from June 2013- June 2017. All cases that presented with breast lump were evaluated with FNAC and the lesions were categorised as C1- C5 as per National Health Service Breast screening programme (NHSBSP) reporting criteria. In 240 cases cytohistopathological correlation was obtained and diagnostic accuracy of FNAC was determined.

Aims: To study the spectrum of benign and malignant breast lesions and the efficacy of FNAC as a diagnostic tool by correlating with histopathological findings.

Results: Statistical analysis showed that sensitivity of FNAC was 99.46% in benign lesions and 96.2 % in malignant lesions. The specificity and positive predictive value of malignant lesions were 99.46% and 98.07% respectively and that of benign lesions were 96.2% and 98.93% respectively.

Conclusions: FNAC serves as a rapid and reliable tool for evaluation of breast lumps with high sensitivity and specificity. However, grey zone lesions of breast which shows atypical / suspicious morphology needs confirmation by biopsy.

Keywords: Fine needle aspiration cytology, Breast lumps, Histopathology, Correlation.

Introduction

Breast carcinoma is the most common cancer in women worldwide accounting for 25% of all cancers. Nearly 1.7 million new cases were diagnosed in 2012 which represents about 12% of all new cancer cases. In the past decade, the incidence of breast cancer has been rising steadily and now ranks as the number one cancer among Indian females, way ahead of cervical cancer with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women. It was estimated that during the year 2012, about 144,937 new cases were diagnosed & 70,218 women died of cancer in India.¹ The increasing incidence of breast cancer and the possible disease curability if detected early emphasises the need for rapid & accurate diagnostic methods.

Breast lesions most commonly present as a palpable lump. The other clinical presentations include pain, nipple discharge or incidental findings. Fine needle aspiration cytology is one of the important components of triple approach which also includes clinical & radiological examination.² The use of all these three modalities increases the diagnostic accuracy rate to over 99%.³ FNAC is highly sensitive, specific, rapid & easy to perform. It is a valuable tool in the work up of all breast abnormalities and has an important role in the pre-operative evaluation of breast lesions. The main purpose of tissue sampling by FNAC

is to delineate malignant from benign lesions and helps in deciding appropriate management.⁴ The present study was conducted with the aim of identifying the spectrum of breast lesions in a tertiary care centre and also to evaluate the diagnostic reliability of FNAC by comparing cytological findings with histopathological diagnosis.

Materials and Methods

This is a 4 year retrospective study undertaken in the department of Pathology from June 2013 to June 2017 in a tertiary care centre in North Malabar. All cases that underwent FNAC were included in the study. Relevant clinical data were obtained from records. During this period, a total of 350 patients presented with breast lump & FNAC was done. Of these 240 cases underwent surgical exploration either in the form of lumpectomy or mastectomy. Majority of the remaining 110 cases were conservatively managed and some were lost to follow up. Information about the patient's age, sex, side of lesion, quadrant involved along with relevant clinical history and duration of symptoms were recorded. After taking informed consent, aspiration was performed on palpable breast lumps under aseptic precautions. FNAC was performed by the technique described by Orell et al.⁵ Aspiration was done using 22 or 23 G needle in a 10 ml syringe. Multiple smears were made from the aspirate & fixed in

95% ethanol & stained using the papanicolau stain. Air dried smears were stained using Giemsa stain. When the aspirate yielded fluid, cytocentrifugation was done and the smears were prepared from sediment and stained. Breast lesions were classified into 5 categories according to NHSBSP (National Health Service Breast Screening Programme) reporting cytological criteria.⁶

C1 (inadequate): Aspirates were classified as inadequate due to hypocellularity, excessive blood or insufficient epithelial cells for confident assessment. C2- (benign): adequate sample showing benign lesions with no evidence of malignancy or atypia. C3- (Atypia probably benign): shows features of benign lesions as in C2 category, but with few atypical features. C4- (suspicious of malignancy): aspirates with atypical features, but a confident diagnosis of malignancy cannot be made. C5- (malignant): adequate smears containing cells characteristic of breast carcinoma. For histopathology the gross specimens were processed routinely and stained by Hematoxylin & Eosin stains and definitive diagnosis was obtained. All cases of ductal carcinoma were graded as per modified Nottingham Bloom Richardson scoring system.⁷

For statistical analysis FNAC results of cases which had biopsy confirmation were further subdivided into two categories, first category being benign/atypical proliferative lesions and second suspicious of carcinoma /carcinoma category. Similarly the biopsy results were also subcategorised as benign/atypical and malignant categories.

Cyto-histopathological correlation was done. Sensitivity, specificity, positive predictive value and negative predictive value of FNAC for benign and malignant lesions and diagnostic accuracy of FNAC as compared to biopsy were calculated using the standard formulas. The results obtained were tabulated and conclusions drawn based on the statistical test analysis

Results

In the present study (n=350) age of the patients ranged from 13 years to 90 years with 10 (2.8%) male and 340 (97.2%) female patients. The majority of patients who underwent FNAC were in the 21-40 age group (41.4%) both in males and females, followed by 41-60 age group (35.1%). (Table 1) Left breast was seen to be more commonly involved- 181 cases (51.7%) than right - 161 cases (46%). Bilateral involvement was seen in 8 (2.3%) cases. The upper and outer quadrant was the commonest site of lump- 156 cases (44.6%) both in benign and malignant cases followed by upper inner quadrant 87 cases (24.8%). 5 cases (1.5%) had lumps involving more than one quadrant. The duration of lump ranged from 5 days to 10 years. Majority of patients had a duration of symptoms ranging from 1-6 months - (Table 2) Out of 350 patients, 274 (78.5%) cases presented with lump only. Painful lumps were seen in 60 (17%) cases. Skin involvement was seen in 7 (2%) patients. Lump with nipple discharge was present in 9 cases (2.5%) (Fig. 1)

Table 1: Age and sex wise distribution of patients enrolled in the study (350 cases)

S.No	Age group	No of cases	percentage	Males	Females
1	<20	24	6.8%	2	22
2	21-40	145	41.5%	5	140
3	41-60	123	35.2%	1	122
4	61-80	56	16%	2	54
5	81-100	2	0.5%	0	2
Total		350	100	10	340

Table 2: Clinical presentation of breast lesions

Side	n	%	Duration of symptoms	n	%	QUADRANT location	n	%
Right	161	46%	<1 month	85	24.3	Upper outer quadrant	156	44.6%
left	181	51.7%	1-6 months	185	52.9%	Upper inner	87	24.7
Bilateral	8	2.3%	6 mon-1 year	36	10.3%	Lower outer	38	10.8
			1-2 years	32	9.1	Lower inner	52	14.8
			2-5 years	8	2.3%	Subareolar	6	1.8%
			>5 years	4	1.1%	Upper inner and upper outer	5	1.5%
						Diffuse vague swelling	6	1.8%
total	350	100		350			350	100

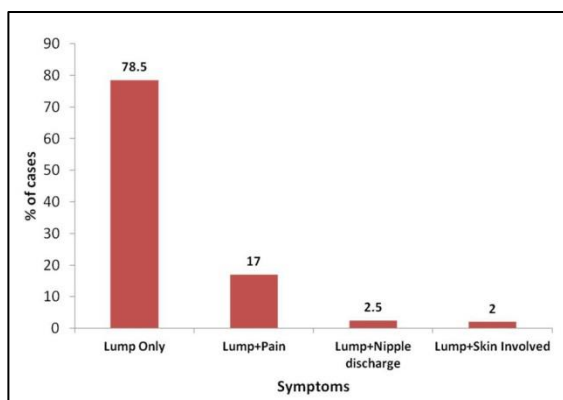


Fig. 1: Types of clinical presentation and incidence

In our study according to NHSBSP guidelines, 9 (2.6%) cases were inadequate and reported as C1

category. C2 included benign lesions like acute mastitis, chronic mastitis, breast abscess, granulomatous lobular mastitis, fibroadenoma, fibrocystic disease, benign phyllodes tumor, galactocele, gynecomastia, epithelial proliferative lesions and duct ectasia. A total of 284 (81.1%) cases were reported in the C2 category. Among this the commonest lesion was fibroadenoma - 146 cases (41.7%) followed by fibrocystic disease -45 cases (12.85%). C3 included cases of proliferative lesions with mild atypia - 5 cases (1.4%).C4 category (suspicious of malignancy) was reported in 8 (2.3%) cases. C5 (malignancy) was reported in 44 cases (12.6%). (Table 3)

Table 3: Category wise cyto histological correlation

Cytological category	FNAC result	n	%	No biopsied	Histopathological examination
C1	inadequate	9	2.6%	-	
C2	Acute mastitis	6	1.71%	-	
	GRANULOMATOUS lobular MASTITIS	7	2%	7	Granulomatous lobular mastitis (7)
	Fibrocystic disease	45	12.8%	27	Fibrocystic disease-(20) Fibroadenoma-(5) Fibroadenoma with fibrocystic change-(2)
	Gynecomastia	9	2.5%	8	Gynecomastia(8)
	Phylloides	3	.82%	3	Phylloides (2) Malignant phylloides (1)
	galactocele	5	1.4%	3	Galactocele (3)
	Breast abscess	15	4.2%	8	Abscess (8)
	Suppurative granulomatous	2	0.5%	1	Granulomatous (1)
	Fibroadenoma	146	41.7%	98	Fibroadenoma (94) Phylloides (3)) Fibroadenomatoid change with foci of UDH and ADH (1)
	Chronic mastitis	9	2.57%	8	Chronic mastitis (8)
	Benign Epithelial proliferative lesion	36	10.2%	20	Fibroadenoma(12) UDH (5) Fibroadenoma with fibrocystic change (3)
	Duct ectasia	1	0.2%	1	Duct ectasia(1)
Total		284	81.1%	184	
C3	PROLIFERATIVE LESION WITH ATYPIA	5	1.42%	4	DCIS(1) Atypical papilloma(1) Extensive FCD with ADH (1) ADH (1)
C4	SUSPICIOUS OF MALIGNANCY	8	2.3%	8	IDC (7) FCD with ADH (1)
C5	malignancy	44	12.6%	44	Medullary (3) MUCINOUS (4) ACC (1)

					IDC with NEC (2) LOBULAR(1) IDC(33)
	Total	350		240	

Cyto histopathological correlation was obtained in 240 cases. The FNAC reports of those cases were classified as benign 184 cases (76.7%), atypical - 4 cases (1.7%), suspicious of malignancy 8 cases (3.3%) and as malignant 44 cases (18.3%). So a total of 188 cases (78.3%) benign/atypical and 52 (21.7%)

malignant/suspicious of malignancy. (Table 4) On histopathological examination 183 cases (76.2%) were benign, 4 cases (1.7%) were atypical and 53 cases (22.1%) were malignant. (Table 4) So a total of 187 (77.9%) benign/atypical category and 53(22.1%) malignant category.

Table 4: Distribution of cases category wise of cytology and biopsy (Histologically confirmed cases n=240)

	Benign	atypical	Susp of malignancy	malignancy	total
Cytology	184(76.7%)	4 (1.7%)	8(3.3%)	44 (18.3%)	240
Biopsy	183(76.2%)	4(1.7%)	0	53(22.1%)	240

Benign lesions were most commonly seen in the 21-40 age group (40.1%) whereas malignancies were seen predominantly in the 41-60 age group (69.9%). No malignancy was detected in females less than 35 years, 5 cases (9.4%) were detected in 35-40 age group. (Fig. 2). The most common benign lesion reported in biopsy was fibroadenoma, a total of 116 cases (48.3%). (Table 3). 3 cases which were reported as fibroadenoma in FNAC turned out to be benign phyllodes tumor by biopsy. Another difficult case we encountered was initially reported as fibroadenoma which on biopsy showed additional foci of atypical ductal hyperplasia (Table 3). Out of 3 benign phylloides reported in FNAC, 2 were benign, 1 was malignant on histopathology. Out of 20 cases which were reported as Benign epithelial proliferative lesion, 12 cases were fibroadenoma, 3 cases were fibroadenoma with fibrocystic change and 5 cases were Usual ductal hyperplasia (UDH).

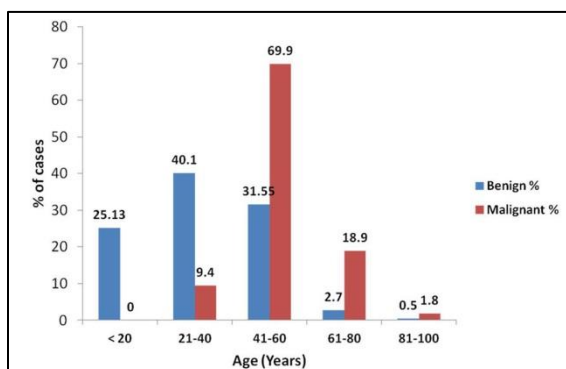


Fig. 2: Distribution of cases according to age group

Out of 5 cases (1.42%) which were reported as proliferative lesion with atypia by FNAC, in 4 cases

biopsy confirmation was obtained. 1 was a case of Ductal Carcinoma in situ (DCIS), another case of atypical papilloma, 1 was a case of atypical ductal hyperplasia (ADH), and 1 was a case of Extensive Fibrocystic disease with foci of ADH. Out of 8 cases of suspicious of malignancy (C4) in 7 cases (87.5%) malignancy was present in histopathology, 1 was a case of fibrocystic disease with ADH. All the cases reported as malignant (C5) in FNAC had 100% concordance on biopsy. Out of 44 malignancy cases, 33 (75%) were Infiltrating Ductal carcinoma (IDC), 3 (6.8%) were medullary carcinomas, 4 (9.1%) were mucinous carcinoma, 2 (4.5%) cases of IDC with neuroendocrine differentiation, 1 (2.3%) case of Lobular carcinoma with areas of Lobular Carcinoma insitu (LCIS) and 1 (2.3%) rare case of Adenoid cystic carcinoma of breast. (Table 3). Out Of 33 cases of IDC, 1 (3.4%) was a 40 year old male patient. Out of 33 cases of IDC, 28(84.9) were grade II, 4 (12.1) were grade III, 1 (3%) grade I.

Statistical analysis showed that the sensitivity of FNAC was 99.46% in benign lesions and 96.2 % in malignant lesions. The specificity and positive predictive value of benign cases were 96.2% and 98.93% respectively. The specificity and positive predictive value of malignant lesions in FNAC were 99.46% and 98.07% respectively. The negative predictive value of benign and malignant lesions were 98.07% and 98.93 % respectively. 186 cases were true negative and 51 cases were true positive for malignancy. The diagnostic accuracy of FNAC in the present study was 98.75%. Percentage of false negative in benign lesions was 1.06% and in malignant lesions was 1.9%. The percentage of false positive in benign and malignant lesions were 1.9% and 1.06% respectively. (Table 5)

Table 5: Accuracy of FNAC in breast lesions in biopsy confirmed cases (n=240)

S. No.	Diagnosis on FNAC	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	%FN	%FP
1	Malignant/suspicious of malignancy	51	186	1	2	96.22%	99.46%	98.07%	98.93%	1.9%	1.06%
2	Benign	186	51	2	1	99.46%	96.2%	98.93%	98.07%	1.06%	1.9%

Table 6: Comparison with previous studies

Authors	Year	Sensitivity	Specificity	PPV	NPV
Srilakshmi HP ³ et al	2013	95.2	100%	100%	95.2%
Ariga et al ⁹	2002	99%	99%	99%	99%
Ranjan Agarwal ¹³ et al	2015	89.5%	100%	100%	94.2%
Hebbar A ²² et al	2013	93.1%	100%	100%	90.4%
Mahajan NA et al ¹⁹	2013	96.77%	98.66%	96.77%	98.6%

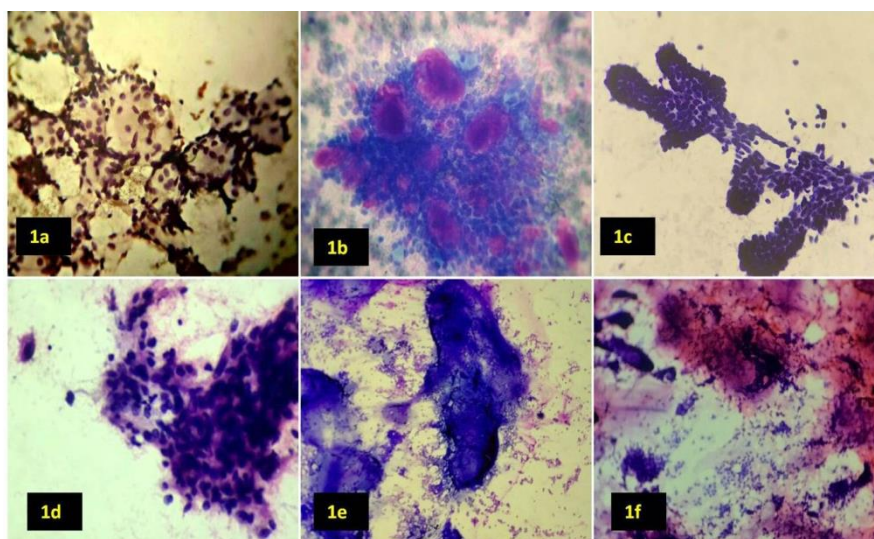


Fig. 3: Photomicrographs of breast cytology 1a. Adenoid cystic carcinoma (PAP) 1b. Adenoid cystic carcinoma (Giemsa) 1c. Fibroadenoma (PAP) 1d. Infiltrating ductal carcinoma (PAP) 1e. Mucinous carcinoma (Giemsa) 1f. Mucinous carcinoma (PAP)



Fig. 4: Gross Images, 2a. Adenoid cystic carcinoma, breast, 2b. Benign phyllodes tumor, 2c. IDC, breast, 2d. Mucinous carcinoma

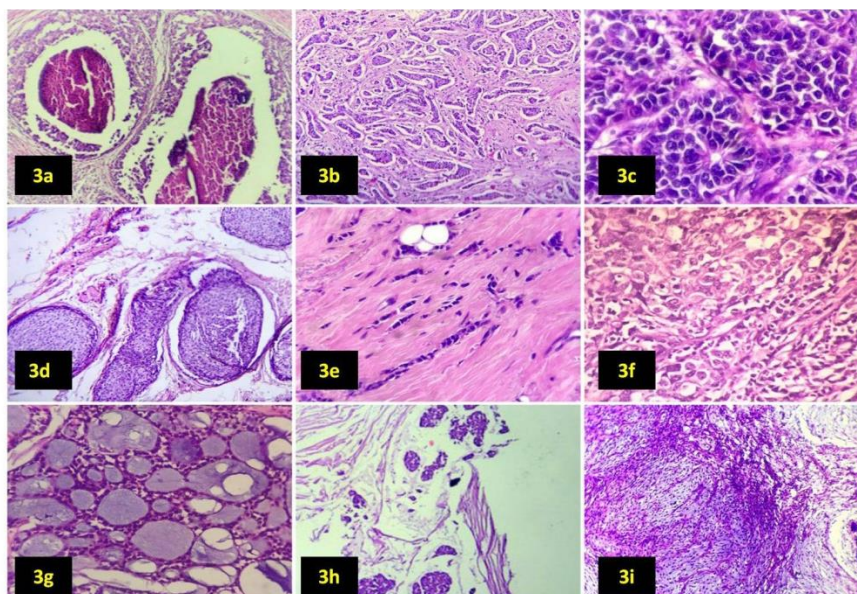


Fig. 5: Photomicrographs of breast histopathology, 3a. DCIS, 3b. IDC(NOS) 3c. IDC breast with neuroendocrine differentiation, 3d. LCIS, 3e. ILC, 3f. Medullary carcinoma, 3g. Adenoid cystic carcinoma, 3h. Mucinous carcinoma, 3i. Benign phyllodes tumor

Discussion

In the present study, maximum incidence of breast lumps was reported in the 21-40 age group. Hussain et al⁸ reported that in their study, maximum incidence of breast lumps was in 31-40 age group. The commonest age group for malignant lesions in our study was 41-60 years, other authors have also reported the same. Ariga et al⁹ and Shresta et al¹⁰ have reported maximum cases of breast cancer in 5th decade of life. Freeman H.P et al¹¹ has reported peak incidence of breast cancer in 6th and 7th decade. In our study, left breast was more commonly involved than right, however previous reports of left sided and right sided breast to be commonly involved have been published. Deshpande et al¹² have reported right breast involvement in 58% of cases in their study. Ranjan Agarwal¹³ et al reported more of right breast involvement in their study. Upper outer quadrant was most commonly involved both in benign and malignant cases. This finding is in accordance with previous studies.^{8,12,13} The majority of patients presented symptoms from 1-6 months. Previous authors have also reported short duration of symptoms. This may be due to the awareness among general population regarding the importance of early detection in our area. The Inadequate sampling rate (C1) in FNAC was only 2.5% in our study. In our institution in most of the cases after FNAC, unstained smear was examined microscopically to assess the adequacy. FNAC procedure was repeated immediately if adequate material was not seen to avoid inadequate sampling. The probable reason for unsuccessful aspiration could be because of extensive fibrosis, cystic

lesion or geographic miss by needle. Out of 9 inadequate samples, 3 were fibrocystic diseases, rest of the 6 cases were lost to follow up. The study by Ranjan Agarwal¹³ et al and Chauhan et al¹⁴ reported inadequate sampling rate of 2% and 4.5% respectively in their studies. The remaining categories were C2 - 83.7%, C3- 1.4% and C4-2.2% and C5-12.5%. The study by Darmola et al¹⁵ and Ranjan Agarwal¹³ et al also reported maximum no of cases in C2 category followed by C5 category. One case which was reported as benign phylloides turned out to be malignant phylloides in biopsy. Jacklin RK¹⁶ et al has also reported that in their study there was a case of malignant phylloides which was initially reported as benign phylloides on FNAC and concluded that in phylloides tumors such problems can arise because of heterogenous nature of these tumors and in such cases core needle biopsy would be useful. In our study one Ductal carcinoma in situ case was reported as proliferative lesion with atypia in FNAC and another case which was reported as suspicious of malignancy in FNAC turned out to be Atypical Ductal hyperplasia. Mitra S et al¹⁷ has also concluded that atypical ductal hyperplasia and in situ carcinomas cannot be confidently picked up by FNAC and their distinction from each other and from invasive carcinoma is difficult. In this study, out of 8 cases which were cytologically diagnosed as C4 (suspicious of malignancy) 7 cases were confirmed to be malignant on histopathology. The study by Bak M et al¹⁸ and study by Ranjan agarwal et al¹³ have also reported that in their studies majority of suspicious of malignancy category lesions were turned out to be malignant in histopathology. Out of 240 cases on histopathology, 187 cases (77.9%) were benign or atypical proliferative lesions and 53 (22.1%) cases were malignant. Shrehta

et al¹⁰ has reported 87.5% cases benign/ atypical while 12.5% cases as malignant / suspicious of malignancy. Mahajan et al¹⁹ reported 64.15% cases as benign/atypical and 29.24% lesions as malignant/suspicious of malignancy. Kamal et al²⁰ reported 69% benign, 1% atypical and 30% malignant in their study.

The commonest benign lesion was fibroadenoma in females and Gynecomastia in males. Infiltrating ductal carcinoma was the commonest malignant lesion. The study by Mahajan et al¹⁹, Kamal et al²⁰, Tiwari et al²¹, showed similar results. In our study, sensitivity of FNAC was 99.46% in benign lesions while 96.2 % in malignant lesions. The specificity and positive predictive value of benign cases were 96.2% and 98.93% respectively while that for malignant lesions were 99.46% and 98.07% respectively. The diagnostic accuracy of FNAC in the present study was 98.75%. Previous studies have also reported high sensitivity and specificity for FNAC in diagnosing breast lesions. Kamal M et al²⁰ reported that in their study, sensitivity of FNAC was 99.25% for benign lesions and 95% for malignant lesions. Specificity and Positive Predictive value for malignant lesions were 99.25% and 98.27% as compared to 95% and 97.79% in benign lesions. Hebbar et al also reported high sensitivity and specificity.²² The statistical data of previous studies are shown in Table 6. True positive cases were 51 (96.2%) and false negative cases were 2(3.7%), 186 cases (99.46%) were true negatives and false positive was 1(0.5%) case. Kamal²⁰ et al reported false positivity of 0.75%, false negativity of 5%, true negative cases 99.25% and true positive cases 95%. False negativity was due to misinterpretation, bloody aspiration, scanty cellularity or drying artefact. Diagnostic efficacy of physical examination, radiological imaging and FNAC (triple test) when taken together increases to over 90%.

FNAC has good sensitivity, specificity and diagnostic accuracy, however it should be noted that a negative FNAC result does not completely rule out possibility of malignancy. The other limitations of FNAC include inability to diagnose lesions if the aspirate is inadequate or if the lesions are very small. In some C3 and C4 grey zone lesions, there is difficulty in classifying breast lesions despite adequate cellularity. In such situations it's advisable to perform a core needle biopsy to avoid misdiagnosis.

Conclusion

The accuracy of FNAC approaches that of histopathology in providing unequivocal diagnosis in breast lesions as it has high sensitivity, specificity and low rate of false negativity and false positivity. FNAC is helpful in preoperative evaluation and deciding further management and can avoid unnecessary surgical intervention.

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Conflict of Interest: The authors declare no conflict of interest

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