



## Correlation of fine needle aspiration cytology (FNAC) with histopathology in palpable breast lesions: A study of 200 cases from a tertiary care center in South India

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### Abstract

**Background:** Palpable breast lesions are one of the commonest presentations in general and oncological surgical practice. Breast cancer is the commonest cancer affecting women worldwide. Fine needle aspiration cytology (FNAC) is an ideal initial diagnostic modality in the management of palpable breast lesions which helps to avoid unnecessary surgical intervention in benign breast lesions and to confirm preoperative diagnosis in malignant breast lesions.

**Materials and Methods:** Cytohistopathological correlation was done in 200 cases who presented with a palpable breast mass in FNA clinic of Dept. of Pathology, Government Medical College, Thrissur, Kerala.

**Results:** A total of 200 cases was studied which included 87 benign cases (43.5%), 105 malignant cases (99 cases diagnosed as carcinoma and 6 cases as suspicious of malignancy) (Total 52.5%), 5 proliferative lesions with atypia (2.5%) and 3 inadequate cases (1.5%). Histopathological diagnosis of all 200 cases was collected and analyzed. There was a discrepancy in 5 cases (2.5%). Sensitivity, specificity, positive predictive value and negative predictive value of FNA for diagnosing benign lesions were found to be 98.8%, 96.3%, 95.6% and 99% and for malignant lesions the values were 96.3%, 98.8%, 99% and 95.6% respectively. The diagnostic accuracy of FNAC in this study was 97.45%.

**Conclusion:** FNAC is a reliable primary screening technique for palpable breast lumps with high diagnostic accuracy and good specificity and positive predictive value, especially for malignant lesions.

**Keywords:** Breast, Palpable, Correlation, Fine Needle Aspiration, Histopathology.

### Introduction

A palpable breast mass is the most common symptom associated with both benign and malignant

diseases of the breast. Palpable breast masses should accurately be classified preoperatively into benign and malignant masses for proper oncologic surgical management and for avoiding unnecessary surgical

intervention. Although benign breast lesions are common, every patient should be evaluated to exclude or confirm malignancy as malignancy is managed by more radical surgery and adjuvant therapy. Breast carcinoma is one of the leading causes of malignancy in females. The ideal diagnosis of palpable breast masses includes triple assessment, which includes clinical examination, imaging (mammography/ ultrasound) and FNAC.

The application of FNA (Fine Needle Aspiration) for the diagnosis of palpable breast masses was first introduced by Martin and Ellis in 1930. The main aim of FNA study of the breast lumps is to establish a preoperative diagnosis for proper oncologic surgical management of malignancies and to avoid unnecessary open biopsy / radical surgery in benign conditions. FNA is simple to carry out, cost-effective, well accepted by the majority of patients, involves minimal discomfort to the patient and can be performed on an outpatient basis.

FNAC of male breast lesions is an equally diagnostically useful procedure. It is cost effective, and the report can be made available on the same day, thus minimizing the anxiety of the patient.

However, FNAC is a procedure with sampling error, sometimes being unable to substitute histopathology. Final confirmation of disease is obtained by histopathological evaluation. This study is undertaken to analyze the correlation between FNA diagnosis and final histopathological diagnosis of palpable breast lesions and hence to assess the utility of FNA as an initial diagnostic tool in the management of breast lesions.

### Materials and Methods

This hospital based retrospective descriptive study was carried out at the Department of Pathology, Government Medical College, Thrissur, Kerala for the duration of one month (June 2018). Data (Age and gender of patients, outpatient/ inpatient number, cytological diagnosis and final histopathological diagnosis) over a period of one year (May 2017 to April 2018) were collected from registers maintained in the department. Patients who did not undergo subsequent histopathological examination

were excluded from the study. 200 cases with breast lumps subjected to FNAC and later confirmed by histopathology were enrolled in the study. FNA was performed using a 23- gauge needle and syringe after obtaining consent, a thorough history taking and clinical examination of the mass. Multiple smears were made from the aspirated material. Smears were carefully labeled and those fixed in 95% ethyl alcohol were stained with Papanicolaou stain and air dried smears were stained using Leishman's stain. In case of cystic swellings with a fluid aspirate, cytocentrifugation was done and the smears were prepared from sediment and stained. Cytological report was categorized according to the National Cancer Institute (NCI) guidelines, into inadequate (C1), benign (C2), atypical, probably benign (C3), suspicious, favor malignancy (C4), and malignant (C5).<sup>1</sup>

Histopathological diagnosis (in trucut biopsy/ excision biopsy/ mastectomy) of all the cases was collected from histopathology registers and analyzed. Data were then subjected to descriptive statistical tabulation and analysis. This study was approved by Institutional Review Board.

### Results

A total of 200 cases was included in the study. There were 197 female patients and 3 male patients (M: F ratio = 0.015: 1).

The age of the patients in the present study varied from 13 to 78 years. Age-wise distribution of the cases is shown in Table 1.

The majority of cases were between 41 and 50 years of age (27.5%). Cytological diagnosis of the cases was categorized as inadequate (C1), benign (C2), atypical, probably benign (C3), suspicious, favor malignancy (C4), and malignant (C5) (Table 2).

Cytological diagnosis of the cases is depicted in Table 3.

There were 87 benign cases (43.5%), 105 malignant cases (99 cases diagnosed as carcinoma and 6 cases as suspicious of malignancy) (Total 52.5%), 5 proliferative lesions with atypia (2.5%) and 3 inadequate cases (1.5%).

Most common cytological diagnosis was carcinoma breast (n=99, 49.5%) followed by fibroadenoma (n=44, 22%). The rest of the cases included benign epithelial proliferative disease (n=16, 8%), fibrocystic disease (n=13, 6.5%), suspicious of malignancy (n=6, 3%), fibrocystic disease with atypia (n=5, 2.5%), granulomatous mastitis and breast abscess (n=4 each, 2%), 2 cases each of gynecomastia, benign Phyllodes tumor and duct papilloma (n=2, 1%) and 3 cases which were inadequate for evaluation (n=3, 1.5%).

Histopathological diagnosis of all 200 cases was collected and analyzed. Table 4 shows cytohistopathological correlation of all cases with cytological and corresponding histopathological diagnosis.

There was a discrepancy between cytological and histopathological diagnosis in 5 cases (2.5%; underlined). For 2 benign cases in FNA (C2; fibrocystic disease and benign Phyllodes tumor), the material obtained for histopathology evaluation was inadequate and hence excluded while calculating sensitivity and specificity.

3 cases diagnosed as C1 category (inadequate for evaluation) in cytology, turned out to be invasive duct carcinomas in histopathology. Out of 87 cases in C2 category (benign), most common diagnosis was fibroadenoma (n=44) followed by benign epithelial proliferative disease (n=16). Among 44 fibroadenomas diagnosed by FNAC, 1 case turned out to be a benign Phyllodes tumor and the rest 43 cases were consistent by biopsy. Among 16 cases of benign epithelial proliferative disease in FNAC, 5 cases each were diagnosed as fibroadenoma and fibrocystic disease, 3 cases as benign phyllodes tumor, 1 case as complex fibroadenoma and 1 case

showed benign breast tissue without a specific pathology in biopsy. 2 cases of granulomatous mastitis in cytology were diagnosed as breast abscess in histopathology. Out of 13 cases diagnosed as fibrocystic disease in cytology, 10 were fibrocystic disease, 1 case of fibroadenomatoid hyperplasia and the rest 2 were inadequate for opinion in biopsy. 1 case of duct papilloma (C2) turned out as IDC with DCIS in biopsy.

In C3 (proliferative disease with atypia), 3 cases were IDCs, 1 case was fibroadenosis with focal atypia but 1 case was diagnosed as fibroadenoma in biopsy. Out of 6 cases suspicious for malignancy in FNA (C4), 5 were malignant and 1 case was fibrocystic disease with atypia in histopathology. All the cases diagnosed as malignant (C5) by FNAC, showed 100% concordance on biopsy. Majority of the malignant cases fell between 41 and 50 years of age (34.3% of malignant cases according to cytological diagnosis; 37% of malignant cases; according to final histopathological diagnosis; table 5).

Statistical analysis showed that the sensitivity of FNAC was 98.8% in benign lesions and 96.3% in malignant lesions (Table 6).

The specificity and positive predictive value of benign cases were 96.3% and 95.6% respectively. The specificity and positive predictive value of malignant lesions in FNAC were 98.8% and 99% respectively. The negative predictive value of benign and malignant lesions was 99% and 95.6% respectively. 89 cases were true positive for benign and 105 cases were true positive for malignancy. The diagnostic accuracy of FNAC in our study was 97.45%.

**Table 1** Age and gender wise distribution of cases (n=200)

Age range of patients	Males	Females	No. of cases	Percentage
10-20	0	18	18	9%
21-30	0	18	18	9%
31-40	0	39	39	19.5%
41-50	1	54	55	27.5%
51-60	0	37	37	18.5%
61-70	0	23	23	11.5%
71-80	2	8	10	5%
<b>Total</b>	<b>3</b>	<b>197</b>	<b>200</b>	<b>100%</b>

**Table 2** Reporting categories on breast FNA

Cytology categories	Explanation
C1	Inadequate
C2	Benign
C3	Atypical, probably benign
C4	Suspicious, favor malignancy
C5	Malignant

**Table 3** Cytological diagnosis of cases (n=200)

Cytological diagnosis	No.of cases	Percentage
Carcinoma breast	99	49.5%
Suspicious of malignancy	6	3%
Fibroadenoma	44	22%
Gynecomastia	2	1%
Benign Phyllodes Tumor	2	1%
Benign epithelial proliferative disease	16	8%
Granulomatous mastitis	4	2%
Breast abscess	4	2%
Fibrocystic disease	13	6.5%
Fibrocystic disease with atypia	5	2.5%
Duct papilloma	2	1%
Inadequate for evaluation	3	1.5%

**Table4.** Cytohistopathological correlation of cases (n=200)

Cytological Category	Cytological diagnosis	No. of cases	Histopathological diagnosis
C1	Inadequate	3	IDC (3)
C2	Fibroadenoma	44	Fibroadenoma (43) Benign Phyllodes tumor (1)
	Gynaecomastia	2	Gynaecomastia (2)
	Benign Phyllodes tumor	2	Benign Phyllodes tumor (1) Inadequate biopsy (1)
	Benign epithelial proliferative disease	16	Fibroadenoma (5) Fibrocystic disease (5) Benign Phyllodes tumor (3) Complex fibroadenoma (1) Benign breast tissue with no evidence of malignancy (1)
	Granulomatous mastitis	4	Granulomatous lobular mastitis (2) Breast abscess (2)
	Breast abscess	4	Breast abscess (4)
	Fibrocystic disease	13	Fibrocystic disease (8) Complex fibroadenoma (2) Fibroadenomatoid hyperplasia (1) Inadequate biopsy (2)
	Duct papilloma	2	Duct papilloma (1) Invasive carcinoma with DCIS (1)
Total		87	87
C3	Proliferative disease with atypia	5	IDC (3) Fibroadenosis with focal atypia (1) Fibroadenoma (1)
C4	Suspicious of malignancy	6	IDC (5) Fibrocystic disease with florid epithelial hyperplasia (1)
C5	Malignancy	99	IDC (92) IDC with apocrine differentiation (2) IDC with high grade DCIS (2) Metaplastic carcinoma (1) Medullary carcinoma (1) Mucinous carcinoma (1)

**Table 5.** Age and gender wise distribution of breast malignancy (according to cytology (C) and histopathology (H))

Age	Males		Females		Total No. of cases		Percentage	
	C	H	C	H	C	H	C	H
10-20	0	0	0	0	0	0	0%	0%
21-30	0	0	1	1	1	1	0.9%	0.9%
31-40	0	0	9	10	9	10	8.5%	9%
41-50	0	0	36	41	36	41	34.3%	37%
51-60	0	0	31	32	31	32	29.5%	28.9%
61-70	0	0	19	18	19	18	18%	16.2%
71-80	1	1	8	8	9	9	8.8%	8%
<b>Total</b>	<b>1</b>	<b>1</b>	<b>104</b>	<b>110</b>	<b>105</b>	<b>111</b>	<b>100%</b>	<b>100%</b>

**Table 6.** Accuracy of FNA in differentiating between benign and malignant breast mass in cases with histopathological confirmation (n=200)

FNA diagnosis	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV
<b>Benign</b>	89	105	4	1	98.8%	96.3%	95.6%	99%
<b>Malignancy/suspicious of malignancy</b>	105	89	1	4	96.3%	98.8%	99%	95.6%

## Discussion

The aim of breast FNA is to establish or exclude malignancy preoperatively in palpable breast mass avoiding unnecessary surgery in benign conditions and to allow subsequent definite treatment planning in malignant masses. Since the first introduction of FNA by Martin and Ellis in 1930, it has been established as an important tool in the evaluation of breast lesions.<sup>2</sup>

Breast cancer is the second most common cancer in the world and the most frequent cancer among women with an estimated 1.67 million new cancer cases diagnosed in 2012 (25% of all cancers).<sup>3</sup> In Kerala, India, around 30% of cancer-affected women have carcinoma breast. Though the incidence of breast cancer is rising steadily in Kerala, the published data on breast cancer in the state is sparse.<sup>4</sup>

In our study the FNA findings were correlated with histopathology results. Out of the 200 cases studied, the rate of inadequate sampling was only 1.5%. In our FNA clinic, FNAs with inadequate material were always repeated whenever the patient was available for a repeat procedure, to increase the sampling yield.

In our study, the most common diagnosis was malignancy. This is in concordance with various studies from other parts of India.<sup>5-7</sup> This may probably be due to the facts that we enrolled only

cases with histopathological confirmation in the study and our institution is a tertiary care referral center. Vasavada et al, Rathi M. et al and Chandanwale SS et al have reported a predominance of benign lesions in their study.<sup>8-10</sup> There was a notable female predominance (F=197; M=3) of the lesions in our study. The maximum incidence of breast lumps in this study was reported in the 41-50 age group. Rathi M et al reported that in their study, the maximum incidence of breast lumps was in 30-39 age group.<sup>9</sup> The commonest age group for malignant lesions in our study was also 41-50 years, followed by 51-60 years. Vasavada et al and Shreshta A et al have also reported similar results.<sup>8, 11</sup> 9 out of 10 cases above 70 years of age were all malignant in our study. Youngest patient with malignancy was 26 years old. Case of a single male patient, 76 years old, diagnosed as malignant with cytohistological correlation, was also noted in our study.

The most common benign lesion in our study was fibroadenoma in females, followed by fibrocystic disease. Similar results were shown by Chandanwale SS et al and Vasavada et al.<sup>8, 10</sup> Most common age group of fibroadenoma was noted as 10-20 years, followed by 20-30 years. The triad of a cellular smear with a bimodal benign pattern, numerous single bipolar oval nuclei and fragments of stroma is virtually diagnostic of fibroadenoma. In the absence of stroma, numerous single bipolar



nuclei are highly suggestive of the diagnosis of fibroadenoma. The considerable degree of overlap in cytological picture of fibroadenoma and benign phyllodes tumor with a scarcity of spindle stromal cells in our case could be the reason for the cytohistological discordance in the case of benign phyllodes tumor diagnosed as fibroadenoma on FNA.

Fragments of myxoid stroma may also be seen in 'fibroadenomatoid hyperplasia'. Fibroadenoma can undergo cystic degeneration, or the ductal structures can become dilated and filled with fluid. Smears from such lesions may contain numerous 'cyst macrophages' and apocrine metaplastic cells and may be interpreted as fibrocystic disease. These are attributed as reasons for diagnosing cases of complex fibroadenoma and fibroadenomatoid hyperplasia as fibrocystic disease on FNA in this study.

Most common benign diagnosis in males was gynecomastia (n=2), which showed 100% cytohistological concordance. This is further supported by Singh A et al and Das et al. who found 100% diagnostic accuracy of fine needle aspiration cytology in cases of gynaecomastia.<sup>12, 13</sup>

In their study of 57 male breast lesions, Singh K et al. have concluded that FNAC of male breast lesions shows excellent specificity, sensitivity and cytohistologic correlation.<sup>14</sup>

Smears of intraductal papilloma are among the most cellular seen on cytology of the breast, with large aggregates distributed all over the slide as well as many dispersed cells.<sup>15</sup> The pattern (cell balls and papillary fragments) also overlaps with that of other papillary lesions. It is difficult to distinguish intracystic or intraductal papillary carcinoma from intraductal papilloma or florid papillomatosis. Solid, finger-like epithelial aggregates with a distinct anatomical border of a row of cuboidal cells can be removed intact from a low-grade invasive carcinoma of particularly cohesive cells by FNB. They can be mistaken for fragments of papilloma. One case of invasive carcinoma with DCIS (in trucut biopsy) was diagnosed as duct papilloma by FNA in our study. So, in papillary lesions, the

definitive diagnosis is best deferred to histopathology.

In our study, 5 out of 6 cases diagnosed as suspicious of malignancy were turned out to be malignant on biopsy. The studies by Vasavada et al and Agarwal R et al have also reported that majority of suspicious of malignancy category lesions were confirmed to be malignant in histopathology.<sup>8,16</sup>

The sensitivity of FNAC was 98.8% in benign lesions and 96.3% in malignant lesions in the present study. The specificity and positive predictive value of benign cases were 96.3% and 95.6% respectively. The specificity and positive predictive value of malignant lesions in FNAC were 98.8% and 99% respectively. The diagnostic accuracy of FNAC in our study was 97.45%. Similar results were shown by various authors.<sup>5-8</sup>

Technical skills of the cytopathologist performing FNA can very much influence the sampling yield. Unsatisfactory cytological smears can be due to faulty FNA technique resulting in poor cell yield and sampling errors due to the nature of lesion itself. False negative results can be due to misinterpretation, hemorrhagic aspiration, scanty material or drying artefact. Provision of adequate sample by an experienced pathologist can prove FNAC as a highly reliable diagnostic tool. Diagnostic efficacy of physical examination, imaging and FNAC (triple test) when combined together, is still higher.

### Conclusions

FNAC is a reliable preoperative diagnostic tool with high diagnostic accuracy in palpable breast masses and helps in the proper surgical management of patients. However, lesions categorized by FNAC as C1, C3, C4 and papillary lesions (of any category) need confirmation by histopathology to eliminate false positive and false negative cases and histopathology remains the gold standard in such cases.

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