

# Cytomorphological overview of fine-needle aspiration breast utilizing the International Academy of Cytology – Yokohama system of reporting



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## ABSTRACT

**Background:** Benign and malignant lesions of breast are one of the most common causes of palpable masses seen in women. Fine-needle aspiration cytology (FNAC) is the important modality of diagnosis of breast lumps. Previously, there were no uniform criteria for reporting breast FNAC. To overcome this problem, the newly designed system – International Academy of Cytology (IAC) – Yokohama system of reporting was implemented in 2016. The system offers a structured report to the patient. **Aims and Objectives:** This study aims to categorize breast FNAC according to the IAC – Yokohama system of reporting, to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of the test, and to analyze the cytomorphological spectrum of various breast lesions. **Materials and Methods:** A total of 210 patients presenting with breast lump in cytology section were subjected to FNAC using a 22 gauge needle under all aseptic precautions. Detailed clinical history was taken. All cytology and histopathology examination slides (wherever available) were thoroughly studied. FNAC smears were reported using IAC – Yokohama system of reporting. **Results:** In our study, benign category (C2) was most commonly seen in 73.33% of cases, followed by 10.48% of cases of atypical probably benign (C3), 2.38% of cases were reported as suspicious (C4), and 11.43% of cases were reported as malignant (C5). Cytohistopathological concordance was seen in 38 cases (88.4%) whereas five cases were reported as discordant. Sensitivity and specificity of the test for the diagnosis of malignancy were 81% and 100%, respectively. PPV was 100%. NPV was 90.90%. Diagnostic accuracy of the test was 93.47%. **Conclusion:** The newer IAC – Yokohama system of reporting of breast FNAC is simple, has clear diagnostic criteria hence boost up the confidence as well has uniformity of reporting by cytopathologist, and increases the understanding and uniformity in assessment by the attending clinician which help in improving the communication between the pathologist and the treating clinician.

**Key words:** Fine-needle aspiration; Fibroadenoma; Breast cancer; Cytomorphology; Histopathology

## INTRODUCTION

Carcinoma of breast is one of the most common causes of malignancy in women worldwide. Carcinoma of breast is now the most common cause of cancer death in woman in less developed countries and it is the second

most common cause of cancer death in more developed countries.<sup>1</sup> In India, carcinoma of cervix was the most common cancer in women but nowadays, carcinoma of breast has overtaken cervical carcinoma with the incidence of 26 per lac women population.<sup>2</sup> The three major modalities for diagnosis of breast lump are clinical

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examination, radiological imaging, and breast cytological examination. These modalities aim at early diagnosis of malignancy so as to offer appropriate treatment or one stage surgeries to patients.<sup>3,4</sup>

Aspiration of breast lump is one of the most commonly performed fine-needle aspiration cytology (FNAC) procedures because of its superficial location, ease to perform, outpatient department procedure, and possible to report in the same day. It is minimally invasive, causes minimum physical or psychological discomfort, and highly acceptable to patient.<sup>5</sup> Previously, there was no uniformity in reporting of breast FNAC and there were no guidelines given in the cytology report to the clinicians for the management of patient.

To overcome these problems, the newly designed system began with a meeting, sponsored by the International Academy of Cytology (IAC), of a group of cytopathologists with an interest in breast fine-needle aspiration biopsy (FNAB) cytology at the International Congress of Cytology in Yokohama in May 2016. The system defines five categories for reporting breast cytology, each with a clear descriptive term for the category, a definition, a risk of malignancy, and a suggested management algorithm.<sup>6</sup> The system is intended for global use, is based on cytomorphology, and includes key diagnostic cytological criteria for each of the many lesions and tumors found in the breast and offers structured reporting to the patient. The system emphasizes that biopsy and smear making techniques of a high standard are essential to optimize quality and enhance breast FNAB diagnosis.<sup>6</sup>

A structured report means using a format of reporting having standard headings, definitions, terminologies, and includes required information.<sup>7,8</sup> The advantage of structured reporting is that, the complete report is reproducible, can be understood internationally by other pathologist provides clear information, and management guidelines to the clinician.<sup>9</sup> A standardized approach will improve the quality of performance of FNAC as well as smear quality.

### Aims and objectives

The aims of the study were as follows:

1. To categorize and interpret breast FNAC according to the IAC – Yokohama system of reporting
2. To calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy for all categories
3. To analyze cytomorphological spectrum of various lesions of breast and to correlate it with histopathological findings wherever available.

## MATERIALS AND METHODS

All patients presented with breast lump coming to the cytology section of our department in the period of 1.5 years, that is, from October 1, 2020, to March 31, 2022, were taken as study population. Informed consent was taken from all the patients.

Type of study – It was a prospective cross-sectional study.

Inclusion criteria and exclusion criteria – All the patients presenting with breast lump coming to our outpatient department were included in the study and were subjected for FNAC. Inadequate and hemorrhagic aspirate were excluded from the study.

Necessary and relevant clinical information and ultrasound (USG) report were taken into account whenever available. Under all aseptic precautions, aspiration of the breast lump was done using a 22 gauge needle. All the cytology slides were stained with hematoxylin and eosin (H and E) stain. Special stains such as Ziehl and Neelsen (ZN) stain and periodic acid Schiff stain were used whenever required. Histopathology slides were also archived and reported wherever available. All histopathology slides were stained with H and E stain. All the cytology cases were categorized by the newly proposed IAC – Yokohama reporting system. Breast FNAC were categorized into five categories: 1 – Insufficient, 2 – benign, 3 – atypical, 4 – suspicious of malignancy, and 5 – malignant. Statistical analysis executed using Microsoft Excel 2011 version.

## RESULTS

In the present study, a total of 210 cases of FNA breast were undertaken. All the patients were female except two cases were males presented with breast lump. The right-sided lump was predominant seen in 101 cases and left sided in 95 cases. Bilateral lump was noted in 14 cases. There was a wide age group range from 16 years to 80 years. The most common age group was 4<sup>th</sup> decade (68 cases) followed by the 5<sup>th</sup> decade (51) and 3<sup>rd</sup> decade (44). The most common category according to the IAC – Yokohama system of reporting was benign (C2). Malignant (C5) diagnosis was seen in 11.43% of cases (Table 1).

Histopathology was available in 43 cases of total 210 cases. There were five cases included in insufficient category (C1) but histopathology was available in only two cases. A total of 154 cases were categorized under benign category (C2). Twenty-six cases were available for histopathology examination (HPE). The most common diagnosis in benign

category was fibroadenoma (75 cases) (Figure 1) followed by fibrocystic disease (30 cases) and granulomatous mastitis (13 cases).

Atypical category (C3) included 22 cases. Five cases were available for HPE. The most common cytology diagnosis in atypical category was proliferating breast lesion with atypia (13 cases) followed by benign phyllodes tumor (four cases) (Figure 1). There were five cases categorized as suspicious of malignancy (C4). Three cases were available for histopathology. All three cases were diagnosed as duct carcinoma on histopathology. Lesions were categorized as malignant (C5) in 24 cases. Only seven were available for histopathology. Out of them, six cases were diagnosed as duct carcinoma and one was diagnosed as mucinous carcinoma (Figure 2, Tables 2 and 2.1).

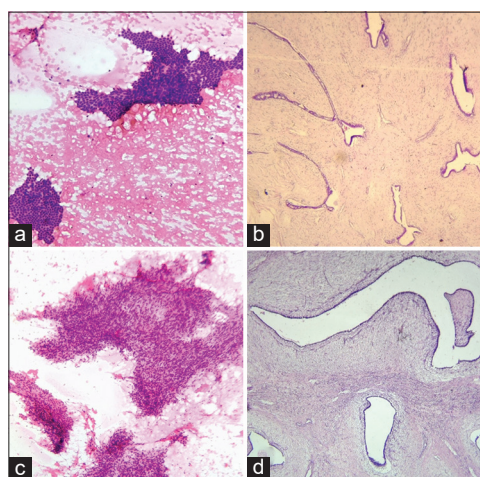
There were five cases where cytology diagnosis did not match with HPE diagnosis. These were labeled as discordant cases (Table 3).

In discordant case no. 1 (Figure 3a and b), FNA was repeated twice due to scant cellularity. In both passes,

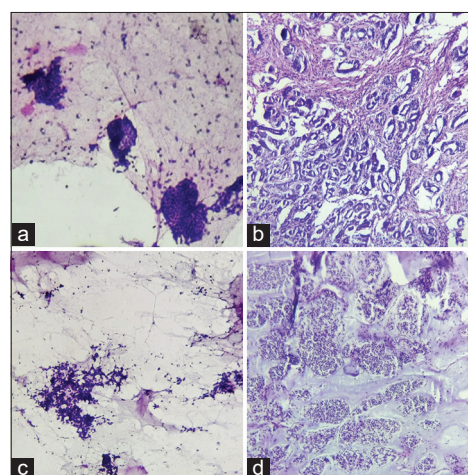
cytology smears were scanty cellular and showed occasional cluster of benign ductal epithelial cells on background of abundant red blood cells. In spite of two passes, cell yield was low so we reported it as insufficient material. Histopathology turned out as pseudoangiomatic stromal hyperplasia (PASH). As there is hyperplasia of stromal elements, our aspirate was scanty. FNA by experienced pathologist and high index

**Table 1: Distribution of cases according to the IAC – Yokohama system of reporting**

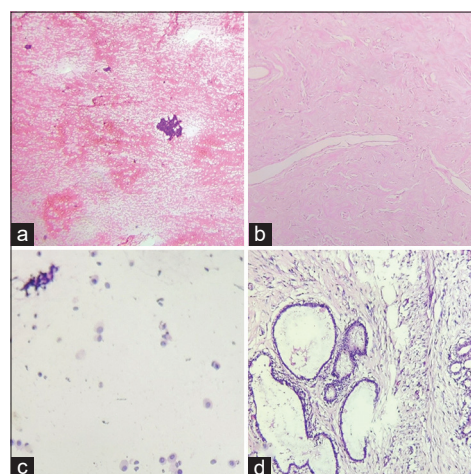
Category	No. of cases	%
Insufficient (C1)	5	2.38
Benign (C2)	154	73.33
Atypical probably benign (C3)	22	10.48
Suspicious (C4)	5	2.38
Malignant (C5)	24	11.43
Total	210	100



**Figure 1:** Fibroadenoma – (a) Cytology smear showing benign, tight cohesive clusters of ductal epithelial cells of breast (H and E ×100). (b) HPE shows proliferating ducts and ductules with fibromyxoid stroma (H and E ×100). Phyllodes tumor – (c) Cytology smears show few sheets of spindle-shaped cells having spindle-shaped nuclei (H and E ×100). (d) HPE shows leaf-like pattern of growth due marked stromal proliferation (H and E ×100)



**Figure 2:** Tubular adenoma – (a) Cytology smear showing benign, tight cohesive clusters of ductal epithelial cells with scattered bare nuclei (H and E ×40). (b) HPE shows closely packed tubules lined by double-layered epithelium. Stroma is scanty (H and E ×100). Mucinous carcinoma – (c) Cytology smears show few clusters of round monomorphic cells on background of abundant mucinous material (H and E ×40). (d) HPE shows plenty clusters of round monomorphic tumor cells floating in the sea of mucin (H and E ×100)



**Figure 3:** Discordant case 1 – (a) Cytology smear showing occasional cluster of benign, ductal epithelial cells of breast on hemorrhagic background, reported as insufficient material (H and E×40). (b) HPE shows hyalinized stroma and few thin channels lined by spindle-shaped cells, reported as PASH (H and E ×100). Discordant case 2: (c) Cytology smears scanty cellularity showing occasional small cluster of benign ductal epithelial cells on background of plenty cyst macrophages, reported as insufficient material (H and E ×400). (d) HPE shows plenty cystically dilated ducts and fibromyxoid stroma, reported as FCD (H and E ×400)



**Table 2: Cytohistopathological correlation**

HPE diagnosis	Cytology diagnosis								
	C1 (5)			C2 (154)					
	FA (75)	FA with FCC (10)	Granulomatous mastitis (12)	Suppurative granulomatous Inflammation (9)	Gynecomastia (2)	Fat necrosis (3)	Galactocele (7)	FCD (30)	Lactating adenoma (2)
Fibroadenoma	18								
FA with FCC		1							
Granulomatous mastitis				1					
Galactocele							1		
Pseudoangiomatous stromal hyperplasia			1						
FCD			1					3	
Tubular adenoma									
Benign Phyllodes									
Borderline phyllodes								1	
Duct carcinoma									1
Mucinous carcinoma									

FA: Fibroadenoma, FCC: Fibrocystic change, FCD: Fibrocystic disease, HPE: Histopathology examination

of suspicion are probably the best remedies to diagnose PASH on FNAC.

In discordant case no. 2 (Figure 3c and d), FNA was scanty cellular with occasional cluster of benign ductal epithelial cells on background of proteinaceous material and abundant cyst macrophages. As aspirate was scanty, a second pass was needed but was not possible as the patient was posted for surgery on the next day and we received a lumpectomy specimen. Hence, cytology report was given as insufficient material and HPE came out as fibrocystic disease. Incorporation of rapid onsite evaluation for clinically benign lesions is probably best remedy here, but is difficult to operate in set up like us due to less availability of workforce.

In discordant case no. 3, FNA (Figure 4a and b) showed moderate cellularity showing few clusters of ductal epithelial cells and background showed occasional cluster showing apocrine metaplasia reported as fibrocystic disease. Here, there were few spindle-shaped cells scattered on the background. HPE was reported as benign phyllodes tumor. If careful clinical examination and FNA by experienced pathologist were done, we probably might not miss the diagnosis on cytology.

In discordant case no. 4 (Figure 5a and b), FNA showed high cellularity with plenty loose clusters of ductal epithelial cells of breast on hemorrhagic background. Few of the clusters were three dimensional with overlapping nuclei. Cells showed moderate pleomorphism. Cytology was reported as proliferating breast lesion with severe atypia. HPE diagnosis offered as infiltrating duct carcinoma. As cytology smears showed only moderate pleomorphism, we offered the diagnosis as proliferating breast lesion with severe atypia. Careful clinical examination of breast lump, an account of cellularity and arrangement of cell clusters, all should be taken into consideration before giving the diagnosis of such lesions.

In discordant case no. 5 (Figure 5c and d), FNA showed high cellularity with relatively benign looking ductal epithelial cells. Background showed few bare nuclei and few cyst macrophages. Cytology diagnosis was offered as fibrocystic disease. HPE diagnosis was given as IDC. As cytology showed relatively benign looking ductal cells, less attention was given to the loose cohesiveness of the clusters and probably the needle did not hit the tumor proper. In such cases, thorough clinical examination and FNA by experienced pathologist can help to arrive at accurate diagnosis on cytology.

In our study, the risk of malignancy was 100% for C4 and C5. It was 0% for C1 (Table 4).

**Table 2.1: Cytohistopathological correlation**

HPE diagnosis	Cytology diagnosis						
	C3 (22)			C4 (5)		C5 (24)	
	FCD with atypia	Proliferating breast lesion without atypia	Proliferating breast lesion with severe atypia	Benign phyllodes	Suspicious of malignancy	Duct carcinoma	Mucinous carcinoma
Fibroadenoma							
FA with FCC							
Granulomatous mastitis							
Galactocele							
PASH							
Fibrocystic disease							
Tubular adenoma		1					
Benign Phyllodes	1			2			
Borderline phyllodes							
Duct carcinoma			1		3	6	
Mucinous carcinoma							1

FA: Fibroadenoma, FCC: Fibrocystic change, FCD: Fibrocystic disease, PASH: Pseudoangiomatous stromal hyperplasia, HPE: Histopathology examination

**Table 3: Discordant diagnosis analysis**

Case No.	Cytology diagnosis	HPE diagnosis
1	Insufficient material	PASH
2	Insufficient material	FCD
3	FCD	Borderline phyllodes
4	FCD	Duct carcinoma
5	Proliferating breast lesion with severe atypia	Duct carcinoma

FCD: Fibrocystic disease, PASH: Pseudoangiomatous stromal hyperplasia, HPE: Histopathology examination

**Table 4: Risk of malignancy**

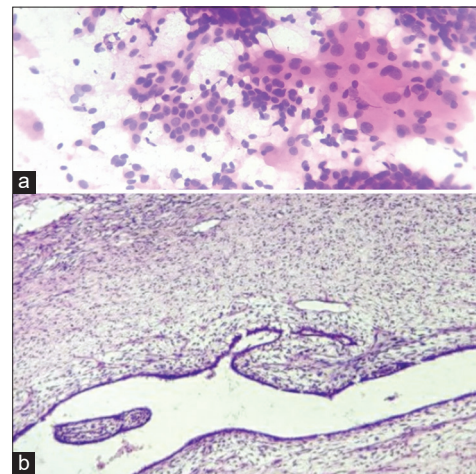
Category	Risk of malignancy (%)
1	00
2	3.8
3	20
4	100
5	100

In our study, we have reported –

- Sensitivity of test for the diagnosis of malignancy – 81%
- Specificity of test for the diagnosis of malignancy – 100%
- PPV – 100%
- NPV – 90.90%
- Diagnostic accuracy of the test – 93.47%.

## DISCUSSION

Breast cancer is the leading cause of malignancy in women worldwide; hence, all the possible majors for early and accurate diagnosis of breast lumps should be applied. Triple examinations, that is, clinical examination, radiological imaging, and cytological examination, are the mainstay of accurate diagnosis of breast lump. However, in centers with



**Figure 4:** Discordant case 3 – (a) Cytology smear showing few clusters of benign, ductal epithelial cells of breast, occasional cluster shows apocrine metaplasia, reported as FCD (H and E ×400). (b) HPE shows few cleft-like spaces surrounded by stromal proliferation by abundant spindle cells reported as benign phyllodes tumor (H and E ×400)

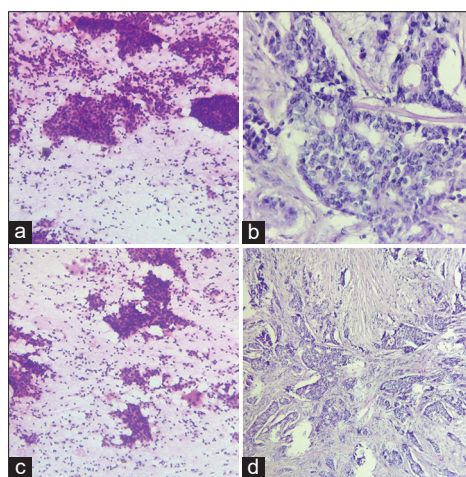
limited resources like us, it is not possible to apply triple test to every single patient presented with breast lump. However, detailed clinical examination, performing the FNAC procedure by experienced pathologist can definitely improve the yield of aspirate and help in improving the cytology diagnosis.

FNAC has limitations in diagnosing certain lesions such as calcification areas, *in situ* carcinomas, and some proliferative tumors where the use of core needle biopsy (CNB) is preferred over FNAC. However, CNB is more invasive, expensive, and is not assessable to many patients due to financial constraints.<sup>10,11</sup>

In patients presenting with deep-seated lumps surrounded by excessive amount of fat, FNAC is difficult to perform

and less reliable and there are chances of missing the diagnosis. Hence, in such cases, USG-guided FNAC by experienced operator is recommended.<sup>12</sup>

The percentage of benign cases in our study is 73.3% which is comparable with other studies.<sup>13,14</sup> The inadequacy rate of the present study is 2.4%, which is in accordance with the recommendation of IAC for inadequate sample that is <5% and comparable with many studies<sup>5,14,15</sup> (Table 5). Our overall findings of the distribution of FNAC samples according to the IAC – Yokohama system of reporting are in concordance with the studies of Panwar et al.,<sup>16</sup> and Agrawal et al.<sup>14</sup> Among the benign diagnosis, the most common diagnosis in our study was fibroadenoma (48.7%) followed by fibrocystic disease (19.5%). Our findings are comparable with the previous studies.<sup>17,18</sup>



**Figure 5:** Discordant case 4 – (a) Cytology smear showing plenty clusters of ductal epithelial cells of breast showing nuclear overlapping at places. Few clusters are loose, reported as proliferating breast lesion with severe atypia (H and E ×100). (b) HPE shows tumor arranged in glandular pattern showing all features of malignancy reported as duct carcinoma (H and E ×400). Discordant case 5: (c) Cytology smears high cellularity showing plenty clusters of benign looking ductal epithelial cells on background plenty bare nuclei and few cyst macrophages, reported as FCD (H and E ×100). (d) HPE shows tumor arranged in glandular pattern invading surrounding stroma, reported as duct carcinoma (H and E ×100)

In our study, atypical category included 10.5% of cases which differ slightly to markedly amongst different studies.<sup>5,13,14,16</sup> In this category, the lesions included were fibrocystic disease with atypia, proliferating breast lesion without atypia, proliferating breast lesion with atypia, and benign phyllodes tumor. This variation among different studies might be due confusion about the various lesions to be included in this category, subjective variation about definition of atypia, and also inclusion of benign phyllodes tumor in this category, as sometimes aspirate is scanty and proportion of stromal elements varies from case to case. Few studies showed that low-grade phyllode tumors are difficult to diagnose on cytology and recommended that all suspect cases should be reviewed and confirmed by an experienced pathologist.<sup>19</sup>

Our findings of suspicious for malignancy<sup>13,16</sup> and positive for malignancy<sup>5,16</sup> are comparable with other studies. Five cases were categorized as suspicious for malignancy, only three cases were received for histopathology and all were confirmed as duct carcinoma. The rate of malignancy in our study was 11.4%. Twenty-four cases were categorized as malignant on cytology, only seven were available for histology and all were diagnosed as carcinoma on histology. Hence, the present study shows 100% cytohistopathological concordance for the diagnosis of malignancy. This is because if a lesion is malignant, then cytology smears showed high cellularity with plenty clusters and sheets of discohesive cells at places showing nuclear overlapping, cells showing all the features of pleomorphism on hemorrhagic background. It shows that FNAC is 100% sensitive for the diagnosis of malignancy and a patient presenting with a malignant breast lump will get the report on the same day and can be started with treatment as early as possible. Hence, FNAC should be strongly recommended for the diagnostic workup of patients presenting with breast lump. In our study, cytohistopathological concordance rate was 88.4% which is comparable with Panwar et al., (89%)<sup>16</sup> and Charusheela and Chandanwale (82.5%).<sup>20</sup>

Table 5: A comparison of the distribution of FNAC samples according to the IAC – Yokohama system of reporting across recent studies					
Categories	Kamatar et al., <sup>13</sup> (%)	Apuruoopa et al., <sup>5</sup> (%)	Panwar et al., <sup>16</sup> (%)	Agrawal et al., <sup>14</sup> (%)	Present study (%)
1	22 (5)	39 (4.3)	3 (1.3)	(4.9)	5 (2.4)
2	332 (71)	522 (58)	186 (82.7)	(65.3)	154 (73.3)
3	7 (1)	160 (17.7)	13 (5.8)	(7.8)	22 (10.5)
4	8 (2)	63 (7.2)	4 (1.8)	(3.3)	5 (2.4)
5	101 (21)	116 (12.8)	19 (8.4)	(18.7)	24 (11.4)
Total	470	900	225	1147	210

Although FNAC is simple, relatively cheap, and outpatient department procedure, it has few drawbacks such as relatively high inadequate rate and suboptimal accuracy in some centers.<sup>21,22</sup>

### Limitations of the study

The sample size is small and the cytohistopathological correlation is available in only 20.47% cases.

## CONCLUSION

The present study showed 81% sensitivity and 100% specificity for the diagnosis of malignancy, 100% PPV, and 90.9% NPV. The newer IAC – Yokohama system of reporting of breast FNAC is simple, has clear diagnostic criteria hence boost up the confidence as well has uniformity of reporting by cytopathologist, and increases the understanding and uniformity in assessment by the attending clinician which help in improving the communication between the pathologist and the treating clinician.

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**Authors Contribution:**

**MPT-** Concept and design of study, prepared first draft of manuscript, and revision of manuscript; **DBN-** Reviewed and guided in improvement of study design, interpreted results; **SST-** Statistical analysis and interpretation, preparation of manuscript; and **SDT-** Reviewed the literature and collection of data.

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