Content available at: https://www.ipinnovative.com/open-access-journals

IP Archives of Cytology and Histopathology Research

Journal homepage: https://www.achr.co.in/

Original Research Article

Reporting breast fine needle aspiration cytology using the international academy of cytology Yokohama system: Experience in a tertiary care centre

Karthik Dhandapani[1,*], Sunitha Shankaralingappa[1], Trupti Patel[1], Sangita Vanik[1], B R Nagarjun[1], Udaya Sundarajan[1]

[1] *Dept. of Oncopathology, The Gujarat Cancer and Research Institute, Ahmedabad, Gujarat, India*

ARTICLE INFO

Article history:
Received 20-09-2023
Accepted 18-10-2023
Available online 30-10-2023

Keywords:
Breast
Cytology
IAC Yokohama system
Breast carcinoma

ABSTRACT

Introduction: In developing countries for all palpable breast lesions, Fine needle aspiration Biopsy (FNAB) is the most suitable test as FNAB is minimally invasive and cost-effective.
Materials and Methods: The present study was undertaken to categorise the Breast Fine Needle Aspiration Biopsy (FNAB) samples according to the IAC Yokohama system of reporting and to assess the Risk of malignancy (ROM) for each category as well as to elucidate other quality indicators of the Breast FNAB.
Results: Among the total 102 cases in which FNAC were performed, 9 were insufficient/ inadequate (8.80%), 11 were benign (10.80%), 5 were atypical (4.95%), 3 were suspicious (2.95%) and the rest 74 FNACs were malignant (72.5%). ROM of insufficient/inadequate, benign, atypical, suspicious and malignant ware 37.5%, 0%, 50%, 100% and 100% respectively. Absolute sensitivity (only category V) was 90.1 and complete sensitivity (including category III to V) was 96.3%. Specificity of IAC Yokohama system is 100% when considering category 5 as positive and is 88.9% when considering category 3 to 5 as positive.
Discussion and Conclusion: The IAC Yokohama Reporting System for breast cytology has high sensitivity, specificity. The ROM in our study done in Indian population ware comparable to the proposed IAC Yokohama system which suggests the IAC Yokohama system has high reproducibility and can be applied in Indian population. Usage of FNAC for the evaluation of breast lumps and categorization based on the Yokohama system helps in ideal management of the patient, reducing the requirement of core needle biopsy.

1. Introduction

Breast lesions range from benign to malignant with intermediate atypical lesions in between. In developing countries, which are medically under-resourced comprises almost 80% of the world's population, where preoperative imaging, core needle biopsy (CNB) and histopathology are not readily available and / or expensive, for all palpable breast lesions, Fine needle aspiration Biopsy (FNAB) is the most suitable test.[1–5] In addition, as FNAB is a minimally invasive, cost-effective and valuable tool for diagnosis and management, it has been readily accepted by patients and clinicians.

A group of experts in cytopathology assisted by oncologists, radiologists and surgeons developed the International Academy of Cytology (IAC) Yokohama System[6–8] based on a review of the literature and the expertise of the IAC breast group to have a standardized reporting system, which will improve the performance, interpretation and reporting of breast FNAB

* *Corresponding author*.
E-mail address: karthik416@gmail.com (K. Dhandapani).

https://doi.org/10.18231/j.achr.2023.039

cytology (FNAC) and clarify communication between cytopathologists and clinicians by linking the reporting system with suggested management options. This system correlates the FNAC smear findings with both clinical and imaging (mammogram/ultrasonogram) findings to arrive at the final diagnosis. Based on the IAC Yokohama system , FNAC from the breast lesions are classified into 5 diagnostic categories: (1) insufficient/ inadequate material, (2) benign, (3) atypical, (4) suspicious of malignancy, and (5) malignant.

The data regarding the quality parameters for IAC Yokoyama system is lacking in Indian setup. The present study was undertaken to standardise the Breast FNAC reporting in our setup, to discuss the approach in diagnosing challenging cases on FNAC and to find out quality parameters and ROM of each category in IAC Yokohama system in Indian population, where FNAC is more often used for initial evaluation of breast lesions

2. Materials and Methods

It was a descriptive, observational study with prospective, consecutive sampling. The study was conducted for a period of 2 years at the Department of Oncopathology in a tertiary cancer centre in western India.

All patients who underwent breast FNACs for the first time in our institute were included in the study. All the required clinical details of the patients were taken from the FNAC request form, electronic case records and patient case files.

FNAC was performed by either under ultrasound guidance or by traditional palpation-based method using 22-25 G needle attached to a 5mL/10ml/20mL syringe. Routine May-Grunwald-Giemsa (MGG) stain was performed on air-dried smears. Papanicolaou (Pap) stain was carried out on wet-fixed smears.

Whenever available, the FNAC smears were correlated with subsequent histopathology slides, either biopsy or surgical specimen and their immunohistochemistry (IHC).

Both Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 20 software were used for statistical analysis. The Risk of Malignancy (ROM) of each category of the IAC Yokohama system were calculated individually. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), False positivity rate, False negativity rate and Accuracy were calculated accordingly for both IAC Yokohama system for breast FNACs and BI-RADS categorization of mammography.

3. Results

A total of 105 consecutive Fine needle aspiration cytology smears (FNAC) from 102 cases were included in the study. Three cases had a repeat FNACs

Median age among the cases was 49 years with an age range of 21 to 76 years. Male: female ratio of 1:101 (A single male patient).

Among the total 102 cases in which FNAC were performed, 9 were insufficient/ inadequate (8.80%), 11 were benign (10.80%), 5 were atypical (4.95%), 3 were suspicious (2.95%) and the rest 74 FNACs were malignant (72.5%). Out of these, 3 cases were lost to follow-up. All the rest of the cases had undergone histopathological examination on which the final diagnosis was made. (Chart 1)

3.1. Insufficient/ Inadequate (Category 1)

Among the nine cases which were in category 1, one case was inadequate (1/9) for diagnosis because of extensive drying causing loss of nuclear details, in spite of the smear being cellular. This case on mammogram was BIRADS 3 and turned out to be fibroadenoma on biopsy. Eight other cases were insufficient (8/9) for diagnosis showing only scattered ductal epithelial cell fragments with haemorrhage not fulfilling the adequacy criteria; 4 among these on mammogram had BIRADS 4 among which 3 turned out to be IBC, NST and one borderline phyllodes tumour on subsequent histopathology examination. Among the remaining 4 cases with BIRADS either 2 or 3, two cases turned out to be Fibroadenoma, one papilloma and one case was lost to follow-up

3.2. Benign (Category 2)

11 Cases were given as benign from the FNAC smears according to IAC Yokohama system

Two cases, on smear had features consistent with Fibroadenoma having stromal fragments along with sheets of ductal and myoepithelial cells and background bare bipolar nuclei (Figure 1). Both these cases turned out to be fibroadenoma on biopsy and further excision.

In four cases, a possibility of mastitis is favoured in view of background inflammatory cells along with histiocytes (Figure 2); all of these cases turned out to be chronic mastitis in final histopathology examination. An interesting finding in all these four cases was that all of the four cases had BIRADS 4 on mammogram.

Another case on FNAC showed many mature squamous cells, sheets of anucleate squames along with mixed inflammatory cells in the background with histiocytic giant cells. This was categorized as benign with possibilities of retroareolar abscess and Infected epidermoid cyst. Excision was done for this case which was consistent with infected epidermoid cyst.

A single case of Gynecomastia was also seen in a 32-year-old male patient smear of which showed benign ductal along with myoepithelial cell clusters with bare bipolar cells in the background. This was proven in subsequent biopsy.

Two cases were given as benign proliferative breast disease; One had sheets of apocrine cells in clusters and singly scattered along with few ductal cell clusters with background foamy macrophages in a proteinaceous background (Figure 3). The other case had large benign ductal cells clusters with myoepithelial cells along with background bare nuclei. Both of these cases did not show significant pleomorphism. On histopathological examination, the first case turned out to be benign fibrocystic disease and the other case became usual ductal hyperplasia.

There was a single case in which the smear showed papillaroid and papillary clusters of ductal cells seen with few myoepithelial cells along with background bare bipolar nuclei (Figure 4). Single scattered cells or pleomorphism was not seen. Considering all these findings on FNAC, it was signed out as benign proliferative breast disease with a possibility of papilloma. This turned out to be Intraductal papilloma.

3.3. Atypical (Category 3)

5 Cases were categorised as atypical on FNAC examination.

Two among these cases with BIRADS of 4 and 5, had singly scattered large cells with moderate pleomorphism in an otherwise scanty cellular smear (Figure 5). Both of these cases turned out to be malignant, breast carcinomas on subsequent histopathology examination.

One of the cases with BIRADS 2 on mammogram had predominantly large monolayered benign ductal with myoepithelial cell clusters; In view of a single small cluster of moderately pleomorphic ductal cells with overlapping, crowding and loss of myoepithelial cells, the FNAC was categorised as atypical. However, this case was lost to follow-up.

One other case with BIRADS 3 on mammogram, showed moderately cellular smear with sheets of many apocrine cells with moderate pleomorphism along with singly scattered atypical apocrine cells. However, in view of inflammation, histiocytes and histiocytic giant cells in the background, this case was categorised as atypical even though cells were showing moderate pleomorphism. This case on subsequent biopsy turned out to be Benign fibrocystic disease related changes.

FNAC smears of one other case with no mammogram evaluation showed background dense inflammation along with many discrete and loosely cohesive ductal cells without myoepithelial cells. As drying artifact was present, pleomorphism and nuclear features were not very well appreciated. This case was also classified as atypical. However, the subsequent biopsy was benign and showed features consistent with mastitis.

*3.4. Suspicious (Category **4**)*

There were three cases which were categorised as suspicious for malignancy under the IAC Yokohama system in our study.

Among them one case had loosely cohesive clusters of ductal cells arranged focally in cribriform pattern with mild pleomorphism along with few singly scattered similar cells with mild pleomorphism (Figure 6). No necrosis was seen. This was given as suspicious for malignancy with possibilities of low-grade DCIS and low-grade breast carcinoma. Subsequent histopathology examination revealed low grade DCIS without invasive component.

One other case which was scantly cellular with few ductal cell clusters and few single cells showing marked pleomorphism in a background showing multiple areas of necrosis. This was given as suspicious of malignancy with possibilities of High-grade DCIS vs Breast carcinoma. This turned out to be IBC, NST. The last case also was paucicellular with predominant haemorrhage with one focus showing many singly lying ductal cells with moderate pleomorphism along with drying artifact. This also was given as suspicious for malignancy with possibility of IBC, NST and Lobular carcinoma. This too turned out to be IBC, NST. All these three cases had a BIRADS of 4a in mammographic examination.

3.5. Malignant (Category V)

Totally 74 cases were given as malignant on FNAC smears.

Among these, 61 cases on FNA smears were moderate to highly cellular, showing many loose clusters of malignant cells with moderate pleomorphism, overlapping, crowding along with many singly scattered similar cells with absence of myoepithelial cells/bare nuclei (Figure 7). Focal patchy areas of necrosis and focal mitosis were noted. Considering all these features, a diagnosis of malignant; breast carcinoma, favouring IBC, NST is given. All these cases turned out to be IBC, NST.

Two of the malignant cases in their smears showed high cellularity, many singly scattered plasmacytoid cells with few intracytoplasmic mucin vacuoles and mild to moderate pleomorphism. In both these cases, a possibility of lobular carcinoma is favoured. 3 other cases had moderate cellularity in the smears showing clusters as well as equal proportion of plasmacytoid single cells with mild to moderate pleomorphism. All these three cases were given as malignant with differential diagnosis of low-grade breast carcinoma and lobular carcinoma (Figure 8). All these five cases turned out to be lobular carcinomas

One case with prominent extracellular mucin in the background along with many cohesive clusters and discrete malignant cells with mild pleomorphism was given as malignant, breast carcinoma, with a possibility of mucinous carcinoma (Figure 8). This finally turned out to be mixed

mucinous carcinoma and IBC-NST.

One each case of cribriform carcinoma, mixed carcinoma (cribriform with IBC, NST) (Figure 8), carcinoma with medullary features and carcinoma with apocrine features each showing typical features of prominent cribriform pattern, prominent lymphocytic infiltrate and abundant cytoplasm with prominent nucleoli respectively in their FNAC smears were also seen in our study. In each of these cases, a diagnosis favouring the possibility of the special type carcinoma was given. One case each of primary neuroendocrine carcinoma of breast, and malignant phyllodes tumour were also seen in our study.

3.6. Risk of malignancy (ROM) of each of these categories

Excluding the three cases which were lost to follow-up, ROM of insufficient/inadequate, benign, atypical, suspicious and malignant are 37.5%, 0%, 50%, 100% and 100% respectively. (Table 1)

3.7. Quality indicators for the IAC Yokohama System for Reporting Breast FNAC

Excluding 3 cases which were lost to follow-up, there were 99 cases for which IAC Yokohama system was used to classify breast FNACs and compared with final histopathology diagnosis. All quality indicators were calculated. (Tables 2 and 3)

Absolute sensitivity (only category 1) was 90.1 and complete sensitivity (including category 3 to 5) was 96.3%. None of the malignant cases were falsely labelled as benign (FNR-0%); However, 3 of the malignant cases were insufficient / inadequate for diagnosis (category 1) (3/81) on FNAC. Specificity of IAC Yokohama system is 100% when considering category 5 as positive and 88.9% when considering category 3 to 5 as positive indicating that IAC Yokohama system in our study has a high specificity with 0% FPR when only category 5 is considered as positive. None of the benign cases fell in suspicious (category 4) or malignant category (category 5). False positivity rate in both Category 4 and category 5 is 0% (FPR-0%). Most of these benign cases were insufficient/inadequate for diagnosis (category 1) (5/18) while two cases were atypical (Category 3) (2/18). Overall accuracy of IAC Yokohama system in our study was 90%.

3.8. Summary of the results

Among the total 102 cases in which FNAC were performed, 9 were insufficient/ inadequate (8.80%), 11 were benign (10.80%), 5 were atypical (4.95%), 3 were suspicious (2.95%) and the rest 74 FNACs were malignant (72.5%). ROM of insufficient/inadequate, benign, atypical, suspicious and malignant are 37.5%, 0%, 50%, 100% and 100% respectively. Absolute sensitivity (only category V) was 90.1 and complete sensitivity (including category III to V) was 96.3%. Specificity of IAC Yokohama system is 100% when considering category 5 as positive and is 88.9% when considering category 3 to 5 as positive. Both False positivity rate (category 5- positive) and False negativity rate (category 2- negative) were 0%. Both Positive predictive value (category 5- positive) and Negative predictive value (category 2- negative) were 100%

4. Discussion

The IAC Yokohama system was introduced as a standardized reporting system for breast FNACs.[6–9] It categorizes breast cytology smears into category 1-insufficient material; category 2-benign; category 3-atypical probably benign; category 4-suspicious for malignancy; and category 5-malignant based on FNAB smear findings, correlating with clinical and imaging findings

4.1. Insufficient/ Inadequate (Category 1)

The IAC Yokohama system has recommended to categorise an FNAC as insufficient/ inadequate when it does not meet the adequacy criteria of 6-7 epithelial fragments, each with 10-20 well preserved and well spread epithelial cells. The above-mentioned criteria for adequacy is not applied if the lesion is a cyst, abscess, spindle cell lesion, scar tissue or a hyalinised fibroadenoma when correlating with radiology. In these scenarios, if the FNAC findings are consistent with the radiology, even when the smear is not adequate as per the IAC Yokohama system, it can be considered adequate. Another exception is if atypical features like dispersal of single epithelial cells, significant nuclear atypia or necrosis are present in the smear, even without the required number of epithelial fragments, these FNACs should be categorised as atypical (category 3) rather than insufficient/inadequate (category 1).[7,8] On histopathology follow-up, most common lesions in our study to show category 1 diagnosis were IBC- NST and fibroadenoma. Both inherent quality of the lesion and FNAC technique affect the nature of the material obtained and the final FNAC categorization. FNACs done by a pathologist with Rapid on-site evaluation (ROSE) reduces the rate of inadequate smears

4.2. Benign (Category 2)

Our cases had a spectrum of inflammatory lesions, proliferative lesions and fibroadenomas.

4.2.1. Reactive atypia in inflammatory lesions

We had four cases which were on FNAC, consistent with chronic mastitis. In the background of inflammation with histiocytes and histiocytic giant cells, these lesions showed sheets of atypical ductal and apocrine cells. However, points which help to differentiate these reactive

atypical cells from malignant lesions are a background of prominent inflammation, clusters of monolayered sheets of epithelial cells with low N:C ratio, uniformity between the cells, nuclei and their chromatin and a more prominent nucleolus.[7,8] Even on radiology, these lesions mimic carcinoma, (all four cases were BIRADS category 4) which underscores the importance of differentiating these lesions from carcinoma on FNAC to prevent mismanagement.

4.2.2. Reactive apocrine cells

One other case in addition to large and small benign epithelial fragments with the typical bimodal population, had sheets of apocrine cells, scattered histiocytes and inflammatory cells in a proteinaceous background. Apocrine cell clusters as seen in our case usually do not have myoepithelial cells and have a little amount of scattered single cells. However overall uniform central nuclei with prominent nucleoli and mild pleomorphism between cells helps the pathologist to differentiate it from carcinoma.[7,8] This case was reported on FNAC as benign proliferative breast disease. Subsequent biopsy was consistent with benign fibrocystic breast disease.

4.2.3. Papillary and papillaroid clusters

Multiple papillaroid and few papillary clusters of epithelial were seen in one case along with benign epithelial fragments showing bimodal population, bare bipolar background nuclei. Presence of bimodal population with myoepithelial cells in the clusters, bare-bipolar nuclei in the background along with absence of single scattered cells, pleomorphism, necrosis helped rule out a carcinoma/ DCIS in this case.[7] However, in view of papillary architecture, a possibility of Intra ductal papilloma was favoured. Final histopathology turned out to be Intraductal papilloma.

4.3. Atypical (Category 3)

Among the 5 atypical cases in our study, two cases had singly scattered large cells with moderate pleomorphism in an otherwise scanty cellular smear. Even though both the cases did not meet the adequacy criteria, IAC Yokohama system recommends categorising these lesions even with scant cellularity as atypical (category 3) as they showed atypical features like prominent single cells and cells with nuclear atypia.[7,8] Both cases were BIRADS 4/5 and they turned out to be malignant, IBC-NST on subsequent histopathology examination.

There were two other cases, one of which showed many apocrine cells in sheets with moderate pleomorphism while other showed few foci of prominent scattered single cells and loose clustering of epithelial cells moderate pleomorphism. Both smears raised the suspicion of malignancy. However, background inflammation was seen in both the smears. Even then, considering moderate pleomorphism of apocrine cells in the first case and prominent dispersed single cells with loose clustering in the second case, both these lesions were categorised as Atypical. However, final histopathology examination revealed the first case to be benign fibrocystic disease related changes while the second case turned out to be chronic mastitis. This highlights that benign inflammatory lesions can show atypical features raising the suspicion of malignancy on FNAC smears.

IAC Yokohama system recommends caution when background inflammation and apocrine cells are present in the smear as inflammation can cause reactive atypia in the epithelial cells and also benign apocrine cells in sheets don't have myoepithelial cells and show moderate dispersal of single cells which mimic carcinoma. However, as mentioned by IAC Yokohama system, low overall cellularity, low N:C ratio, with absence of atypical features (marked anisonucleosis, increased nuclear size, coarse chromatin with perinucleolar clearing, large spiculated irregular nucleoli and 3-dimensional (3-D) or cribriform tissue fragments) helps differentiate these changes seen in benign breast disease from apocrine carcinoma.[7,8]

4.4. Suspicious (Category 4)

4.4.1. DCIS vs IBC

One case on FNAC smears showed moderate cellularity with clusters and singly scattered malignant cells with mild pleomorphism. Clusters showed focal cribriform architecture with scant myoepithelial cells. No bare bipolar nuclei were seen. No necrosis/mitosis noted. These features can be seen overlappingly in both low-grade DCIS and in low-grade breast carcinoma. However, in view of cells showing only mild pleomorphism, correlating with BIRADS, given as suspicious for malignancy with possibilities of low-grade DCIS and low-grade breast carcinoma as recommended by IAC Yokohama system[7] to prevent false positive diagnosis. This on consecutive histopathology examination was proven to be Low grade DCIS without invasive component.

Next case which was given as suspicious for malignancy showed scant- moderate cellularity on the FNAC smear with small clusters and singly scattered malignant cells showing moderate to marked pleomorphism with mitosis and multiple foci of granular necrosis. Based on IAC Yokohama system[7,8], scanty cellular smear of malignant cells with background necrosis and BIRADS of 4A correlates with High grade DCIS. However, Invasive Breast carcinoma cannot be ruled out. IAC Yokohama system recommends to classify these lesions as suspicious for malignancy to avoid false positivity. Bases on the above findings, possibilities of high-grade DCIS and high-grade breast carcinoma were suggested in this case. On subsequent histopathology, this case turned out to be IBC, NST.

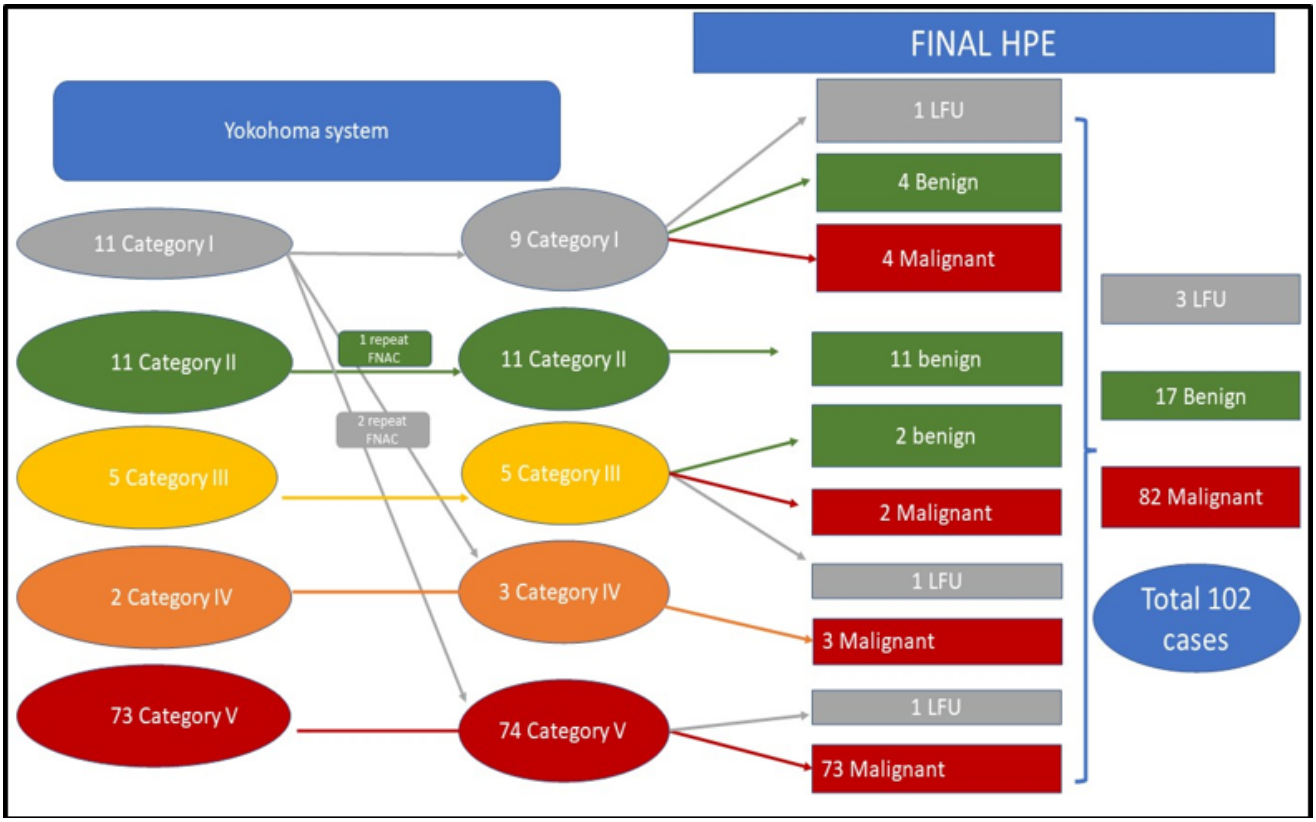

Chart 1: Total distribution of cases and their final diagnosis

Table 1: Risk of malignancy (ROM) of each category inthe IAC yokohama system category

	Final category		Total	ROM
	Benign	Malignant		
1- Insufficient/ Inadequate	5	3	8	37.5% (3/8)
2- Benign	11	0	11	0% (0/11)
3- Atypical	2	2	4	50% (2/4)
4- Suspicious	0	3	3	100% (3/3)
5- Malignant	0	73	73	100% (73/73)

Table 2: Distribution of Cases in the IACyokohama system correlating with final histopathology

			Final category		Total
			Benign	Malignant	
FNAC category	I- Insufficient/ Inadequate	Percentage (No. of cases)	27.8% (5)	3.7% (3)	8.1% (8)
	II- Benign	Percentage (No. of cases)	61.1% (11)	0.0% (0)	11% (11.1)
	III- Atypical	Percentage (No. of cases)	11.11% (2)	2.5% (2)	4.% (4)
	IV- Suspicious	Percentage (No. of cases)	0.0% (0)	3.7% (3)	3% (3)
	V- Malignant	Percentage (No. of cases)	0.0% (0)	90.1% (73)	73.7% (73)
Total		Percentage (No. of cases)	100.0% (18)	100.0% (81)	100.0% (99)

Table 3: Quality indicators for the IAC yokohama system for reporting breast FNAC

1.	Absolute sensitivity (category 5, malignant) – 90.1%
2.	Complete sensitivity (categories 3, 4, and 5, atypical, suspicious, and malignant)- 96.3%
3.	Specificity (considering category 5 as positive) – 100%
4.	Specificity (considering category 3 to 5 as positive) - 88.9%
5.	Accuracy- 90%
6.	PPV for category 3, atypical -50%
7.	PPV for category 4, suspicious -100%
8.	PPV for category 5, malignant -100%
9.	NPV for category 2, benign -100%
10.	False-negative rate (category 2, benign)- 0%(0/11)
11.	False-positive rate (category 5, malignant)- 0%(0/74%)

Table 4: Risk of malignancy (ROM) in each category comparing with other studies

FNAC category	Insufficient (%)	Benign (%)	Atypical (%)	Suspicious for malignancy (%)	Malignant (%)
Hoda et al [10]	30.3	4.7	51.5	85.4	98.7
Kamatar et al [11]	0	4	66	83	99
Montezuma et al [12]	4.8	1.4	13	97	100
Nargund et al [13]	7.6	16.26	65.38	83.33	99.18
Wong et al [14]	2.6	1.7	15.7	84.6	99.5
De Rosa et al [15]	49.6	4.9	20.7	78.7	98.8
Dixit et al [16]	33.3%,	0.5%,	13.3%,	83.3%	100
Oosthuizen et al [17]	11	3	28	56	100
Ahuja et al [18]	5	1.5	17.4	81.8	100
Present study	37.5	0	50	100%	100

Table 5: Quality indicators in each category comparing with other studies

Quality indicators	Hoda et al [10]	Montezuma et al [12]	Wong et al [14]	De Rosa et al [15]	Ahuja et al [18]	Dixit et al [16]	Present study
Sensitivity (Category 3-5 - positive)	96.3%	98.3%	98.9%	98.9%	97.2%	95%,	96.3%
Specificity (Category 3-5 - positive)	98.8%	54.8%	62.1%	46.3%	86.0%	99.5%	88.9%
PPV (only category 5 - positive)	98.7%	100%	100%	98.8%	100%	98.27%	100%
NPV (only category 2- negative)	95.3%	98.6%	98.3%	95.1%	98.5%	98.6%	100%
Accuracy (Category 3-5 - positive)	-	68.2%	80.2%	82.7%	89.6%	98.5%	90%

4.5. Malignant (Category 5)

4.5.1. IBC- NST

Among the malignant cases, 61 cases showed unequivocal features of malignant, breast carcinoma showing moderate to highly cellular smears with many small loose clusters and singly scattered malignant cells showing moderate to marked pleomorphism with overlapping. Moderate cytoplasm, coarse to opened chromatin and conspicuous to prominent nucleoli were seen. As recommended by IAC Yokohama system [7], correlating with this constellation of FNAB smear findings and a concordant clinical and imaging finding, a diagnosis of malignant, breast carcinoma was given. All of these cases turned out to be Invasive breast carcinoma, NST.

4.5.2. Low grade IBC vs low grade DCIS

FNAB smear of the two other cases showed many small loose clusters of malignant cells with cribriforming, single scattered cells with moderate pleomorphism and loss of myoepithelial cells and background bare bipolar nuclei. In both these case, possibility of low-grade IBC- NST was suggested. On final histopathology, one case turned out to be mixed carcinoma (IBC-NST + cribriform carcinoma) and the other, pure invasive cribriform carcinoma.

Even though low-grade DCIS can show cribriform pattern with many single cells showing mild pleomorphism, according to IAC Yokohama system, important

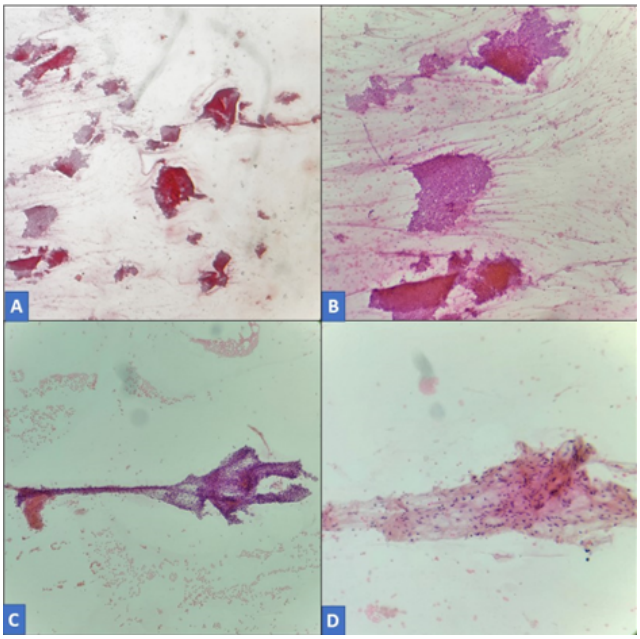

Fig. 1: A case of fibroadenoma: **A,B:** Large monolayered clusters with bimodal population (10x, Pap); **C:** Staghorn clusters (20x, Pap); **D:** Stromal fragments (20x Pap)

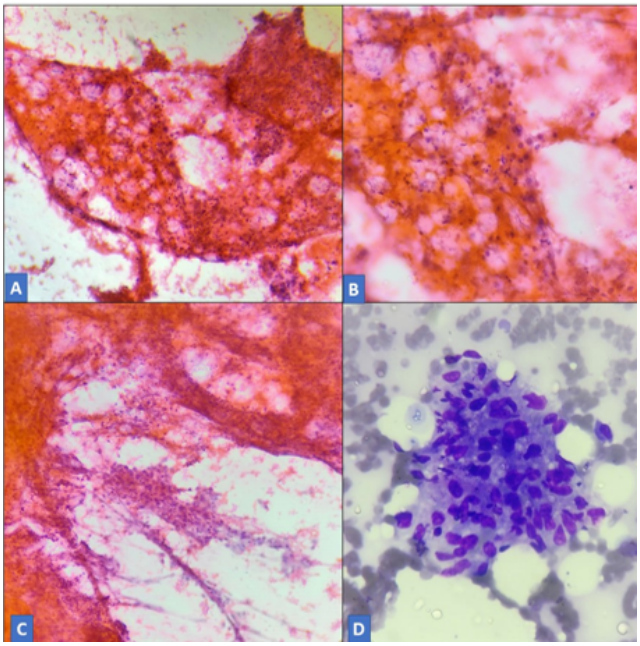

Fig. 2: A case of Chronic mastitis: **A,B:** Stromal fragments showing dense inflammation (20x, Pap); **C:** Dense inflammation along with monolayered ductal cells (20x, Pap); **D:** Ill formed Granuloma (40x, MGG)

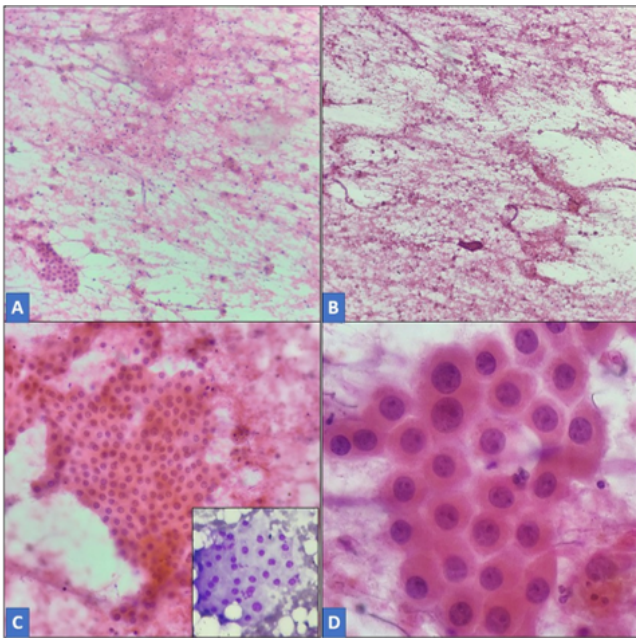

Fig. 3: A case of Benign fibrocystic disease showing **A,B:** Inflammatory background with monolayered Apocrine cells (10x, Pap); **C,D:** Monolayered bland looking Apocrine cells (C: 20x, Pap, **D:** 40x, Pap, Inset: 40x, MGG)

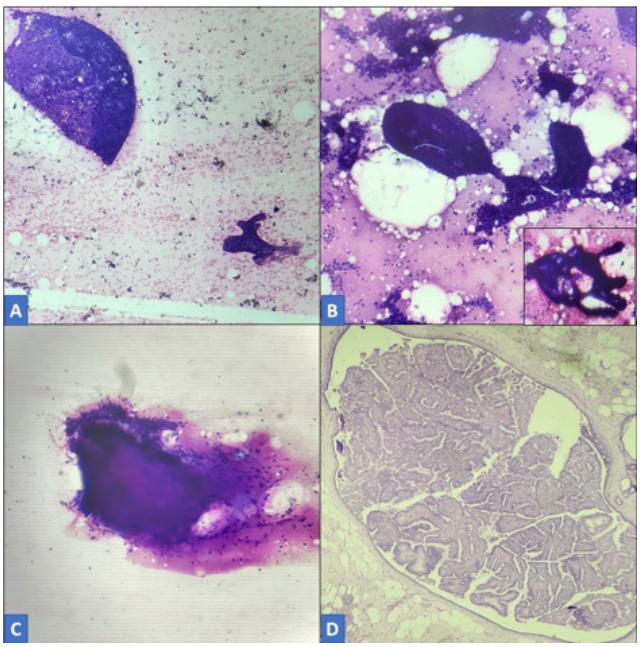

Fig. 4: A case of Intra ductal papilloma with **A:** Large monolayered sheet of cells with bimodal population along with smaller papillaroid clusters (10x, Pap) **B:** Papillaroid clusters with many bare nuclei in background (20x, Pap); **C:** Ductal cell clusters attached to fibroelastotic stroma with capillary streak (20x, Pap); **D:** Specimen showing Intraductal papilloma (10x, Hand E)

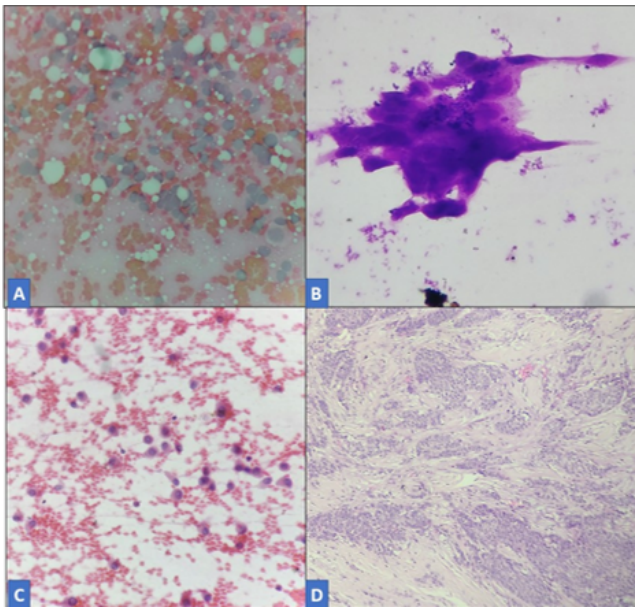

Fig. 5: A,B,C: Two cases with singly scattered and occasional clusters of atypical cells showing moderate pleomorphism given as 'Category 3- Atypical' (A, C 20x, Pap; **B:** 40x, MGG) **D:** Subsequent Histopathology examination showing IBC-NST (10x, H and E)

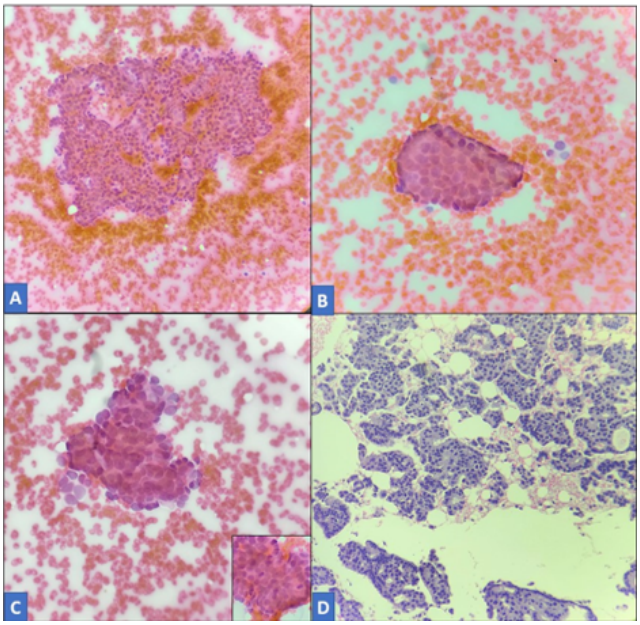

Fig. 6: A case given as 'Category 4- Suspicious for malignancy'; **A:** Large sheet of ductal cells with mild pleomorphism and sparse myoepithelial cells (20x, Pap); **B,C:** Ductal cell clusters with overlapping, mild pleomorphism and absent myoepithelial cells (Inset- cribriform pattern in clusters) (40x, Pap); **D:** Subsequent biopsy showing Low grade DCIS (20x, H and E)

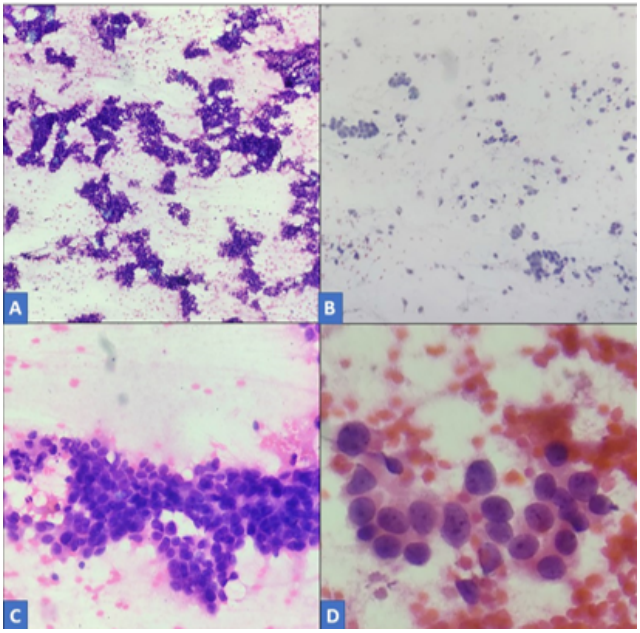

Fig. 7: Cases of IBC- NST given as 'Category 5- Malignant'; **A,B:** Highly cellular with nests, sheets and singly scattered malignant cells (**A**, **B:** 10x, Pap); **C,D:** cells show moderate pleomorphism with crowded overlapped nuclei (**C:** 20x, Pap; **D:** 40x, Pap)

differentiating point to distinguish low grade DCIS from low grade invasive carcinoma is while the former has mostly had large epithelial fragments, the later will have small loose overlapping epithelial clusters. Also, presence of a mass lesion strongly supports the diagnosis of invasive carcinoma rather than DCIS as only 2% of mass lesions will be pure DCIS.[7,8]

4.6. Quality indicators and ROM of various categories of IAC Yokohama system

In the largest meta-analysis till now on breast lesions done by Hoda et al[19] which included 33,341 breast FNABs from 27 studies, ROM for insufficient material, benign, atypical, suspicious, and malignant were 30.3, 4.7, 51.5, 85.4, and 98.7%, respectively. The complete sensitivity (including category III to V) and specificity were 96.3 and 98.8%, correspondingly. The PPV and NPV were 98.7 and 95.3%, correspondingly. The false negative and false-positive rates were 3.7 and 1.0%, respectively showing high sensitivity and specificity for breast FNACs using IAC Yokohama system with an increasing ROM from category II to category V (benign to malignant).[14,19]

This was similar to our study where ROM of insufficient/inadequate, benign, atypical, suspicious and malignant were 37.5%, 0%, 50%, 100% and 100% respectively. Absolute sensitivity (only category V) was 90.1% while complete sensitivity (including category III to V) was 96.3%. Specificity of IAC Yokohama system is

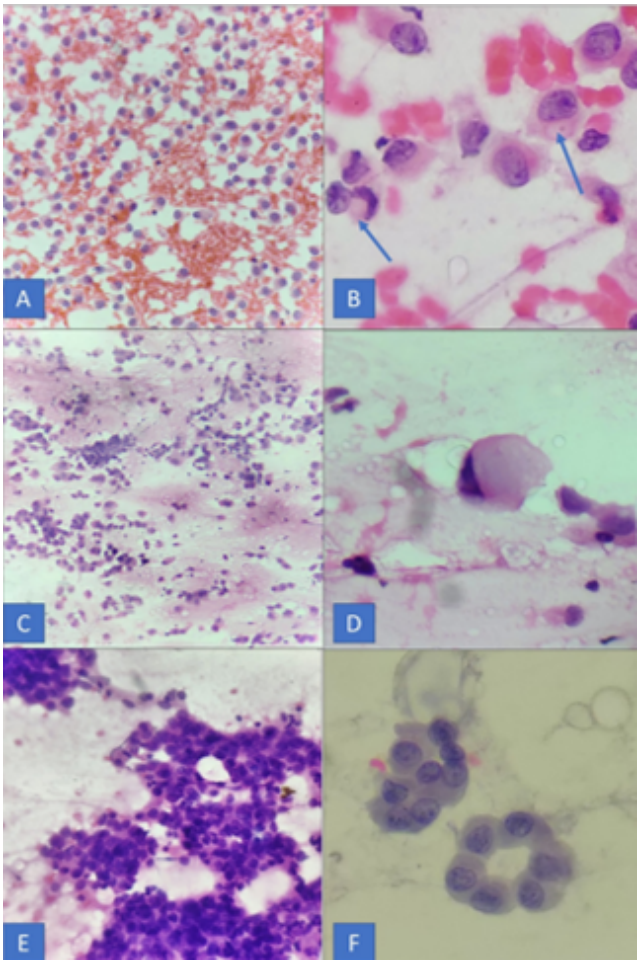

Fig. 8: A,B: Lobular Carcinoma; **A:** Singly scattered malignant cells with eccentric nuclei and mild pleomorphism (20x, Pap); **B:** Cells show intracytoplasmic mucin vacuoles (Arrow) (40x, Pap); **C,D:** Mixed Mucinous carcinoma with IBC-NST; **C:** Nests and singly scattered malignant cells with moderate cytoplasm and mild pleomorphism in a mucinous background (10x, Pap); **D:** Focal intra cytoplasmic mucin seen (40x, Pap); **E,F:** Invasive Cribriform Carcinoma; **E:** Cribriform pattern seen (20x, Pap); **F:** Tubular Pattern (40x, pap).

100% when considering category 5 as positive and 88.9% when considering category 3 to 5 as positive indicating that IAC Yokohama system in our study has high specificity. Overall accuracy of IAC Yokohama system for breast lesions in our study was 90%

Proportion of cases in each category in the multiple studies done[10,13] are insufficient - 3.6-40%, benign- 24 - 74%, atypical- 0.6% - 13.7%, suspicious for malignancy- 0.7 - 4.7% and malignant- 1.6 -59%. Our study had a lower proportion in benign category (10.8%) and a higher proportion in malignant category (72.5%) as the study was conducted in a referral cancer centre. Ideal inadequate rate recommended by The IAC Yokohama system[7,8] is less than 5%. An inadequate rate of 5–20% requires a review in FNAB practice. An inadequate rate > 20% suggests a need to alter technique. ROSE reduces inadequacy rate considerably as proven by study done by wong et al (17.1% without ROSE to 4.0% with ROSE) and increased the number in the "malignant" category (17.9 to 39.0%).[10]

Risk of malignancy (ROM) in each category in various studies are insufficient – 5 - 49.5%, benign- 0.5- 16.26%, atypical- 13 – 66 %, suspicious for malignancy- 56-97% and malignant- 98.7 – 100%. These were similar to our study where ROM of insufficient/inadequate, benign, atypical, suspicious and malignant were 37.5%, 0%, 50%, 100% and 100% respectively(Table 4).[13,19]

Sensitivity, specificity, PPV, NPV and accuracy of the IAC Yokohama system in the multiple studies published till date are 96.3-98.9%, 46.3- 99.5%, 98.7 -100%, 95.1 -98.6% and 68.2 to 98.5% respectively.[10,12–14,18,19] Comparing this in our study Sensitivity, specificity, PPV, NPV and accuracy were 96.3%, 88.9%, 100%, 100% and 90% respectively (Table 5). Recent meta-analysis and review done have also shown that the implementation of the system appears to be successful with high level of diagnostic accuracy.[16,20] They found out that when only "Malignant" interpretations were regarded as cytologically positive, the pooled FPR was lower (0.75%; 95% CI, .39%-1.42%) but it was at the expense of sensitivity (76.61%; 95% CI, 70.05%-82.10%).[16]

Overall, the IAC Yokohama system for breast FNAB has a high sensitivity, relatively high specificity, accuracy and high PPV and NPV.

5. Conclusion

Our study, one of the largest in Indian population done till date to validate The IAC Yokohama Reporting System for breast cytology, has found that IAC Yokohama system has high sensitivity, specificity with negligible false positive and false negative rate and high positive predictive value and negative predictive value. We have also discussed in detail the diagnostic difficulties and approach to Breast FNACs. Challenging cases which require detailed workup include apocrine lesions, inflammatory lesions, and IBC vs DCIS. The ROM and other quality indicators of various categories in our study done are comparable to the proposed IAC Yokohama system which suggests the IAC Yokohama system has high reproducibility and can be applied in Indian population.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Field A, Zarka MA. ractical Cytopathology: A Diagnostic Approach E-Book: A Volume in the Pattern Recognition Series. 1st edn. Elsevier; 2016.
2. Cibas ES, Ducatman BS. Diagnostic Principles and Clinical Correlates. 4th edn_. Saunders; 2014.
3. Ciatto S, Cariaggi P, Bulgaresi P, Confortini M, Bonardi R. Fine needle aspiration cytology of the breast: review of 9533 consecutive cases. *Breast*. 1993;2(2):87–90. doi:10.1016/0960-9776(93)90163-A.
4. Chaiwun B, Settakorn J, Ya-In C, Wisedmongkol W, Rangdaeng S, Thorner P, et al. Effectiveness of fine-needle aspiration cytology of breast: analysis of 2,375 cases from northern Thailand. *Diagn Cytopathol*. 2002;26(3):201–5.
5. Ukah CO, Oluwasola OA. The clinical effectiveness of fine needle aspiration biopsy in patients with palpable breast lesions seen at the University College Hospital, Ibadan, Nigeria: A 10-year retrospective study. *J Cytol*. 2011;28(3):111–3.
6. Field AS, Schmitt F, Vielh P. IAC Standardized Reporting of Breast Fine-Needle Aspiration Biopsy Cytology. *Acta Cytol*. 2017;61(1):3–6.
7. Field AS, Raymond WA, Rickard M, Arnold L, Brachtel EF, Chaiwun B, et al. The International Academy of Cytology Yokohama System for Reporting Breast Fine-Needle Aspiration Biopsy Cytopathology. *Acta Cytol*. 2019;63(4):257–73.
8. Field AS, Raymond WA, Rickard M, Arnold L, Brachtel E, Chaiwun B, et al. The International Academy of Cytology Yokohama System for Reporting Breast Fine-Needle Aspiration Biopsy Cytopathology. *Acta Cytol*. 2020;63(4):257–63.
9. Field A, Mak A. A prospective study of the diagnostic accuracy of cytological criteria in the FNAB diagnosis of breast papillomas. *Diagn Cytopathol*. 2007;35(8):465–75.
10. Wong S, Rickard M, Earls P, Arnold L, Bako B, Field AS, et al. The International Academy of Cytology Yokohama System for Reporting Breast Fine Needle Aspiration Biopsy Cytopathology: A Single Institutional Retrospective Study of the Application of the System Categories and the Impact of Rapid Onsite Evaluation. *Acta Cytol*. 2019;63(4):280–91.
11. Nargund A, Mohan R, Pai M, Sadasivan B, Dharmalingam P, Premalata C, et al. Demystifying Breast FNAC's Based on the International Academy of Cytology, Yokohama Breast Cytopathology System- A Retrospective Study. *J Clin Diagn Res*. 2021;15(3):EC01–5.
12. Ahuja S, Malviya A. Categorization of Breast Fine Needle Aspirates Using the International Academy of Cytology Yokohama System Along with Assessment of Risk of Malignancy and Diagnostic Accuracy in a Tertiary Care Centre. *J Cytol*. 2021;38(3):158–63.
13. Dixit N, Trivedi S, Bansal VK. A retrospective analysis of 512 cases of breast fine needle aspiration cytology utilizing the recently proposed IAC Yokohama system for reporting breast cytopathology. *Diagn Cytopathol*. 2021;49(9):1022–31.
14. Montezuma D, Malheiros D, Schmitt FC. Breast Fine Needle Aspiration Biopsy Cytology Using the Newly Proposed IAC Yokohama System for Reporting Breast Cytopathology: The Experience of a Single Institution. *Acta Cytol*. 2019;63(4):274–9.
15. Oosthuizen M, Razack R, Edge J, Schubert PT. Classification of Male Breast Lesions According to the IAC Yokohama System for Reporting Breast Cytopathology. *Acta Cytol*. 2021;65(2):132–9.
16. Nikas IP, Vey JA, Proctor T, Alrawashdeh MM, Ishak A, Ko HM, et al. The Use of the International Academy of Cytology Yokohama System for Reporting Breast Fine-Needle Aspiration Biopsy: A Systematic Review and Meta-Analysis. *Am J Clin Pathol*. 2023;159(2):138–45.
17. Kamatar P, Athanikar V, Dinesh U. Breast Fine needle Aspiration Biopsy Cytology Reporting using International Academy of Cytology Yokohama System-Two Year Retrospective Study in Tertiary Care Centre in Southern India. *National J Lab Med*. 2019;8(4):PO01–3.
18. Rosa FD, Migliatico I, Vigliar E, Salatiello M, Pisapia P, Iaccarino A, et al. The continuing role of breast fine-needle aspiration biopsy after the introduction of the IAC Yokohama System For Reporting Breast Fine Needle Aspiration Biopsy Cytopathology. *Diagn Cytopathol*. 2020;48(12):1244–53.
19. Hoda RS, Brachtel EF. International Academy of Cytology Yokohama System for Reporting Breast Fine-Needle Aspiration Biopsy Cytopathology: A Review of Predictive Values and Risks of Malignancy. *Acta Cytol*. 2019;63(4):292–301.
20. Yu W, Gan Q, Gong Y. The Yokohama System for Reporting Breast Cytopathology. *J Clin Trans Pathol*. 2023;3(2):99–105.

Author biography

Karthik Dhandapani, Assistant Professor

Sunitha Shankaralingappa, Assistant Professor

Trupti Patel, Associate Professor

Sangita Vanik, Assistant Professor

B R Nagarjun, Senior Resident

Udaya Sundarajan, Senior Resident

Cite this article: Dhandapani K, Shankaralingappa S, Patel T, Vanik S, Nagarjun BR, Sundarajan U. Reporting breast fine needle aspiration cytology using the international academy of cytology Yokohama system: Experience in a tertiary care centre. *IP Arch Cytol Histopathology Res* 2023;8(3):169-179.