

ORIGINAL ARTICLE

Utility of the IAC Yokohama System for Reporting Breast Fine Needle Aspiration Cytology: A Cytohistological Correlation Study

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ABSTRACT

Background: Breast lumps require prompt and reliable assessment because malignant lesions may be clinically indistinguishable from benign conditions at presentation. Fine-needle aspiration cytology (FNAC) remains a practical first-line investigation in many hospitals because it is quick, inexpensive and minimally invasive. The International Academy of Cytology (IAC) Yokohama reporting system groups breast FNAC findings into five diagnostic categories linked to an estimated risk of malignancy (ROM). Rapid on-site evaluation (ROSE) can additionally confirm whether aspirated material is adequate before the patient leaves the procedure area.

Objective: To determine the diagnostic performance of the IAC Yokohama system for breast FNAC at three cytological positivity thresholds. Additional objectives were to describe the distribution of cases within the five Yokohama categories, estimate the ROM for each category and examine the usefulness of ROSE in prospective samples.

Methods: This cross-sectional analytical study was undertaken in the Department of Pathology, JSS Medical College, Mysore, over 42 months. A total of 180 patients with palpable breast lumps and available cytological and histopathological diagnoses were studied. The dataset included 86 retrospective cases and 94 prospective cases. In the prospective arm, FNAC was performed using aseptic precautions and smear adequacy was checked on site with toluidine blue staining. Each cytology specimen was assigned to category C1, C2, C3, C4 or C5 according to the IAC Yokohama system. Histopathology was treated as the reference standard. Diagnostic indices were calculated for three positive-test definitions: C5 alone; C4 plus C5; and C3 plus C4 plus C5.

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Results: Of the 180 aspirates, 8 (4.4%) were categorized as C1, 106 (58.9%) as C2, 14 (7.8%) as C3, 2 (1.1%) as C4 and 50 (27.8%) as C5. The category-wise ROM was 25% for C1, 0.94% for C2, 35.7% for C3, 100% for C4 and 98% for C5. The most inclusive threshold (C3-C5 positive) yielded the greatest sensitivity (98.3%), whereas the C5-only and C4-C5 thresholds both showed a specificity of 99.1%. The best overall diagnostic accuracy was obtained when C4 and C5 were regarded as positive (95.3%). Among cases assessed with ROSE, inadequate smears accounted for 3.2%.

Conclusion: Classification of breast FNAC using the IAC Yokohama system produced clinically meaningful ROM estimates and showed strong agreement with histopathology, especially for benign and malignant categories. A positivity threshold that included suspicious and malignant aspirates provided the most balanced diagnostic performance. ROSE was associated with a low proportion of inadequate samples in the prospective component and may improve the efficiency of FNAC-based evaluation.

KEYWORDS:

• Breast lump • Fine-needle aspiration cytology • IAC Yokohama system • Risk of malignancy • Rapid on-site evaluation • Histopathology

INTRODUCTION

Breast cancer now represents a major component of cancer care among women in India and globally. In India, it has moved ahead of cervical cancer in relative frequency, creating a need for diagnostic pathways that are accurate, timely and feasible in routine practice.¹ The evaluation of a palpable breast lump generally combines clinical assessment, imaging and tissue or cellular examination. Cytopathological and histopathological interpretation are therefore central to treatment planning.²

FNAC continues to be valuable, particularly in settings where cost, access to biopsy services and waiting time are important concerns. As a component of triple assessment, it can provide early information about whether a lesion is likely to be benign or malignant and can assist the clinician in selecting further management.^{3,4}

A major limitation of descriptive breast cytology reports is variability in terminology and in the clinical interpretation of borderline findings. The IAC Yokohama system was introduced to address this issue by assigning breast aspirates to five categories: inadequate/insufficient (C1), benign (C2), atypical (C3), suspicious for malignancy (C4) and malignant (C5).⁵ The categories are linked to an increasing probability of malignancy and are intended to support consistent communication between pathologists and treating teams.

In addition to defining diagnostic labels, the Yokohama framework addresses sample handling, smear preparation, reporting practice, ancillary tests and clinical correlation.⁵ ROSE complements this approach because adequacy can be assessed during the procedure itself, allowing immediate repeat aspiration when the first sample is scant or non-representative.²

A reporting format that is understood in the same way by cytopathologists, surgeons and radiologists is likely to facilitate risk-based decisions and reduce avoidable delays. It may be particularly relevant in institutions where FNAC is frequently used for initial assessment of breast masses.⁵

The present study was designed to evaluate the application of the IAC Yokohama system in a tertiary care centre using histopathology for correlation. The analysis focused on category distribution, category-specific ROM, diagnostic performance under three thresholds of positivity and the contribution of ROSE to specimen adequacy in prospective cases.

MATERIALS AND METHODS

Study design and setting

A cross-sectional analytical study was conducted in the Department of Pathology, JSS Medical College, Mysore. The observation period extended over 42 months and comprised

a retrospective phase from November 2021 to April 2023 and a prospective phase from May 2023 to April 2025.

Study participants

Patients of any age and either sex presenting with a palpable breast lump were eligible when both a cytological diagnosis and a subsequent histopathological diagnosis were available. After institutional ethics approval and, for the prospective component, informed consent, 180 eligible cases were included. Cases with recurrent malignant disease, absent histopathological follow-up or insufficient clinical documentation were excluded; approximately 30 cases met one or more of these exclusion conditions.

Cytological procedure and smear processing

The prospective component comprised 94 cases. Aspirates were collected under aseptic conditions. A rapid toluidine blue-stained smear was reviewed at the time of the procedure for adequacy assessment through ROSE. Additional air-dried smears were processed with May-Grunwald-Giemsa stain, while alcohol-fixed smears were stained with Papanicolaou and hematoxylin and eosin stains. For the retrospective component, 86 previously prepared FNAC slides were retrieved and reassessed.

Cytological categorization and reference standard

All aspirates were categorized using the five-tier IAC Yokohama system: C1 - inadequate, C2 - benign, C3 - atypical, C4 - suspicious for malignancy and C5 - malignant. The corresponding histopathological diagnosis was used as the reference standard for cytohistological correlation and for estimating the ROM.

Diagnostic thresholds

The diagnostic performance of the classification was explored using three increasingly inclusive definitions of a positive cytology result: Group A considered only C5 as positive; Group B considered C4 and C5 as positive; and Group C considered C3, C4 and C5 as positive. This approach permitted evaluation of how inclusion of indeterminate categories altered sensitivity and specificity.

Bias control

Cytological interpretation and histopathological reporting were performed independently. At the time of cytological reporting, the interpreting cytopathologist was not aware of the final histopathological diagnosis. Where feasible, histopathological interpretation was undertaken without reference to the preceding Yokohama category, with the intention of limiting observer-related bias.

Sample size

The study included all consecutive eligible cases with both cytological and histopathological information during the defined study period. This inclusive approach was adopted because the investigation combined retrospective and prospective observational data and aimed to avoid selective sampling of available correlated cases.

Statistical analysis

Data were compiled and analysed using Statistical Package for the Social Sciences (SPSS), version 26.0. Clinical, demographic, radiological and cytological variables were summarized descriptively. ROM was calculated separately for each Yokohama category using histopathological outcome. For each of the three positivity thresholds, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were calculated. Specimen adequacy among prospective ROSE-assessed cases was also documented.

RESULTS

Clinical and radiological profile

The analysis included 180 patients whose ages ranged from 12 to 79 years; the mean age was 40.8 years. Women accounted for 178 cases (98.9%), while two patients (1.1%) were male. A unilateral lump was more frequent than bilateral presentation, and 51.7% of lesions were located in the left breast. A painless lump was the presenting symptom in 70% of patients, and 20% presented with a painful lump. The remaining patients reported features such as nipple discharge, cutaneous change or reduced appetite.

Breast Imaging Reporting and Data System

(BI-RADS) information was available for 145 cases. Among these, category II lesions comprised 30.4% and category III lesions 32.4%; categories IV and V represented 25.5% and 11.7%, respectively.

Distribution of Yokohama categories

On FNAC classification, C2 was the most frequent category, with 106 cases (58.9%)

(Table 1). Fibroadenoma was the leading benign cytological diagnosis, occurring in 60 cases (33.3%). Other benign findings included benign breast disease and proliferative breast disease (6.1% each), mastitis (5.0%), fibrocystic change and lipoma (3.3% each), and isolated cases of duct ectasia, benign phyllodes tumour and gynecomastia (0.6% each).

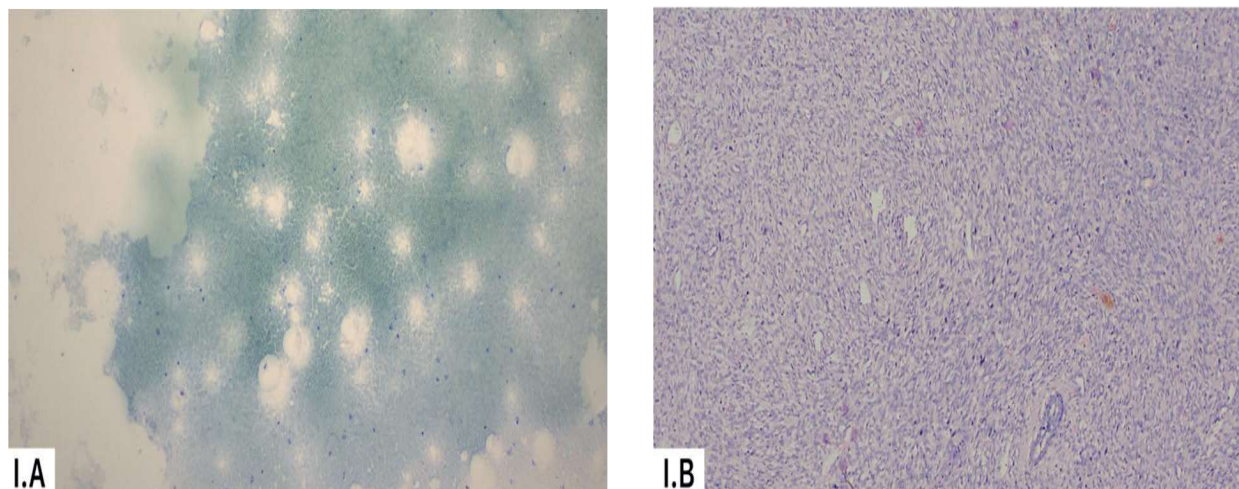


Figure 1: The microscopic cytological features and Yokohama categorization of breast FNAC and ROSE with corresponding histopathological diagnoses. [I.A: ROSE C1, Inadequate (Toluidine blue, X100); I.B: Corresponding histopathology showing Benign Phyllodes tumor (H&E, X100)].

Table 1: Distribution of FNAC diagnoses according to IAC Yokohama System

FNAC Diagnoses	Frequency (N)	Percentage (%)	IAC Yokohama Category
Inadequate	8	4.4	Category 1 (n=8, 4.4%)
Fibroadenoma	60	33.3	
Benign breast disease	11	6.1	Category 2 (n=106, 58.9%)
Proliferative breast disease	11	6.1	
Mastitis	9	5.0	
Fibrocystic breast disease	6	3.3	
Lipoma	6	3.3	
Duct ectasia	1	0.6	
Benign phyllodes	1	0.6	
Gynecomastia	1	0.6	
Atypical	5	2.8	Category 3 (n=14, 7.8%)
Proliferative breast disease with atypia	4	2.2	
Atypical ductal hyperplasia	2	1.1	
Papillary lesion	3	1.7	Category 4 (n=2, 1.1%)
Suspicious for breast carcinoma	2	1.1	
Breast carcinoma	50	27.8	Category 5 (n=50, 27.8%)

Fifty aspirates (27.8%) were placed in C5 and were reported cytologically as malignant. Fourteen cases (7.8%) were categorized as C3, including proliferative breast disease

with atypia, atypical ductal hyperplasia and papillary lesions. Only two aspirates (1.1%) were assigned to C4, while eight samples (4.4%) were inadequate and categorized as C1.

ROSE findings

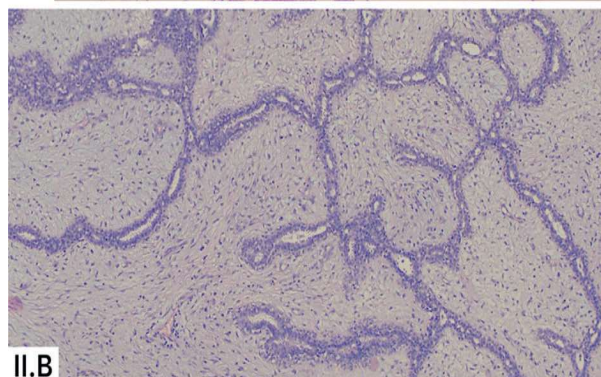
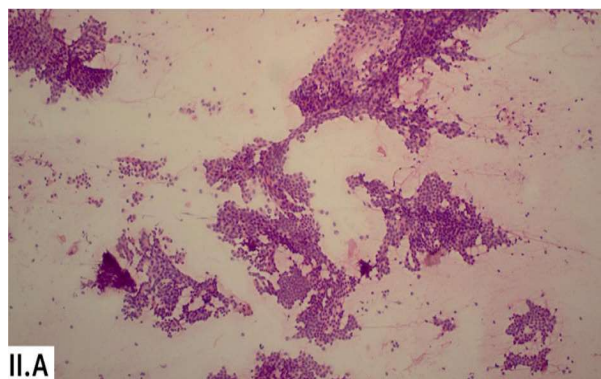


Figure 2: The microscopic cytological features and Yokohama categorization of breast FNAC and ROSE with corresponding histopathological diagnoses. [II.A: C2 category, Benign, Fibroadenoma (H&E, X100); II.B: Corresponding histopathology showing Fibroadenoma (H&E, X100)].

Table 2: Distribution of breast lesions using ROSE according to IAC Yokohama System

ROSE Category	Frequency (N)	Percentage (%)
C1	3	3.2
C2	60	63.8
C3	0	0.0
C4	0	0.0
C5	31	33.0
Total	94	100

ROSE was used in all 94 prospectively sampled cases. Of these, 60 cases (63.8%) were assigned to C2, 31 cases (33.0%) to C5 and three cases (3.2%) to C1. None of the ROSE-assessed specimens was reported as C3 or C4 (Table 2). Thus, the inadequate rate within the ROSE group was 3.2%.

Cytohistological correlation (Figures 1-5) and risk of malignancy

The correlation between cytological assessment, including ROSE where available, and histopathological diagnosis is presented in Table 3. Among the eight C1 samples, histopathology showed malignancy in two cases, giving an ROM of 25%. Of the 106 C2 aspirates, 105 were benign on histopathology

and one was malignant, resulting in an ROM of 0.94%. In category C3, five of 14 lesions were malignant on histopathology, corresponding to an ROM of 35.7%. Both C4 cases were malignant on tissue examination, while 49 of the 50 C5 cases were histologically malignant.

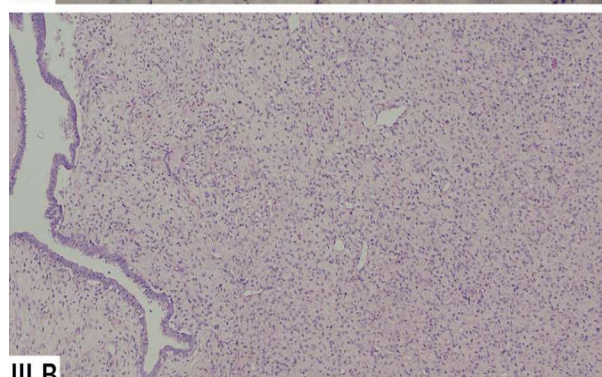
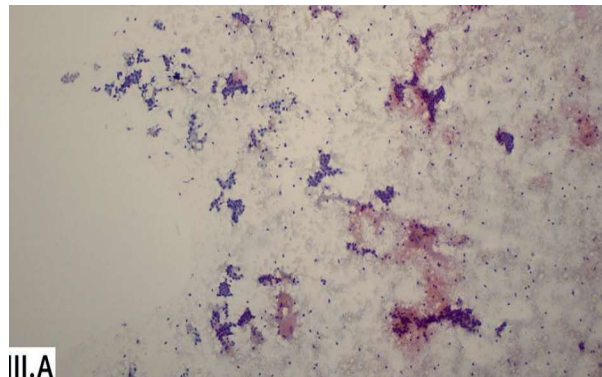


Figure 3: The microscopic cytological features and Yokohama categorization of breast FNAC and ROSE with corresponding histopathological diagnoses. [III.A: C3 category, Atypical (PAP, X100); III.B: Corresponding histopathology showing Borderline Phyllodes tumor (H&E, X100)].

Table 3: Correlation of Cytological Diagnoses with Histopathological Diagnoses

Cytological diagnoses	Histopathological Diagnoses		
	Benign	Malignant	Total
C1	6	2	8
C2	105	1	106
C3	9	5	14
C4	0	2	2
C5	1	49	50
Total	120	60	180

Agreement with histopathology was greatest at the definite ends of the cytological spectrum: 99.1% of C2 cases were confirmed as benign and 98.0% of C5 cases were confirmed as malignant. The greater proportion of discordant findings within C3 indicates the need for tissue confirmation and clinical-radiological correlation when atypical cytology is reported.

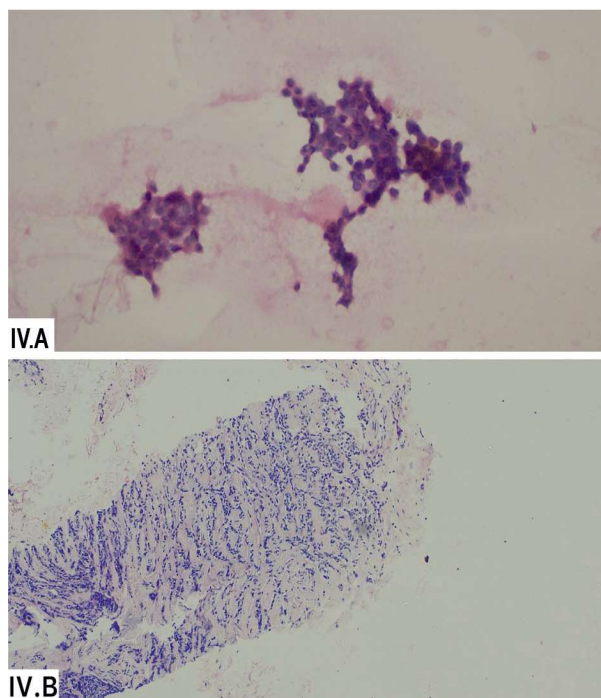


Figure 4: The microscopic cytological features and Yokohama categorization of breast FNAC and ROSE with corresponding histopathological diagnoses. [IV.A: C4 category, Suspicious for malignancy (H&E, X400); IV.B: Corresponding histopathology showing Breast carcinoma (H&E, X100)]

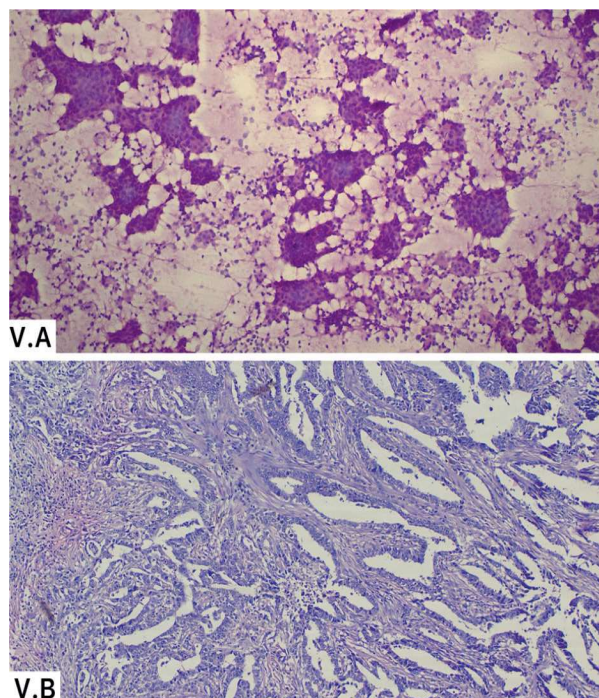


Figure 5: The microscopic cytological features and Yokohama categorization of breast FNAC and ROSE with corresponding histopathological diagnoses. [V.A: C5 category, Malignant, Breast carcinoma (H&E, X100); V.B: Corresponding histopathology showing Invasive breast carcinoma (H&E, X100)]

Table 4: Comparison of Diagnostic Performance Parameters Across Groups

Parameter	Group A	Group B	Group C
Sensitivity	84.5%	87.9%	98.3%
Specificity	99.1%	99.1%	92.1%
Positive Predictive Value (PPV)	98.0%	98.1%	86.4%
Negative Predictive Value (NPV)	92.6%	94.2%	99.1%
Diagnostic accuracy	94.2%	95.3%	94.2%

The ROM values across categories were: C1 - 25%; C2 - 0.94%; C3 - 35.7%; C4 - 100%; and C5 - 98%. Except for the limited number of C1 cases, the pattern demonstrates a marked rise in malignant outcome from the benign category to the suspicious and malignant categories.

Diagnostic performance at three thresholds

Group A, which treated C5 alone as a positive result, produced a sensitivity of 84.5% and a specificity of 99.1%. Group B, in which C4 and C5 were positive, increased sensitivity to 87.9% while retaining a specificity of 99.1%. Group C, which additionally included C3 as positive, provided the greatest sensitivity at 98.3%, with a specificity of 92.1%. The highest overall diagnostic accuracy was observed in Group B (95.3%), compared with 94.2% for Groups A and C (Table 4).

DISCUSSION

The present analysis evaluated breast FNAC reporting under the IAC Yokohama framework in a tertiary care institution and correlated each category with histopathology. This is clinically relevant in a setting where breast cancer contributes substantially to the cancer burden among Indian women and where practical diagnostic strategies are required for patients presenting with palpable lesions.⁶

Assessment of a breast mass is strongest when clinical examination, imaging and pathological sampling are interpreted together. FNAC and core needle biopsy contribute tissue-based information within this triple assessment approach, and FNAC continues to offer a rapid means of separating many benign lesions from cases requiring urgent evaluation for malignancy.⁷

The Yokohama system improves the usefulness of breast cytology by translating smear findings into categories with distinct clinical implications rather than relying on variable narrative terminology.⁵ In this study, most aspirates were benign (C2), followed by malignant (C5), with a smaller number of atypical, suspicious or inadequate aspirates.

The proportion of inadequate aspirates in the present series was 4.4%. This is close to the rates reported by Yadav et al. (3.8%) and Joshi et al. (1.1%), and lower than figures reported by Munjal et al. (15.3%) and Agarwal et al. (7.1%).^{8,10-12} A plausible contributor to this low proportion is the use of ROSE in the prospective component, since inadequate material can be recognized and resampled during the same visit.

Benign aspirates constituted 58.9% of the series, a result similar to the proportion described by Joshi et al. (57.7%).⁸ Differences from other studies may relate to referral practices, population characteristics and the proportion of patients presenting with radiologically concerning lesions.^{10,11,13}

The atypical category accounted for 7.8% of cases, which is broadly consistent with observations by Agarwal et al., Yadav et al. and Ahuja et al.^{10,12,13} Rohilla et al. recorded a higher frequency of atypical diagnoses (26.9%), illustrating that category assignment can vary with interpretation and the types of lesions encountered.¹⁴

Only two cases (1.1%) were classified as suspicious for malignancy. Similar small proportions have been described in earlier series, including those by Munjal et al., Montezuma et al. and Yadav et al.^{10,11,15} The malignant category constituted 27.8% of the present cohort, which may reflect the case mix of a tertiary referral hospital.

Role of rapid on-site evaluation

The prospective component provided an opportunity to examine the practical contribution of ROSE. Among the 94 patients evaluated on site, the inadequate rate was 3.2%, and most specimens could be categorized as benign or malignant during initial review. Wong et al. documented a reduction in inadequate samples from 17.1% to 4.0% after introduction of ROSE, and Field et al. reported a comparable decline from 17% to 4%.^{7,9} Agrawal et al. also reported a low inadequate rate of 1.8% with on-site assessment.²

ROSE is particularly useful because adequacy is verified while the procedure is still in progress. When cellularity is insufficient, a repeat aspirate can be obtained immediately rather than recalling the patient after a nondiagnostic report. Previous reports have also described fewer atypical or suspicious interpretations after the introduction of ROSE,

which may improve clinical triage and reduce uncertainty for patients.^{2,7,9}

Risk of malignancy and diagnostic performance

The category-specific ROM in this study generally increased in the expected direction, from less than 1% in benign aspirates to 98% in malignant aspirates. The C3 and C4 categories showed ROM values of 35.7% and 100%, respectively. Although the C4 estimate was based on only two cases and should be interpreted cautiously, these results support the need for further tissue evaluation when cytological findings are indeterminate or suspicious.

Cytohystological concordance was particularly strong for C2 and C5. When only C5 was treated as positive (Group A), specificity and PPV were very high, indicating that a malignant cytology result was highly reliable. The Group A sensitivity (84.5%) and accuracy (94.2%) were comparable to the figures described in studies by Yadav et al., Munjal et al. and Ahuja et al.^{10,11,13}

Including suspicious cases with malignant cases (Group B) increased sensitivity to 87.9% while maintaining 99.1% specificity. This definition gave the best diagnostic accuracy in the present study (95.3%) and produced results similar to those reported by Yadav et al., Ahuja et al. and Munjal et al.^{10,11,13} For routine practice, this threshold offers a clinically useful balance because a suspicious aspirate usually requires prompt confirmatory tissue diagnosis or definitive management planning.

The broadest threshold (Group C) maximized sensitivity (98.3%) and NPV (99.1%) by treating atypical aspirates as positive. The expected consequence was lower specificity (92.1%) and PPV (86.4%), because some atypical lesions were benign on histopathology. A similar sensitivity-specificity trade-off has been observed in other studies once the atypical group is included in the positive arm.^{10-12,15}

Taken together, the three thresholds serve different clinical priorities. C5 alone gives the greatest certainty for a malignant call; combining C4 with C5 offers the most balanced performance in this dataset; and inclusion of C3 provides the highest sensitivity where the immediate concern is to avoid overlooking malignancy. Interpretation should therefore be

made in conjunction with imaging and clinical findings rather than in isolation.

Strengths and limitations

Important strengths of this study are the application of a recognized cytological reporting framework, availability of histopathological correlation for included cases and inclusion of a prospective group in which ROSE was used. The assessment of three positivity thresholds also provides information that is directly relevant to clinical decision-making.

Several limitations must be considered. The data were obtained from a single tertiary care centre and the sample size was modest; therefore, the findings may not represent all clinical settings. The retrospective component may be affected by incomplete documentation and selection bias. Restriction of the correlation analysis to cases with histopathological follow-up could introduce verification bias and may inflate estimates of diagnostic performance. The atypical and suspicious categories are inherently subject to interobserver variation, and the small number of C4 cases limits the precision of its ROM estimate. ROSE was available only for the prospective group, preventing uniform adequacy comparison across all patients. In addition, ancillary techniques such as immunocytochemistry and molecular testing were not used for diagnostically challenging lesions.

CONCLUSION

The IAC Yokohama system provided a structured method for reporting breast FNAC and showed good correlation with histopathology in this study, especially within the clearly benign and clearly malignant categories. The increasing ROM across diagnostic categories supports its use for risk-based clinical communication. Among the diagnostic thresholds assessed, classifying both suspicious and malignant aspirates as positive produced the highest overall accuracy, while inclusion of atypical cases maximized sensitivity.

In the prospective cases, ROSE was associated with a low rate of inadequate specimens and enabled prompt assessment of smear adequacy. When incorporated into a triple assessment pathway, Yokohama-based FNAC reporting with ROSE may assist clinicians in

selecting further biopsy or management in a timely and consistent manner.

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Conflict of Interest

The authors declare that they have no conflict of interest related to this work.

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