

The Yokohama Paradigm: Assessing Fine-Needle Aspiration Biopsy for Breast Lesions with Enhanced Diagnostic Precision

Dr Silla Alisha Patro¹, Dr Meenakshi Mohapatro², Dr Lipsa Priyadarshini³, Dr Devidutta Ramani Ranjan Rout⁴, Prof. Dr. Lity Mohanty⁵

¹Assistant professor, Department of Pathology, VIMSAR, Burla

²Assistant Professor, Department of Pathology, SCB Medical College and Hospital, Cuttack, Odisha

³Assistant professor, Department of Pathology, VIMSAR, Burla

⁴Senior Resident (SR), Department of Pathology, PRM Medical college, Baripada

⁵Professor and HOD, Department of Pathology, SCB Medical College and Hospital, Cuttack, Odisha

*Corresponding Author: Dr Meenakshi Mohapatro

Assistant Professor, Department of Pathology, SCB Medical College and Hospital, Cuttack, Odisha

KEYWORDS	ABSTRACT:
diagnostic accuracy, cytopathology, yokohama system, fine-needle aspiration biopsy (fnab), breast cancer	<p>Background: Breast cancer is the most common malignancy in women, with rising incidence in India. FNAB is a key diagnostic tool, but reporting inconsistencies exist. The IAC Yokohama System standardizes FNAB cytology, improving clinical communication and patient management.</p> <p>Methods: A cross-sectional study at SCB Medical College (2020-2022) included 210 patients with breast lumps. FNAB was performed, and smears were stained with H&E, Pap, and Diff-Quik. Diagnoses followed the Yokohama System, with histopathological correlation. Statistical analysis assessed diagnostic accuracy, sensitivity, specificity, PPV, NPV, and risk of malignancy (ROM).</p> <p>Results & Discussion: Among 210 FNA procedures, the majority of cases occurred in the 31-40-year age group, with the upper outer quadrant being the most common site (40%). Benign lesions (47.6%) were most frequent, followed by malignant cases (43.8%). The risk of malignancy ranged from 17.44% (Category II) to 97.4% (Category V). Sensitivity and specificity were assessed against histopathology, with statistical significance ($\chi^2 = 138.88$, $p < 0.05$). FNAB demonstrated high diagnostic accuracy, aiding in distinguishing benign from malignant lesions. The five-tier Yokohama classification improved clinician-pathologist communication, risk assessment, and preoperative decision-making.</p> <p>Conclusion: The Yokohama System enhances FNAB's reliability, supporting its wider adoption to improve breast cancer diagnosis and patient outcomes.</p>

INTRODUCTION

Breast cancer remains the most prevalent malignancy among women and is the leading cause of cancer-related mortality in this population [1]. Its incidence continues to rise globally, underscoring the need for efficient diagnostic modalities. Fine Needle Aspiration Biopsy (FNAB) has long been recognized as a reliable and cost-effective technique for evaluating breast lesions [2]. While Core Needle Biopsy (CNB) provides additional advantages, such as assessing tumor invasion, histologic grading, hormone receptor status, and HER2 expression, FNAB remains highly valuable, particularly in resource-limited settings. The triple test, which includes clinical examination, mammography and/or ultrasonography, and cytology, plays a crucial role in breast cancer diagnosis [2].

To enhance the consistency and reliability of cytologic reporting, the International Academy of Cytology (IAC) introduced the Yokohama System for Breast Cytology in 2019. This standardized, tiered classification framework aims to improve the clarity of FNAB cytology reports, thereby facilitating better clinical interpretation and decision-making [3]. Given its affordability and accessibility, FNAB continues to be a frontline diagnostic tool, particularly in low-resource healthcare settings. This study aims to classify and interpret Fine Needle Aspiration (FNA) smears of breast lesions using the IAC Yokohama System, calculate the risk of malignancy (ROM) for each category, and determine the sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy. By evaluating the diagnostic performance of FNAB within a tertiary care hospital setting, this study seeks to reinforce its clinical applicability and prognostic significance.

MATERIAL AND METHODS

This cross-sectional, observational study was conducted over a period of two years, from November 2020 to August 2022, in the Department of Pathology, SCB Medical College and Hospital, Cuttack. A total of 210 patients with clinically detected breast lumps, referred from the Surgery Outpatient Department (OPD) to the Cytology Section, were included based on specific inclusion criteria. Patients who were pregnant or lactating, those who did not provide consent for FNAB and biopsy, and those unwilling to participate in the study were excluded. Ethical approval for the study was obtained from the Institutional Ethics Committee (IEC) under application number 741.

Under aseptic precautions, FNAB was performed using a 10 mL disposable syringe with a 22–26-gauge needle. Relevant clinical history, including age, gender, duration of symptoms, onset, presence of pain, and history of recurrence, was recorded. A rapid on-site examination (ROSE) was performed to assess sample adequacy [4,5]. A thorough clinical examination of the lump, including its site, size, number, consistency, and fixity to the overlying skin, was conducted. The aspirated material was smeared onto clean glass slides, with one slide air-dried and the other fixed with ethanol. The fixed smear was stained using Hematoxylin and Eosin (H&E), Papanicolaou (Pap) stain, and Diff-Quik stain for cytological evaluation. Cytological diagnoses were categorized according to the International Academy of Cytology (IAC) Yokohama System for Breast Cytology. Patients were subsequently referred to the Department of Surgery for core needle biopsy, lumpectomy, or mastectomy, followed by histopathological examination to confirm the diagnosis and evaluate the accuracy of the Yokohama cytology grading system.

RESULT

The present study was conducted in the Department of Pathology, S.C.B. Medical College and Hospital, Cuttack, over a period of two years (October 2020–November 2022). A total of 210 fine-needle aspiration (FNA) procedures were performed on breast lumps, and cases were classified into five categories according to the International Academy of Cytology (IAC) Yokohama System for Reporting Breast Cytopathology.

The majority of lesions were observed in the 31–40-year age group (34.76%) (Table 1). The most common tumor location was the upper outer quadrant of the breast, accounting for 83 cases (40%), followed by the lower outer quadrant (48 cases, 23%), the upper inner quadrant (43 cases, 20%), and the lower inner quadrant (36 cases, 17%), with a predominance on the left side.

Among the study population, core needle biopsy was the most frequently performed surgical procedure (90 cases, 52.02%), followed by modified radical mastectomy (49 cases, 28.32%) and lumpectomy (34 cases, 19.65%).

Benign lesions (Category II) were the most prevalent, comprising 100 cases (47.6%), followed by malignant lesions (Category V) with 92 cases (43.8%). The "suspicious for malignancy" category (Category IV) included 7 cases (3.35%), while the "insufficient" (Category I) and "atypical" (Category III) categories accounted for 6 (2.8%) and 5 (2.3%) cases, respectively (Table 2). Fibroadenoma was the most commonly encountered benign lesion (Figure 1).

"Atypical," "suspicious for malignancy," and "malignant" were regarded as positive test results. Cases with negative cytological findings but diagnosed as carcinoma on histopathological examination were classified as false-negative (FN).

The Atypical category encompassed cases exhibiting predominantly benign cytologic features yet harboring subtle malignant indicators, such as benign phyllodes tumors (Figure 3) and ductal carcinoma of the breast (Figure 4).

The sensitivity and specificity of cytological diagnosis were assessed in correlation with histopathological findings. Of the 210 cases, 176 underwent definitive surgical procedures, including lumpectomy, core needle biopsy, or mastectomy. Among the six cases classified as "insufficient," three were successfully followed up, but as per Acta Cytologica guidelines, these cases were excluded from the final statistical analysis.

TABLE 1: AGE WISE DISTRIBUTION OF BREAST LESIONS

AGE IN YEARS	NO. OF PATIENTS	%
11-----20	3	1.42
21-----30	13	6.19
31-----40	73	34.76
41-----50	61	29.04
51-----60	32	15.23
61-----70	13	6.19
71-----80	15	7.14

TABLE 2: DIFFERENT CATEGORIES OF FNA CYTOLOGY AS PER YOKOHAMA BREAST CYTOLOGY GRADING SYSTEM

YOKAHAMA SYSTEM CATEGORY	NO. OF CASES	NO. OF CASES WITH HISTOPATHOLOGICAL FOLLOW UP	BENIGN	MALIGNANT	ROM (RISK OF MALIGNANCY) IN %
I(INSUFFICIENT)	6	3	1	2	66.67
II(BENIGN)	100	86	71	15	17.44
III(ATYPICAL)	5	5	3	2	40
IV (SUSPICIOUS OF MALIGNANCY)	7	5	1	4	80
V(MALIGNANT)	92	77	2	75	97.4

TABLE 3: SENSITIVITY SPECIFICITY OF BREAST LESIONS

THE YOKAHAMA BREAST CYTOLOGY GRADING SYSTEM	HISTOPATHOLOGICAL CORRELATION (CNB/LUMPECTOMY/MASTECTOMY)		TOTAL
	MALIGNANT (POSITIVE)	BENIGN (NEGATIVE)	
MALIGNANT	81(TP)	06(FP)	87
BENIGN	15(FN)	71(TN)	86
TOTAL	96	77	173

TABLE 4: STATISTICAL ANALYSIS

YOKAHAMA SYSTEM(Screening)	Biopsy Test (Confirmatory)		
	NEGATIVE=0	POSITIVE=1	Total
NEGATIVE=0	81	5	86
POSITIVE=1	4	83	87
Total Cases	85	88	173

FIGURE-1. Hematoxylin and eosin, 100x fibroadenoma of breast.

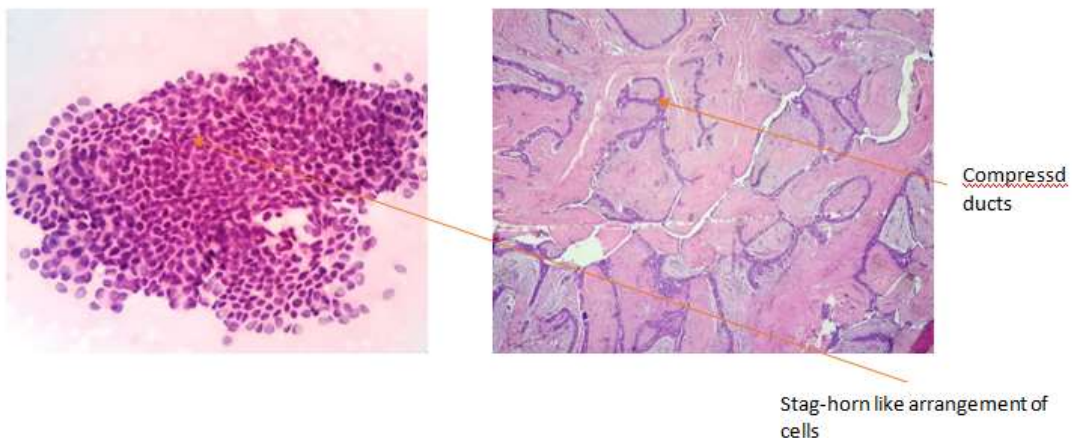


FIGURE-2. Diff quik stained cytosmear (400X) of insufficient material from breast lesions.

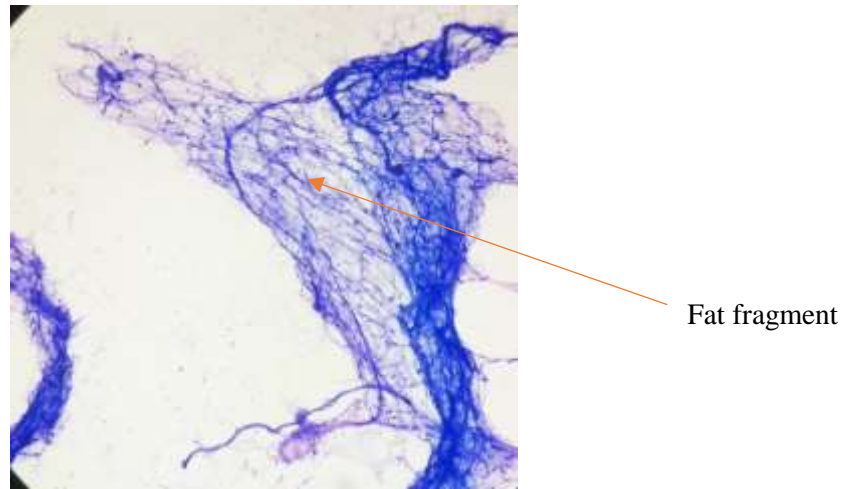


FIGURE-3. Hematoxylin and eosin, 400x phyllodes tumor of breast

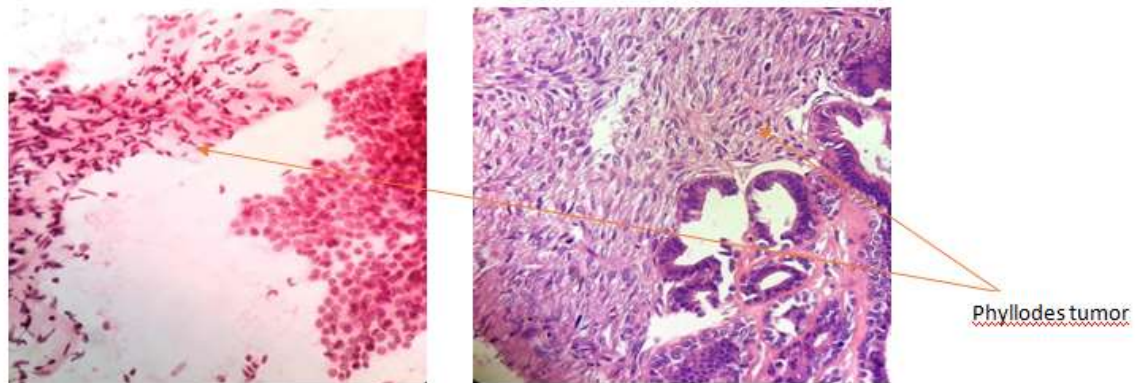
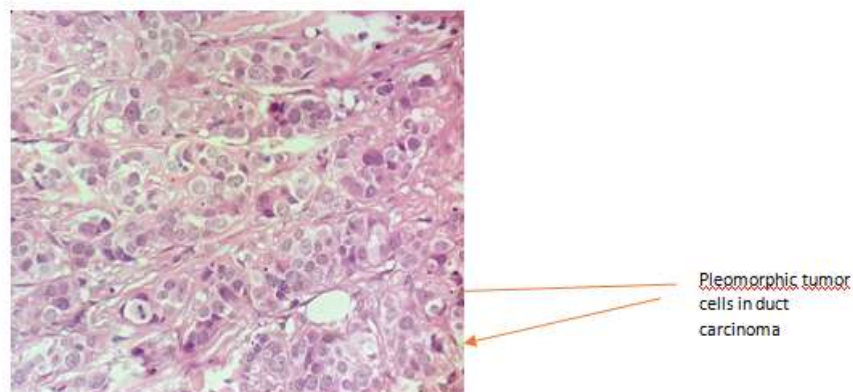


FIGURE-4. Hematoxylin and eosin, 400x duct carcinoma breast.



STATISTIC ANALYSIS

All the statistical analysis were performed by Microsoft Excel 2019 (Microsoft corporation, Redmond, Washington, USA). The statistical calculations were performed using IBM SPSS Statistics (IBM SPSS Statistics for Windows, Version 20.0)

Chi-square test was used to assess the effect of gender independent variable on the results of histopathological and cytological tests. Chi square value was calculated (138.8882). Our study is statistically significant ($p < 0.05$) (Table -3)

DISCUSSION

Fine-needle aspiration biopsy (FNAB) of the breast remains a highly accurate diagnostic modality, offering the dual advantages of cost-effectiveness and rapid turnaround. Breast lump is a common complaint presented by patients at the surgical OPDs with an apprehension of possible malignancy being extremely common [6,7]. The risk of malignancy (ROM) associated with the various diagnostic categories exhibits statistically significant variations. Notably, cases deemed insufficient (figure 2) but exhibiting concordant benign cytological features were not subjected to further evaluation, inadvertently excluding a substantial cohort of true-negative cases [8]. Among the atypical cases, two were subsequently diagnosed as carcinoma upon histopathological examination [9]. Diagnostic misinterpretation arose due to the presence of a few benign bipolar nuclei and only mild anisonucleosis within the epithelial cells, underscoring the challenges inherent in cytomorphological assessment. Nevertheless, the ROM for the malignant category was found to be satisfactory. Granulomatous mastitis, a well-documented cytologic mimic of malignancy, further exemplifies the potential diagnostic pitfalls of FNAB.

The International Academy of Cytology (IAC) Yokohama System for Reporting Breast Cytopathology represents a pivotal advancement in cytologic reporting, providing an evidence-based, five-tier classification system designed to enhance diagnostic clarity and standardization. This system stratifies FNAC findings into five categories—Insufficient, Benign, Atypical, Suspicious for Malignancy, and Malignant—each correlated with a distinct ROM [10]: 2.6-4.8%, 1.4-2.3%, 13-15.7%, 84.6-97.1%, and 99.0-100%, respectively (Table 2).

Our study encompassed 210 patients presenting with breast lumps, all of whom underwent FNAC. Subsequently, in 173 patients who proceeded to surgical excision, FNAC diagnoses were correlated histopathologically at SCB Medical College and Hospital. The age range of the study cohort spanned 11 to 80 years, with the highest prevalence observed in the 31-40 years age group, followed by the 41-50 years cohort (Table 1). The most frequently encountered pathology was fibroadenoma, affecting 100 patients (Table 2), aligning with findings reported by Monalyn et al [11]. In our study, the benign category constituted the majority of cases (100 cases, 47.6%), followed by the malignant category (92 cases, 43.8%) (Table 2), which aligns with observations from Nutan et al [12], Akansha et al [13] and Ying Ping et al. The Insufficient category comprised six cases (2.8%), primarily due to fluid aspiration, cyst macrophages, fat fragments, and hemorrhage.

Of the 92 cases categorized as malignant on FNAB cytology, 77 underwent follow-up, yielding an ROM of 97.4% (Table 2). The sensitivity and specificity of FNAB in our study were 84.37% and 92.2%, respectively (Table 4), with an overall diagnostic accuracy of 87.86%.

The IAC Yokohama System establishes a universal lexicon for cytopathologic reporting, thereby enhancing interobserver reproducibility and diagnostic reliability. Our findings corroborate recent studies validating the Yokohama system as a robust tiered classification schema that optimizes breast cytology reporting and facilitates judicious clinical management. Additionally, the study underscores the indispensable role of clinical-radiological correlation and ancillary investigations in refining cytologic interpretations, thereby ensuring optimal patient care. The study faced certain limitations. The COVID-19 pandemic restricted the sample size within the designated study period, affecting the overall data collection. Additionally, ancillary molecular techniques, such as genetic studies, were not available at our institution, limiting the scope of advanced diagnostic evaluations. Furthermore, for deep-seated or non-palpable lesions, the use of ultrasound-guided FNAC could have potentially improved the diagnostic yield and accuracy, but this facility was not incorporated into the study.

CONCLUSION

The YOKOHAMA breast cytology grading system serves as a meticulously structured and standardized reporting framework, demonstrating commendable diagnostic accuracy. Its implementation facilitates early detection while simultaneously curbing the incidence of unwarranted surgical interventions. Although core-needle biopsy remains the gold standard for definitive breast cancer diagnosis, we advocate that FNAB continues to hold a pivotal role in the evaluation of breast lesions. This study underscores its clinical utility in mitigating diagnostic ambiguity and misinterpretation. A risk-stratification approach has been devised to provide clinicians with a strategic roadmap for subsequent management, while also delineating the associated risk of malignancy (ROM).

Acknowledgements

The authors are showing their gratitude to SCB Medical College (Department of pathology and surgery), for providing spontaneous support in terms of resources and facilities regarding this entire research study.

Conflicts of interest

All authors clearly stated that they do not have any conflicts of interests.

Ethics approval

The ethical approval was acquired from institutional ethical committee of SCB Medical College and Hospital, Ethics Committee Registration no-ECR/84/Inst/OR/2013/RR-20, Dt -04/06/2021

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, et al.: [GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012 v1.0: IARC cancerbase No. 11](#). International Agency for Research on Cancer (IARC). 2013, 0:11.
2. Field AS, Raymond WA, Rickard M, et al.: [Breast fine needle aspiration biopsy cytology: the potential impact of the International Academy of Cytology Yokohama System for Reporting Breast Fine Needle Aspiration Biopsy Cytopathology and the use of rapid on-site evaluation](#). Journal of the American Society of Cytopathology. 2020, 9:103-111. [10.1016/j.jasc.2019.10.004](#)
3. Krishnamurthy S: [Relevance and impact of the International Academy of Cytology Yokohama System for standardized reporting of breast fine-needle aspiration biopsy cytology](#). Journal of American Society of Cytopathology. 2020, 9:63-66. [10.1016/j.jasc.2019.12.001](#)
4. [Utility of Rapid On-Site Evaluation of Transbronchial Needle Aspirates](#). 2005, 72:182-88. [10.1159/000084050](#) or <https://pubmed.ncbi.nlm.nih.gov/15824529/>
5. Baram D, Garcia RB, Richman PS.: [Impact of rapid on-site cytologic evaluation during transbronchial needle aspiration](#). The Journal Chest. 2005, 128:869-75. [10.1378/chest.128.2.869](#)
6. Hughes JE, Royle GT, Buchanan R, et al.: [Depression and social stress among patients with benign breast disease](#). The British Journal of Surgery. 1986, 73:997-999. [10.1002/bjs.1800731217](#)
7. Ellman R, Angel N, Moss S, et al.: [Psychiatric morbidity associated with screening for breast cancer](#). The British Journal of Cancer. 1989, 60:781-784. [10.1038/bjc.1989.359](#)
8. Wong YP, Vincent James EP, Mohammad Azhar MAA, et al.: [Implementation of the International Academy of Cytology Yokohama standardized reporting for breast cytopathology: An 8-year retrospective study](#). Diagnostic Cytopathology. 2021, 49:718-726. [10.1002/dc.24731](#)
9. Homesh N A, Issa M A, El-Sofiani H A: [The diagnostic accuracy of fine needle aspiration cytology versus core needle biopsy for palpable breast lump\(s\)](#). The Saudi Medical Journal. 2005, 26:42-46.
10. Field AS, Raymond WA, Rickard M, et al.: [The International Academy of Cytology Yokohama System for reporting breast fine-needle aspiration biopsy cytopathology](#). Acta Cytologica. 2019, 63:257-273. [10.1159/000499509](#)
11. 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](#). Diagnostic Cytopathology. 2021, 49:1022-1031. [10.1002/dc.24808](#)
12. Marabi M, Aphivatanasiri C, Jamidi SK, et al.: [The International Academy of Cytology Yokohama System for Reporting Breast Cytopathology showed improved diagnostic accuracy](#). The Journal Cancer Cytopathology. 2021, 129:852-864. [10.1002/cncy.22451](#)
13. Agarwal A, Singh D, Mehan A, et al.: [Accuracy of the International Academy of Cytology Yokohama system of breast cytology reporting for fine needle aspiration biopsy of the breast in a dedicated breast care setting](#). Diagnostic Cytopathology. 2021, 49:195-202. [10.1002/dc.24632](#)