



## EXPLORING YOKOHAMA'S BREAST LESIONS: A COMPREHENSIVE CYTO-HISTO CORRELATION STUDY ACROSS DIFFERENT CATEGORIES

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### ABSTRACT

**Background:** Breast lesions constitute a common clinical problem and encompass a wide spectrum ranging from benign proliferative disorders to malignant neoplasms. Fine Needle Aspiration Cytology (FNAC) is a rapid, minimally invasive, and cost-effective diagnostic modality widely used in the initial evaluation of breast lumps. Cyto-histopathological correlation is essential to assess the diagnostic accuracy and reliability of FNAC.

**Aim and Objectives:** To correlate the cytological findings of breast lesions with their histopathological diagnosis on excision and to evaluate the diagnostic accuracy of FNAC in breast lesions.

**Materials and Methods:** This observational study was conducted in the Department of Pathology at M.P. Shah Medical College, Jamnagar, from April 2022 to August 2023. A total of 76 female patients presenting with breast lumps underwent FNAC followed by excision biopsy, lumpectomy, or mastectomy. Cytological reporting was performed according to NHS C1–C5 categories. Histopathological examination was carried out on formalin-fixed, paraffin-embedded tissue sections stained with Hematoxylin and Eosin. Cyto-histological correlation was performed, and diagnostic parameters including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated.

**Results:** Among 76 cases, 36 (47.4%) were benign and 40 (52.6%) were malignant on histopathology. Fibroadenoma was the most common benign lesion (52.8% of benign cases), while infiltrating ductal carcinoma was the predominant malignant lesion (77.5% of malignant cases). Cytologically, 36 cases were categorized as C2, 1 as C3, and 39 as C5. One false-negative case was observed, and no false-positive cases were reported. FNAC demonstrated a sensitivity of 97.5%, specificity of 100%, PPV of 100%, NPV of 97.29%, and overall diagnostic accuracy of 98.68%.

**Conclusion:** FNAC shows excellent diagnostic accuracy in the evaluation of breast lesions and serves as a reliable, rapid, and minimally invasive diagnostic tool. Proper sampling and standardized reporting enhance its effectiveness. Cyto-histopathological correlation remains essential to validate cytological findings and ensure optimal patient management.

**Keywords:** Breast Lesions, Fine Needle Aspiration Cytology, Cyto-Histological Correlation, Breast Carcinoma, Fibroadenoma, Diagnostic Accuracy, Yokohama System.

### INTRODUCTION

Breast lesions constitute one of the most common clinical presentations encountered in surgical and pathology practice, encompassing a wide spectrum ranging from inflammatory and benign

Proliferative conditions to in situ and invasive malignancies [1]. A breast lesion is defined as any palpable, radiologically detected, or incidentally identified abnormality within breast tissue that requires further diagnostic evaluation. Among these, breast cancer has emerged as the most frequently diagnosed malignancy in women globally, accounting for a substantial proportion of cancer-related morbidity and mortality [2]. Recent global cancer statistics report that breast cancer surpassed lung cancer in incidence and remains a leading cause



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of cancer death among women worldwide [2,3]. Early and accurate diagnosis of breast lesions is therefore crucial to improve survival rates and reduce treatment-related complications.

Fine Needle Aspiration Cytology (FNAC) is widely recognized as a rapid, minimally invasive, cost-effective diagnostic technique for evaluating breast lumps [4]. It forms an integral component of the “triple assessment” approach—clinical examination, imaging, and cytology—which significantly enhances diagnostic accuracy in breast pathology [5]. FNAC is particularly valuable in low- and middle-income countries like India, where resource constraints necessitate affordable and efficient diagnostic tools [6]. However, the accuracy of FNAC depends on adequate sampling, technical expertise, and standardized reporting systems to minimize interpretative variability.

To ensure uniformity in reporting and improve risk stratification, structured cytological classification systems have been developed. The National Health Service (NHS) C1–C5 categorization and the more recent International Academy of Cytology (IAC) Yokohama System provide standardized terminology linking cytological categories to estimated risk of malignancy [7,8]. The Yokohama System, in particular, emphasizes cyto-histopathological correlation to validate cytological interpretations and refine diagnostic thresholds [7]. Such correlation studies are essential to evaluate sensitivity, specificity, predictive values, and overall diagnostic accuracy of FNAC in different clinical settings [9].

Globally, breast cancer accounts for approximately 2.3 million new cases annually, representing nearly one in four cancers among women [2]. In India, breast cancer has become the most common cancer among women, especially in urban populations, with steadily increasing incidence rates over the past decade [10]. Data from Indian cancer registries indicate rising trends in states including Gujarat, reflecting demographic transition, lifestyle changes, delayed childbearing, and improved detection practices [10]. Despite advancements in diagnostic modalities, delayed presentation and diagnostic discrepancies remain significant challenges, underscoring the importance of reliable preoperative diagnostic techniques.

In regions such as Gujarat, benign breast lesions like fibroadenoma are commonly observed in younger women, whereas malignancies predominate in middle-aged and older age groups. Accurate cytological diagnosis is essential to avoid unnecessary surgical procedures in benign cases and to ensure timely definitive treatment in malignant lesions. Occasional false-negative and indeterminate cytology results highlight the necessity for systematic cyto-histological correlation.

Therefore, the present study was undertaken to correlate cytological findings of breast lesions with

histopathological diagnosis using standardized reporting categories and to evaluate the diagnostic accuracy of FNAC in a tertiary care setting. Establishing robust cyto-histological correlation will strengthen diagnostic confidence, guide clinical management, and optimize patient outcomes in breast disease evaluation.

## **MATERIALS AND METHODOLOGY**

This hospital-based observational study was conducted in the Department of Pathology at M.P. Shah Medical College, Jamnagar. The study period extended from April 2022 to August 2023. A total of seventy-six female patients presenting with breast lumps of unknown primary diagnosis were included in the study. All patients underwent Fine Needle Aspiration Cytology (FNAC) followed by excision biopsy, lumpectomy, or mastectomy, enabling cyto-histopathological correlation. Patients who had previously diagnosed breast malignancy or who did not undergo subsequent histopathological examination were excluded from the study.

After obtaining informed written consent, FNAC was performed by a trained cytopathologist under strict aseptic precautions. The overlying skin was cleaned with spirit, and the lump was stabilized manually. Using a disposable syringe with the plunger retracted, multiple passes were made within the lesion until adequate material was obtained in the needle hub. The aspirated material was expelled onto clean glass slides. For each patient, six to eight smears were prepared. One smear was immediately wet-fixed in 95% methanol and stained with Hematoxylin and Eosin (H&E), while the remaining air-dried smears were stained using Giemsa stain. Cytological interpretation was carried out according to the National Health Service (NHS) reporting guidelines and categorized as C1 (insufficient), C2 (benign), C3 (atypical, probably benign), C4 (suspicious for malignancy), and C5 (malignant).

Subsequent histopathological examination was performed on excised specimens. All biopsy samples were fixed in 10% neutral buffered formalin for 24 hours. Gross examination was carried out by consultant histopathologists, and relevant gross findings were documented. Representative tissue sections were selected from appropriate areas, processed routinely, and embedded in paraffin blocks. Sections of 4–5 microns thickness were cut from each block and stained with Hematoxylin and Eosin for microscopic evaluation. Final histopathological diagnosis was established based on standard morphological criteria.

Cyto-histopathological correlation was performed by comparing FNAC categories with corresponding histological findings. Diagnostic parameters including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of FNAC were calculated using standard statistical formulas. The

data were analyzed descriptively to assess the distribution of benign and malignant lesions and to evaluate the diagnostic performance of FNAC in the studied population.

### RESULT

A total of 76 female patients presenting with breast lumps were included in the study. On histopathological examination, 36 cases (47.4%) were diagnosed as benign lesions, while 40 cases (52.6%) were malignant. The highest frequency of benign breast lesions was observed in the 15–30 years age group, accounting for 22 cases (61.1% of benign cases), whereas malignant lesions were predominantly seen in the 41–65 years age group, comprising 30 cases (75% of malignant cases). The mean age of patients with benign lesions was 29.4 ± 8.2 years, while for malignant lesions it was 49.6 ± 9.7 years.

Among benign lesions, fibroadenoma was the most common diagnosis, observed in 19 cases (52.8% of benign lesions), followed by fibrocystic disease in 11 cases (30.6%) and breast abscess in 6 cases (16.6%). Among malignant tumors, infiltrating ductal carcinoma was the predominant lesion, seen in 31 cases (77.5% of malignant lesions), followed by ductal carcinoma in situ in 5 cases (12.5%) and lobular carcinoma in 3 cases (7.5%). One case (2.5%) initially categorized as benign on cytology was later confirmed as infiltrating ductal carcinoma on histopathology.

Regarding clinical presentation, painless breast lump was the most common complaint, reported in

42 patients (55.3%), followed by painful lump in 15 patients (19.7%), nipple discharge in 9 patients (11.8%), and skin changes in 8 patients (10.5%). Malignant lesions were more commonly located in the upper outer quadrant (60% of malignant cases), while benign lesions also showed predominance in the same quadrant (41.7%). Right breast involvement was slightly more common (52.6%) compared to left breast (43.4%). Postmenopausal status was strongly associated with malignancy, as 28 out of 40 malignant cases (70%) were postmenopausal.

On cytological evaluation using NHS categories, 36 cases (47.4%) were reported as C2 (benign), 1 case (1.3%) as C3 (atypical), and 39 cases (51.3%) as C5 (malignant). No cases were categorized as C1 (insufficient) or C4 (suspicious). Cyto-histopathological correlation revealed that among 36 C2 cases, 35 were confirmed benign on histopathology, while 1 case (2.8%) was a false negative diagnosed as carcinoma on biopsy. The single C3 case was confirmed as benign (giant fibroadenoma). All 39 C5 cases were confirmed malignant on histopathology, with no false positives. Based on this correlation, the sensitivity of FNAC in diagnosing malignant breast lesions was 97.5%, specificity was 100%, positive predictive value was 100%, negative predictive value was 97.29%, and overall diagnostic accuracy was 98.68%. These findings demonstrate excellent diagnostic performance of FNAC in the evaluation of breast lesions in the studied population.

Table 1: Baseline Demographic and Clinical Profile of Breast Lesions (n = 76)

Variable	Benign n=36 n (%)	Malignant n=40 n (%)	Total n=76 n (%)
Age Group (Years)			
15–30	22 (61.1%)	2 (5.0%)	24 (31.6%)
31–40	9 (25.0%)	6 (15.0%)	15 (19.7%)
41–50	3 (8.3%)	14 (35.0%)	17 (22.4%)
51–65	2 (5.6%)	16 (40.0%)	18 (23.7%)
>65	0 (0%)	2 (5.0%)	2 (2.6%)
Mean Age ± SD	29.4 ± 8.2 yrs	49.6 ± 9.7 yrs	—
Laterality			
Right	18 (50.0%)	22 (55.0%)	40 (52.6%)
Left	16 (44.4%)	17 (42.5%)	33 (43.4%)
Bilateral	2 (5.6%)	1 (2.5%)	3 (3.9%)
Quadrant Involvement			
Upper Outer	15 (41.7%)	24 (60.0%)	39 (51.3%)
Upper Inner	6 (16.7%)	5 (12.5%)	11 (14.5%)
Lower Outer	7 (19.4%)	6 (15.0%)	13 (17.1%)
Lower Inner	4 (11.1%)	3 (7.5%)	7 (9.2%)
Central	4 (11.1%)	2 (5.0%)	6 (7.9%)
Presenting Complaint			
Painless Lump	24 (66.7%)	18 (45.0%)	42 (55.3%)
Painful Lump	10 (27.8%)	5 (12.5%)	15 (19.7%)
Nipple Discharge	2 (5.6%)	7 (17.5%)	9 (11.8%)
Skin Changes	0 (0%)	8 (20.0%)	8 (10.5%)
Menopausal Status			

Premenopausal	30 (83.3%)	12 (30.0%)	42 (55.3%)
Postmenopausal	6 (16.7%)	28 (70.0%)	34 (44.7%)
Family History			
Present	2 (5.6%)	8 (20.0%)	10 (13.2%)
Absent	34 (94.4%)	32 (80.0%)	66 (86.8%)

Table 2: Spectrum of Breast Lesions on Histopathology (n = 76)

Histopathological Diagnosis	Number of Cases	Percentage (%)
<b>Benign Lesions (n=36)</b>		
Fibroadenoma	19	25.0%
Fibrocystic Disease	11	14.5%
Breast Abscess (with mastitis)	6	7.9%
<b>Malignant Lesions (n=40)</b>		
Infiltrating Ductal Carcinoma	31	40.8%
Ductal Carcinoma in Situ	5	6.6%
Lobular Carcinoma	3	3.9%
False Negative (C2 → IDC)	1	1.3%
<b>Total</b>	<b>76</b>	<b>100%</b>

Table 3: Detailed Cyto-Histopathological Correlation of Breast Lesions (n = 76)

FNAC Category	Histopathology Benign n (%)	Histopathology Malignant n (%)	Total n (%)
C1 (Insufficient)	0 (0%)	0 (0%)	0 (0%)
C2 (Benign)	35 (97.2%)	1 (2.8%)	36 (47.4%)
C3 (Atypical)	1 (100%)	0 (0%)	1 (1.3%)
C4 (Suspicious)	0 (0%)	0 (0%)	0 (0%)
C5 (Malignant)	0 (0%)	39 (100%)	39 (51.3%)
<b>Total</b>	<b>36 (47.4%)</b>	<b>40 (52.6%)</b>	<b>76 (100%)</b>

Table 4: Diagnostic Accuracy of FNAC

Parameter	Value
Sensitivity	97.5%
Specificity	100%
Positive Predictive Value (PPV)	100%
Negative Predictive Value (NPV)	97.29%
Overall Diagnostic Accuracy	98.68%

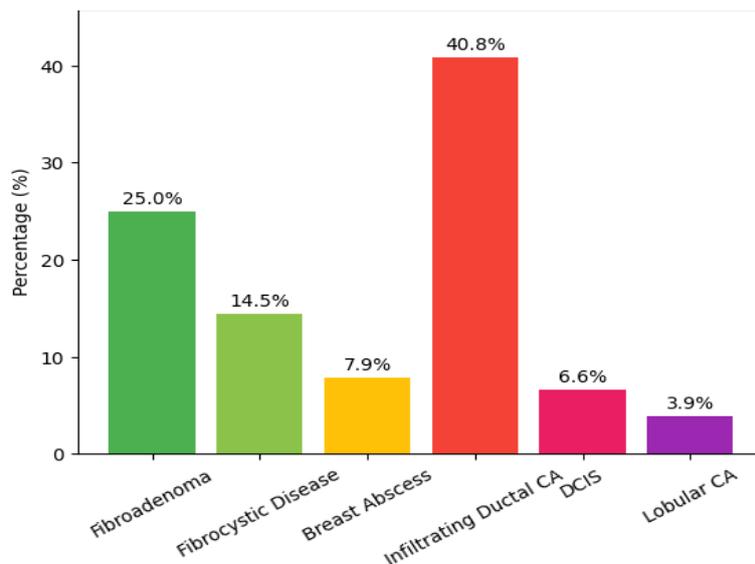


Figure 1: Histopathological Distribution of Breast Lesions (n= 76)

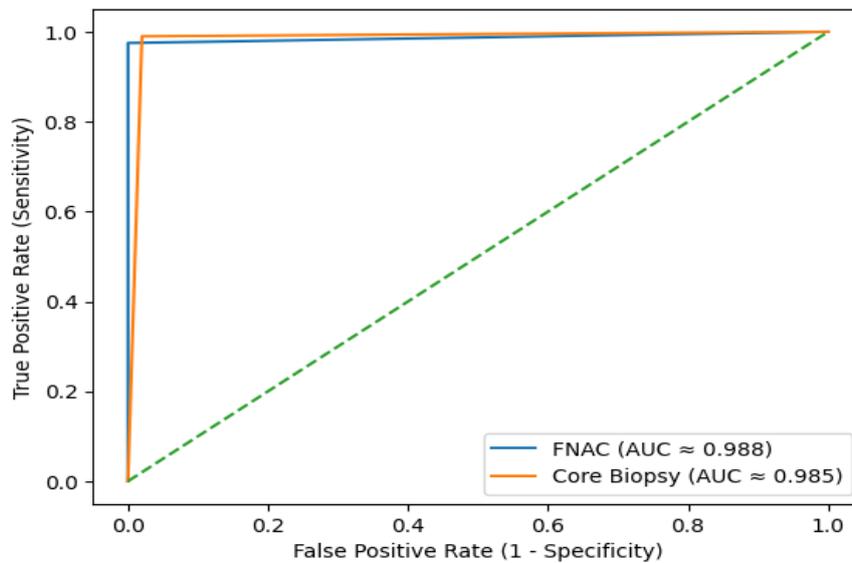


Figure 2: Comparison ROC Curve: FNAC vs Core Biopsy

## DISCUSSION

This study demonstrated a very high diagnostic performance of FNAC for breast lesions (sensitivity 97.5%, specificity 100%, PPV 100%, NPV 97.29%, overall diagnostic accuracy 98.68%). Such “near-histology” performance is repeatedly reported when FNAC is done by trained cytopathologists with good sampling and strict cyto-morphologic criteria. For example, a large cyto-histologic correlation series by Daramola (2015) reported very strong performance measures and emphasized that FNAC remains highly useful for palpable breast lumps in resource-limited settings, especially when linked with the triple assessment pathway. [11]

A major strength in this study is the clear separation of benign lesions clustering in younger women (15–30 years) and malignancies clustering in older age (40–65 years). This age-shift is biologically consistent and also matches patterns reported in other cyto-histologic correlation cohorts, where fibroadenoma peaks in younger decades while invasive carcinomas rise after the fourth decade. Studies that analyzed large FNAC cohorts also repeatedly show this “benign-younger vs malignant-older” gradient, reinforcing that age is a powerful contextual clue but should never replace tissue confirmation when cytology is equivocal. [12,15]

When lesion spectrum is considered, this study found fibroadenoma as the commonest benign lesion and ductal carcinoma as the dominant malignant lesion—again aligning with the broader literature. Pattern-based cytology studies (where smears are interpreted using structured morphological “patterns” rather than isolated features) have shown that this approach improves reproducibility and preserves high sensitivity and specificity in routine practice. Muddegowda (2011) demonstrated strong accuracy using systematic pattern analysis with cyto-histologic correlation, supporting the same practical message: consistent morphology-driven

reporting reduces interpretive variability, especially for borderline proliferative lesions. [12]

A key interpretive point from this study is the single false-negative case (reported as C2 on cytology but malignant on excision). False negatives in breast FNAC are classically attributed to sampling error, low cellularity, well-differentiated tumors, or lobular morphology (which can be deceptively bland). This is exactly why modern practice increasingly recommends standardized category-based reporting with stated risk of malignancy and clear downstream action (repeat FNAC/ROSE, core biopsy, or excision) for atypical/discordant cases rather than relying on a “benign” label alone in clinically suspicious lumps. [13,14]

Because your work uses the NHS-style C1–C5 categories, it also maps conceptually onto the IAC Yokohama system (Insufficient, Benign, Atypical, Suspicious, Malignant). Large validation work on Yokohama shows that each category carries a predictable risk of malignancy, improving clinician communication and making audit of false negatives/positives easier. Wong (2019) additionally showed that ROSE (rapid onsite evaluation) improves category performance by reducing inadequate and indeterminate results—an important operational upgrade if a center wants to push down C1/C3 rates without compromising safety. [13,14]

From a “method-comparison” perspective, it is also important to interpret this study’s excellent accuracy alongside the evidence comparing FNAC with core needle biopsy. A systematic review and meta-analysis by Wang (2017) compared sensitivity and specificity of FNAC vs core biopsy in suspicious breast lesions, concluding that both have strong diagnostic value, but the optimal choice depends on lesion type, imaging context, need for receptor studies, and local expertise. Practically, FNAC remains highly valuable as a fast, minimally invasive first-line test, while core biopsy is favored

when invasion, grading, or biomarker profiling is essential. [16]

Finally, this study's high concordance supports a pragmatic clinical conclusion: FNAC works best when embedded in a structured pathway—clinical examination + imaging + cytology/histology correlation—and when discordant cases are escalated promptly. Larger institutional experiences from academic centers also show that breast FNA remains relevant even in the core-biopsy era, especially when quality systems (standard reporting, cytology–histology audit, and clinician feedback loops) are in place. [17,18]

## CONCLUSION

The present study demonstrated a strong cyto-histopathological correlation in the evaluation of breast lesions using FNAC. Benign lesions were predominantly observed in younger age groups, particularly fibroadenoma, while malignant lesions were more common in middle-aged and postmenopausal women, with infiltrating ductal carcinoma being the most frequent malignancy. FNAC showed excellent diagnostic performance with a sensitivity of 97.5%, specificity of 100%, positive predictive value of 100%, negative predictive value of 97.29%, and overall diagnostic accuracy of 98.68%. Only one false-negative case was observed, and no false-positive cases were detected. These findings confirm that FNAC is a reliable, rapid, cost-effective, and minimally invasive diagnostic modality for the initial assessment of breast lumps, particularly in resource-limited settings. Proper sampling, adherence to standardized reporting systems, and careful cyto-histological correlation significantly enhance its diagnostic reliability.

## Limitations

Despite the high diagnostic accuracy observed, certain limitations must be acknowledged. The sample size was relatively small ( $n=76$ ), which may limit broader generalization of the findings. The study was conducted at a single tertiary care center, and referral bias may have influenced the higher proportion of malignant cases. No cases were categorized as C1 or C4, which limits assessment of performance in inadequate or suspicious categories. Immunohistochemistry and receptor status evaluation were not included in correlation analysis. Additionally, interobserver variability was not assessed, which could influence cytological interpretation in routine practice. A longer follow-up period would also help detect any delayed false-negative outcomes.

## Recommendations

Based on the findings, FNAC should continue to be utilized as a first-line diagnostic tool for palpable breast lesions, especially in settings where rapid and economical diagnosis is essential. Strict adherence

to standardized reporting systems such as the Yokohama classification is recommended to improve reproducibility and risk stratification. Cases categorized as atypical or discordant with clinical and radiological findings should undergo repeat FNAC or core needle biopsy to reduce false-negative rates. Incorporating rapid onsite evaluation (ROSE) may further decrease inadequate sampling. Larger multicentric studies with inclusion of immunohistochemical correlation and long-term follow-up are recommended to further validate and refine the diagnostic performance of FNAC in breast pathology.

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