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Original Article

Correlation of Cytological and Histopathological Findings in Breast Lesions

Dr Navreet[1], Rajul Rastogi[2]
1 Department of Pathology, Tertiary Care Teaching Hospital and Medical College
2 Department of Pathology, Tertiary Care Teaching Hospital and Medical College

Corresponding Author:

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Abstract-

Fine needle aspiration cytology (FNAC) is a rapid, minimally invasive, and cost-effective first-line investigation for the evaluation of palpable breast lesions. Histopathological examination of the excised specimen remains the gold standard, and correlation between the two is essential to validate the diagnostic reliability of cytology in routine practice. **Objective:** To correlate cytological findings on FNAC, categorised according to the International Academy of Cytology (IAC) Yokohama System, with histopathological diagnosis in patients presenting with breast lesions, and to determine the sensitivity, specificity, and diagnostic accuracy of FNAC. **Methods:** This prospective study was conducted over 18 months and included 150 patients with palpable breast lesions who underwent FNAC followed by histopathological examination of the excised specimen. FNAC smears were categorised into five IAC Yokohama categories (C1–C5), and findings were compared with the final histopathological diagnosis taken as the gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated. **Results:** Fibroadenoma was the most common benign lesion on histopathology (38.7%), and invasive ductal carcinoma the most common malignant lesion (21.3%). Overall cytohistological concordance was 96.0% (144/150). Considering C4 and C5 categories as positive for malignancy, FNAC demonstrated a sensitivity of 94.9%, specificity of 99.0%, positive predictive value of 97.4%, negative predictive value of 98.1%, and an overall diagnostic accuracy of 97.9%. Discordance was largely confined to fibroepithelial and atypical lesions, where cytomorphological overlap between cellular fibroadenoma and low-grade phyllodes tumour, or between proliferative breast disease with atypia and carcinoma, accounted for most discrepant cases. **Conclusion:** FNAC shows excellent correlation with histopathology and remains a highly sensitive and specific first-line diagnostic modality for breast lesions. However, given the recognised diagnostic overlap in fibroepithelial and atypical categories, histopathological confirmation remains essential before definitive surgical management, particularly in cytologically equivocal cases.

Keywords: *Breast lesions; Fine needle aspiration cytology; Histopathology; Cytohistological correlation; IAC Yokohama System; Fibroadenoma.*

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer among women worldwide and the leading cause of cancer-related death in women in many regions, with an estimated 2.29 million new cases recorded globally in 2022, accounting for 11.5% of all cancer diagnoses (1). In India, breast cancer has overtaken cervical cancer to become the most common malignancy among women, with approximately 192,000 new cases reported in a single year, representing a substantial proportion of the overall cancer burden in the country (1,2). Against this backdrop, the rapid and accurate diagnostic evaluation of palpable breast lumps is of considerable clinical importance, both to expedite appropriate management of malignant lesions and to avoid unnecessary surgical intervention for the many benign conditions that present similarly.

Fine needle aspiration cytology (FNAC) has, for several decades, occupied a central role in the pre-operative triage of breast lesions, forming one component of the 'triple assessment' alongside clinical examination and imaging (3). Its principal advantages lie in its simplicity, low cost, minimal invasiveness, and the ability to provide a same-day or near-immediate preliminary diagnosis in an outpatient setting, thereby guiding further management without the need for an initial surgical procedure (3,4). However, FNAC is not without limitations: cytomorphological overlap between certain benign and malignant entities, particularly fibroepithelial lesions such as fibroadenoma and phyllodes tumour, and the

diagnostically challenging category of proliferative breast disease with atypia, can give rise to discordant results that necessitate cytohistological correlation to validate diagnostic accuracy (3,5).
To address the historical inconsistency in breast cytology reporting terminology, the International Academy of Cytology (IAC) introduced the Yokohama System for Reporting Breast Cytopathology, which standardises FNAC findings into five categories: C1 (insufficient/inadequate), C2 (benign), C3 (atypical, probably benign), C4 (suspicious for malignancy), and C5 (malignant) (6,7). This system assigns each category an associated risk of malignancy (ROM) and a corresponding suggested clinical management pathway, and has been shown in several validation studies to improve diagnostic accuracy and inter-observer reproducibility compared with earlier, non-standardised reporting practices (8,9).

Numerous studies correlating FNAC with histopathology, taken as the reference gold standard, have consistently demonstrated high diagnostic performance for breast cytology. A study correlating FNAC, cell-block, and histopathological diagnosis of breast lesions reported a sensitivity of 94.5%, specificity of 100%, PPV of 100%, and NPV of 97.0%, with the principal discordance arising from a case of proliferative breast disease with atypia that was subsequently diagnosed as invasive ductal carcinoma on histopathology (10). Similarly, a study of 125 cases found 98.4% concordance between FNAC and histopathology, with a sensitivity of 91.66%, specificity of 100%, and overall diagnostic accuracy of 98.4% (11). A study applying systematic pattern analysis to FNAC smears of breast lesions, correlated with histopathology in 225 cases, reported a sensitivity of 94.5%, specificity of 98%, and diagnostic accuracy of 97% (12). Meta-analytic data spanning multiple studies have shown that, when unsatisfactory samples are excluded, FNAC achieves a pooled sensitivity of approximately 92.7% and specificity of approximately 94.8% for the diagnosis of breast malignancy (13).

Despite this generally favourable diagnostic performance, the literature consistently identifies specific categories of cytohistological discordance, particularly involving fibroepithelial lesions and lesions showing epithelial atypia, where sampling limitations and cytomorphological overlap can lead to either false-negative or false-positive cytological interpretation (5,9,14). Continued correlation of FNAC with histopathology, ideally using the standardised IAC Yokohama categorisation, therefore remains essential both to monitor and benchmark local diagnostic performance and to identify recurring patterns of discordance that may inform refinements in cytological interpretation. The present study was undertaken to correlate FNAC findings, categorised according to the IAC Yokohama System, with histopathological diagnosis in patients with palpable breast lesions, and to determine the sensitivity, specificity, and overall diagnostic accuracy of FNAC at our centre.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted in the Department of Pathology at a tertiary care teaching hospital and medical college over a period of 18 months, following approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrolment.

Study Population

All patients presenting with a palpable breast lump to the surgical outpatient department, who subsequently underwent FNAC followed by surgical excision (lumpectomy, wide local excision, or mastectomy) with histopathological examination of the excised specimen, were considered for inclusion. A total of 150 patients in whom both FNAC and a corresponding histopathological specimen were available for correlation were enrolled consecutively. Patients in whom FNAC was performed but no subsequent histopathological specimen was available, those who defaulted from follow-up or declined surgical intervention, and cases with non-breast (axillary or chest wall soft tissue) lesions were excluded.

FNAC Technique and Reporting

FNAC was performed using a 23–25 gauge needle attached to a 10 mL syringe, with the lesion immobilised between two fingers and multiple passes made in different directions to ensure adequate cellular yield. Aspirated material was expressed onto glass slides; both air-dried smears stained with May-Grünwald-Giemsa and wet-fixed smears stained with Papanicolaou and/or haematoxylin and eosin stains were prepared for each case. Smears were examined independently by two cytopathologists, with discordant readings resolved by consensus, and were categorised according to the IAC Yokohama System for Reporting Breast Cytopathology into five categories: C1 (insufficient/inadequate), C2 (benign), C3 (atypical, probably benign), C4 (suspicious for malignancy), and C5 (malignant).

Histopathological Processing

Surgically excised specimens were fixed in 10% neutral buffered formalin, grossed, and processed routinely, with paraffin-embedded sections cut at 4–5 micron thickness and stained with haematoxylin and eosin. Sections were examined by a consultant histopathologist blinded to the original cytological category at the time of microscopic evaluation, and a final histopathological diagnosis was rendered according to standard World Health Organization classification criteria for breast

tumours, with immunohistochemistry performed where required to resolve diagnostic ambiguity (for example, in differentiating cellular fibroadenoma from phyllodes tumour, or in confirming invasive carcinoma).

Statistical Analysis

Histopathological diagnosis was considered the gold standard against which FNAC findings were correlated. For the purpose of calculating diagnostic accuracy, C4 and C5 categories were considered cytologically positive for malignancy, while C2 and C3 categories were considered cytologically negative for malignancy; C1 (insufficient) cases were excluded from the 2×2 contingency analysis but were reported descriptively. Sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were calculated using standard formulae. Data were analysed using SPSS software, and categorical variables were expressed as frequencies and percentages.

RESULTS

A total of 150 patients with palpable breast lesions who underwent both FNAC and subsequent histopathological examination were included in the study. The demographic and clinical characteristics of the study population are summarised in Table 1.

Table 1. Demographic and clinical characteristics of the study population (N = 150)

Characteristic	Value	Percentage / Range
Total patients (n)	150	100%
Female	146	97.3%
Male	4	2.7%
Mean age, years (± SD)	38.6 ± 13.4	Range 14–78
Age group ≤30 years	54	36.0%
Age group 31–50 years	62	41.3%
Age group >50 years	34	22.7%
Right breast	71	47.3%
Left breast	76	50.7%
Bilateral	3	2.0%
Cases with concordant cyto-histopathological diagnosis	144	96.0%

The study population showed a marked female predominance (97.3%), with a mean age of 38.6 ± 13.4 years. Breast lesions were almost equally distributed between the right and left breast, with a small proportion of bilateral presentations. Overall cytohistological concordance was observed in 144 of 150 cases (96.0%).

Table 2. Distribution of FNAC findings according to the IAC Yokohama System for Reporting Breast Cytopathology

FNAC Category (IAC Yokohama System)	No. of Cases	Percentage (%)
C1 — Insufficient/Inadequate	6	4.0%
C2 — Benign	94	62.7%
C3 — Atypical (probably benign)	12	8.0%
C4 — Suspicious of malignancy	10	6.7%
C5 — Malignant	28	18.6%
Total	150	100.0

The majority of FNAC samples were categorised as benign (C2, 62.7%), followed by malignant (C5, 18.6%). Atypical (C3) and suspicious for malignancy (C4) categories together accounted for 14.7% of cases, reflecting the diagnostically challenging subset of lesions in which cytomorphological features did not permit confident categorisation as definitively benign or malignant. Insufficient or inadequate aspirates (C1) comprised 4.0% of the total cases.

Table 3. Spectrum of histopathological diagnoses among the study population

Histopathological Diagnosis	No. of Cases	Percentage (%)
Fibroadenoma	58	38.7%
Fibrocystic disease / fibrocystic change	16	10.7%
Benign phyllodes tumour	10	6.7%
Granulomatous mastitis / chronic mastitis	8	5.3%
Gynaecomastia	3	2.0%
Invasive ductal carcinoma (NST)	32	21.3%
Ductal carcinoma in situ	6	4.0%
Invasive lobular carcinoma	4	2.7%
Malignant phyllodes tumour	2	1.3%
Atypical ductal hyperplasia	6	4.0%
Other benign lesions (fat necrosis, galactocoele)	5	3.3%
Total	150	100.0

Fibroadenoma was the single most common histopathological diagnosis, accounting for over a third of all cases (38.7%), consistent with its recognised position as the most frequent benign breast lesion in young women. Invasive ductal carcinoma (no special type) was the most common malignant diagnosis (21.3%), followed by ductal carcinoma in situ (4.0%) and invasive lobular carcinoma (2.7%). Benign lesions collectively accounted for 66.7% of cases, while malignant and atypical/borderline lesions accounted for the remaining 33.3%.

Table 4. Cross-tabulation of FNAC categorisation versus final histopathological diagnosis (2×2 contingency table)

FNAC Diagnosis	Malignant on Histopathology	Benign on Histopathology	Total
Malignant / Suspicious (C4 + C5)	37	1	38
Benign / Atypical (C2 + C3)	2	104	106
Insufficient (C1, excluded from 2×2 analysis)	—	—	6
Total	39	105	144

Of the 144 cases included in the 2×2 contingency analysis (excluding 6 insufficient C1 cases), 37 of 39 lesions cytologically categorised as suspicious or malignant (C4/C5) were confirmed malignant on histopathology, while 104 of 106 lesions cytologically categorised as benign or atypical (C2/C3) were confirmed benign on histopathology. There was one false-positive case, in which a cellular fibroadenoma was cytologically categorised as suspicious for malignancy (C4) due to increased cellularity and mild nuclear atypia, but proved benign on histopathology. There were two false-negative cases, both initially categorised as atypical (C3) on cytology, which were subsequently diagnosed as low-grade invasive ductal carcinoma on histopathological examination.

Table 5. Diagnostic performance of FNAC in relation to histopathology (gold standard)

Statistical Parameter	Value	Fraction
Sensitivity	94.9%	(37/39)
Specificity	99.0%	(104/105)
Positive predictive value (PPV)	97.4%	(37/38)
Negative predictive value (NPV)	98.1%	(104/106)
Diagnostic accuracy	97.9%	(141/144)

False positive rate	1.0%	(1/105)
False negative rate	5.1%	(2/39)

FNAC demonstrated a sensitivity of 94.9%, specificity of 99.0%, positive predictive value of 97.4%, negative predictive value of 98.1%, and an overall diagnostic accuracy of 97.9% for distinguishing malignant from benign breast lesions, when C4 and C5 categories were considered cytologically positive for malignancy. The false-positive rate was low at 1.0%, while the false-negative rate was 5.1%, reflecting the two atypical (C3) cases that were ultimately diagnosed as malignant on histopathology.

DISCUSSION

The present study demonstrates an overall cytohistological concordance of 96.0%, with FNAC achieving a sensitivity of 94.9%, specificity of 99.0%, and diagnostic accuracy of 97.9% when compared against histopathology as the gold standard. These findings affirm the continued reliability of FNAC as a first-line diagnostic tool for breast lesions and are concordant with the substantial existing body of comparative literature on this subject (10,11,12).

Our sensitivity and specificity figures closely parallel those reported in a prospective study correlating cytological, cell-block, and histopathological diagnosis of breast lesions, which found a sensitivity of 94.5%, specificity of 100%, PPV of 100%, and NPV of 97.0% (10), as well as a separate correlation study of 125 cases that reported a sensitivity of 91.66%, specificity of 100%, and an overall accuracy of 98.4% (11). The application of systematic pattern analysis to FNAC smears in another large series of 225 cytohistologically correlated cases similarly yielded a sensitivity of 94.5%, specificity of 98%, and diagnostic accuracy of 97%, figures that are virtually indistinguishable from those obtained in our cohort (12). This consistency across multiple independent studies, despite differences in patient population, sample size, and reporting methodology, underscores the robustness and reproducibility of FNAC as a diagnostic tool for breast lesions when performed and interpreted by experienced personnel.

The distribution of histopathological diagnoses in our study, with fibroadenoma as the most common benign lesion and invasive ductal carcinoma as the most common malignant lesion, mirrors the pattern consistently described in the literature on breast lesion spectra. A study applying the IAC Yokohama classification system similarly identified fibroadenoma as the most common benign lesion (56.06%) and ductal carcinoma as the most common malignant lesion (96.15% of malignant cases) (8), while comparable proportions of fibroadenoma and ductal carcinoma as the leading benign and malignant diagnoses, respectively, have been reported in several other Yokohama-based correlation studies (9,14). This consistency reflects the relatively stable epidemiological pattern of breast disease across populations, with fibroadenoma predominating in younger women and invasive carcinoma in older age groups.

The discordant cases identified in our series were instructive and consistent with previously described patterns of diagnostic difficulty. The single false-positive case arose from a cellular fibroadenoma misclassified as suspicious for malignancy due to increased cellularity and nuclear atypia, a recognised pitfall given the well-documented cytomorphological overlap between cellular fibroadenoma, phyllodes tumour, and low-grade carcinoma on FNAC smears (5,9). Similarly, both false-negative cases in our study arose from the atypical (C3) category, in which proliferative breast disease with atypia was subsequently diagnosed as carcinoma on histopathology — a discordance pattern that has been specifically highlighted in previous correlation studies as the principal source of cytohistological discrepancy in breast FNAC (10,14). This recurring vulnerability of the atypical category across multiple independent studies reinforces the IAC Yokohama System's own categorisation of C3 lesions as carrying an intermediate but non-trivial risk of malignancy, for which histopathological confirmation, rather than cytology alone, should guide definitive management (6,9).

Limitations of the present study include its single-centre design and the inherent selection bias of including only those patients in whom histopathological correlation was subsequently available, which may exclude lesions managed conservatively without surgical excision and could therefore modestly overestimate diagnostic performance relative to the true clinical population. The relatively small number of cases in the atypical and suspicious categories also limits the precision of category-specific risk-of-malignancy estimates. Larger, multicentre studies with longer follow-up of cytologically benign cases managed conservatively would further strengthen the generalisability of these findings.

CONCLUSION

FNAC demonstrates excellent correlation with histopathology in the evaluation of breast lesions, with high sensitivity, specificity, and overall diagnostic accuracy in the present study. Use of the standardised IAC Yokohama System for Reporting Breast Cytopathology facilitates consistent categorisation and risk stratification, supporting its continued role as a reliable, rapid, and cost-effective first-line investigation in the diagnostic work-up of palpable breast lesions. However, given the recognised cytomorphological overlap in fibroepithelial and atypical lesions, cytological findings in these

categories should be interpreted with caution, and histopathological correlation remains essential before definitive surgical decision-making.

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