ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 18, Issue 12, 2025

Online - 2455-3891
Print - 0974-2441

Research Article

HARMONIZING THE TAPESTRY OF BREAST LESIONS IN WOMEN: AN INTEGRATED EXPLORATION OF CLINICAL, RADIOLOGICAL, CYTOLOGICAL, HISTOPATHOLOGICAL, AND IMMUNOHISTOCHEMICAL PATTERNS

SANGEETHA NAGALINGAM[1], BALAJI VENKATARAMAN[2], SWETHA MURALIDHARAN[1]

[1]Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Chengalpattu, Tamil Nadu, India.
[2]Department of Surgery, Chengalpattu Medical College and Hospital, Chengalpattu, Tamil Nadu, India.
*Corresponding author: Sangeetha Nagalingam; Email: sangeethanagalingam86@gmail.com

Received: 14 August 2025, Revised and Accepted: 09 October 2025

ABSTRACT

Objectives: The study aimed to evaluate and compare the diagnostic validity of clinical examination, radiological imaging, Breast Imaging Reporting and Data System (BIRADS), and cytological examination in women presenting with breast lumps, using histopathology as the gold standard.

Methods: A cross-sectional study was conducted among 96 women with palpable breast lumps at a tertiary teaching hospital over a 2-year period. Each patient underwent clinical examination, mammography (BIRADS scoring), and fine-needle aspiration cytology. The triple test scores were analyzed for diagnostic concordance, and histopathological examination was performed in all cases. Statistical analysis included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and 95% confidence intervals (CIs).

Results: Among 96 participants, 61 (63.5%) had benign and 35 (36.5%) had malignant lesions confirmed histopathologically. Clinical diagnosis showed the highest sensitivity (93.5%; 95% CI: 78.6–98.2), cytology showed perfect specificity (100%; 95% CI: 94.1–100), and radiology demonstrated moderate sensitivity (77.4%; 95% CI: 59.2–88.7) and specificity (96.9%; 95% CI: 88.2–99.5). The triple test achieved an overall concordance rate of 83.3%. PPV and NPV for clinical, radiological, and cytological evaluations were 93.5%, 77.4%, 100%, and 96.9%, 96.9%, 100%, respectively.

Conclusion: The triple assessment method provides a highly accurate, non-invasive, and cost-effective diagnostic approach for breast lumps. Clinical examination and cytology together offer optimal diagnostic reliability. Integrating histopathology and immunohistochemistry enhances diagnostic precision and guides treatment, particularly in resource-limited settings.

Keywords: Breast lump, Breast imaging reporting and data system, Fine-needle aspiration cytology, Histopathology, Triple test, Diagnostic validity.

 DOI: http://dx.doi.org/10.22159/ajpcr.2025v18i12.57255. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Breast lumps are one of the most common presenting complaints among women across all age groups. Defined as localized swellings or masses differing from surrounding breast tissue, lumps can be cystic or solid and may be benign or malignant. Their clinical presentation varies, often accompanied by pain, nipple discharge, or skin changes. In women with dense breast tissue, smaller or deeper lumps may be difficult to detect.

In India, benign breast lesions account for 1.5 out of every 1000 hospital admissions among women, with fibroadenoma being the most common, followed by fibrocystic disease, phyllodes tumor, and fibroadenosis. Fine-needle aspiration cytology (FNAC), a minimally invasive outpatient procedure, is easy, cost-effective, and produces speedy and accurate results when properly administered. Inadequacies in each of these individual tests have led to a combined approach, known as the triple test, which includes clinical, radiological, and cytological assessment. By providing an accurate pre-operative diagnosis, the triple test helps clinicians design appropriate treatment plans. Follow-up immunohistochemical methods can then be used to confirm morphological diagnoses [1,2].

Many studies evaluating breast lumps use single diagnostic methods. Only a few use a multidisciplinary approach (e.g., clinical, radiological, cytological, histopathological, and immunohistochemical methods) to diagnose and differentiate breast lumps. The present study thus aimed to compare the surgical ward admissions, and 8.1 out of 1000 of admissions of female patients [2]. A recent review of breast pathologies shows fibroadenoma to be the most common lesion type, followed by cystosarcoma phyllodes, fibrocystic disease, inflammatory lesions, and fibroadenosis [3]. Early and accurate diagnosis is critical for distinguishing malignant from benign conditions and guiding management strategies. Diagnostic tools include breast self-examination, clinical breast examination, mammography, and FNAC. Each modality, while useful, has limitations when used independently. The triple assessment method, combining clinical, radiological, and cytological evaluation, has emerged as a reliable approach, improving pre-operative accuracy and minimizing diagnostic errors.

Objectives

This study aimed to assess the diagnostic validity of clinical, radiological, and cytological evaluations in detecting benign and malignant breast lesions, using histopathological examination as the gold standard. The central hypothesis was that the combined triple test provides higher diagnostic accuracy than any individual component.

METHODS

Study design and setting

A hospital-based cross-sectional study was conducted in the Department of Pathology, [Chennai Medical College Hospital and Research Centre, Irungalur, Trichy], from study period of two years.

Sample size

A total of 96 women presenting with palpable breast lumps were included.

Ethical approval
The study was approved by the Institutional Animal and Human Ethics Committee (IEC Approval No: IEC/2021/105) (Figs. 1 and 2). Informed consent was obtained from all participants; for minors, parental consent was obtained (Fig. 3).

Inclusion criteria
Female patients of any age presenting with palpable breast lumps.

Patients who consent to all diagnostic procedures (clinical, radiological, cytological, and histopathological).

Exclusion criteria
Patients with recurrent breast disease or post-surgical breast changes (Figs. 4-7).

Patients with incomplete diagnostic data.

Triple test evaluation
Each patient underwent:
1. Clinical examination: Performed by a single experienced examiner through inspection and palpation of both breasts and axillae.
2. Radiological assessment: Mammography findings were scored using the Breast Imaging Reporting and Data System (BIRADS) classification (0–5).
3. Cytological assessment: FNAC was performed, and smears were stained with Papanicolaou and Giemsa stains.

Histopathological and immunohistochemistry (IHC) evaluation
All specimens underwent Hematoxylin and Eosin staining and were graded using the Modified Scarff-Bloom–Richardson system. Malignant cases were further analyzed for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2/neu using IHC.

Triple test scoring
Each component was scored: 1 – Benign, 2 – suspicious, 3 – malignant.

Scores of 3 (benign concordance) or 9 (malignant concordance) indicated agreement; all other scores were deemed discordant.

Statistical analysis
Data were analyzed using the Statistical Package for the Social Sciences v26. Diagnostic validity parameters – sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and 95% confidence intervals (CI) – were calculated. Mean ± standard deviation (SD) was used for continuous variables.

RESULTS

The majority of participants (44.8%) were in the 20–40 years age group, representing the peak age range for benign breast diseases such as fibroadenoma. Only 12.5% of participants were below 20 years, whereas another 12.5% were above 60 years, where the likelihood of malignancy increases. The mean age of presentation was 41.2±13.7 years, aligning with previous epidemiological studies in similar populations (Table 1).

Fibroadenoma was the most frequently diagnosed lesion clinically, accounting for 57.3% of all cases, consistent with its known high prevalence among women under 40 years. Carcinoma was clinically suspected in 32.3% of patients, indicating a significant proportion of potentially malignant presentations in this cohort (Table 2). Fibroadenosis and phyllodes tumors were infrequent, comprising 5.2% and 3.1%, respectively.

BIRADS 2 (benign) lesions were the most common (40.6%), followed by BIRADS 5 (highly suggestive of malignancy) at 26.1%. The relatively small proportion of BIRADS 3 and 4 (15.6% and 5.2%, respectively) indicates that most radiological findings were clearly benign or malignant (Table 6). The presence of 9.4% of cases categorized as BIRADS 0 (incomplete assessment) reflects limitations due to dense parenchyma or inconclusive mammographic features (Table 3).

Fibroadenoma accounted for nearly half (48%) of cytological findings, confirming its clinical predominance.

Duct papilloma was identified in 25% of cases – an unusually high frequency, suggesting potential overrepresentation of ductal proliferative changes in cytological sampling. Carcinoma constituted 16.6% of cytological diagnoses, correlating closely with histopathological outcomes (Table 4). The absence of duct papilloma in histopathology (Table 5) suggests possible cytological misclassification, which warrants mention in the discussion.

Histopathology confirmed fibroadenoma in 46.8% of cases and invasive carcinoma in 30.2%, closely matching clinical suspicion. Fibrocystic disease and fibroadenosis together comprised approximately 11.3%

Table 1: Age distribution in the present study

Age group in years	Frequency	Percentages
<20	12	12.5
20–40	43	44.8
41–60	29	30.2
>60	12	12.5

Table 2: Clinical diagnosis of lesion

Lesion type	Frequency	Percentages
Fibrocystic disease	2	2.1
Fibroadenosis	5	5.2
Fibroadenoma	55	57.3
Phyllodes tumor	3	3.1
Carcinoma	31	32.3

Table 3: Radiological (BIRADS) classification

BIRADS category	Frequency	Percentages
0	9	9.4
1	3	3.1
2	39	40.6
3	15	15.6
4	5	5.2
5	25	26.1

BIRADS: Breast imaging reporting and data system

Table 4: Cytological diagnosis of lesion

Lesion	Frequency	Percentages
Fibroadenoma	46	48
Duct papilloma	24	25
Fibrocystic disease	10	10.4
Carcinoma	16	16.6

Table 5: Histopathological diagnosis of lesion

Lesion	Frequency	Percentages
Fibroadenoma	45	46.8
Fibrocystic disease	7	7.2
Fibroadenosis	4	4.1
Benign phyllodes	3	3.1
Invasive carcinoma	29	30.2
Others	8	8.6

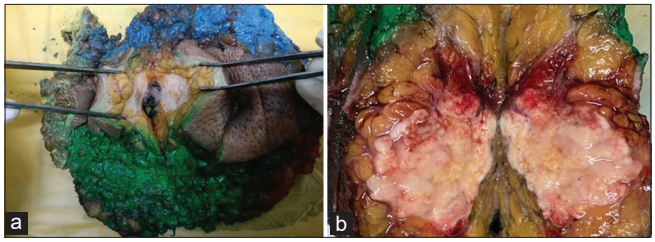

Fig. 1: Images of lesions and histopathological slides. (a and b) The modified radical mastectomy specimen shows a well-defined gray white, hard, solid mass in the central quadrant

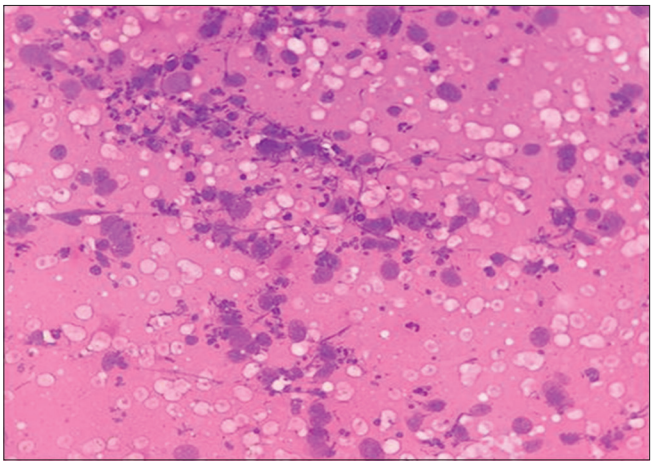

Fig. 2: Cells exhibit marked nuclear anisocytosis with pleomorphic nuclei and irregular nuclear membrane – Fine-needle aspiration, carcinoma breast (Hematoxylin and Eosin, ×40)

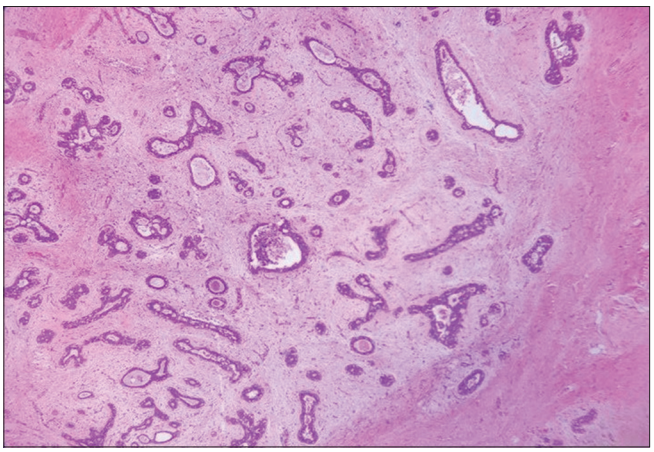

Fig. 3: Well circumscribed neoplasm with proliferating ducts compressed in intracanalicular and pericanalicular pattern by proliferating fibromyxoid stroma – fibroadenoma (Hematoxylin and Eosin, ×10)

of benign lesions. Benign phyllodes tumors represented a small subset (3.1%). "Others" included rare entities such as nodular sclerosing adenosis and atypical hyperplasias (Figs. 8-10).

Clinical examination achieved the highest sensitivity (93.5%) and a specificity of 96.9%, emphasizing its reliability in initial evaluation. Cytology demonstrated perfect specificity (100%) and no false negatives, confirming its diagnostic accuracy for malignancy. Radiological assessment showed moderate sensitivity (77.4%) but high specificity (96.9%), limited by breast density in younger women. The PPV and NPV for cytology were both 100%, underscoring its strength as a confirmatory diagnostic tool.

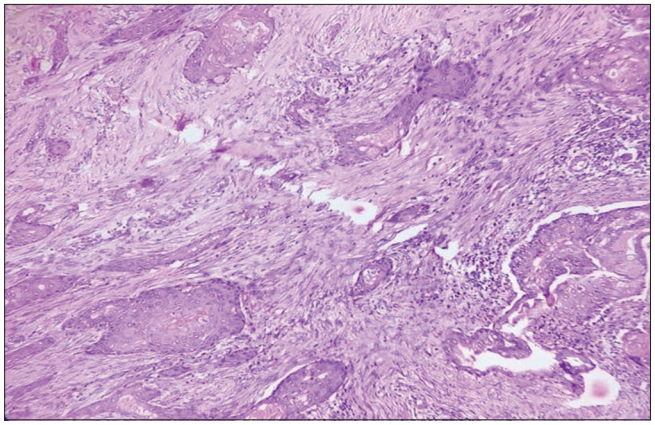

Fig. 4: Metaplastic carcinoma with 90% of tumour cells with squamoid differentiation (Hematoxylin and Eosin, ×10)

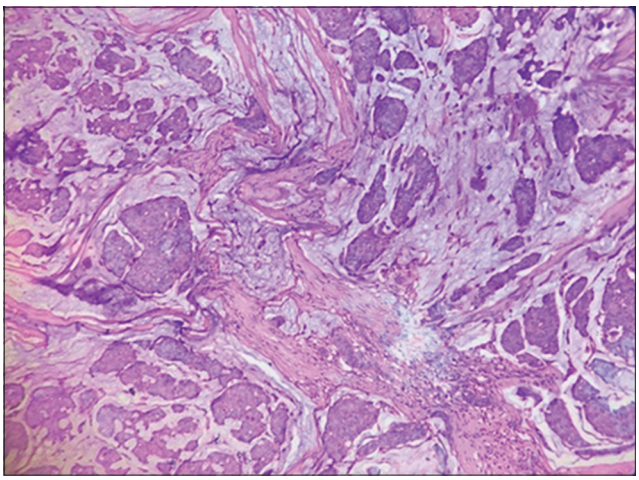

Fig. 5: Clusters of tumor cells floating in pools of extracellular mucin separated by fibrous septa – invasive mucinous carcinoma breast (Hematoxylin and Eosin, ×10)

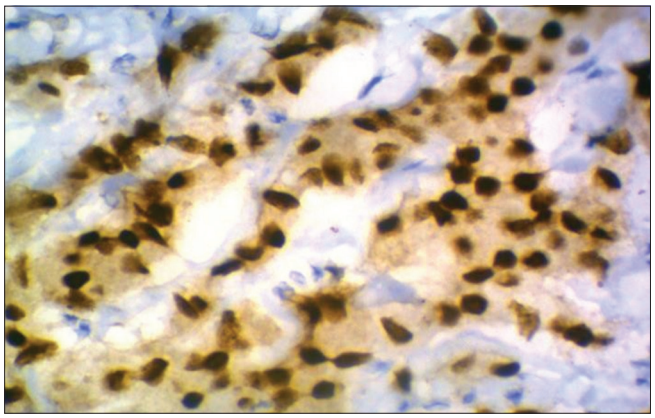

Fig. 6: Immunohistochemistry (×40) showing Estrogen receptor positivity with score 8 (Allred score)

DISCUSSION

In this study of 96 women presenting with palpable breast lumps, we found an overall concordance rate of 83.3% for the triple assessment method – a finding consistent with earlier foundational work by Morris *et al*. [5], who first demonstrated the utility of the triple test in palpable breast masses [4]. Clinical examination achieved a sensitivity of 93.5%, whereas FNAC reached a specificity of 100% in our series. Radiological

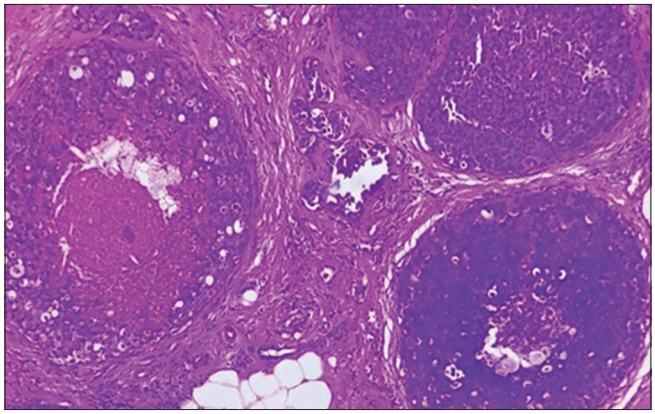

Fig. 7: Neoplastic intraductal proliferation of tumor cells, high nuclear grade with expansile comedo necrosis – Ductal Carcinoma *in situ* (Hematoxylin and Eosin, ×40)

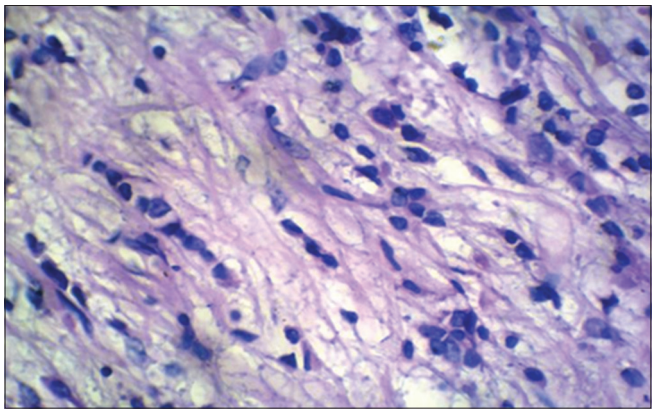

Fig. 8: Invasive lobular carcinoma (Hematoxylin and Eosin, x40)

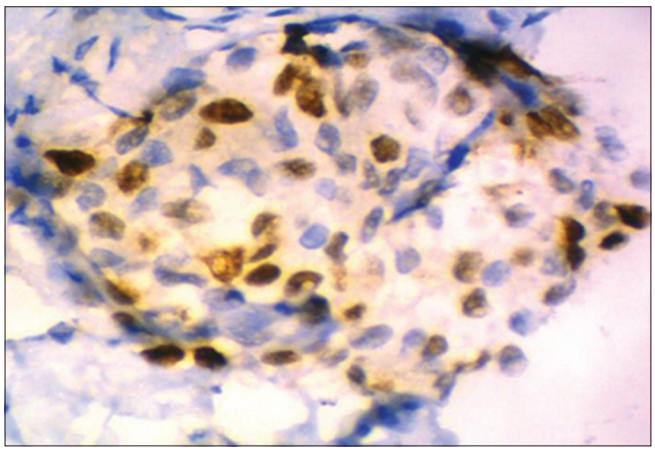

Fig. 9: Immunohistochemistry (×40) showing progesterone receptor with score 5

assessment (via BIRADS scoring) had a lower sensitivity of 77.4% but maintained high specificity at 96.9%.

Our observations are consistent with the classic findings of Morris *et al.* [5], who reported that a concordant triple test result is almost 100% accurate in distinguishing benign from malignant breast lesions. More recent evidence, such as that of Agarwal *et al.* [6], similarly emphasized the high diagnostic precision of combined clinical, radiological, and cytological assessment, reporting sensitivities above 95% and

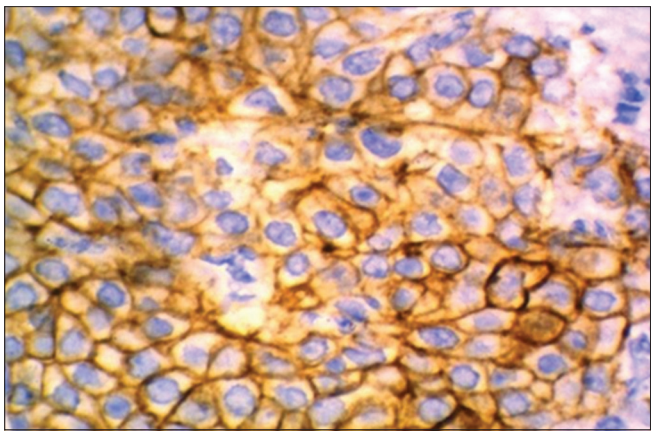

Fig. 10: Immunohistochemistry (×40) showing human epidermal growth factor receptor 2/neu with score 3 – all red scoring system

Table 6: Diagnostic validity of the study

Parameter	Clinical (%)	Radiological (%)	Cytological (%)
True positive	29	24	24
True negative	63	62	65
False positive	2	7	7
False negative	2	3	0
Sensitivity	93.50	77.40	77.40
Specificity	96.90	96.90	100
PPV	93.50	77.40	100
NPV	96.90	96.90	100

PPV: Positive predictive value, NPV: Negative predictive value

specificities exceeding 90%. Our results for cytology align with more recent work. The perfect specificity in our FNAC results underscores its role as a rule-in test for malignancy, indicating that when FNAC finds malignancy, it is very reliable – but we must acknowledge that sensitivity may be variable based on operator and institutional factors.

The somewhat lower sensitivity of radiological assessment observed in our cohort is compatible with clinical experience showing decreased mammographic sensitivity in women with dense breasts or those younger than the typical screening age. For example, in a 2024 study by Sharma *et al.* [7], focusing on 301 consecutive breast lumps, certain clinical features – including non-mobility and hard consistency – differentiated benign from malignant lesions, highlighting the importance of clinical examination in tandem with imaging. This is in agreement with Rao *et al.* [8], who observed that FNAC maintains both high sensitivity (92%) and specificity (98%) when performed by experienced cytopathologists. Similarly, Smita Balwantrao Sankaye *et al.* [9] reported FNAC as a rapid, cost-effective, and highly reliable method for pre-operative evaluation of breast masses, particularly in developing countries.

The high sensitivity of clinical examination in our study mirrors findings by Gana *et al.* [10], who found that a modified triple test using clinical evaluation, ultrasound, and core biopsy achieved 100% diagnostic accuracy. Our results also align with Reddy *et al.* [11], who demonstrated that when properly standardized, clinical assessment remains indispensable for the early identification of suspicious lesions in resource-limited settings.

A noteworthy finding in our dataset is the high reported frequency of "duct papilloma" in cytology (25.0%), which did not correspond with histopathological classification. This discrepancy likely reflects the inherent limitations of FNAC in sampling papillary and intraductal lesions, where cytologic features overlap with benign ductal hyperplasia, papilloma, or may yield insufficient representative material. Studies

such as that by Ogbuanya *et al.* [12] caution that FNAC's utility in intraductal/papillary lesions is limited, and urge histologic correlation when cytology is suggestive of papilloma but imaging/clinical features are ambiguous. For our practice, this reinforces the need to flag cytology-imaging discordance for expedited core or excisional biopsy.

A multicentric analysis by Adda *et al.* [13] reaffirmed the diagnostic value of the triple test, reporting an overall accuracy of 95%, comparable to our results. Similarly, Rao *et al*. [8] and Singh *et al*. [14] emphasized the synergistic advantage of combining modalities over individual tests, particularly in regions with limited access to advanced imaging. Smita Balwantrao Sankaye *et al.* [9] further demonstrated that implementing the triple test reduces unnecessary biopsies and improves diagnostic confidence among clinicians.

From a clinical-pathway perspective, our results support a pragmatic algorithm: begin with a thorough clinical examination, followed by FNAC for palpable lumps where imaging is unremarkable or equivocal. If FNAC indicates malignancy, surgical planning may proceed. If FNAC is benign and clinical/imaging concordant, conservative follow-up may be justified. But if any discordance arises (e.g., suspicious imaging, atypical cytology, and dense breast tissue), a core needle biopsy or excisional biopsy should be triggered. This strategy mirrors recent findings by Gana *et al.* [10], who reported 100% sensitivity and specificity for their modified triple test (clinical+ultrasound+core biopsy) in resource-limited settings.

Our findings substantiate that the triple assessment method remains the gold standard for diagnosing breast lumps, combining simplicity, cost-effectiveness, and high accuracy. In clinical practice – especially within resource-limited healthcare systems – combining clinical examination and cytology offers the most efficient diagnostic pathway. Radiology and histopathology serve as vital adjuncts in discordant or suspicious cases. This approach not only streamlines diagnosis but also optimizes patient management and minimizes unnecessary invasive procedures, as also advocated by Smita Balwantrao Sankaye *et al*. and Rao *et al.* [8,9].

Study limitations

- Relatively small sample size (n=96)
- Single-center study limits generalizability
- Potential verification bias, as all patients underwent biopsy
- Minor data inconsistencies in lesion categorization
- Future studies should include multicentric data and standardized imaging protocols.

Clinical implications

The findings suggest that in resource-constrained settings, a combined approach of clinical examination and cytology can effectively guide diagnosis, reserving radiological evaluation and biopsy for discordant or suspicious cases.

CONCLUSION

The triple assessment method – combining clinical, radiological, and cytological evaluation – is a robust, accurate, and cost-effective diagnostic protocol for breast lumps.

Clinical examination offers the highest sensitivity, cytology the greatest specificity, and their integration minimizes false negatives. The addition of histopathology and IHC enhances diagnostic confidence and aids in personalized treatment planning.

ETHICAL APPROVAL

Institutional Human Ethics Committee approval obtained (IAEC/2022/105).

AUTHOR CONTRIBUTIONS

All authors contributed equally to study conception, data acquisition, analysis, and manuscript preparation.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING

No external funding was received for this study.

REFERENCES

1. Baron RH, Walsh A. 9 facts everyone should know about breast cancer. Am J Nurs. 1995;95(7):29-33.
2. Ajitha MB, Srinivasan N, Shivaswamy BS, Abhishek V. A systematic study on fibroadenoma of the breast. Int J Biol Adv Res. 2012;3(12):302-7.
3. Rangabashyam N, Gnanaprakasam D, Krishnaraj B, Manohar V, Vijayalakshmi SR. Spectrum of benign breast lesions in Madras. J R Coll Surg Edinb. 1983;28(6):369-73.
4. Na SP, Houserková D. Role of various modalities in breast imaging. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2007;151(2):209-18.
5. Morris KT, Pommier RF, Morris A, Schmidt WA, Beagle G, Alexander PW, et al. Usefulness of the triple test score for palpable breast masses. Arch Surg. 2001;136(9):1008-13.
6. Agarwal NK, Choudhury DN, Minocha A. Diagnostic accuracy of fine needle aspiration cytology, Triple test and tru-cut biopsy in the detection of breast lesion. Asian Pac J Cancer Care. 2023;8(1):34-42.
7. Sharma SK, Singh S, Kumar S. Role of clinical examination in the evaluation of patients with breast lumps: A cytopathological study. World Acad Sci J. 2024;6(3):152-60.
8. Apuroopa M, Chakravarthy VK, Rao DR. Application of Yokohama system for reporting breast fine needle aspiration cytology in correlation with histopathological and radiological findings. Ann Pathol Lab Med. 2020;7:A210-5.
9. Sankaye SB, Dongre SD. Cytological study of palpable breast lumps presenting in an Indian rural setup. Indian J Med Paediatr Oncol. 2014;35:159-64.
10. Gana SG, Olarinoye- Akorede SA, Samaila MO, Yusufu lM. Modified triple assessment in palpable breast lumps: A prospective study. Eur Soc Med J. 2025;7(2):142-50.
11. Jagadev S, Kustagi SS, Balaji C, Reddy KS, Bhaarat BN. Assessing the efficacy of the modified triple test in the diagnosis of palpable breast lumps. Int J Acad Med Pharm. 2024;6(1):215-9.
12. Ogbuanya, AUO, Anyanwu SN, Iyare EF, Nwigwe CG. The role of fine needle aspiration cytology in triple assessment of patients with malignant breast lumps. Niger J Surg. 2021;26(1):35-41.
13. El-Bolkainy TM, Shabaan HA, Abodeif WT, El-Bolkainy MN, El-Tony A. Intra-operative diagnosis of breast mass-lesions: Comparison of the validity of touch smear preparation and frozen section techniques. J Egypt Natl Canc Inst. 2008 Mar;20(1):63-9. PMID 19847283
14. Sharma SK, Singh S and Kumar S. Role of clinical examination in the evaluation of patients with breast lumps: A cytopathological study. World Acad Sci J. 2024;6:33.