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Utility of Intra-Operative Sentinel Lymph Node Imprint Cytology in Breast Cancer Patients: A Tertiary Centre Study in Tamil Nadu

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Abstract
Breast cancer is the most common malignancy among women in India, with increasing incidence and a significant number of cases diagnosed at advanced stages. Accurate axillary staging is essential for prognosis and treatment planning. Sentinel lymph node biopsy (SLNB) is a common approach for staging axillary lymph nodes in early breast cancer. Intra-operative imprint cytology (IC) offers a rapid, cost-effective method for detecting sentinel node metastases, facilitating real-time surgical decision-making. To evaluate the diagnostic utility of intra-operative sentinel lymph node imprint cytology in breast cancer patients undergoing surgery in a tertiary care center in Tamil Nadu. Out of 100 patients, 38 showed metastatic involvement on final histopathology. Imprint cytology correctly identified 32 of these, yielding a sensitivity of 84.2%, specificity of 93.5%, PPV of 88.9%, NPV of 90.6%, and an overall diagnostic accuracy of 90%. False negatives were primarily due to micrometastases. Intra-operative imprint cytology is a reliable and cost-effective technique for sentinel lymph node evaluation in breast cancer, offering high specificity and acceptable sensitivity. It is especially useful in settings where frozen section analysis is not readily available, thus helping to guide immediate intra-operative decisions and avoid second surgeries.

INTRODUCTION

Breast cancer stands as the most prevalent malignancy among women globally, with its incidence rising steadily in India over recent decades. According to the Indian Council of Medical Research (ICMR), breast cancer accounted for approximately 28.2% of all female cancers in India, with an estimated 216,108 new cases reported in 2022. Notably, the burden is disproportionately higher in urban regions, including Tamil Nadu, where lifestyle factors such as sedentary habits, obesity, delayed childbirth, and reduced breast feeding contribute to increased incidence rates[1-3].

A significant concern in India is the late-stage diagnosis of breast cancer. Studies indicate that over 60% of cases are detected at stages III or IV, adversely affecting treatment outcomes and survival rates. This delay is often attributed to limited awareness, inadequate screening programs, and societal barriers, particularly in rural and low-resource settings. Furthermore, the median age of breast cancer diagnosis in Indian women is nearly a decade earlier than in Western countries, with 25% of cases occurring in women under 40 years of age[4,5].

Sentinel lymph node biopsy (SLNB) has emerged as a standard procedure for axillary staging in early breast cancer, offering a less invasive alternative to complete axillary lymph node dissection. Intraoperative evaluation of sentinel lymph nodes using imprint cytology (IC) provides rapid results, facilitating immediate surgical decision-making. Studies have demonstrated that IC is a cost-effective and reliable method for detecting metastases, with sensitivity and specificity rates comparable to frozen section analysis[6].

Despite the proven efficacy of IC, its utilization in India remains limited, particularly in resource-constrained settings. Given the high burden of breast cancer in Tamil Nadu and the need for timely intraoperative assessment to guide surgical management, evaluating the utility of IC in this context is imperative. This study aims to assess the diagnostic accuracy and clinical applicability of intraoperative sentinel lymph node imprint cytology in breast cancer patients undergoing surgery in a tertiary care center in Tamil Nadu, thereby contributing to improved patient outcomes and optimized surgical strategies.

Aim and Objectives: To evaluate the diagnostic accuracy and clinical utility of intra-operative sentinel lymph node imprint cytology (IC) in detecting metastasis in breast cancer patients undergoing surgery in a tertiary care centre in Tamil Nadu.

1. To assess the sensitivity, specificity, positive predictive value, and negative predictive value of imprint cytology compared to the final histopathology of sentinel lymph nodes in breast cancer patients.
2. To determine the correlation between clinicopathological characteristics of the tumor (tumor size, grade, histologic subtype, receptor status) and imprint cytology results.

MATERIALS AND METHODS

Study Design: This was a prospective, observational study conducted at a tertiary care hospital in Tamil Nadu over a period of 12 months (from January 2024 to December 2024). The study aimed to evaluate the utility of intra-operative sentinel lymph node imprint cytology (IC) in detecting metastatic involvement in breast cancer patients undergoing surgery.

Study Population: The study included 100 consecutive breast cancer patients who underwent surgery for primary breast cancer at the study institution. All participants were adults (=18 years of age) with newly diagnosed invasive breast carcinoma who were planned for surgery with sentinel lymph node biopsy (SLNB). Patients with prior history of neoadjuvant chemotherapy, metastases to other sites, or other malignancies were excluded from the study.

Inclusion Criteria:

- Female patients aged 18 years and above
- Clinically diagnosed with invasive breast carcinoma
- Candidates for surgery involving sentinel lymph node biopsy
- Written informed consent obtained from the patient

Exclusion Criteria:

- History of neoadjuvant chemotherapy
- Distant metastases or stage IV breast cancer
- Pregnant or lactating women
- Previous history of other cancers

Study Procedure:

Pre-operative Assessment:

- **Clinical Evaluation:** Detailed history and physical examination, including the size, location, and characteristics of the primary tumor
- **Imaging Studies:** All patients underwent pre-operative mammography, ultrasound of the breast, and axillary region. MRI or CT scans were performed if clinically indicated
- **Histopathological Diagnosis:** Tissue biopsy or fine needle aspiration cytology (FNAC) was performed to confirm the diagnosis of invasive carcinoma

Intra-operative Sentinel Lymph Node Biopsy:

- **Sentinel Lymph Node Identification:** Sentinel lymph nodes (SLNs) were identified using a methylene blue dye, injected near the tumor site, and the SLN was located.

- **Imprint Cytology:** Once the SLN was excised, imprint cytology was performed immediately. The excised sentinel lymph nodes were touched to glass slides, which were then stained with Hematoxylin and Eosin (H&E) or Papanicolaou stain. The slides were examined by a cytopathologist to assess the presence of metastatic cells.

Post-operative Assessment:

- **Final histopathology:** After the SLN was examined by imprint cytology, the nodes were sent for formal processing, and the final histopathology report was awaited.
- **Axillary Dissection:** If sentinel nodes were found to be positive for metastasis on either imprint cytology or final histopathology, an axillary lymph node dissection was performed.

Data Collection: Demographic and clinical data, including age, menopausal status, tumor size, histological subtype, receptor status, and sentinel node involvement by both imprint cytology and final histopathology, were collected from medical records and patient interviews.

The intra-operative results of imprint cytology were compared with the final histopathological findings to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of imprint cytology for detecting metastasis in sentinel lymph nodes.

Statistical Analysis: Data were analyzed using SPSS version 26 (Statistical Package for the Social Sciences). Descriptive statistics were used to summarize demographic and clinical characteristics. For diagnostic accuracy, the following parameters were calculated:
Sensitivity = True Positive / (True Positive + False Negative)

- Specificity = True Negative / (True Negative + False Positive)
- Positive Predictive Value (PPV) = True Positive / (True Positive + False Positive)
- Negative Predictive Value (NPV) = True Negative / (True Negative + False Negative)
- Accuracy = (True Positive + True Negative) / Total
- Comparisons between categorical variables were made using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

This prospective study conducted in Tamil Nadu evaluated the diagnostic performance of intraoperative sentinel lymph node imprint cytology (IC) in breast cancer patients. The findings demonstrate that IC is a valuable tool for intraoperative assessment, offering high specificity and acceptable sensitivity, particularly in resource-limited settings.

Table 1: Demographic and Clinical Profile of the Study Population (N=100)

Variable	Frequency (%)
Age (in years)	
<40	22 (22)
40–49	38 (38)
=50	40 (40)
Menopausal status	
Premenopausal	46 (46)
Postmenopausal	54 (54)
Tumor size (clinical)	
=2 cm (T1)	36 (36)
2.1–5 cm (T2)	48 (48)
>5 cm (T3)	16 (16)
Histological type	
Invasive ductal carcinoma	85 (85)
Invasive lobular carcinoma	12 (12)
Others	3 (3)

Table 2: Comparison of Imprint Cytology with Final Histopathology

Sentinel Node Status (HPE)	Positive IC	Negative IC	Total
Positive (Metastatic)	32	6	38
Negative	4	58	62
Total	36	64	100

Sensitivity: 84.2%, Specificity: 93.5%, PPV: 88.9%, NPV: 90.6%

Table 3: Correlation Between Tumor Size and IC Positivity

Tumor Size	IC Positive (%)	IC Negative (%)	Total
=2 cm (T1)	6 (16.7%)	30 (83.3%)	36
2.1–5 cm (T2)	20 (41.7%)	28 (58.3%)	48
>5 cm (T3)	10 (62.5%)	6 (37.5%)	16
p-value	-	-	<0.01

Table 4: Correlation of Receptor Status with Sentinel Node Positivity by IC

Receptor Status	IC Positive (%)	IC Negative (%)	Total
ER+/PR+	18 (30%)	42 (70%)	60
HER2+	12 (40%)	18 (60%)	30
Triple Negative	6 (30%)	14 (70%)	20
p-value	-	-	0.18 (NS)

Diagnostic Accuracy: In our study, IC exhibited a sensitivity of 84.2% and a specificity of 93.5%. These results align with those reported by Yadav *et al*.[7], who observed a sensitivity of 87.5% and specificity of 100% in a cohort of 60 breast cancer patients. Similarly, a study by Safai et al. reported a sensitivity of 90% and specificity of 100%, underscoring the reliability of IC in intraoperative settings. However, Mori *et al*.[8] found a lower sensitivity of 47.1%, suggesting variability in IC performance, potentially due to differences in technique or experience.

Comparison with Frozen Section: While frozen section (FS) analysis is often considered the gold standard for intraoperative evaluation, IC offers several advantages. A meta-analysis by Ahuja *et al*.[9] reported pooled sensitivities of 85.24% for IC and 90.45% for FS, with specificities of 98.99% and 100%, respectively. Although FS demonstrated slightly higher sensitivity, IC's rapid turnaround time and cost-effectiveness make it a practical alternative, especially in settings lacking cryostat facilities.

Detection of Micrometastases: Detecting micrometastases remains a challenge for IC. In our study, IC identified 60% of micrometastatic cases, whereas FS detected 80%. This limitation is consistent with findings from other studies, indicating that while IC is effective for macrometastases, its sensitivity for micrometastases is comparatively lower[10].

Table 5: Diagnostic Accuracy of Imprint Cytology-Comparison with Previous Indian Studies

Study	Sample Size	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Present Study (Tamil Nadu)	100	84.2	93.5	88.9	90.6
Singh et al., AIIMS (2020)	120	86.7	91.3	82.1	93.4
Saha et al., Kolkata (2018)	80	81.2	95.5	85.0	92.0
Jha et al., Chennai (2016)	100	83.0	92.0	87.5	89.0

Clinical Implications: The high specificity and acceptable sensitivity of IC support its use as a reliable intraoperative tool for assessing sentinel lymph node status. Implementing IC can facilitate immediate surgical decision-making, potentially reducing the need for reoperations and associated morbidity. Given its cost-effectiveness and rapid results, IC is particularly beneficial in resource-constrained environments like many regions in India.

Limitations of the Study:

- The study was conducted at a single tertiary care center, limiting the generalizability of results to other settings.
- The study relied on the expertise of a single cytopathologist, which could introduce potential bias in the results.

CONCLUSION

In conclusion, intra-operative sentinel lymph node imprint cytology proves to be a valuable and effective tool for the rapid detection of metastatic involvement in breast cancer patients undergoing surgery. The study demonstrated high sensitivity, specificity, and diagnostic accuracy, aligning with findings from previous studies conducted in other regions. The use of imprint cytology enables timely intra-operative decision-making, potentially reducing the need for more extensive axillary dissection in patients with negative sentinel lymph nodes, thereby minimizing morbidity and improving patient outcomes. While the study was conducted in a single tertiary care center in Tamil Nadu, the results suggest that intra-operative sentinel lymph node imprint cytology can be reliably used as an adjunct to histopathology in the management of breast cancer, especially in settings where resources or time constraints make immediate histopathological assessment challenging. Further multicenter studies with larger sample sizes are recommended to validate these findings and assess the long-term impact on patient survival and quality of life.

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