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Cross-Sectional Study to Determine the Metastatic Involvement of Blue Lymph Nodes in Axillary Reverse Mapping After Axillary Lymph Node Dissection (ALND) in Females with Locally Advanced Breast Carcinoma Post Neoadjuvant Chemotherapy in the Tertiary Care Centre in Central India

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ABSTRACT

Background: Axillary lymph node dissection (ALND) remains integral to surgical management of locally advanced breast cancer (LABC) but carries notable morbidity, particularly upper limb lymphedema. Axillary Reverse Mapping (ARM) has been introduced to preserve arm lymphatic drainage; however, its oncological safety is debated due to potential tumor involvement in ARM nodes.
Objective: To assess the frequency of metastatic involvement in ARM-identified lymph nodes in patients with LABC treated with neoadjuvant chemotherapy (NACT).
Methods: This cross-sectional study included 75 patients with LABC undergoing modified radical mastectomy with ALND. ARM was performed using methylene blue dye injected into the ipsilateral upper limb. Identified ARM nodes were excised separately and subjected to histopathological examination. Associations between ARM node metastasis and clinicopathological variables were analyzed using Chi-square and unpaired t-tests.
Results: ARM nodes were successfully identified in 80% of cases. Metastatic involvement was observed in 18% of these nodes. A statistically significant association was found between ARM node positivity and both clinical stage and nodal burden (p=0.04). No significant correlation was noted with patient age, tumor size, or histological grade.
Conclusion: The presence of metastasis in a considerable proportion of ARM nodes raises concerns regarding their preservation in LABC. Routine ARM node conservation cannot be recommended; a selective approach incorporating intraoperative evaluation may be more appropriate.

Keywords*: Breast cancer, Axillary reverse mapping, ALND, Lymphedema, Neoadjuvant chemotherapy.*

INTRODUCTION

Breast cancer continues to represent a major global health burden and is a leading contributor to cancer-related mortality among women. Locally advanced breast cancer encompasses tumors with extensive local spread, including significant nodal involvement or invasion of adjacent structures[1].

Despite advances in systemic therapy, ALND remains a key component for regional disease control and staging. However, its association with postoperative complications—particularly lymphedema—has prompted exploration of less morbid alternatives[2].

Axillary Reverse Mapping (ARM) is based on the concept of preserving lymphatic channels draining the upper limb during axillary surgery. While technically feasible, concerns persist regarding oncological safety due to possible overlap between breast and arm lymphatic pathways[3].

This study was conducted to evaluate the incidence of metastatic involvement in ARM nodes in patients undergoing surgery following neoadjuvant chemotherapy.

AIMS AND OBJECTIVES

Primary Objectives:

1. To identify ARM lymph nodes intraoperatively during ALND
2. To determine the rate of metastatic involvement in these nodes
3. To assess their relevance in predicting axillary disease status

Secondary Objective:

To examine the relationship between ARM node involvement and clinicopathological factors

MATERIALS AND METHODS

Study Design: Cross-sectional observational study
Setting: Department of General Surgery, MY Hospital, Indore
Sample Size: 75 patients

INCLUSION CRITERIA:

- Female patients aged >18 years
- Diagnosed with LABC
- Completed neoadjuvant chemotherapy
- Planned for modified radical mastectomy with ALND

PROCEDURE:

A volume of 2–4 ml methylene blue dye was injected into the ipsilateral upper limb prior to surgery. During axillary dissection, blue-stained lymphatics and nodes were identified as ARM nodes. These were excised separately and sent for histopathological analysis independent of standard axillary specimens.

STATISTICAL ANALYSIS:

Data were analyzed using JAMOVI software. Associations between categorical variables were evaluated using Chi-square test, while continuous variables were analyzed using unpaired t-test. A p-value <0.05 was considered statistically significant.

RESULTS:

Table 01: Age distribution of the patients

Age Group	No.	Percentage	P Value
18-30	05	6.7	$\chi^2 = 16.68$
31-40	15	20	df = 4
41-50	25	33.3	$p \approx 0.002$
51-60	20	26.7	
More than 60	10	13.3	
Total	75	100	

There is a statistically significant difference in the distribution of participants across age groups ($p \approx 0.002$). The majority of participants were concentrated in the 41–50 and 51–60 age groups, indicating that the sample is not evenly distributed across all age categories.

Table 02: Clinical Characteristics of Patients Included in the Study

Variable	Category	Frequency (n)	Percentage (%)	P Value
Tumor Site	Upper Outer Quadrant	30	40.0	$\chi^2 = 34.04$ df = 5 p < 0.0001 (highly significant)
	Central	15	20.0	
	Lower Outer Quadrant	10	13.3	
	Upper Inner Quadrant	08	10.7	
	Diffuse	07	9.3	
	Lower Inner Quadrant	05	6.7	
Received Neoadjuvant Chemotherapy	Yes	75	100	-
	No	00	00	
Clinical Stage	I	00	00	For $\chi^2 = 91.66$ with df = 3: p < 0.0001
	II	25	33.3	
	III	50	66.7	
	IV	00	00	

Tumor sites are not evenly distributed. There is a clear predominance of tumors in certain locations. Most common site: Upper Outer Quadrant (40%)

Least common: Lower Inner Quadrant (6.7%). There is a highly statistically significant difference in the distribution of tumor sites. The upper outer quadrant was the most commonly affected site, indicating a non-uniform distribution of tumor location among the study participants. Chi-square goodness-of-fit test applied.

All 75 patients (100%) received neoadjuvant chemotherapy, while none (0%) did not receive it.This indicates complete uniformity in treatment every subject in the study was given neoadjuvant chemotherapy.The p-value is extremely small (< 0.05). This means the distribution of patients across clinical stages is not equal. There is a statistically significant difference, with most patients concentrated in Stage III

Table 03: Operative and Histopathological Parameters of Patients in Whom ARM Node(s)/Lymphatics identified

Parameter	Category	Frequency (n)	Percentage (%)	P Value
Type of Surgery	MRM	75	100	-

Parameter	Category	Frequency (n)	Percentage (%)	P Value
	BCS + ALND	00	00	
ARM Node Identified	Yes	60	80.0	$\chi 2 \approx 27.0$, df=1, $p<0.0001$
	No	15	20.0	
ARM Lymphatic Identified	Yes	55	73.3	$\chi 2 \approx 16.33$, df=1, $p<0.0001$
	No	20	26.7	
ARM Node and Lymphatic	Both	50	66.7	$\chi 2 \approx 18.85$, df=1, $p<0.0001$
	Either of Two	15	20.0	
Number of ARM Nodes	1	20	26.7	$\chi^2 = 2.5$, df = 2, p = 0.28.
	2	25	33.3	
	≥3	15	20.0	

For "Number of ARM Nodes," percentages are based on total 75 patients; the sum (60) equals the number with nodes identified. All patients (100%) underwent MRM.There was a statistically significant difference in ARM node identification, with a higher proportion of patients showing identifiable ARM nodes (80%). There was a statistically significant difference in ARM lymphatic identification ($\chi^2 = 16.33$, $p < 0.0001$), with most patients showing identifiable lymphatics (73.3%). There was a statistically significant predominance of patients with both ARM node and lymphatic identified.There was no statistically significant difference in the distribution of the number of ARM nodes identified.

Table 04: Correlation of ARM Nodes/Lymphatics Identification with Clinicopathological Parameters

Parameter	**Category**	**ARM Identified (n)**	**ARM Not Identified (n)**	**P-value**
ARM Age	<50	38	7	Chi-square ≈ 1.29 p ≈ 0.25
	≥50	22	8	
Tumor Size	T1–T2	15	5	Chi-square ≈ 0.31 p ≈ 0.57
	T3–T4	45	10	
Nodal Status	N0	32	8	Chi-square ≈ 2.06 p ≈ 0.41
	N+	28	7	
Stage	Early	20	5	Chi-square ≈ 0.00 p ≈ 0.049
	Advanced	40	10	
	I	8	2	Chi-square ≈ 0.59

Parameter	Category	ARM Identified (n)	ARM Not Identified (n)	P-value
Histological Grade	II	28	7	p ≈ 0.97
	III	24	6	

All totals sum to 75 patients (60 ARM identified, 15 not identified).
Age: Among patients aged <50 years, ARM nodes were identified in 38 cases compared to 22 cases in those ≥50 years. However, this difference was not statistically significant (p ≈ 0.25), indicating that age did not influence ARM identification.

Tumor Size: ARM nodes were identified in 15 patients with T1–T2 tumors and 45 patients with T3–T4 tumors. The association was not statistically significant (p ≈ 0.57), suggesting tumor size had no significant effect on ARM identification.

Nodal Status: In node-negative (N0) patients, ARM nodes were identified in 32 cases, while in node-positive (N+) patients, 28 cases showed identification. This difference was also not statistically significant (p ≈ 0.41).

Stage: ARM identification was seen in 20 early-stage and 40 advanced-stage patients. The p-value (≈ 0.049) indicates a statistically significant association, suggesting that stage may influence ARM node identification. However, the Chi-square value reported (≈ 0.00) appears inconsistent with the p-value and may require verification.

Histological Grade: ARM nodes were identified across all grades (Grade I: 8, Grade II: 28, Grade III: 24), with no statistically significant association (p ≈ 0.97), indicating tumor grade does not affect ARM identification.

Table 05: ARM Nodes of Identified

ARM Nodes of Identified	Frequency (n)	Percentage (%)*	P-value
Positive	11	18	For $\chi^2 = 24.06$ with df = 1: p < 0.0001
Negative	49	82	
	60	100	

The p-value is highly significant (< 0.05)
This means the observed distribution is not equal.There are significantly more negative ARM nodes (82%) than positive (18%).

Table 06: Correlation of identified ARM Nodes metastatic involvement with Clinicopathological Parameters

Parameter	Category	ARM Identified (n)	Positive ARM nodes (n)	P-value
ARM Age	<50	38	6	Chi-square ≈ 0.7 p ≈ 0.35
	≥50	22	5	
Tumor Size	T1–T2	15	1	Chi-square ≈ 0.3 p ≈ 0.57
	T3–T4	45	10	

Parameter	Category	ARM Identified (n)	Positive ARM nodes (n)	P-value
Nodal Status	N0	32	3	Chi-square ≈ 3.57 p ≈ 0.04
	N+	28	8	
Stage	Early	20	1	Chi-square ≈ 4.2 p ≈ 0.04
	Advanced	40	10	
Histological Grade	I	8	1	Chi-square ≈ 2.0 p ≈ 0.3
	II	28	4	
	III	24	6	

All totals sum to 75 patients (60 ARM identified, 15 not identified).
Age: Out of 38 patients aged <50 years, 6 (15.8%) had metastatic ARM nodes, whereas among 22 patients aged ≥50 years, 5 (22.7%) showed positivity.

This difference was not statistically significant ($\chi^2 \approx 0.7$, $p > 0.05$).
Tumor Size: Among C T1–T2 tumors 2 (13.3%) had metastatic ARM nodes, compared to 9 (20.0%) in 45 patient with T3–T4 tumors .The association between tumor size and ARM node metastasis was not statistically significant ($\chi^2 \approx 0.3$, $p > 0.05$)..

Nodal Status: Among 32 node-negative patients (N0), 3 (9.4%) had metastatic ARM nodes, whereas in 28 node-positive patients (N+), 8 patients (28%) showed involvement.

Although a higher proportion was observed in node-positive cases, the association was statistically significant ($\chi^2 \approx 3.57$, $p < 0.05$).

Stage: Among early-stage patients (n=20), 1 (5%) had metastatic ARM nodes, compared to 10 (25%) among advanced-stage patients (n=40).

This difference was found to be statistically significant ($\chi^2 \approx 4.2$, $p \approx 0.04$).
Histological Grade: Metastatic ARM node involvement was observed in 1 patient with Grade 1 tumor(n=8), 4 patients with Grade 2 tumor(n=28), 6 patients with Grade 3 tumor(n=24)

Although a rising trend was seen with increasing tumor grade, the association was not statistically significant ($\chi^2 \approx 2.0$, $p > 0.05$).

DISCUSSION
The present study demonstrates that ARM nodes may harbor metastatic disease in a notable subset of patients with LABC [4-6]. The observed rate of 18% falls within the range reported in existing literature [7]. These findings indicate that lymphatic drainage pathways of the breast and upper limb are not entirely distinct, supporting the concept of anatomical crossover [8]. Patients with higher nodal burden and advanced stage appear more likely to exhibit ARM node involvement [9]. Although neoadjuvant chemotherapy reduces tumor load, it may not completely eradicate microscopic disease within lymphatic channels. Therefore, preservation of ARM nodes without assessment could potentially leave residual disease [10].

CONCLUSION
ARM technique shows a high identification rate and is technically feasible. Metastatic involvement in ARM nodes is not negligible. Routine preservation of ARM nodes in LABC is not advisable. Selective preservation guided by intraoperative or pathological assessment may improve safety.

LIMITATIONS

- Single-center design limits generalizability
- Lack of long-term follow-up data
- Survival and recurrence outcomes were not evaluated

Declaration by Authors

- **Ethical Aproval**: Approved
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- **Conflict of interest**: The Authors declare no conflict of interest.

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