Original Article

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Pathology Section

Patterns of Reaction in Non Metastatic Lymph Nodes of Breast Carcinoma: A Cross-sectional Study

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ABSTRACT

Introduction: Lymph nodes draining breast carcinoma exhibit reactive patterns reflecting tumour-immune interactions. While lymph node metastasis is a well-established prognostic factor, the clinical significance of reactive patterns in non metastatic nodes remains underexplored. Understanding these patterns may provide insights into host immune response and potential prognostic implications.

Aim: To evaluate the patterns of reaction in non metastatic lymph nodes in breast carcinoma and analyse their association with tumour size, grade, stage, and receptor status {Oestrogen Receptor (ER), Progesterone Receptor (PR), Human Epidermal Growth Factor Receptor 2 (HER2/neu), Ki67}.

Materials and Methods: A cross-sectional study was conducted at the Department of Pathology in RL Jalappa Hospital and Research Centre, Kolar, Karnataka, India. Patients diagnosed with invasive ductal carcinoma (no special type) who underwent mastectomy between January 2022 and December 2024 were included. A total of 80 patients meeting inclusion criteria were enrolled. Histopathological examination of 1,063 non metastatic lymph nodes was performed. Data were analysed using Chi-square test, Fisher's-exact test for small samples, and Generalised Estimating Equations (GEE) to account for patient-level clustering. Bonferroni correction for multiple comparisons was applied (adjusted α=0.00625).

Results: Among 1,063 non metastatic lymph nodes examined, 111 (10.4%) showed reactive changes, predominantly Sinus Histiocytosis (SH) (85.6%), followed by Germinal Centre Predominance (GCP) (9.9%) and Lymphocyte Predominance (LP) (4.5%). Tumour size showed significant association with reactive patterns (p=0.001, remains significant after Bonferroni correction). Molecular subtype also correlated significantly (p=0.002, remains significant after correction). Ki67 proliferation index showed association (p=0.009) but did not remain significant after Bonferroni correction (α=0.00625). Luminal A tumours showed exclusively SH, while other subtypes displayed varied patterns. ER, PR, and HER2 status showed no significant association.

Conclusion: Non metastatic lymph nodes exhibit diverse reactive patterns that correlate significantly with tumour size and molecular subtype after rigorous statistical correction. These findings highlight the complex interplay between tumour biology and nodal immunity, with potential prognostic implications.

Keywords: Breast neoplasms, Immunologic factors, Ki-67 antigen, Lymph nodes, Neoplasm staging, Oestrogen receptors, Progesterone receptors, Receptor ErbB-2

INTRODUCTION

Breast carcinoma remains the most frequently diagnosed malignancy in women globally, with approximately 2.3 million new cases reported worldwide in 2020, representing a substantial burden on healthcare systems [1]. Axillary lymph node status stands as one of the most powerful prognostic indicators in breast cancer, significantly influencing treatment decisions, staging, and survival outcomes [2]. However, the biological significance of lymph nodes extends beyond mere anatomical sites of metastatic spread. Regional lymph nodes serve as critical immunological organs that orchestrate adaptive immune responses against circulating tumour antigens, and their morphological patterns reflect the complex tumour-immune interactions occurring in the draining lymphoid tissue [3,4].

Non metastatic lymph nodes in patients with breast carcinoma frequently exhibit distinct reactive patterns, including Sinus Histiocytosis (SH), Germinal Centre Predominance (GCP) and Lymphocyte Predominance (LP) lymphocyte depletion, granulomatous reaction, and vascular transformation of sinuses, as classified by the World Health Organisation (WHO) [5]. These morphological patterns are not merely incidental findings but represent active immune responses to tumour antigens and may carry prognostic significance. Recent immunological studies have demonstrated that the tumour-draining lymph node microenvironment plays a pivotal role in shaping anti-tumour immunity, with specific reactive patterns correlating with T-cell priming, B-cell activation, and production of tumour-specific antibodies [6,7]. Emerging evidence suggests that immune-activated regional lymph nodes predict favourable survival in certain malignancies, including triple-negative breast cancer, highlighting the clinical relevance of characterising these patterns [8].

The molecular classification of breast cancer based on hormone receptor status {Oestrogen Receptor (ER), Progesterone Receptor (PR)}, Human-epidermal Growth Factor Receptor 2 (HER2), and proliferation index (Ki67) has revolutionised treatment approaches and prognostic assessment [9]. Different molecular subtypes exhibit varying degrees of immunogenicity, with triple-negative and HER2-enriched tumours demonstrating higher tumour-infiltrating lymphocytes and enhanced immune activation compared to luminal subtypes [10,11]. However, limited data exist on whether these molecular characteristics influence the patterns of immune reactions in draining lymph nodes. Understanding such associations could provide valuable insights into tumour-host immune interactions and potentially identify patients who might benefit from immunotherapy or have different prognostic trajectories.

Despite the recognised importance of lymph node biology in cancer immunity, most studies have focused on metastatic involvement, with relatively sparse investigation of reactive patterns in tumour-free lymph nodes. Previous studies have reported variable prevalence of different reactive patterns, with SH being the most commonly observed, but correlations with modern biomarkers and molecular subtypes remain inadequately explored [12,13].

Many studies that reactive patterns in non metastatic lymph nodes reflect the immunogenic properties of primary breast tumours and correlate with molecular subtypes, proliferative activity, and tumour characteristics. Specifically, many studies propose that highly proliferative tumours and immunogenic molecular subtypes (triple-negative and HER2-enriched) elicit more diverse and pronounced immune reactions in regional lymph nodes compared to less immunogenic luminal A tumours.

Hence, the present study aimed to evaluate the morphological patterns of immune reactions in non metastatic lymph nodes in patients with breast carcinoma, to analyse the association between reactive lymph node patterns and clinicopathological parameters including tumour size, grade, and TNM stage and to investigate correlations between lymph node reactive patterns and immunohistochemical markers (ER, PR, HER2neu, Ki67) and molecular subtypes.

1. To evaluate the morphological patterns of immune reactions in non metastatic lymph nodes in patients with breast carcinoma.
2. To analyse the association between reactive lymph node patterns and clinicopathological parameters including tumour size, grade, and TNM stage.
3. To investigate correlations between lymph node reactive patterns and IHC markers (ER, PR, HER2neu, Ki67) and molecular subtypes.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the Department of Pathology, RL Jalappa Hospital and Research Centre, Tamaka, Kolar, Karnataka, India, a tertiary care teaching hospital affiliated with Sri Devaraj Urs Academy of Higher Education and Research. The study was approved by the Institutional Ethics Committee (IEC No: SDUAHER/R&D/CEC/SDUMC-PG/70/NF/-2025-26). As this was a retrospective analysis of archival pathological specimens, the requirement for informed consent was waived by the ethics committee.

Sample size calculation: All patients diagnosed with breast carcinoma who underwent mastectomy with axillary lymph node dissection at study Institution between January 2022 and December 2024 were screened for eligibility. Sample size was calculated based on the proportion of LP pattern (13.3%) reported in a previous study [5], using the formula: $n=Z^2_1-\alpha/2\times P(1-P)/d^2$, where $Z_1-\alpha/2=1.96$ (for 95% confidence level), P=0.133, and d=0.075 (absolute precision). This yielded a minimum required sample size of 77 patients. 80 consecutive eligible patients were enrolled.

Inclusion criteria: Patients were included if they: (1) underwent mastectomy with axillary lymph node dissection; (2) had histopathologically confirmed Invasive Ductal Carcinoma, No Special Type (IDC-NST); and (3) had adequate archival tissue blocks and slides available for review.

Exclusion criteria: Cases were excluded if they: (1) underwent only lumpectomy or core needle biopsy; (2) had histological types other than IDC-NST; (3) had incomplete Immunohistochemistry (IHC) data; or (4) had inadequate tissue quality precluding accurate assessment.

Study Procedure

Specimen processing and histopathological examination: All mastectomy specimens were received fresh in the Department of Pathology, fixed in 10% neutral buffered formalin for 24-48 hours, and grossed according to the College of American Pathologists (CAP) protocol. Tissue sections were processed routinely, embedded in paraffin, sectioned at 4-5 µm thickness, and stained with Haematoxylin and Eosin (H&E). All axillary lymph nodes were carefully dissected, measured, and processed separately.

Classification of lymph node reactive patterns: Lymph nodes were first categorised as metastatic or non metastatic based on the presence or absence of tumour deposits. Non metastatic lymph nodes were then evaluated for reactive patterns and classified according to WHO criteria into six categories [5]: (1) SH - expansion of sinuses with increased histiocytes; (2) GCP - expansion of B-cell follicles with prominent germinal centres; (3) LP - expansion of paracortical T-cell zones; (4) Lymphocyte depletion (LD) - marked reduction in lymphoid cells; (5) Granulomatous reaction; and (6) Vascular transformation of sinuses. In cases showing mixed patterns, the predominant pattern occupying the largest area was recorded. No patient showed multiple different reactive patterns across their lymph nodes; all reactive nodes from a given patient demonstrated the same predominant pattern. To ensure reproducibility, 20% of cases (16 patients) were independently reviewed by two pathologists. Interobserver agreement was assessed using Cohen's kappa coefficient, which demonstrated substantial agreement (κ=0.82, 95% CI: 0.71-0.93).

Immunohistochemistry (IHC) and Scoring: IHC staining was performed on representative tumour sections using commercially available antibodies: (ER, clone ID5), (PR, clone EP2), HER2/neu (clone EP3), and Ki67 (clone MIB-1). Staining was performed using an automated immunostainer with appropriate positive and negative controls. ER and PR expression was scored using the Allred scoring system (range 0-8). An Allred score of 0-2 was classified as negative, while scores of 3-8 were considered positive, consistent with current American Society of Clinical Oncology (ASCO)/ College of American Pathologists (CAP) guidelines. HER2 expression was scored according to ASCO/CAP 2018 guidelines: 0 (no staining), 1+ (faint/incomplete membrane staining), 2+ (weak to moderate complete membrane staining), and 3+ (strong complete membrane staining). Scores of 0 and 1+ were classified as negative, 3+ as positive, and 2+ as equivocal. For the present study, HER2 2+ (equivocal) cases were classified as HER2-negative for molecular subtype determination, as Fluorescence In Situ Hybridisation (FISH) testing was not available. Ki67 proliferation index was assessed by counting at least 500 tumour cells in hot spot areas. A cut-off of <14% was used to define low proliferation, while ≥14% indicated high proliferation, following St. Gallen consensus [14-16].

Molecular subtype classification: Breast cancers were classified into molecular subtypes based on IHC surrogates following St. Gallen consensus criteria: (1) Luminal A - ER-positive and/or PR-positive, HER2-negative, Ki67 <14%; (2) Luminal B (HER2-negative) - ER-positive and/or PR-positive, HER2-negative, Ki67 ≥14%; (3) HER2-enriched - HER2-positive regardless of ER/PR status; (4) Triple-negative - ER-negative, PR-negative, and HER2-negative [14-16].

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel 2019 and analysed using Statistical package for Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated for all variables. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. The primary unit of analysis was individual lymph nodes rather than patients, consistent with pathology literature examining tissue-level morphological patterns. Associations between reactive patterns and clinicopathological parameters (tumour size, grade, stage) and IHC markers (ER, PR, HER2, Ki67, molecular subtypes) were assessed using Chi-square test or Fisher's-exact test. Fisher's-exact test was employed when expected cell frequencies were less than 5 in more than 20% of cells. To account for potential clustering of multiple lymph nodes within individual patients, sensitivity analyses were performed using GEE with an exchangeable correlation structure and robust standard errors. To address multiple comparisons, Bonferroni correction was applied. Eight primary comparisons were

planned (tumour size, grade, stage, ER, PR, HER2, Ki67, molecular subtype), yielding an adjusted significance threshold of $\alpha = 0.05/8 = 0.00625$. Results are reported with both uncorrected and Bonferroni-corrected p-values. A two-tailed p-value <0.05 was considered statistically significant for uncorrected analyses, while p<0.00625 indicated significance after correction for multiple testing.

RESULTS

Baseline characteristics: The present study included 80 patients diagnosed with IDC-NST, who underwent mastectomy with axillary lymph node dissection. The mean age of patients was 52.2 ± 12.7 years (range: 28-84 years). All patients were female. The mean tumour size was 5.60 ± 2.85 cm (range: 2.0-18.0 cm), with 53.8% of tumours measuring 2-5 cm and 46.2% larger than 5 cm. Histological grading revealed 55.0% Grade I, 38.7% Grade II, and 6.3% Grade III tumours. The majority of patients presented with Stage II (52.5%) or Stage III (45.0%) disease, and lowest patients presented with Stage I comprised of 2.5%.

Lymph node examination and distribution of reactive patterns: A total of 1,265 axillary lymph nodes were examined across the 80 patients, with a mean of 15.81 ± 7.19 lymph nodes per patient. Of these, 202 lymph nodes (16.0%) showed metastatic involvement, while 1,063 lymph nodes (84.0%) were free of metastasis. Among the 1,063 non metastatic lymph nodes, 111 nodes (10.4% of non metastatic lymph nodes) demonstrated morphological evidence of reactive changes, while 952 nodes (89.6%) showed no reactive pattern.

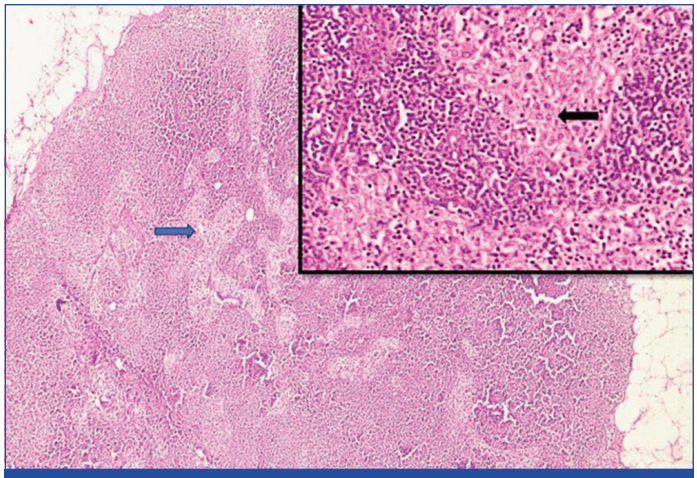
At the patient level, 28 of 80 patients (35.0%) had at least one reactive lymph node. Among these 28 patients: 15 patients (53.5%) had 1-2 reactive nodes, 8 patients (28.6%) had 3-5 reactive nodes, and 5 patients (17.9%) had more than 5 reactive nodes. The remaining 52 patients (65.0%) showed no reactive changes in any examined non metastatic lymph nodes. No patient showed mixed patterns of reactive changes; all reactive nodes from a given patient demonstrated the same predominant pattern.

The distribution of reactive patterns is shown in [Table/Fig-1]. Among the 111 reactive lymph nodes, SH was the most prevalent pattern, observed in 95 nodes (85.6%). GCP was identified in 11 nodes (9.9%), while LP was noted in five nodes (4.5%). None of the lymph nodes showed lymphocyte depletion, granulomatous reaction, or vascular transformation of sinuses. SH emerged as the dominant reactive pattern, as shown in [Table/Fig-2].

Association with clinicopathological parameters: Analysis revealed that tumour size had a highly significant correlation with reactive patterns (p=0.001) [Table/Fig-3]. After Bonferroni correction (adjusted α=0.00625), this association remained statistically significant. Tumours measuring 2-5 cm predominantly showed SH (83.3%) accompanied by GCP (16.7%), with no LP. In contrast, tumours larger than 5 cm exhibited SH (88.9%) with increased LP (11.1%), while no GCP was observed. This differential distribution suggests that tumour size influences the type of immune response in regional lymph nodes.

Reactive pattern	n (%)
Sinus Histiocytosis (SH)	95 (85.6)
Germinal Centre Predominance (GCP)	11 (9.9)
Lymphocyte Predominance (LP)	5 (4.5)
Lymphocyte Depletion (LD)	0
Granulomatous Reaction	0
Vascular Transformation of Sinus	0
Total	111 (100.0)

[Table/Fig-1]: Distribution of reactive patterns in non metastatic lymph nodes (n=111 reactive nodes).
*Out of 1,063 non metastatic lymph nodes, only 111 (10.4%) showed reactive patterns



[Table/Fig-2]: Stained microscopic image of lymph node with Sinus Histiocytosis (SH) pattern; (blue arrow indicates dilated sinus) (H&E stained 100X); inset shows microscopic image of macrophages within sinus (black arrow indicates macrophages within the sinus) (H&E stained 400X).

Parameters	SH n (%)	GCP n (%)	LP n (%)	Total nodes	p-value
Tumour size					
2-5 cm	55 (83.3%)	11 (16.7%)	0	66	0.001†
>5 cm	40 (88.9%)	0	5 (11.1%)	45	
Tumour grade					
Grade I	39 (90.7%)	2 (4.7%)	2 (4.7%)	43	0.496
Grade II	49 (83.1%)	7 (11.9%)	3 (5.1%)	59	
Grade III	7 (77.8%)	2 (22.2%)	0	9	
TNM stage					
Stage I	5 (100.0%)	0	0	5	0.167
Stage II	29 (74.4%)	7 (17.9%)	3 (7.7%)	39	
Stage III	61 (91.0%)	4 (6.0%)	2 (3.0%)	67	
Total	95 (85.6%)	11 (9.9%)	5 (4.5%)	111	

[Table/Fig-3]: Association of reactive patterns with clinicopathological parameters (N=111 reactive lymph nodes).
†Remains statistically significant after Bonferroni correction (adjusted α=0.00625)

Tumour grade did not show statistically significant association with reactive patterns (p=0.496), and TNM stage showed no significant correlation (p=0.167). SH remained the predominant pattern across all grades and stages.

Association with IHC markers and molecular subtypes: Assessment of IHC markers revealed that Ki67 proliferation index showed association with reactive lymph node patterns (p=0.009) [Table/Fig-4].

All lymph nodes from tumours with low Ki67 (<14%) demonstrated exclusively SH (100%), whereas high Ki67 tumours (≥14%) showed more diverse patterns including GCP (14.9%) and LP (6.8%). However, after Bonferroni correction (adjusted α=0.00625), this association did not reach statistical significance.

Molecular subtyping showed a strong association with reactive patterns (p=0.002), which remained statistically significant after Bonferroni correction. Luminal A tumours exhibited exclusively SH (100%), while Luminal B, HER2-enriched, and triple-negative tumours demonstrated a broader spectrum of reactive responses, particularly increased GCP and LP patterns. Luminal B tumours showed the highest proportion of GCP (31.6%). In contrast, ER, PR, and HER2neu status individually showed no statistically significant association with reactive patterns.

Biomarkers	SH n (%)	GCP n (%)	LP n (%)	Total nodes	p-value
ER status					
Negative (0-2)	44 (84.6%)	5 (9.6%)	3 (5.8%)	52	0.833
Positive (3-8)	51 (86.4%)	6 (10.2%)	2 (3.4%)	59	

PR status					
Negative (0-2)	50 (86.2%)	5 (8.6%)	3 (5.2%)	58	0.848
Positive (3-8)	45 (84.9%)	6 (11.3%)	2 (3.8%)	53	
HER2neu status					
Negative (0/1+/2+)	65 (83.3%)	10 (12.8%)	3 (3.8%)	78	0.266
Positive (3+)	30 (90.9%)	1 (3.0%)	2 (6.1%)	33	
Ki67 status					
Low (<14%)	37 (100.0%)	0	0	37	0.009*
High (≥14%)	58 (78.3%)	11 (14.9%)	5 (6.8%)	74	
Molecular subtype					
Luminal A	30 (100.0%)	0	0	30	0.002†
Luminal B	13 (68.4%)	6 (31.6%)	0	19	
HER2 enriched	30 (90.9%)	1 (3.0%)	2 (6.1%)	33	
Triple negative	22 (75.9%)	4 (13.8%)	3 (10.3%)	29	

[Table/Fig-4]: Association of reactive patterns with IHC markers and molecular subtypes (n=111 reactive lymph nodes).
*Significant at α=0.05 but does not remain significant after Bonferroni correction (α=0.00625)
†Remains statistically significant after Bonferroni correction (adjusted α=0.00625)

DISCUSSION

Breast carcinoma is the most common malignancy among females worldwide and the second most common cancer in India after cervical cancer. In India, the disease-specific mortality of breast cancer is approximately 50%. In the Kolar region, breast cancer accounts for about 6.41% of all malignancies. Globally, it constitutes nearly 10.4% of all cancers in women. Breast cancer is a heterogeneous disease with wide variations in morphology, molecular characteristics, and therapeutic response. Therefore, accurate assessment of prognostic factors for each patient has become increasingly important in guiding management [2,5].

A wide range of prognostic parameters has been evaluated in breast carcinoma, broadly categorised into histopathological and molecular factors. The histopathological features are practical, cost-effective, and provide reliable diagnostic as well as prognostic information. Among them, axillary lymph node status is one of the most powerful predictors of outcome and significantly influences patient morbidity and mortality [2,5]. Histological examination remains the most accurate method for lymph node staging, surpassing both clinical and radiological assessment. Patients with axillary lymph node metastasis have a four- to eight fold higher mortality rate compared to node-negative individuals, along with an increased risk of distant recurrence [5].

The present study comprehensively evaluated reactive patterns in non metastatic lymph nodes draining breast carcinoma and their correlation with clinicopathological and IHC parameters. The findings demonstrate that SH is the predominant reactive pattern (85.6%), with significant associations observed with tumour size (p=0.001) and molecular subtype (p=0.002), both remaining significant after Bonferroni correction for multiple testing (α=0.00625). Ki67 proliferation index showed showed a non significant trend that did not withstand multiple comparison correction.

The prevalence of SH in the present study (85.6%) is notably higher than reported in several previous investigations. Khetarpal S et al., observed SH in only 12.10% of ductal carcinomas [3]. This 7-fold difference may be attributed to several methodological factors: (1) In the present study, lymph nodes were analysed at the individual node level (111 nodes from 80 patients) whereas other studies analysed at the case level; (2) All non IDC-NST histologies were excluded, creating a more homogeneous cohort; (3) Classification here, prioritised the single predominant pattern per node, while mixed patterns were common in other series; (4) Geographic and population differences may influence immune responses. The exclusive focus on IDC-NST and stringent classification methodology may account for the higher prevalence in this cohort.

The significant association between tumour size and reactive lymph node patterns (p=0.001, remains significant after Bonferroni correction) represents a key finding. Tumours measuring 2-5 cm predominantly showed SH with GCP, whereas larger tumours (>5 cm) exhibited LP. This size-dependent variation suggests that tumour burden influences both the nature and intensity of lymph node immune responses. The shift toward LP in larger tumours may reflect enhanced paracortical T-cell zone activation in response to greater antigenic load.

The association between Ki67 and reactive patterns (p=0.009) did not withstand rigorous Bonferroni correction (α=0.00625), suggesting this finding should be interpreted with caution. However, the trend toward more diverse patterns in high-proliferation tumours (with GCP and LP observed exclusively in Ki67-high tumours) warrants further investigation in larger cohorts.

The molecular subtype classification showed a robust association with reactive patterns (p=0.002, remains significant after Bonferroni correction), with distinct immunological profiles across subtypes. Luminal A tumours exhibited exclusively SH (100%), while Luminal B, HER2-enriched, and triple-negative tumours demonstrated broader spectrum of reactive responses. This finding aligns with established understanding that different breast cancer molecular subtypes exhibit varying degrees of immunogenicity [10,11]. Triple-negative breast cancer is recognised as the most immunogenic subtype with higher tumour-infiltrating lymphocytes and enhanced immune activation signatures [13,17]. The varied reactive patterns observed in triple-negative tumours (75.9% SH, 13.8% GCP, 10.3% LP) reflect this heightened immunogenicity.

The clinical implications of these findings are multifaceted. The strong association between reactive patterns and molecular subtypes suggests that lymph node immune responses mirror the immunogenic properties of primary tumours. This correlation could potentially be utilised for risk stratification. Patients with Luminal A tumours showing uniform SH may have different surveillance strategies compared to triple-negative or HER2-enriched tumours exhibiting varied reactive patterns. Furthermore, identification of specific reactive patterns may help identify patients who might benefit from immunotherapy.

Limitation(s)

The present study has several important limitations that must be acknowledged. First, the retrospective cross-sectional design limits causal inference and assessment of temporal relationships between reactive patterns and clinical outcomes. Second, the single-center nature may limit generalisability to other populations with different demographic and genetic backgrounds. Third, lack of long-term follow-up data precluded survival analysis and assessment of prognostic significance of reactive patterns. Fourth, small numbers in certain subgroups (GCP n=11, LP n=5) limited statistical power for subgroup analyses.

Fifth, and most significantly, the primary unit of analysis was individual lymph nodes rather than patients, while tumour-related variables (size, grade, stage) are patient-level characteristics. This creates a fundamental mismatch whereby multiple lymph nodes from the same patient contribute to the analysis despite sharing identical tumour characteristics, potentially inflating sample size and violating independence assumptions. Although we attempted to address this through GEEs with robust standard errors to account for patient-level clustering, and observed that no patient demonstrated mixed reactive patterns (all reactive nodes from a given patient showed the same pattern), the associations between patient-level variables and node-level patterns should be interpreted with appropriate caution. This analytical approach follows precedent in pathology literature examining tissue-level morphological patterns, but future studies employing patient-level analysis or more sophisticated multilevel modeling approaches would provide more definitive evidence.

Sixth, potential confounders were not accounted such as neoadjuvant therapy status or patient co-morbidities that might influence immune responses. Seventh, molecular subtype classification was based on IHC surrogates rather than genomic profiling, which may not fully capture biological heterogeneity. Despite these limitations, our comprehensive lymph node-wise analysis provides valuable insights into immune responses in breast cancer draining lymph nodes.

CONCLUSION(S)

This cross-sectional study demonstrates that SH is the most prevalent reactive pattern (85.6%) in non metastatic lymph nodes of breast carcinoma patients. Luminal A tumours exhibited exclusively SH, whereas Luminal B, HER2-enriched, and triple-negative subtypes demonstrated more heterogeneous immune responses including germinal centre and LP patterns, reflecting their higher immunogenicity thus consistent with the study hypothesis. These findings suggest that lymph node immune responses are influenced by tumour biology and molecular subtype. Understanding these patterns may provide additional insights into host-tumour immune interactions and contribute to refining prognostic assessment in breast cancer management. Future prospective multicenter studies with long-term follow-up are warranted to establish the prognostic significance of these reactive patterns and their potential utility in guiding therapeutic decisions and patient stratification for immunotherapy.

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