International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 23s, 2025
https://theaspd.com/index.php

Association Between Neutrophil-To-Lymphocyte Ratio and Immunohistochemical Subtypes (ER, PR, HER2/Neu) In Patients with Breast Cancer

Dr. Vishwanathan[1], Dr. Karthika[1], Balaji M.B[2]
[1]Department of Pathology, Saveetha Medical College & Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Thandalam, Chennai - 602105, Tamil Nadu, India
[2]Department of Biochemistry, Saveetha Medical College & Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Thandalam, Chennai - 602105, Tamil Nadu, India.

Abstract

Background: *Breast cancer is the most common malignancy among women worldwide. Molecular subtyping using immunohistochemical (IHC) markers estrogen receptor (ER), progesterone receptor (PR), and HER2/neu is essential for prognosis and therapeutic planning. The neutrophil-to-lymphocyte ratio (NLR), a systemic inflammatory marker, is emerging as a potential prognostic indicator.*

Aim: *To evaluate the association between NLR and IHC subtypes of invasive breast carcinoma and explore its prognostic relevance.*

Methods: *A retrospective analysis was conducted on 50 newly diagnosed, untreated invasive breast carcinoma patients at Saveetha Medical College between February 2024 and March 2025. NLR was calculated from complete blood counts. IHC subtypes were determined based on ER, PR, and HER2/neu expression. Patients with infections, autoimmune diseases, or on immunosuppressive therapy were excluded.*

Results: *Mean NLR differed significantly among IHC subtypes ($p = 0.02$). The highest NLR values were observed in HER2-enriched and triple-negative breast cancer (TNBC) subtypes, whereas Luminal A demonstrated the lowest values.*

Conclusion: *Elevated NLR is associated with more aggressive IHC subtypes and may serve as a cost-effective prognostic tool, particularly in resource-limited settings.*

Keywords: *Breast cancer, Neutrophil-to-lymphocyte ratio, Immunohistochemistry, ER, PR, HER2/neu.*

INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy and a leading cause of cancer-related mortality among women. The disease's heterogeneity necessitates precise classification, and IHC profiling using markers such as ER, PR, and HER2/neu plays a pivotal role in distinguishing biologically distinct subtypes. These subtypes Luminal A, Luminal B, HER2-enriched, and triple-negative breast cancer (TNBC) differ markedly in prognosis and therapeutic response [1]. In recent years, systemic inflammatory markers have been studied as potential prognostic tools in oncology. One such marker, the neutrophil-to-lymphocyte ratio (NLR), is easily derived from routine complete blood counts and reflects the balance between innate (neutrophilic) and adaptive (lymphocytic) immune responses. Elevated NLR has been associated with poor outcomes in various cancers, including breast carcinoma [2]. This study explores the association between NLR and IHC subtypes of breast cancer to determine if NLR can serve as a prognostic biomarker in the diagnostic workup (Figure 1). Breast cancer is a biologically diverse disease with varying clinical behaviors. IHC markers like ER, PR, and HER2 classify it into subtypes: Luminal A/B, HER2-enriched, and TNBC [3]. These subtypes guide prognosis and therapy. NLR is a systemic inflammatory marker derived from complete blood counts. Elevated NLR is linked to poor outcomes in several cancers. This study aims to investigate NLR's relationship with IHC subtypes in breast cancer [4].

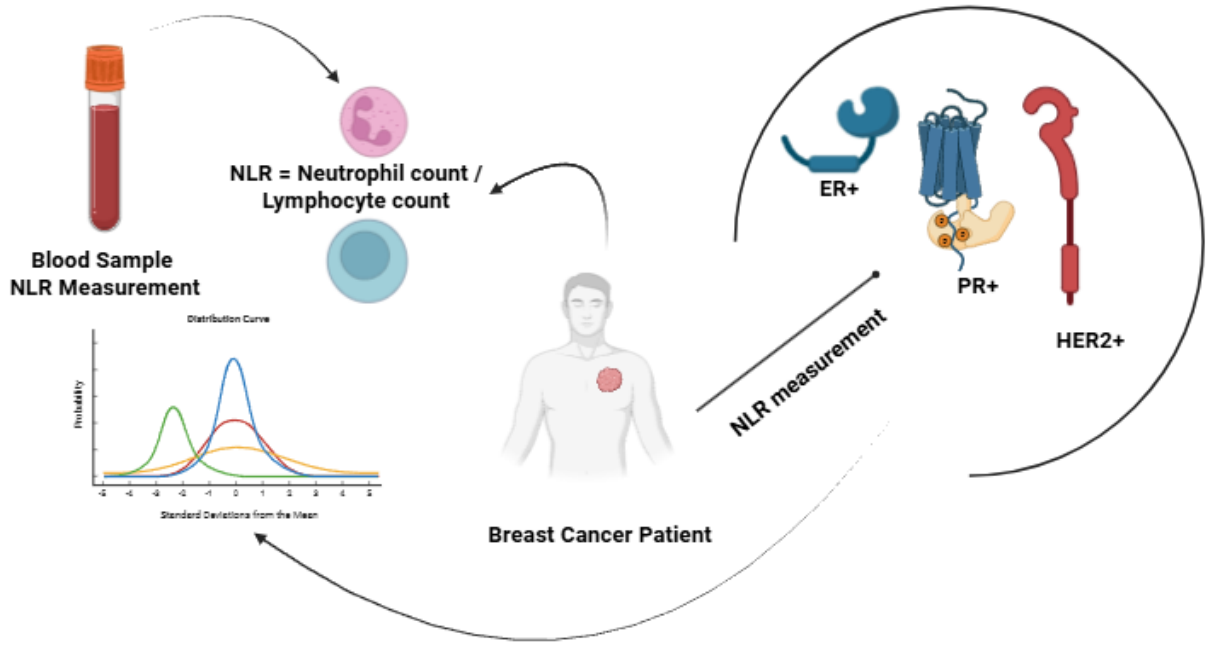

Figure 1. Workflow showing NLR calculation from blood samples and its comparison across breast cancer IHC subtypes (ER+, PR+, HER2+).

Materials and Methods

Design: Retrospective observational study
Site: Saveetha Medical College, Chennai
Period: Feb 2024 – Mar 2025
Sample: 50 invasive breast carcinoma cases

Inclusion Criteria:

- New, untreated invasive carcinoma
- CBC and IHC reports available

Exclusion Criteria:

- Active infection
- Autoimmune/chronic inflammatory diseases
- Corticosteroid or immunosuppressive use

Procedure:

 NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count from pre-treatment CBC results [5].
 IHC profiling was done using formalin-fixed paraffin-embedded (FFPE) tissue sections stained for ER, PR, and HER2/neu using standard protocols [6].
 based on receptor status, tumors were classified into subtypes: Luminal A, Luminal B, HER2-enriched, and TNBC [7].
 Statistical analysis was conducted to evaluate the significance of differences in NLR between subtypes ($p < 0.05$ considered statistically significant).

- NLR = absolute neutrophils / absolute lymphocytes
- IHC markers ER, PR, HER2 used to subtype tumors

Results

- Among the 50 patients, NLR showed considerable variation between different IHC subtypes.
- The highest NLR values were observed in HER2-enriched and TNBC subtypes.
- Luminal A tumors had the lowest mean NLR values.
- The mean NLR was statistically significantly different among subtypes ($p = 0.02$), suggesting an association between NLR and tumor aggressiveness.

A statistically significant variation in mean NLR values was found among subtypes (**$p = 0.02$**).

Table 1: NLR by IHC Subtype

Subtype	No. of Patients	Mean NLR	Prognostic Category
Luminal A	15	2.1	Favorable
Luminal B	12	2.7	Intermediate
HER2-enriched	10	3.8	Aggressive
Triple Negative (TNBC)	13	4.1	Aggressive

Pie Chart (Verbal Representation):

- Luminal A – 30%
- Luminal B – 24%
- HER2-enriched – 20%
- TNBC – 26%

HER2 and TNBC subtypes had the highest NLR, indicating aggressive tumor biology.

DISCUSSION

The findings of this study are consistent with previous literature that associates elevated NLR with worse prognosis in breast cancer. Inflammatory responses play a crucial role in cancer progression, and a high neutrophil count may support tumor growth by promoting angiogenesis, suppressing cytotoxic immune responses, and facilitating metastasis [8]. On the other hand, a lower lymphocyte count may reflect compromised cell-mediated immunity. In this context, NLR serves as a surrogate biomarker for systemic inflammation and immune dysregulation. The study revealed that HER2-enriched and TNBC subtypes known for their aggressive naturecorrelated with higher NLR values [9 -12]. This supports the hypothesis that inflammation may contribute to the pathogenesis and progression of aggressive breast cancers [13]. Given that NLR can be measured from routine blood tests, it offers a low-cost and easily accessible prognostic tool, especially beneficial in resource-limited settings where molecular testing may not be feasible for all patients. NLR reflects the balance of neutrophil-driven inflammation and lymphocyte-mediated immune response [14]. This study found high NLR values in HER2 and TNBC groups, aligning with their known poor prognosis. Given its accessibility and cost-effectiveness, NLR can be a valuable adjunct in prognostic assessment, particularly where molecular testing is limited. Further multicenter studies are needed for validation [15].

Conclusion

This study demonstrates a statistically significant association between elevated neutrophil-to-lymphocyte ratio and aggressive immunohistochemical subtypes of breast cancer. NLR may serve as a simple, non-invasive, and cost-effective marker for risk stratification and prognostication in clinical settings. Further studies with larger cohorts and long-term follow-up are warranted to validate these findings and integrate NLR into breast cancer management protocols.

REFERENCES

1. Azab B, Bhatt VR, Phookan J, et al. Usefulness of the neutrophil-to-lymphocyte ratio in predicting short- and long-term mortality in breast cancer patients. Ann Surg Oncol. 2012;19(1):217–224.
2. ASCO/CAP Guidelines for ER, PR, and HER2 Testing in Breast Cancer.
3. Guthrie GJ, et al. The systemic inflammation-based neutrophil–lymphocyte ratio. Oncol Hematol. 2013;88(1):218–230.
4. Ahmad, Aamir. 2020. Breast Cancer Metastasis and Drug Resistance: Challenges and Progress. Springer.
5. Aydiner, Adnan, Abdullah İğci, and Atilla Soran. 2019. Breast Disease: Management and Therapies. Volume 2.
6. Lakhani, Sunil R., and International Agency for Research on Cancer. 2012. WHO Classification of Tumours of the Breast. World Health Organization.
7. Liu, Chao, Feifei Teng, Alberto Traverso, and Shicheng Guo. 2024. Novel Immune Markers and Predictive Models for Immunotherapy and Prognosis in Breast and Gynecological Cancers. Frontiers Media SA.
8. Mishra, Anand Kumar, Amit Agarwal, Rajeev Parameswaran, and Kul Ranjan Singh. 2022. Endocrine Surgery: A South Asian Perspective. CRC Press.
9. Roizen, Michael F., and Mehmet Oz. 2015. You: Staying Young: The Owner's Manual for Looking Good & Feeling Great. Simon and Schuster.
10. Shao, Zhi-Ming, Yi-Zhou Jiang, Zhijie Jason Liu, and Shengtao Zhou. 2022. Predictive, Prognostic Biomarkers and Therapeutic Targets in Breast Cancer. Frontiers Media SA.
11. Tierney, Lawrence M., Sanjay Saint, and Mary A. Whooley. 2010. CURRENT Essentials of Medicine, Fourth Edition. McGraw Hill Professional.

12. Wernick, Miles N., and John N. Aarsvold. 2004. Emission Tomography: The Fundamentals of PET and SPECT. Academic Press.
13. Baskar, Gomathy. 2025. "GPX4 in Triple-Negative Breast Cancer: A Key Regulator of Ferroptosis and Therapeutic Target." Cancer Genetics 296-297 (June):76–83.
14. Kumaravel, Aravindan, and Muthuvel Esakki. 2024. "Comparing CD10 Expression With the Clinicopathological Features and Hormone Status of Invasive Breast Cancer." Cureus 16 (9): e69836.
15. P, Yashaswinii, Evangeline P. Christina, Sukumar Ramaswami, Harish Sl, and Paarthipan Natarajan. 2024. "Comparative Evaluation of USG-Guided Single Tissue Marker Versus Multiple Tissue Marker Placements in Breast Malignancy Patients Undergoing Neoadjuvant Chemotherapy for Tumor Localization." Cureus 16 (7): e65355.