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A Clinical Study to Evaluate the Prognostic Value of the Neutrophil-to-Lymphocyte Ratio in Libyan Women with Breast Cancer

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Abstract:

Background: Cancer has emerged as one of the most pressing health challenges of the 21st century, surpassing many infectious and chronic diseases in its global impact. While multiple environmental, genetic, and lifestyle-related factors can contribute to cancer development, the efficiency of the immune system plays a pivotal role in preventing it. Breast cancer is one of the most common malignancies affecting women, representing a major challenge in early diagnosis and prognosis. Despite the remarkable advances achieved in diagnostic techniques, there remains a pressing need for simple, reliable, and cost-effective biomarkers that can enhance clinical assessment and support treatment decision-making. **Objective:** The aim of this study that the research seeks to analyze the predictive value of the neutrophil-to-lymphocyte ratio (NLR) as a simple and accessible biomarker that could be utilized in the clinical assessment of breast cancer patients. **Methods**: This study is a prospective descriptive investigation designed to raise awareness about cancers and their underlying causes, with a particular emphasis on immune-inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR). The primary aim was to assess the predictive and diagnostic value of the neutrophil-to-lymphocyte ratio (NLR) in cancer patients using real patient data. **Results**: The analysis revealed a high prevalence of elevated neutrophil-to-lymphocyte ratio (NLR) (>3) across the sample. This elevation was particularly associated with advanced stages of cancer and with older age groups (>50 years). Patients younger than 30 years exhibited exclusively normal neutrophil-to-lymphocyte ratio (NLR) values. These findings reinforce the prognostic role of neutrophil-to-lymphocyte ratio (NLR) as a low-cost and clinically valuable biomarker. **Conclusion:** The present study evaluated the prognostic value of the neutrophil-to-lymphocyte ratio (NLR) in Libyan breast cancer patients. The findings demonstrated that the majority of patients (80%) had elevated neutrophil-to-lymphocyte ratio (NLR) values (>3), with higher prevalence observed in advanced cancer stages and in older age groups. These results strongly support the role of neutrophil-to-lymphocyte ratio (NLR) as a biomarker of systemic inflammation and cancer progression.

Keywords: Brest cancer, Neutrophil, Lymphocyte, Neutrophil-to-Lymphocyte ratio (NLR).

Introduction

In light of the rapid and concerning rise in cancer cases, cancer has emerged as one of the most pressing health challenges of the 21st century, surpassing many infectious and chronic diseases in its global impact (Katsura *et al*., 2022), (Chen, J *et al*., 2015) and (Chen, F *et al*., 2022). While multiple environmental, genetic, and lifestyle-related factors can contribute to cancer development, the efficiency of the immune system plays a pivotal role in preventing it (Li, J *et al*., 2024) and (Chen, C *et al*., 2018). As the body's first line of defense, the immune system not only combats infections but also detects and corrects cellular abnormalities that may otherwise

progress into malignancies. Scientific research highlights that the immune system performs a dual role: defense and surveillance (Liu, J *et al*., 2022). It constantly monitors cellular activity, identifies irregularities, and triggers corrective responses to suppress potential tumor formation. Breast cancer provides a clear and practical example of this interaction, as it remains the most common malignancy among women worldwide and demonstrates a strong association between immune health and disease progression (Katsura *et al*., 2022) and (Nemoto, D *et al*., 2021). The emergence of immunotherapy as a modern treatment paradigm further emphasizes the importance of harnessing immune power in fighting cancer cells, offering new avenues for more effective and less toxic therapies compared to conventional methods (Zhang, W *et al*., 2023). Given these insights, raising awareness becomes not only a matter of disease management but also a crucial preventive strategy. Promoting a healthy lifestyle that strengthens immune function—including balanced nutrition, regular physical activity, sufficient sleep, and stress reduction—is essential (Templeton, A *et al*., 2014). At the same time, expanding the application of immunotherapy and investing in cancer research represent urgent needs, particularly in resource-limited settings. Increasing public understanding of the link between immunity and cancer is no longer optional but rather a necessary health and social priority (Pistelli, M *et al*., 2015). It contributes to reducing the burden of cancer, improving quality of life, and enhancing recovery outcomes. Against this backdrop. The neutrophil-to-lymphocyte ratio (NLR) has emerged as an important inflammatory marker that has been reported to correlate with various tumor characteristics, including tumor size, degree of invasion, and the presence of lymphatic metastases. However, the reliability and predictive accuracy of neutrophil-to-lymphocyte ratio (NLR) as a clinical indicator for breast cancer remain subjects of ongoing scientific debate (Koh, C *et a*l., 2015), (Kim, K *et al*., 2021) and (Ivars Rubio *et al*., 2019). This uncertainty is particularly evident in the absence of local studies that consider the demographic, genetic, and environmental factors specific to Libyan female patients (Islam, M *et al* ., 2024), (Grassadonia, A *et al*., 2021) and (Gong, P *et al*., 2021). The present study aims to elucidate the vital relationship between the immune system and cancer, with a specific focus on breast cancer as both a scientific case study and a public health awareness example (Fridman, W *et al*.,2012), (Faria, S *et al*., 2016) and (Ethier, J *et al*., 2017). Ultimately, this work contributes to broader efforts toward building a culture of health grounded in prevention, knowledge, and effective immune response.

Material and methods

This study is a prospective descriptive investigation designed to raise awareness about cancers and their underlying causes, with a particular emphasis on immune-inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR). The primary aim was to assess the predictive and diagnostic value of neutrophil-to-lymphocyte ratio (NLR) in cancer patients using real patient data.

Study Duration

There was no fixed time frame for the study, as the analysis was conducted on precollected retrospective data. The project was initiated and completed after receiving institutional approval and data clearance.

Place of Study

The study was conducted using a non-interventional observational design. Data were collected from three medical centers in Libya. Sabratha Medical Center, Misrata Oncology Center and Al-Tibbi Hospital. This study did not have a fixed sample size; instead, it followed a convenience sampling approach, where all eligible patients who met the inclusion criteria during the data collection phase were considered for analysis.

Participants and Inclusion Criteria

Participants included adult patients (aged mid-twenties and above) who were diagnosed with various types of cancer. **Inclusion criteria:** Histologically confirmed malignancy (any type). Availability of complete blood count (CBC) data. Willingness to participate and complete a structured medical questionnaire. Accessible medical file with clinical data. **Exclusion criteria**: Incomplete blood test results. Missing clinical data in medical records. History of autoimmune diseases or chronic infections that could alter inflammatory markers.

Data Collection

Data collection consisted of two main components: **1.** Structured Medical Questionnaire: A self-reported tool designed to capture demographic data (age, gender, residence), clinical history, comorbidities, and treatment information. **2.** Laboratory and Clinical Records: Complete blood count (CBC) reports were retrieved from hospital databases. Particular attention was given to the absolute neutrophil count and lymphocyte count, from which the neutrophil-to-lymphocyte ratio (NLR) was calculated manually for each patient (neutrophil-to-lymphocyte ratio (NLR) = Absolute Neutrophil count (ANC) / Absolute Lymphocyte count (ALC)). All data were anonymized before analysis to ensure patient privacy and confidentiality.

Data Type and Variables

Quantitative variables: Neutrophil count, lymphocyte count, calculated neutrophil-to-lymphocyte ratio (NLR) values. **Categorical variables**: Type of cancer, gender, age group, comorbidities. **Derived variables:** High or low neutrophil-to-lymphocyte ratio (NLR) based on established clinical cut-off points (if available in literature or defined in the study).

Ethical Considerations

The study was reviewed and approved by the local ethical committees of the participating institutions. Since data were derived from pre-existing hospital records and blood test results, and patients were not subjected to any experimental procedure, no direct ethical risk was associated. All patient data were handled with strict confidentiality.

Data management and statistical analysis

Data were analyzed using SPSS. Cross-tabulations and Chi-square tests were performed to assess the relationship between the neutrophil-to-lymphocyte ratio (NLR) categories and clinical variables. A p-value < 0.05 was considered statistically significant.

Results and discussion

Distribution of participants according to the neutrophil-to-lymphocyte ratio (NLR)

Were evaluate the association between neutrophil-to-lymphocyte Ratio (NLR) and normal reference range (neutrophil-to-lymphocyte Ratio (NLR) 1–3). There is a statistically significant elevation in the neutrophil-to-lymphocyte ratio (NLR) among patients compared to expected values under normal physiological conditions ($p = 0.001$), were is high 63.8%, normal 34% and low 2.1%. As shown in graph 1.

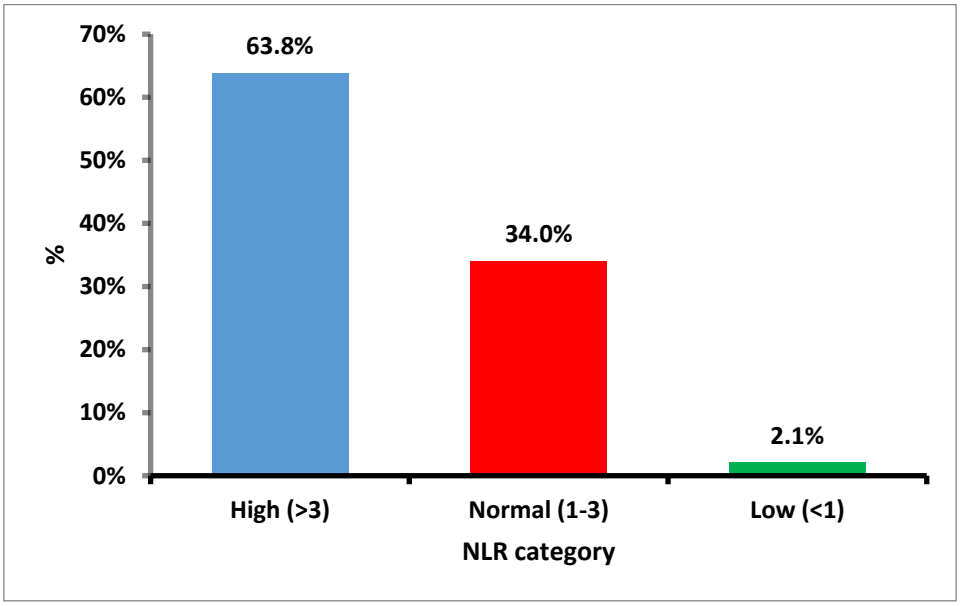
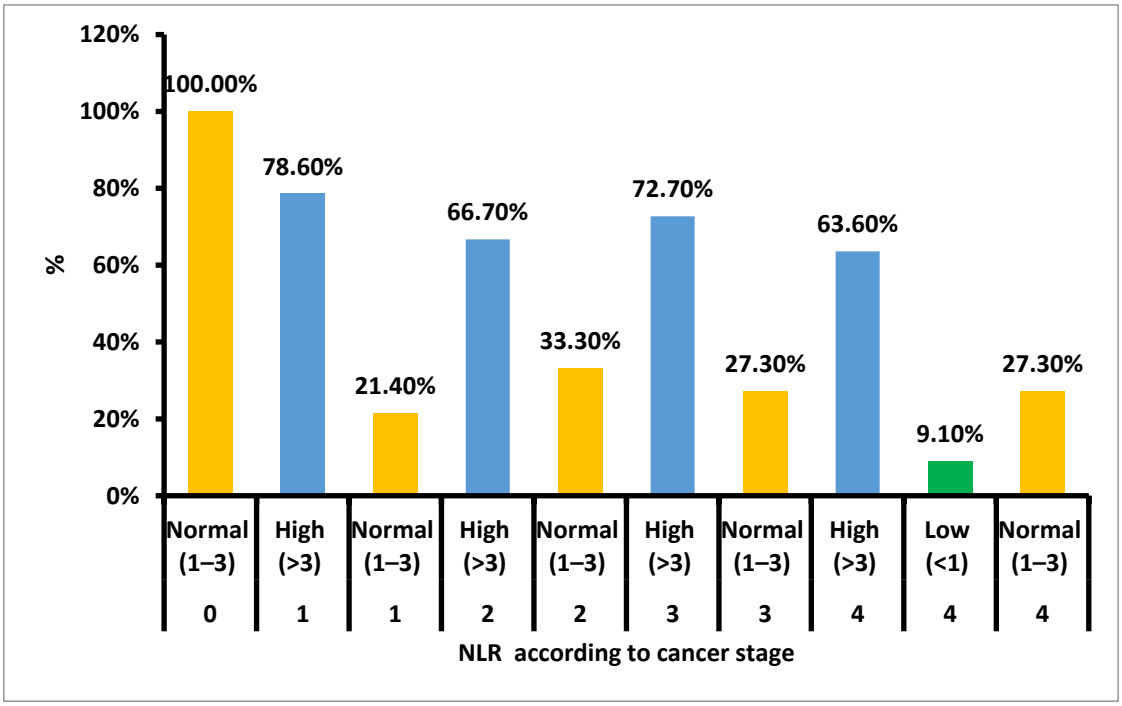


Figure 1. Distribution of participants according to NLR

Distribution of the neutrophil-to-lymphocyte ratio (NLR) categories according to cancer stage

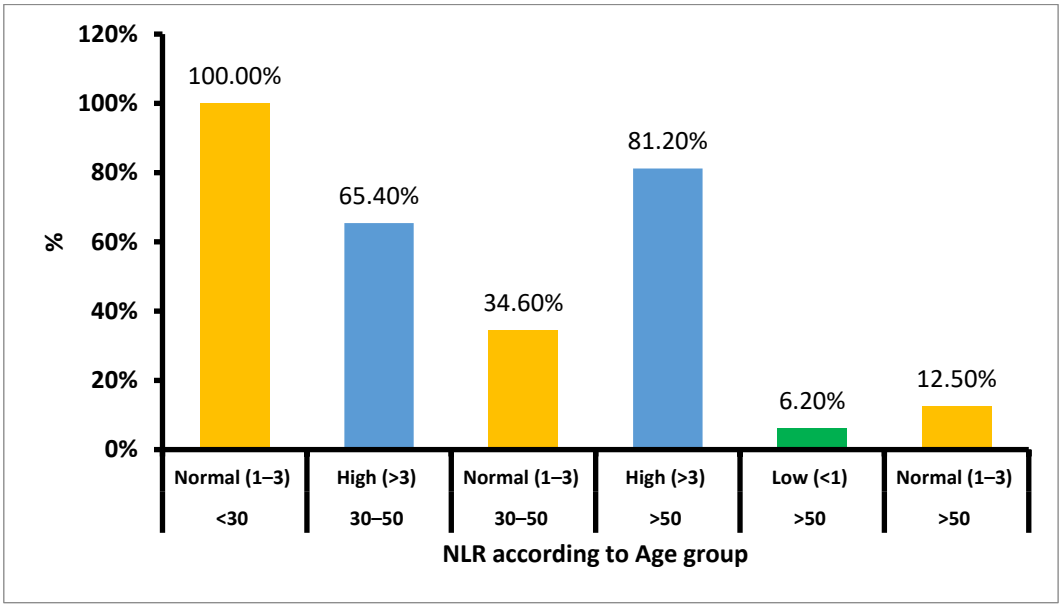
There is a statistically significant (p value= 0.043) association between neutrophil-to-lymphocyte Ratio (NLR) and cancer stage. Elevated neutrophil-to-lymphocyte Ratio (NLR) is more frequent in advanced stages (3 – 4), suggesting its potential as a prognostic marker As shown in graph 2.



figure(2) Distribution of NLR according to cancer stage

Distribution of the neutrophil-to-lymphocyte ratio (NLR) categories according to age group

There is a statistically significantly (p value = 0.024) associated with age. So Patients >50 years show a higher prevalence of elevated neutrophil-to-lymphocyte Ratio (NLR), indicating increased systemic inflammation with age. As shown in graph 3.



Figure(3) Distribution of NLR according to age group

Overall, the analysis revealed a high prevalence of elevated neutrophil-to-lymphocyte Ratio (NLR) (>3) across the sample. This elevation was particularly associated with advanced stages of cancer and with older age groups (>50 years). Patients younger than 30 years exhibited exclusively normal neutrophil-to-lymphocyte Ratio (NLR) values. These findings reinforce the prognostic role of neutrophil-to-lymphocyte Ratio (NLR) as a low-cost and clinically valuable biomarker. The present study evaluated the prognostic value of the neutrophil-to-lymphocyte ratio (NLR) in Libyan breast cancer patients. The findings demonstrated that the majority of patients (80%) had elevated neutrophil-to-lymphocyte Ratio (NLR) values (>3), with higher prevalence observed in advanced cancer stages and in older age groups. These results strongly support the role of neutrophil-to-lymphocyte Ratio (NLR) as a biomarker of systemic inflammation and cancer progression. Similar findings have been consistently reported in international studies. Pistelli et al. (2015) and Liu *et al*. (2022) highlighted that elevated neutrophil-to-lymphocyte Ratio (NLR) is associated with poor overall survival (OS) and disease-free survival (DFS) in breast cancer patients. Likewise, Kim *et al*. (2021) and Nemoto *et al*. (2021) confirmed that higher neutrophil-to-lymphocyte Ratio (NLR) values were more frequent among patients in advanced stages of the disease. Differences between the present study and some international reports could be attributed to the relatively small sample size, regional variations in patient characteristics, and the retrospective design. Nevertheless, the consistency of elevated neutrophil-to-lymphocyte Ratio (NLR) as an indicator of poor prognosis highlights its clinical importance.

Conclusion

This study has clearly demonstrated the critical link between immune system activity and cancer development, with a specific focus on triple-negative breast cancer (TNBC) as a representative and clinically significant model. By integrating both international evidence and local data from Libyan patients, the findings highlight the neutrophil-to-lymphocyte ratio (NLR) as a simple, cost-effective, and clinically valuable biomarker of systemic inflammation and disease prognosis. The results showed that the majority of patients (80%) presented with elevated NLR values (>3), with strong correlations observed between high NLR, advanced cancer stage, and older age groups. These findings are consistent with international studies, such as those by Pistelli *et al*. (2015), Kim et al. (2021), Nemoto *et al*. (2021), and Liu *et al*. (2022), which collectively confirm that elevated NLR is significantly associated with reduced overall survival (OS) and disease-free survival (DFS). Importantly, the present study strengthens the argument that NLR reflects the underlying balance between immune surveillance and chronic inflammation, both of which play central roles in cancer progression.

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