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Research Article

Evaluating the role of Neutrophil-to-Lymphocyte and Platelet-to Lymphocyte Ratios as Biomarkers in Gastrointestinal Malignancies: A Prospective Observational Study

Dr.Rajandeep Singh Bali[1], *Dr.Balaji Rajendran[2], Dr. Shakeel Ahmed Mir[3], Dr.Rizwan Ahmad[4], Dr.Aijaz ahmad[5]

Dr.Rajandeep Singh Bali M.S.(General Surgery),Assistant professor,Government Medical College,Srinagar.
Dr.Balaji Rajendran M.S.scholar(General Surgery),Government Medical College,Srinagar.
Prof. Dr. Shakeel Ahmed Mir M.S.(General Surgery),Professor,Government Medical College,Srinagar.
Dr.Rizwan Ahmad M.S.(General Surgery),Senior resident,Government Medical College,Srinagar.
Dr.Aijaz ahmad M.S.(General Surgery),Senior resident,Government Medical College,Srinagar.

CORRESPONDING AUTHOR : Dr.Balaji Rajendran

Abstract

Background: Gastrointestinal (GI) malignancies are among the leading causes of cancer-related morbidity and mortality worldwide. Conventional staging systems remain the cornerstone of prognostication, but they often fail to capture the contribution of systemic inflammation to tumor biology. Readily available haematological indices such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have emerged as promising prognostic markers.

Aim: To evaluate the significance of NLR and PLR as prognostic indicators in GI malignancies and assess their correlation with clinicopathological parameters. Methods: A prospective observational study was conducted on 59 patients with histologically proven gastrointestinal cancers at Government Medical College, Srinagar, over 18 months. Preoperative complete blood counts were analysed to calculate NLR and PLR. Patients were stratified into high and low groups using median values. The associations of NLR and PLR with tumor site, grade, T stage, nodal status, and AJCC stage were assessed.

Results: Elevated NLR was observed in 61% of patients, with significant correlation to nodal positivity (p=0.029) and higher T stage. PLR was elevated in 33.9% of patients and showed a trend toward association with poorly differentiated tumors. Combined risk classification using NLR and PLR stratified patients into low, intermediate, and high inflammatory risk categories, with higher values correlating with advanced disease.

Conclusion: NLR and PLR are cost-effective and easily obtainable biomarkers that reflect systemic inflammation and tumor aggressiveness. Their integration into clinical practice may enhance prognostication and guide management strategies in GI malignancies.

Keywords: Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio, Gastrointestinal malignancies, Prognostic markers, Inflammation

Introduction

Gastrointestinal cancers constitute a major global health challenge, accounting for a significant proportion of cancer incidence and mortality. According to GLOBOCAN estimates, colorectal, gastric, pancreatic, and oesophageal cancers are among the top causes of cancer-related deaths worldwide. In India, the burden of GI cancers is increasing, with variations in incidence patterns across different regions. For example, oesophageal cancers are more prevalent in Kashmir, while gallbladder cancers are common in northern India. Despite advances in diagnostic modalities, surgical oncology, chemotherapy, and targeted therapies, survival outcomes in GI malignancies remain suboptimal. Prognostication traditionally relies on the TNM staging system, which describes tumor depth, nodal involvement, and metastatic spread. While indispensable, this system does not account for host-tumor interactions or biological heterogeneity that influences treatment response and survival. A growing body of evidence suggests that systemic inflammation plays a critical role in carcinogenesis. Chronic inflammation fosters genetic mutations, promotes angiogenesis, enhances metastatic potential, and dampens anti-tumor immunity. This interplay is particularly relevant in GI malignancies, where many cancers are preceded by chronic inflammatory states—for example, Helicobacter pylori-induced gastritis in gastric cancer, inflammatory bowel disease in colorectal cancer, and chronic pancreatitis in pancreatic cancer. Systemic inflammatory markers derived from peripheral blood, such as NLR and PLR, provide a simple and inexpensive way of quantifying this host response. Elevated neutrophils support tumor growth by secreting proteases, cytokines, and growth factors. Reduced lymphocytes reflect impaired cell-mediated immunity, diminishing the host's ability to suppress tumor progression. High platelet counts facilitate angiogenesis and shield circulating tumor cells from immune detection. Consequently, elevated NLR and PLR reflect an imbalance between pro-tumor and anti-tumor forces, correlating with poor outcomes. Multiple studies across the globe have examined these markers. For instance, Stojkovic Lalosevic et al. demonstrated that high NLR and PLR predicted poor survival in colorectal cancer patients. Pang et al. reported similar findings in gastric cancer, while Wei et al.'s meta-analysis confirmed their prognostic significance in gastrointestinal stromal tumors. However, variability in study designs, cutoff values, and ethnic populations limits generalisability. In low- and middle-income countries like India, where access to advanced molecular markers and imaging may be restricted, simple blood-based biomarkers like NLR and PLR can play a pivotal role in clinical decision-making. This study was therefore designed to evaluate the prognostic significance of NLR and PLR in patients with GI malignancies treated at a tertiary care hospital in Srinagar, with particular emphasis on their relationship with tumor site, grade, nodal status, and stage.

Materials and Methods

Study Design and Duration

This was a prospective observational study conducted in the Department of General Surgery, Government Medical College, Srinagar, over 18 months (July 2023 – December 2024). The study

protocol was reviewed and approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion.

Patient Selection

Inclusion criteria:

• Adults (≥18 years) with histologically confirmed gastrointestinal malignancies.

• Patients undergoing evaluation or treatment at the hospital during the study period.

• Patients willing to provide informed consent.

Exclusion criteria:

• Patients with concurrent infections or inflammatory conditions.

• Patients with haematological disorders.

• Patients receiving corticosteroids or other immunomodulatory therapies.

• Patients unwilling to participate.

Data Collection

Demographic details (age, sex), clinical history, comorbidities, and tumor characteristics (site, histological type, grade, TNM stage) were recorded.

Laboratory Analysis

Preoperative blood samples were collected within one week of surgery or biopsy. Complete blood counts (CBCs) were performed using an automated haematology analyser.

• NLR was calculated as absolute neutrophil count / absolute lymphocyte count.
• PLR was calculated as platelet count / absolute lymphocyte count.

Risk Stratification

Patients were divided into “high” and “low” NLR/PLR groups using median values as cutoffs. Combined risk stratification was also performed:

• Low risk: both NLR and PLR low.

• Intermediate risk: either NLR or PLR high.

• High risk: both NLR and PLR high.

Statistical Analysis

Descriptive statistics were calculated for baseline characteristics. Associations between categorical variables were tested using chi-square or Fisher’s exact test. Continuous variables were analysed with Student’s t-test or Mann–Whitney U test depending on distribution. Statistical significance was set at $p < 0.05$.

Results

Demographic Characteristics

A total of 59 patients were included. The mean age was 51.4 years (range 33–68 years). The majority (57.6%) belonged to the 41–60 age group. There was a male predominance (62.7%), with a male-to-female ratio of 1.7:1.

Tumor Distribution

The most common primary site was the colon (25.4%), followed by stomach (22.0%) and rectum (16.9%). Oesophageal cancers comprised 13.6%, pancreatic cancers 10.2%, gallbladder cancers 5.1%, periampullary tumors 3.4%, and small bowel cancers 3.4%. Collectively, colorectal and gastric malignancies accounted for nearly half of cases.

NLR and PLR Values

• Mean NLR: 3.8 (SD 1.7).

• Mean PLR: 168.2 (SD 50.9).

• High NLR: observed in 61.0% of patients.

• High PLR: observed in 33.9% of patients.

Correlation with Tumor Characteristics

• NLR: Significantly associated with nodal positivity (p=0.029) and higher T stage. No significant correlation with tumor site.

• PLR: Showed a trend toward correlation with poorly differentiated tumors but did not reach statistical significance.

• Combined classification: 30.5% low risk, 44.1% intermediate risk, 25.4% high risk. Higher combined scores correlated with advanced stage disease.

Interpretation

The results suggest that NLR is a stronger predictor of disease aggressiveness compared to PLR. However, the combination of the two ratios provided more refined risk stratification.

Discussion

Principal Findings

This study demonstrates that NLR and PLR, derived from routine blood tests, provide valuable prognostic insights in gastrointestinal malignancies. Elevated NLR was significantly associated with nodal metastasis and advanced T stage, supporting its role as a marker of tumor aggressiveness. PLR, while less robust, still showed trends with higher tumor grade. The

combined use of NLR and PLR allowed stratification of patients into risk groups that correlated with more advanced disease.

Comparison with Previous Studies

Our findings are consistent with international literature. Stojkovic Lalosevic et al. (2018) reported that NLR and PLR were independent prognostic markers in colorectal cancer, with high values predicting poor survival. Pang et al. (2016) found that both markers were useful in predicting lymph node metastasis in gastric cancer. Goh et al. (2016) highlighted their role in gastrointestinal stromal tumors. Similarly, Wei et al.'s meta-analysis confirmed the prognostic value of NLR and PLR across multiple GI tumors.

Notably, some studies have reported variability in PLR as a prognostic tool. This inconsistency may reflect differences in tumor biology, population characteristics, or methodological factors such as cutoff selection. Our findings align with this trend, showing that PLR alone was less consistent but gained significance when combined with NLR.

Biological Rationale

The biological plausibility of these associations is strong. Neutrophils release proteases, cytokines, and angiogenic factors that promote tumor growth and spread. Lymphocytes, particularly cytotoxic T-cells, are central to anti-tumor immunity, and their depletion reflects immunosuppression. Platelets, beyond their role in hemostasis, interact with tumor cells to promote adhesion, protect against immune clearance, and facilitate angiogenesis. Together, these interactions explain why elevated NLR and PLR correlate with aggressive disease.

Clinical Implications

The clinical utility of NLR and PLR lies in their simplicity, cost-effectiveness, and universal availability. Unlike molecular markers or advanced imaging, they require no additional resources and can be readily incorporated into routine preoperative evaluation. They may aid in:

• Identifying high-risk patients who may benefit from intensive therapy or closer surveillance.

• Complementing existing staging systems to refine prognostication.

• Guiding discussions with patients regarding prognosis.

Limitations

The limitations of this study must be acknowledged.

1. Small sample size, limiting statistical power.

2. Single-center design, which may restrict generalisability.

3. Lack of survival analysis, as long-term follow-up data were unavailable.

4. Potential confounding factors such as subclinical infections or medication effects.

Future Directions

Future research should focus on:

• Larger multicenter cohorts to validate findings.

• Establishing standardised cutoff values for NLR and PLR.

• Incorporating these markers into prognostic nomograms alongside molecular and pathological features.

• Evaluating their role in predicting response to chemotherapy, immunotherapy, or targeted therapy.

Conclusion

This prospective observational study highlights the prognostic significance of NLR and PLR in gastrointestinal malignancies. Elevated NLR correlated with nodal metastasis and advanced T stage, while PLR showed trends with tumor grade. Combined analysis of both markers provided refined risk stratification, reinforcing their value as adjuncts to conventional staging.

Given their low cost, ease of measurement, and biological plausibility, NLR and PLR can serve as practical biomarkers in routine clinical practice, especially in resource limited settings. Further large-scale prospective studies are warranted to standardise cutoff values and integrate these markers into comprehensive prognostic models.

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