RESEARCH PAPER

Lymphocyte to Monocyte Ratio: A Pathfinder in Solid Tumor Prognosis

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ABSTRACT

Introduction: The behaviour of solid tumours depends not only on the malignant cells themselves but also on the host inflammatory response. Blood-based inflammatory markers derived from routine complete blood count have therefore gained interest as simple and inexpensive indicators of tumour behaviour. Among them, the lymphocyte-to-monocyte ratio (LMR) may be particularly relevant because it reflects the balance between host immune defence and tumour-associated inflammation.

Objective: To evaluate the association between pretreatment lymphocyte-to-monocyte ratio and histological grade in patients with histopathologically confirmed solid tumours, and to compare its performance with neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio.

Materials & Methods: This retrospective cross-sectional study included 72 patients with histopathologically confirmed solid tumours. Pretreatment complete blood count parameters were obtained from institutional records, and LMR, NLR, and PLR were calculated. The association between inflammatory biomarkers and histological grade was analysed using appropriate statistical tools. A p-value <0.05 was considered statistically significant.

Results: All three inflammatory biomarkers demonstrated significant associations with histological grade ($p < 0.001$). LMR showed a progressive decline from Grade I to Grade III tumours, whereas NLR and PLR increased with advancing tumour grade. Notably, LMR demonstrated the strongest discriminatory ability, with significant differences across all histological grades, while NLR and PLR primarily differentiated high-grade tumours from the lower grades.

Conclusion: Pretreatment LMR was more consistently associated with histological tumour grade than NLR or PLR in the present study. As an inexpensive and routinely available parameter derived from complete blood count, LMR may complement conventional histopathological assessment and aid prognostic stratification in patients with solid tumours. Larger prospective studies are warranted to validate its clinical utility.

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INTRODUCTION:

Solid tumours account for a large proportion of cancers encountered in routine clinical practice and remain an important cause of cancer-related mortality despite advances in diagnosis and treatment.[1] In India as well, the burden of solid malignancies continues to increase, contributing substantially to cancer-related morbidity and mortality. [2] Histopathological examination remains the gold standard for diagnosis, while tumour grade continues to be one of the most important indicators of biological behaviour and prognosis. However, we often encounter tumours with similar histological grades that behave differently during follow-up. This suggests that histopathological assessment alone may not completely explain tumour behaviour and highlights the need for additional markers that are simple, objective, and readily available.

The behaviour of a tumour depends not only on the malignant cells themselves but also on the host immune

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response.[3] Inflammatory cells within the tumour microenvironment influence cell proliferation, angiogenesis, invasion, and metastasis through continuous interaction with tumour cells.[4,5]] For this reason, inflammatory biomarkers measured in peripheral blood have been evaluated as additional indicators of tumour behaviour and prognosis.[4-6]

Routine complete blood count provides several inflammatory indices that can be calculated without additional laboratory investigations. Because these parameters are inexpensive, reproducible, and routinely available, they have been widely evaluated as potential prognostic biomarkers in patients with solid tumours.[6] Among these, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been widely studied and have shown associations with tumour progression and survival in several malignancies.[7-9] Elevated neutrophil counts reflect an enhanced systemic inflammatory response, while increased platelet counts contribute to tumour growth and angiogenesis.[4,5] Although these biomarkers provide useful prognostic information, they primarily reflect individual components of the inflammatory response.[7-9]

The lymphocyte-to-monocyte ratio (LMR) offers a different perspective because it reflects the balance between host immune defence and tumour-associated inflammation.[10,11] Lymphocytes play an important role in recognising and eliminating malignant cells, whereas monocytes differentiate into tumour-associated macrophages that promote tumour progression and suppress the immune response.[4,5] A low LMR therefore reflects reduced antitumour immunity together with increased tumour-promoting inflammation, making it a biologically relevant marker for assessing tumour behaviour.[10,11]

Previous studies have shown that low pretreatment LMR is associated with adverse clinicopathological features and poorer survival in several solid malignancies.[10-14] However, most studies have focused on survival outcomes or treatment response. [10-14] Comparatively fewer studies have examined whether pretreatment LMR is associated with histological grade across different solid tumours. Since histological grading is routinely performed in pathologic practice and forms an integral part of prognostic assessment, establishing this relationship may provide additional information that is readily applicable in daily clinical practice.

The present study was therefore undertaken to evaluate the association between pretreatment lymphocyte-to-monocyte ratio and histological grade in patients with histopathologically confirmed solid tumours. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio were analysed for comparison to determine whether LMR provides additional value as a simple inflammatory biomarker that can complement conventional histopathological evaluation.

MATERIALS AND METHODS

This retrospective descriptive cross-sectional study was carried out in the Department of Pathology, Tagore Medical College and Hospital, Chennai, after obtaining approval from the Institutional Ethics Committee (IEC REF No. **17/NOVEMBER/2023**), (IEC PROTOCOL NO: PP NO:13/NOVEMBER/2023).

A total of 72 patients with histopathologically confirmed solid tumours diagnosed between January 2019 and April 2023 were included. Pretreatment complete blood count reports and corresponding histopathology records were retrieved from the departmental database. Only patients who underwent surgery as the primary treatment and had an available pretreatment complete blood count were included. Patients who had received chemotherapy, radiotherapy, hormonal therapy, immunotherapy, or had incomplete records were excluded.

Patient age, sex, tumour type, histological grade, total white blood cell count, neutrophil count, lymphocyte count, monocyte count, and platelet count were recorded. The lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) were calculated from the pretreatment complete blood count. LMR was the primary biomarker evaluated, while NLR and PLR were analysed for comparison.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation, and categorical variables as frequency and percentage. Differences in inflammatory biomarkers across histological grades were analysed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 72 patients with histopathologically confirmed solid tumours were included in the study. The mean age of the study population was **61.1 ± 10.1 years** (range, 38–82 years). Females constituted **54.2% (n = 39)** of the study population, while males accounted for **45.8% (n = 33)**. Grade II tumours were the most common (**50.0%**), followed by Grade I (**26.4%**) and Grade III (**23.6%**). Breast carcinoma was the predominant tumour type (**24/72, 33.3%**) (Table 1).

Table 1: Clinicopathological characteristics of the study population (n = 72)

Variable	Category	value
Age (years)	Mean ± SD	61.1 ± 10.1
Sex	Male	33 (45.8%)
	Female	39 (54.2%)

Histological Grade	Grade I	19 (26.4%)
	Grade II	36 (50.0%)
	Grade III	17 (23.6%)
Tumour Type	Breast	24 (33.3%)
	Thyroid	9 (12.5%)
	Colon	8 (11.1%)
	Cervix	6 (8.3%)
	Prostate	4 (5.6%)
	Gastric	4 (5.6%)
	Oral	4 (5.6%)
	Ovary	3 (4.2%)
	Skin	3 (4.2%)
	Endometrium	2 (2.8%)

Table 2. Comparison of inflammatory biomarkers according to histological grade

Biomarker	**Grade I (n = 19) Mean ± SD**	**Grade II (n = 36) Mean ± SD**	**Grade III (n = 17) Mean ± SD**	**F statistic**	**P value**	**Significant post hoc comparison***
LMR	4.93 ± 1.28 (95% CI: 4.32–5.55)	3.29 ± 0.81 (95% CI: 3.02–3.56)	2.02 ± 0.66 (95% CI: 1.68–2.36)	44.87	**<0.001**	I vs II, I vs III, II vs III
NLR	2.03 ± 0.75 (95% CI: 1.78–2.51)	2.82 ± 0.86 (95% CI: 2.55–3.14)	4.39 ± 1.67 (95% CI: 3.56–5.27)	20.79	**<0.001**	I vs III, II vs III
PLR	109.58 ± 52.90 (95% CI: 84.09–135.08)	157.66 ± 85.75 (95% CI: 128.64–186.67)	276.19 ± 137.99 (95% CI: 205.24–347.14)	14.98	**<0.001**	I vs III, II vs III

The mean pretreatment LMR showed a progressive decline with increasing histological grade, decreasing from **4.93 ± 1.28** in Grade I tumours to **3.29 ± 0.81** in Grade II and **2.02 ± 0.66** in Grade III tumours. In contrast, both NLR and PLR increased with increasing tumour grade. The mean NLR increased from **2.03 ± 0.75** in Grade I to **4.39 ± 1.67** in Grade III tumours, while the mean PLR increased from **109.58 ± 52.90** to **276.19 ± 137.99** across the same grades (Table 2).

One-way analysis of variance demonstrated statistically significant differences in all three inflammatory biomarkers according to histological grade. LMR showed the strongest association with tumour grade (**$F = 44.87$, $p < 0.001$**), followed by NLR (**$F = 20.79$, $p < 0.001$**) and PLR (**$F = 14.98$, $p < 0.001$**)(Table 2).

Post hoc analysis using Tukey's test demonstrated significant differences in LMR between all three histological grades ($p < 0.001$). In contrast, significant differences in NLR and PLR were observed mainly between Grade III tumours and the lower histological grades(Table 2).

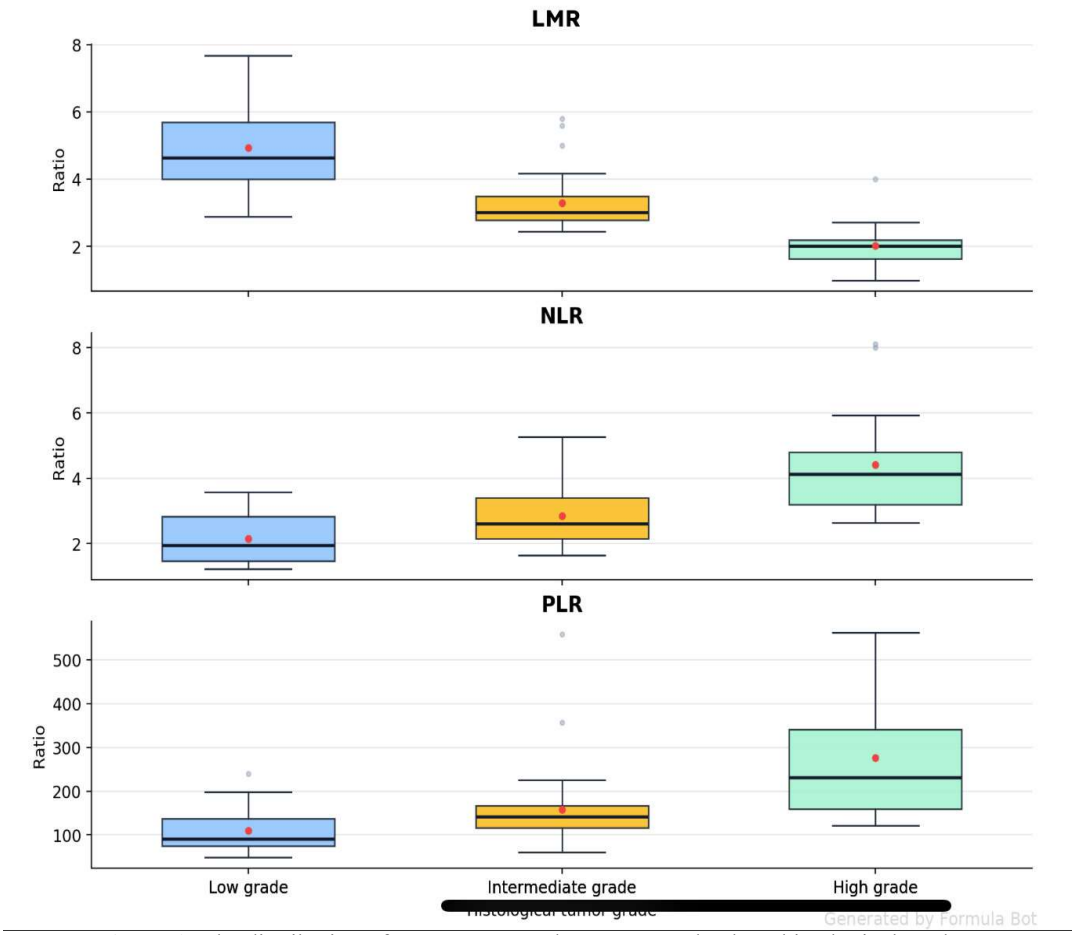

Figure 1: The distribution of LMR, NLR, and PLR across the three histological grades:

DISCUSSION

The present study evaluated the association between pretreatment inflammatory biomarkers and histological grade in patients with solid tumours. Within our study population, LMR decreased steadily from Grade I to Grade III tumours, whereas both NLR and PLR increased with increasing tumour grade. LMR also showed significant differences between all three histological grades, while NLR and PLR mainly differentiated Grade III tumours from the lower grades. Taken together, these findings suggest that LMR reflects tumour differentiation more consistently than the other inflammatory biomarkers evaluated in this study.

The findings are biologically plausible. Tumour behaviour depends not only on the malignant cells themselves but also on the host immune response.[3] Lymphocytes contribute to immune surveillance by recognising and eliminating malignant cells, whereas circulating monocytes differentiate into tumour-associated macrophages within the tumour microenvironment.[4,5] These macrophages promote tumour growth through angiogenesis, immune suppression, extracellular matrix remodelling, and tumour invasion.[4,5] A reduction in LMR therefore reflects reduced host immune surveillance together with increased tumour-associated inflammation, which may explain the progressive decline in LMR with increasing histological grade observed in the present study.

The findings of the present study are consistent with previous reports evaluating LMR in solid malignancies. Nishijima *et al.* reported that patients with a low pretreatment LMR had poorer survival and less favourable clinicopathological features across different solid tumours.[10] Similarly, Teng *et al.* found that reduced LMR was associated with adverse clinical outcomes and suggested that it reflects both tumour aggressiveness and the host inflammatory response.[11] While these studies primarily evaluated survival, the present study demonstrates that LMR is also associated with histological tumour grade. This suggests that changes in the systemic inflammatory response may parallel tumour differentiation even before long-term clinical outcomes become apparent.

NLR and PLR were also significantly associated with histological grade in the present study, with both biomarkers increasing as tumour grade advanced. Similar observations have been reported in previous studies.[7-9,13,14] However, on post hoc analysis, both biomarkers showed greater overlap between Grade I and Grade II tumours, whereas LMR remained significantly different

across all three histological grades. This finding suggests that LMR may reflect tumour differentiation more consistently than NLR and PLR within our study population. A possible explanation is that LMR incorporates both the host immune response and tumour-associated inflammatory activity, whereas NLR and PLR predominantly reflect individual components of the systemic inflammatory response.

One of the practical advantages of LMR is that it is derived from a routine pretreatment complete blood count without additional investigations or cost.[15,16] This makes it particularly relevant in routine pathological practice and resource-limited settings. Although LMR should not replace established prognostic parameters such as tumour stage or histological grade, it may serve as a useful adjunct when interpreted alongside routine clinicopathological findings.

LIMITATIONS

The findings of this study should be interpreted in the context of its design. The study was retrospective, conducted at a single institution, and included a relatively small cohort representing different types of solid tumours. Although the inclusion of multiple tumour types reflects routine pathological practice, it may also have introduced biological heterogeneity. In addition, follow-up data on survival, recurrence, and treatment response were not available, limiting assessment of the prognostic value of LMR beyond its association with histological grade. Future prospective multicentre studies involving larger, tumour-specific cohorts are needed to validate these findings and establish clinically meaningful LMR cut-off values.

CONCLUSION

The present study demonstrates a significant association between pretreatment LMR and histological grade in patients with solid tumours. Compared with NLR and PLR, LMR showed a closer association with tumour differentiation within our study population. As LMR can be obtained from a routine pretreatment complete blood count without additional cost or laboratory investigations, it may serve as a practical adjunct to conventional histopathological assessment. Future multicentre prospective studies with long-term follow-up should evaluate the clinical utility of LMR across different solid tumours and establish standardized cut-off values for routine clinical practice.

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