THE ASSOCIATION BETWEEN PERIPHERAL BLOOD NEUTROPHIL-TO-LYMPHOCYTE AND PLATELET-TO-LYMPHOCYTE RATIOS WITH CLINICAL AND LABORATORY CHARACTERISTICS IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

Ta Viet Hung[1,2], Tran Minh Duc[3], Do Khac Dai[2], Nguyen Thi Hien Hanh[1,2]
Vu Hong Anh[1,2], Nguyen Trung Kien[1,2]*

Abstract

Objectives: To analyze the association between peripheral blood neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) with clinical and laboratory characteristics in patients with hepatocellular carcinoma (HCC). ***Methods:*** A cross-sectional descriptive study was conducted on 60 newly diagnosed HCC patients who had not received any treatment. These patients came for examination and treatment at the Department of Gastroenterology and Hepatology, Military Hospital 103, from April 2023 to April 2024. ***Results:*** The patients had a mean age of 61.5 years, predominantly male (96.7%), with a median tumor size of 6.4cm, and 21.7% presented with metastasis. The median value of AFP was 965.3 ng/mL, CRP was 13.8 ng/mL, ALBI score was -2.06, NLR was 2.6, and PLR was 104.9. No significant differences in NLR or PLR were observed across subgroups by age, liver function, tumor number/size, or metastasis. NLR correlated positively with AST (r = 0.41), CRP (r = 0.51), ALBI score (r = 0.36), and negatively with albumin (r = -0.38) and prothrombin ratio (r = -0.31), while PLR showed only a weak positive correlation with CRP (r = 0.28). ***Conclusion:*** NLR and PLR were associated with markers of liver injury and systemic inflammation. NLR showed moderate correlations with AST, CRP, ALBI score, albumin, and prothrombin ratio, whereas PLR demonstrated only a weak correlation with CRP.

Keywords: Neutrophil-to-lymphocyte ratio; Platelet-to-lymphocyte ratio; Hepatocellular carcinoma; Clinical and laboratory characteristics.

---

[1]Military Hospital 103, Vietnam Military Medical University
[2]Vietnam Military Medical University
[3]Military Institute of Traditional Medicine
[*]Corresponding author: Nguyen Trung Kien (bs.ntkien@gmail.com)
Date received: 29/7/2025
Date accepted: 10/9/2025
http://doi.org/10.56535/jmpm.v50si4.1477

INTRODUCTION

Hepatocellular carcinoma is the most common primary liver cancer, accounting for 85 - 90% of cases. It ranks sixth globally in cancer incidence and third in cancer-related deaths. Despite advances in diagnosis and treatment, the 5-year survival rate remains low at around 2.3% [1]. Chronic inflammation is key in HCC development, promoting cancer cell growth, invasion, angiogenesis, metastasis, and immune suppression. Simple markers, such as NLR and PLR, are gaining interest as indirect indicators of inflammation and immune status. Elevated NLR reflects strong inflammation and suppressed immunity, both linked to worse outcomes. PLR also correlates with systemic inflammation and cancer progression [2]. Several studies have shown the associations between NLR, PLR, and various clinical, laboratory features in HCC, including age [3], liver function (Child-Pugh score) [4, 5], tumor size, number, and vascular invasion [6 - 8], as well as liver enzymes (AST, ALT), AFP, and disease stage [9, 10]. We conducted this study with the objective: *To analyze the association between peripheral blood NLR and PLR with clinical and laboratory characteristics in patients with HCC.*

MATERIALS AND METHODS

1. Subjects

Including 60 patients newly diagnosed with HCC who had not received any prior therapeutic intervention, treated at the Department of Gastroenterology and Hepatology, Military Hospital 103, from April 2023 to April 2024.

* *Inclusion criteria:* Patients diagnosed with HCC according to the diagnostic criteria issued by the Ministry of Health of Vietnam in 2020; first-time diagnosis of HCC without any prior therapeutic intervention; patients ≥ 18 years who provided informed consent to participate in the study.

* *Exclusion criteria:* Patients with other malignancies; patients with acute or chronic inflammatory diseases at the time of diagnosis, or with comorbidities that may affect bone marrow function or confound hematological results (intoxication, renal failure, hematopoietic disorders, cardiovascular disease, other organ malignancies, immunosuppressive therapy, hematologic malignancies, thrombocytopenia, or autoimmune disorders); patients with active bleeding;

use of hematopoietic-stimulating agents within one month before blood testing, immunomodulatory drugs within 7 days before sampling, or blood transfusion within 14 days before testing.

2. Methods

* *Study design:* A cross-sectional descriptive study.

* *Sample size and selection:* Convenience sampling was applied. All patients who met the inclusion criteria and did not violate any exclusion criteria were enrolled in the study.

* *Study process:*

Data collection included: Age; sex; Child-Pugh score; tumor number and size; metastatic status; laboratory parameters including complete blood cell count, prothrombin time; and biochemical indices such as albumin (g/L), AST (U/L), ALT (U/L), total bilirubin (µmol/L), CRP (ng/mL), and AFP (ng/mL).

Calculation of NLR, PLR, and ALBI score:

- NLR = Absolute neutrophil count (G/L) / Absolute lymphocyte count (G/L).

- PLR = Platelet count (G/L) / Absolute lymphocyte count (G/L).

- ALBI = (log10 bilirubin × 0.66) + (albumin × -0.085), where bilirubin is in µmol/L and albumin in g/L.

- The ALBI grade is classified into three categories: Grade 1 with an ALBI score ≤ -2.60, grade 2 with a score ranging from > -2.60 to ≤ -1.39, and grade 3 with a score of > -1.39.

Analysis of the association between peripheral blood NLR, PLR, and clinical variables, including age, hepatic impairment (Child-Pugh classification), and tumor characteristics (number, size, metastasis). Correlation between NLR and PLR with biochemical indices (albumin, AST, ALT, prothrombin index, total bilirubin, CRP, and AFP) was also evaluated.

* *Data analysis:* Data were processed using SPSS version 22.0. A p-value < 0.05 was considered statistically significant.

3. Ethics

The study was approved by the Ethics Committee of Military Hospital 103 (Decision No. 2030/HĐĐĐ, dated June 23th, 2023). Military Hospital 103 granted permission for the use and publication of the research data. The authors declare to have no conflicts of interest in this study.

RESULTS

Table 1. General characteristics of the study group.

Characteristics		$\bar{X} \pm SD$ or Median (IQR) or n (%)
Age		61.47 ± 11.06
Gender	Male	58 (96.7)
	Female	2 (3.3)
Number of tumors		1.96 ± 0.9
Tumor size (cm)		6.4 (4.05 - 8.87)
Metastasis		13 (21.7)
Albumin (g/L)		34.52 ± 6.15
AST (U/L)		95.12 (56.1 - 219.06)
ALT (U/L)		60.42 (38.54 - 96.56)
Total bilirubin (µmol/L)		20.75 (13.3 - 49.85)
Prothrombin (%)		74.43 ± 17.54
CRP (ng/mL)		13.84 (2.05 - 47.34)
AFP (ng/mL)		965.34 (13.2 - 3000)
ALBI score		-2.06 (-2.57 - -1.44)
NLR		2.6 (1.72 - 4.48)
PLR		104.86 (83.12 - 161.14)

The mean age of the patients was 61.47 ± 11.06 years, including 96.7% of males. The average number of tumors was 1.96 ± 0.9, and the median tumor size was 6.4cm. Metastasis was identified in 13 patients (21.7%). The median CRP concentration was 13.84 ng/mL, while AFP levels reached a median of 965.34 ng/mL. The ALBI score had a median of -2.06. Hematological indices showed a median NLR of 2.6 and a median PLR of 104.86.

Table 2. The association between NLR, PLR, and age.

Indices		Age group		p
		< 60 (n = 25)	≥ 60 (n = 35)	
NLR	Median (IQR)	2.43 (1.64 - 3.76)	2.79 (1.69 - 5.59)	> 0.05
PLR	Median (IQR)	99.66 (83.25 - 132.52)	108.64 (81.92 - 165.48)	> 0.05

There was no significant difference in the median values of NLR and PLR between patients aged ≥ 60 years and those aged < 60 years (p > 0.05)

Table 3. The association between NLR, PLR, and Child-Pugh score.

Indices		Child-Pugh A (n = 38)	Child-Pugh B (n = 12)	Child-Pugh C (n = 10)	p
NLR	Median (IQR)	2.46 (1.68 - 3.68)	3.85 (1.80 - 5.33)	3.68 (1.81 - 5.79)	> 0.05
PLR	Median (IQR)	106.44 (76.15 - 158.91)	105.94 (91.62 - 204.16)	100.99 (82.72 - 133.00)	> 0.05

Patients classified as Child-Pugh B and C exhibited higher median NLR values than those in the Child-Pugh A group. However, the differences were not statistically significant (p > 0.05). The median PLR values were comparable among all three Child-Pugh classes (p > 0.05).

Table 4. The association between NLR, PLR, and tumor characteristics.

Characteristics		NLR Median (IQR)	PLR Median (IQR)
Tumor number	1 tumor (n = 25)	2.79 (1.78 - 4.65)	107.75 (82.14 - 160.03)
	2 tumors (n = 12)	2.59 (1.68 - 4.52)	105.42 (78.61 - 125.25)
	≥ 3 tumors (n = 23)	2.43 (1.68 - 4.5)	99.90 (82.98 - 174.75)
	p	> 0.05	> 0.05

Characteristics		NLR Median (IQR)	PLR Median (IQR)
Tumor size	< 5cm (n = 23)	2.48 (1.65 - 3.94)	99.90 (74.15 - 125.42)
	5 - 10cm (n = 27)	2.57 (1.59 - 4.42)	110.85 (91.34 - 174.5)
	> 10cm (n = 10)	2.93 (2.35 - 5.68)	111.67 (93.57 - 183.97)
	p	> 0.05	> 0.05
Metastatic status	Yes (n = 13)	3.93 (2.41 - 6.11)	101.03 (83.2 - 201.83)
	No (n = 47)	2.43 (1.68 - 3.87)	105.12 (81.9 - 140.05)
	p	> 0.05	> 0.05

There were no significant differences in NLR and PLR median values among subgroups categorized by tumor number, tumor size, or metastatic status ($p > 0.05$).

Table 5. Correlation between NLR, PLR, and laboratory indices.

Indices	NLR		PLR	
	Correlation coefficient (r)	p	Correlation coefficient (r)	p
Albumin (g/L)	-0.38	< 0.005	-0.03	> 0.05
AST (U/L)	0.41	< 0.005	0.10	> 0.05
ALT (U/L)	0.12	> 0.05	0.06	> 0.05
Total bilirubin (µmol/L)	0.24	> 0.05	0.001	> 0.05
Prothrombin (%)	-0.31	< 0.05	0.05	> 0.05
CRP (ng/mL)	0.51	< 0.005	0.28	< 0.05
AFP (ng/mL)	-0.03	> 0.05	0.01	> 0.05
ALBI score	0.36	< 0.01	0.01	> 0.05

NLR demonstrated a moderate positive correlation with AST, CRP, and ALBI score with correlation coefficients of $r = 0.41$, 0.51, and 0.36, respectively ($p < 0.01$). In contrast, weak negative correlations were observed between NLR and both albumin concentration ($r = -0.38$, $p < 0.005$) and prothrombin index ($r = -0.31$, $p < 0.05$). PLR exhibited a weak positive correlation with CRP levels ($r = 0.28$, $p < 0.05$), while no significant correlations were found with other biochemical parameters.

DISCUSSION

In our study, the mean age was 61.47 years, with a majority of males (96.7%). The average number of tumors was 1.96 ± 0.9, and the median tumor size was 6.4cm. Metastasis was identified in 13 patients (21.7%). Our results were consistent with the study of Sagnelli et al. (2020), who emphasized that HCC incidence increases with age and occurs more frequently in males due to both biological and exposure-related risk factors. This study also showed that elevated AFP was a common feature in patients with progressive HCC [1]. The inflammatory profile in our patients was characterized by a median CRP of 13.84 ng/mL, a median NLR of 2.6, and a median PLR of 104.86. These values are lower than the cut-off points, which are often associated with poor prognosis in HCC. Wang et al. demonstrated that preoperative NLR and PLR above specific thresholds were independent predictors of worse survival in resectable HCC [9]. Similarly, Taussig et al. highlighted the association between elevated NLR and disease progression or advanced stages of HCC [4]. Yang et al. also reported that higher PLR was an adverse prognostic marker in patients undergoing curative resection [5].

Table 2 shows that both NLR and PLR tended to be higher in patients aged ≥ 60 years compared to those < 60 years; however, these differences did not reach statistical significance. This finding is partly consistent with the report by Wang et al. (2019), which demonstrated that patients with higher PLR values had a significantly older mean age than those with lower PLR (52.54 ± 10.60 vs. 48.82 ± 12.07 years, p = 0.02). Similarly, patients with elevated NLR also showed a slightly higher mean age compared to those with lower NLR, although this difference was not statistically significant (51.28 ± 11.33 vs. 49.00 ± 12.47 years, p = 0.06) [9].

When evaluating the association between NLR and PLR with the severity of liver dysfunction using the Child-Pugh classification, we observed no statistically significant differences in NLR or PLR across the Child-Pugh classes. However, other studies have reported contrasting results. Taussig MD et al. (2017) identified Child-Pugh class B and elevated NLR as poor prognostic indicators for treatment response and disease progression [4]. Similarly, Yang HJ et al. (2017) reported that higher PLR was associated with more severe hepatic dysfunction as indicated by higher Child-Pugh scores [5]. These discrepancies suggest

further research is needed to clarify the relationship between systemic inflammatory indices and liver function.

Regarding tumor characteristics, our findings showed that NLR tended to be higher in patients with multiple tumors and/or larger tumor sizes. The lowest NLR was observed in patients with a single tumor measuring < 5cm, while the highest NLR values were noted in patients with ≥ 2 tumors of larger dimensions. PLR was highest in the subgroup with tumors measuring between 5 - 10cm. However, these differences did not reach statistical significance, possibly due to the limited sample size. Wong L et al. (2019) reported elevated NLR in patients with tumors ≥ 5cm, tumor rupture, or vascular invasion [6]. Such associations may reflect increased systemic inflammatory activation in patients with more aggressive tumor features. Wang D et al. (2019) hypothesized that: (1) elevated neutrophil and platelet counts contribute to the secretion of various growth and inflammatory factors, thereby promoting the proliferation of tumor and stromal cells, modulating the tumor microenvironment, and facilitating tumor progression; (2) larger tumor size represents a higher tumor burden, which is associated with significantly reduced lymphocyte counts and weakened antitumor immune responses, ultimately promoting tumor growth [9].

While it is not statistically significant, both NLR and PLR tended to be higher in patients with extrahepatic metastases. This trend may be attributed to our cohort's small number of metastatic cases, as most patients were diagnosed at relatively earlier stages. Nonetheless, several studies have reported stronger associations. Li X et al. (2014) found that high NLR was associated with extrahepatic metastasis, portal vein thrombosis, and ascites [7]. Chen Y et al. (2021) reported significantly increased PLR in patients with metastasis ($p = 0.001$) [8]. These findings suggest that NLR and PLR may reflect systemic inflammation secondary to tumor progression. In patients with HCC presenting with multifocal disease and/or vascular invasion, heightened neutrophil and platelet counts may indicate stronger inflammatory responses, whereas decreased lymphocyte counts may reflect impaired immune surveillance, favoring metastatic spread.

In our correlation analysis between NLR and PLR with laboratory parameters in table 5, we found a moderate positive correlation between NLR and AST ($r = 0.41$, $p < 0.005$), CRP ($r = 0.51$, $p < 0.005$), ALBI score ($r = 0.36$, $p < 0.01$) and weak negative correlations between NLR and both albumin ($r = -0.38$, $p < 0.005$) and prothrombin

index ($r = -0.31$, $p < 0.05$). For PLR, only a weak positive correlation was observed with CRP ($r = 0.28$, $p < 0.05$). These findings are consistent with a study by Wang C et al. (2020), which reported that high NLR was associated with elevated AST and bilirubin levels, decreased albumin, and lower red blood cell counts [10]. Similarly, Wang D et al. (2019) found that both NLR and PLR were associated with ALT, AST, AFP levels, and disease stage [9]. These correlations further support the utility of NLR and PLR as potential markers for disease progression and cancer-related inflammation.

CONCLUSION

In 60 patients with HCC (mean age 61.5 years, 96.7% male), the median tumor size was 6.4cm, and 21.7% had extrahepatic metastasis. The median AFP, CRP, ALBI, NLR, and PLR were 965.3 ng/mL, 13.8 ng/mL, -2.06, 2.6, and 104.9, respectively. NLR showed positive correlations with AST ($r = 0.41$), CRP ($r = 0.51$), ALBI ($r = 0.36$), and negative correlations with albumin ($r = -0.38$) and prothrombin ratio ($r = -0.31$). PLR correlated weakly with CRP ($r = 0.28$). These findings indicate that NLR may be a more relevant indicator of systemic inflammation and liver dysfunction in HCC.

REFERENCES

1. Sagnelli E, Macera M. Epidemiological and etiological variations in hepatocellular carcinoma. *Infection*. 2020; 48(1):7-17.

2. Lu HR, Zhu PF, Deng YY, et al. Predictive value of NLR and PLR for immune-related adverse events: a systematic review and meta-analysis. *Clin Transl Oncol*. 2024; 26(5):1106-1116.

3. Jebbor A, Zrara A. Age-and gender-specific reference intervals for systemic inflammatory indicators in healthy Moroccan adults. *Clin Lab*. 2024; 70(1).

4. Taussig MD, Irene Koran ME, Mouli SK, et al. Neutrophil to lymphocyte ratio predicts disease progression following intra-arterial therapy of hepatocellular carcinoma. *HPB (Oxford)*. 2017; 19(5):458-464.

5. Yang HJ, Jiang JH, Liu QA, et al. Preoperative platelet-to-lymphocyte ratio is a valuable prognostic biomarker in patients with hepatocellular carcinoma undergoing curative liver resection. *Tumour Biol*. 2017; 39(6):1010428317707375.

6. Wong L, Bozhilov K, Hernandez B, et al. Underlying liver disease and advanced stage liver cancer are associated with elevated neutrophil-lymphocyte ratio. *Clin Mol Hepatol*. 2019; 25(3):305-316.

7. Li X, Chen ZH, Ma XK, et al. Neutrophil-to-lymphocyte ratio acts as a prognostic factor for patients with advanced hepatocellular carcinoma. *Tumour Biol*. 2014; 35(11):11057-11063.

8. Chen Y, Zeng J, Guo P, et al. Prognostic significance of platelet-to-lymphocyte ratio (PLR) in extrahepatic metastasis of hepatocellular carcinoma after curative resection. *Cancer Manag Res*. 2021; 13:1395-1405.

9. Wang D, Bai N, Hu X, et al. Preoperative inflammatory markers of NLR and PLR as indicators of poor prognosis in resectable HCC. *PeerJ*. 2019; 7:e7132.

10. Wang C, Wang M, Zhang X, et al. The neutrophil-to-lymphocyte ratio is a predictive factor for the survival of patients with hepatocellular carcinoma undergoing transarterial chemoembolization. *Ann Transl Med*. 2020; 8(8):541.