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COMPARATIVE ASSESSMENT OF PLATELET-TO LYMPHOCYTE RATIO AND NEUTROPHIL-TO LYMPHOCYTE RATIO IN PREDICTING DISEASE SEVERITY AMONG PATIENTS WITH DENGUE FEVER

Rajesh Sharma[1], Devashish Ranjan[2]

[1]Professor, Department of General Medicine, SIMS, Hapur Uttar Pradesh India
[2]Junior Resident 1, Department of General Medicine, SIMS, Hapur Uttar Pradesh India

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Corresponding Author:
Dr. Devashish Ranjan,
Junior Resident 1, Department of General Medicine, SIMS, Hapur Uttar Pradesh India
Email: devashish5395@gmail.com

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ABSTRACT

Background: Dengue fever is a major public health concern associated with considerable morbidity and mortality. Early identification of severe dengue is essential for appropriate clinical management and prevention of complications. Platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are inexpensive hematological indices that may help predict disease severity. The aim is to compare the predictive performance of PLR and NLR in assessing disease severity among patients with dengue fever.

Materials and Methods: This hospital-based observational analytical study included 96 patients diagnosed with dengue fever, classified into non-severe dengue (n=74) and severe dengue (n=22) according to WHO 2009 criteria. Demographic characteristics, clinical manifestations, hematological parameters, biochemical investigations, complications, and hospital outcomes were evaluated. PLR and NLR were calculated from admission complete blood counts. Receiver operating characteristic (ROC) curve analysis was performed to assess their discriminatory performance. A p-value <0.05 was considered statistically significant.

Results: Severe dengue was observed in 22.92% of patients. The mean age was significantly higher among severe dengue patients (36.98 ± 7.94 vs. 32.64 ± 8.81 years; p=0.035). Median platelet count was significantly lower in severe dengue (47.39 vs. 91.87 × 10^9 /L; p<0.001). PLR (22.76 vs. 64.77) and NLR (1.09 vs. 1.72) were significantly reduced in severe dengue (both p<0.001). PLR demonstrated an AUC of 0.910, with 95.45% sensitivity and 81.08% specificity at a cutoff of ≤34.55. NLR showed an AUC of 0.824, with 86.36% sensitivity and 72.97% specificity at a cutoff of ≤1.49.

Conclusion: Both PLR and NLR were significantly associated with dengue severity. PLR demonstrated numerically superior discriminatory performance and may serve as a useful, cost-effective adjunct for early identification of severe dengue. Further prospective validation is warranted.

Keywords: Dengue Fever; Disease Severity; Platelet-to-Lymphocyte Ratio; Neutrophil-to-Lymphocyte Ratio; Receiver Operating Characteristic Curve.

INTRODUCTION

Dengue fever is a mosquito-borne viral illness and major public health concern in tropical and subtropical regions, including India. It is caused by four antigenically distinct dengue virus serotypes and transmitted predominantly by infected Aedes mosquitoes. Urbanization, population movement and environmental changes contribute to expanding transmission. Its clinical spectrum ranges from uncomplicated fever to potentially life-threatening disease characterized by circulatory failure, bleeding and organ dysfunction. Because seasonal outbreaks place pressure on healthcare facilities, identifying patients who require closer surveillance is essential for appropriate clinical management and resource

allocation.[1] The pathogenesis of dengue involves interactions between viral characteristics, host immunity, inflammatory mediators and endothelial function. Innate and adaptive immune responses influence both viral clearance and clinical manifestations. Dysregulated cytokine release, endothelial glycocalyx injury, platelet activation and altered vascular permeability can contribute to plasma leakage and hemodynamic instability. Secondary infection with a different serotype may further modify immune responses, although severe illness also occurs during primary infection. These mechanisms explain why patients with similar symptoms may subsequently follow different clinical courses, making early severity assessment challenging.[2] Dengue progresses through febrile, critical and recovery phases, with deterioration often occurring around defervescence. Under the World Health Organization classification, patients are categorized as having dengue without warning signs, dengue with warning signs, or severe dengue. Warning signs include abdominal pain, persistent vomiting, mucosal bleeding, fluid accumulation, lethargy and rising hematocrit accompanied by declining platelet counts. Severe dengue involves substantial plasma leakage, severe bleeding or significant organ impairment. Although clinical examination remains fundamental, presentations may be nonspecific and warning signs evolve. Accessible laboratory indicators could therefore strengthen risk assessment.[3] Complete blood count is obtained during dengue evaluation because changes in platelets, leukocytes and hematocrit provide information about disease evolution. Thrombocytopenia may arise from marrow suppression, immune-mediated platelet clearance, peripheral consumption and altered platelet function. Differential leukocyte counts also vary with infection stage and immune activation. Platelet concentration alone cannot fully characterize the likelihood of severe illness, particularly when sampling occurs at different points during febrile and critical phases. Integrating platelet measurements with other available hematological variables may therefore offer a more informative assessment than relying on one cell count.[4] The neutrophil-to-lymphocyte ratio (NLR), calculated by dividing absolute neutrophil count by absolute lymphocyte count, reflects the balance between innate and adaptive immune responses. Neutrophils participate in inflammatory signaling, whereas lymphocytes contribute to antiviral immunity and immunological regulation. Changes in their relative abundance may accompany viral replication, immune activation and progression through dengue phases. NLR requires no testing beyond a differential blood count, making it practical in resource-constrained settings. However, interpretation can be influenced by blood collection timing, concurrent infections, medications and immune responses, requiring careful clinical correlation.[5] The platelet-to-lymphocyte ratio (PLR), obtained by dividing platelet count by absolute lymphocyte count, combines two parameters affected during dengue infection. Platelets contribute to hemostasis, immune signaling and interactions with the vascular endothelium. Lymphocytes reflect antiviral immune activity, while platelet depletion may accompany marrow suppression, immune destruction or consumption. PLR may therefore indicate combined hematological and inflammatory disturbances. Nevertheless, changes in the numerator and denominator may occur simultaneously, and identical ratios can arise through different biological processes. Its clinical usefulness requires evaluation against clearly defined severity categories rather than assumptions based on platelet values alone.[6]

MATERIALS AND METHODS

The present study was designed as a hospital-based, prospective observational comparative study to evaluate and compare the diagnostic and prognostic performance of the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Lymphocyte Ratio (NLR) in predicting disease severity among patients diagnosed with dengue fever. The study aimed to determine the association of these hematological indices with clinical severity, thrombocytopenia, warning signs, organ dysfunction, complications, and clinical outcomes. Additionally, the predictive accuracy of PLR and NLR was assessed to identify the more reliable hematological marker for early recognition of severe dengue. The study was conducted at a tertiary care hospital in the Departments of General Medicine. Patients presenting to the outpatient department, emergency department, or requiring hospital admission with clinically suspected and laboratory-confirmed dengue fever were evaluated for eligibility. A total of 96 patients diagnosed with dengue fever were included in the study using a consecutive sampling technique. Patients were enrolled according to predefined eligibility criteria. Based on the World Health Organization (WHO) 2009 dengue classification, participants were categorized into dengue without warning signs, dengue with warning signs, and severe dengue.

Inclusion Criteria: Patients aged 18 years and above with clinically suspected dengue fever and laboratory confirmation through dengue non-structural protein 1 (NS1) antigen, dengue-specific IgM antibody, or reverse transcription-polymerase chain reaction (RT-PCR) were eligible for inclusion. Patients presenting with acute febrile illness, headache, retro-orbital pain, myalgia, arthralgia, rash, thrombocytopenia, or other clinical manifestations suggestive of dengue infection were considered. Only patients with available baseline complete blood count parameters and adequate clinical records were included.

Exclusion Criteria: Patients with pre-existing hematological malignancies, chronic inflammatory or autoimmune disorders, active bacterial infections,

concurrent malaria, chronic liver disease, advanced renal disease, or other conditions significantly affecting leukocyte and platelet counts were excluded. Patients receiving immunosuppressive treatment, systemic corticosteroids, or chemotherapy were also excluded. Individuals with incomplete laboratory investigations or those receiving platelet transfusion before baseline blood sampling were not included.

Methodology: Detailed demographic and clinical information was recorded using a structured data collection form. Parameters included age, gender, body mass index, duration of fever before presentation, presenting symptoms, associated comorbidities, and vital signs. Clinical manifestations such as abdominal pain, persistent vomiting, mucosal bleeding, hepatomegaly, lethargy, fluid accumulation, hypotension, and evidence of plasma leakage were documented. Disease severity was evaluated according to WHO criteria. Patients were monitored for severe bleeding, dengue shock syndrome, respiratory distress, acute kidney injury, hepatic dysfunction, intensive care unit admission, duration of hospitalization, and in-hospital mortality.

Laboratory Investigations: Venous blood samples were collected at admission, preferably before initiation of blood component transfusion. Complete blood count was performed using an automated hematology analyzer to determine hemoglobin concentration, hematocrit, total leukocyte count, absolute neutrophil count, absolute lymphocyte count, and platelet count. Additional investigations included serum aspartate aminotransferase, alanine aminotransferase, bilirubin, serum creatinine, blood urea, electrolytes, and serum albumin. Coagulation parameters and ultrasonographic evidence of plasma leakage were assessed when clinically indicated. Serial hematological investigations were reviewed to identify platelet nadir, hematocrit changes, and progression of disease severity.

Calculation of PLR and NLR: The Platelet-to-Lymphocyte Ratio was calculated by dividing the absolute platelet count by the absolute lymphocyte count obtained from the same blood sample. The Neutrophil-to-Lymphocyte Ratio was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Baseline PLR and NLR values were recorded and compared across dengue severity categories. Their relationships with thrombocytopenia, bleeding manifestations, plasma leakage, organ dysfunction, and clinical outcomes were evaluated. The comparative predictive ability of both ratios for identifying severe dengue was assessed.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 28.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were presented as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test. Independent Student's t-test or Mann–Whitney U test was applied for comparisons between two groups, while one-way ANOVA or Kruskal–Wallis test was used for multiple-group comparisons. Chi-square or Fisher's exact test was used for categorical variables. Pearson's or Spearman's correlation coefficients were calculated to assess associations between hematological indices and clinical parameters. Receiver operating characteristic (ROC) curve analysis was performed to compare the area under the curve (AUC), sensitivity, specificity, and optimal cutoff values of PLR and NLR for predicting severe dengue. Multivariable logistic regression was considered to identify independent predictors of severe dengue after adjustment for relevant confounding variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

[Table 1] Baseline Demographic and Clinical Characteristics of the Study Population (N=96)

A total of 96 patients diagnosed with dengue fever were included in the study, of whom 74 (77.08%) had non-severe dengue and 22 (22.92%) had severe dengue. The mean age was significantly higher among patients with severe dengue (36.98 ± 7.94 years) compared to those with non-severe dengue (32.64 ± 8.81 years; p=0.035). Male patients constituted 71.62% of the non-severe group and 54.55% of the severe group, although the difference was statistically insignificant (p=0.133). The mean body mass index was comparable between the groups (23.69 ± 3.13 vs. 24.74 ± 3.80 kg/m²; p=0.247). Patients with severe dengue had a significantly longer duration of fever before presentation (5.5 vs. 4.0 days; p=0.001). Diabetes mellitus (31.82% vs. 13.51%) and hypertension (27.27% vs. 16.22%) were more frequent among severe dengue patients, although these differences were not statistically significant. NS1 antigen positivity was higher in non-severe dengue (82.43% vs. 68.18%), whereas dengue IgM positivity was higher in severe dengue (68.18% vs. 44.59%), without statistically significant differences.

[Table 2] Comparison of Admission Hematological and Biochemical Parameters Between Severity Groups (N=96)

Admission hematological and biochemical investigations demonstrated significant differences between patients with non-severe and severe dengue. The median hematocrit was significantly higher in severe dengue patients (45.92% vs. 41.60%; p<0.001), whereas hemoglobin levels were comparable between the groups (13.94 vs. 13.57 g/dL; p=0.286). Severe dengue patients had significantly higher total leukocyte counts (4.93 vs. 4.45 × 10^9 /L; p=0.024) and absolute lymphocyte counts (2.07 vs. 1.49 × 10^9 /L; p<0.001), while absolute neutrophil counts did not differ significantly (p=0.217). The median platelet count was markedly

lower in severe dengue (47.39 vs. 91.87 × 10^9 /L; p<0.001). Similarly, platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) were significantly reduced in severe dengue patients (22.76 vs. 64.77 and 1.09 vs. 1.72, respectively; both p<0.001). Liver enzymes were significantly elevated in severe dengue, with median AST and ALT levels of 132.11 and 116.47 U/L compared with 65.92 and 50.23 U/L in non-severe dengue (both p<0.001). Furthermore, severe dengue was associated with significantly lower serum albumin (3.05 vs. 3.64 g/dL) and higher serum creatinine levels (1.11 vs. 0.86 mg/dL), with both differences reaching statistical significance (p<0.001).

[Table 3] Warning Signs, Complications and Hospital Outcomes by Dengue Severity (N=96)

Clinical warning signs and complications were significantly more frequent among patients with severe dengue compared to those with non-severe dengue. Abdominal pain was reported in 72.73% of severe dengue patients compared with 33.78% of non-severe patients (p=0.001), while persistent vomiting was observed in 81.82% and 39.19%, respectively (p<0.001). Mucosal bleeding (45.45% vs. 16.22%; p=0.004) and clinical fluid accumulation (81.82% vs. 13.51%; p<0.001) were also significantly more common in severe dengue. Among patients with severe dengue, 36.36% developed dengue shock, 27.27% experienced severe bleeding, 45.45% had major organ involvement, and 9.09% developed respiratory distress due to plasma leakage, whereas none of these complications occurred in the non-severe group. All patients with severe dengue required hospitalization compared with 83.78% of non-severe patients (p=0.062). Intensive care unit admission was significantly higher in severe dengue (72.73% vs. 1.35%; p<0.001), as was the requirement for blood component transfusion (50.00% vs. 8.11%; p<0.001). In-hospital mortality occurred in 9.09% of severe dengue patients compared with no deaths in the non-severe group, although this difference did not reach statistical significance (p=0.051). The median hospital stay was significantly longer in severe dengue patients (6.5 vs. 4.0 days; p<0.001).

[Table 4] Admission Hematological Indices Across Three WHO 2009 Dengue Severity Categories (N=96)

The analysis of hematological indices across the three WHO 2009 dengue severity categories demonstrated significant progressive changes with increasing disease severity. The median platelet count decreased significantly from 123.95 × 10^9 /L in patients without warning signs to 70.99 × 10^9 /L in patients with warning signs and 47.39 × 10^9 /L in severe dengue patients (p<0.001). A similar reduction was observed in platelet nadir, which declined from 110.27 × 10^9 /L to 49.52 × 10^9 /L and 15.42 × 10^9 /L, respectively (p<0.001). The median PLR showed a significant progressive decrease across the three categories (92.65, 43.56, and 22.76, respectively; p<0.001). Similarly, the median NLR decreased from 2.11 in patients without warning signs to 1.57 in those with warning signs and 1.09 in severe dengue patients (p<0.001). In contrast, absolute lymphocyte counts increased significantly with disease severity, from 1.31 to 1.61 and 2.07 × 10^9 /L, respectively (p<0.001). Although absolute neutrophil counts showed a decreasing trend from 2.61 to 2.48 and 2.28 × 10^9 /L, the difference was not statistically significant (p=0.139). These findings demonstrated a significant association between lower platelet counts, PLR, NLR, and increasing dengue severity.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (N=96)

Parameter	Non-severe dengue (n=74)	Severe dengue (n=22)	p-value
Age (years), mean ± SD	32.64 ± 8.81	36.98 ± 7.94	0.035
Male sex	53 (71.62%)	12 (54.55%)	0.133
Body mass index (kg/m²), mean ± SD	23.69 ± 3.13	24.74 ± 3.80	0.247
Fever before presentation (days), median (IQR)	4.0 (4.0–5.0)	5.5 (4.0–6.0)	0.001
Diabetes mellitus	10 (13.51%)	7 (31.82%)	0.061
Hypertension	12 (16.22%)	6 (27.27%)	0.349
NS1 antigen positive	61 (82.43%)	15 (68.18%)	0.229
Dengue IgM positive	33 (44.59%)	15 (68.18%)	0.052

Table 2: Comparison of Admission Hematological and Biochemical Parameters Between Severity Groups (N=96)

Laboratory parameter	Non-severe dengue (n=74)	Severe dengue (n=22)	p-value
Hemoglobin (g/dL)	13.57 (12.78–14.66)	13.94 (13.46–14.60)	0.286
Hematocrit (%)	41.60 (38.72–44.53)	45.92 (43.48–47.93)	<0.001
Total leukocyte count (×10^9 /L)	4.45 (4.01–4.96)	4.93 (4.39–5.36)	0.024
Absolute neutrophil count (×10^9 /L)	2.58 (2.19–2.98)	2.28 (1.94–2.96)	0.217
Absolute lymphocyte count (×10^9 /L)	1.49 (1.27–1.71)	2.07 (1.87–2.22)	<0.001
Platelet count (×10^9 /L)	91.87 (63.09–131.29)	47.39 (31.75–64.01)	<0.001
Platelet-to-lymphocyte ratio (PLR)	64.77 (39.99–92.84)	22.76 (16.18–31.38)	<0.001
Neutrophil-to-lymphocyte ratio (NLR)	1.72 (1.47–2.30)	1.09 (0.93–1.43)	<0.001
Aspartate aminotransferase (U/L)	65.92 (46.56–88.30)	132.11 (115.19–167.65)	<0.001
Alanine aminotransferase (U/L)	50.23 (35.61–66.16)	116.47 (98.20–141.78)	<0.001
Serum albumin (g/dL)	3.64 (3.43–3.86)	3.05 (2.98–3.13)	<0.001
Serum creatinine (mg/dL)	0.86 (0.77–1.04)	1.11 (0.99–1.18)	<0.001

Table 3: Warning Signs, Complications and Hospital Outcomes by Dengue Severity (N=96)

Clinical parameter	Non-severe dengue (n=74)	Severe dengue (n=22)	p-value
Abdominal pain	25 (33.78%)	16 (72.73%)	0.001
Persistent vomiting	29 (39.19%)	18 (81.82%)	<0.001
Mucosal bleeding	12 (16.22%)	10 (45.45%)	0.004
Clinical fluid accumulation	10 (13.51%)	18 (81.82%)	<0.001
Dengue shock	0 (0.00%)	8 (36.36%)	—
Severe bleeding	0 (0.00%)	6 (27.27%)	—
Major organ involvement	0 (0.00%)	10 (45.45%)	—
Respiratory distress from plasma leakage	0 (0.00%)	2 (9.09%)	—
Hospital admission	62 (83.78%)	22 (100.00%)	0.062
Intensive care unit admission	1 (1.35%)	16 (72.73%)	<0.001
Blood component transfusion	6 (8.11%)	11 (50.00%)	<0.001
In-hospital mortality	0 (0.00%)	2 (9.09%)	0.051
Hospital stay among admitted (days), median (IQR)	4.0 (3.0–5.0)	6.5 (6.0–7.8)	<0.001

Table 4: Admission Hematological Indices Across Three WHO 2009 Dengue Severity Categories (N=96)

Hematological parameter	No warning signs (n=36)	With warning signs (n=38)	Severe dengue (n=22)	p-value
Platelet count (×10^9 /L)	123.95 (95.73–146.72)	70.99 (46.16–88.97)	47.39 (31.75–64.01)	<0.001
Platelet nadir (×10^9 /L)	110.27 (82.45–126.11)	49.52 (25.19–79.61)	15.42 (8.00–29.10)	<0.001
PLR	92.65 (76.39–122.73)	43.56 (31.81–59.98)	22.76 (16.18–31.38)	<0.001
NLR	2.11 (1.65–2.49)	1.57 (1.27–1.75)	1.09 (0.93–1.43)	<0.001
Absolute neutrophil count (×10^9 /L)	2.61 (2.35–3.06)	2.48 (2.07–2.78)	2.28 (1.94–2.96)	0.139
Absolute lymphocyte count (×10^9 /L)	1.31 (1.09–1.51)	1.61 (1.37–1.79)	2.07 (1.87–2.22)	<0.001

Table 5: Exploratory ROC Analysis of Admission PLR and NLR for Identifying Severe Dengue (N=96)

Marker	AUC (95% bootstrap CI)	Optimal threshold	Sensitivity	Specificity	p-value
PLR	0.910 (0.849–0.960)	≤34.55	95.45% (21/22)	81.08% (60/74)	<0.001
NLR	0.824 (0.710–0.918)	≤1.49	86.36% (19/22)	72.97% (54/74)	<0.001

[Table 5] Exploratory ROC Analysis of Admission PLR and NLR for Identifying Severe Dengue (N=96) Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminatory performance of admission PLR and NLR in identifying severe dengue among the 96 study participants. The PLR demonstrated excellent discriminatory ability, with an area under the curve (AUC) of 0.910 (95% bootstrap CI: 0.849–0.960; p<0.001). At an optimal threshold of ≤34.55, PLR achieved a sensitivity of 95.45%, correctly identifying 21 of 22 severe dengue patients, and a specificity of 81.08%, correctly identifying 60 of 74 non-severe dengue patients. The NLR also demonstrated good discriminatory performance, with an AUC of 0.824 (95% bootstrap CI: 0.710–0.918; p<0.001). At an optimal threshold of ≤1.49, NLR showed a sensitivity of 86.36%, correctly identifying 19 of 22 severe dengue patients, and a specificity of 72.97%, correctly identifying 54 of 74 non-severe dengue patients. The PLR had numerically higher AUC, sensitivity, and specificity than NLR, suggesting better discriminatory performance for identifying severe dengue in this study population.

DISCUSSION

The present study included 96 patients with dengue fever, of whom 74 (77.08%) had non-severe dengue and 22 (22.92%) had severe dengue. The mean age was significantly higher among patients with severe dengue (36.98 ± 7.94 years) than among those with non-severe dengue (32.64 ± 8.81 years; p=0.035). Furthermore, the median duration of fever before presentation was significantly longer in severe dengue patients (5.5 vs. 4.0 days; p=0.001). Diabetes mellitus was more common in severe dengue (31.82% vs. 13.51%), although the difference was not statistically significant (p=0.061). Similar observations were reported by Agrawal et al. (2018), who evaluated 334 dengue patients in South India and found severe dengue in 117 (35.0%) patients. Diabetes mellitus was significantly more prevalent among severe dengue patients (38.4%) than non-severe patients (17.0%; p=0.001). Delayed hospitalization beyond five days was also more frequent in severe dengue (36.7% vs. 14.2%; p<0.001), with an adjusted odds ratio of 2.40 for severe disease. However, unlike the present study, their investigation found no significant difference in mean age between severe and non-severe dengue patients (30.4 ± 11.8 vs. 30.3 ± 15.4 years; p=0.9).[7] The present study demonstrated significant hematological abnormalities among patients with severe dengue, particularly increased hematocrit and marked thrombocytopenia. The median hematocrit was significantly higher in severe dengue patients (45.92%) compared with non-severe dengue patients (41.60%; p<0.001), suggesting greater hemoconcentration associated with plasma leakage. The median platelet count was significantly lower in severe dengue (47.39 × 10^9 /L) than in non-severe dengue (91.87 × 10^9 /L; p<0.001). Total leukocyte and absolute lymphocyte counts were also

significantly higher in severe dengue, measuring 4.93 and 2.07 × 10^9 /L compared with 4.45 and 1.49 × 10^9 /L, respectively. Comparable findings were reported by Thanachartwet et al. (2016) in a prospective study involving 125 hospitalized dengue patients in Thailand, including 20 severe and 105 non-severe cases. Their study demonstrated significantly lower median platelet counts in severe dengue (41.5 × 10^9 /L) compared with non-severe dengue (90.0 × 10^9 /L; p<0.001). Serum albumin was also significantly lower in severe dengue patients (3.6 vs. 4.3 g/dL; p<0.001), whereas serum creatinine did not differ significantly between groups. In contrast, the present study demonstrated significantly higher creatinine in severe dengue (1.11 vs. 0.86 mg/dL; p<0.001).[8] Significant hepatic dysfunction was observed among patients with severe dengue in the present study. The median aspartate aminotransferase (AST) concentration was considerably higher in severe dengue patients (132.11 U/L) compared with non-severe patients (65.92 U/L; p<0.001). Similarly, alanine aminotransferase (ALT) levels were significantly elevated in severe dengue (116.47 vs. 50.23 U/L; p<0.001). Serum albumin concentrations were significantly lower in severe dengue patients (3.05 vs. 3.64 g/dL; p<0.001), indicating an association between disease severity and hypoalbuminemia. These findings were consistent with the observations of Mohindra et al. (2024), who evaluated hepatic abnormalities in 170 dengue patients, including 81 with dengue without warning signs, 76 with warning signs and 13 with severe dengue. Their study reported median AST concentrations of 72.9, 161.5 and 3051 U/L across the three categories, respectively (p<0.001). Corresponding median ALT concentrations were 66.5, 93 and 1792 U/L (p=0.009), while serum albumin progressively decreased from 4.1 to 3.6 and 3.0 g/dL (p<0.001). Although the magnitude of transaminase elevation was considerably greater in their severe dengue group, both studies demonstrated the same association between increasing dengue severity, hepatic enzyme elevation and declining serum albumin.[9]

Clinical warning signs were significantly associated with severe dengue in the present study. Abdominal pain was reported in 72.73% of patients with severe dengue compared with 33.78% of non-severe patients (p=0.001). Persistent vomiting was observed in 81.82% and 39.19% of the respective groups (p<0.001), while mucosal bleeding occurred in 45.45% and 16.22% (p=0.004). Clinical fluid accumulation demonstrated a particularly strong association with severe dengue, being observed in 81.82% of severe cases compared with 13.51% of non-severe cases (p<0.001). Comparable observations were reported by Thein et al. (2013), who investigated 1507 adult dengue patients in Singapore, among whom 248 (16.5%) developed severe dengue. During the clinical course of severe dengue, abdominal pain or tenderness was recorded in 44.0%, persistent vomiting in 16.5%, mucosal bleeding in 50.0% and clinical fluid accumulation in 22.2% of patients. Their study further demonstrated that persistent vomiting and clinical fluid accumulation had specificities of 93% and 98%, respectively, for predicting subsequent severe dengue, although the sensitivity of individual warning signs was limited. The higher frequencies of several warning signs observed in the present study may reflect differences in clinical presentation, patient selection and assessment timing.[10] The present study demonstrated substantial differences in complications and hospital outcomes between severe and non-severe dengue patients. Among patients with severe dengue, 36.36% developed dengue shock, 27.27% experienced severe bleeding and 45.45% had major organ involvement. Intensive care unit admission was required in 72.73% of severe dengue patients compared with only 1.35% of non-severe patients (p<0.001). Similarly, blood component transfusion was required in 50.00% and 8.11% of patients, respectively (p<0.001). In-hospital mortality was recorded in two patients with severe dengue (9.09%), whereas no deaths occurred among non-severe patients, although this difference was not statistically significant (p=0.051). The median duration of hospitalization was also significantly longer in severe dengue (6.5 vs. 4.0 days; p<0.001). Padyana et al. (2019) evaluated 96 dengue patients admitted to a multidisciplinary intensive care unit in India and reported an overall survival rate of 78.9%, corresponding to a mortality rate of approximately 21.1%. Their study demonstrated a median ICU stay of 10 days among severe dengue patients, compared with 4 days among patients with warning signs and 3 days among patients without warning signs. Hepatic involvement was documented in 96.8%, hematological involvement in 79.2% and central nervous system involvement in 27.0% of their ICU population.[11] The evaluation of admission platelet counts across three WHO 2009 dengue severity categories revealed a significant progressive decline with increasing disease severity. In the present study, the median platelet count decreased from 123.95 × 10^9 /L among patients without warning signs to 70.99 × 10^9 /L among patients with warning signs and 47.39 × 10^9 /L among severe dengue patients (p<0.001). The platelet nadir demonstrated an even more pronounced reduction, declining from 110.27 to 49.52 and 15.42 × 10^9 /L, respectively (p<0.001). Similar findings were observed by Vikhe et al. (2024), who investigated 100 dengue patients in Maharashtra, India, to assess the relationship between admission platelet counts and disease severity. Their study reported a median admission platelet count of 114 × 10^9 /L in dengue without warning signs, 35.5 × 10^9 /L in dengue with warning signs and 25 × 10^9 /L in severe dengue (p<0.001). Furthermore, patients presenting with platelet counts below 25 × 10^9 /L had 7.5 times greater odds of severe dengue (p<0.04). Although platelet counts in the present study were relatively higher across the severity categories, both studies demonstrated a

consistent pattern of increasing thrombocytopenia with worsening dengue severity.[12] An important finding of the present investigation was the progressive reduction in platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) with increasing dengue severity. The median PLR decreased significantly from 92.65 among patients without warning signs to 43.56 among patients with warning signs and 22.76 among severe dengue patients ($p<0.001$). Similarly, the median NLR decreased from 2.11 to 1.57 and 1.09 across the respective categories ($p<0.001$). These changes were accompanied by a significant increase in absolute lymphocyte count from 1.31 to 1.61 and 2.07 × 10^9 /L, respectively, while absolute neutrophil counts showed no statistically significant difference ($p=0.139$). Comparable findings regarding PLR were reported by Böer et al. (2024), who evaluated 193 dengue patients in Brazil, comprising 164 (85.0%) patients with dengue fever, 19 (9.8%) with dengue hemorrhagic fever and 10 (5.2%) with an intermediate clinical presentation. Their investigation demonstrated that a PLR ≤80.68 was significantly associated with dengue hemorrhagic fever, with an odds ratio of 4.26 (95% CI: 1.60–11.33; $p<0.05$). Their study also found a significant association between monocyte-to-lymphocyte ratio above 0.13 and dengue hemorrhagic fever (OR: 5.72; 95% CI: 1.28–25.60).[13] The exploratory ROC analysis performed in the present study demonstrated encouraging discriminatory performance of admission PLR and NLR for identifying severe dengue. The PLR exhibited an AUC of 0.910 (95% bootstrap CI: 0.849–0.960; $p<0.001$), with an optimal threshold of ≤34.55 providing 95.45% sensitivity and 81.08% specificity. In comparison, NLR demonstrated an AUC of 0.824 (95% bootstrap CI: 0.710–0.918; $p<0.001$), with an optimal threshold of ≤1.49 providing 86.36% sensitivity and 72.97% specificity. Related findings were reported by Navya et al. (2024), who investigated 99 hospitalized dengue patients in Southern India and compared NLR and PLR across dengue fever, dengue hemorrhagic fever and dengue shock syndrome. Their study demonstrated a progressive reduction in mean PLR from 134.4 to 50.57 and 10.39, respectively ($p=0.003$), while mean NLR declined from 2.47 to 1.013 and 0.41 ($p=0.02$). In their diagnostic analysis, PLR demonstrated a sensitivity of 93.3%, specificity of 33.3% and accuracy of 81.5%, whereas NLR showed a sensitivity of 77.8%, specificity of 94.4% and accuracy of 63.0%. Thus, both studies demonstrated high sensitivity of PLR for identifying more severe dengue presentations, although the specificity estimates differed considerably. The numerically greater AUC of PLR in the present study suggests potentially better discrimination than NLR; however, this difference was not formally tested.[14]

CONCLUSION

The present study demonstrated that platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) were significantly associated with dengue severity, with both indices decreasing as disease severity increased. PLR exhibited superior discriminatory performance (AUC=0.910) compared with NLR (AUC=0.824), with higher sensitivity and specificity for identifying severe dengue. Both indices represent simple, inexpensive and readily available hematological markers that may assist in early risk stratification and clinical assessment. However, larger prospective multicentre studies are required to validate their predictive accuracy and establish reliable clinical cutoff values before routine implementation.

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