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The Role of Neutrophil to Lymphocyte Ratio in Dengue Hemorrhagic Fever and Dengue Shock Syndrome: A Narrative Systematic Review

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ABSTRACT

This systematic review aimed to evaluate the diagnostic and prognostic utility of the neutrophil-to-lymphocyte ratio (NLR) in distinguishing disease severity among patients with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The review emphasizes the biomarker's role in early detection and risk stratification. Literature searches were conducted in PubMed, Scopus, ScienceDirect, Cochrane Library, and manual searching from inception to May 2025. Only articles published in English and involving human subjects were considered. Studies were included if they reported NLR values among patients with DHF or DSS and assessed the relationship between NLR and clinical severity. The initial database search yielded 1.794 records. After removing duplicates and screening titles, abstracts, and full texts, 15 eligible studies were selected. Quality appraisal was performed using the Joanna Briggs Institute (JBI) and Newcastle–Ottawa Scale (NOS) checklists. Two independent reviewers extracted data on study design, sample size, NLR measurement, severity classification, and key statistical outcomes. Disagreements were resolved by consensus. The majority of studies reported a significant association between higher NLR and increased dengue severity, particularly in patients with DSS. However, there was notable heterogeneity in cut-off values, timing of NLR measurement, and reference standards used. A few studies suggested that lower NLR may occur at critical or late stages. NLR demonstrates potential as a simple, cost-effective biomarker for identifying severe dengue, including DHF and DSS. Nonetheless, variation in methodologies and inconsistent cut-offs limit its generalizability. Further standardized, prospective studies are warranted to establish its diagnostic thresholds and timing of use.

Keywords: *Biomarkers (MeSH); Blood Cell Count (MeSH); Disease Progression (MeSH); Hemorrhage (MeSH); Humans (MeSH); Immunity (MeSH); Lymphocytes (MeSH); Neutrophils (MeSH); Prognosis (MeSH); Risk Asessment (MeSH); Severe Dengue (MeSH).*

1. INTRODUCTION

Dengue is a mosquito-borne viral illness that continues to pose a major threat to public health in tropical and subtropical regions, particularly in Asia, Latin America, and parts of Africa. The disease is caused by four antigenically distinct serotypes of the dengue virus (DENV 1–4), all of which are capable of causing a spectrum of clinical manifestations ranging from mild febrile illness to severe, life-threatening complications(de Almeida et al., 2025). While most cases are self-limiting, a significant proportion progress to Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS), both of which are associated with increased mortality if not recognized and managed early. According to the World Health Organization (WHO), DSS is the most severe form of dengue and represents the critical phase of the illness, characterized by plasma leakage, circulatory collapse, and multiorgan dysfunction (Witte et al., 2024).

Recent research has focused on identifying more dynamic and accessible biomarkers. Among these, the neutrophil-to-lymphocyte ratio (NLR) has emerged as a promising parameter reflecting systemic inflammation, based on leukocyte differentials obtained from routine complete blood count tests (Zahorec, 2021). The utility of NLR has been widely studied

in infectious, cardiovascular, and malignant diseases, as it integrates two components of the innate and adaptive immune response (Buonacera et al., 2022).

In dengue, alterations in neutrophil and lymphocyte counts have been shown to correlate with disease stage and severity, with several studies indicating that high or decreasing NLR values may be predictive of clinical deterioration (Song et al., 2021). However, the interpretation of NLR in dengue remains complex, as differing patterns have been observed between patients with DHF and those progressing to DSS.

The biological rationale for using NLR in dengue is supported by the temporal changes in leukocyte subsets during infection. In the early febrile phase, neutrophilia predominates as part of the acute-phase response(Rawat et al., 2021). As the infection transitions into the critical phase, particularly in DHF and DSS, lymphocyte activation increases, while bone marrow suppression and neutrophil apoptosis may occur, resulting in a relative decline in NLR. This paradoxical reduction has been observed in several clinical studies and may signal immunological exhaustion or severe endothelial activation (Calderón-Peláez et al., 2022) (Hasanah et al., 2023).

Some studies have proposed that a declining NLR may actually be more indicative of severe progression, possibly reflecting immune exhaustion or bone marrow suppression seen in late dengue stages (mahayanti & Suardamana, 2024). This contrasts with findings in other infections where elevated NLR is commonly associated with worse prognosis.

2. METHODS

Review Framework and Registration

This review was conducted in alignment with the PRISMA 2020 reporting standards and was prospectively registered in the PROSPERO database (CRD420251055441).

Inclusion and Exclusion Criteria

Eligible studies included observational research—such as cross-sectional, cohort, retrospective, and case-control designs—that evaluated neutrophil-to-lymphocyte ratio (NLR) among patients diagnosed with Dengue Hemorrhagic Fever (DHF) and/or Dengue Shock Syndrome (DSS). We included only full-text articles published in English. Studies were excluded if they lacked stratification between DHF and DSS or did not report NLR values. Additionally, reviews, abstracts, case reports, non-human studies, and editorials were excluded.

Literature Search and Screening

A comprehensive search strategy was applied to five electronic databases: PubMed, Scopus, ScienceDirect, Cochrane Library, and manual hand searching. No restriction on publication date was applied. The final search was completed in May 2025 using the search terms: ("neutrophil to lymphocyte ratio" OR "NLR") AND ("dengue hemorrhagic fever" OR "DHF" OR "dengue shock syndrome" OR "DSS"). Search results were imported into Mendeley for de-duplication. Two reviewers (DD and PW) screened titles and abstracts independently, followed by full-text evaluation. Any discrepancies were resolved through discussion with a third reviewer (YH).

Data Collection Process

Three reviewers (DD, YH, and PW) independently extracted data from included studies using a standardized form. Extracted data included first author, publication year, country, study design, sample size, dengue classification, NLR values, statistical tests, and key conclusions. Disagreements were resolved through consensus.

Assessment of Methodological Quality

Risk of bias was appraised using the Joanna Briggs Institute (JBI) critical appraisal tools for cross-sectional and cohort studies, and the Newcastle-Ottawa Scale (NOS) for case-control and prospective cohort studies. JBI tools evaluated elements such as participant selection, measurement validity, and statistical analysis. NOS domains included selection, comparability, and outcome/exposure assessment. Two independent reviewers (DD and YH) performed all assessments, resolving conflicts through discussion.

Data Synthesis Strategy

Due to heterogeneity in study design, participant characteristics, and NLR reporting, a meta-analysis was not conducted. Findings were synthesized descriptively, with emphasis on trends in NLR values across DHF and DSS severity groups.

3. RESULTS

Search Outcome and Study Selection

The initial database search yielded 1.794 records. After removing duplicates, 25 articles were retained for full-text assessment. Fifteen studies met all inclusion criteria and were incorporated into the final synthesis. The PRISMA flow diagram (**Figure 1**) outlines the selection process and reasons for exclusion.

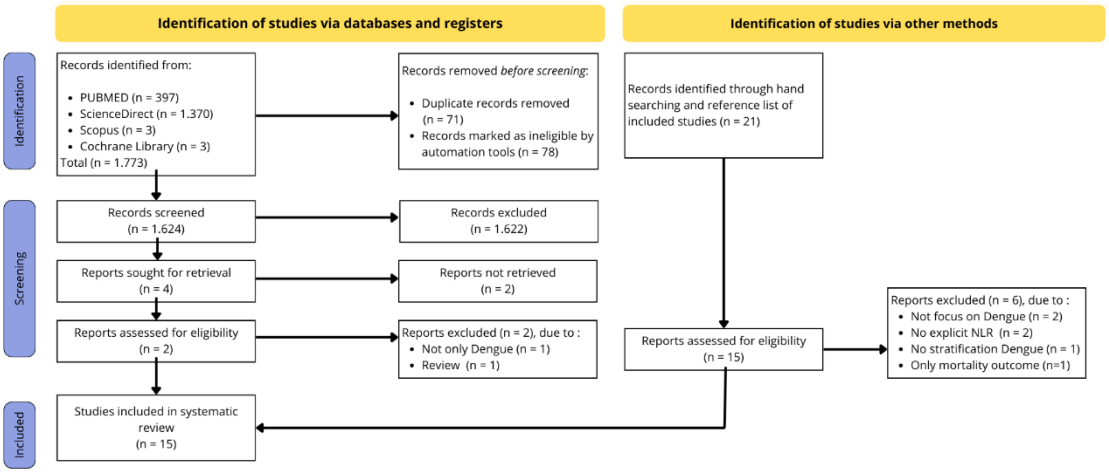

Figure 1. Prisma Diagram

Risk of Bias Evaluation

Among the 15 included studies, 10 were assessed using the JBI checklist for cross-sectional designs, with most receiving scores of 6 out of 8. The remaining five studies (four retrospective or case-control and one cohort design) were assessed using the Newcastle–Ottawa Scale (NOS), scoring between 6 and 7 out of 9. Common limitations included lack of adjustment for potential confounders, incomplete outcome data, and limited clarity in participant selection or follow-up procedures. Full appraisal results are presented in **Table 1**.

Table 1. STUDY QUALITY ASESSMENT

First Author	Year	Assessment Tool	Score
Navya et al.	2024	JBI	6/8
Amri et al.	2025	NOS	6/9
Wazib et al.	2025	NOS	7/9
Sadgir et al.	2023	NOS	6/9
Pribadi et al.	2025	JBI	6/8
Sajjad et al.	2025	JBI	6/8
Ishaque et al.	2021	JBI	7/8
Deshapande et al.	2024	NOS	6/9
Gauri et al.	2022	JBI	6/8
Ashma et al.	2023	JBI	6/8
Mahayanti and Suardamana	2023	JBI	6/8
Maulida et al.	2023	JBI	6/8
Koundinya et al.	2021	NOS	6/9
Irmayanti et al.	2017	JBI	6/8
Böer et al.	2024	NOS	7/9

JBI = Joanna Briggs Institute; NOS = Newcastle-Ottawa Scale

Overview of Included Studies

This review synthesized data from 15 observational studies published between 2017 and 2025, encompassing a total of 1,462 patients. The studies originated from Indonesia (n = 6), India (n = 5), Pakistan (n = 2), Bangladesh (n = 1), and Brazil (n = 1). The 15 included studies comprised 10 cross-sectional studies, 3 retrospective studies, and 2 cohort studies, with the majority evaluating hospitalized patients during the acute or critical phase of dengue infection. Six studies assessed comparisons between DHF and DSS, including investigations by Navya et al., Amri et al., Wazib et al., Mahayanti and Suardamana, Gauri et al., and Koundinya et al. Seven studies focused exclusively on DHF or related warning signs—such as platelet dynamics, plasma leakage, or clinical grading—as seen in studies by Sadgir, Pribadi, Ashma, Maulida, Irmayanti, Deshapande, and Ishaque. One study by Gauri et al. specifically examined DSS patients without comparison groups, while another by Böer et al. included DF, DHF, and an intermediate severity classification. This diversity in clinical focus and study design allowed a comprehensive evaluation of NLR's role across various manifestations of dengue severity. The included studies. The included studies data are shown in **Table 2**.

Table 2. SUMMARY OF INCLUDED STUDIES REPORTING NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) IN DENGUE PATIENTS WITH SEVERITY CLASSIFICATION

Study	Year	Country	Study Design	Sample Size	Group Comparison	Reported NLR Values	Statistical Test Used	Key Findings / Notes
Navya et al.(Navya et al., 2024)	2024	India	Cross-sectional	99	DF, DHF, DSS	DF: 2.47, DHF: 1.01, DSS: 0.41	ANOVA, Chi-square, ROC	Significant decrease from DF to DSS
Amri et al.(Amri et al., 2025)	2025	Indonesia	Cross-sectional (Retrospective)	100	DHF, DSS	DHF: 1.28, DSS: 2.07	Mann–Whitney U test, Chi-square	Lower NLR in DSS
Wazib et al.(Wazib et al., 2025)	2025	Bangladesh	Case-control	42	DSS vs non-DSS (control)	DSS: 2.5 [1.7–3.0], Control: 1.4 [0.8–2.0]	Mann–Whitney U test, Chi-square test (with Odds Ratio and CI).	NLR significantly higher in DSS group
Sadgir et al.(Sadgir et al., 2023)	2023	India	Retrospective	100	DHF	NLR <2 in 76% NLR ≥2 in 24%	Chi-square	Majority of dengue patients had NLR <2
Pribadi et al.(Pribadi et al., 2025)	2025	Indonesia	Prospective cohort	30 (pediatric)	DHF patients: platelet ↑ vs platelet ↓	NLR < 0.8 associated with platelet	Chi-square / Fisher's exact test, ROC, OR	Low NLR (<0.8) predicted platelet recovery
Sajjad et al.(Sajjad et al., 2025)	2025	Pakistan	Cross-sectional	136	DF	Mean NLR: 2.2; 41% had low NLR	Spearman correlation, Shapiro-	No correlation between NLR and hospital stay; 41% had low NLR

							Wilk test	(mean 2.2)
Ishaque et al.(Ishaque et al., 2022)	2021	Pakistan	Cross-sectional	141	Early vs Late NLR reversal; correlated with DHF progression	Day 5: Early 0.73 vs Late 1.76	Chi-square, Fisher's Exact	Late NLR reversal strongly associated with DHF
Deshapande et al.(Deshapande et al., 2024)	2024	India	Retrospective	100	Dengue without warning vs. warning signs vs. severe dengue	Normal NLR: 58%, High NLR: 42%	Chi-square	No significant association between NLR and dengue severity
Gauri et al.(Gauri et al., 2022)	2022	India	Cross-sectional	99	DSS	0.85 ± 0.29	Mann–Whitney U, Chi-square	DSS only
Ashma et al.(Ashma et al., 2023)	2023	Indonesia	Cross-sectional	70	DHF (plasma leakage vs non)	Median: 2.43 (range 0.31–9.52)	K–S, Spearman, Regression	NLR positively correlated with hemoconcentration (r = 0.314, p = 0.008)
Mahayanti and Suardamana(mahayanti & Suardamana, 2024)	2023	Indonesia	Cross-sectional (retrospective)	56	DHF with/without shock	With shock: 1.30 ± 0.52; No shock: 3.06 ± 0.96	Mann–Whitney U test	A statistically significant difference was observed between the groups
Maulida et al.(Maulida et al., 2023)	2023	Indonesia	Cross-sectional	74	DHF (no group stratified	<3.13: 61%, >3.13: 39%	Multiple linear regression	Weak correlation between NLR and platelet count (r = 0.259, p = 0.026); NLR mostly norma
Koundinya et al.(Koundinya et al., 2021)	2021	India	Retrospective observational	30	NLR vs bleeding and shock	NLR <0.1 (n=1), 0.2–0.4 (n=4), 0.5–0.9 (n=8), 1–2 (n=7), >2 (n=10); mean NLR: 2.12 (range: 0.1–8.2)	Chi-square, p=0.001	Lower NLR (<1) was significantly associated with bleeding and shock. Strong correlation with severity (p=0.001).

Irmayanti et al.(Irmayanti et al., 2017)	2017	Indonesia	Retrospective	96 (52 Grade I, 44 Grade II)	Grade I vs Grade II DHF	Grade I: 2.19, Grade II: 0.80	Mann–Whitney, Spearman	NLR significantly lower in more severe DHF; r = -0.68, p < 0.001
Böer et al.(Monteiro BÖER et al., 2024)	2024	Brazil	Retrospective cohort	193	DF (n=164), Intermediate DF/DHF (n=10), DHF (n=19)	Median NLR: DF 1.58, Intermediate 1.73, DHF 1.15	Mann–Whitney, Kruskal–Wallis, ROC	PLR & MLR more predictive for DHF; NLR trend declined during illness but not predictive alone.

DF = Dengue Fever; DHF = Dengue Hemorrhagic Fever; DSS = Dengue Shock Syndrome; NLR = Neutrophil-to-Lymphocyte Ratio; ROC = Receiver Operating Characteristic Curve; K-S = Kolmogorov–Smirnov

NLR Trends and Comparisons Across Severity Groups

The neutrophil-to-lymphocyte ratio (NLR) emerged as a consistently reported hematologic marker across the reviewed studies, particularly in relation to disease severity. In studies that stratified patients into DF, DHF, and DSS categories, a downward trend in NLR values was consistently observed as clinical severity increased. For example, Navya et al. (2024) reported mean NLR values of 2.47 in DF, 1.01 in DHF, and 0.41 in DSS, indicating a statistically significant inverse association between NLR and severity. Amri et al. (2025) reported a significantly higher NLR in DSS (2.07) compared to DHF (1.28), supporting the role of NLR as a marker of disease severity in pediatric dengue patients.. Mahayanti and Suardamana (2023) demonstrated significantly lower NLR in DHF patients with shock (1.30 ± 0.52) than in those without shock (3.06 ± 0.96; $p < 0.0001$).

Gauri et al. (2022), focusing exclusively on DSS, reported a mean NLR of 0.85 ± 0.29, reinforcing the pattern of low NLR values in severe cases. In contrast, NLR values in studies focusing solely on DHF remained relatively stable between 1.1 and 2.4, with representative data from studies by Deshapande et al. (2024), Maulida et al. (2023), and Pribadi et al. (2025). Pediatric-specific data confirmed similar trends with mean NLR values ranging from 1.21 to 1.27. Irmayanti et al. (2017) further substantiated this trend by demonstrating that NLR values were significantly lower in grade II DHF patients (0.80) than in grade I DHF patients (2.19), with a strong negative correlation ($r = –0.68$, $p < 0.001$).

Unique contributions were also made by studies with dynamic analysis. Ishaque et al. (2021) reported that late NLR reversal (Day 5 value of 1.76 vs. early reversal of 0.73) was strongly associated with progression to DHF (80.9% vs. 8.3%, $p < 0.05$), suggesting the temporal trajectory of NLR could inform prognosis. Ashma et al. (2023) reported a positive correlation between NLR and hemoconcentration ($r = 0.314$, $p = 0.008$), indicating relevance in early plasma leakage detection. Koundinya et al. (2021) further demonstrated that lower NLR values (<1) were significantly associated with bleeding and shock ($p = 0.001$), reinforcing its prognostic utility. Meanwhile, Böer et al. (2024) found no significant differences in NLR between DF and DHF (1.58 vs. 1.15; $p = 0.284$), although PLR and MLR showed greater predictive value.

Summary of Diagnostic and Prognostic Value

Several studies applied ROC analysis to assess the diagnostic performance of NLR. Navya et al. (2024) reported a specificity of 94.4% for identifying severe dengue using NLR. Wazib et al. (2025) demonstrated that an NLR ≥2 on the third day of dengue infection was significantly associated with a higher risk of developing dengue shock syndrome (DSS), supporting the utility of NLR in prognostic assessment. Despite methodological heterogeneity that precluded meta-analysis, narrative findings across studies consistently support the role of NLR as a low-cost, accessible biomarker for dengue severity assessment. Its availability from routine CBC testing makes it especially valuable in resource-limited endemic settings.

4. DISCUSSION

This systematic review reveals a consistent trend across the included studies indicating that the neutrophil-to-lymphocyte ratio (NLR) declines as dengue severity progresses from Dengue Hemorrhagic Fever (DHF) to Dengue Shock Syndrome (DSS). This pattern, observed across various populations and study designs, reinforces the potential utility of NLR as a clinical biomarker for stratifying dengue severity. In particular, studies by Navya et al. (2024) reported lower NLR values in DSS than in DHF (Navya et al., 2024**)**. Sajjad et al. reported a mean NLR of 2.2 in mild dengue (DF) cases, with 41%

showing low NLR values. Although not stratified by severity, this provides a useful baseline (Sajjad et al., 2025). A similar finding was reported by **Mahayanti and Suardamana (2024)** demonstrated significantly lower NLR values in DHF patients with shock (mean 1.30) compared to those without shock (mean 3.06), further validating the inverse relationship between NLR and disease severity (Mahayanti & Suardamana, 2024). In addition, the study by Koundinya et al. (2021) contributed further support for the inverse relationship between NLR and disease severity (Koundinya et al., 2021). This inverse association was also demonstrated in the study by Irmayanti et al. (2017), where patients with grade II DHF had significantly lower NLR values than those with grade I DHF (Irmayanti et al., 2017). However, a contrasting result was reported by Wazib et al. (2025), who found that NLR values were significantly higher in DSS patients compared to non-DSS controls, with NLR ≥2 associated with a tenfold increased risk of DSS (OR = 10.2), suggesting a positive rather than inverse relationship between NLR and disease severity (Wazib et al., 2025).

The biological plausibility of these findings can be explained by the immune response dynamics in dengue infection. During the early febrile phase, neutrophilia may be observed as part of the host innate immune response. However, as the disease advances to the critical phase—especially in DSS—bone marrow suppression, neutrophil apoptosis, and increased lymphocyte activation occur (Leliefeld et al., 2016). These changes lead to decreased neutrophil counts and relative lymphocytosis, resulting in a paradoxical reduction in NLR in patients with more severe disease (Biswas et al., 2022).

Neutrophils play a protective role during acute viral infections by phagocytosing viral particles, releasing antimicrobial enzymes like MPO and lactoferrin, and producing reactive oxygen species (ROS) to limit viral replication (Fontoura et al., 2021). However, in severe cases, excessive activation of neutrophils and the formation of neutrophil extracellular traps (NETs) may contribute to host tissue damage, vascular leakage, and immune-mediated pathology, especially during the critical phase of dengue infection (Ma et al., 2021). Neutrophils exhibit functional heterogeneity, with subsets that may either promote viral clearance or amplify immunopathology (Chan et al., 2022). Autophagy plays a dual role during viral infections by either promoting antiviral defense or being hijacked by viruses such as dengue to support replication and immune evasion (Chen et al., 2023). **During viral infections, including dengue, lymphocytes undergo metabolic reprogramming—such as upregulated glycolysis and mitochondrial metabolism—to support activation, differentiation, and effector functions** (Chapman & Chi, 2022). Several studies in this review, including those by Ashma et al. (2023) and Gauri et al. (2022), support this mechanism by demonstrating lower NLR values in DSS and its association with clinical parameters such as hemoconcentration, plasma leakage, and thrombocytopenia (Ashma et al., 2023) (Gauri et al., 2022).

Dynamic trends also play a significant role. In Ishaque et al. (2021), delayed reversal of the NLR—marked by a slower shift from neutrophil to lymphocyte predominance—was strongly associated with progression from DF to DHF. This highlights the importance of not only absolute NLR values but also their temporal pattern in clinical prognostication(Ishaque et al., 2022). Although most studies in this review reported NLR at a single time point, this finding underscores the potential added value of serial NLR monitoring.

Among the studies referenced in this review, several—such as Navya et al. (2024)—explicitly evaluated the diagnostic performance of NLR through receiver operating characteristic (ROC) analysis. Navya et al. reported a high specificity of 94.4% for NLR in predicting severe dengue (Navya et al., 2024). Although not included in the final synthesis due to overlapping disease comparison with COVID-19, the study by Hasanah et al. (2023) provides valuable additional insight. This study demonstrated that an NLR cut-off of <0.39 could predict DHF with shock with 93.2% sensitivity and 83.3% specificity, highlighting the discriminative utility of NLR when integrated with platelet count metrics (Hasanah et al., 2023; Böer et al. 2024), though reporting non-significant differences in NLR between DF and DHF (median 1.58 vs. 1.15; p = 0.284), still reinforced the trend of lower NLR in more severe disease and highlighted the added predictive value of PLR and MLR (Monteiro BÖER et al., 2024). *Thrombocytopenia in viral infections, including dengue, results not only from platelet consumption and decreased production, but also from active immunomodulatory roles of platelets, which can interact directly with viruses and immune cells to influence disease severity and outcome* (Raadsen et al., 2021).

It is also noteworthy that pediatric studies, such as those by Pribadi et al. (2025) and Deshapande et al. (2024), reported NLR values within the expected DHF range but did not include DSS cases, limiting the ability to generalize their findings to the most severe spectrum. Nonetheless, the consistency of NLR values across DHF studies in both adult and pediatric populations highlights its robustness as a hematological marker in this clinical category (Pribadi et al., 2025; Deshapande et al., 2024; Yuditya et al. 2020), although excluded from the main synthesis due to lack of reported group-wise NLR values, was included in the discussion for its compelling findings. This study demonstrated a statistically significant negative correlation between NLR and dengue severity (p = 0.000; contingency coefficient –0.733), indicating that lower NLR values were associated with higher severity grades (Yuditya & Sudirgo, 2020).

An another retrospective cohort study by Agrawal et al. (2023) demonstrated that a higher neutrophil-to-lymphocyte ratio (NLR) at admission was associated with adverse outcomes in dengue patients, highlighting its potential as an early prognostic marker (Agrawal et al., 2023). Although the study by Prajapati (2024) did not meet inclusion criteria for the main synthesis due to the absence of DHF/DSS stratification, it contributed supplementary value by demonstrating a significant association between NLR, platelet count, and duration of illness. This supports the broader trend in this review of NLR functioning as a

dynamic, severity-linked inflammatory marker in dengue(Prajapati, 2024). Together, these findings support the growing consideration of NLR in early warning scores, particularly in settings with limited diagnostic infrastructure.

This systematic review highlights the potential role of the neutrophil-to-lymphocyte ratio (NLR) as a clinical biomarker for stratifying dengue severity. Several studies demonstrated a consistent inverse association between NLR values and disease progression. For instance, Navya et al. (2024) reported a significant decline in mean NLR from 2.47 in Dengue Fever (DF) to 1.01 in Dengue Hemorrhagic Fever (DHF), and 0.41 in Dengue Shock Syndrome (DSS) (Navya et al., 2024). Similar findings were observed in the study by Mahayanti and Suardamana (2024), where patients with DSS had a significantly lower mean NLR (1.30 ± 0.52) compared to those without shock (3.06 ± 0.96, $p < 0.0001$) (mahayanti & Suardamana, 2024). Irmayanti et al. (2017) further supported this pattern, showing that patients with grade II DHF had a lower NLR (0.80) than those with grade I (2.19). In line with these, Koundinya et al. (2021) found that NLR <1 was significantly associated with bleeding and shock manifestations ($p = 0.001$), reinforcing its prognostic utility (Irmayanti et al., 2017). However, contrasting results were reported by Wazib et al. (2025) and Amri et al. (2025), both of whom found higher NLR values in DSS patients compared to less severe forms, indicating that the relationship may vary depending on the population or timing of measurement (Wazib et al., 2025). Additionally, studies such as those by Sajjad et al. (2025), Maulida et al. (2023), and Ashma et al. (2023) reported weak or non-significant associations, suggesting that NLR alone may not reliably predict severity (Sajjad et al., 2025) (Maulida et al., 2023) (Ashma et al., 2023). The majority of current evidence supports an inverse relationship between NLR and dengue severity, although its predictive accuracy is likely to improve when interpreted in conjunction with other clinical and hematological parameters.

5. CONCLUSION

This systematic review reveals that the neutrophil-to-lymphocyte ratio (NLR) tends to decline with increasing severity of dengue, particularly from Dengue Fever (DF) to Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). Most studies demonstrated significantly lower NLR values in patients with severe manifestations, including shock and bleeding, supporting its potential as a prognostic marker. However, a few studies reported opposite trends or non-significant associations, possibly due to differences in study populations, disease phase at the time of measurement, and analytical methods. Despite this variability, the overall body of evidence suggests that NLR remains a promising, low-cost, and widely accessible biomarker for early risk stratification and guiding clinical decisions in dengue management, particularly in resource-limited settings. Further prospective studies with standardized timing and severity classification are needed to confirm its utility and refine its diagnostic thresholds.

6. LIMITATION

While this review provides consistent findings across multiple studies, some limitations should be acknowledged. The timing of NLR measurement varied between studies, and not all used uniform criteria to define DHF and DSS, which may influence the comparability of results. In addition, most studies were cross-sectional or retrospective, limiting the ability to observe dynamic changes in NLR over time. Despite these variations, the overall trend of declining NLR with increasing dengue severity remained consistent and supports the potential value of NLR in clinical practice.

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