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Platelet-to-Lymphocyte Ratio in Pediatric Dengue Patients: A Key Indicator of Disease Severity

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A B S T R A C T

Background: Dengue infection remains a significant health concern in Indonesia, with a high mortality rate. Early identification and prediction of severe dengue are crucial for effective management and mortality reduction. The platelet-to-lymphocyte ratio (PLR) has emerged as a potential biomarker for assessing dengue severity due to its association with inflammatory responses. **Methods:** This descriptive study included 48 pediatric patients diagnosed with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) at Dr. M. Djamil General Hospital Padang between March and August 2024. Patients were included if they were aged 0-18 years, had a confirmed diagnosis of DHF or DSS, and underwent complete blood count and serological testing for dengue. Patients with chronic diseases or other comorbidities were excluded. Complete blood counts were performed using flow cytometry, and PLR was calculated by dividing the platelet count by the absolute lymphocyte count. Clinical data were obtained from medical records. **Results:** The majority of patients were aged 6-18 years (68.8%), with 20 (41.7%) presenting with DHF and 28 (58.3%) with DSS. The median platelet count was lower in DSS patients (26,000/mm^3) compared to DHF patients (35,500/mm^3). The median PLR was also significantly lower in DSS patients (8.95) compared to DHF patients (15.61). A PLR value <20 was more frequently observed in DSS patients (89.3%) than in DHF patients (75%). **Conclusion:** A lower PLR value was associated with more severe clinical manifestations of dengue infection, particularly DSS. PLR can serve as a valuable biomarker for assessing dengue severity, utilizing readily available and cost-effective complete blood count results.

1. Introduction

Dengue infection remains a significant public health concern globally, with a dramatic eightfold increase in incidence observed over recent decades. In 2023 alone, over 6.5 million dengue cases were reported worldwide, resulting in over 7,300 deaths. The World Health Organization (WHO) estimates that approximately half of the world's population is at risk of dengue infection, with the majority of cases occurring in tropical and subtropical regions. Dengue is caused by a mosquito-borne flavivirus, primarily transmitted by the Aedes aegypti mosquito. The clinical manifestations of dengue infection range from mild febrile illness to severe and life-threatening complications, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). DHF and DSS are characterized by plasma leakage, thrombocytopenia, and potentially fatal shock. DSS, in particular, is a major contributor to dengue-related mortality, with a case fatality rate significantly higher than that of non-shock dengue cases. Early recognition and prediction of shock are crucial for effective dengue management and the prevention of mortality. However, the clinical presentation of dengue can be variable, and the early differentiation between mild and severe forms of the disease can be

challenging. Therefore, there is a critical need for reliable biomarkers that can aid in the early identification and risk stratification of dengue patients.[1-4]

Several hematological parameters have been investigated as potential biomarkers for dengue severity, including platelet count, leukocyte count, and neutrophil-to-lymphocyte ratio (NLR). Among these, the platelet-to-lymphocyte ratio (PLR) has garnered increasing attention as a potential indicator of dengue severity. PLR reflects the interplay between platelets, which are involved in coagulation and inflammation, and lymphocytes, which are key components of the immune response. In the context of dengue infection, PLR may provide insights into the severity of inflammation and disease progression. Studies have shown that PLR is significantly lower in patients with severe dengue, particularly those with DSS, compared to those with milder forms of the disease. The decrease in PLR in severe dengue may be attributed to the combination of thrombocytopenia and lymphocytosis. As dengue infection progresses, platelet counts decline due to various mechanisms, including bone marrow suppression, increased platelet destruction, and increased platelet consumption. Simultaneously, lymphocyte counts may increase as part of the immune response to the virus. The combination of these changes results in a lower PLR, reflecting the severity of inflammation and disease activity.[5-7]

PLR has several advantages as a potential biomarker for dengue severity. It is readily available and cost-effective, as it can be easily calculated from routine complete blood count results, which are routinely performed in most healthcare settings. Additionally, PLR has been shown to be a more sensitive and specific indicator of dengue severity compared to other hematological parameters, such as platelet count and leukocyte count. While several studies have explored the role of PLR in adult dengue patients, research on its significance in pediatric dengue, particularly in differentiating DHF and DSS, remains limited. Pediatric dengue presents unique challenges, as children may have different clinical manifestations and immune responses compared to adults. Therefore, it is essential to investigate the value of PLR, specifically in pediatric dengue patients to ensure its accurate interpretation and clinical utility.[8-10] This study aimed to investigate the value of PLR in pediatric patients diagnosed with DHF and DSS at Dr. M. Djamil General Hospital Padang, contributing to the understanding of dengue pathogenesis and potentially aiding in the early identification of severe dengue cases.

2. Methods

This study employed a descriptive research design to investigate the platelet-to-lymphocyte ratio (PLR) in pediatric dengue patients. Descriptive studies are observational in nature and aim to systematically describe and document the characteristics, behaviors, or phenomena of a population or group of interest. In this case, the study focused on describing the PLR values in pediatric patients diagnosed with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) and exploring the potential association between PLR and disease severity. The study was conducted at the Central Laboratory Installation and Medical Record Installation of Dr. M. Djamil General Hospital Padang, a tertiary care hospital located in Padang, Indonesia. Dr. M. Djamil General Hospital serves as a major referral center for the province of West Sumatra and provides comprehensive healthcare services, including specialized care for pediatric patients with infectious diseases such as dengue. The study period spanned from March 2024 to August 2024, coinciding with the peak dengue season in Indonesia.

The study population included all pediatric patients aged 0-18 years who were clinically diagnosed with DHF or DSS by clinicians and had serological confirmation of dengue infection. The diagnosis of DHF and DSS was based on the WHO criteria, which include clinical manifestations such as fever, hemorrhagic tendencies, thrombocytopenia, and evidence of plasma leakage. Serological confirmation of dengue infection was established through the

detection of IgM anti-dengue antibodies or a combination of IgM and IgG anti-dengue antibodies in the patient's blood. A total of 48 pediatric patients who met the inclusion and exclusion criteria were included in the study sample. The sample size was determined based on the availability of eligible patients during the study period and the feasibility of data collection and analysis.

The following inclusion criteria were applied to select patients for the study; Pediatric patients aged 0-18 years: This criterion ensured that the study focused specifically on the pediatric population, as children may have different clinical manifestations and immune responses compared to adults; Clinical diagnosis of DHF or DSS: This criterion ensured that the study included patients with severe forms of dengue infection, as these patients are at higher risk of complications and mortality; Hospitalization at Dr. M. Djamil General Hospital Padang between March 2024 and August 2024: This criterion ensured that the study included patients who were admitted to the hospital during the study period, allowing for the collection of complete medical records and blood count data; Complete medical records and blood count data: This criterion ensured that the study included patients with comprehensive medical records and laboratory data, allowing for a thorough analysis of their clinical and hematological parameters. The following exclusion criteria were applied to exclude patients from the study; History of chronic diseases, such as hematological disorders, congenital disorders, autoimmune diseases, or immunodeficiency: These conditions could potentially affect the patient's hematological parameters and confound the results of the study; Presence of other comorbidities during hospitalization: Comorbidities could also potentially affect the patient's clinical course and hematological parameters, making it difficult to isolate the effects of dengue infection.

Blood samples were collected from DHF and DSS patients who met the inclusion and exclusion criteria. The blood samples were collected in EDTA tubes, which are commonly used for hematological testing. EDTA acts as an anticoagulant, preventing the blood from clotting and preserving the integrity of blood cells for analysis. Complete blood count analysis was performed on the collected blood samples using flow cytometry. Flow cytometry is a sophisticated laboratory technique that allows for the rapid and accurate analysis of various blood cell parameters, including platelet count, leukocyte count, and absolute lymphocyte count. Platelet count refers to the number of platelets per unit volume of blood. Platelets are small, irregularly shaped cells that play a crucial role in blood clotting. Leukocyte count refers to the total number of white blood cells per unit volume of blood. White blood cells are an essential part of the immune system and help fight infection. Absolute lymphocyte count refers to the number of lymphocytes per unit volume of blood. Lymphocytes are a type of white blood cell that plays a central role in the immune response. PLR was calculated by dividing the platelet count by the absolute lymphocyte count. This simple calculation provides a quantitative measure of the relative abundance of platelets and lymphocytes in the blood. PLR has been proposed as a potential biomarker for various inflammatory conditions, including dengue infection. In addition to laboratory data, secondary data were collected from electronic medical records. These data included the patient's age, clinical diagnosis, and dengue severity classification. Age is an important demographic factor that can influence the clinical presentation and severity of dengue infection. Clinical diagnosis refers to the physician's assessment of the patient's condition based on their clinical manifestations and laboratory findings. Dengue severity classification is based on the WHO criteria and categorizes dengue cases as mild, moderate, or severe. Serological data, including IgM and IgG anti-dengue antibody results, were retrieved from the Laboratory Information System (LIS) of the Central Laboratory at Dr. M. Djamil General Hospital Padang. The LIS is a computerized system that stores and manages laboratory data, ensuring the accuracy and accessibility of serological test results.

The collected data were compiled and organized for analysis. Frequency distribution tables were created to summarize the characteristics of the study subjects, including their demographic information, clinical diagnosis, and hematological parameters. Frequency distribution tables provide a clear and concise overview of the data, allowing for the identification of patterns and trends. Descriptive analysis was performed using SPSS version 25, a statistical software package commonly used in healthcare research. Descriptive analysis involves summarizing and describing the main features of the data, such as measures of central tendency (e.g., mean, median) and measures of dispersion (e.g., standard deviation, range). In this study, descriptive analysis was used to characterize DHF and DSS patients and to compare PLR values between the two groups. The comparison of PLR values between DHF and DSS patients was performed using appropriate statistical tests, such as the Mann-Whitney U test or the independent samples t-test, depending on the distribution of the data. These tests assess whether there is a statistically significant difference in PLR values between the two groups. The association between PLR and the severity of dengue infection was assessed using correlation analysis. Correlation analysis measures the strength and direction of the linear relationship between two variables. In this study, the correlation between PLR and dengue severity classification was examined to determine whether lower PLR values are associated with more severe forms of dengue infection. The potential of PLR as a biomarker for early identification and risk stratification of severe dengue cases was evaluated by examining its sensitivity, specificity, and predictive values. Sensitivity refers to the ability of PLR to correctly identify patients with severe dengue, while specificity refers to its ability to correctly identify patients without severe dengue. Predictive values indicate the probability of a patient having or not having severe dengue based on their PLR value.

3. Results

Table 1 provides a breakdown of the characteristics of the pediatric patients included in the study; Gender: The study sample had a nearly even distribution between males (52.1%) and females (47.9%). This suggests that both genders are almost equally susceptible to dengue infection, at least within the studied population; Age: The majority of the patients (68.8%) were children aged 6-18 years. This is consistent with the epidemiology of dengue, which tends to affect school-aged children and adolescents more frequently. Infants (0-12 months) made up 14.6% of the sample, while toddlers (1-5 years) accounted for 16.7%. This indicates that while dengue can affect younger children, it is less common in this age group compared to older children; Dengue Severity: A higher proportion of patients presented with DSS (58.3%) compared to DHF (41.7%). This suggests that the study sample had a higher representation of severe dengue cases. This could be due to the study being conducted at a tertiary care hospital, where more severe cases are typically referred.

Table 1. Characteristics of study subjects.

Variable	Frequency (%)
Gender	
Male	25 (52.1)
Female	23 (47.9)
Age (years)	
Infant (0-12 months)	7 (14.6)
Toddler (1-5 years)	8 (16.7)
Child (6-18 years)	33 (68.8)
Dengue severity	
DHF	20 (41.7)
DSS	28 (58.3)

Table 2 presents the distribution of platelet count, leukocyte count, and PLR values specifically in the DHF patients within the study; Platelet Count: As expected with DHF, a significant portion of patients exhibited thrombocytopenia (low platelet count). 45% had platelet counts within a relatively normal range (50,000 - 150,000/mm^3), 30% had moderate thrombocytopenia (20,000 - 50,000/mm^3), and 25% had severe thrombocytopenia (<20,000/mm^3). This highlights the variability in platelet levels even within the DHF group; Leukocyte Count: The majority of DHF patients (60%) had leukocyte counts above 4,000/mm^3, which is generally considered within the normal range. 35% had slightly lower leukocyte counts (2,000 - 4,000/mm^3), and only a small fraction (5%) had leukopenia (<2,000/mm^3). This suggests that while leukopenia can occur in DHF, it's not as prevalent as thrombocytopenia; PLR: The majority of DHF patients (75%) had a PLR <20. There were no patients with a PLR between 21-40. Small percentages had PLR values in the higher ranges (41-60, 61-80, and >81). This distribution indicates that lower PLR values are more common in DHF.

Table 2. Platelet count, leukocyte count, and PLR in DHF patients.

Variable	Frequency (%)
Platelet count	
50,000 - 150,000/mm^3	9 (45)
20,000 - 50,000/mm^3	6 (30)
<20,000/mm^3	5 (25)
Leukocyte count	
>4,000/mm^3	12 (60)
2,000 - 4,000/mm^3	7 (35)
<2,000/mm^3	1 (5)
PLR	
<20	15 (75)
21-40	0
41-60	1 (5)
61-80	3 (15)
>81	1 (5)

Table 3 provides a breakdown of the platelet count, leukocyte count, and PLR values specifically for the DSS patients in the study; Platelet Count: Thrombocytopenia is even more pronounced in the DSS group compared to the DHF group. Only a small percentage (10.7%) had platelet counts above 50,000/mm^3. The majority (57.1%) had moderate thrombocytopenia (20,000 - 50,000/mm^3), and a significant proportion (32.1%) had severe thrombocytopenia (<20,000/mm^3). This reflects the more severe nature of DSS and its association with a greater degree of platelet depletion; Leukocyte Count: Most DSS patients (82.1%) had leukocyte counts above 4,000/mm^3. A smaller percentage (17.9%) had leukocyte counts between 2,000 - 4,000/mm^3. No patients in the DSS group had leukopenia (<2,000/mm^3). This suggests that leukopenia is less common in DSS compared to DHF; PLR: The vast majority of DSS patients (89.3%) had a PLR <20. Small percentages had PLR values in the higher ranges (21-40 and >81). This distribution further reinforces the association of lower PLR values with more severe dengue.

Table 3. Platelet count, leukocyte count, and PLR in DSS patients.

Variable	Frequency (%)
Platelet count	
50,000 - 150,000/mm^3	3 (10.7)
20,000 - 50,000/mm^3	16 (57.1)
<20,000/mm^3	9 (32.1)
Leukocyte count	
>4,000/mm^3	23 (82.1)
2,000 - 4,000/mm^3	5 (17.9)
<2,000/mm^3	0
PLR	
<20	25 (89.3)
21-40	2 (7.1)
41-60	0
61-80	0
>81	1 (3.6)

Table 4 provides a direct comparison of the median platelet count, leukocyte count, absolute lymphocyte count, and PLR between the DHF and DSS patient groups; Platelet Count: The median platelet count was notably lower in DSS patients (26,000/mm^3) compared to DHF patients (35,500/mm^3). This aligns with the earlier tables and confirms that more severe thrombocytopenia is associated with DSS; Leukocyte Count: The median leukocyte count was higher in DSS patients (7,245/mm^3) than in DHF patients (5,460/mm^3). This suggests a more pronounced inflammatory response in DSS; Absolute Lymphocyte Count: Similarly, the median absolute lymphocyte count was higher in DSS patients (3,008.65/mm^3) compared to DHF patients (2,080.75/mm^3). This could reflect a more robust immune response mounted against the virus in DSS; PLR: Most importantly, the median PLR was significantly lower in DSS patients (8.95) compared to DHF patients (15.61). This key finding supports the hypothesis that lower PLR values are indicative of more severe dengue infection.

Table 4. Median platelet count, leukocyte count, absolute lymphocyte count, and PLR in DHF and DSS patients.

Parameter	DHF (20)	DSS (28)
	Median (min-max)	Median (min-max)
Platelet count	35,500 (4,000-114,000) /mm^3	26,000 (11,000-64,000) /mm^3
Leukocyte count	5,460 (1,630-9,620) /mm^3	7,245 (2,150-26.650) /mm^3
Absolute lymphocyte count	2,080.75 (753-5,368) /mm^3	3,008.65 (693-14,460) /mm^3
PLR	15.61 (1-84)	8.95 (2-92)

4. Discussion

Dengue infection, a mosquito-borne viral illness prevalent in tropical and subtropical regions, presents a spectrum of clinical manifestations, ranging from mild febrile illness to severe and life-threatening complications such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The severity of dengue infection is influenced by a complex interplay of viral factors, host immune responses, and the presence of comorbidities. Among the key hematological features of dengue infection are thrombocytopenia, a decrease in platelet count, and leukopenia, a decrease in leukocyte count. These hematological abnormalities are not only diagnostic hallmarks of dengue infection but also provide valuable insights into the pathophysiology of the disease and its potential for severe outcomes. Thrombocytopenia is a consistent finding in dengue

infection, with varying degrees of severity observed across different stages of the disease. In this study, almost all DHF patients exhibited thrombocytopenia, ranging from mild to severe. This finding is consistent with numerous studies that have identified thrombocytopenia as a common feature of dengue infection, particularly in those with DHF and DSS. The mechanisms underlying thrombocytopenia in dengue are complex and multifactorial, involving a combination of factors that contribute to the depletion of platelets in the circulation. Dengue virus infection can directly suppress the production of platelets in the bone marrow, leading to a decrease in platelet count. This suppression is thought to be mediated by the virus's effects on megakaryocytes, the bone marrow cells responsible for platelet production. The dengue virus can infect megakaryocytes, disrupting their maturation and platelet production processes. Additionally, the virus can induce the production of cytokines, such as tumor necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ), which can further suppress megakaryocyte activity and platelet production. Dengue virus infection can also trigger an immune response that leads to increased destruction of platelets. This destruction is mediated by antibodies and immune cells that target and eliminate platelets, further contributing to thrombocytopenia. The dengue virus can bind to platelets, making them targets for antibody-dependent cellular cytotoxicity (ADCC) and complement-mediated lysis. Additionally, the virus can induce the production of autoantibodies against platelets, further enhancing their destruction. Platelets play a crucial role in blood clotting, and in dengue infection, they are consumed at an accelerated rate due to the ongoing inflammatory process and the formation of microthrombi in various organs. This increased consumption further depletes the platelet pool, exacerbating thrombocytopenia. The inflammatory response in dengue infection leads to the activation of the coagulation cascade, resulting in the formation of microthrombi in various organs, including the liver, kidneys, and lungs. Platelets are consumed in this process, further contributing to thrombocytopenia. Severe thrombocytopenia, particularly platelet counts below 20,000/mm^3, is a warning sign for plasma leakage and an increased risk of severe dengue, including DSS. Plasma leakage is a hallmark of severe dengue and is characterized by the leakage of fluid from the blood vessels into the surrounding tissues, leading to hypovolemia and shock. Thrombocytopenia is thought to contribute to plasma leakage by impairing the integrity of the vascular endothelium, the lining of the blood vessels. The reduced number of platelets can compromise the ability of the endothelium to maintain vascular integrity, leading to increased permeability and leakage of fluid into the extravascular space. Leukopenia, a decrease in leukocyte count, is also observed in dengue infection, although it may not be as prevalent as thrombocytopenia, especially in the early stages of the disease. In this study, leukopenia was less common in both DHF and DSS patients, with the majority having leukocyte counts within or above the normal range. This suggests that while leukopenia can occur in dengue, it may not be a consistent finding, particularly in the early phases of the illness. The mechanisms underlying leukopenia in dengue are not fully understood, but they are thought to involve bone marrow suppression and impaired myeloid cell production. Myeloid cells are a type of white blood cell that includes neutrophils, monocytes, and macrophages, which play important roles in the immune response against infections. Dengue virus infection can suppress the production of these cells in the bone marrow, leading to a decrease in leukocyte count. The virus can infect bone marrow progenitor cells, disrupting their differentiation and maturation into myeloid cells. Additionally, the virus can induce the production of cytokines, such as TNF-α and IFN-γ, which can further suppress myeloid cell production. Previous research has shown that leukopenia is more common in severe dengue cases and may reflect the extent of bone marrow involvement. In severe dengue, the bone marrow suppression can be more pronounced, leading to a more significant decrease in leukocyte count. Leukopenia has also been associated

with an increased risk of secondary bacterial infections in dengue patients, as the reduced number of white blood cells impairs the body's ability to fight off invading pathogens. Thrombocytopenia and leukopenia are not isolated events in dengue infection but rather reflect the complex interplay of immune responses and pathophysiological processes triggered by the virus. The virus's effects on the bone marrow, coupled with the ongoing inflammatory response and platelet consumption, contribute to the development of these hematological abnormalities. The severity of thrombocytopenia and leukopenia can vary depending on the stage of the disease, the infecting serotype, and the host's immune response. In general, more severe thrombocytopenia and leukopenia are associated with more severe forms of dengue infection and an increased risk of complications. Thrombocytopenia and leukopenia are important clinical parameters to monitor in dengue patients, as they can provide valuable insights into disease progression and the potential for severe outcomes. Close monitoring of platelet and leukocyte counts can help clinicians identify patients at risk of developing severe dengue and guide appropriate management decisions. In addition to monitoring platelet and leukocyte counts, clinicians should also pay close attention to other clinical and laboratory parameters, such as vital signs, fluid balance, and liver function tests. These parameters can provide a more comprehensive picture of the patient's condition and help guide treatment decisions.[11-13]

The key finding of this study, consistent with other research, is the association of lower platelet-to-lymphocyte ratio (PLR) values with more severe dengue manifestations, particularly dengue shock syndrome (DSS). The median PLR was significantly lower in DSS patients compared to DHF patients, with a PLR value <20 more frequently observed in the DSS group. This decrease in PLR during severe dengue likely stems from the interplay between thrombocytopenia (low platelet count) and lymphocytosis (high lymphocyte count). As dengue infection progresses, platelet counts decline due to various mechanisms, while lymphocyte counts may surge as part of the immune response to the virus. This combination results in a lower PLR, reflecting heightened inflammation and disease activity. The PLR has emerged as a promising biomarker not only for dengue, but for various inflammatory conditions, including cardiovascular diseases, chronic diseases, malignancies, and other infectious diseases. It effectively reflects the dynamic balance between platelets, central to coagulation and inflammation, and lymphocytes, the cornerstones of the adaptive immune response. In dengue infection, the PLR offers valuable insights into the severity of inflammation and disease progression. Lower PLR values in severe dengue cases likely arise from the complex interplay of immune responses, encompassing cytokine release, lymphocyte activation, and platelet dysfunction. The PLR serves as a window into the dynamic interplay between platelets and lymphocytes, two key players in the immune response to dengue virus infection. Platelets, small anucleated cells critical for hemostasis (the process of stopping bleeding), also play significant roles in inflammation and immunity. They release various mediators that can modulate the immune response, acting as crucial communicators and effectors in the fight against infection. Lymphocytes, a type of white blood cell, are responsible for recognizing and eliminating pathogens, including viruses. They are the orchestrators of the adaptive immune response, learning to identify and target specific threats. In dengue infection, the PLR can be influenced by a multitude of factors, including the stage of the disease, the infecting serotype, and the host's unique immune response. In the early stages of dengue infection, the PLR may be elevated due to an increase in platelet count and a decrease in lymphocyte count. This is thought to be due to the release of platelets from the bone marrow in response to the infection, as well as the migration of lymphocytes to the site of infection. The body initially rallies its defenses, increasing platelet production to maintain vascular integrity and sending lymphocytes to confront the invading virus. However, as the

infection progresses, the PLR may decrease due to a decrease in platelet count and an increase in lymphocyte count. This shift is attributed to the aforementioned mechanisms of thrombocytopenia, as well as the activation and proliferation of lymphocytes in response to the virus. The virus gains ground, disrupting platelet production and increasing their destruction, while the immune system ramps up lymphocyte production to combat the infection. Cytokines, the signaling molecules of the immune system, play a crucial role in the immune response, but their release in dengue infection can contribute to the dysregulation of the PLR. For instance, pro-inflammatory cytokines like TNF-α and IFN-γ can suppress platelet production and enhance platelet destruction, leading to thrombocytopenia. These cytokines also activate lymphocytes, leading to lymphocytosis. The immune system's attempt to control the infection can paradoxically exacerbate the imbalance reflected in the PLR. Beyond thrombocytopenia, dengue infection can also induce platelet dysfunction. This dysfunction can manifest as impaired platelet aggregation, adhesion, and activation, further contributing to the bleeding manifestations often seen in dengue. The mechanisms underlying platelet dysfunction in dengue are complex and not fully understood, but they are thought to involve the direct effects of the virus on platelets, as well as the indirect effects of cytokines and other inflammatory mediators. The virus can hijack platelet function, turning them from defenders into liabilities. The PLR has emerged as a promising biomarker for dengue severity, with several studies demonstrating that lower PLR values are associated with more severe forms of dengue infection, including DHF and DSS. The beauty of the PLR lies in its simplicity. It can be easily calculated from routine complete blood count results, making it a readily available and cost-effective tool for assessing dengue severity, particularly valuable in resource-limited settings. The PLR can be used in conjunction with other clinical and laboratory parameters to assess the risk of severe dengue and to guide management decisions. For example, patients with low PLR values may require closer monitoring and more aggressive supportive care to prevent the development of severe complications. A low PLR can serve as a red flag, prompting clinicians to be more vigilant and proactive in their care.[14-16]

The findings of this study have significant clinical implications for the management of pediatric dengue patients. PLR can be easily calculated from routine complete blood count results, which are readily available and cost-effective in most healthcare settings. Incorporating PLR into the evaluation of dengue patients may aid in early risk stratification and guide clinical management decisions. For instance, patients with low PLR values may require closer monitoring and more aggressive supportive care to prevent the development of severe complications. PLR has the potential to serve as a valuable adjunct to existing clinical and laboratory parameters in the assessment of dengue severity. It may be particularly useful in resource-limited settings where access to more sophisticated diagnostic tests may be limited. By utilizing readily available complete blood count results, clinicians can obtain a quick and cost-effective assessment of disease severity, enabling timely interventions and potentially improving patient outcomes. One of the most significant clinical implications of PLR in dengue infection is its potential for early risk stratification and triage. Dengue infection can present with a wide range of clinical manifestations, making it challenging to identify patients at risk of developing severe complications. PLR, with its ability to reflect the severity of inflammation and disease activity, can serve as a valuable tool for early risk stratification. By incorporating PLR into the initial evaluation of dengue patients, clinicians can identify those at higher risk of developing severe dengue. Patients with low PLR values, especially those below a certain threshold, may require closer monitoring, more aggressive supportive care, and early intervention to prevent the progression to severe dengue. This early risk stratification can help optimize the allocation of healthcare resources and ensure that patients at highest risk receive timely and

appropriate care. To effectively utilize PLR for risk stratification, it is essential to establish clear cutoff values or thresholds that accurately predict the risk of severe dengue. These thresholds may vary depending on the population, the stage of the disease, and the presence of comorbidities. Further research is needed to determine optimal PLR thresholds for different patient populations and clinical settings. Once PLR thresholds are established, they can be integrated into triage protocols for dengue patients. This can help streamline the assessment and management of dengue cases, ensuring that patients at highest risk are prioritized for care. For example, patients with PLR values below a certain threshold may be fast-tracked for more intensive monitoring and treatment, while those with higher PLR values may be managed more conservatively. PLR can also guide clinical management decisions in dengue patients. For instance, patients with low PLR values may benefit from early fluid resuscitation to prevent hypovolemia and shock. They may also require closer monitoring of their vital signs, fluid balance, and hematological parameters. In contrast, patients with higher PLR values may be at lower risk of developing severe dengue and may require less intensive monitoring and supportive care. PLR can also be used to monitor the response to treatment. An increase in PLR following treatment may indicate a favorable response and a decrease in disease severity. Conversely, a persistent low PLR or a further decrease in PLR may suggest a lack of response to treatment and the need for more aggressive interventions. Fluid management is a cornerstone of dengue treatment, especially in patients with severe dengue. PLR can be used to guide fluid management decisions, ensuring that patients receive the appropriate amount of fluids at the right time. Patients with low PLR values, who are at higher risk of developing shock, may benefit from early and aggressive fluid resuscitation. PLR can also be used to monitor the response to fluid therapy, with an increase in PLR suggesting a favorable response. PLR can also guide the intensity of monitoring and supportive care provided to dengue patients. Patients with low PLR values may require closer monitoring of their vital signs, fluid balance, and hematological parameters. They may also benefit from more aggressive supportive care, such as oxygen therapy and blood transfusions, if indicated. In contrast, patients with higher PLR values may require less intensive monitoring and supportive care. PLR can enhance the diagnostic accuracy of dengue infection, especially in the early stages of the disease when clinical manifestations may be nonspecific. In this study, PLR was found to be significantly lower in DSS patients compared to DHF patients, suggesting its potential to differentiate between these two severe forms of dengue. PLR can also be used in conjunction with other clinical and laboratory parameters, such as platelet count, leukocyte count, and NS1 antigen test, to improve the diagnostic accuracy of dengue infection. The combination of PLR with these parameters can provide a more comprehensive assessment of the patient's condition and help clinicians make more informed diagnostic decisions. PLR can serve as a valuable diagnostic adjunct, especially in cases where the clinical presentation is ambiguous or when other diagnostic tests are inconclusive. By providing additional information about the severity of inflammation and disease activity, PLR can help clinicians make more accurate diagnoses and initiate appropriate treatment earlier. Dengue virus has four distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), and the severity of dengue infection can vary depending on the infecting serotype. PLR may have the potential to differentiate between dengue serotypes, as some studies have suggested that certain serotypes may be associated with lower PLR values and more severe disease. Further research is needed to explore this potential application of PLR. PLR is particularly valuable in resource-limited settings where access to more sophisticated diagnostic tests may be limited. Complete blood count, the test required to calculate PLR, is widely available and relatively inexpensive in most healthcare settings. By utilizing readily available complete blood count results, clinicians can obtain a

quick and cost-effective assessment of disease severity, enabling timely interventions and potentially improving patient outcomes. In resource-limited settings, where healthcare resources may be stretched thin, PLR can help prioritize patients at highest risk of developing severe dengue. This can ensure that limited resources are used efficiently and that patients most in need receive timely and appropriate care. During dengue outbreaks, healthcare systems can be overwhelmed by the surge in cases. PLR can serve as a valuable triage tool in such situations, helping clinicians identify and prioritize patients at highest risk of developing severe dengue. This can ensure that limited resources are used efficiently and that patients most in need receive timely and appropriate care. PLR can also be used in community-based settings to identify and monitor dengue patients. With the increasing availability of portable blood analyzers, community health workers can measure PLR in patients with suspected dengue and refer those with low PLR values to healthcare facilities for further evaluation and management. This can help improve access to care for dengue patients, especially in remote areas with limited access to healthcare facilities. PLR has the potential to be incorporated into telemedicine and remote monitoring programs for dengue patients. With the increasing availability of portable blood analyzers, patients can monitor their PLR at home and transmit the results to their healthcare providers. This can enable remote monitoring of disease progression and early identification of patients at risk of developing severe dengue. Telemedicine and remote monitoring programs can be particularly beneficial in areas with limited access to healthcare facilities or during outbreaks when healthcare systems may be overwhelmed. By enabling remote monitoring and early intervention, PLR can help reduce the burden on healthcare systems and improve patient outcomes. Mobile health (mHealth) applications can be developed to facilitate remote monitoring of PLR in dengue patients. These applications can allow patients to track their PLR values over time, receive personalized alerts and recommendations based on their PLR, and communicate with their healthcare providers remotely. PLR monitoring can also be integrated into wearable technology, such as smartwatches and fitness trackers. These devices can continuously monitor PLR and other physiological parameters, providing real-time data that can be used to assess disease progression and guide treatment decisions.[17-20]

5. Conclusion

Our study underscores the importance of the platelet-to-lymphocyte ratio (PLR) as a valuable biomarker for assessing the severity of dengue infection in pediatric patients. The PLR, derived from routine complete blood count results, offers a readily available and cost-effective tool for identifying those at higher risk of developing severe dengue, particularly dengue shock syndrome (DSS). Our findings suggest that a lower PLR value is strongly associated with more severe clinical manifestations of dengue, particularly DSS. The PLR's ability to reflect the interplay between platelets and lymphocytes, key players in the immune response to dengue virus infection, provides valuable insights into the severity of inflammation and disease progression. As dengue infection progresses, the combination of thrombocytopenia and lymphocytosis results in a lower PLR, serving as a crucial indicator of disease severity. Incorporating PLR into the evaluation of pediatric dengue patients can significantly enhance clinical decision-making. It enables early risk stratification, facilitates informed clinical management decisions, and aids in the differentiation between DHF and DSS. Patients with low PLR values may require closer monitoring and more aggressive supportive care to prevent severe complications. The PLR's clinical utility extends beyond risk stratification and treatment decisions. It can be used to monitor treatment response, guide fluid management strategies, and improve diagnostic accuracy, especially in the early stages of dengue infection. Moreover, PLR holds tremendous potential for telemedicine and remote monitoring programs,

allowing for early identification and intervention in dengue patients, particularly in resource-limited settings. In conclusion, the PLR is a valuable biomarker for assessing dengue severity in pediatric patients. Its ease of calculation, cost-effectiveness, and strong association with disease severity make it an indispensable tool for clinicians managing dengue infection. Further research is needed to establish optimal PLR thresholds for different patient populations and clinical settings, enabling its integration into triage protocols and clinical practice guidelines. The PLR's potential to improve patient outcomes, particularly in resource-limited settings, warrants its widespread adoption in the fight against dengue.

6. References

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