Research Article

Correlation Between Neutrophil-to-Lymphocyte Ratio (NLR) and Length of Hospital Stay in Pediatric Patients with Dengue Hemorrhagic Fever

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Abstract

Dengue hemorrhagic fever (DHF) is a tropical infectious disease that remains a serious global health concern. During the critical phase of the illness, the neutrophil-to-lymphocyte ratio (NLR) decreases, exacerbating the infection and facilitating dengue virus replication in mononuclear blood cells. A lower NLR value is thought to be associated with a longer duration of hospitalization. This study aims to investigate the correlation between NLR and the length of hospitalization in pediatric patients with DHF at Mohammad Hoesin Hospital, Palembang. This study employed an analytical observational cross-sectional design using secondary data collected from August to December 2023. A total of 67 children met the inclusion criteria. The predominant characteristics included age 5–10 years (52.2%), male (47.8%), female (52.2%), DHF grade II (46.3%), and a history of 5 days of fever (44.8%). Bivariate analysis revealed no correlation between NLR and the length of hospitalization in pediatric DHF patients (p=0.068; r=0.224). To conclude, there is no correlation between the NLR value and the duration of hospitalization in pediatric DHF patients at Mohammad Hoesin Hospital, Palembang.
Keywords: *neutrophil-to-lymphocyte ratio, immune response, dengue hemorrhagic fever, hospitalization.*

Korelasi antara Rasio Neutrofil-Limfosit dan Lama Rawat Inap pada Pasien Anak dengan Demam Berdarah Dengue

Abstrak

Demam berdarah dengue (DBD) merupakan penyakit infeksi tropis yang masih menjadi masalah kesehatan global yang serius. Selama fase kritis penyakit, rasio neutrofil-limfosit (RNL) menurun, yang dapat memperburuk infeksi dan replikasi virus dengue dalam sel darah mononuklear. Nilai RNL yang lebih rendah diduga berhubungan dengan durasi rawat inap yang lebih lama. Penelitian ini bertujuan untuk mengevaluasi hubungan antara RNL dengan lama rawat inap pada pasien DBD anak di RS Mohammad Hoesin, Palembang. Penelitian ini menggunakan desain observasional analitik dengan pendekatan potong lintang berdasarkan data sekunder yang dikumpulkan pada Agustus hingga Desember 2023. Sebanyak 67 pasien memenuhi kriteria inklusi. Karakteristik utama meliputi usia 5–10 tahun (52,2%), laki-laki (47,8%), perempuan (52,2%), DBD derajat II (46,3%), dan riwayat demam selama 5 hari (44,8%). Analisis bivariat menunjukkan tidak ada hubungan bermakna antara RNL dengan lama rawat inap pada pasien anak dengan DBD (p=0,068; r=0,224). Dapat disimpulkan bahwa tidak ada korelasi antara RNL dan lama rawat inap pada pasien DBD anak di RS Mohammad Hoesin, Palembang.

Kata kunci: *rasio neutrofil-limfosit; respon imun, demam berdarah dengue, rawat inap.*

Introduction

Dengue hemorrhagic fever (DHF) is an infectious disease that has become a significant global health concern, particularly in tropical and subtropical regions, over the past few decades. This disease is caused by the dengue virus, which belongs to the Flaviviridae family and the Flavivirus genus. Transmission occurs through the bite of mosquitoes from the Aedes genus, especially *Aedes albopictus* and *Aedes aegypti*.[1,2]

The World Health Organization predicted in 2022, that between 100 and 400 million cases of dengue cases are recorded each year, putting half of the world's population at risk.[3] Asia accounts for approximately 70% of global dengue cases, making it the region with the highest burden. In Southeast Asia, DHF is a leading cause of morbidity and mortality, with Indonesia contributing 57% of the regional total.[4] Children in Indonesia are particularly vulnerable to dengue infection. Between 2016 and 2019, the incidence of dengue cases among children aged 0–14 years reached 54.74%, 51.66%, 51.76%, and 53.08%, respectively, and remained high in 2020 at 53.41%.[5] In 2016, children aged 5–14 were the largest group affected (43.44%), followed by those aged 15–44 (33.25%). According to the Indonesian Ministry of Health, as of February 20, 2022, 13,776 dengue cases were reported, with 145 resulting in death. The highest numbers were reported in Bandung (598 cases), followed by Depok (394), and Bogor as well as Sumedang (347 each), while Cirebon reported 317 cases.[6] In South Sumatra, the Central Bureau of Statistics recorded a rise in dengue cases in Palembang, from 1,135 cases in 2021 to 2,854 cases in 2022.[7]

Leukocytes play a crucial role in combating infection through phagocytosis and antibody production, which help eliminate or neutralize invading pathogens. Neutrophils and lymphocytes are the primary leukocyte subtypes involved in the inflammatory and immune responses. As such, the balance between these cell types can be used to assess the body's immune response.[8]

Dengue infection progresses through three phases: febrile, critical, and recovery.[9,10] A predominance of neutrophils marks the febrile phase, while the critical phase is characterized by plasma leakage, increased hematocrit, and leukopenia, typically occurring as the fever subsides. The recovery phase involves the cessation of plasma leakage and is often accompanied by clinical improvement. Some patients may experience bradycardia during this phase, referred to as recovery bradycardia.[1,11]

The mechanism of plasma leakage in DHF may result from thrombocytopenia and coagulation disorders. A strong immune and inflammatory response can activate endothelial cells in blood vessels, altering their structure and function, contributing to plasma leakage.[11,13–15] During the critical phase, a decrease in neutrophil and lymphocyte counts results in a lower neutrophil-to-lymphocyte ratio (NLR), which exacerbatess infection and facilitates dengue virus replication in mononuclear blood cells. Increased vascular permeability during this phase causes plasma leakage into the peritoneal cavity, pleural space, and interstitial tissues, collectively called the "third space." A lower NLR is hypothesized to correlate with a longer duration of hospitalization.[11,14–18]

The NLR is calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. It has been associated with both mortality and length of hospitalization in various infectious conditions, including DHF. A study by Yasmina[19] reported a correlation between NLR and the length of hospitalization in sepsis patients. Conversely, research by Thaharatin[20] found no correlation between length of stay and NLR in ischemic stroke patients. However, studies examining the correlation between NLR and hospitalization duration in DHF patients remain limited. Therefore, this study aims to investigate the correlation between NLR and the length of hospital stay in pediatric DHF patients admitted to the inpatient clinic of Mohammad Hoesin Hospital in Palembang.

Methods

This study employed an analytical observational design with a cross-sectional approach to assess the correlation between NLR and the length of hospital stay in pediatric DHF patients. The research utilized secondary data from the medical records department and the central laboratory of Mohammad

Hoesin Hospital, Palembang, from August to December 2023.

A total-sampling technique was used. Pediatric inpatients diagnosed with DHF who fulfilled the criteria for inclusion were included for analysis. Inclusion criteria were as follows: (1) Paediatric inpatients diagnosed with DHF at Mohammad Hoesin Hospital between January 1st 2020 and October 30th 2023; (2) Availability of laboratory data on neutrophil and lymphocyte counts; (3) Availability of complete hospitalization data, including dates of admission and discharge; (4) Availability of complete demographic data (name, age, and gender); and (5) Aged between 5 and 18 years.

Meanwhile, exclusion criteria included: (1) Incomplete medical record or laboratory data; (2) Paediatric patients with coexisting infections that could affect NLR, such as bacterial infections (typhoid fever, pulmonary tuberculosis, urinary tract infections, and pneumonia) or viral infections (including COVID-19); (3) Paediatric patients with hematologic disorders that could influence NLR, including leukaemia, thalassemia, and idiopathic thrombocytopenic purpura (ITP); (4) Patients with a history of immunodeficiency disorders, such as HIV; (5) Patients with a history of sepsis; (6) Patients with a history of autoimmune diseases; and (7) Patients with a history of immunosuppressive therapy or blood transfusion.

The variables in this study were age, gender, degree of DHF, neutrophil count, lymphocyte count, NLR, and length of hospital stay. Clinical degree of DHF is classified into four categories: (1) Degree I is characterized by fever and nonspecific symptoms, as well as a positive tourniquet test result; (2) Degree II is characterized by spontaneous bleeding on the skin or other bleeding, in addition to the symptoms present in Grade I; (3) Degree III is characterized by circulatory failure; and (4) Degree IV is characterized by severe shock, where the pulse cannot be felt and blood pressure cannot be measured. The neutrophil and lymphocyte counts used are absolute values. NLR is calculated by comparing the number of neutrophils and lymphocytes measured in peripheral blood. NLR calculation uses the following formula:

$$NLR = \frac{Absolute\ neutrophil}{Absolute\ lymphocyte}$$

Data processing was conducted using univariate and bivariate analyses. Univariate analysis was applied to age, gender, degree of DHF, neutrophil count, and lymphocyte count. Bivariate analysis was used to examine the correlation between NLR and the length of hospital stay in DHF patients. The collected data were processed using IBM SPSS Statistic 24 (IBM, Armonk, United States). This research has received ethical approval from the Faculty of Medicine, Sriwijaya University, with the number 375-2023.

Results

In this study, 67 pediatric patients diagnosed with DHF and treated at Mohammad Hoesin Hospital between January 2020 and October 2023 met the inclusion and exclusion criteria. The characteristics of 67 patients are detailed in Table 1. Most patients were in the paediatric age group of 5–10 years (52.2%). Of these, 35 respondents were female (52.2%), and 32 were male (47.8%). Regarding the clinical grade of DHF, 31 respondents were classified as having grade 2 DHF (46.3%). In terms of fever onset, 30 respondents (44.8%) presented to the emergency department at Mohammad Hoesin Hospital, Palembang, with a complaint of fever lasting for 5 days. For further statistical analysis, the normality test results showed that the research variables, including neutrophil count, lymphocyte count, length of hospital stay, and NLR, were not normally distributed. Consequently, the Spearman rank correlation test was used to perform the correlation analysis.

Table 2 presents the descriptive statistics for neutrophil and lymphocyte counts, length of hospitalization, and neutrophil-to-lymphocyte ratio (NLR) in pediatric patients with DHF at Mohammad Hoesin Hospital, Palembang.

The results show that the median absolute neutrophil count of the patients was 2,186.10 cells/mm³ (IQR: 2,213.92–3,228.22 cells/mm³), with the lowest value being 444 cells/mm³ and the highest value being 12,272 cells/mm³. The median lymphocyte count among the patients was 1,501.77 cells/mm³ (IQR: 1,831.61–2,564.23 cells/mm³), with the lowest value being 290 cells/mm³ and the highest value 7,380 cells/mm³. The length of stay had a median value of 4 days (range: 2–8 days). For the NLR, the median value was 1.12 (range: 0.28–13.00).

Table 1. Characteristics of Pediatric Dengue Hemorrhagic Fever Patients

Characteristic (n=67)	Frequency (n)	Percentage (%)
Age		
Child age: 5-10 years	35	52.2
Early adolescence: 11-14 years	19	28.4
Middle-teenage age: 15-18 years	13	19.4
Gender		
Male	32	47.8
Female	35	52.2
Clinical Degree of DHF		
Degree I	13	19.4
Degree II	31	46.3
Degree III	14	20.9
Degree IV	9	13.4
Onset of Fever		
Day 1	0	0
Day 2	1	1.5
Day 3	4	6.0
Day 4	19	28.4
Day 5	30	44.8
Day 6	9	13.4
Day 7	4	6.0
Length of Hospitalization		
Day 2	9	13.4
Day 3	21	31.3
Day 4	15	22.4
Day 5	15	22.4
Day 6	5	7.5
Day 7	1	1.5
Day 8	1	1.5

Table 2. Neutrophil and Lymphocyte Counts, Length of Hospitalization, and NLR (n=67)

Variable	Median	Min-Max	Mean	SD
Neutrophils	2186.1	444-12272	2721.07	2079.16
Lymphocytes	1853.7	290-7380	2197.92	1501.77
Length of Hospitalization	4	2-8	3.84	1.24
NLR	1.12	0.28-13.00	1.62	1.88

The correlation between NLR and the length of hospital stay in pediatric patients with dengue hemorrhagic fever at Mohammad Hoesin Hospital Palembang was measured using Spearman analysis, which demonstrated no significant correlation (n=67; p=0.068; r=0.224). In this study, the p-value (0.068) indicates that the correlation between NLR and the length of hospitalization was not statistically significant (p>0.05). The correlation coefficient (r=0.224) suggests a weak positive correlation, implying that higher NLR values were slightly associated with longer hospital stays, although the relationship was not significant.

Discussion

Characteristics of Research Respondents

Most respondents (52.2%) were children aged 5–10 years, indicating that this age group was most affected in the study population. These findings are consistent with the research conducted by Hussain et al[21], which reported an average age of 5.7 ± 3.07 years for dengue haemorrhagic fever patients in their population. These findings are aligned with a study by Sasmono et al[22] who reported the median age of patients in Ambon was significantly lower (9 years, IQR = 4–16 years) than that in Batam (15 years, IQR = 6–26 years) and Banjarmasin (16 years, IQR

= 10–23 years). Female-to-male ratios of 1:1.15 and 1:1.1.1 were also reported, respectively; male patients were more prevalent in Ambon and Batam. Nevertheless, no statistically significant differences between the groups were found. The proportion of men to women in Banjarmasin was equal.[22]

While dengue fever is a virus that may afflict people of any age, children under 18 account for almost 90% of cases. Children are 15 times more likely than adults to die during a second illness episode. The most typical sign of dengue fever in youngsters is still fever, which is followed by vomiting and stomach discomfort. Dengue fever (DF), DHF, and dengue shock syndrome (DSS) are the three severity-based categories into which the clinical symptoms of dengue fever divided.[21, 22]

Most respondents (46.3%) were diagnosed with grade II DHF, and 44.8% presented to the emergency room after experiencing 5 days of fever. These results are consistent with the findings of Utama et al[23] who reported that, out of 468 instances of DENV infection, 187 cases had DF (40%), 270 cases had DHF grades I and II (57.7%), and 11 cases had grade III and IV dengue fever symptoms or unusual presentations (2.3%).[23] Similar to the study by Lim et al,[24] which found that the average duration of fever before the first visit was approximately 3.4 days for both groups, the overall duration of illness was significantly longer in patients with confirmed dengue fever (6.5 days) compared to those who did not suffer from dengue fever (5.7 days).[24] The results of this study were also consistent with the research by Sinha et al[25], which found the highest incidence in children aged 5 to 10 years (50.4 per 1000 person-years, 95% CI: 36.5 to 67.8). The average duration of an acute dengue fever episode was 6.9 (1.7) days.[25] These results are also consistent with the research by Thein et al[26] which reported that the median number of days of illness (from the onset of fever) at the time of admission was 4 days (5th–95th percentile = 2–6).

Distribution of Neutrophil Counts in Patients with Dengue Haemorrhagic Fever

The median absolute neutrophil count (ANC) among patients was 2,186.10 cells/mm³, ranging from 444 to 12,272 cells/mm³. These results are in line with Thein et al,[26] who found that throughout hospitalization, 1,579 (82.2%) patients had an ANC <1.5×10⁹/L, and that 227 (11.8%), 856 (44.6%), and 496 (25.8%) patients had severe, moderate, and mild neutropenia, respectively. Additionally, the results align with the study by Osuna-Ramos et al,[27] which reported that neutrophil levels in dengue patients were 2×10³/μL (IQR = 1.9).

DF is a mosquito-borne viral disease that primarily affects populations in tropical and subtropical regions and has become a growing global health concern. In recent years, it has also posed a significant risk to international travellers, highlighting the need for further training in the clinical management of dengue fever, particularly for physicians in non-endemic regions. DF is often characterized by thrombocytopenia and leukopenia, with neutropenia reported less frequently. Neutrophils play a crucial role in initiating and maintaining immune responses to microorganisms. Individuals with severe neutropenia (defined as ANC <0.5×10⁹/L) are at an increased risk of developing secondary bacterial infections, and prophylactic antibiotics are often administered to these patients. The clinical relevance of acute neutropenia in DF is still unknown, and there is currently little research on the condition. Especially, it is unclear if preventative antibiotic therapy is required and if dengue patients with severe neutropenia are more likely to develop subsequent bacterial infections.[26]

Leukopenia is a common finding in DHF patients and is an important diagnostic marker. The reduction in the total leukocyte count in DHF patients is primarily attributed to a decrease in neutrophils. While neutropenia in dengue infection has been documented, it is less commonly observed. Severe neutropenia has not been shown to correlate with an increased risk of secondary bacterial infections; however, it may result from the infection of leukocytes by the dengue virus. Infected cells, such as Langerhans and dendritic cells, migrate to the lymph nodes from the site of infection, where they recruit macrophages and monocytes, which then become targets for infection. The suppression of white blood cell production in the bone marrow by the dengue virus may contribute to leukocyte depletion.[29]

Distribution of Lymphocyte Counts in Patients with Dengue Haemorrhagic Fever

The median lymphocyte count among respondents was 1,501.77 cells/mm³, ranging from

290 to 7,380 cells/mm³. These findings align with the research of Osuna-Ramos et al,[7] which reported a lymphocyte count of 0.9×10³/μL in DF patients. Variations in the DENV genome, sub-genomic RNA, viral non-structural protein 1 (NS1), memory cross-reactive T cells, anti-DENV NS1 antibodies, antibody-dependent enhancement (ADE), and autoimmunity are some of the viral and host factors that affect the pathophysiology of dengue fever. According to several studies, the pathophysiology of DHF is partly mediated by cross-reactive T cells, which are active during secondary heterotypic infection. Patients with severe DHF have more T cells during the early stages of recovery than patients with less severe cases. T cells are activated by exposure to an antigen. The non-structural proteins NS3 and NS5 include the majority of CD8+ T cell peaks. High cross-reactivity and poor avidity were seen in CD8+ T cells activated in heterologous secondary DENV infections, which were ineffective in eliminating newly infectious virus serotypes. Activated DENV-specific cross-reactive T cells produced greater amounts of cytokines and chemokines in dengue fever patients, suggesting a positive correlation between the severity of dengue-related illness and cross-reactive T cell activation. Interleukin-10 has pleiotropic effects on inflammation and immunoregulation, indicating that it may be a key player in DENV pathogenesis. It is evident that DHF/DSS patients have greater IL-10 levels than DHF patients.[29, 30]

There is considerable debate over the connection between viral replication and IL-10, although it seems most probable that IL-10 plays a part by suppressing the antiviral IFN response. Type 2 T-helper cells, CD4+CD25+Foxp3+ regulatory T cells, and monocytes/macrophages are the primary cells that generate IL-10. CD4+CD25 regulatory T cells are very prevalent in acute dengue infections. Additionally, it has been demonstrated that ADE infection alone induces IL-10, but DENV infection alone does not. It is implied that DENV and ADE control the synthesis of IL-10, which benefits DHF/DSS patients. High levels of viral infection in cells with Fcγ receptors are caused by extrinsic ADE infection, whereas intrinsic ADE actions through IL-10 inhibit the activation of IFN-mediated antiviral responses. The expression of MHC class II antigens and co-stimulatory molecules, proinflammatory activation, TLR-mediated antiviral IFN responses, IL-2, IL-12, TNF-α, and IFN-γ production, and more all depend on NF-κB, which IL-10 blocks. Moreover, during the immunological response to DENV infection, increased IL-10 synthesis suppresses the activity of antiviral NK cells. This process may be in charge of extending viral infection and preventing IL-10. The incidence of DHF/DSS development is determined by high viremia titers, which ADE brings in DENV infection. A normal lymphocyte count may result from this.[29,30]

The number of atypical lymphocytes (AL) is a research parameter obtained during a complete blood count. These AL have an increased percentage of nucleic acid and a characteristic scattering property that can detect an increased fluorescence signal. In dengue fever patients, an increase in lymphocytes with atypical features has been associated with secondary dengue infection, indicating the role of the immunological response and differences in cytokines produced during the first and subsequent exposure to the disease. This may be caused by an increased immune response due to secondary viral exposure. Antigen exposure causes a more severe form of clinical disease.[11] The substantial rise in anti-dengue immunoglobulin-G (IgG) antibodies following secondary dengue infection may be explained by the suspicion that these cells reflect an antibody immunological response to the dengue virus. Patients with dengue infection have been discovered to have atypical plasmacytoid lymphocytes, which are also associated with noticeably higher IgG levels.[31]

Distribution of the Neutrophil-to-Lymphocyte Ratio

The median NLR among patients in this study was 1.12, with values ranging from 0.28 to 13.00. These findings are consistent with the research by Osuna-Ramos et al,[27] which reported an NLR of 2.1 (IQR = 2.7) in patients with DHF. These results are also in accordance with the research of Katepui et al,[28] which showed that most DHF respondents had neutrophil counts less than 2,800 cells/μL and NLR less than 2.8. The ratio of absolute numbers of neutrophils and lymphocytes, known as the NLR, is used to predict inflammation. In the immune response that occurs in a person's body, neutrophils and lymphocytes, which make up 80% of all leukocyte cells, are the cells that respond to

infection and inflammation.[32] A straightforward metric for rapidly determining the level of inflammation is the NLR. Dengue fever is a systemic disease in which leukopenia and thrombocytopenia have been identified as common haematological disorders due to endothelial involvement that causes excessive plasma leakage due to an immunological response that can be seen from the NLR. The NLR ratio has been extensively studied in many infectious diseases, including dengue fever.[27] NLR was significantly lower in dengue fever patients compared with malaria patients due to an increased percentage and number of total lymphocytes, as well as an increased percentage and number of atypical lymphocytes.[28] Most of the body's immune response can be described by the proportion of these two cells. Viral infections can cause disturbances in the proportion of neutrophils and lymphocytes because they cause apoptosis in neutrophils, so that the NLR can be correlated with the severity of the disease, namely, the more severe the apoptosis process, the more severe the disease, which also affects the length of time the patient is hospitalized.[32]

Length of Hospitalization in Patients with Dengue Haemorrhagic Fever

The median length of hospital stay among respondents was 4 days, ranging from 2 to 8 days. The results of this study are in accordance with the research of Hussain et al,[21] which shows the average duration from disease onset to hospitalization is 4.2 ±2.1 days. These results are also in line with research by Thein et al,[26] which shows the median length of stay (LOS) in hospitals is 5 days (5th–95th = 3–8). DHF is a disease caused by infection with the DEN-1, 2, 3, or 4 viruses, which are transmitted through the bite of *Aedes albopictus* and *Aedes aegypti* that have previously been infected with the dengue virus by other dengue-infected individuals. The incubation period for dengue fever is when the dengue virus infects humans until it causes clinical symptoms, between 3 and 14 days, with an average of 4 and 7 days. The *Aedes aegypti* becomes infective 8–12 days after sucking on the blood of a previous dengue-infected individual. An infected individual will have symptoms in the form of a sudden high fever continuously for 2–7 days, which causes bleeding manifestations such as petechiae, purpura, ecchymosis, and epistaxis, liver enlargement, thrombocytopenia, haemoconcentration, with or without shock. DHF is currently a public health problem in Indonesia, which is known to increase in the number of patients, and its spread is becoming more widespread. Dengue extraordinary incidence (KLB) usually occurs in endemic areas and is related to the arrival of the rainy season, so it can result in increased dengue vector activity during the rainy season, which can cause the transmission of dengue disease to humans via the *Aedes* vector. Due to its morbidity and mortality, dengue fever is the most mosquito-transmitted disease.[33] Several factors can influence the occurrence of dengue fever. Factors influencing this are age, gender, platelets, and leukocytes, which can indirectly affect the length of treatment for dengue fever in hospitals.[34]

Correlation of Neutrophil-to-Lymphocyte Ratio and Length of Hospitalization

Several studies have attempted to predict the development of severe dengue infection during the acute febrile phase of the disease using various clinical and laboratory indicators. Most of these nations have employed laboratory measures as a preliminary indicator of dengue fever severity. It is well recognized that dengue fever is a non-inflammatory illness. Consequently, it is not anticipated that dengue fever will increase inflammatory indicators such as the NLR. Aside from that, one of the characteristics of the dengue virus is its capacity to inhibit bone marrow leukocyte generation, particularly neutrophil production, resulting in extreme neutropenia. The ANC has been employed in recent research to predict severe dengue illness. However, this study requires further validation in other regions and age groups.[34]

This study’s results show no significant correlation between the NLR value and the length of stay for paediatric patients with dengue haemorrhagic fever at Mohammad Hoesin Hospital, Palembang (p=0.068; r=0.224). The study's findings are consistent with those of Prayon et al,[32] who demonstrated elevated NLR during the dengue fever's feverish phase. The dengue virus is a public health issue affecting society and the economy. Along with the endemic region's expansion, the prevalence of dengue virus

infection rises annually. Tropical and subtropical regions are common places to get DHF, particularly in cities. Leukocytes' physiological immunological reaction to stress, including severe trauma, major surgery, tissue damage, and sepsis, is to produce more neutrophils and fewer lymphocytes. The neutrophil lymphocyte stress factor (NLSF), the ratio of the blood's neutrophil to lymphocyte proportion, can also indicate immune response stress. In patients with systemic inflammation, the neutrophil/lymphocyte ratio can be utilized as a clinical assessment since it will rise in cases of severe infection or systemic inflammation. Because of systemic inflammation or severe infection, a neutrophil/lymphocyte ratio of less than 5 under physiological settings (normally 75% neutrophils and lymphocytes >15%) might be greater than 6 in pathological situations.[26] Research by Yuditya[34] shows that the results aligned with this study, and the conclusion is that NLR and dengue fever severity did not significantly correlate (p=0.63). Things that can influence the results are the quality and type of equipment used, the examination skills of laboratory personnel, and taking blood samples on different fever days (2nd–7th fever days).[25] On the other hand, other factors can influence the length of stay for dengue haemorrhagic fever patients, namely age, clinical grade, comorbidities, and immune status. This allows for an insignificant correlation between the NLR variable and the length of stay in this study.

Strengths and Weaknesses of the Study

The strength of this study is that research related to the correlation between NLR and the length of hospitalization of dengue fever patients has never been conducted in the population of Mohammad Hoesin Hospital, Palembang. This study can serve as initial data for further research, particularly regarding predictive markers for the length of hospital stay in paediatric patients with DHF. A limitation of this study is the variation in the onset of fever, which may influence the pathogenesis of the disease and specific inflammatory markers.

Conclusion

The study found that most respondents were children aged 5–10 years, with an approximately equal distribution between male and female participants. Clinically, most patients were diagnosed with grade II DHF, and 44.8% presented to the emergency room after experiencing five days of fever. Regarding laboratory findings, the median ANC was 2,721.07 cells/mm³, while the mean lymphocyte count was 2,197.92 cells/mm³. The NLR had a mean value of 1.62. Regarding the clinical course, the average length of hospital stay was 3.57 days. No significant correlation was found between NLR and the length of hospital stay in paediatric DHF patients.

References

1. Salim MF, Syairaji M, Wahyuli KT, Muslim NNA. Pengembangan sistem informasi surveilans demam berdarah dengue berbasis mobile sebagai sistem peringatan dini outbreak di Kota Yogyakarta. J Kesehatan Vokasional. 2021;6:99. doi: 10.22146/jkesvo.61245
2. Roy SK, Bhattacharjee S. Dengue virus: epidemiology, biology, and disease aetiology. Can J Microbiol. 2021;67:687–702. doi: 10.1139/cjm-2020-0572
3. World Health Organization. Dengue and severe dengue [internet]. World Health Organization. 2022 [cited 2025 Jan 11]. Available from https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.
4. World Health Organization. Dengue and severe dengue. [internet]. World Health Organization. 2023 [cited 2025 Jan 11]. Available from https://www-who-int.translate.goog/news-room/fact-sheets/detail/dengue-and-severe-dengue?_x_tr_sl=en&_x_tr_tl=id&_x_tr_hl=id&_x_tr_pto=tc.
5. Kementerian Kesehatan Republik Indonesia. Tatalaksana infeksi dengue anak dan remaja. 2021.
6. Rizaty MA. Musim penghujan, terjadi 13.776 kasus DBD pada awal 2022 [internet]. Databoks. 2022 [cited 2025 Jan 11]. Available from https://databoks.katadata.co.id/datapublish/2022/03/01/musim-penghujan-terjadi-13776-kasus-dbd-pada-awal-2022.
7. Badan Pusat Statistik. Jumlah kasus penyakit menurut jenis penyakit (kasus) [internet]. Badan Pusat Statistik. 2023 [cited 2025 Jan 11]. Available from https://sumsel.bps.go.id/indicator/30/368/1/jumlah-kasus-10-penyakit-terbanyak.html
8. John DV, Lin YS, Perng GC. Biomarkers of severe dengue disease - a review. J Biomed Sci. 2015;22:1–13. doi: 10.1186/s12929-015-0191-6
9. Mulik V, Dad N, Buhmaid S. Dengue in pregnancy. Eur J Obstet Gynecol Reprod Biol. 2021;261:205–10. doi: 10.1016/j.ejogrb.2021.04.035
10. Hasan S, Jamdar S, Alalowi M, Al-Ageel, Al-Beaiji S. Dengue virus: a global human threat: review of literature. J Int Soc Prev Community Dent. 2016;6:1-6. doi: 10.4103/2231-0762.175416

11. Ummaimah EA, Syahrul Z. Hubungan rasio neutrofil-limfosit dengan skor sequential organ failure assessment pada pasien sepsis di intensive care unit RSUP Dr. M. Djamil Padang. J Kesehatan Andalas. 2020;9:1–6. doi: 10.25077/jka.v9i1S.1150
12. Halstead S, D V. Dengue shock syndrome - an overview [internet]. ScienceDirect Topics. 2023 [cited 2025 Jan 11]. Available from https://www.sciencedirect.com/topics/medicine-and-dentistry/dengue-shock-syndrome.
13. Prijanto SA, Wayan I, Suryawan B, Kadek I. Rasio neutrofil-limfosit sebagai prediktor kejadian syok pada demam berdarah dengue pada anak di Rumah Sakit Umum Daerah Wangaya, Denpasar. Sari Pediatri. 2023;24:19–25. doi: 10.14238/sp24.5.2023.307-13
14. Nisa K. Karakteristik infeksi dengue dengan kebocoran plasma [thesis]. 2018. Unpublished thesis.
15. Parveen S, Riaz Z, Saeed S, Ishaque U, Sultana M, Faiz Z, et al. Dengue hemorrhagic fever: a growing global menace. Journal of water and health. 2023;21(11):1632-50. doi: 0.2166/wh.2023.114
16. Wang WH, Urbina AN, Chang MR, Assavalapsakul W, Lu PL, Chen YH, et al. Dengue hemorrhagic fever–A systemic literature review of current perspectives on pathogenesis, prevention and control. Journal of Microbiology, Immunology and Infection. 2020;53(6):963-78. doi: 10.1016/j.jmii.2020.03.007
17. Widoyono A. Penyakit tropis: epidemiologi, penularan, pencegahan dan pemberantasannya. Jakarta: Erlangga; 2008.
18. Martina BEE, Koraka P, Osterhaus ADME. Dengue virus pathogenesis: an integrated view. Clin Microbiol Rev. 2009;22:564–81. doi: 10.1128/CMR.00035-09
19. Yasmina D. Hubungan neutrofil limfosit rasio dengan length of hospitalization pada pasien sepsis akibat pneumonia [thesis]. 2022. Unpublished thesis.
20. Wulandari TG. Hubungan antara rasio jumlah neutrofil limfosit dengan length of hospitalization pada pasien stroke iskemik di RSUD Dr. H. Abdul Moeloek Provinsi Lampung. Lampung: Fakultas Kedokteran UNILA; 2020.
21. Hussain W, Shaikh M, Hanif M, Ashfaq M, Ahmed H, Nisa BU. Pattern and outcome of dengue fever in a pediatric tertiary hospital: a retrospective report. Cureus. 2021;13:e14110. doi: 10.7759/cureus.14164
22. Sasmono RT, Santoso MS, Pamai YWB, Yohan B, Afida AM, Denis D, et al. Distinct dengue disease epidemiology, clinical, and diagnosis features in Indonesia's western, central, and eastern regions, 2017–2019. Front Med. 2020;7:582235. doi: 10.3389/fmed.2020.582235
23. Made SUI, Lukman N, Sukmawati DD, Alisjahbana B, Alam A, Murniati D, et al. Dengue viral infection in Indonesia: epidemiology, diagnostic challenges, and mutations from an observational cohort study. PLoS Negl Trop Dis. 2019;13:e0007785. doi: 10.1371/journal.pntd.0007785
24. Lim JK, Chanthavanich P, Limkittikul K, Lee J, Sirivichayakul C, Lee KS, et al. Clinical and epidemiologic characteristics associated with dengue fever in 2011–2016 in Bang Phae district, Ratchaburi province, Thailand. PLoS Negl Trop Dis. 2021;15:e0009513. doi: 10.1371/journal.pntd.0009513.
25. Sinha B, Goyal N, Kumar M, Choudhary A, Arya A, Revi A, et al. Incidence of lab-confirmed dengue fever in a pediatric cohort in Delhi, India. PLoS Negl Trop Dis. 2022;16:e0010333. doi: 10.1371/journal.pntd.0010333
26. Thein TL, Lye DC, Leo YS, Wong JGX, Hao Y, Wilder-Smith A, et al. Severe neutropenia in dengue patients: prevalence and significance. Am J Trop Med Hyg. 2014;90:984–7. doi: 10.4269/ajtmh.14-0004
27. Osuna-Ramos JF, Reyes-Ruiz JM, Ochoa-Ramírez LA, Jesús-González LAD, Ramos-Payán R, Farfan-Morales CN, et al. The usefulness of peripheral blood cell counts to distinguish COVID-19 from dengue during acute infection. Trop Med Infect Dis. 2022;7:20. doi: 10.3390/tropicalmed7020020
28. Kotepui M, PhunPhuech B, Phiwklam N, Uthaisar K. Differentiating between dengue fever and malaria using hematological parameters in endemic areas of Thailand. Infect Dis Poverty. 2017;6:27. doi: 10.1186/s40249-017-0238-x
29. Yuntoharjo PJ, Arkhaesi N, Hardian H. Perbandingan antara nilai rasio neutrofil limfosit (NLCR) pada anak dengan demam dengue dan demam berdarah dengue. Hardian JKD. 2018;7:801–12. doi: 10.14710/dmj.v7i2.20741
30. Suriantina NG. Aplikasi survival lama perawatan pasien demam berdarah dengue di Rumah Sakit Permata Bunda Malang. J Ilm Kesehatan Media Husada. 2022;5:179-90. doi: 10.33475/jikmh.v5i2.177
31. Suryandari AE, Anasari T. Faktor-faktor yang mempengaruhi lama perawatan pasien demam berdarah dengue. Bina Cipta Husada Purwokerto. 2022;13.
32. Prayon KM, Oncog AS. Absolute neutrophil counts and neutrophil to lymphocyte ratio as early predictive markers of dengue severity among children admitted in Governor Celestino Gallares Memorial Hospital: a 5-year retrospective study. Acta Scientific Paediatrics. 2022;5:37-45. doi: 10.31080/ASPE.2022.05.0537
33. Irmayanti I, Nurulita A, Sennang N. Neutrophil/lymphocyte count ratio on dengue hemorrhagic fever. Indones J Clin Pathol Med Lab. 2017;23:234–9. doi: 10.24293/ijcpml.v23i3.1200
34. Yuditya DC, Sudirgo I. The relation between neutrophil lymphocyte count ratio (NLCR) and dengue infection grade of severity in adult patients in RS Muhammadiyah Ahmad Dahlan Kediri in January 2019. STRADA J Ilm Kesehatan. 2020;9:20–5. doi: 10.30994/sjik.v9i1.265