

CORRELATION OF NEUTROPHIL LYMPHOCYTE RATIO (NLR) AND PLATELET LYMPHOCYTE RATIO (PLR) IN CHILDREN WITH DENGUE HEMORRHAGIC FEVER (DHF) INFECTION IN NORTHERN KALIMANTAN

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ABSTRACT

Background: Dengue fever is a viral infection transmitted to humans through the bite of an infected mosquito. This inflammation causes active immune cells such as neutrophils, lymphocytes, and platelets. When inflammation occurs, there will be a physiological response in the form of a decrease in the number of lymphocytes and an increase in the number of neutrophils. The ratio of neutrophils and lymphocytes is also called the Neutrophil Lymphocyte Ratio (NLR). This infection also causes a decrease in platelets and lymphocytes simultaneously. This can be worsening the patient's condition. The ratio of platelets and lymphocytes is also called Platelet lymphocyte ratio (PLR). NLR and PLR are important biomarkers of inflammation in supporting the diagnosis of DHF, allowing clinicians to immediately treat DHF cases, especially in children.

Method: This study used a retrospective observational study design with a cross sectional approach. The sampling technique used in this study was total sampling. The data collection technique in this study was observation of medical record data of DHF pediatric patients. To analyze the correlation between NLR and PLR in children with DHF infection, a correlation statistical test was used

Result: The results showed that the average value of NLR is 1,187 and PLR is 1536,74. And the results of this study also show a significant correlation between NLR and PLR with the correlation coefficient showing a strong positive correlation ($r > 0.70$, $p\text{-value} < 0.001$).

Conclusion: There is a significant correlation between NLR and PLR in children with dengue infection.

Keywords: DHF, NLR, PLR

INTRODUCTION

Dengue fever (DHF) is a viral infection transmitted to humans through the bite of an infected mosquito. Dengue is widely found in tropical and subtropical climates around the world, mostly in urban and semi-urban areas. DHF can affect anyone including children. Children are at risk of DHF especially those under 15 years old because children often spend time at home playing, resting and living in a humid and unsanitary environment (Irma, 2023; Kemenkes RI, 2017; Sandra, dkk. 2019; WHO, 2023).

Dengue infection is often asymptomatic or only causes mild symptoms but the virus sometimes triggers more severe cases and even cause death. Dengue virus infection

causes the release of inflammatory mediators such as cytokines (e.g., $\text{TNF-}\alpha$, interleukin-6) and vasoactive factors. These pro-inflammatory cytokines could cause damage to capillary endothelial cells, resulting in increased vascular permeability. The increased of capillary permeability and in severe cases increased fluid and protein loss could trigger dengue shock syndrome (SSD), where blood flow decreases drastically resulting in significantly reduced blood volume, threatening oxygen supply to body tissues. When the immune response out of control, it leads to capillary leak syndrome and complications such as shock (Bhatt P Dkk, 2021; Cristina M, Padovani and Kingsley Yin.2024; Pongpayung, 2024; Solórzano Victor Edgar Fiestas, dkk,2021).

When dengue virus infects, there is a rapid activation of the innate and adaptive immune system. Immune cells such as macrophages will identify the virus and trigger the release of various signaling molecules such as cytokines and chemokines. In severe dengue infection, excessive release of cytokines, 'known as "cytokine storm", can occur. This cytokine storm causes strong inflammation, and triggers blood vessel damage, increasing vascular permeability and causing plasma leakage (Marvianto, dkk., 2023; Navya PT, dkk.,2024).

This inflammation causes the activation of immune cells such as neutrophils, lymphocytes and platelets. Neutrophils play an important role in the initial response of identifying and eliminating pathogens. Lymphocytes function in modulating specific immune responses and increasing antibody production. During inflammation platelets will secrete substances that can attract neutrophils and lymphocytes to the site of inflammation. There fore causing interactions in the healing process and infection control (Navya PT, dkk.,2024; Tulk, S. E., & Conroy, A. L, 2019).

When inflammation occurs, there will be a physiological response in the form of a decrease in the number of lymphocytes and an increase in the number of neutrophils due to an imbalance in the inflammatory response. The ratio of neutrophils and lymphocytes is also called the Neutrophil Lymphocyte Ratio (NLR). This infection also causing a decrease in platelets and lymphocytes simultaneously. This could be worsen the patient's condition. The platelet and lymphocyte ratio is also called Platelet lymphocyte ratio (PLR) (Navya PT, dkk.,2024).

NLR and PLR are biomarkers of inflammation and prognostic markers in various diseases. In dengue, inflammation is caused by an excessive immune system response, where NLR has a role in identifying non-severe dengue cases. Whereas PLR

shows effective accuracy in identifying severe cases. NLR is an active inflammatory component as well as lymphocytes as a regulatory and protective component (Solórzano Victor Edgar Fiestas, dkk, 2021).

NLR and PLR are important biomarkers of inflammation in supporting the diagnostic of dengue disease, are allowing the clinicians to immediately treat DHF cases, especially in children. To determine the number of NLR and PLR in the blood, routine hematology laboratory tests can be done (Hoffbrand, A dkk, 2016; Rodak, B. F, dkk. 2016; Navya PT, dkk.,2024).

The results of research by PT Navya et al in 2024 showed that the NLR and PLR can be used as biomarkers of inflammation and prognostic markers in various diseases. In dengue fever, inflammation occurs due to excessive immune system response, where NLR has a role in identifying cases of dengue fever that are not severe. While PLR shows effective accuracy in identifying severe cases. While research by Aisya Nailatul Ashma, et al in 2023 showed there was a significant positive correlation between NLR and hemocontrast in Dengue infection.

METHODS

This study used a retrospective observational study design with a cross sectional approach. The sampling technique used in this study was total sampling, where all respondents who met the inclusion and exclusion criteria. Inclusion criteria were pediatric patients aged 3 months - 14 years who had been diagnosed with DHF with NS1 (+) laboratory examination results, had complete examination data which included the number of neutrophils, lymphocytes, and platelets needed to calculate the NLR and PLR values. Exclusion criteria were no history of comorbid diseases, incomplete laboratory data, pediatric patients with DHF and positive tubex, and negative NS1 and laboratory results

with children who received immunosuppressant or corticosteroid therapy within 30 days before the study.

The data collection technique in this study was observation of medical record data of DHF pediatric patients. The data generated in this study were secondary data in the form of respondent characteristics data, NLR and PLR data. To analyze the correlation between NLR and PLR in children with DHF infection, the correlation statistical test was used. The results of the analysis will be presented in tables or graphs.

RESULTS AND DISCUSSION

The characteristics of respondents at the Nunukan Regency General Hospital, Tarakan City General Hospital, and Dr.H. Soemarno Sosroatmodjo Tanjung Selor Hospital were analyzed based on gender, age, Tourniquet test, and the presence of spontaneous bleeding. For age characteristics based on the data obtained, it is divided into 3 age groups of children, namely infants and toddlers <5 years, children 5-9 years and teenage 10-18 years.

An overview of the characteristics of respondents can be seen in the table below:

Table 1. Characteristics of respondents

Characteristics	Frequency	Percentage (%)
Gender		
Male	25	43,9%
Female	32	56,1%
Age		
Infants and Toddlers (< 5 years)	8	14%
Children (5-9 Years)	29	50,9%
Teenagers (10-18 Years)	20	35,1%
Tourniquet Test		
Positive	100	100%
Spontaneous Bleeding		
Negative	45	78,9%
Positive	12	21,1%

The table above is showing the characteristics of respondents based on gender show that more women (56.1%) suffered from DHF than men (43.9%). In this study, the age characteristics were dominated by children

(50.9%). The table above also shows that all respondents in pediatric DHF patients had positive tourniquet test results indicating fragile blood vessel wall permeability (the presence of petechiae or small red spots on the skin in the area where tourniquet pressure is applied, usually in the amount of more than 10 petechiae per square inch. These petechiae indicate capillary fragility and increased vascular wall permeability). As for the characteristic of spontaneous bleeding, only 21.1% of respondents showed positive results, which means that most respondents did not experience spontaneous bleeding despite indications of capillary fragility.

3.1. Overview of NLR and PLR in children with dengue infection

Table 1. Overview of NLR and PLR in children with dengue infection

Variable	n	Mean	Min	Max	Std. Deviation
NLR	57	1,187	0,08	8,51	1,388
PLR	57	1536,74	150,00	9367,09	1381,272

Based on the table above, it can be seen that the average value of NLR is 1,187 and the average PLR is 1536,74.

3.2 Correlation between NLR and PLR in children with dengue infection

Table 2. Correlation of NLR and PLR in children with dengue infection

Variable	n	Coefficient of correlation	P value
NLR	57	0,741	< 0,001
PLR	57		

The results showed a significant correlation between NLR and PLR with the correlation coefficient (r) showing a strong positive correlation ($r > 0.70$, $p\text{-value} < 0.001$). The $p\text{-value} < 0.001$ indicates that the correlation between NLR and PLR is highly statistically significant, meaning that it is almost certain that the correlation does not occur by chance. The correlation between NLR and PLR in children with DHF infection is very important in the severity of dengue virus infection and its impact on the immune system.

DHF infection affects the number of blood cells in the body, including neutrophils, lymphocytes and platelets. These changes consistently affect the NLR and PLR values. This study is in line with research conducted by PT Navya et al, (2024). In a study conducted by PT Navya, et al on 99 DHF patients who were treated, had similarities in the average results with a range of minimum to maximum values. So the conclusion is that an increase in NLR followed by an increase in PLR indicates a significant inflammatory response in pediatric patients with dengue infection, where an increase in neutrophils and a decrease in lymphocytes and platelets contribute to changes in the value of these two parameters. Thus, NLR and PLR could be potential indicators in assessing the severity of inflammation in children with dengue infection.

This study found a close correlation between NLR and PLR values in children with DHF infection. This correlation can be explained by the pathophysiological mechanism of DHF which is characterized by tourniquet test (+) and spontaneous bleeding in children with DHF, immune dysregulation and significant changes in hematological parameters during the disease phase. NLR is an inflammatory parameter that reflects the balance between innate (neutrophils) and adaptive (lymphocytes) immune responses. Elevated NLR in children with DHF indicates a significant systemic inflammatory response due to dengue virus infection.

Meanwhile, high NLR reflects the interaction between thrombocytopenia and lymphocytosis, which is often found in DHF patients due to increased platelet destruction and release of proinflammatory cytokines. This study shows that the increase in NLR is directly proportional to the severity of dengue infection, where high NLR values are often found in patients with higher severity, such as dengue with dengue shock syndrome (DSS). Similarly, a significant increase in PLR reflects disturbances in hemostasis and immune

hyperactivity that may contribute to the worsening of the patient's condition.

These two ratios are important indicators in monitoring the severity of dengue infection in children (Solorzano Victor Edgar Fiestas, 2021). So monitoring NLR and PLR can help in assessing the progressivity of DHF in children, especially in predicting the risk of worsening conditions and simple biomarkers in decision making related to patient management.

CONCLUSION

Based on the results of study conducted at the Nunukan Regency General Hospital, Tarakan City General Hospital, and Dr. H. Soemarno Sosroatmodjo Tanjung Selor Hospital, regarding the correlation between NLR and PLR in children with DHF infection, it can be concluded that the average NLR in children with DHF infection is 1.187 and the average PLR in children with DHF infection is 1536.74. There is a significant correlation between NLR and PLR in children with dengue infection with $r > 0.70$ and $p\text{-value} < 0.001$.

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CONFLICT OF INTEREST

The author declares there is no conflict of interest

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