International Summit on Science Technology and Humanity
ISETH 2024
ISSN: 2615-1588 (online)

Correlation of Eosinophil-basophil Count and Ratio with Length of Stay in Children Dengue Infection

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Abstract

Purpose: *This study purpose is to determine the correlation between the number of absolute eosinophils, absolute basophils, and eosinophil-basophil ratio (EBR) with the length of stay of pediatric patients with dengue virus infection.*
Methodology: *The study design used cross-sectional. The samples used in this study were taken from routine hematologic laboratory medical record data for the period January-October 2024, using consecutive non-probability sampling technique.*
Results: *49 samples were obtained and met the restriction criteria as subjects of this study. The results of the Spearman correlation bivariate test showed that the number of absolute eosinophil count, absolute basophil count, and EBR with length of stay had statistical data results respectively p = 0.139, p = 0.993, and p = 0.536.*
Applications/Originality/Value: *This study provides a reference in laboratory results to determine the length of stay (LOS) in children with dengue virus infection.*

Introduction

Dengue virus infection is an arthropod-borne disease that often attacks humans in tropical and subtropical areas (Kotepui et al., 2017). This infection is caused by DENV (dengue virus) (Shahid Ansari et al., 2021). According to WHO (2022) (World Health Organizations), the incidence of dengue virus infection is estimated to occur as many as 390 million cases each year. From 2015 to 2019, the number of dengue virus infections in Southeast Asia continued to increase (Sutriyawan et al., 2022). In 2022, Indonesia recorded 143,000 cases with the 5-14 age group as the most affected (Kemenkes, 2022).

Common clinical symptoms in patients with dengue virus infection include fever, headache, rash, thrombocytopenia, and leukopenia. Certain conditions such as thrombocytopenia (platelets <100,000/mm3), bleeding manifestations (petechiae, ecchymosis, purpura), to plasma leakage (hematocrit > 20% normal) require hospitalization (Nugraheni et al., 2023). Management of pediatric patients with dengue virus infection requires careful clinical assessment to determine the severity of the disease and predict the length of stay (Nayar et al., 2019). Factors such as initial clinical conditions, response to therapy, and complications affect the length of stay. Predicting the length of stay can help plan medical resources (Maesarah et al., 2023).

The main laboratory parameters for the management of dengue virus infection are hemoglobin, hematocrit, and platelets (Nugraheni et al., 2023). Research by Macchia et al. (2023) stated a relationship between the number of eosinophils and viral infections in the respiratory system, for example SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2). Eosinophils modulate the immune response to viruses through their role as APCs (antigen presenting cells) and through Th2 inflammation (Constantine & Klion, 2022; Gaur et al., 2022). However, the clinical significance of eosinophil antiviral responses in the respiratory system remains unclear because most studies have been conducted in vitro (Rupani et al., 2024). In dengue virus infection, eosinophils decrease in the acute phase and then increase in the convalescent phase (Maesarah et al., 2023). Shirley & Brindha (2023) stated that an increase in the number of eosinophils can be a marker of recovery from dengue virus infection. This requires further study because the number of eosinophils can be a parameter for predicting the length of stay of patients.

Basophils are known to help reduce the risk of severe COVID-19 (coronavirus disease) (Murdaca et al., 2021). In dengue virus infection, the number of basophils indicates recovery from spinal cord suppression during the convalescent phase (Nayar et al., 2019). The usefulness of basophils is still debated although it is known that basophils can be a parameter of recovery from dengue virus infection (Joshi et al., 2018). The interaction between basophils and endothelial cells can increase the accumulation of eosinophils, which can worsen inflammation and affect the length of stay (Cheng et al., 2015). The eosinophil-basophil ratio (EBR) measures the relationship between the number of eosinophils and basophils in the

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blood circulation. EBR describes immunological balance and has the potential as a prognostic marker (Joshi et al., 2018; Nayar et al., 2019). Research on the correlation of EBR with the length of stay in pediatric patients with dengue virus infection has not been further studied.

Based on the above explanation, it is necessary to conduct a study to determine the correlation between the number of absolute eosinophils, absolute basophils, and eosinophil-basophil ratio (EBR) with the length of stay of pediatric patients with dengue virus infection. The researcher hopes that the results of the study can add to the list of literature related to similar sciences and can expand the reference material for further research.

Method

The study was conducted in analytical observational study. The study design used was cross-sectional, conducted at PKU Muhammadiyah Sampangan Surakarta Hospital in November 2024. The data used in this study were secondary data from patient medical records. The samples used in this study were taken from routine hematologic laboratory medical record data for the period between January and October 2024, using consecutive non-probability sampling technique.

Absolute eosinophil count in this study means the absolute number of reddish-orange granular cells in human blood circulation, the data of which was taken using laboratory results when the patient entered the emergency room. Absolute basophil count means the absolute number of polymorphonuclear leukocytes in the blood circulation, cells that are characterized by dark blue granules covering their nuclei, which are obtained using laboratory results when the patient is admitted to the emergency room. EBR means a ratio that measures the ratio between the number of eosinophils and basophils in the bloodstream, data is taken using laboratory results when the patient is admitted to the emergency room. Length of stay (LOS) means the duration of one period of hospitalization for a child patient with dengue virus infection starts from the day of admission to the hospital until the patient is allowed to be treated at home. It can be calculated by finding the difference between the date of discharge from hospital and the date of admission of hospitalization.

Univariate analysis in this study was conducted to describe the distribution of samples based on the absolute number of eosinophils, the distribution of samples based on the absolute number of basophils, the distribution of samples based on the eosinophil-basophil ratio, and the distribution of samples based on the length of stay using the Shapiro-Wilk test because the sample size needed were under fifty. Bivariate analysis used the Spearman correlation test, because it is known that the data distribution is not normal according to the Shapiro-Wilk test. If the Spearman test obtains a p value <0.05, then there is a significant relationship between the variables studied in this study.

Results

This research was conducted at PKU Muhammadiyah Sampangan Surakarta. Research sampling was conducted using consecutive non-probability sampling techniques on cases of dengue virus infection that occurred between January and October 2024. There were 49 medical records obtained that could be used as subjects of this research.

Research Samples Distribution

The distribution of research samples in this study are shown in Table 1 below.

Table 1. Characteristics of Research Samples

Variable	Frequency (%)	Med (Min–Max)
Age (years)		10 (1-14)
0-5	8 (16.3)	
6-10	22 (44.9)	
11-14	19 (36.7)	
Total	49 (100)	
Sex		-
Male	20 (40.8)	
Female	29 (59.2)	
Total	49 (100)	
Leukosit (/mm^3)	-	2770 (185-9120)
Absolute eosinophil count (/mm^3)	-	2,66 (0–96.30)
Absolute basophil count (/mm^3)	-	0 (0–277)
Eosinophil-Basophil Ratio	-	0 (0–0,07)
Length of stay (days)	-	3 (2–6)

Based on table 1, the characteristic data showed a total of 49 subjects (100%). Based on age characteristics, the age of subjects diagnosed with dengue virus infection was mostly 6-10 years old with a frequency of 22 (44.9%). Characteristics based on gender, the most subjetcs were found to be female 29 (59.2%).

Based on the characteristic data, the median leukocyte data was 2770 with a minimum value of 185 and a mazimum of 9120. The median absolute eosinophil count was 2,66 with a minimum value of 0 and a maximum of 96.30. The median absolute basophil count was 0 with a minimum value of 0 and a maximum of 0.07. Based on the characteristics of length of stay, the median was 3 with a minimum value of 2 and a maximum of 6.

Correlation Between Research Variables

Correlation between two variables in this study was analyzed through bivariate analysis with Spearman test, the results of the analysis are in Table 2 below.

Table 2. Hypothesis Analysis of Absolute Eosinophil Count, Basophil Count, and Eosionophil-Basophil Ratio with Length of Stay

Variable	Length of stay	
	r	p
Absolute eosinophil count	-0,214	0,139
Absolute basophil count	-0,001	0,993
Eosinophil-basophil ratio	-0,091	0,536

Note: r: correlation coefficient; p: probability of obtaining result, p<0,05 is significant

The results of the Spearman correlation bivariate test showed that the absolute eosinophil count and length of stay had statistical data results of p = 0,139 and r = -0,214. The correlation coefficient (r-value) shows a weak negative relationship between the two variables. However, because p > 0,05, the relationship between the two variables is declared insignificant. The results of the Spearman correlation bivariate test showed that the absolute basophil count and length of stay had statistical data results of p = 0,993 and r= -0,001. The correlation coefficient (r-value) shows a weak negative relationship between variables. However, because p > 0,05, the relationship between the two variables is declared insignificant. The results of the Spearman correlation bivariate test showed that EBR and length of stay had statistical data results of p = 0,536 and r = -0,0091. The correlation coefficient (r-value) shows a weak negative relationship between variables. However, because p > 0,05, the relationship between the two variables is declared insignificant.

Discussion

Based on the characteristic distribution data, it was found that the age group most likely to experience dengue virus infection was 6-10 years. This is in line with research by (Mishra et al., 2021). This is because children often play in open areas with puddles of water that provide vectors and facilitate exposure to dengue virus infection. In the rainy season, puddles of water will increase and create ideal conditions for mosquitoes as vectors to breed. The presence of puddles or unmaintained water reservoirs increases the risk of dengue virus infection. Children have an immune system that is not fully mature compared to adults, so they are more susceptible to viral infections. The child's less effective immune system results in minimal formation of specific antibodies against DENV so that cytokine secretion by macrophages is less effective and results in suboptimal inhibition of DENV replication (Arfan et al., 2024).

Characteristic distribution data shows that there are more females than males. This is in accordance with research by Putra et al in 2020 which conducted research in Bali. This is due to hormonal effects. Estrogen levels in women can affect the production of leptin, which plays a role in regulating the body's immunity. This can make women more susceptible to dengue virus infection if estrogen levels are low (Novitasari et al., 2015). In addition, women theoretically tend to have a stronger immune response than men. This is stated to be related to the high frequency of CD4 + T-cells and the effect of producing large amounts of antibodies. However, this immune response can be reversed if the antibodies produced are not effective in neutralizing DENV (Mauvais-Jarvis et al., 2020).

Correlation Between Absolute Eosinophil Count with Length of Stay

From the results of the bivariate test, it was found that the absolute eosinophil count was negatively related and did not correlate significantly with the length of stay. This is indicated by a p value = 0,139 and a correlation coefficient value of r = -0,214, which means the correlation strength is weak. Because p> 0,05, it can be concluded that the absolute eosinophil count is not strong enough to be used as a parameter or predictive factor for the length of stay of patients. This is in line with research by Nayar et al. (2019), that the study conducted did not find any statistical significance in predicting the

severity and length of stay for dengue virus infection. This is because eosinopenia that occurs in the acute phase of the disease and an increase to normal levels can be confused by the possibility of other conditions. In some cases, the number of eosinophils can increase more than in the infected body condition. In a study comparing dengue virus and malaria infections, it was found that a low eosinophil count is a characteristic of dengue infection (Kotepui et al., 2017).

The percentage of eosinophil count may increase in the convalescent phase along with other hematological parameters in predicting recovery. However, this theory is not strong enough to support the number of eosinophils as a marker of recovery (Chaloemwong et al., 2018; Sihombing et al., 2023). Infections or other conditions may show different eosinophil responses, so it is concluded that the number of eosinophils does not play a direct role in the pathogenesis of dengue virus infection (Musaddad et al., 2023). The main pathogenesis of dengue virus infection is more influenced by complex inflammatory mechanisms involving cytokines and other immune cells, such as neutrophils, monocytes, and lymphocytes (Cherie et al., 2024; Mallhi et al., 2017). In addition, a decrease in the number of eosinophils or eosinopenia is a systemic effect due to suppression of production due to the dominance of IFN-γ cytokines as an acute phase response to viral infection (Cherie et al., 2024).

Correlation Between Absolute Basophil Count with Length of Stay

The absolute basophil count was stated to be negatively related and not significantly correlated with the length of stay. This is indicated by the p value = 0,993 and the correlation coefficient value of r = -0,001, which means that the higher the basophil count, the longer the hospitalization tends to decrease. However, because p> 0,05, the relationship between the two is not strong enough to be considered statistically relevant. It can be concluded that the absolute basophil count is less relevant if used as a parameter or predictive factor for the length of stay of patients. This is in accordance with the research of Chaloemwong et al. (2018) which retrospectively examined the role of hematological parameters in the diagnosis of dengue infection, stated that the percentage of basophils did not change significantly in patients with dengue virus infection studied. This may be due to the effect of recovery from spinal cord suppression during infection. Spinal cord suppression occurs for a range of 3-4 days of infection, then the body's immune response works to eliminate infected cells. The decrease in basophils is likely a protective mechanism to limit the severity of injury to marrow stem cells during the process of eradicating infected cells. In addition, during the eradication process, DENV-infected cells do not interact with basophils. Research by Susanti et al. (2022) found that although there were fluctuations in the number of basophils in dengue infection patients, these changes do not correlate with clinical severity or length of stay. Therefore, the absolute number of basophils is not one of the main factors for predicting the length of stay of patients.

Other studies have shown that the absolute basophil count has not been established as a reliable indicator to predict the severity of the disease or the length of stay of patients with dengue virus infection (Shahid Ansari et al. (2021). In theory, basophils play a role in allergic responses and immune function, but the mechanism is still unclear. The immune response to dengue virus infection is complex and involves various types of cells, but basophils do not play a central role in the pathogenesis or clinical outcomes of dengue virus infection (Chaloemwong et al., 2018; King et al., 2020). Research conducted by Efiariza et al. (2024) showed that an increase in the number of atypical lymphocytes was more frequently observed in cases of severe dengue infection than in mild cases, confirming that lymphocytes atypical play a greater role than basophils in determining the clinical outcome of dengue infection.

Correlation Between Eosinophil-Basophil Ratio with Length of Stay

The eosinophil-basophil ratio (EBR) showed a negative relationship with the length of stay. This is indicated by a p value of 0,536 and a correlation coefficient value of r = -0,091, which means that the higher the number of basophils, the longer the length of stay tends to decrease. However, because p> 0,05, the relationship between the two is not strong enough to be considered statistically relevant. In theory, the higher the EBR, the shorter the length of stay. However, because the p value was 0,536 (p>0,05), the relationship between EBR and length of stay was declared not statistically significantly correlated. Thus, it can be concluded that EBR is less relevant when used as a parameter or prediction of patient length of stay. Research that discusses the effect of EBR on length of stay significantly has not been clearly found, although in theory EBR reflects the dynamics of the immune response during infection. During dengue virus infection, eosinopenia will tend to occur and will return to normal towards the convalescent phase (Kotepui et al., 2017). A study stated that patients with dengue virus infection studied had normal basophil levels, indicating that basophil levels did not fluctuate significantly with clinical outcomes such as length of stay (Sihombing et al., 2023). In addition, it was stated in a study by (Chaloemwong et al., 2018) that changes in eosinophil and basophil levels were due to suppression of the spinal cord which was then followed by a mechanism for eradicating cells infected with DENV. However, it is said that DENV-infected endothelial cells do not interact with eosinophils or basophils. Thus, there is no strong and relevant evidence to support the correlation

between EBR and length of stay in dengue virus infection. Further research is needed to examine the role of EBR as a clinical predictor and length of stay in patients with dengue virus infection.

In this study, there was no significant relationship between each variable and length of stay. The limitation of this study is the relatively minimum number of samples for certain reasons. In addition, the tendency of limited references regarding EBR as one variable makes this study only able to rely on sources related to eosinophils and basophils separately. Other reference sources may be needed as a comparison of the results studied.

Conclusions

Based on the cross-sectional study that has been conducted, it can be concluded that statistically there is an insignificant correlation between the absolute eosinophil count and the length of stay of pediatric patients with dengue virus infection with p = 0,139 (p>0,05). Statistical results between the absolute basophil count also showed an insignificant relationship with p = 0,993 (p>0,05). An insignificant relationship was also found between the eosinophil-basophil ratio (EBR) and the length of stay of pediatric patients with dengue virus infection with p = 0,536 (p>0,05). Thus, the third variable can be stated as less relevant as a parameter for predicting the length of stay of pediatric patients with dengue virus infection. Further research needs to be conducted based on other risk factors and using the limitations of this study as learning and evaluation.

Acknowledgement

The author wishes to express gratitude to Faculty of Medicine of Universitas Muhammadiyah Surakarta, PKU Muhammadiyah Sampangan Surakarta, and to all parties who have played a role and supported the completion of the writing of this study.

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