

## Blood Parameters and Length of Hospitalization in Pediatric Dengue Virus Infection Patients

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### Abstract

This research aims to evaluate the correlation between erythrocyte level, hematocrit, hemoglobin, and Hb/RDW ratio with the length of hospitalization in pediatric patients with DVI. This observational study used a cross-sectional design and analyzed secondary data from 41 pediatric DVI patients at PKU Muhammadiyah Sampangan Surakarta Hospital. The correlation between hematological parameters and length of hospitalization was analyzed using the Spearman test. Laboratory results showed a mean erythrocyte count of 5.05 million cells/nL (SD 0.61), a median hematocrit of 39.5%, hemoglobin of 13.6 g/dL, and Hb/RDW ratio of 1.03. Bivariate correlation test showed erythrocyte level ( $r = 0.027$ ,  $p = 0.867$ ), hematocrit ( $r = -0.004$ ,  $p = 0.983$ ), hemoglobin ( $r = 0.079$ ,  $p = 0.625$ ), and Hb/RDW ratio ( $r = 0.116$ ,  $p = 0.472$ ) showed no significant association with length of hospitalization. This study provides insights into the relationship between hematological parameters and the length of hospital stay in pediatric dengue patients. While no significant correlation was found, it highlights the complexity of factors influencing outcomes and the need to explore other prognostic markers. Conducted in an Indonesian endemic region, the research contributes to understanding DVI management and underscores the importance of a comprehensive, multifactorial approach to improving patient care strategies.

Keywords: Erythrocytes, Hematocrit, Hemoglobin, Hb/RDW Ratio, Length of Hospitalization for Dengue Virus Infection

### Introduction

Dengue virus infection (DVI) is a viral infection transmitted through the bite of the *Aedes aegypti* mosquito (World Health Organization, 2023). The World Health Organization (WHO) reported that there were 5,2 million cases of dengue infection worldwide in 2019, and the Southeast Asia region had the highest number of cases, which amounted to 658.301 cases (World Health Organization, 2020). Dengue virus infection in Indonesia continues to increase, reaching 143.000 cases by the end of 2022. The highest number of cases occurred in the provinces of West Java, East Java, and Central Java (Kemenkes RI, 2023). The mortality rate in Central Java in 2021 was 2.7%, an increase from 2020 which was 1.9%. Deaths due to dengue occurred in 25 regencies/cities in Central Java with the highest number in Surakarta City (Dinas Kesehatan Provinsi Jawa Tengah, 2021). Surakarta City is classified as a dengue-endemic area, with 166 cases reported in 2022, an increase from 41 cases in 2021 (Dinkes Kota Surakarta, 2022).

An estimated 500.000 of the 50 million DVI patients require hospitalization each year and nearly 90% of them are children (Cahyani et al., 2020). The prevalence of DVI is higher in children because their immune system is not fully developed, making them more susceptible to viral infections (Fadilla et al., 2020). Children are at a higher risk of contracting dengue infection because they tend to spend more time engaging in outdoor activities (Hernawan and Afrizal, 2020). The length of hospitalization for DVI patients typically ranges from 2-7 days, unless the patient experiences shock, the length of hospitalization becomes longer (Syahwal, 2018). The length of hospitalization of DVI patients is related to the severity, which can be measured by complete blood laboratory tests including erythrocyte count, hemoglobin levels (Hb), and hematocrit levels (Hct) (Maesarah et al., 2023).

Based on research by Marsudi (2022) stated that erythrocyte levels in DVI patients vary depending on the severity. Patients infected with dengue virus in the early phase of the erythrocyte count can be normal or slightly decreased, while if hemoconcentration occurs, erythrocyte levels tend to increase (Marsudi et al., 2022). Hemoconcentration is a condition of increased cell concentration in the blood due to plasma leakage, which can cause

hypovolemic shock. If hypovolemic shock occurs, it can worsen the severity of DVI patients which will impact on the length of hospitalization (Maulin and Irma, 2023).

Hemoconcentration is also related to hematocrit values, an increase in hematocrit is one indicator of hemoconcentration (Pritanti and Notopuro, 2019). Research conducted by Cahyani et al. (2020) showed that there was a statistically significant relationship between the amount of hematocrit and the length of hospitalization in DVI patients (Cahyani et al., 2020). Another study has shown that hematocrit has no relationship with the severity of DVI, which means there is no relationship with the length of hospitalization (Syumarta et al., 2014). Research from Tuzzahra (2016) stated that hematocrit values were not related to the length of hospitalization of dengue infection patients at the South Tangerang City Hospital (Tuzzahra, 2016). Apart from being related to hematocrit, hemoconcentration also causes an increase in haemoglobin (Recker et al., 2024).

Hemoglobin levels in the first few days are generally normal or slightly decreased because the dengue virus is still in the replication stage, but then the levels will increase following the increase in hemoconcentration and are the earliest hematological abnormalities found in DVI patients (Tuntun and Ayunani, 2018). Study from Recker et al. (2024) also said that hemoglobin increases when hemoconcentration occurs (Recker et al., 2024). Previous studies have shown that high hemoglobin levels at the time of hospital admission can be a factor in the length of hospitalization (Recker et al., 2024). Another study stated that hemoglobin is not related to the severity of DVI patients (Oehadian et al., 2021).

Red Blood Cell Distribution Width (RDW) is one of the results of a complete blood test which is a variation in the size or area of erythrocytes (Idris et al., 2019). Hemoglobin-to-Red Blood Cell Distribution Width ratio or Hb/RDW ratio is a measurement that combines the results of a hemoglobin test with RDW. Hb/RDW ratio is associated with infection and is a biomarker of inflammation (Chen et al., 2024). There are studies that suggest that the Hb/RDW ratio can be a prognosis parameter in patients with hepatitis B virus infection (Yu et al., 2022). However, there are no studies that discuss the relationship between Hb/RDW ratio and DVI, especially the length of hospitalization of pediatric DVI patients.

Based on the explanation above, there are several contradictory studies and a limited number of related articles. This study was conducted to determine the correlation between erythrocyte levels, hematocrit, hemoglobin, and Hb/RDW ratio with the length of hospitalization in pediatric DVI patients. The results of this study are expected to be an indicator for assessing the length of hospitalization in pediatric DVI patients.

## Method

This study used a correlative observational design with a cross-sectional approach. This study was conducted at the Medical Record Installation of PKU Muhammadiyah Sampangan Hospital, Pasar Kliwon, Surakarta from October to November 2024. The target population in this study were pediatric dengue virus infection patients, while the actual population were pediatric dengue virus infection patients who were hospitalized at PKU Muhammadiyah Sampangan Hospital, Surakarta. The sample size used in this study was 41 samples. The sample size was calculated using the sample size formula for research on correlative analysis of numerical data. Sampling was carried out using consecutive non-probability sampling. Inclusion criteria used in this study were pediatric patients aged 0-18 years with a diagnosis of DVI and obtained positive anti-dengue IgG and/or IgM. Exclusion criteria in this study were patients with other infections such as typhoid fever.

The independent variables in this study were erythrocyte levels, hematocrit, hemoglobin, and Hb/RDW ratio. The dependent variable in this study was the length of hospitalization in pediatric DVI patients. Secondary data used in this study were obtained from medical records of dengue infection patients who underwent treatment at PKU Muhammadiyah Sampangan Hospital. Data management and analysis used in this study was statistical analysis using Jeffreys's Amazing Statistics Program software version 0.16.1.0 (Amsterdam University). This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Muhammadiyah Surakarta University under the protocol number 5385/C.1/KEPK-FKUMS/XI/2024.

## Result and Discussion

Based on data obtained from the medical records department of PKU Muhammadiyah Sampangan Hospital, a total of 41 samples were collected and the results of the univariate analysis are presented in Table 1.

**Table 1.** Univariate Test Results

Variables	Result
Length of hospitalization (days)	3 (1)**
Erythrocytes (million cells/uL)	5,05 (0,61)*
Hematocrit (%)	39,5 (4,8)**
Hemoglobin (gr/dL)	13,6 (1,2)**
Hb/RDW ratio	1,03 (0,12)**
Degree of severity of dengue infection	
Without warning sign (%)	65,85
Warning sign (%)	34,14
Severe dengue (%)	0

Note: \*normal data: mean (standard deviation), \*\*abnormal data: median (Interquartile Range)

Table 1 shows the univariate test result for various variables analyzed in this study. The analysis of the length of hospitalization revealed a median of 3 days. From the laboratory data of pediatric dengue infection patients, the mean erythrocyte count was 5.05 million cells/nL (SD 0.61 million cells/nL), which is within the normal range for children, indicating that erythrocyte levels were not significantly altered by the dengue infection. The median hematocrit value was 39.5%, which is also within the normal range for children (approximately 35-45%). The median hemoglobin level was 13.6 g/dL, which is within the normal range for children (12-16 g/dL), indicating that hemoglobin levels remained stable despite the infection. And the median Hb/RDW ratio was 1.03. In this study, the values of these hematological parameters suggest that the majority of patients did not experience severe complications such as significant bleeding or plasma leakage. Regarding the severity of dengue infection, the majority of subjects had dengue infection without warning signs (66%), while the remaining 34% were patients with warning signs. No cases of severe dengue were observed in this study, which aligns with the relatively normal hematological values observed across the study participants.

Table 2 presents the bivariate correlation test results between hematological parameters and the length of hospitalization in pediatric dengue patients. The correlation between length of hospitalization and erythrocyte count yielded an  $r$ -value of 0.027 with a  $p$ -value of 0.867, indicating no significant correlation. Similarly, hematocrit showed an  $r$ -value of -0.004 and a  $p$ -value of 0.983, also indicating no significant relationship. Hemoglobin levels demonstrated an  $r$ -value of 0.079 with a  $p$ -value of 0.625, while the Hb/RDW ratio had an  $r$ -value of 0.116 with a  $p$ -value of 0.472. None of the hematological parameters studied here showed a statistically significant correlation with length of hospitalization ( $p > 0.05$ ) in pediatric dengue virus infection patients at PKU Muhammadiyah Sampangan Hospital, Surakarta. The complete results of the bivariate analysis are presented in Table 2.

**Table 2.** Bivariate Correlation Test Results

Correlation	r-value	p-value
Length of hospitalization - Erythrocytes	0,027	0,867
Length of hospitalization - Hematocrit	-0,004	0,983
Length of hospitalization - Hemoglobin	0,079	0,625
Length of hospitalization - Hb/RDW ratio	0,116	0,472

### **Relationship between erythrocyte levels and length of hospitalization**

Bivariate analysis using the *Spearman* method showed a very low and statistically insignificant correlation between erythrocyte levels and length of hospitalization of patients with dengue virus infection ( $r = 0.027$  and  $p = 0.876$ ). This finding is inconsistent with the initial hypothesis that hematological parameters, including erythrocyte levels, may play a significant role in predicting the length of hospitalization. The observed differences could be attributed to

variations in study populations, differences in the severity of the disease, or limitations in the sample size used in this research. These results are in line with the research of Marsudi et al. (2022) which states that the average results of erythrocytes of dengue virus infection patients are normal and not associated with length of hospitalization (Marsudi et al., 2022). These results are also supported by research from Kusdianto et al. (2021) which explains that erythrocyte levels in DVI patients without bleeding will remain stable throughout the course of the disease (Kusdianto et al., 2021).

The number of erythrocytes is relatively stable in patients with dengue infection because the dengue virus does not cause direct erythrocyte destruction, so the number of erythrocytes remains stable during the course of the disease (Hidayatullah and Aisyah, 2018). Erythrocyte stability is also influenced by the body's mechanism that always maintains the number of erythrocytes by increasing bone marrow production so that the number of erythrocytes remains stable unless heavy bleeding or other complications occur (Indricuan et al., 2020). In this study, the majority of participants were classified as having mild to moderate dengue infection, with 66% categorized as having no warning signs, 34% presenting with warning signs, and none experiencing severe dengue. This distribution of disease severity may also explain the lack of significant changes in erythrocyte counts. Significant changes in the number of erythrocytes only occur in cases with severe complications, such as massive gastrointestinal bleeding or severe anemia due to hemolysis. However, this condition rarely occurs in pediatric patients with dengue (Nugraha, 2017).

### ***Relationship between hematocrit levels and length of hospitalization***

Spearman test results showed that the values of  $r = -0.004$  and  $p = 0.983$  which indicates that hematocrit does not have a statistically significant relationship with the length of hospitalization in pediatric patients with dengue virus infection. These results are in line with the research of Syumarta et al. (2014) which showed that there was no significant relationship between hematocrit and length of hospitalization with a  $p$  value  $>0.05$  and  $r = 0.059$ . The results of this study are also supported by the research of Ugi & Damayanti (2018) with a  $p$  value  $= 0.067$  which stated that there was no significant relationship between hematocrit levels and length of hospitalization (Ugi and Damayanti, 2019). However, this study is different from research from Cahyani et al. (2020) which states that there was a significant relationship between hematocrit levels and length of hospitalization. This is due to differences in the number of samples and research locations (Cahyani et al., 2020).

Hematocrit is often used as a parameter of plasma leakage which is one of the typical signs of the critical phase of dengue infection (Rodrigo et al., 2021). Plasma leakage causes hemoconcentration which is characterized by an increase in hematocrit. Hematocrit levels usually increase only in the critical phase which lasts for a short time and the value can return to normal with adequate intravenous fluid therapy (Ardlianti et al., 2022). Longer hospitalization usually occurs in patients who experience plasma leakage (Rachim, 2019). Plasma leakage is one of the sign of severe dengue (Rachim, 2019). In this study, the absence of subjects with severe dengue likely contributed to the lack of a significant relationship between hematocrit levels and hospitalization duration. The predominantly mild to moderate cases in this study population did not exhibit the plasma leakage or hemoconcentration that are typically linked to extended hospitalization periods. These results emphasize the need to explore other factors that may influence hospitalization length in patients with dengue virus infection.

### ***Relationship between hemoglobin levels and length of hospitalization***

Based on the Spearman test, the results obtained  $r = 0.079$  and  $p = 0.625$  showed that there was no significant correlation between hemoglobin levels and the length of hospitalization of pediatric DVI patients. This result is in line with the research of Oehadian et al. (2021) which states that hemoglobin is not associated with the length of hospitalization of DVI patients (Oehadian et al., 2021). This study is also supported by the research of Handayani et al. (2022) which shows that there is no significant relationship between hemoglobin levels and the length of hospitalization of pediatric DVI patients with the result of  $p = 0.073$  (Handayani et al., 2022). The results of this study are not in line with the research of Recker et al. (2024) which states that high hemoglobin levels at the time of admission can be a factor in longer length of hospitalization. The difference with this study is that patients with elevated hemoglobin and hematocrit levels will increase the possibility of plasma leakage which has an impact on severe dengue. Whereas in our study there were no subjects who experienced severe dengue.

Dengue infection patients who experience hemoconcentration will experience an increase in hemoglobin levels, but if overcome by intravenous fluid administration it will quickly return to normal values (Ardlianti et al., 2022).

Dengue virus does not cause direct erythrocyte damage, so hemoglobin levels tend to be stable unless there is massive bleeding (Handayani et al., 2022). Meanwhile, decreased hemoglobin usually occurs in patients with severe bleeding complications, but this case is rare in pediatric patients. Hemoglobin abnormalities are not only caused by dengue infection, but can also be caused by other conditions such as pregnancy, anemia, leukemia, chronic renal failure, and malaria (Bere and Sudrajat, 2024).

### ***Relationship between Hb/RDW ratio and length of hospitalization***

Bivariate analysis using the *Spearman* method showed that the Hb/RDW ratio was not correlated and not statistically associated with the length of hospitalization of dengue virus infection patients ( $r = 0.027$  and  $p = 0.876$ ). No previous studies have examined the Hb/RDW ratio with the length of hospitalization in DVI patients. The Hb/RDW ratio is a hematological parameter used to evaluate variations in erythrocyte size (anisocytosis) in the context of hemoglobin levels (Rahamim et al., 2022). This parameter is often associated with various clinical conditions, including chronic inflammation, anemia, or other hematological disorders (Chen et al., 2024). However, dengue fever is an acute infectious disease characterized by a rapid onset and progression. Therefore, it is unlikely that the Hb/RDW ratio would be significantly impacted by the infection in a way that would correlate with the length of hospitalization. The primary factors that influence the length of hospitalization in DVI patients, such as the development of shock, severe bleeding, or organ complications, are not directly related to changes in the Hb/RDW ratio (Sari et al., 2021).

There are several limitations in this study. The sample size of 41 pediatric DVI patients may not be large enough to be fully representative of the broader population. We cannot generalize the results as it was performed in a small patient population. The study is conducted in a single hospital, the results may not reflect diverse conditions in other healthcare facilities. The study predominantly included patients with mild to moderate dengue, with no cases of severe dengue, which may have contributed to the lack of significant findings, as severe cases typically show more marked changes in hematological parameters. In addition, this study only focused on hematological parameters, without evaluating other potential factors that influence the length of hospitalization. These limitations suggest the need for further research to validate and expand upon these findings. A larger, multicenter study with a more diverse patient population and prospective data collection would provide more robust conclusions and better insights into the role of hematological parameters in predicting hospitalization duration in pediatric DVI patients.

## **Conclusions**

The results of this research indicated that there was no statistically significant correlation between erythrocyte levels, hematocrit, hemoglobin, Hb/RDW ratio, and the length of hospitalization in pediatric patients with dengue virus infection (DVI). This suggests that these hematological parameters do not serve as reliable predictors of hospitalization duration in this cohort. The absence of significant hematological changes such as hemoconcentration, which is typically observed in more severe cases of dengue, supports this finding. Hemoconcentration, often linked to plasma leakage and increased hematocrit levels, did not occur in a significant proportion of the study participants. Most of the subjects in this study had mild to moderate severity of DVI, with a majority experiencing dengue infection without warning signs. These milder cases did not exhibit the complications that are often associated with longer hospitalization periods, such as severe bleeding or organ involvement. Given that severe cases of dengue can lead to more substantial hematological disturbances and longer hospitalization, further research is needed with a larger sample size and more varied disease severities to better understand the factors that influence the length of hospitalization in pediatric DVI patients. Future studies could explore the role of other clinical markers or complications that may contribute to prolonged hospital stays.

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