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Correlation of Dengue Infection Severity with Abdominal Pain, Delta Hematocrit, Platelet Count, and Delta Hematocrit-Platelet Ratio in Pediatric Patients

Dinda Dwi Agustina[1], Metana Puspitasari[1], Safari Wahyu Jatmiko [1*]

[1] Faculty of Medicine, Universitas Muhammadiyah Surakarta, Surakarta, Indonesia

Abstract

Purpose: *This study aimed to determine the correlation between the severity of dengue infection and abdominal pain, delta hematocrit, platelet levels, and the delta hematocrit-platelet ratio.*
Methodology: *the study used a correlational observational design with a cross-sectional approach. Data were obtained from the medical records of dengue infection patients at PKU Muhammadiyah Sampangan Hospital from October–November 2024. A total of 39 samples were selected using a consecutive non-probability sampling technique. Data analysis was performed using JASP statistical software version 0.19.1.0.*
Results: *The study revealed no significant relationship between the severity of dengue infection and abdominal pain (p=0.089), delta hematocrit (p=0.589), platelet levels (p=0.068), or the delta hematocrit-platelet ratio (p=0.740).*
Applications/Originality/Value: This study provides valuable insights into the limitations of individual clinical and laboratory parameters, emphasizing the need for a comprehensive approach to assessing dengue severity in pediatric patients.

Introduction

Dengue virus infection is an arboviral disease primarily transmitted by Aedes aegypti and Aedes albopictus mosquitoes. The transmission of dengue infection tends to rise with the onset of the rainy season (Bestari and Siahaan, 2018). The World Health Organization (WHO, 2020) reported a significant increase in dengue cases globally from 2000 to 2019, with a 46% rise in Southeast Asia between 2015 and 2019. Kemenkes RI (2022) also reported an increase in dengue cases from 2000 to 2019, with a 46% rise in Southeast Asia during the same period. In Central Java, 12,994 dengue cases were recorded in 2022, while in Surakarta City, 99 dengue cases were reported in 2023 (Dinkes Jawa Tengah, 2022; Dinkes Kota Surakarta, 2023). These rising figures highlight the significant impact of dengue infection in various regions, necessitating enhanced prevention and control efforts to reduce the incidence.

Dengue infection can be asymptomatic or symptomatic, with symptoms typically resolving within 1-2 weeks (WHO, 2024). The WHO revised the classification of dengue infection based on its severity in 2009, categorizing it into dengue fever without warning signs, dengue fever with warning signs, and severe dengue (Zein and Farhanah, 2015). Symptoms of dengue infection without warning signs include fever accompanied by nausea and vomiting, skin rash, bone, joint, or retro-orbital spain, a positive tourniquet test, and leukopenia. Meanwhile, symptoms of dengue with warning signs include abdominal pain, persistent vomiting, mucosal bleeding, lethargy, hepatomegaly >2 cm, increased hematocrit, decreased platelet count, and leukopenia. Dengue infection is considered severe if there is significant plasma leakage, severe bleeding, and serious organ complications (WHO, 2009). Abdominal pain is one of the easily observable warning signs.

According to the 2009 WHO classification, one of the warning signs of dengue infection is abdominal pain (WHO, 2009). This pain can be caused by liver enlargement and gastrointestinal bleeding and is a risk factor for developing Dengue Shock Syndrome (DSS) (Idrus et al., 2023; Podung et al., 2021). Research by Edwin and Olivia Budiarta (2019) showed that dengue patients with abdominal pain have a sevenfold higher risk of experiencing DSS. However, a study by Sari and Darmawan (2010) found that abdominal pain was not statistically significant in

* Corresponding author: safari.wahyu@ums.ac.id

association with the incidence of shock in pediatric dengue infections. Dengue infection is also associated with changes in hematological profiles, including increased hematocrit levels and decreased platelet counts.

Patients with dengue infection commonly experience increased hematocrit levels or hemoconcentration (Syed Abas et al., 2022). Hemoconcentration in dengue patients can begin on the third day of illness (Kamuh et al., 2015). Elevated hematocrit levels may indicate plasma leakage (Made et al., 2022; Pathak et al., 2021), which typically occurs during the critical phase, from the fourth to the seventh day (Atira et al., 2023; Rodrigo et al., 2021). Delta hematocrit is the difference between hematocrit levels measured on the fourth and fifth days. A study by Handayani et al. (2022) found a significant correlation between hematocrit levels and the severity of dengue hemorrhagic fever. However, research conducted by (Maulin and Irma (2023) did not find such a correlation.

A decrease in platelet levels, known as thrombocytopenia, is a key laboratory indicator for diagnosing dengue hemorrhagic fever, with a notable decline typically observed around the fourth day of illness (Ervinda Faradiana & Adimayanti, 2023; Halim & Rifai, 2024). Studies have explored the relationship between platelet levels and the severity of dengue hemorrhagic fever, yielding mixed results. Research conducted by Maulin and Irma (2023) identified a negative correlation, suggesting that lower platelet levels are associated with increased severity of the disease. However, a study by Putri et al. (2023) found no significant relationship between platelet levels and disease severity. These contrasting findings highlight the complexity of the clinical manifestations and laboratory parameters associated with dengue hemorrhagic fever.

The delta hematocrit-platelet ratio can serve as a diagnostic tool for dengue patients, with increased hematocrit levels and decreased platelet counts indicating the severity of the infection. The higher the hematocrit and the lower the platelet count, the more severe the dengue infection experienced by the patient (Atira et al., 2023)This study aims to divide the delta hematocrit value by the platelet count to determine the correlation between this ratio and the severity of dengue infection. If a correlation is found, future research could establish threshold values for the delta hematocrit-platelet ratio to assess infection severity. A study by Manik and Ramadhan (2021) reported a hematocrit-to-platelet ratio 1:2.8 in pediatric dengue patients at Universitas Kristen Indonesia Hospital.

The high incidence of dengue infection in Indonesia highlights the need for evaluation based on clinical symptoms and laboratory results to assess the severity of the disease. This study aims to determine the relationship between the severity of dengue infection and abdominal pain, delta hematocrit, platelet count, and the delta hematocrit-platelet ratio. The findings are expected to serve as indicators for assessing the severity of dengue infection.

Method

This study utilized a correlational observational design with a cross-sectional approach to examine the relationships between key variables. The research was conducted at the Medical Records Department of PKU Muhammadiyah Sampangan Hospital over a period from October to November 2024. A total of 39 participants were included in the study, selected through consecutive non-probability sampling to ensure practicality and relevance. The independent variables assessed in this study included abdominal pain, delta hematocrit, platelet count, and the delta hematocrit-platelet ratio. The severity of dengue infection served as the dependent variable. Data for the research were derived from secondary sources, specifically the medical records of patients diagnosed and treated for dengue infection at the hospital. To analyze the relationships between the variables, different statistical tests were employed. The Chi-Square test was used to evaluate the correlation between ordinal and nominal variables, while the Spearman test was applied to assess correlations involving ordinal and ratio variables. All data management and statistical analyses were conducted using Jeffreys's Amazing Statistics Program (JASP) software, version 0.19.1.0, developed by Amsterdam University. This rigorous analytical framework ensured the accuracy and reliability of the findings.

Results and Discussion

This study was conducted at PKU Muhammadiyah Sampangan Hospital from October to November 2024. The subjects of this study were pediatric patients under 15 years old with dengue infection who were treated at PKU Muhammadiyah Sampangan Hospital. A total of 37 research subjects were involved, and their characteristics are presented in Table 1.

Table 1. Univariate Test Results

Variabel	Result
The severity level of dengue infection	
Without warning sign (%)	53.8
Warning sign (%)	46.2
Severe dengue (%)	0
Abdominal pain	
Without abdominal pain (%)	64.1
With abdominal pain (%)	35.9
Hematocrit (%)	
The fourth day*	39.4 (3.25)
Fifth dayⱡ	39.22 (4.12)
Delta hematocrit*	2.2 (2,45)
Platelet (thousand /mm3)ⱡ	109.87 (39.27)
Delta hematokrit-platelet ratio*	0.031 (0.035)

Note: ⱡ data presented as mean (SD), * data presented as median (IQR)

Table 2. Bivariate Test Results

Correlation	r-value	p-value	VS-MPR
DKID-NA	0.272	0.089	1.707
DKID-DH	-0.089	0.589	1
DKID-Plt	-0.295	0.068	2.004
DKID-RDH Plt	0.055	0.74	1

Note: (DKID-NA): Severity of Dengue Infection - Abdominal Pain, (DKID-DH): Severity of Dengue Infection - Delta Hematocrit, (DKID-Plt): Severity of Dengue Infection - Platelet, (DKID-RDH Plt): Severity of Dengue Infection - Delta Hematocrit-Platelet Ratio.

The Chi-Square correlation test indicated that the relationship between abdominal pain and the severity of dengue infection had a p-value of 0.089 and an r-value of 0.272, suggesting a weak positive correlation. However, as the result was not statistically significant ($p > 0.05$), it implies that abdominal pain alone cannot reliably predict the severity of dengue infection. Similarly, the Spearman correlation test for delta hematocrit showed a p-value of 0.589 and an r-value of -0.089, indicating a weak negative correlation, meaning that an increase in delta hematocrit was slightly associated with a decrease in severity. However, this relationship was also statistically insignificant. Regarding platelet count, the test produced a p-value of 0.068 and an r-value of -0.295, demonstrating a weak negative correlation, suggesting that lower platelet levels may correspond to higher disease severity. Nonetheless, the lack of statistical significance ($p > 0.05$) renders this association unreliable as a predictive measure. Finally, the Spearman test for the delta hematocrit-platelet ratio yielded a p-value of 0.74 and an r-value of 0.055, revealing a weak positive correlation that was similarly not statistically significant. These findings collectively highlight that while weak correlations exist between these variables and the severity of dengue infection, none are strong or statistically substantial enough to be used as reliable clinical indicators.

The Relationship Between Abdominal Pain and the Severity Level of Dengue Infection

Based on the results of the chi-square test, no significant relationship was found between the severity of dengue infection and the presence of abdominal pain ($p = 0.089$). In this study, only 26.64% of patients reported experiencing abdominal pain, a proportion that highlights its limited prevalence among the participants. Among patients with dengue infection who exhibited warning signs, 44.4% experienced abdominal pain. This symptom in dengue patients is often attributed to liver involvement, which may manifest as hepatomegaly caused by the replication of the dengue virus in hepatocytes and Kupffer cells (Ahmed, 2015; Idrus et al., 2023). The extent of liver damage and the resulting symptoms, such as abdominal pain, depend on the immune response to the dengue virus, which can vary among individuals (Alam et al., 2023).

The findings of this study align with prior research conducted by Sari & Darmawan (2010), which similarly found no statistically significant relationship between the severity of dengue infection and the occurrence of abdominal pain. However, contrasting results were reported by Edwin and Olivia Budiarta (2019), who observed that abdominal pain significantly increases the risk of developing Dengue Shock Syndrome (DSS) by sevenfold. In their study, among 43 patients who developed DSS, 76.6% reported experiencing abdominal pain. This observation suggests that in severe cases, such as DSS, abdominal pain may arise from more severe complications, including gastrointestinal bleeding and extensive hepatomegaly. Another specific cause of acute abdominal pain is acute hepatitis, which is a common complication observed in dengue fever. This condition arises because one of the phases of dengue virus replication occurs in the liver, leading to significant liver damage. The virus directly invades hepatocytes, which can disrupt normal liver function and stimulate processes such as inflammation and apoptosis of liver cells, resulting in further liver injury (Gupta et al., 2017).

The Relationship Between Delta Hematocrit and the Severity Level of Dengue Infection

The delta hematocrit variable in this study did not demonstrate a significant relationship with the severity of dengue infection ($p = 0.589$, $r = -0.089$). Delta hematocrit, as defined in this study, represents the difference in hematocrit levels measured on the fourth and fifth days after the onset of fever. Hematocrit levels often rise due to plasma leakage, a hallmark of severe dengue infection (Ayunani et al., 2017). However, the results of this study indicate that 53.8% of patients experienced dengue infection without warning signs. In such cases, plasma leakage is usually minimal, resulting in insignificant changes in hematocrit levels. Hematocrit levels are determined not only by plasma volume but also by the number of erythrocytes (Maulin & Irma, 2023). Hematocrit is essentially the ratio of erythrocyte volume to the total blood volume, meaning that both the number and size of erythrocytes influence its value. Conditions such as anemia, blood loss, or reduced erythrocyte size can lead to lower hematocrit levels due to decreased blood viscosity (Putri et al., 2023). Therefore, hematocrit measurements alone may not fully reflect plasma leakage in all cases, as they are also affected by underlying hematological factors. The critical phase of dengue infection typically begins on the third day and lasts until the seventh day. The recovery phase occurs 48–72 hours after the critical phase. This suggests that by the fifth day after fever onset, patients may already be entering the recovery phase, during which hematocrit levels begin to decline (Nugraheni et al., 2023). Hematocrit levels increase when the viral load in the blood rises. The elevated viral load activates T cells, leading to a cytokine storm. This excessive release of cytokines causes an increase in vascular permeability, which results in endothelial damage and plasma leakage (Permatasari et al., 2020). The disruption of endothelial integrity due to the cytokine storm not only contributes to hemoconcentration but also exacerbates the severity of dengue infection.

The findings of this study are consistent with the results of research conducted by Putri et al. (2023), which found no significant correlation between hematocrit levels and the severity of dengue hemorrhagic fever (DHF). This suggests that hematocrit levels alone may not be a reliable indicator of disease severity, particularly without other corroborating clinical or laboratory markers. However, these results contrast those reported by Handayani et al. (2022), who observed a significant relationship between hematocrit levels and the severity of dengue infection. According to research by Sihombing & Salim (2023), 53.8% of DHF patients had normal hematocrit levels, indicating that not all DHF patients experience increased hematocrit levels. It is also important to note that plasma leakage indicators are not solely reliant on the rise in hematocrit levels. Clinical guidelines emphasize that a decrease in hematocrit of >20% following fluid therapy is also considered a diagnostic indicator of plasma leakage (Hidayat et al., 2017).

The Relationship Between Platelet Levels and the Severity Level of Dengue Infection

In this study, the Spearman test revealed a non-significant relationship between platelet levels and the severity of dengue infection ($p = 0.068$, $r = -0.295$). While it is well-established that a decrease in platelet levels often correlates with an increase in hematocrit levels-reflecting plasma leakage during dengue infection-the findings from this study suggest that the rise in hematocrit was not statistically significant. This lack of a substantial increase in hematocrit may explain the absence of a significant decrease in platelet levels observed. The relationship between platelet levels and hematocrit during dengue infection is complex, as various pathological mechanisms and physiological responses interact and contribute to the observed changes. Dengue infection typically leads to thrombocytopenia or a decrease in platelet levels, which is a hallmark of the disease. Thrombocytopenia in dengue infection is primarily caused by bone marrow suppression resulting from the replication of the dengue virus within the bone marrow. This viral activity can inhibit the proliferation of hematopoietic progenitor cells, which are critical for the production of platelets, leading to a state of bone marrow hypocellularity. The suppression of these progenitor cells disrupts the normal hematopoietic process, significantly reducing platelet production. In addition to the suppression of progenitor cell proliferation, the maturation of megakaryocytes, which are the precursor cells responsible for platelet formation, may also be impaired. This impairment further exacerbates the reduction in platelet levels, as immature megakaryocytes fail to produce sufficient functional platelets (Alifa et al., 2022). The disruption of these processes ultimately results in the observed thrombocytopenia seen in dengue infection. Therefore, while platelet levels are typically expected to decrease during severe dengue cases due to these underlying mechanisms, the absence of a significant change in hematocrit levels in this study may explain the lack of a corresponding decrease in platelet levels.

The findings of this study align with those reported by (Putri et al. (2023), who found no significant relationship between platelet levels and the severity of dengue infection. This suggests that platelet levels, although commonly used as a marker in the clinical management of dengue, may not consistently correlate with disease severity in all patient populations. However, these results contrast with the study conducted by (Handayani et al. (2022), which found a significant correlation between platelet levels and the severity of dengue infection. In this study, while the r-value suggested a weak negative relationship between platelet levels and the severity of dengue infection, the p-value indicated that this relationship was not statistically significant. Interestingly, the VS-MPR (Validity and Statistical-Mathematical Prediction Ratio) values in this study supported the alternative hypothesis on two occasions, suggesting a potential trend that warrants further exploration. Further research with a larger sample size is recommended to obtain more definitive results.

The Relationship Between the Delta Hematocrit-Platelet Ratio and the Severity Level of Dengue Infection

This study found no significant relationship between the delta hematocrit-platelet ratio and the severity of dengue infection ($p = 0.74$, $r = 0.055$). To date, limited research has explored the ratio of delta hematocrit to platelet levels in dengue-infected patients. The absence of a significant association highlights the complexity of the interactions between these two parameters during dengue infection. In this study, no substantial increase in hematocrit levels was observed between the fourth and fifth days after the onset of fever. The average hematocrit level recorded on the fourth day was 40.23%, while on the fifth day it was 39.22%. A paired t-test yielded a p-value of 0.054, indicating no significant difference between hematocrit levels on these two days. These findings suggest a declining trend in hematocrit levels between the fourth and fifth days. An increase in hematocrit levels in dengue infection is typically linked to plasma leakage, a hallmark of the disease, while the observed reduction in platelet levels is associated with impaired platelet production in the bone marrow (Alifa et al., 2022; Rahat et al., 2020). An increase in hematocrit levels in dengue infection patients is typically associated with plasma leakage, while a decrease in platelet levels is linked to reduced platelet production in the bone marrow (Atira et al., 2023). This sequence may explain the lack of a relationship between the delta hematocrit-platelet ratio and the severity of dengue infection in this study.

Conclusions

This study, conducted at PKU Muhammadiyah Sampangan Hospital, examined the correlation between dengue infection severity and several clinical and laboratory parameters in pediatric patients, including abdominal pain, delta hematocrit, platelet levels, and the delta hematocrit-platelet ratio. The findings revealed no significant relationship between these parameters and the severity of dengue infection. Although abdominal pain is recognized as a warning sign of dengue, the study found no significant association with disease severity, possibly due to the absence of severe cases like Dengue Shock Syndrome (DSS) among the participants. Similarly, delta hematocrit, often linked to plasma leakage, showed no correlation with severity, which could be influenced by the timing of measurements or individual variability. Platelet levels, typically reduced in dengue infection due to bone marrow suppression, also did not significantly correlate with disease severity in this study. Additionally, the delta hematocrit-platelet ratio, proposed as a diagnostic tool, was not a reliable indicator of severity in this population. These findings suggest that these parameters alone are insufficient to assess dengue severity. Further research with larger sample sizes and more diverse patient groups is recommended to better understand the relationships between these indicators and disease outcomes.

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