

## ORIGINAL RESEARCH REPORT

## Hematology Profiles and Disease Severity of Pediatric Dengue Virus Infection at a Tertiary Hospital in Surabaya, Indonesia

Annisa Fira Salsabila<sup>1</sup>, Juniastuti<sup>2\*</sup>, Dominicus Husada<sup>3</sup>, Dwiyantri Puspitasari<sup>4</sup>

<sup>1</sup>Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

<sup>2</sup>Department of Clinical Microbiology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia; Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

<sup>3</sup>Department of Child Health, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia; Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

<sup>4</sup>European Society for Paediatric Infectious Diseases, Bathgate, Scotland, The United Kingdom.

---

**Article Info****Article history:**

Received 08-12-2023

Revised 02-01-2024

Accepted 06-01-2024

Published 10-01-2024

---

**Keywords:**

Dengue virus infection

Dengue fever

Dengue hemorrhagic fever

Hematology profile

Pediatric

**\*Corresponding author:**

Juniastuti

junssf@fk.unair.ac.id

---

**ABSTRACT**

**Background:** The escalating incidence of dengue cases in Surabaya, Indonesia, underscores the imperative to comprehend the hematology profiles and disease severity in pediatric patients affected by dengue virus infections (DVI). As the prevalence of DVI continues to surge, understanding the nuanced clinical manifestations becomes paramount for effective management and mitigation of the disease burden. **Objective:** This study aimed to characterize the hematology profiles and the disease severity of dengue virus infections (DVI) among pediatric patients hospitalized at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia throughout 2019. **Material and Method:** A retrospective descriptive cross-sectional study was conducted using secondary data from medical records. Pediatric patients aged six months to 18 years were enrolled. A total sampling method comprised 67 patients meeting the inclusion criteria. **Result:** Severe thrombocytopenia was most commonly observed in dengue hemorrhagic fever (DHF) III cases (36.4%), while leukopenia was predominant in DF cases (42.2%). High hematocrit levels were more prevalent in DHF III cases (27.3%), and high hemoglobin levels were most frequently identified in DHF II and DHF III cases (33% in each case). Significant differences in DVI severity were observed in platelets and hemoglobin levels ( $p=0.0002$  and  $p=0.0066$ , respectively) but not in leukocyte and hematocrit levels. **Conclusion:** Mild thrombocytopenia was prevalent in Dengue Fever (DF), while severe thrombocytopenia was most prevalent in Dengue Hemorrhagic Fever (DHF) grade III. Leukopenia was prominent in DF patients, and platelets and hemoglobin levels varied across severity of DVI. These findings provide insights for improved clinical management and diagnostic criteria refinement.

---

**How to cite:**

Salsabila, A.F., Juniastuti., Husada, D., et al. 2024. Hematology Profiles and Disease Severity of Pediatric Dengue Virus Infection at a Tertiary Hospital in Surabaya, Indonesia. *Majalah Biomorfologi-Biomorphology Journal*, 34(1): 1-9.

**Majalah Biomorfologi (Biomorphology Journal)** p.ISSN:0215-8833, e.ISSN: 2716-0920

doi: [10.20473/mbiom.v34i1.2024.1-9](https://doi.org/10.20473/mbiom.v34i1.2024.1-9)



Copyright: © 2024 by the authors. Open access publication under the terms and condition of the Creative Commons Attribution 4.0 International license (CC.BY 4.0).

## Highlights

1. Dengue virus infections exhibit a spectrum of clinical manifestations, ranging from asymptomatic cases to severe disease, with the potential for fatalities if not managed effectively.
2. Hematology factors significantly contribute to the severity of dengue virus infection.

## BACKGROUND

The number of dengue cases has been steadily increasing over time. According to the World Health Organization (WHO), there were 5.2 million cases of dengue fever in 2019, with 658,301 cases in Southeast Asia (Chong, et al., 2023; World Health Organization, 2023). Dengue is an arboviral illness, with around 40% of the worldwide population at risk of contracting the disease, particularly in the tropical and subtropical parts of the world (Laily, et al., 2020; Wardhani, et al., 2023). Recently, in 2019, there were 138,127 cases of dengue in Indonesia. In Surabaya, the incidence of dengue hemorrhagic fever (DHF) in 2019 was 9.56 per 100,000 population, with 277 cases (Minister of Health of The Republic of Indonesia, 2019; Surabaya City Health Office, 2020). The dengue virus causes Dengue Virus Infection (DVI). This virus has four serotypes: DENV-1, DENV-2, DENV-3, and DENV-4 (Mikhael, et al., 2022). Clinical manifestations of dengue virus infections range from asymptomatic to severe disease, potentially leading to fatalities if not appropriately managed. Symptomatic cases are categorized as dengue fever (DF), dengue hemorrhagic fever (DHF), dengue shock syndrome (DSS), and expanded dengue syndrome (World Health Organization, 2022). Dengue virus infections include primary and secondary infections, with latter infections often associated with bleeding, circulatory failure, and Dengue Shock Syndrome (DSS) (Marvianto, et al., 2023).

Diagnosing dengue requires laboratory testing to confirm the diagnosis alongside clinical symptoms. Patients with DHF may exhibit thrombocytopenia, leukopenia, increased hematocrit, and increased hemoglobin (Silitonga, et al., 2020; World Health Organization, 2022). A previous study reported that dengue patients showed higher levels of hemoglobin and hematocrit from day 3 to day 8 ( $p < 0.001$ ), lower white blood cell counts from day 2 to day 5 ( $p < 0.001$ ), and lower platelet counts from day 3 to day 8 ( $p < 0.001$ ) (Chaloemwong, et al., 2018). However, another study showed no correlation between average white blood cell count and the clinical severity of dengue virus infection on the third and fourth day of fever but did find a correlation between average platelet count and hematocrit with clinical severity in pediatric patients on the fourth day of fever (Aini, et al., 2016).

## OBJECTIVE

This study aimed to explore the complete blood count profile and severity grading of dengue virus infections among patients hospitalized in the pediatric inpatient ward at Dr. Soetomo General Academic Hospital, a tertiary hospital in Surabaya, Indonesia, during the year 2019. Information regarding this matter might significantly contribute to healthcare professionals to enhance response for DVI management in pediatric patients.

## MATERIAL AND METHOD

This cross-sectional descriptive study utilized secondary data collected through medical records of children aged six months to 18 years admitted with a new suspected DVI at the Department of Pediatrics of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to December 2019. Participants were included if the medical records assigned the International Classification of Diagnosis (ICD)-10 code A90-A91 (“Dengue fever [classical dengue]” and “Dengue hemorrhagic fever,” respectively) during hospitalization. A total sampling of 67 pediatric patients aged six months to 18 years were included. The case definition, clinical diagnosis, and management of dengue fever in children were based on the World Health Organization (2022) guidelines. They were categorized as dengue fever and dengue hemorrhagic fever (DHF) I, II, III, and IV. The diagnosis of dengue fever was

confirmed based on relevant and consistent clinical information. Patients were excluded when they had no supporting serological confirmation for DVI. Data regarding Hb levels, Hct, WBC, platelet count, and the severity of DVI were obtained from the medical records. Chi-square or Fisher's exact test was employed to analyze differences in hematology parameters across different grades of DVI severity. Statistical significance was determined if  $p < 0.05$ . All statistical analyses were conducted using the [IBM SPSS Statistics](#) for Mac, version 26.0 (IBM Corp., Armonk, N.Y., USA). Data were visualized using GraphPad Prism ver. 9 software for Mac.

## RESULT

A total of 310 pediatric patients were admitted to Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, during the study period. Only 67 patients fulfilled the inclusion and exclusion criteria, comprising 42 males (63%) and 25 females (37%). The predominant age group was 6 to under 12, encompassing 36 patients (54%). Regarding the clinical severity of dengue virus infection among those patients, the most prevalent manifestation was Dengue Fever, observed in 23 patients (34%), followed by Dengue Hemorrhagic Fever (DHF) I (30%), DHF III (16%), and DHF II (15%) while the least common presentation was DHF grade IV, documented in 3 patients (5%) ([Table 1](#)).

Table 1. Characteristic of pediatric DHF sample patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to December 2019.

Characteristics	Total
Age	
6 month - <6 years	10 (15%)
6-<12 years	36 (54%)
12-18 years	21 (31%)
Sex	
Male	42 (63%)
Female	25 (37%)
Severity	
Dengue Fever	23 (34%)
Dengue Hemorrhagic Fever I	20 (30%)
Dengue Hemorrhagic Fever II	10 (15%)
Dengue Hemorrhagic Fever III	11 (16%)
Dengue Hemorrhagic Fever IV	3 (5%)

Based on the platelet count, mild thrombocytopenia was most commonly found in Dengue Fever (DF) cases, with the highest severity level (14, 73.7%). Severe thrombocytopenia was most frequently encountered in cases of Dengue Hemorrhagic Fever (DHF) grade III (8, 36.4%). Regarding the leukocyte count, leukopenia was most prevalent in cases of DF (19, 42.2%) ([Fig. 1-A](#)). DHF grade I (1, 33.3%) and DHF grade III (2, 66.7%) had leukocytosis ([Fig. 1-B](#)). Regarding hematocrit levels, high hematocrit was most frequently observed in cases of DHF grade III (5, 27.3%) ([Fig 1-D](#)). Based on hemoglobin levels, normal hemoglobin was most commonly found in cases of DHF grade III (6, 33.3%) ([Fig 1-C](#)). There were significant differences in platelets ( $p=0.0002$ ) and hemoglobin ( $p=0.0066$ ) levels across different severity of DVI ([Table 2](#)).

Table 2. Complete blood count based on the DVI severity.

Complete blood count	Severity					p-value†
	DF	DHF I	DHF II	DHF III	DHF IV	
Platelets						
Normal	3 (100%)	0	0	0	0	
Mild thrombocytopenia	14 (73.7%)	5 (26.3%)	0	0	0	
Moderate thrombocytopenia	5 (21.7%)	9 (39.1%)	4 (17.4%)	3 (13.0%)	2 (8.7%)	
Severe thrombocytopenia	1 (4.5%)	6 (27.3%)	6 (27.3%)	8 (36.4%)	1 (4.5%)	
Leukocyte						
Leukopenia	19 (42.2%)	12(26.7%)	6 (13.3%)	6 (13.3%)	2 (4.4%)	
Normal	4 (21.1%)	7 (36.8%)	4 (21.1%)	3 (15.8%)	1 (5.3%)	
Leukocytoses	0	1 (33.3%)	0	2 (66.7%)	0	0.0002*
Hematocrit						
Low	4 (33.3%)	4 (33.3%)	1 (8.3%)	2 (16.7%)	1 (8.3%)	
Normal	18 (42.9%)	12(28.3%)	6 (14.3%)	4 (9.5%)	2 (4.8%)	
High	1 (7.7%)	4 (30.7%)	3 (23.1%)	5 (38.5%)	0	
Hemoglobin						
Low	2 (22.2%)	4 (44.4%)	0	2 (22.2%)	1 (11.1%)	
Normal	20 (50.0%)	12 (30.0%)	4 (10.0%)	3 (7.5%)	1 (2.5%)	
High	1 (5.6%)	4 (22.2%)	6 (33.3%)	6 (33.3%)	1 (5.6%)	

†Chi-square or Fisher's Exact Test

\*Significant differences (p&lt;0.05)

## DISCUSSION

Across new pediatric patients with suspected DVI in Dr. Soetomo General Hospital, we identified that dengue fever (34%) was the most prevalent grade of severity, followed by DHF I (30%), DHF III (16%), DHF II (15%), and DHF IV (5%). Following the natural progression of the disease, cases of suspected DVI were identified based on a comprehensive clinical history of the presence of fever during the third to seventh days. Dengue Fever (DF) 's higher prevalence than Dengue Hemorrhagic Fever (DHF) can be attributed to several factors, including variations in host susceptibility, viral strain characteristics, and the complex interplay of immune responses. Factors such as individual immunity, previous exposure to different dengue virus serotypes, and variations in vector competence among mosquito populations may contribute to the predominance of DF over DHF. Additionally, environmental and socio-economic factors and healthcare infrastructure can influence the transmission dynamics and clinical outcomes, leading to a higher incidence of the milder form of the disease, highlighting regional context as an essential consideration for public health management (Guillena, et al., 2013). This study revealed mild thrombocytopenia was most prevalent in DF. In line with these findings, previous studies highlighted that normal platelet counts and mild thrombocytopenia are commonly seen in laboratory tests of DF patients (World Health Organization, 2022). Severe thrombocytopenia was found in one DF (4.5%) patient. This might correlate with the severity of clinical symptoms, possibly influenced by co-infections or underlying conditions that were not documented in the medical records. Severe thrombocytopenia was most commonly found in pediatric patients with DHF grade III (36.4%) (Giri, et al., 2016).

Previous retrospective studies have shown that less than 20,000 cells/mm<sup>3</sup> platelet counts were present in pediatric DHF patients. In line with these findings, prior research confirmed that dengue patients typically experience thrombocytopenia, making them more susceptible to bleeding (Laoprasopwattana, et al., 2017). This condition occurs due to platelet destruction and dysfunction resulting from cytokine storms. There were significant differences in platelet levels across different severity of DVI (Buntubatu, et al., 2017).

This investigation revealed a predominant occurrence of leukopenia in DF (42.2%) patients, with the lowest prevalence observed in DHF grade IV (4.4%). These findings are consistent with the prior studies indicating that most DVI patients exhibit leukopenia (Yanti, et al., 2021; Wisanti, et al., 2022).

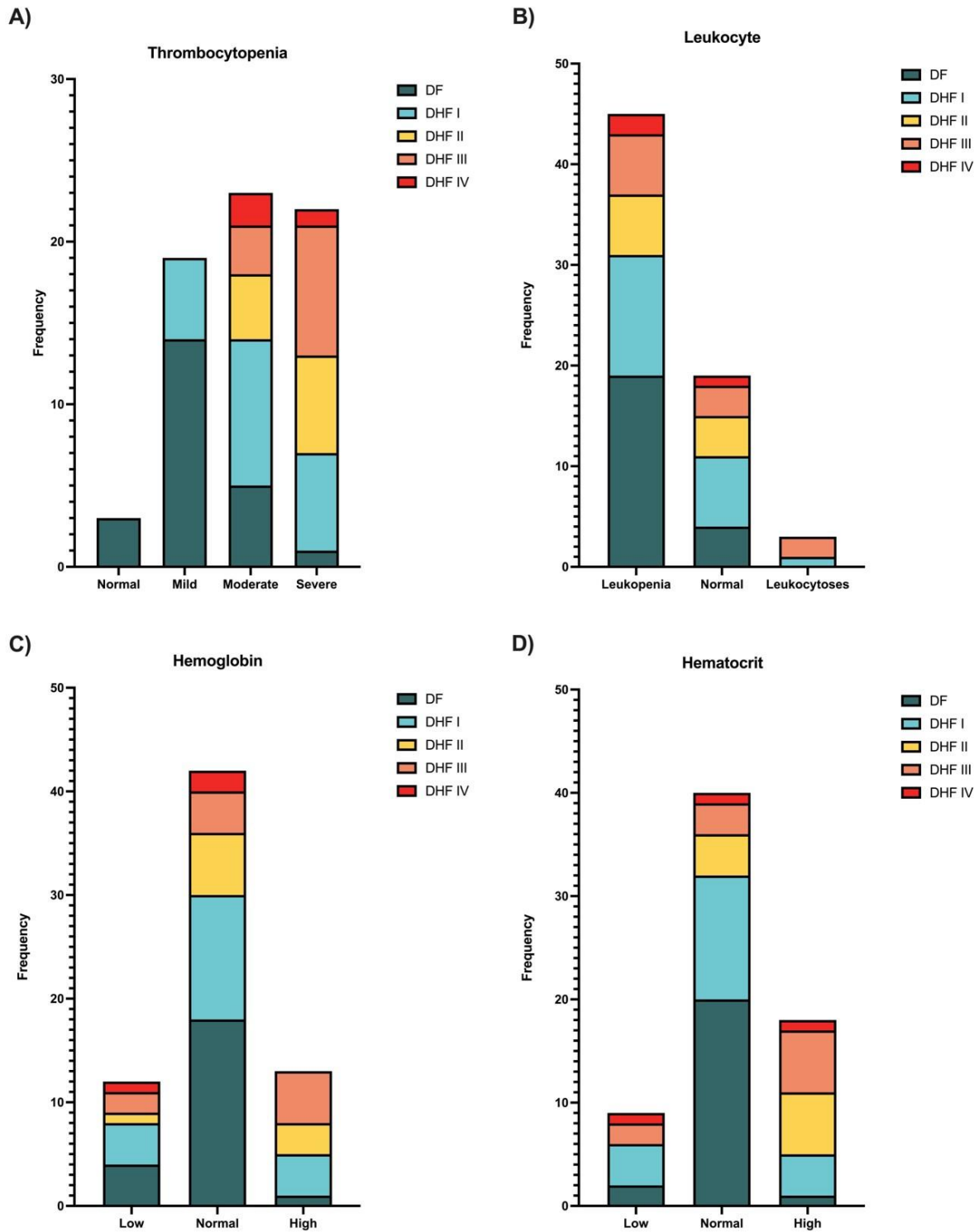


Figure 1. Hematology parameters across varying DVI severity (A–D).

Leukopenia is attributed to bone marrow suppression, stemming from either direct viral infection or the indirect impact of proinflammatory cytokines. Its peak is typically reached just before fever subsidence, with a return to normal levels within 2-3 days after defervescence (Masihor, et al., 2013). Notably, this study identified leukocytosis in three patients, potentially linked to a urinary tract infection in one patient. Elevated leukocyte counts are indicative of a systemic inflammatory response, with leukocytosis also associated with bacterial infections, typically manifesting as mild to moderate increases (11,000 - 30,000/ $\mu$ L) (Riley & Rupert, 2015; Lorensia, et al., 2016).

Hemoconcentration is a recognized phenomenon associated with complement activation in dengue patients, particularly through C3a and C5a, which can enhance immune cell chemotaxis and inflammatory responses, potentially causing plasma leakage (Bhatt, et al., 2021). However, this study did not observe a significant difference in hemoconcentration. Most pediatric dengue patients with normal hematocrit levels exhibited this condition, with the highest severity observed in DF at 42.9% and the lowest in DHF grade IV at 4.8%. Similarly, prior studies by Hidayat, et al., (2021) reported predominantly normal hematocrit levels, which can be influenced by factors such as intravenous fluid administration before referral to a referral hospital like Dr. Soetomo General Academic Hospital, Surabaya. In this study, twelve patients recorded sequentially low hematocrit levels, likely indicating severe bleeding based on decreasing platelet counts. The normal or low hematocrit values may be attributed to bleeding or anemia, affecting the red blood cell count and consequently influencing the hematocrit value (Kusdianto, et al., 2021).

In dengue infection, heightened hemoglobin levels, typically due to hemoconcentration resulting from plasma leakage, are well-documented (Ralapanawa, et al., 2018). This study reveals a significant difference in hemoglobin levels. However, most pediatric dengue patients with normal hemoglobin concentrations displayed this condition. The investigation identified that the highest prevalence of normal hemoglobin levels was evident in pediatric patients with DF at the most severe classification (50%), contrasting with the lowest prevalence observed in DHF grade IV cases (2.5%). These findings aligned with earlier research where hemoglobin assessments predominantly reported normal levels (Vebriani, et al., 2016; Hidayat, et al., 2021). The observed variation may be attributed to the influence of rapid fluid administration in hospital settings (Rosenberger, et al., 2016). Identifying nine patients with low hemoglobin levels in this study was noteworthy. These results substantiated the notion that hemoglobin levels had parallel alterations in hematocrit values and, in severe cases, indicated bleeding and anemia (Handayani, et al., 2022).

### **Strength and limitations**

Investigating dengue virus infections (DVI) among pediatric patients at a tertiary hospital of Dr. Soetomo General Academic Hospital in Surabaya in 2019 was challenging. The study's reliance on secondary data from medical records meant that the researchers were distanced from directly observing outcomes. This constraint underscores the need for a cautious interpretation of the results, recognizing the inherent limitations of using pre-existing medical records. Furthermore, the study grapples with constraints in the methodology related to blood sample collection. The limit of acquiring blood samples only once hindered the ability to fully capture the dynamic changes in hematology profiles over time. A continuous and longitudinal data collection approach would be more appropriate to provide a more comprehensive and nuanced understanding of these profiles. This would allow for a more accurate representation of the fluctuations in hematology parameters, contributing to a richer comprehension of the disease progression within specific timeframes. Additionally, the study faces challenges in determining the duration of fever, relying on patients' self-diagnosis. This introduces an element of subjectivity and potential variability in reporting, affecting the precision of the data related to the duration of fever in the analysis. In summary, while the study endeavors to shed light on the hematology aspects and severity of DVI in pediatric patients, it is crucial to acknowledge and consider these limitations in interpreting findings. Recognizing these constraints is fundamental in ensuring a balanced and informed understanding of the implications and applications of the research outcomes.



## CONCLUSION

Mild thrombocytopenia was predominant in Dengue Fever (DF). In contrast, severe thrombocytopenia was most prevalent in Dengue Hemorrhagic Fever (DHF) grade III, which corresponds with the escalating severity of dengue virus infection and accelerated shock events. Leukopenia was prominent in DF patients. There were significant differences in platelets and hemoglobin levels across different severity of DVI. However, no significant differences were observed between leukocyte and hematocrit with the seriousness of DVI. Overall, these findings contribute valuable insights into the hematology manifestations of pediatric dengue infections, paving the way for enhanced clinical management and diagnostic criteria refinement.

## Acknowledgment

The authors extend their heartfelt gratitude to all participants who willingly participated in this study. Additionally, sincere appreciation is conveyed to the Department of Pediatrics of Dr. Soetomo General Academic Hospital for granting necessary permissions during the data collection process.

## Conflict of Interest

All authors have no conflict of interest.

## Ethic Consideration

The protocol of this study has been approved by the Health Research Ethics Committee of Dr. Soetomo General Hospital with a reference number of 1229/LOE/301.4.2/II/2023 on 16-02-2023.

## Funding Disclosure

This study did not receive any funding.

## Author Contribution

AFS, J, DP, and DH contributes to analysis and interpretation of the data; drafting of the article; critical revision of the article for important intellectual content; final approval of the article; provision of study materials or patients; and statistical expertise. AFS, J, DP contributes to conception and design; and administrative, technical, or logistic support. AFS contributes to collection and assembly of data.

## REFERENCES

- Aini, Z. M., Arimaswati, A., Rezika, M. F. 2016. Hubungan rerata hasil pemeriksaan laboratorium terhadap derajat klinis infeksi virus dengue pada pasien anak di Rumah Sakit Santa Anna Tahun 2016. Seminar Nasional Teknologi Terapan Berbasis Kearifan Lokal, 2(1): 517–522. Available at: <http://ojs.uho.ac.id/index.php/snt2bkl/article/download/9725/7055>.
- Bhatt, P., Sabeena, S. P., Varma, M., et al. 2021. Current understanding of the pathogenesis of dengue virus infection. *Current Microbiology*, 78(1): 17–32. doi: [10.1007/s00284-020-02284-w](https://doi.org/10.1007/s00284-020-02284-w).
- Buntubatu, S., Arguni, E., Indrawanti, R., et al. 2017. Status nutrisi sebagai faktor risiko sindrom syok dengue. *Sari Pediatri*, 18(3): 226. doi: [10.14238/sp18.3.2016.226-32](https://doi.org/10.14238/sp18.3.2016.226-32).
- Chaloemwong, J., Tantiworawit, A., Rattanathammethee, T., et al. 2018. Useful clinical features and hematological parameters for the diagnosis of dengue infection in patients with acute febrile illness: a retrospective study. *BMC Hematology*, 18(1): 20. doi: [10.1186/s12878-018-0116-1](https://doi.org/10.1186/s12878-018-0116-1).
- Chong, V., Tan, J. Z. L., Arasoo, V. J. T. 2023. Dengue in pregnancy: A Southeast Asian perspective. *Tropical Medicine and Infectious Disease*, 8(2): 86. doi: [10.3390/tropicalmed8020086](https://doi.org/10.3390/tropicalmed8020086).
- Giri, R., Agarwal, K., Verma, S., et al. 2016. A study to correlate level of thrombocytopenia with dengue seropositive patients and frequency of bleeding pattern. *Scholars Journal of Applied Medical Sciences (SJAMS)*, 4(1c): 214–218. doi: [10.36347/sjams.2016.v04i01.040](https://doi.org/10.36347/sjams.2016.v04i01.040).
- Guillena, J. B., Opena, E. L. L., Baguio, M. L. 2013. Prevalence of dengue fever (DF) and dengue hemorrhagic fever (DHF): A description and forecasting in Iligan City, Philippines. *Mindanao Journal of Science and Technology*, 11(1). Available at: <https://ejournals.ph/article.php?id=10502>.
- Handayani, N. M. D., Udiyani, D. P. C., Mahayani, N. P. A. 2022. Hubungan kadar trombosit, hematokrit, dan hemoglobin dengan derajat demam berdarah dengue pada pasien anak yang rawat

- inap di BRSU Tabanan. *AMJ (Aesculapius Medical Journal)*, 2(2): 130–136. Available at: <https://www.ejournal.warmadewa.ac.id/index.php/amj/article/view/5304>.
- Hidayat., Triwahyuni, T., Zulfian, Z., et al. 2021. Comparison of hematological abnormalities between primary and secondary dengue infection patient at Regional General Hospital Dr. H. Abdul Moeloek, Lampung. *Jurnal Ilmu dan Teknologi Kesehatan Terpadu (JITKT)*, 1(1): 28–37. doi: [10.53579/jitkt.v1i1.9](https://doi.org/10.53579/jitkt.v1i1.9).
- IBM Corp. 2019. IBM SPSS statistics for windows, version 26.0. Armonk, NY: IBM Corp
- Kusdianto, M. M., Asmin, E., Latuconsina, V. Z. 2021. Hubungan jumlah hematokrit dan trombosit dengan derajat keparahan pasien infeksi dengue di RSUD DR. M. Haulussy Ambon periode 2019. *PAMERI: Pattimura Medical Review*, 2(2): 127–144. doi: [10.30598/pamerivol2issue2page127-144](https://doi.org/10.30598/pamerivol2issue2page127-144).
- Laily, F. I., Rossyanti, L., Sulistiawati. 2020. The effect of DHF education on DHF prevention knowledge of 5<sup>th</sup> and 6<sup>th</sup> grade students of SDN Purwotengah II Mojokerto. *Juxta: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga*, 11(2): 51-55. doi: [10.20473/juxta.V11I22020.51-55](https://doi.org/10.20473/juxta.V11I22020.51-55).
- Laoprasopwattana, K., Binsaai, J., Pruekprasert, P., et al. 2017. Prothrombin time prolongation was the most important indicator of severe bleeding in children with severe dengue viral infection. *Journal of Tropical Pediatrics*, 63(4): 314–320. doi: [10.1093/tropej/fmw097](https://doi.org/10.1093/tropej/fmw097).
- Lorensia, A., Ikawati, Z., Andayani, T. M., et al. 2016. Post-therapy leukocytosis events after intravenous aminophylline compared to the nebulized salbutamol in asthma exacerbations patients. *Indonesian Journal of Clinical Pharmacy*, 5(3): 149–159. doi: [10.15416/ijcp.2016.5.3.149](https://doi.org/10.15416/ijcp.2016.5.3.149).
- Marvianto, D., Ratih, O. D., Nadya Wijaya, K. F. 2023. Infeksi dengue sekunder: Patofisiologi, diagnosis, dan implikasi klinis. *Cermin Dunia Kedokteran*, 50(2): 70–74. doi: [10.55175/cdk.v50i2.518](https://doi.org/10.55175/cdk.v50i2.518).
- Masihor, J. J. G., Mantik, M. F. J., Memah, M., et al. 2013. Hubungan jumlah trombosit dan jumlah leukosit pada pasien anak demam berdarah dengue. *e-Biomedik*, 1(1). doi: [10.35790/ebm.1.1.2013.4152](https://doi.org/10.35790/ebm.1.1.2013.4152).
- Mikhael, K., Husada, D., Lestari, P., 2022. Profile of dengue fever complication in infant at Tertiary Referral Hospital in East Java, Indonesia. *Biomolecular and Health Science Journal*, 5(1): 11–15. doi: [10.20473/bhsj.v5i1.34827](https://doi.org/10.20473/bhsj.v5i1.34827).
- Minister of Health of The Republic of Indonesia. 2019. Profil kesehatan Indonesia tahun 2019. Jakarta: Kementerian Kesehatan Republik Indonesia. Available at: [https://www.kemkes.go.id/app\\_asset/file\\_content\\_download/Profil-Kesehatan-Indonesia-2019.pdf](https://www.kemkes.go.id/app_asset/file_content_download/Profil-Kesehatan-Indonesia-2019.pdf).
- Ralapanawa, U., Alawattegama, A. T. M., Gunrathne, M., et al. 2018. Value of peripheral blood count for dengue severity prediction. *BMC Research Notes*, 11(1): 400. doi: [10.1186/s13104-018-3505-4](https://doi.org/10.1186/s13104-018-3505-4).
- Riley, L. K., Rupert, J. 2015. Evaluation of patients with leukocytosis. *American Family Physician*, 92(11): 1004–11. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26760415>.
- Rosenberger, K. D., Lum, L., Alexander, N., et al. 2016. Vascular leakage in dengue – clinical spectrum and influence of parenteral fluid therapy. *Tropical Medicine & International Health*, 21(3): 445–453. doi: [10.1111/tmi.12666](https://doi.org/10.1111/tmi.12666).
- Silitonga, P., Dewi, B. E., Bustamam, A., et al. 2020. Correlation between laboratory characteristics and clinical degree of dengue as an initial stage in a development of machine learning predictor program. in, p. 030008. doi: [10.1063/5.0023932](https://doi.org/10.1063/5.0023932).
- Surabaya City Health Office. 2020. Profil kesehatan 2019. Surabaya. Available at: [https://dinkes.surabaya.go.id/portalv2/dokumen/Profil Kesehatan Kota Surabaya 2019.pdf](https://dinkes.surabaya.go.id/portalv2/dokumen/Profil%20Kesehatan%20Kota%20Surabaya%202019.pdf).
- Vebriani, L., Wardana, Z., Fridayanti. 2016. Karakteristik hematologi pasien demam berdarah dengue di bagian penyakit dalam RSUD Arifin Achmad Provinsi Riau periode 1 Januari – 31 Desember 2013. *Jurnal Online Mahasiswa Fakultas Kedokteran Universitas Riau*, 3(1). Available at: <https://www.neliti.com/id/publications/189003/karakteristik-hematologi-pasien-demam-berdarah-dengue-di-bagian-penyakit-dalam-r>.
- Wardhani, P., Yohan, B., Tanzilia, M., et al. 2023, Genetic characterization of dengue virus 4 complete genomes from East Java, Indonesia. *Virus Genes*, 59(1): 36-44. doi: [10.1007/s11262-022-01942-4](https://doi.org/10.1007/s11262-022-01942-4).
- Wisanti, R., Gongga, V. N., Hartanto, W., et al. 2022. Referat jumlah leukosit sebagai prediktor perburukan trombositopenia pada pasien demam dengue anak. *Jurnal Health Sains*, 3(2): 289–297. doi: [10.46799/jhs.v3i2.426](https://doi.org/10.46799/jhs.v3i2.426).
- World Health Organization. 2022. Guidelines for the clinical diagnosis and treatment of Dengue, Chikungunya, and Zika. WHO. Available at: <https://www.who.int/publications/i/item/978927>



5124871.

World Health Organization. 2023. Dengue and severe dengue. WHO. Available at: <https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>.

Yanti, E. L., Suryawan, I. W. B., Widiassa, M. 2021. Hubungan derajat leukopenia terhadap tingkat keparahan penyakit Demam Berdarah Dengue (DBD) pada pasien anak yang dirawat di Ruang Kaswari RSUD Wangaya, Denpasar, Indonesia. *Intisari Sains Medis*, 12(3): 908–911. doi: [10.15562/ism.v12i3.1160](https://doi.org/10.15562/ism.v12i3.1160).