

Albumin globulin ratio in children with dengue virus infection at Prof. Dr. R. D. Kandou Hospital, Manado Indonesia

by Novie Rampengan

Submission date: 02-Feb-2023 10:21AM (UTC+0700)

Submission ID: 2004516340

File name: Albumin_globulin_ratio_in_children_with_dengue.pdf (615.18K)

Word count: 4809

Character count: 23272



Published by DiscoverSys

Albumin globulin ratio in children with dengue virus infection at Prof. Dr. R. D. Kandou Hospital, Manado Indonesia



CrossMark

Novie Homenta Rampengan,^{1*} Dasril Daud,² Sarah Warouw,¹ Idham Jaya Ganda²

ABSTRACT

Backgrounds: Dengue virus infection (DVI) consists of mild-to-severe manifestations. The increasing hematocrit of 20% is used for detecting leakage of plasma, but it is a single parameter that is easily influenced by certain factors. It is necessary to examine the ratio of albumin/globulin which is more stable. The purpose of this study is to find out the ratio of albumin/globulin against various degrees of DVI.

Methods: This is an analytic observational study with a cross-sectional and prospective cohort. The study was conducted at the Prof. Dr. R.D. Kandou Hospital, Pancaran Kasih Hospital, and R.W. Monginsidi Hospital from March 2013 to October 2014. The sample is obtained from at least 38 children for each group of DVI. Data were analyzed using SPSS 15, with significant value at $p \leq 0.05$.

Results: There were 164 children with DVI during the study, but we analyzed only 39 patients with DF, 39 patients with DHF, and 41 patients with DSS. All patients with DF had a albumin/globulin ratio ≥ 1.2 , whereas 4 DHF patients and 5 DSS patients had a albumin/globulin ratio ≥ 1.2 .

Conclusions: There were significant differences in the ratio of albumin/globulin between DF, DHF, and DSS groups. It is emphasized that in the evaluation of plasma leakage using the ratio of albumin/globulin the changing levels of albumin should be considered. We should keep in mind also that there are other factors that can affect the synthesis of albumin.

Keywords: Ratio of albumin/globulin, Dengue virus infection, DF, DHF, DSS

Cite This Article: Rampengan, N.H., Daud, D., Warouw, S., Ganda, I.J. 2017. Albumin globulin ratio in children with dengue virus infection at Prof. Dr. R. D. Kandou Hospital, Manado Indonesia. *Bali Medical Journal* 5(3): 562-567. DOI:10.15562/bmj.v5i3.569

¹Department of Child Health, Medical School, Sam Ratulangi University, Manado, Indonesia

²Department of Child Health, Medical School, Hasanuddin University, Makassar, Indonesia

*Correspondence/Reprint request to: Novie Homenta Rampengan, Department of Child Health, Medical School, Sam Ratulangi University, Prof. Dr. R.D. Kandou General Hospital, Jl Raya Tanawanko, Manado 95263, Indonesia. novierampengan@yahoo.com, novierampengan@hotmail.com

Received: 30 October 2016
Accepted: 11 December 2016
Published: 29 December 2016

INTRODUCTION

Dengue virus infection (DVI), notably dengue hemorrhagic fever (DHF), is still a health threat in the world because it is a cause of serious morbidity and mortality, particularly in tropical and subtropical regions, including Indonesia.^{1,2} Each year an estimated 50 million cases of DVI with 500,000 cases of dengue and at least 24,000 cases were reported dead.^{3,4}

In Asia, DHF/dengue shock syndrome (DSS) is currently the main cause of patients admitted to hospital, with a high mortality rate ranging from 0.5 to 5%.^{5,6} In Indonesia, the incidence of DHF has increased prominently from 37.11‰ in 2004 to 60.06‰ in 2008.⁷

Dengue virus infection can cause a spectrum of clinical manifestations, varying from self-limited fever, namely dengue fever (DF), to the severe form, DHF, and can lead to shock or death.³ Theoretically, DF is a relatively mild disease whereas DHF is a disease that can be life-threatening if it is not detected or addressed adequately.⁸ The increasing of vascular permeability and vasculopathy is a sign of DHF and DSS and what distinguishes it from DF.⁹ The state of plasma leakage that occurs in DHF with shock within no more than 48 hours and generally after 48 hours

will be followed by immediate and spontaneous improvement.¹⁰

Based on the protocol of the World Health Organization (WHO) in 1997, DHF can be distinguished from the DF base on increasing hematocrit, pleural effusion, or ascites.⁸ Other way to detect the leakage of plasma is by chest X-ray, ultrasound, and hypoalbuminemia. The leakage of plasma can happen when albumin levels ≤ 3.5 g% or there are changes in albumin level of 0.5 g%.¹¹ Nevertheless, all the means mentioned above is a single parameter that can be influenced by certain factors, such as hematocrit values found normal in DVI patients with anemia, bleeding, and fluid therapy; therefore, there is a need to have more stable parameters that can be assessed using the ratio of albumin/globulin.¹² A study using the ratio of albumin/globulin was conducted on patients with systemic inflammatory response syndrome (SIRS) and on patients who suffered from burns and sepsis. The normal value of the ratio of albumin/globulin is 1.2–1.5.^{13,14} A research on the assessment of ratio of albumin/globulin conducted on people with burns were associated with severity of disease, but the research on the DVI has never been reported. Besides, it has huge clinical significance in the early detection of plasma leakage in DVI.^{13,14}

MATERIALS AND METHODS

This is an analytical observational study with a cross-sectional and prospective cohort. The study was conducted at Prof. Dr. R.D. Kandou Manado Hospital, PancaranKasih Hospital and R.W. Monginsidi Hospital from March 2013 to October 2014. The examination of blood samples was carried out in the laboratory department of Prof. Dr. R.D. Kandou Manado Hospital, Manado Clinical Laboratory and Prodia Jakarta Laboratory. The samples were obtained from at least 38 children for each study group (DF, DHF, DSS) with $\alpha = 0.05$, power 80%, and $r = 0.4$.¹⁵ The inclusion criteria were patients aged 1–15 years diagnosed with DVI (DF, DHF, DSS), which is based on WHO criteria in 1997 as well as the child and parent/guardian who agreed to provide informed consent, while the exclusion criteria on patients suffering from a viral illness or other bacteria is based on clinical examination and laboratory. However, patients who received corticosteroids and suffered poor nutrition and obesity as well as DSS patients who were referred and having hospital admission showing the signs of shock were not found. There is also criteria of drop-out, namely a blood sample lysis, wherein patients whose parents refused to do a second blood

sampling (48 hours after the first blood sample/in case of worsening) or third blood sample (48 hours after the deterioration).

Initial blood sampling was taken when patients were diagnosed with DF, DHF, and DSS; the second blood sampling was performed when patients experienced worsening within a duration ≥ 48 hours after the initial/first blood sampling. The third blood sampling was done within a period ≥ 48 hours after the second blood sampling. This study was approved by the Department of Biomedical Research Ethics Committee Prof. Dr. R.D. Kandou Manado Hospital. We compared the ratio of albumin/globulin from first blood samples between DF, DHF, and DSS. We then compared the ratio at the beginning from the first blood sampling to second/third blood sampling. There was a leakage in plasma when the ratio of albumin/globulin < 1.2 . Data were analyzed using a statistical software package, version 15 (SPSS 15); with chi-square test and one way t-test. It is said to be significant if the p value ≤ 0.05 .

RESULTS

During the study period, there were 164 children with DVI treated in hospital. After anamnesis and

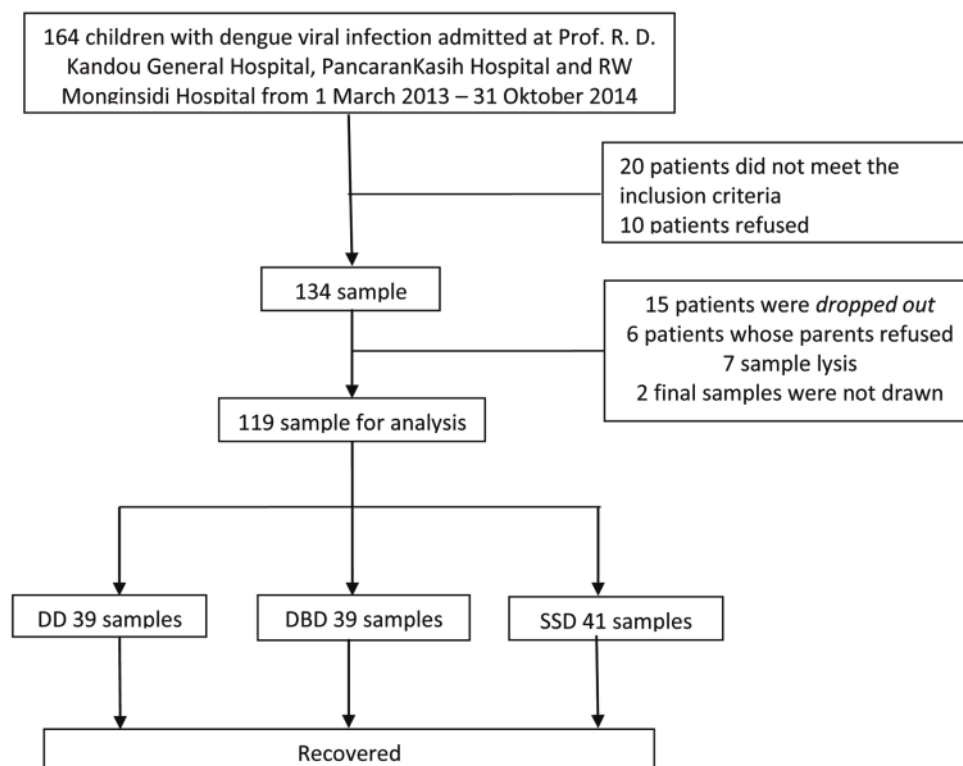


Figure 1 The study population

further inspection, there were 20 children who did not meet the inclusion criteria and 10 children whose parents who did not agree; therefore, the remaining samples of the study were 134. Furthermore, 15 samples were dropped out since 6 parents/guardians refused, 7 samples were lysis, and 2 blood samples were both unsuccessfully taken so that the remaining 119 samples were divided into 3 groups consisting of 39 patients with DF, 39 patients with DHF, and 41 patients with DSS for analysis. At the end of the study, all the subjects of the study were healed (Figure 1).

In the study planned, the blood sampling was taken 3 times from the subject in case of clinical deterioration from DF to DHF or from DHF to DSS. During the study period, there were no subjects who experienced clinical deterioration, so that the samplings of all study subjects were only taken 2 times, namely initial blood samples diagnosed for DVI (DF, DHF, DSS) and ≥ 48 hours later.

Characteristics of the study sampling based on the severity of DVI (DF, DHF, DSS) can be seen in Table 1 below.

Table 1 Characteristics of the study sampling based on the severity of the dengue viral infection (DF, DHF, DSS)

Variable	DF (n = 39)	DHF (n = 39)	DSS (n = 41)	P
Gender (%)				
Man	17 (43.6)	15 (38.5)	19 (46.3)	0.385*
Women	22 (56.4)	24 (61.5)	22 (53.7)	
Nutritional status (%)				
Under weight	7 (17.9)	7 (17.9)	8 (19.5)	0.978*
Good nutrition	32 (82.1)	32 (82.1)	33 (80.5)	
Age (year)				
Average	7.76	8.95	7.06	0.011**
SD	3.00	2.51	2.87	
95% CI	6.68–8.63	8.14–9.77	6.15–7.97	
Median	7.92	8.92	6.5	
Span	1.42–12.92	4–13.3	2.08–12.3	
Interval of fever (day)				
Rerata				
SD	2.6	4.1	4.4	<0.001**
95% CI	0.60	0.8	0.7	
Median	2.37–2.76	3.84–4.37	4.2–4.63	
Span	3.00	4	4	
Laboratorium	1–3	3–6	4–6	
Blood sample I				
Hematokrite, %	36.99 (3.43)	42.59 (2.99)	45.35 (3.44)	
Albumin, g/dl	3.88 (0.41)	3.39 (0.51)	2.63 (0.54)	
Globulin, g/dl	3.06 (0.37)	3.79 (0.84)	3.51 (1.23)	
Albumin/Globulin	1.31 (0.15)	0.94 (0.26)	0.85 (0.32)	
Blood sample II				
Hematokrite, %	36.76 (3.35)	35.79 (2.8)	35.34 (2.77)	
Albumin, g/dl	3.89 (0.48)	3.81 (0.4)	3.51 (0.54)	
Globulin, g/dl	3.12 (0.54)	3.14 (0.67)	3.05 (0.81)	
Albumin/Globulin	1.29 (0.32)	1.25 (0.28)	1.21 (0.31)	

Ket: SD = standard deviation * = χ^2 test (Chi Square) ** = one way ANOVA test

Table 1 shows that there were no significant differences in gender distribution and nutritional status ($p > 0.05$). Of the entire samples obtained, there were 51 boys who were classified as follows: 17 in the DF group, 15 in the DHF group, and 19 in the DSS group. More females were found than males in each group, with 22 children in the DF group, 24 in the DHF group, and 22 in the DSS group. Based on nutritional status, we found that the research samples were dominated by good nutrition (81.5%). The distribution of good nutritional status based on group was obtained, with 32 children in DF and DHF group, respectively, and 33 children in the DSS group.

All the subjects were in the age range of 1.42–13.3 years, with the mean age of patients with DF at 7.76 (SD 3.0) years, mean age of patients with DHF at 8.95 (SD 2.51) years, and the mean age of patients with DSS at 7.06 (SD 2.87) years. The ANOVA test results of the patients' age show that there is a significant difference between the DF, DHF, and DSS groups, with $p = 0.011$ ($p < 0.05$), followed by Benferroni test. Those experiencing DHF were older than those who have DF or DSS. In the age group of DF and DHF, and DF and DSS, there are no significant differences, with $p = 0.128$ and $p = 1.000$ ($p > 0.05$), respectively, while in the age group of DHF and DSS there was a significant difference, with $p = 0.009$ ($p < 0.01$).

Result of the ANOVA for duration of fever showed there was a very significant difference between the DF, DHF, and DSS groups, with $p < 0.001$ ($p < 0.01$), followed by Benferroni test. There was a very significant difference with $p < 0.001$ ($p < 0.01$) in duration of fever in DF and DHF group, and DF and DSS group, whereas in DHF and DSS group there was no significant difference, with $p = 0.147$ ($p > 0.05$).

Table 1 shows that in the initial/first blood sampling at DF group, there was no hemoconcentration based on hematocrit level whereas in the DHF and DSS group there was hemoconcentration which was equal to the ratio of albumin/globulin in the DF group, which was ≥ 1.2 and for the DHF and DSS group the majority ratio of albumin/globulin was < 1.2 . In the second blood samples obtained, there was no hemoconcentration from hematocrit or the ratio of albumin/globulin on DF, DHF, or DSS group.

Based on the above results, we found that there was no difference in the ratio of albumin/globulin in the second blood samples of the patients with DF, DHF, and DSS; therefore, the comparative analysis of the ratio of albumin/globulin between the first and second blood sample in DF, DHF, and DSS group was not conducted. However, analysis of the ratio of albumin/globulin with varying degrees of

Table 2 Analysis of the relationship of albumin/globulin <1.2 and ≥ 1.2 with clinical degree of dengue viral infection (DF, DHF, DSS)

The degree of clinical	Albumin/globulin		<i>p</i> *
	<1.2 (<i>n</i> = 71)	≥ 1.2 (<i>n</i> = 48)	
DF	0	39	<0.001
DHF	35	4	
DSS	36	5	

*X² test

clinical dengue (DF, DHF, DSS) on a sample of the first group (Table 2) was conducted.

Table 2 shows there was a significant relationship between the ratio of albumin/globulin <1.2 and the ratio of albumin/globulin ≥ 1.2 patients with clinical degrees of DVI (DF, DHF, DSS). In the DF group, none had a ratio of albumin / globulin <1.2. In the DHF group there were 4 of the 39 patients, and in DSS group there were 5 of 41 patients that had the ratio of albumin/globulin ≥ 1.2 .

DISCUSSION

Dengue virus infection is a dangerous viral infection transmitted to humans through mosquito bites. Clinical spectrum of DVI varies from DF to a small portion to life-threatening disorder characterized by hemostasis, endothelial permeability, thrombocytopenia, and coagulation (DHF). Vascular leakage is a characteristic of DHF which indicates the presence of vascular endothelial damage. Changes in vascular permeability can trigger hypovolemic shock known as DSS.

Data on patient characteristics of the study in DVI (DF, DHF, DSS) show that there were more females than males in the age range of 6–10 years (Table 1). A study in Semarang showed more females (14 out of the 26 children, 53.8%) suffered from DHF and DSS (16 out of 23 children, 69.6%).¹⁶ The opposite was found in a study in Brazil; there were more male patients in the group without plasma leakage (33 out of 56 children, 59%), with plasma leakage (31 out of 49 children, 63%), and the group of healthy children (9 out of the 15 children, 60%).¹⁷

Based on the age of the subjects, we found significant differences in mean age between the DF, DHF, and DSS groups, with a mean age of 7–9 years. Age is one factor that influences the susceptibility to DVI. In Indonesia, Philippines, Thailand, and Malaysia, DHF affects mostly children during the age span of 5–9 years.¹⁸ These results are similar with the results of a study conducted in Jakarta, wherein it was found that the highest percentage of dengue cases was noticed in children in the age group of 5–14

years (36%), followed by those aged below 5 years (31%), those in the age range of 15–44 years (22%), and those aged above 45 years (11%).¹⁹ Several studies were reported that young age is associated with the occurrence of DSS.^{20,21} A study in Denpasar reported the mean age of subjects with DSS group 7.5 (SD 2.5) years,²² and a study in Semarang found a mean age of 8 years (range 6–10 years) for both subjects with DHF and with DSS.¹⁶

Shock in patients with DHF is more common in children with good nutritional status; it is associated with increased antigen antibody reaction resulting in more severe infection.^{18,23} This study found a different result; there was no effect of the nutritional status on DVI. This is due to the characteristic of the study sample. This study shows the frequencies of DF, DHF, and DSS were more common in children with good nutritional status (80%) compared to those with malnutrition status (20%). Studies in Thailand and Vietnam showed a significant association between nutritional status and severity of dengue; the risk for complications of dengue in normal children is 3.2 times higher compared to malnourished children.²⁴ The same result was reported by two other researchers who showed obesity as a risk factor in the severity of dengue.^{25,26} This is in contrast to the studies in Latin America, El Salvador, which did not see the connection between nutritional status and the severity of dengue.²⁷

The duration of fever determines the clinical course of DHF and the ratio of albumin/globulin. In the early days of DHF, dengue virus viremia was still going on and the infected macrophages produced cytokines.²⁸ This study shows a very significant difference of duration of fever between DF (2.56 days), DHF (4.1 days), and DSS (4.41 days) groups. This is similar to a study in Brazil which showed a significantly different duration of fever in patients with plasma leakage compared to patients without plasma leakage in DVI.¹⁷

Furthermore, the study results show that all patients in the DF group (39 subjects) did not experience leakage of plasma, whereas those in the DHF group (39 subjects) and DSS group (41 subjects) had plasma leakage with one or more markers of plasma leakage according to WHO criteria, 1997. The grouping of patients into DHF and DSS is based on several clinical and laboratory parameters of DHF/DSS according to WHO criteria, 1997. Moreover, there is an increase in hematocrit $\geq 20\%$ and the presence of pleural effusion or RLD photo and/or thickening of the gallbladder/ascites on ultrasound. Hematocrit can be influenced by the presence of anemia, bleeding, hydration status, fluid, and often we do not have the initial laboratory data that can be used as the initial benchmark. Chest X-ray also

has weaknesses. It can only detect the presence of fluid effusion in a relatively large number and it is difficult to do in series (for ethical reasons, no additional information on the diagnosis and treatment of patients was collected and thus there may have been technical difficulties during diagnosis. The abdominal ultrasound in this study also was not performed on all patients because of the technical difficulties of implementation. The use of the ratio of albumin/globulin, hematocrit, albumin, and the differences in albumin, x-rays, and ultrasound are the parameters of plasma leakage that should be interpreted with the same time, to improve the accuracy of these parameters as a marker of plasma leakage.²⁹⁻³²

Moreover, in this study, in the DF group there was no subject that had a ratio of albumin/globulin <1.2, while in the DHF and DSS group we found 4 patients and 5 patients, respectively, who had albumin/globulin ≥ 1.2 . This is possible because the parameter of albumin/globulin can be influenced by the severity of leakage of albumin and globulin plasma, so that both can be out of the intravascular space together and cannot meaningfully reduce the levels of albumin/globulin. Further analysis showed that in 4 patients and 5 patients (in DHF and DSS group, respectively) had a ratio of albumin/globulin ≥ 1.2 showing albumin level <3.5 g/dl and the changing level of albumin from the beginning till the end of study at > 0.5 g/dl. This is a sign of plasma leakage by WHO criteria, 2011. In this case, in evaluating plasma leakage using the ratio of albumin/globulin we should consider the levels of albumin and the changing level of albumin. We should keep in mind also that there are other factors that affect the synthesis of albumin. In this study, it is found out that duration of fever influenced the ratio of albumin/globulin.³⁰

Albumin molecule has a smaller size (69 kDa) compared to globulin molecules (90–156 kDa), resulting in the state of increased vascular permeability; the albumin has relatively more leakage than globulin at an early stage; consequently, the ratio of albumin and globulin was reversed. In more severe cases an increasing pore size of the blood vessels can lead to leakage of good albumin and globulin molecules, thus resulting in no reversal in the ratio of albumin and globulin.¹⁴

In addition, albumin and globulin were affected by vascular permeability, and by the reduction of synthesis, by reduction through the gastrointestinal tract and kidneys, as well as by reducing the lymphatic backflow.³³

In [24](#)'s study, the ratio of serum albumin/globulin was significantly different between the DF, DHF, and DSS groups. The ratio of serum levels of initial/first albumin/globulin in DHF and DSS

groups was significantly lower than the DF group. Dengue shock syndrome group has a lower ratio of the initial serum albumin/globulin than the DHF group but this difference was not significant.

This study also shows that there was a decrease in the ratio of the initial levels of albumin/globulin in all groups at different degrees. According to Wills, a light increase in the capillary permeability results in relatively slow leakage of albumin and gives time to activate the mechanism of regulation of homeostasis compared to the massive leak. If the leak exceeds the capacity of regulation, there will be hemoconcentration followed by cardiovascular disorders. Thus, in DF the capillary leak was light or only small, so hemoconcentration did not occur. Wills also reports that the levels of IgG, transferrin, and albumin in patients with secondary DVI will be reduced in patients who experienced shock than those who are in convalescence. There are significant differences in the levels of albumin in moderate-to-severe shock patients because they had lower albumin levels than patients who experienced only a mild shock.^{34,35}

REFERENCES

1. Kurane I. Dengue hemorrhagic fever with special emphasis on immunopathogenesis. *Comp ImmunolMicrobiol Infect Dis*2007; 30:329-40.
2. Srikiatkachorn A. Plasma leakage in dengue hemorrhagic fever. *ThromHaemost* 2009;102:1042-9.
3. Hottz E, Tolley ND, Zimmerman GA, Weyrich AS, Bozza FA. Platelets in dengue infection. 2011. DDMECdoi: 10.1016/j.ddmec.2011.09.001.
4. Dewi BE, Takasaki T, Kurane I. Peripheral blood mononuclear cells increase the permeability of dengue virus-infected endothelial cells in association with downregulation of vascular endothelial cadherin. *J Gen Virol*2008; 89:642-52.
5. WHO. Dengue, dengue haemorrhagic fever and dengue shock syndrome in the context of the IMCI. [6](#)HO-FCH-CAH 2005.
6. Sosohtikul D, Seksrn P, Pongsewalak S, Thisyakorn U, Lusher J. Activation of endothelial cells, coagulation and fibrinolysis in children with Dengue virus infection. *Thromb Haemost* 2007; 97:627-34.
7. Ministry of Health Indonesia. Indonesian Health Profile 2008.
8. Ng CFS, Lum LCS, Ismail NA, Tan LH, Tan CPL. Clinician's diagnostic practice of dengue infections. *J ClinVirol*2007; [5](#)202-6.
9. Bandyopadhyay S, Lum LCS, Kroeger A. Classifying dengue: a review of the difficulties in using the WHO cases classification for dengue hemorrhagic fever. *Trop Med IntHealth*2006; 8:1238-55.
10. Srikiatkachorn A, Ajariyakhajorn C, Endy TP, et al. Virus-induced decline in solublevascular endothelial growth-receptor 2 is associated with plasma leakage in dengue-hemorrhagic fever. *J Virol* 2007; 81: 1592-600.
11. Kalayanaroj S. Dengue classification: Current WHO vs the newly suggested classification for better clinical application? *J Med AssocThai*2011; 94(3):74-84.
12. Mitchel M, Djamiatun K, Faradz SMH, Koenders MMJE, de Mast Q, Van der Ven AJAM. High plasma mid regional pro-andrenomedulin levels in children with severe dengue virus infections. *J ClinVir*2011; 50:8-12.

13. Kumar P, D'Souza J, Bhaskara KG, Bharadwaj S. Serum protein level in conjunction with serum albumin/globulin ratio as an indicator of severity of changes in capillary permeability. *Burns* 2003; 29:628-9.
14. Kumar P. Grading of severity of the condition in burn patients by serum protein and albumin/globulin studies. *Ann Plast Surg* 2010; 65(1):74-9.
15. Madiyono B, Moeslichan S, Sastroasmoro S, Budiman I, Purwanto H. Approximate sample size. Sastroasmoro S, Ismael S, ed. In: basics of clinical research methodology 4th eds. SagungSeto Jakarta 2011; 348-82.
16. Mitchel M, van der Ven AJAM, Djamiatun K, et al. Imbalance of Angiopoietin 1 and Angiopoietin-2 in severe dengue and relationship with thrombocytopenia, endothelial activation and vascular stability. *Am J Trop Hyg* 2012; 87(5):943-6.
17. Van der Weg CAM, Pannuti CS, Van den Ham HJ, et al. Serum Angiopoietin-2 and soluble VEGF receptor 2 are surrogate markers for plasma leakage in patients with acute dengue virus infection. *J Clin Virol* 2014; 60:328-35.
18. Soedarmo SP. The problem of dengue hemorrhagic in Indonesia. In: Dengue hemorrhagic fever. Book publisher faculty of medicine, Indonesia University. Jakarta. 2005.
19. Karyanti MR, Hadinegoro SR. Changes in the epidemiology of dengue hemorrhagic fever in Indonesia. *Sari Pediatri* 2009; 10:424-32.
20. Pawitan JA. Dengue virus infection: predictors for severe dengue. *Acta Med Indones* 2011; 43:129-35.
21. Guzman MG, Kouri G, Bravo J, Valdes L, Vasquez S, Halstead SB. Effect of age on outcome of secondary dengue 2 infections. *Int J Infect Dis* 2002; 6: 118-24.
22. Saniathi E, Arhana BNP, Suandi IKG, Sidiarta IGL. Obesity as a risk factor of dengue shock syndrome. *Sari Pediatri* 2009; 11:238-43.
23. Soegijanto S, Yotopranoto S, Salamun. Dengue hemorrhagic fever: overview and findings in new era 2013. Airlangga University Press. Surabaya. 2004.
24. Huang NT, Lan NT, Lei HY, et al. Association between sex, nutritional status, severity of dengue hemorrhagic fever, and immune status in infants with dengue hemorrhagic fever. *Am. J. Trop. Med. Hyg* 2005; 72:370-4.
25. Kalayanaroj S, Nimmannitya S. Is dengue severity related to nutritional status?. *Southeast Asian J Trop Med Public Health* 2005; 36(2):378-84.
26. Pichainarong N, Mongkalagoon N, Kalayanaroj S, Chaveepojnkamjorn W. Relation between bodysize and severity of dengue hemorrhagic fever among children aged 0 - 14 years. *Southeast Asian J Trop Med Public Health* 2006; 37(2):283-8.
27. Maron GM, Clara AW, Diddle JW, et al. Association between nutritional status and severity of dengue infection in children in El Salvador. *Am J Trop Med Hyg* 2010; 82:324-9.
28. Baratawidjaja KG. Basic immunology 7th eds. Faculty of Medicine, Indonesia University. Jakarta. 2006.
29. WHO. Update on the principles and use of rapid test in dengue 2009.
30. WHO. Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. 2011.
31. Rampengan TH. Tropical infectious diseases in children 2nd eds. EGC, Jakarta 2008: 122-49.
32. Hadinegoro SR, Moedjito I, Chairulfatah A. Guidelines for diagnosis and management of dengue viral infection in children. 1st eds. Book publisher from Indonesian Pediatric Association, Jakarta 2014; 37-42.
33. Liu M, Chan CP, Yan BP, Zhang Q, Lam YY, Li RJ et al. Albumin levels predict survival in patients with heart failure and preserved ejection fraction. *Eur J Heart Fail* 2012; 14(1):39-44.
34. Wills BA, Dung NM, Loan HT. Comparison of Three Fluid Solutions for Resuscitation in Dengue Shock Syndrome. *N Engl J Med* 2004; 353; 9: 877-89.
35. Luplertlop N, Misse D. MMP Cellular responses to dengue infection-induced vascular leakage. *J Infect Dis* 2008; 197:298-301.



¹ This work is licensed under a Creative Commons Attribution

Albumin globulin ratio in children with dengue virus infection at Prof. Dr. R. D. Kandou Hospital, Manado Indonesia

ORIGINALITY REPORT

11%

SIMILARITY INDEX

9%

INTERNET SOURCES

6%

PUBLICATIONS

%

STUDENT PAPERS

PRIMARY SOURCES

1	erepo.unud.ac.id Internet Source	2%
2	bmcinfectdis.biomedcentral.com Internet Source	2%
3	biomarkerres.biomedcentral.com Internet Source	1%
4	dr.ntu.edu.sg Internet Source	1%
5	Anshula Tayal, Sushil Kumar Kabra, Rakesh Lodha. "Management of Dengue: An Updated Review", Indian Journal of Pediatrics, 2022 Publication	1%
6	www.frontiersin.org Internet Source	1%
7	www.thaiscience.info Internet Source	<1%
8	docksci.com Internet Source	<1%

9

Anna Beltrame, Alessandra Arzese, Alessandro Camporese, Giada Rorato et al. "Acute Renal Failure Due to Visceral Leishmaniasis by Successfully Treated With a Single High Dose of Liposomal Amphotericin B", Journal of Travel Medicine, 2008

Publication

<1 %

10

apps.who.int

Internet Source

<1 %

11

www.paediatricaindonesiana.org

Internet Source

<1 %

12

Koichi Kikuta, Hirofumi Yasue, Michihiro Yoshimura, Etsuo Morita et al. "Increased plasma levels of B-type natriuretic peptide in patients with unstable angina", American Heart Journal, 1996

Publication

<1 %

13

brieflands.com

Internet Source

<1 %

14

qmro.qmul.ac.uk

Internet Source

<1 %

15

D. D. Chadee, B. Shivnauth, S. C. Rawlins, A. A. Chen. "Climate, mosquito indices and the epidemiology of dengue fever in Trinidad (2002–2004)", Annals of Tropical Medicine & Parasitology, 2013

Publication

<1 %

16	media.neliti.com Internet Source	<1 %
17	123dok.com Internet Source	<1 %
18	Gunadharma Suryani, Seilly Yunita Jehosua, Khosama Herlyani, Chia Zhi-Jien, Lim Kheng-Seang. "Attitudes toward epilepsy in Indonesia", <i>Epilepsy & Behavior</i> , 2021 Publication	<1 %
19	mycosphere.org Internet Source	<1 %
20	journals.sagepub.com Internet Source	<1 %
21	repository.lppm.unila.ac.id Internet Source	<1 %
22	www.canjsurg.ca Internet Source	<1 %
23	www.researchgate.net Internet Source	<1 %
24	Mei-Chuan Kuo, Po-Liang Lu, Jer-Ming Chang, Ming-Yen Lin, Jih-Jin Tsai, Yen-Hsu Chen, Ko Chang, Hung-Chun Chen, Shang-Jyh Hwang. "Impact of Renal Failure on the Outcome of Dengue Viral Infection", <i>Clinical Journal of the American Society of Nephrology</i> , 2008 Publication	<1 %

25 Yutaka Okagawa, Tetsuya Sumiyoshi, Takayuki Imagawa, Hiroya Sakano et al. "Clinical factors associated with acute abdominal symptoms induced by gastric anisakiasis: A multicenter retrospective cohort study", Research Square Platform LLC, 2023
Publication <1 %

26 hdl.handle.net
Internet Source <1 %

27 www.ijss-sn.com
Internet Source <1 %

Exclude quotes Off

Exclude matches Off

Exclude bibliography Off