

**CORRELATION OF DAYS OF FEVER AND THE NUMBER OF TROMBOSITES
ON SECONDARY AND PRIMARY DENGUE
HEMORRHAGIC FEVER INFECTION**

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ABSTRACT

Dengue Hemorrhagic Fever (DHF) is caused by four variants of the Dengue Hemorrhagic Fever (DHF) virus of the Flaviviridae family (DENV-1, DENV-2, DENV-3, and DENV-4). These four variants are indistinguishable clinically. The occurrence of platelet deterioration is sometimes not accompanied by positive IgG and IgM DHF results, nor can they be negative. In DHF sufferers, platelet decline will decrease steadily during the 3rd to 6th day and will increase on the 7th day. This research is retrospective analytical with cross sectional approach. The samples were 15 patients of Secondary DHF and 15 Primary DHF who have fulfilled the inclusion criteria. The day of fever when the patient came to the Poli Internal Medicine Dr. Soetomo Hospital is known from the patient's history, while the results of IgG and IgM DHF examination and platelet count are performed in KLINIKA Surabaya laboratory. The result of this study used correlation parametric test (Pearson's test), to know the relationship of day of fever and platelet count in Secondary and Primary DHF patients with $\alpha = 0,05$. Result of day of fever with $p = .659$ ($p > 0.05$). The result of thrombocyte count with Pearson's test ($p = .042$) ($p < 0.05$) showed a correlation of platelet count between Secondary and Primary DHF patients. It was concluded that there was a significant correlation the number of platelets between Secondary and Primary DHF.

Key words: Day of fever, Platelet Count, Secondary DHF Patient, Primary DHF Patient.

INTRODUCTION

The number of Dengue Hemorrhagic Fever in 2014 until mid-December recorded in 34 provinces in Indonesia as many as 71,668 people, and 641 of them died. This figure is lower than the previous year, in 2013 with the number of people as many as 112,511 people and the number of cases died as many as 871 people (Balitbangkes, 2015).

Dengue virus until now known 4 serotypes DENV-1, DENV-2, DENV-3, and DENV-4 included in Arthropod Borne Virus (Arbovirus) group B family Flaviviridae. All four serotypes of this virus have been found in various regions in Indonesia. Research in Indonesia show that Dengue-3 is closely related to severe dengue cases

and is the most widely distributed followed by Dengue-2, Dengue-1 and Dengue-4 serotype. Incubation period usually ranges from 4-7 days followed by a sudden high fever lasting for 2-7 days. Fever can come down on the 3rd day then up again, and on the 6th or 7th day the fever suddenly goes down (Setiati TE, 2006; C.P. Simmons, 2012).

Thrombocyte count is usually found during illness between 3-7 days to about 100,000 / mm³. Platelet count decreases in patients who have been tested positive for IgG and IgM DHF or just IgG DHF or IgM DHF. Patients with negative both IgG and IgM DHF outcomes how the impression of platelet count. So far, no researcher has examined platelet count in patients with

secondary and primary DHF. Also is there day of fever difference with the decrease in platelet counts in secondary and primary DHF.

The sample of the study was obtained from inpatients in RSUD Dr. Soetomo, and platelet test were performed by Sysmex KX-21 and IgG and IgM DHF levels were performed with Bioline rapid test, and the days of fever were recorded on the patient arrival to the Hospital.

MATERIAL AND METHOD

This research is an observational analytic with cross sectional approach. The population of the study were all patient of Tropic Infection RSUD Dr. Soetomo Surabaya. All patients with fever were noted the day of fever, then IgG and IgM DHF were examined with Rapid Test, then into 2 groups with IgG and IgM DHF positive, and IgG or IgM positive is classified as secondary DHF infection, and patients with IgG and IgM DHF negative, are classified as primary DHF infection. The total sample size was 30 where the patients with secondary DBD and primary DBD were each 15 samples. The reagents used are Rapid test IgG and IgM DHF SD Bioline. Platelet examination is done automatically with Sysmex KX 21 in Klinika laboratory.

RESULTS

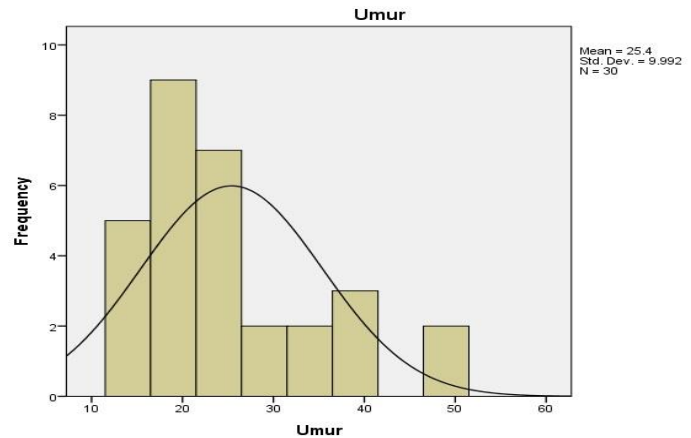


Figure 4.1 Hitogram Age of respondents where seen in the age group 17-21 years is the highest suffer from fever of secondary and primary DHF on 9 patient or 30% (9/30).

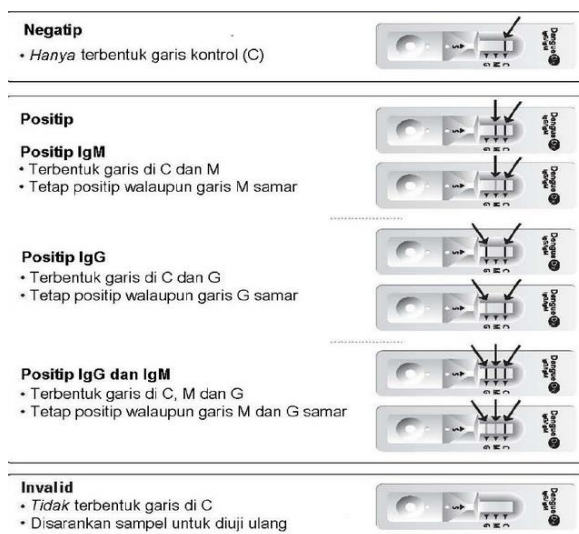
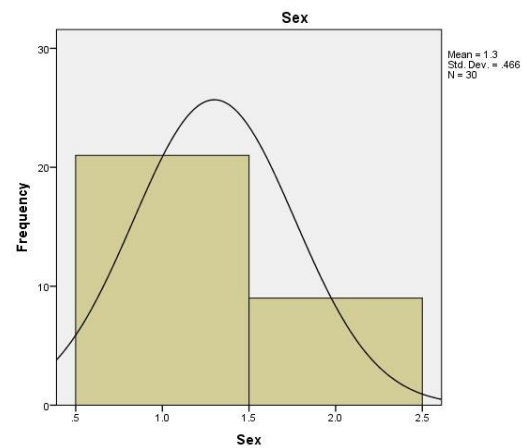


Figure The result of SD Bioline

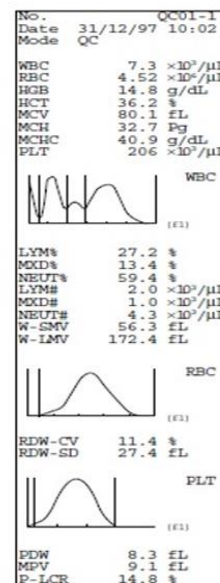


Figure 5-2-18: Example of Analysis Result Printing

Figure 4.2 Histogram Gender of respondents which seen in the group Men as many as 21 patient or 70% is highest suffered from secondary and primary DHF, while in the group of women as many as 9 patient or 30% (9/30).

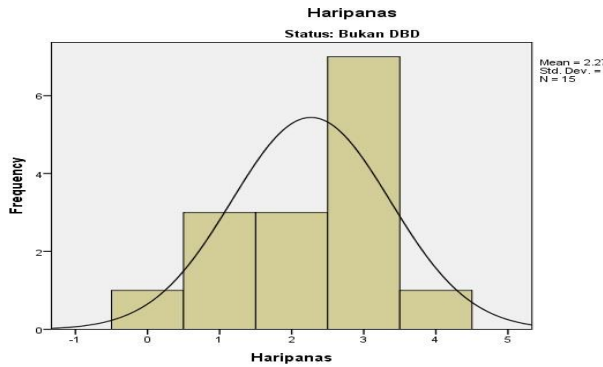


Figure 4.3 Histogram The day of fever of the primary DHF patient, which was seen in the 5th day of fever group of 7 patient or 46.7% (7/15) was the highest day of fever that came to the hospital.

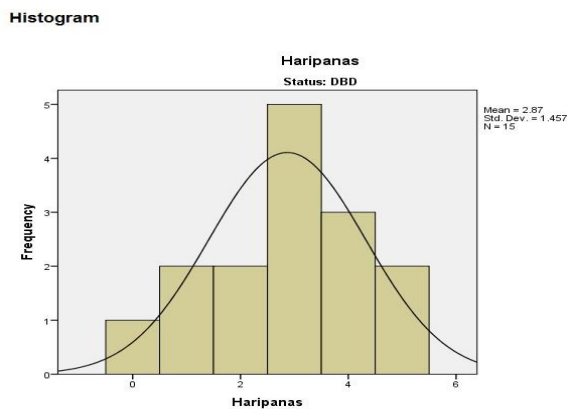


Figure 4.4 Histogram The day of fever during secondary DHF patient, which was seen 5 people in the 5th Day of fever or 33.3% (5/15) was the highest day of fever that came to the hospital.

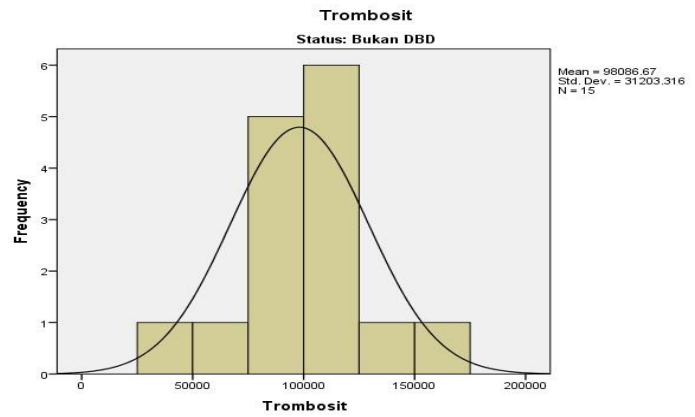


Figure 4.5 Hitogram platelet count in primary DHF patient, where seen in the platelet count group of 100,000-124,000 as many as 6 patient or 40% is the highest platelet count coming to the hospital.

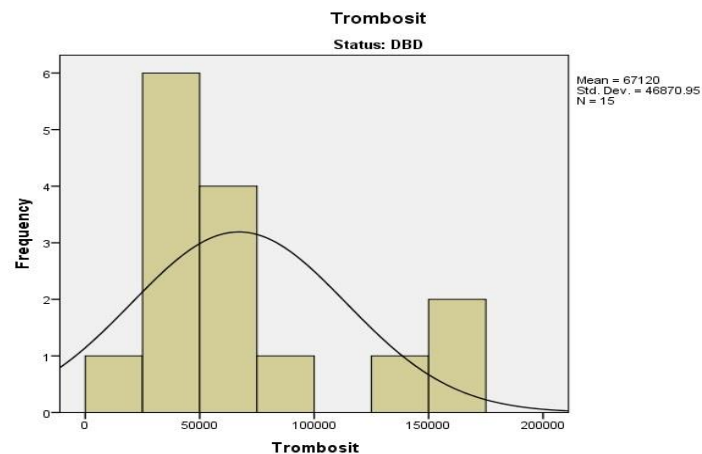


Figure 4.5 Hitogram Thrombocyte count in the secondary DBD patient, where seen in the platelet count group 25,000-49,000 as many as 6 patient or 40% is the highest platelet count coming to the Hospital.

Correlations

			Haripanas	Status	Trombosit
Kendall's tau_b	Haripanas	Correlation Coefficient	1.000	.217	-.089
		Sig. (2-tailed)	.	.196	.526
		N	30	30	30
	Status	Correlation Coefficient	.217	1.000	-.373*
		Sig. (2-tailed)	.196	.	.016
		N	30	30	30
	Trombosit	Correlation Coefficient	-.089	-.373*	1.000
		Sig. (2-tailed)	.526	.016	.
		N	30	30	30
Spearman's rho	Haripanas	Correlation Coefficient	1.000	.240	-.101
		Sig. (2-tailed)	.	.201	.597
		N	30	30	30
	Status	Correlation Coefficient	.240	1.000	-.447*
		Sig. (2-tailed)	.201	.	.013
		N	30	30	30
	Trombosit	Correlation Coefficient	-.101	-.447*	1.000
		Sig. (2-tailed)	.597	.013	.
		N	30	30	30

*. Correlation is significant at the 0.05 level (2-tailed).

Kendall's and Spearman's non parametric test results showed days of fever in secondary DBF patients and primary DHF there was no correlation in which Kendall's correlation coefficient test = -0.217; $p = 0.196$ ($p > 0.05$) and Spearman's test correlation coefficient = -0.240; $p = 0.201$ ($p > 0.05$) with weak correlation strength. Whereas the number of platelets in secondary and primary DHF there is a correlation in which the results with Kendall's correlation coefficient test = -0.373; $p = 0.016$ ($p < 0.05$) and Spearman's test correlation coefficient = -0.447; $p = 0.013$ ($p < 0.05$) show negative correlation with strong correlation strength.

DISCUSSION

The mean age of secondary DHF and primary-DHF patients was the subject of this study 25.4 years and the most sex were male, this result was in accordance with Endo Dardjito 2005 results in which age > 15 years and 72% were Men as much as 58%.

The result of the day of fever shows no significant correlation in secondary DHF and primary DHF patients, but the most the day of fever that came to RSUD Dr.

Soetomo that after experiencing the fever on the 5th day, this result is also obtained on the research Andi Alfia in 2011. It can be concluded that the people believes that if the day of fever of the fifth day does not go down and down, worrying about suffering from dengue fever. One of the typical symptoms of dengue fever is 2-7 days. These symptoms appear as the body's response to dengue virus infection and as the body's defense mechanism against DHF virus (Mayeti, 2010; Rena, 2009).

Result of research of platelet count in patient primary DHF got result of platelet count between 100.000-124.000 / mm³ and in secondary DHF sufferer got result of platelet count most between 25.000-49.000 and this result almost same with result of research of Putu Diani Wirayanti 2015 in patients with dengue fever degree I obtained 103000 / mm³ platelet mean and in dengue hemorrhagic patients grade II obtained mean platelet count were 94.000 / mm³. From the results of this study the number of platelets between secondary DHF and primary DHF patients who come to the hospital on the 5th day is very different meaningful. This suggests that in

secondary DHF patients the number of platelets count decreased to 25.000 / mm³ as a result of a second infection with different DHF virus variants. A natural infection by one of the four DENV Serotypes (DENV-1, DENV-2, DENV-3, DENV-4) produces long-lasting immunity to reinfection by the same serotype, but the heterotypic protection is temporary. This condition is called in primary infection as seen in patients with dengue fever that looks fresh and there are some people are not aware that he was once infected with the virus Dengue. In this case it may be that IgG and IgM levels have not formed or are only positive for DHF IgM alone. In the second infection, both IgG and IgM-positive IgG or IgM DHF results from IgM DHF acute phase have passed and most of these individuals will develop more severe DHF or DSS as a result of being infected by a serotype different from the first DHF infection serotype. This situation indicates that previous dengue infection has developed antibody-dependent enhancement (ADE) is a risk factor for developing more severe disease (Halstead, 1988; Cummings DAT, 2005).

In the body, the primary DHF virus antibody infects will recognize the second viral antigen DHF infection, resulting in antibody antigen bonds that will interact with complement, causing permeability of blood vessels (the ability of blood vessel walls penetrate the liquid), so that some components of fluid and white blood cells outward to body tissues, and platelet function to the wound of body platelets decreases. These events cause the results of blood tests found thrombocytopenia (decreased platelet count), leukopenia (decreased white blood cell count), and increased hemotocrit (increased blood cell concentration due to reduced blood fluid to the tissues) (BA Bouchard, 2001). Due to thrombocytopenia, people with Dengue virus infection have a blood clotting disorder that often encountered red spots on the skin called petechiae. Patients are also susceptible to bleeding such as

bleeding gums, nosebleeds, and gastrointestinal bleeding (S. B. Halstead, 1988).

CONCLUSIONS

Based on data presentation and discussion, it can be concluded that the day of fever correlates positively but not significant in secondary and primary DHF patients, but for platelet count there is negative and significant correlation in secondary and primary DHF patient. This shows the faster the number of decreased platelets occur, meaning the stage of dengue suffered more severe in secondary stage DHF is more severe than the primary DHF.

REFERENCES

- Alvarez M, Rodriguez R, Bernardo L, Vasquez S, Morier L, et al. 2006. Dengue hemorrhagic fever caused by sequential dengue 1-3 infections at a long interval: Havana epidemic, 2001–2002. *Am. J. Trop. Med. Hyg.* 75:1113–17
- Balitbangkes Pusat Komunikasi Publik Sekretariat Jenderal Kementerian Kesehatan RI. Nomor hotline <kode lokal> 500-567; SMS 081281562620, faksimili: (021) 52921669, dan alamat email kontak [at] kemkes [dot] go [dot] id.
- B. A. Bouchard and P. B. Tracy, "Platelets, leukocytes, and coagulation," *Current Opinion in Hematology*, vol. 8, no. 5, pp. 263–269, 2001
- C.P. Simmons, J. J. Farrar, N. van Vinh Chau, and B. Wills, "Current concepts: dengue," *The New England Journal of Medicine*, vol. 366, no. 15, pp. 1423–1432, 2012.
- Cummings DAT, Schwartz IB, Billings L, Schaw LB, Burke DS., 2005. Dynamic effects of antibody-dependent enhancement on the fitness of viruses. *Proc. Natl. Acad. Sci. USA* 102:15259–64.

- Favier C, Schmit D, Muller-Graf CDM, Cazelles B, Degallier N, et al. 2005. Influence of spatial heterogeneity on an emerging infectious disease: the case of dengue epidemics. *Proc. Biol. Sci.* 272:1171–77.
- Ferguson NM, Donnelly CA, Anderson RM. 1999. Transmission dynamics and epidemiology of dengue: insights from age-stratified sero-prevalence surveys. *Philos. Trans. R. Soc. London B* 354:757–68.
- J. Mongkolsapaya, W. Dejnirattisai, X.N. Xu et al. ,2003. “Original antigenic sin and apoptosis in the pathogenesis of dengue hemorrhagic fever,” *Nature Medicine*, vol. 9, no. 7, pp. 921–927.
- Ooi EE, Gubler DJ. Dengue in Southeast Asia: epidemiological characteristics and strategic challenges in disease prevention. *Cad Saude Publica*. 2008; 25: S115-S124
- Setiati TE, Wagenaar JF, de Kruif MD, Mairuhu ATA, van Gorp ECM, Soemantri A. Changing epidemiology of dengue haemorrhagic fever in Indonesia. *Dengue Bull.* 2006;30:1–14.
- SD Technical Information, 2003a. Part III. Principle, Test Method and Limitation.
- SD Technical Information, 2003b. Comparison of SD BIOLINE Dengue IgG/IgM vs Panbio “Dengue Duo IgM and IgG Rapid Strip Test”.
- S. B. Halstead, 1988. “Pathogenesis of dengue: challenges to molecular biology,” *Science*, vol. 239, no. 4839, pp. 476–481.
- Z. M. Ruggeri and G. L. Mendolicchio, 2007. “Adhesion mechanisms in platelet function,” *Circulation Research*, vol. 100, no. 12, pp.1673–1685