

## Association between Hemoconcentration and longer hospitalization day of Dengue patients

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Christine Ernita Banggai, Vivi Lisdawati, Sulianti, Dyani Kusumowardhani, Iman Firmansyah, Maya Marinda Montain

Prof. Dr. Sulianti Saroso Infectious Disease Hospital, North Jakarta, Indonesia

Corresponding address: Christine Ernita Banggai, SKM, MARS

e-mail: ita.banggai@gmail.com

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### **Abstrak**

**Latar Belakang:** Identifikasi dini kondisi klinis serta penanganan yang tepat terhadap pasien dengue merupakan hal penting untuk mencegah perkembangan penyakit menjadi lebih berat. Hal ini akan berdampak positif bagi perawatan pasien yang menjadi lebih singkat dan dengan sendirinya biaya semakin rendah. Tujuan penelitian adalah untuk mengetahui faktor-faktor yang mempengaruhi lama perawatan pasien dengue di RSPI Prof. Dr. Sulianti Saroso.

**Metode:** Studi potong lintang secara random sampling yang dilakukan terhadap catatan medis pasien dengue yang dirawat inap di RSPI Prof. Dr. Sulianti Saroso periode Januari 2014 s/d Desember 2015. Analisis dilakukan secara multivariat dengan regresi Cox.

**Hasil:** Pada 153 sampel catatan medis pasien dengue yang dianalisis, hasil menunjukkan terdapat 41,2% pasien yang dirawat lebih dari 5 hari. Kondisi hemokonsentrasi memiliki pengaruh signifikan dan berisiko 1,8 kali lebih besar untuk lama perawatan pasien lebih dari 5 hari di rumah sakit [aRR=1.75; P=0.003].

**Kesimpulan:** Kondisi hemokonsentrasi pada pasien dengue memiliki risiko lebih besar untuk lama waktu perawatan. (*Health Science Journal of Indonesia 2017;8(1):19-24*)

**Kata kunci:** Dengue, hemokonsentrasi, lama perawatan

### **Abstract**

**Background:** Early identification of clinical conditions and proper treatment to dengue patients is essential to prevent the development of more severe condition. This can lead to shorter length of stay and lower cost of patient care in hospitals. The objective of this study was to determine the factors that affect length of stay of dengue patients in RSPI Prof. Dr. Sulianti Saroso.

**Methods:** A cross-sectional study conducted by random sampling on the medical records of dengue patients hospitalized in RSPI Prof. Dr. Sulianti Saroso period January 2014-December 2015. Multivariate analyzes were performed with Cox regression.

**Results:** There were 153 samples of dengue patient's medical record for analysis, 41.2% of them were hospitalized over 5 days. Hemoconcentration were significant and had higher risk by 1,8 times to length of stay more than 5 days [aRR = 1.75; P = 0.003].

**Conclusion:** Hemoconcentration in dengue patients had higher risk to length of stay. (*Health Science Journal of Indonesia 2017;8(1):19-24*)

**Keywords:** Dengue, hemoconcentration, length of stay

The dengue infection is a disease caused by a virus carried by the mosquito *Aedes aegypti* which spreads rapidly, shifting from the urban areas to the rural areas.<sup>1</sup> The incidence rate of Dengue Hemorrhagic Fever (DHF) in Indonesia increased from 39.8 per 100,000 peoples in 2014 to 50.75 per 100,000 peoples in 2015, and for the area of Special Capital Region of Jakarta, the incidence rates in 2014 and 2015 were 83.34 per 100,000 peoples and 48.67 per 100,000 peoples respectively.<sup>2,3</sup> DHF is one of the diseases listed among the top ten diseases in the inpatient care facility of RSPI Prof. Dr. Sulianti Saroso (RSPI-SS) every year. Based on the hospital's reports, there were 338 cases in 2012, 484 cases in 2013, 583 cases in 2014, and 442 cases in 2015. As for the number of death from DHF and Dengue Shock Syndrome (DSS), there was 1 case in 2012, there were 5 cases in 2013, 8 cases in 2014, and 5 cases in 2015. Meanwhile, it is also known that the length of hospital stay of patients with dengue in 2014-2015 quite varied, i.e. from 2 up to 15 days, and the average was 5,3 days.<sup>4</sup>

Because of the variability of the length of hospital stay of dengue patients in RSPI-SS, so the hospital wants to know various factors that can affect the length of stay of patients with dengue. It is expected that understanding of the factors can improve the quality of service to patients with dengue and prevent the patients' condition from worsening. This study is conducted in order to identify the factors that affect length of stay of dengue patients in RSPI-SS. The research ethics are issued by the Committee for Health Research Ethics of RSPI-SS Number: 01/KE/I/2016.

**METHODS**

This study is a cross sectional study with retrospective analysis of the medical records of patients with dengue

receiving inpatient care in RSPI-SS within the period of January 2014-December 2015. In total, there were 981 medical records of the patients diagnosed with dengue infection receiving inpatient care during the period from January 2014 to December 2015, then samples were selected using the randomize sampling method and 260 medical records were obtained (Lemeshow size). From this number, there were 107 medical records which have not inclusion criteria (did not have complete data), so the number of samples further analyzed were 153 medical records of patients with dengue.

The secondary data were collected using Case Report Form (CRF) consisting of In-Patient Data Form and Physical and Laboratory Examination Monitoring Form. The data collected covered the patients' age, sex, payment method, duration of fever before admission to the hospital, hemorrhage symptoms, the time the serological tests were performed, final diagnosis, hemoconcentration, thrombocytopenia, leukopenia, and the results of serological tests. The data on the results of IgG and IgM serological tests are grouped into the following: IgG(-)/IgM(-); IgG(-)/IgM(+); IgG(+)/IgM(-); IgG(+)/IgM(+).<sup>5</sup>

An analysis was conducted to identify the dominant factor affecting the length of hospital stay of patients with dengue of more than 5 days. From the results of cross tabulation of the independent variable and the length of hospital stay variable, a prevalence of more than 10% was achieved. This study employed Cox regression analysis using the Stata software version 12.<sup>6</sup>

**RESULTS**

The characteristics of 153 patients with dengue by their age and sex as shown in the medical records obtained can be seen in Figure 1.

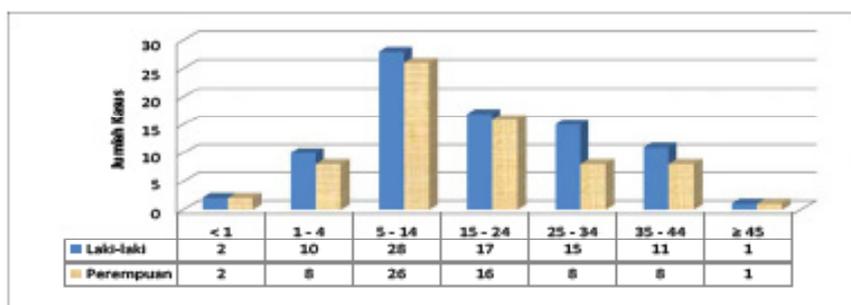


Figure 1. Characteristics of dengue patients in the Inpatient Care Facility of RSPI-SS within the period of January 2014-December 2015 by age and sex

In Figure 1, it can be seen that the highest number of patients with dengue receiving inpatient care in RSPI-SS from January 2014 to December 2015 is found in the age group of 5-14 years, in which they are almost evenly distributed in the male and female sex groups. Analysis was continued on the length of stay of patients with dengue and the results can be seen in Table 1.

Table 1 shows the distribution of patients with dengue with length of stay of more than 5 days and of 5 days or less, distributed by age, sex, and payment method when receiving inpatient care. The age grouping used in this study is the age groups of < 1 year, 1-4 years, 5-14 years, 15-24 years, 25-34 years, 35-44 years and  $\geq 45$  years.<sup>6</sup> From 153 patients with dengue in RSPI SS (with the age range of 0-47 years), the highest number of patients is found in the age group of 5-14 years, i.e. as many as 54 patients (35.3%), 51.9% of which are male.

The average of length of hospital stay of 153 dengue patients was 5,3 days so as for the outcome analysis of the length of hospital stay of patients with dengue, those with length of stay of more than 6 days were observed. The results obtained indicate that there were 90 patients receiving inpatient care for  $\leq 5$  days (58.8%) and 63 patients receiving inpatient care for

> 5 days (41.2%).

Bivariate analysis was then conducted on the clinical and laboratory characteristics, and the results can be seen in Table 2.

In Table 2, it can be seen that variables of duration of fever of 3 days or more before admission to the hospital and hemoconcentration with a P value of < 0.25 are considered potential to be included as candidates in the multivariate analysis. Further, the multivariate analysis was conducted in three phases, namely the stepwise, enter and robust models, resulting in two factors remaining in the final model, namely the duration of fever of 3 days or more before admission to the hospital, and hemoconcentration. The results of the multivariate analysis can be seen in Table 3.

Table 3 shows that hemoconcentration condition significantly related to length of stay of patients of more than 5 days in the hospital. If compared to the subjects who did not have hemoconcentration, the subjects with hemoconcentration have a 1.8 times greater risk of staying for more than 5 days [aRR=1.75; P=0.003]. Meanwhile, the duration of fever of more than 3 days before hospitalization [aRR=0.58; P=0.003], was not a risk factor for length of stay of patients for more than 5 days in hospital.

Table 1. Demographic characteristics of dengue patients with the length of hospital stay in RSPI-SS from January 2014 to December 2015

Variables	Stay $\leq 5$ days (n = 90)		Stay >5 days (n = 63)		95% Confidence Interval	p
	n	%	n	%		
Age						
< 1 year	3	75	1	25	Reference	
1 – 4 years	8	44.4	10	55.6	0.28 – 17.36	0.446
5 – 14 years	33	61.1	21	38.9	0.21 – 11.6	0.666
15 – 24 years	21	63.6	12	36.4	0.19 – 11.19	0.719
25 – 34 years	14	60.9	9	39.1	0.19 – 12.35	0.671
35 – 44 years	11	57.9	8	42.1	0.21 – 13.47	0.623
$\geq 45$ years	0	0	2	100	0.36 – 44.11	0.258
Sex						
Male	49	58.3	35	41.7	Reference	
Female	41	59.4	28	40.6	0.59 – 1.60	0.917
Payment method						
Patients with insurance coverage	32	60.4	21	39.6	Reference	
Patients with no insurance coverage	23	56.1	18	43.9	0.59 – 2.08	0.749
General	35	59.3	24	40.7	0.57 – 1.84	0.930

Table 2. Clinical and laboratory characteristics with length of hospital stay

Variables	Stay ≤ 5 days (n = 90)		Stay > 5 days (n = 63)		Crude Relative Risk	95% Confidence Interval	P
	n	%	n	%			
Clinical characteristics							
Fever before inpatient care							
3 days or less	20	40.8	29	59.2	1.00	Reference	
More than 3 days	70	67.3	34	32.7	0.55	0.34 – 0.91	<b>0.019</b>
Hemorrhage							
No	15	53.6	13	46.4	1.00	Reference	
Yes	75	60	50	40	0.86	0.47 – 1.59	0.632
Final diagnosis							
Dengue fever	10	50	10	50	1.00	Reference	
Dengue hemorrhagic fever	80	60.2	53	39.8	0.80	0.41 – 1.57	0.510
Hemoconcentration							
Normal	63	69.2	28	30.8	1.00	Reference	
Hemoconcentration	27	43.5	35	56.5	1.83	1.12 – 3.02	<b>0.017</b>
Thrombocytopenia							
Normal	35	54.7	29	45.3	1.00	Reference	
Thrombocytopenia	55	61.8	34	38.2	0.84	0.51 – 1.38	0.500
Leukopenia							
Normal	37	57.8	27	42.2	1.00	Reference	
Leukopenia	53	59.6	36	40.4	0.96	0.58 – 1.58	0.869
Laboratory characteristics							
Serological test results							
IgG(-) IgM(-)	19	67.9	9	32.1	1.00	Reference	
IgG(-) IgM(+)	15	62.5	9	37.5	0.75	0.30 – 1.89	0.542
IgG(+) IgM(-)	12	44.4	15	55.6	1.11	0.49 – 2.54	0.803
IgG(+) IgM(+)	54	64.3	30	35.7	0.71	0.34 – 1.50	0.376

Table 3. Relationship between clinical factors and length of hospital stay of more than 5 days

	Stay ≤ 5 days (n = 90)		Stay > 5 days (n = 63)		Adjusted Relative Risk (aRR)	95% Confidence Interval	P
	n	%	n	%			
Fever before inpatient care							
Fever 3 days or less	20	40.8	29	59.2	1.00	Rujukan	
Fever more than 3 days	70	67.3	34	32.7	0.58	0.41 – 0.83	0.003
Hemoconcentration							
Normal	63	69.2	28	30.8	1.00	Rujukan	
Hemoconcentration	27	43.5	35	56.5	<b>1.75</b>	1.20 – 2.53	<b>0.003</b>

## DISCUSSION

The study used secondary data derived from the medical records of patients who already had the results of IgG and IgM serological tests for DHF. The dependent variable is the length of hospital stay that is divided into two categories: 1) the length of hospital stay of 5 days or less and 2) the length of hospital stay of more than 5 days. The determination of the two categories was based on categories that used in previous studies<sup>7</sup>, which is not much different from the average length of hospital stay of

dengue patients in RSPI Prof. Sulianti Saroso that is 5.3 days. There were 10 independent variables studied, and they were adjusted to the available data in the medical records.

Of the 153 subjects used in the study, it was found that 62 subjects (40.5%) experienced hemoconcentration, and they are distributed into two groups, i.e. 27 subjects (43.5%) with a length of hospital stay of 5 days or less, and 35 subjects (56.5%) with a length of hospital stay of more than 5 days. The data on hemoconcentration were obtained based on the percentage of the increase

of the hematocrit level from the lowest one to the highest one recorded in the medical records of patients during the inpatient care. Based on DHF Control Guideline in Indonesia in 2013, the hemoconcentration condition for dengue fever is indicated by an increase of hematocrit level of more than 10% and dengue hemorrhagic fever of more than 20%.

The results of the study show that dengue patients who experienced hemoconcentration had a 1.8 times greater risk of a longer length of hospital stay of more than 5 days. Hemoconcentration conditions or increased hematocrit of more than 20% indicate the presence of plasma leakage due to increased capillary permeability. A decrease in body temperature accompanied by an increase in capillary permeability and plasma leakage indicates the onset of the critical phase of the disease, i.e. on the third to the sixth day of fever/illness.<sup>1,8</sup> This is consistent with the results of previous studies that showed an increase in hematocrit percentage of 23.79% which provides the patients with DHF a risk of more than 2.5 times to experience shock than the percentage of the increase in hematocrit of 20.28%.<sup>9</sup>

The laboratory parameters used for the diagnosis of DHF are the condition of thrombocytopenia and hemoconcentration or pleural effusion, ascites or hypoproteinemia.<sup>8</sup> Meanwhile in this study, not all samples that were diagnosed with dengue hemorrhagic fever were proven to experience hemoconcentration. The results of the study are in line with that of the previous studies conducted in India by Pooransingh, et al and in Indonesia by Kusumaningtyas, et al and Rasyada, et al which showed that not all dengue patients experienced hemoconcentration.<sup>10,11,12</sup>

Delay in the identification of hemoconcentration conditions and improper handling, especially in terms of fluid therapy when there is plasma leakage can lead to various complications such as advance pleural effusion, acute pulmonary congestion, and or cardiac failure and impaired electrolyte/metabolite.<sup>1</sup> Progression of the disease towards a more severe condition in dengue patients who experienced hemoconcentration causes the patients to have a longer length of hospital stay of more than 5 days.

In this study, the duration of fever for more than 3 days before hospitalization was protective variable which means not a risk factor for the patients' length of hospital stay of more five days [aRR=0.58; P=0.003]. The largest proportion (67.3%) was present in fever for more than 3 days and length of hospital

stay for 5 days or less. Plausability biologic showed that the patients that hospitalized after had fever of more than 3 days (delayed hospitalization), did not have long treatment because of the patients have no complications such as hepatomegaly, gastrointestinal bleeding and acute kidney injury that can aggravate the condition of dengue patients.<sup>13,14,15</sup>

In conclusion, hemoconcentration significantly related and had higher risk to length of stay more than 5 days in RSPI Prof. Dr. Sulianti Saroso. Consultation as early as possible at the health care facility will accelerate the identification of the dengue patient's clinical condition and reduce the risk of disease progression towards a severe dengue which do not require longer treatment. Longer treatment will result in a financial burden both for the patient and the hospital.

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