COMORBID FACTORS AND DURATION OF ILLNESS IN DENGUE HEMORRHAGIC FEVER PATIENTS AT UNIVERSITAS AIRLANGGA HOSPITAL, SURABAYA, INDONESIA

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ABSTRACT

Dengue hemorrhagic fever (DHF) continues to prevail in Indonesia annually. Individuals afflicted with dengue hemorrhagic fever may exhibit distinct clinical manifestations, and these can vary based on individual factors. Numerous elements can contribute to this diversity. Typically, adult patients with comorbidities face a less favorable prognosis for the primary disease. This study aimed to examine the impact of comorbid factors on the severity of DHF, as well as its duration. The comorbidities considered in this research encompassed hypertension, diabetes mellitus, and obesity. This research employed an analytical approach and was conducted at Universitas Airlangga Hospital from January to December 2022. Medical records served as the primary data source for this study. A total of 121 patient samples were collected based on specific criteria. The criteria included adults (>18 years) treated at Universitas Airlangga Hospital, who had no comorbid diseases other than those under study, and possessed complete medical record data. The sampling technique employed in this research was total sampling, which adhered to the inclusion and exclusion criteria. This research demonstrated that comorbid factors were not associated with the severity of DHF ($p<0.05$), while the duration of illness in DHF patients was correlated with the severity of the disease ($p=0.027$).

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INTRODUCTION

Indonesia is a tropical country. With changing seasons, several infections pose a threat to the society. Infectious diseases are often caused by microorganisms such as parasites, bacteria, fungi, and viruses. This is associated with the conditions of temperature, rainfall, and air humidity in tropical countries, which are conducive to the growth and development of microorganisms responsible for tropical disease infections[1]. One significant contributor to tropical infectious diseases in Indonesia is viruses, and among them is the

dengue virus. The virus is transmitted to humans through mosquitoes, specifically *Aedes aegypti* and *Aedes albopictus*, which are prevalent in various locations. This virus can lead to dengue hemorrhagic fever (DHF), an acute disease caused by a virus serotype from the genus Flavivirus, family Flaviviridae, with clinical manifestations characterized by bleeding that may result in shock and even death[2]. DHF can be a feared occurrence in the community due to its relatively fast and easy transmission. Within just one month in endemic areas, the number of dengue cases can reach up to tens of people[3]. The transmission of dengue fever is widespread in tropical regions, with risk variations depending on temperature, humidity, rainfall, and urbanization[4].

According to data from the Indonesian Ministry of Health (2021), dengue cases were reported in 456 districts or cities across 34 provinces as of the 51st week of 2021, with a total of 51,048 patients. Deaths caused by dengue fever occurred in 167 districts or cities, reaching a total of 472 people. Based on information from the East Java Provincial Health Service, the number of dengue fever patients in East Java in January 2022 reached 1,220, with 21 fatalities[5].

According to the health service's data[3], the city of Surabaya experiences an annual increase. In 2020, the incidence rate per 100,000 population was 2.51, which increased to 3.80 in 2021. Temporary data for 2022 from January to March recorded a rate of 3.70. DHF exhibits clinical manifestations and degrees of severity that depend on individual factors and the virulence of the virus. Differences in clinical characteristics and disease severity may indicate the impact of serological status, immunological background, comorbid factors, and socioeconomic status[6].

Comorbidities means the presence of more than one disease or condition occurring in an individual at the same time. Comorbidities are described as chronic or long-term conditions[7]. Comorbidities are congenital diseases suffered by humans in addition to the main disease. Common comorbid diseases in Indonesia include hypertension, diabetes, obesity, and heart disease[8]. According to the Indonesian Ministry of Health[3], the estimated number of hypertension cases in Indonesia in 2021 was 63,309,620 people, with a death toll of 427,218 people. Diabetes in Indonesia reached 6.2%, equivalent to more than 10.8 million cases in the year 2020. Meanwhile, the prevalence of obesity in Indonesia doubled from 19.1% in 2017 to 35.4% in 2018.

Generally, comorbid diseases can worsen the prognosis and increase the severity of the main disease. For instance, research conducted by Senewe et al. in 2021 showed that the prognosis for DHF is determined by the severity of the disease, length of treatment, age, and nutritional condition of the patient. Generally, the prognosis for grades one and two is good, while degrees three and four depend on the length of disease detection. In cases of dengue fever accompanied by complications, the prognosis is poor[9]. In patients with chronic diseases, their immune systems will be weakened, making them more susceptible to infections and other diseases[10]. This indicates that patients with comorbidities are more prone to infections from other diseases[11].

Patients who have contracted DHF will experience varying durations of illness based on factors such as the patient's characteristics, the clinical manifestations

observed, and laboratory test results. The length of fever before hospital admission is a contributing factor to the duration of hospital stay for dengue fever patients. Additionally, this duration can be influenced by indicators of plasma leakage and leukocyte count[12].

Previous research results have shown that DHF manifests in several degrees of severity, and various comorbid diseases can exacerbate the prognosis of the primary ailment. However, research comparing DHF patients with and without comorbidities is still very limited. Therefore, further investigation on this matter is necessary. This study aimed to analyze the characteristics of DHF patients with comorbid diseases and to assess the impact of the duration of illness on the severity of dengue fever at Universitas Airlangga Hospital from January to December 2022.

MATERIALS AND METHODS

This research had obtained ethical approval from the Universitas Airlangga Hospital research ethics committee with reference number 105/KEP/2022. It was conducted as an analytic study, utilizing samples derived from the medical records of Universitas Airlangga Hospital spanning from January to December 2022. During the data collection process at Universitas Airlangga Hospital, a total of 284 medical records of patients with DHF were initially identified. However, due to some samples not meeting the inclusion and exclusion criteria, a total of 121 patients were included in this study.

After collection, the data were sorted based on specified variables, including the presence of comorbid diseases, the duration of the patient's illness, and the severity status of the patient. Data processing was performed using IBM SPSS to examine the relationship between dependent and independent variables. The Fisher exact test was employed in this research, as it did not fulfill the requirements for using the Chi-square test.

The severity of DHF is classified based on the[13] criteria, as follows: DF (Dengue Fever), DHF Grade I, DHF Grade II, DHF Grade III, and DHF Grade IV. The classification of the severity levels of DHF is based on different signs, symptoms, and laboratory results at each level. The severity of DHF can be assessed through the clinical manifestations of the patient, physical examination results, and laboratory test outcomes[14]. Patients experiencing vomiting or gum bleeding have a higher risk of developing severe DHF, but further examinations are still needed to determine the severity grade experienced by dengue fever patients[15].

RESULTS

It is evident that the majority of patients with an illness duration exceeding 7 days were diagnosed with dengue fever, accounting for 46.6%, whereas 36.3% had grade 1 DHF, and 17.1% had grade 2 DHF. In contrast, among the group with an illness duration of less than 7 days, dengue fever patients constituted the highest percentage at 69.6%, followed by grade 1 DHF at 21.2% (Table 1).

Table 1. Duration of illness based on DHF severity degree

Duration of illness	DHF severity								Total			
	DF		DHF 1		DHF 2		DHF 3		Σ	%	α	p-*value*
	Σ	%	Σ	%	Σ	%	Σ	%				
<7 days	23	69.6	7	21.2	2	6.1	1	3.1	33	100		
>7 days	41	46.6	32	36.3	15	17.1	0	0	88	100	0.05	0.027
Totals	64	52.9	39	32.2	17	14.1	1	0.8	121	100		

Table 2. Comorbid based on DHF severity

Comorbid	DHF severity								Total			
	DF		DHF 1		DHF 2		DHF 3		Σ	%	α	P value
Hypertension	Σ	%	Σ	%	Σ	%	Σ	%				
Yes	11	61.1	3	16.7	4	22.2	0	0	18	100	0.05	0.350
No	53	51.6	36	34.9	13	12.6	1	0.9	103	100		
Diabetes Mellitus	Σ	%	Σ	%	Σ	%	Σ	%				
Yes	2	40	2	40	1	20	0	0	5	100	0.05	0.706
No	62	53.4	37	31.9	16	13.8	1	0.9	116	100		
Obesity	Σ	%	Σ	%	Σ	%	Σ	%				
Yes	2	50	2	50	0	0	0	0	4	100	0.05	1.000
No	5	62.5	3	37.5	0	0	0	0	12	100		

In a descriptive analysis, it can be concluded that a significant proportion of grade 2 dengue fever patients experienced an illness duration exceeding 7 days. The results of the statistical tests employing Fisher's Exact Test yielded a p-value of 0.027 (0.05), indicating a statistically significant relationship between the length of the patient's illness and the severity of dengue fever among patients treated at Universitas Airlangga Hospital.

Based on the presence of comorbid diseases in Table 2, the majority of patients at Universitas Airlangga Hospital experienced hypertension, totaling 18 patients. The majority of patients with comorbid diseases had dengue fever, with 11 patients (61.1%) experiencing dengue fever, 4 patients (22.2%) with dengue fever grade 2, and 3 patients (16.7%) with dengue fever grade 1. Descriptively, it can be concluded that 61.1% of DHF patients also had hypertension.

Based on the results of statistical tests using Fisher's Exact Test, the p-value was 0.35 (p>0.05). Therefore, it can be concluded that the comorbid factor of hypertension has no significant relationship with the severity of DHF in patients treated at Universitas Airlangga Hospital.

DHF patients with comorbid diabetes mellitus most frequently experienced dengue fever at 40%, DHF grade I at 40%, and DHF grade II at 20%. Meanwhile, the majority of DHF patients without diabetes mellitus experienced dengue fever at 53.4%, 31.9% for grade I DHF, 13.8% for grade II DHF, and 0.9% for grade III DHF. Descriptively, it can be concluded that the majority of DHF patients with diabetes mellitus had dengue fever and 40% had grade I dengue fever. Based on the results of statistical tests using Fisher's Exact Test, the p-value was 0.706 (p> 0.05), so it can be concluded that the comorbid factor of diabetes mellitus had no

relationship with the severity of DHF in patients treated at Universitas Airlangga Hospital.

DHF patients with obesity comorbidities mostly experienced dengue fever at 50% and DHF grade I at 50%. Meanwhile, the majority of DHF patients without obesity experienced dengue fever at 62.5% and grade I DHF at 37.5%. Descriptively, it can be concluded that the majority of DHF patients with obesity had dengue fever, and 50% had grade I dengue fever. Based on the results of statistical tests using Fisher's Exact Test, the p-value was 1.000 (0.05), so it can be concluded that the comorbid factor of obesity had no relationship with the severity of DHF in patients treated at Universitas Airlangga Hospital.

DISCUSSION

Based on the research conducted from January to December 2022, it was observed that DHF patients with a duration of illness greater than 7 days outnumbered those with a duration of illness less than 7 days. The average duration of illness among hospitalized patients was 8.4 days, ranging from 5 to 13 days. The length of a patient's stay is influenced by the duration of illness before admission to the hospital, the presence of complications, signs of plasma leakage, and the leukocyte count. Additionally, the length of a patient's stay can be determined by the severity of the dengue fever experienced by the patient[11]. Statistical tests using Fisher's Exact Test yielded a p=0.027 (p<0.05). Therefore, it can be concluded that the duration of the patient's illness is correlated with the severity of dengue fever in patients treated at Universitas Airlangga Hospital.

The duration of the patient's illness is calculated from the time the patient first experiences the symptoms. These symptoms may include fever, headache, muscle aches, or others. The duration of the illness is calculated in conjunction with the length of stay until discharge from the hospital. The length of hospitalization can serve as an indicator for monitoring the condition of dengue fever patients. DHF patients need to be hospitalized if hemoglobin and hematocrit values are normal, with platelet levels <100,000, or if hemoglobin and hematocrit levels increase with normal or decreased platelets. Additionally, hospitalization is warranted if there are complaints and signs of hypotension, bleeding, organ disorders, comorbid factors (such as pregnancy, diabetes mellitus, hypertension), as well as complications of hyperthermia and convulsions[16].

Comorbid for DHF patients treated at Universitas Airlangga Hospital who had hypertension accounted for 14.8% of the total patients treated during the same period. Among this group, DHF patients with hypertension experienced a longer duration of illness (>7 days) compared to those with a duration of <7 days. This indicated that patients with hypertension tend to have a prolonged illness duration compared to those without hypertension. The degrees of severity observed in DHF patients with hypertension were mostly dengue fever, grade I dengue fever, and grade II dengue fever. Among these severity levels, the longest duration of illness was observed in cases lasting >7 days.

Elderly patients and individuals with pre-existing hypertension exhibit elevated systolic and diastolic blood pressure levels during dengue infection[17].

Hypertension could serve as a risk factor for the progression of dengue fever to severe dengue. The study investigated patients' blood pressure, revealing an increase in both systolic and diastolic blood pressure in correlation with the duration of the illness. Nevertheless, it is important to note some limitations in this research, specifically that the administration of fluids can influence blood pressure, potentially masking the effects of plasma leakage.

DHF patients with comorbid diabetes mellitus treated at Universitas Airlangga Hospital accounted for 4.1% of the total patients treated during the same period. A higher number of patients were observed with an illness duration of more than 7 days compared to those with a duration of less than 7 days. The degrees of severity experienced by DHF patients with diabetes mellitus were mainly dengue fever, grade 2 DHF, and grade 1 DHF.

Diabetes mellitus can lead to insulin deficiency, which may result in damage to antibodies and cause a weakened immune system, making the body more susceptible to infections and other diseases[18]. Diabetic patients infected with dengue fever experience more severe thrombocytopenia and are at a higher risk of developing DHF/DSS. Another study also suggest that diabetes mellitus does not correlate strongly with DHF. This lack of correlation may be attributed to the glycemic status and diabetes control, which do not appear to play a significant role in the development of the severity of DHF[19].

Patients with comorbid obesity who experienced DHF accounted for 33.3% of all patients with complete BMI data in the RSUA medical records. According to these figures, all patients had an illness duration exceeding 7 days. The predominant final diagnoses for the severity of DHF in patients with obesity were dengue fever and grade 1 dengue fever.

Based on research conducted by Kharisma[20], individuals with overweight and obese nutritional statuses have a higher risk of experiencing Dengue Shock Syndrome (DSS). Essentially, nutritional status is a crucial element in determining one's health status. Nutritional status is a factor that influences a person's immune system, affecting their ability to combat infections. Those with excessive nutritional status (overweight) or obesity tend to be more susceptible to severe dengue infection[20]. This is in contrast to individuals with deficient or poor nutritional status and those with normal nutritional status, who tend to exhibit a protective factor against the incidence of severe dengue[21]. The findings of this study confirmed a study by Utomo et al[22], who stated that individuals with a fat/over nutritional status are five times more likely to experience increased severity of DHF compared to patients with good nutritional status[22]. According to Prihatiningrum & Wildan[23], the risk of shock in dengue patients can occur in patients with nutritional status which makes them more susceptible to experiencing severe dengue fever compared to those with poor nutritional status[23].

This contradicts the findings of a study conducted by Salsabila et al.[24], which concluded that the overall nutritional status does not correlate with the occurrence of Dengue Shock Syndrome (DSS)[24]. This conclusion is also supported by Trang et al. (2015)[25], who asserted that there is no significant relationship between nutritional status and the incidence of dengue, aligning with earlier research data, making it a subject of controversy[25]. In individuals with poor or deficient nutritional status, as well as those with normal nutrition, lipid levels

are lower compared to those with better nutrition. This lower lipid level may result in an insufficient virus replication process, potentially explaining why patients with poor or deficient nutritional status and those with normal nutrition are less prone to severe dengue infections[26].

CONCLUSION

Comorbid diseases do not exhibit a significant relationship with the severity of DHF. However, the duration of illness in patients with DHF does show a significant correlation with the severity of the condition.

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CONFLICT OF INTEREST

All Authors have no conflict of interest.

ETHICS CONSIDERATION

This research received ethical clearance from KEPK Ethic Universitas Airlangga Hospital. With number 105/KEP/2022 and date of approval on 20 October 2022.

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AUTHOR CONTRIBUTION

All authors contributed to the process of conducting this research.

REFERENCES

1. Binsasi E, Bano EN, Salsinha CN. Analisis Model Penyebaran Penyakit Demam Berdarah Dengue Di Kota Kefamenanu. *Statmat J Stat Dan Mat*. 2021;3(1):1.
2. Sukohar. Demam Berdarah Dengue (DBD). *Medula*. 2014;2(2):1-15. doi:10.35952/jik.v1i2.80
3. Kemenkes. *Data DBD Indonesia*.; 2021.
4. Xu C, Pang J, Hsu JP, Leo YS, Lye DCB. Differences in clinical features and dengue severity between local and migrant Chinese with dengue infection in Singapore. *PLoS One*. 2018;13(8):1-10.
5. Philipus Senewe F, Endah Pracoyo N, Marina R, Letelay AM, Sulistiyowati N, Upaya Kesehatan Masyarakat P. Pengaruh Penyakit Penyerta/Komorbid Dan Karakteristik Individu Dengan Kejadian Covid-19 Di Kota Bogor Tahun 2020. *J Ekol Kesehat*. 2021;20(2):69-79.
6. Yusoff NSBM. *Demam Berdarah Dengue*. Vol 2.; 2010.
7. Ndera ML, Supriyatni N, Rahayu A. Faktor Komorbid terhadap Covid-19 di Puskesmas Kota Tahun 2020. *J Biosainstek*. 2021;3(2):1-9.
8. Tule NRS. *Systematic Review: Identifikasi Faktor Jenis Kelamin Dan Kelompok Usia Pada Pasien Demam Berdarah Dengue Dengan Pendekatan Kasus Trombositopenia*. 2020.
9. Rachim, W., Subronto, Y.W., Laksanawati, I.S. *Faktor-Faktor yang Berpengaruh terhadap Lama Rawat Inap Pasien Demam Berdarah Dengue*. 2019
10. Suhendro, Nainggolan L, Chen K, Pohan HT. *Demam berdarah dengue. Buku ajar ilmu penyakit dalam jilid III*. Edisi ke-5. Jakarta: Pusat Penerbitan Departemen Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Indonesia. 2015. pp. 539□58.
11. Yeung W, Lye DCB, Thein TL, Chen Y, Leo YS. Blood pressure trend in

hospitalized adult dengue patients. *PLoS One*. 2020;15(7):1-11. doi:10.1371/journal.pone.0235166
12. Lestari, Zulkarnain, Sijid SA. Diabetes Melitus: Review Etiologi, Patofisiologi, Gejala, Penyebab, Cara Pemeriksaan, Cara Pengobatan dan Cara Pencegahan. *UIN Alauddin Makassar*. 2021;(November):237-241. http://journal.uin-alauddin.ac.id/index.php/psb
13. Chen CY, Lee MY, Lin K Der, et al. Diabetes mellitus increases severity of thrombocytopenia in dengue-infected patients. *Int J Mol Sci*. 2015;16(2):3820-3830.
14. Kharisma PL, Muhyi A, Rachmi E. Hubungan Status Gizi, Jenis Kelamin dengan Derajat Infeksi Dengue pada Anak di RSUD Abdul Wahab Sjahranie Samarinda. *J Sains dan Kesehat*. 2022;3(3):376-382.
15. Buntubatu S, Arguni E, Indrawanti R, Laksono IS, Prawirohartono EP. Status Nutrisi sebagai Faktor Risiko Sindrom Syok Dengue. *Sari Pediatr*. 2017;18(3):226.
16. Utomo WC. *Hubungan Status Gizi Terhadap Derajat Keparahan Demam Berdarah Dengue Pada Anak Usia 0-14 Tahun Periode Januari Desember 2016 Di Rs Pku Muhammadiyah Yogyakarta*. 2018.
17. Prihatiningrum RM. *Perbedaan Angka Kejadian Antara Anak Status Gizi Baik Dan Status Gizi Kurang Dengan Kejadian Demam Berdarah Dengue Di Rsud Kota Surakarta*. 2016.
18. Salsabila O, Shodikin MA, Rachmawati DA. Analisis Faktor Risiko Terjadinya Sindrom Syok Dengue Pada Anak di RSD dr. Soebandi Kabupaten Jember. *J Agromedicine Med Sci*. 2017;3(1):56.
19. Trang NTH, Long NP, Hue TTM, et al. Association between nutritional status and dengue infection: A systematic review and meta-analysis. *BMC Infect Dis*. 2016;16(1):1-11.
20. Zulkipli MS, Dahlui M, Jamil N, et al. The association between obesity and dengue severity among pediatric patients: A systematic review and meta-analysis. *PLoS Negl Trop Dis*. 2018;12(2):1-22.
21. Buntubatu S, Arguni E, Indrawanti R, et al. Status Nutrisi sebagai Faktor Risiko Sindrom Syok Dengu. *Sari Pediatr* 2017; 18: 226.
22. Utomo W. Hubungan Srarus Gizi terhadap Derajat Keparahan Demam Berdarah Dengue pada Anak 0-14 Tahun Pediode Januari Desember 2016 di Rs Pku Muhammadiyah Yogyakarta. 2018.
23. Prihatiningrum Rm, Wildan M. Perbedaan Angka Kejadian Antara Anak Status Gizi Baik dan Gizi Kurang dengan Kejadian Demam Berdarah Dengue di RSUD Kota Surakarta. 2016.
24. Salsabila O, Shodikin M, Rachmawati D. Analisi Faktor Risiko Terjadinya Sindrom SYok Dengue Pada Anak di RSD dr. Soebandi Kabupaten JEmber. *J Agromedicine Med Sci* 2017; 3: 56.
25. Trang NTH, Long NP, Hue TTM, et al. Association between nutritional status and dengue infection: A systematic review and meta-analysis. *BMC Infect Dis*. 2016; 16:1-11.
26. Zulkipli MS. Dahlui M, Jamil, et al. The association between obesity and dengue severity among pediatric patients: A systematic review and meta-analysis, *PLoS Negl Trop Dis* 2018; 12: 1-22.