EFFECT OF SOCIODEMOGRAPHIC AND CLINICAL FACTORS ON LENGTH OF HOSPITAL STAY FOR ADULT DENGUE PATIENTS: A RETROSPECTIVE STUDY AT A TERTIARY CARE HOSPITAL, JAKARTA, INDONESIA

Ifael Yerosias Mauleti¹, Krishna Adi Wibisana¹, Nurul Husna Muchtar², Vivi Lisdawati²,Kartika Afrida Fauzia³, Achmad Shidiq³, Harimat Hendarwan^{3,4}, Seung Hwan Lee⁵ and Ika Saptarini^{3,6}

¹Department of Internal Medicine, ²Directorate of Human Resources, Education and Research, Fatmawati General Hospital, Jakarta; ³Research Center for Preclinical and Clinical Medicine, National Research and Innovation Agency, Bogor; ⁴Indonesia Maju University, Jakarta, Indonesia; ⁵Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea; ⁶Doctoral Program in Medical Sciences, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

Abstract. Dengue infection is prevalent, yet data on factors associated with prolonged hospital stays are limited. This study aimed to identify factors related to prolonged hospital stays in adult patients admitted with dengue infection at a tertiary hospital. We conducted an observational retrospective cohort study utilizing secondary data from medical records between 2020 and 2024. Clinically confirmed dengue patients were divided into two groups based on hospital stay duration, namely ≤4 days and >4 days. We compared clinical and laboratory characteristics using appropriate statistical methods. Of the 272 patients, 48% had prolonged hospital stays, with a mean hospital stay of 4.7 ± 1.6 days. Multivariate analysis revealed that patients with comorbidities (adjusted odds ratio (aOR) = 2.08) had an increased likelihood of prolonged hospital stays. Patients admitted to the hospital after 4 days of illness had a 0.27 lower likelihood of experiencing prolonged hospital stays. Nadir platelet counts <20×10³ cells/µl, low white blood cell counts, vomiting, and low hemoglobin level were predictors of prolonged hospital stay (aORs = 3.47, 2.74, 1.93, and 1.92, respectively). Our research indicated that comorbidities of adult dengue patients, viz low hemoglobin, low platelet and white blood cell counts, and vomiting, are significantly associated with prolonged hospital stay, factors that the attending clinicians should take into consideration.

Keywords: dengue, comorbidity, healthcare, length of hospital stay

Correspondence: Ika Saptarini, Research Center for Preclinical and Clinical Medicine, National Research and Innovation Agency, Jl. Raya Jakarta - Bogor KM 46, Bogor 16911, Indonesia

Tel: +62 82122716063 E-mail: ikas003@brin.go.id

INTRODUCTION

Dengue is a viral disease transmitted by mosquitoes, resulting from infection with one of the four antigenically different serotypes of the dengue virus (Yang et al, 2021). Dengue is extensively prevalent globally in numerous tropical and subtropical areas, thus imposing a considerable strain on the public health systems (Du et al, 2021; Yang et al, 2021). The range of illnesses extends from mild, self-limiting conditions such as dengue fever (DF) to more severe and acute manifestations, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) (WHO SEARO, 2011). The World Health Organization (WHO) estimates that over 40% of the global population reside in regions at risk of dengue transmission, and the increase in dengue infection is particularly pronounced in Asia, with around 1.8 billion individuals at risk of the disease (WHO, 2009). Adult dengue subjects carry a non-negligible mortality burden. Although the overall case-fatality rates have fallen below 1% with early diagnosis and appropriate care, adult case-fatality rates of 5.4% have been reported during dengue hemorrhagic fever epidemics. Severe dengue mortality may range from 2-5% even with treatment, rising to as high as 20% when management is delayed or unavailable (Ong et al, 2007).

In Indonesia, dengue was first identified in Surabaya and Jakarta in 1968, emerging as a public health issue (Setiati *et al*, 2006). Since 2014, it has been present in all provinces, and by 2019, it had spread to 481 of the 514 regions and cities of the country. Dengue incidence in Indonesia has increased over the past 50 years,

with the highest number of cases reported in 2009 and 2016, with incidence rate of 68 and 78 per 100,000 respectively (Harapan et al, 2019). Based on the 2023 Ministry of Health report, the incidence rate of dengue infection in Indonesia is 41 per 100,000, down from 52 per 100,000 in 2022 (Ministry of Health Republic of Indonesia, 2023). During the COVID-19 pandemic, dengue prevalence rose to 59.0 million cases, with a pronounced peak of 6.3 million cases among 10-14 years of age group; however, substantial prevalence persisted across all adult age groups, such that, even excluding pediatric patients, dengue remained the second-highest viral disease burden after COVID-19 in the country (Li et al, 2024).

Despite low fatality rates, a significant number of dengue patients are hospitalized annually, imposing a substantial economic burden on the health systems, particularly in low- and middle-income countries (LMICs) (Luh et al, 2018). The duration of

hospitalization, and consequently the medical care needed, may range from several days to weeks. Management of adult dengue in Indonesia and elsewhere remains purely supportive, focused on judicious fluid resuscitation, dynamic monitoring of hematocrit and platelet counts, and symptomatic relief with paracetamol, since no specific antiviral therapy is currently available (Recker et al, 2024). The extent to which supportive care can directly impact the immunopathology of dengue and, therefore, influence the clinical progression of the virus is uncertain (Recker et al, 2024). Dengue vaccination, not widely included in Indonesia national programs and largely depending on private funding, demonstrates strong preventive potential when combined with rigorous vectorcontrol strategies (Suwantika et al, 2020).

Extensive scientific research has focused on identifying immunopathologic markers associated with or predictive of

disease severity (Oliveira et al, 2017; Tissera et al, 2017). On the other hand, limited research has been focused on the length of hospital stay and its related factors (Recker et al, 2024). Prolonged length of hospital stay is one that exceeds the expected or typical duration for a given condition and correlates with negative consequences for patients and healthcare facilities, including increased complications, unfavorable outcomes, and elevated care costs, which impose a substantial economic burden on hospitals. There is significant interest in managing hospital resources, especially concerning dengue disease; consequently, hospitals aim to minimize the length of hospital stays (Ruangkriengsin and Phisalprapa, 2014; Rayamajhi et al, 2024). The length of hospital stay is a comprehensive metric for assessing healthcare resource utilization, associated costs and disease severity. Therefore, predicting patients who need early intervention and those who require a moderate amount of intervention

to prevent prolonged hospital stays is crucial.

In this study, we analyzed dengue hospitalization data collected from a tertiary hospital in Jakarta over five years to improve our understanding of the risk factors associated with prolonged hospital stay. Our analysis included demographic, clinical and laboratory results associated with prolonged hospital stay. These results should provide important health and economic implications for tertiary hospitals in Indonesia and other LMICs where dengue is endemic.

MATERIALS AND METHODS

Study design and subjects

An observational retrospective cohort study was conducted utilizing secondary data obtained from the medical records between January 2020 and March 2024 of Fatmawati General Hospital, a tertiary care and teaching hospital with 798 beds in Jakarta, Indonesia. As one of eight primary referral

centers in Jakarta, its responsibility covers an area within a 5 km radius containing approximately 12.4 million residents (Silalahi et al, 2020). At Fatmawati General Hospital, the medical records library is complemented by an electronic medical record system that was piloted in 2016 and fully integrated in 2020. We restricted our study to all hospitalized dengue patients aged 18 years or older, thereby excluding all pediatric dengue cases. To ensure the completeness and integrity of the collected data, we omitted any patients with missing or incomplete records. Anonymized medical data were retrieved from Fatmawati General Hospital computerized central information system.

We included all patients aged ≥18 years who met our study criteria and for whom complete clinical and laboratory data were available; notably, this cohort also encompassed individuals who, despite lacking NS1 or IgM confirmation, were managed clinically as dengue cases during

their hospitalization. Therefore, to ensure that our study cohort accurately reflected standard clinical practice at our study site, we incorporated patients who received empirical dengue management in the absence of NS1 or IgM/IgG serological confirmation. Upon the patients' discharge, the outcome was also documented.

Data collection

Previous studies have reported a median hospital stay of 3-4 days for patients with dengue infection (Khan et al, 2008; Lye et al, 2008). Other studies defined prolonged hospital stay based on the median or mean length (Mallhi et al, 2017; Ansari et al, 2021). Consequently, we established a cut-off length of >4 days for prolonged hospital stay, given that the median hospital stay in this study was 4 days and the mean was 5 days. Patients with a hospital stay ≤4 days were compared to those with stays >4 days to identify possible predictors of prolonged hospital stay. Data on patients' demographic, socioeconomic and

clinical sign/symptom profiles were documented upon admission. Clinical and laboratory findings were recorded daily throughout the hospital stay until discharge. Patients' age was divided into two groups: <45 years and ≥45 years, consistent with prior research that employed 45 years as the threshold for dichotomizing age groups (Guzmán et al, 2002; Low et al, 2011). Education was categorized into three groups: attended junior high school or lower, attended senior high school, and graduated with a Bachelor's degree or higher. Insurance coverage was the national security insurance (JKN) or others. Severity was categorized as dengue fever (DF) and dengue hemorrhagic fever (DHF) according to the WHO's criteria (WHO, 1997). Low hemoglobin levels are defined as female <11.6 g/dl and male <13.2 g/ dl. Elevated hematocrit levels are defined as >40% in female adults, and >46% and 42% in males ≤60 and >60 years of age, respectively. Patients with unconfirmed dengue were defined as those with negative

NS1 or IgM test results or those not tested.

Statistical analysis

Comparison of categorical variables between two groups was conducted using the χ^2 test, provided that at least five participants were in a given category. An independent Student's *t*-test was performed to compare continuous variables. A variable with a *p*-value <0.25 in a bivariate analysis was chosen for a subsequent logistic regression analysis to assess the association between a prolonged hospital stay and a potential predictor, with a p-value ≤ 0.05 considered statistically significant. Analysis was performed using the STATA 15.1 SE (StataCorp LLC, College Station, TX).

Ethical consideration

The study protocols were approved by an ethical review committee of Fatmawati General Hospital (approval no. PP.08.02/D. XXI.18/206/2024). Due to the use of secondary data, prior written

informed consent was not required for the study.

RESULTS

Adult dengue patients (n =272), mean \pm SD age of 34.8 \pm 14.3 years, were selected according to the procedure shown in Fig 1. From 432 hospital-reported dengue cases, 106 were excluded due to unavailable medical records, age under 18 years, or non-dengue diagnoses, leaving 326 cases. A further 54 with incomplete data were excluded, resulting in 272 patients with complete clinical and laboratory information. Among these, diagnostic testing showed varied NS1 and IgM results, with 184 patients never serologically confirmed but managed clinically as dengue. DF and DHF was diagnosed in 31% and 69% of the patients respectively. The vast majority of patients (92%) were covered by the national security insurance (JKN). Eighty-five out of the 272 participants were confirmed to have dengue infection by an NS1 or IgM test (Table 1). Almost a quarter of patients (23.5%) had comorbidities, with the highest frequency being hypertension (8.8%), followed by diabetes mellitus (7.4%) and then kidney disease (2.6%). Fever was the most common symptom (87%), followed by nausea (85%). Low hemoglobin levels and WBC counts were present in 38 and 77% respectively, of the subjects, while 54% had high hematocrit. One hundred and thirty-one patients (48%) experienced prolonged hospital stay (>4 days) (Table 1).

To identify factors independently associated with prolonged hospital stay, those with a p-value <0.25 in a bivariate analysis using χ^2 or Student's *t*-test (Table 1) were subjected to a multivariate analysis. Out of 27 variables, 11 had *p*-values <0.25 (Table 1). At admission, we collected data on subjects' demographics, and during hospitalization we recorded clinical and laboratory findings from the enrolled patients. We paid particular attention to laboratory measurements outside the upper or lower normal limits established

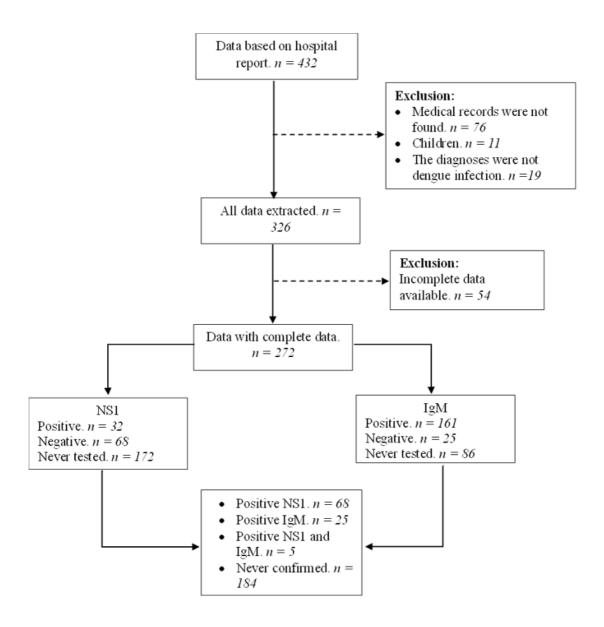


Fig 1 - Flow chart of sample selection

IgG: immunoglobulin G; IgM: immunoglobulin M; NS1: nonstructural protein 1

Table 1

Comparison of characteristics of patients according to presence or absence of prolonged stay, Fatmawati General Hospital, Jakarta, Indonesia, January 2020 - March 2024

Variable	Frequency, n (%)*		p-value [†]
	LOS ≤4 days	LOS >4 days	-
Age group			0.544
<45 years (N = 201)	102 (51)	99 (49)	
≥45 years (N = 71)	39 (55)	32 (45)	
Sex			0.042
Female $(N = 128)$	58 (45)	70 (55)	
Male $(N = 144)$	83 (58)	61 (42)	
Education level			0.407
Junior high school or below (N = 40)	22 (55)	18 (45)	
Senior high school (N = 136)	65 (48)	71 (52)	
Bachelor's degree or above (N = 96)	54 (56)	42 (44)	
Working status			0.986
Working $(N = 147)$	76 (52)	71 (48)	
Student $(N = 53)$	28 (53)	25 (47)	
Not working $(N = 72)$	37 (51)	35 (49)	
Insurance coverage			0.391
National insurance ($N = 251$)	132 (53)	119 (47)	
Others $(N = 21)$	9 (43)	12 (57)	
Definitive diagnosis			0.006
Not confirmed ‡ (N = 184)	106 (58)	78 (42)	
Confirmed $(N = 88)$	35 (40)	53 (60)	

Southeast Asian J Trop Med Public Health

Table 1 (cont)

Variable	Frequen	Frequency, n (%) *	
	LOS ≤4 days	LOS >4 days	-
Severity			0.288
DF (N = 85)	40 (47)	45 (53)	
DHF (N = 187)	101 (54)	86 (46)	
With comorbidity			0.077
No $(N = 208)$	114 (55)	94 (45)	
Yes (N = 64)	27 (42)	37 (58)	
Days of illness before admission			< 0.001
≤4 days (N = 180)	76 (42)	104 (58)	
>4 days (N = 92)	65 (71)	27 (29)	
Fever			0.003
No $(N = 36)$	27 (75)	9 (25)	
Yes (N = 236)	114 (48)	122 (52)	
Headache			0.025
No $(N = 108)$	65 (60)	43 (40)	
Yes $(N = 164)$	76 (46)	88 (54)	
Retro orbital pain			0.943
No $(N = 253)$	131 (52)	122 (48)	
Yes (N = 19)	10 (53)	9 (47)	
Myalgia			0.757
No $(N = 179)$	94 (52)	85 (48)	
Yes (N = 93)	47 (50)	46 (50)	
Arthralgia			0.290
No $(N = 215)$	115 (53)	100 (47)	
Yes (N = 57)	26 (46)	31 (54)	

Table 1 (cont)

Variable	Frequen	Frequency, n (%) *	
	LOS ≤4 days	LOS >4 days	-
Rash			0.549
No $(N = 224)$	118 (53)	106 (47)	
Yes (N = 48)	23 (48)	25 (52)	
Nausea			0.800
No $(N = 41)$	22 (54)	19 (46)	
Yes $(N = 231)$	119 (51)	112 (49)	
Vomiting			0.004
No (N = 145)	87 (60)	58 (40)	
Yes (N = 127)	54 (43)	73 (57)	
Bleeding			0.209
No $(N = 228)$	122 (53.5)	106 (46.5)	
Yes (N = 44)	19 (43.2)	25 (56.8)	
Coinfection			0.686
Absent $(N = 253)$	132 (52)	121 (48)	
Suspected/confirmed (N = 19)	9 (47)	10 (53)	
Hemoglobin level			0.084
Normal (N = 168)	47 (45)	57 (55)	
Low^{\S} (N = 104)	94 (56)	74 (44)	
Platelet count			0.040
$>100\times10^{3} \text{ cells/}\mu l \text{ (N = 34)}$	23 (68)	11 (32)	
$>50\times10^3 - 100\times10^3 \text{ cells/}\mu\text{l (N = 78)}$	46 (59)	32 (41)	
$20 \times 10^3 - 50 \times 10^3 \text{ cells/} \mu \text{l (N = 87)}$	41 (47)	46 (54)	
$<20\times10^{3} \text{ cells/}\mu\text{l (N = 73)}$	31 (43)	42 (57)	

Table 1 (cont)

Variable	Frequency, n (%)*		<i>p-</i> value [†]
	LOS ≤4 days	LOS >4 days	-
Elevated hematocrit			0.370
No $(N = 126)$	69 (55)	57 (45)	
Yes $(N = 146)$	72 (49)	74 (51)	
White blood cell count			< 0.001
$>5 \times 10^3 \text{ cells/} \mu l \text{ (N = 62)}$	46 (74)	16 (26)	
$\leq 5 \times 10^3 \text{ cells/} \mu l \text{ (N = 210)}$	95 (45)	115 (55)	
Systolic (mmHg), mean ± SD	131 ± 15	129 ± 15	0.520
Diastolic (mmHg), mean ± SD	90 ± 68	83 ± 11	0.284
Pulse (per minute), mean ± SD	105 ± 78	103 ± 15	0.758

*Unless otherwise stated; *Significantly different when p-value ≤ 0.05 ; *Negative NS1 or IgM results, or never been tested; *Female <11.6 g/dl, male <13.2 g/dl; \parallel >40% in female adults, >46% and >42% in males ≤ 60 and >60 years of age, respectively

DF: dengue fever, DHF: dengue hemorrhagic fever, g/dl: gram per deciliter; IgM: immunoglobulin M; LOS: length of stay; mmHg: millimeters of mercury; NS1: non-structural protein 1; SD: standard deviation; μ l: microliter

by Fatmawati General Hospital as these outlying parameters might be associated with prolonged hospital stay. Patients with comorbidities, confirmed dengue results using NS1 or IgM test and ≤4 days of illness before admission experienced a higher percent prolonged hospital stay. Interestingly, male

participants had a lower percent prolonged hospital stay. Patients who experienced fever, headache and/or vomiting had a higher percent prolonged hospital stay. Surprisingly, disease severity is not significant in the bivariate analysis, but was included in the multivariate analysis because

this parameter might have an independent role in determining the length of hospitalization.

In the multivariate analysis (Table 2), we observed that comorbidity, days of illness before admission, vomiting, platelet count, hemoglobin level, and WBC count are significantly associated with prolonged hospital stay. Patients with comorbidities were 2.08 (95% CI: 1.02-4.25, p-value = 0.045) times more likely to experience prolonged hospital stay than those without comorbidity. Predictors of prolonged hospital stay were the following (in order of decreasing adjusted odds ratio (aOR): nadir platelet counts <20×10³ cells/ μl (aOR = 3.47), low WBC and hemoglobin counts (aORs = 2.28 and 1.92 respectively), and vomiting (aOR = 1.95). Admission to the hospital after 4 days of illness had a lower risk of prolonged hospitalization than admission within 4 days of illness (aOR = 0.27). Disease severity demonstrated a nonsignificant association, with DHF cases exhibiting lower odds than DF (aOR = 0.54; p-value = 0.06). Fever (aOR = 2.03; p-value = 0.129), headache (aOR = 1.95; p-value = 0.087), and bleeding (aOR = 1.50; p-value = 0.299) were associated with higher odds but did not achieve statistical significance, indicating no independent predictive value in the adjusted model.

DISCUSSION

The disease burden from dengue significantly impacts healthcare costs, particularly in low- and middle-income countries where dengue is endemic. Identifying dengue patients at high risk for prolonged hospital stay may help mitigate the disease burden. We assessed various characteristics linked to prolonged hospital stays in dengue patients at tertiary care facilities. Comorbidity was one of the predictors of prolonged hospital stay, consistent with previous studies (Mallhi et al, 2017; Kunti et al, 2024; Nabila et al, 2024). It has been suggested that worsening comorbid conditions rather than dengue infection may

Southeast Asian J Trop Med Public Health

 $\label{eq:table 2} Table~2$ Multivariate analysis to evaluate risk factors of prolonged hospital stay $^{\! ^{\star}}$

, and the second	1 0	1 5
Variable	aOR (95% CI)	<i>p</i> -value
Sex		
Female	Reference	
Male	0.58 (0.33 - 1.01)	0.057
Comorbidity		
No	Reference	
Yes	2.08 (1.02 - 4.25)	0.045
Definitive diagnosis		
Not confirmed [‡]	Reference	
Confirmed	1.28 (0.70 - 2.34)	0.790
Severity		
DF	Reference	
DHF	0.54 (0.28 - 1.02)	0.06
Days of illness before admission		
≤4 days	Reference	
>4 days	0.27 (0.14 - 0.49)	< 0.001
Fever		
No	Reference	
Yes	2.03 (0.93 - 2.89)	0.129
Headache		
No	Reference	
Yes	1.95 (0.92 - 2.96)	0.087
Vomiting		
No	Reference	
Yes	1.93 (1.10 - 3.48)	0.022

Table 2 (cont)

Variable	aOR (95% CI)	<i>p</i> -value	
Bleeding			
No	Reference		
Yes	1.50 (0.70 - 3.22)	0.299	
Hemoglobin level			
Normal	Reference		
Low^{\dagger}	1.92 (1.05 - 3.48)	0.033	
Platelet count			
>100×10³ cells/µl	Reference		
>50×10³ - 100×10³ cells/μl	1.42 (0.51 - 3.94)	0.507	
20×10^3 - 50×10^3 cells/ μ l	2.74 (0.95 - 7.88)	0.062	
<20×10³ cells/μl	3.47 (1.19 - 10.12)	0.022	
White blood cell count			
>5×10³ cells/µl	Reference		
≤5×10³ cells/μl	2.74 (1.25 - 5.98) 0.011		

*Data from Table 1; [‡]Negative NS1 or IgM result, or not been tested; [†]Female <11.6 g/dl, male <13.2 g/dl

aOR: adjusted odds ratio; CI: confidence interval; DF: dengue fever, DHF; dengue hemorrhagic fever; g/dl: gram per deciliter; IgM: immunoglobulin M; NS1: non-structural protein 1; µl: microliter

be responsible for the prolonged hospital stay (Mallhi *et al*, 2017; Fonseca-Portilla *et al*, 2021; Owens *et al*, 2022). However, it is also possible that the disease severity contributes to this, as comorbidity is a recognized trigger of severe

organ involvement in dengue (Willeam Peter et al, 2019).

During hospitalization, vomiting was a predictor of prolonged hospital stays. Vomiting is one of the gastrointestinal manifestations of dengue and is

used as a warning sign based on the WHO's criteria (WHO, 2009). The presence of warning signs among dengue patients may prompt doctors to prolong hospitalization due to the lack of reliable early predictors of severity. Several reports emphasize the importance of individual warning signs as tools to recognize patients at high risk of severe illness and death (Mallhi *et al*, 2017; Thein *et al*, 2013).

Previous studies reported that days of illness before hospital admission were negatively associated with hospital stay (Simmons et al, 2015; Nabila et al, 2024; Recker et al, 2024). This phenomenon is similar to a leadtime bias. Dengue has three clinical phases: febrile, which occurs over 2-7 days; critical phase, which follows the febrile phase if patients develop DHF and usually occurs on Days 3-6 and lasts 24-48 hours; and convalescence, which involves both cessation of plasma leakage and reabsorption of leaked fluids (Simmons et al, 2015).

Regarding laboratory findings, we found that low platelet and WBC counts were predictors of prolonged hospital stay, also reported in previous studies (Khalil et al, 2014; Prattay et al, 2022; Recker et al, 2024). We observed that platelet counts in dengue patients reached their nadir, on average, on the 3rd day of hospitalization. A gradual increase until Day 8 or the final day of hospital stay indicates a favorable treatment outcome. This shows the necessity for careful monitoring of dengue patients' platelet counts in the early phase of the infection when they are likely to experience the lowest levels and may require platelet transfusion: this is not warranted for those with mild or moderate thrombocytopenia (Khalil et al, 2014; Prattay et al, 2022). Recker et al (2024) reported that WBC count is significantly associated with the length of hospital stay. Leukopenia represents the most significant hematological alteration observed in dengue. In the recovery phase, WBC counts increase, followed by an increase in platelet count after 3 to 4 days. Although WBC count is not a criterion for discharging dengue patients, WBC production during the recovery phase is a more reliable indicator of disease recovery than platelet production (Rasool *et al*, 2014).

We observed that low hemoglobin levels were associated with prolonged hospital stay. This finding may reflect the clinical course of dengue infection. Hemoglobin levels in the initial days are usually normal or slightly decreased due to erythropoiesis suppression that occurs mainly during the fever phase and is restored in the critical phase (Day et al, 2024). Subsequently, hemoglobin level rises with the increase in hemoconcentration, the earliest hematologic abnormality found in DHF. However, in severe dengue conditions accompanied by spontaneous bleeding, hemoglobin level decreases significantly, with worsening manifestations (Hassan et al, 2020). DF individuals have higher hemoglobin levels in the earlier days of fever than DHF patients (Day et al, 2024).

As alluded to in aforementioned comments, more severe disease manifestation may be associated with longer hospitalization, but our data was inconclusive. A previous study found that a more severe disease is associated with a shorter hospital stay (Hernández Bautista et al, 2024); however, the authors cautioned that time from symptom onset to admission may also play a role. We did not find that bleeding is significantly linked to prolonged hospital stay. This finding might be due to the categorization of bleeding employed in our study, which defined bleeding as any occurrence, irrespective of its type.

Two major limitations in the current study that warrant consideration. Firstly, this was a retrospective analysis conducted at a single institution, and the results may not be generalizable to other hospitals. Secondly, the data collected were from a secondary source, and might be biased due to the absence of a standardized management protocol for dengue infection; the admission and discharge criteria may differ among clinicians treating the patients.

However, the strength of this study lies in our effort to include a large and heterogeneous cohort of dengue patients. We believe the findings enhanced understanding of clinical-laboratory factors linked to extended hospitalization in adult dengue patients. This underscores the need for additional research and a strategic management protocol to mitigate the disease burden. Several reports have emphasized the importance of warning signs among individual dengue patients as predictors of high risk of severe morbidity and possible mortality (Thein et al, 2013; Mallhi et al, 2017).

In conclusion, our study demonstrated that among adult dengue patients, comorbidity, vomiting, low platelet and WBC counts, and a drop-in hemoglobin level increased the odds of prolonged hospital stay. However, prolonged hospital stay is significantly inversely correlated with the duration of illness prior

to hospital admission. We caution that variations between cases and broader shifts in factors may render general predictive factors insufficiently specific for individual patients. Nonetheless, clinicians managing dengue patients should be aware of the factors associated with longer hospital stays, thereby allowing time and resources to be allocated to patients at risk, leading to a reduction in the predicted prolonged hospital stay. In addition, our findings should be valuable for providers and hospital staff to ensure that dengue patients receive the most appropriate treatment. Future prospective research should be conducted to validate our predictors and should also include mechanism-based investigations. Developing and externally validating a composite risk score that combines demographic, clinical and laboratory data should enable even earlier intervention. Accompanying economic evaluations will be crucial to guide cost-effective implementations of dengue treatment in resourcelimited settings such as Indonesia.

ACKNOWLEDGEMENTS

The authors thank the data collection team and all healthcare workers at Fatmawati General Hospital for their valuable contributions. This research was supported by the Bio&Medical Technology Development Program of the National Research Foundation (NRF), funded by the Korean government (MSIT) (no. RS-2025-15373195).

CONFLICT OF INTEREST DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

- Ansari MS, Jain D, Harikumar H, et al.

 Identification of predictors and model for predicting prolonged length of stay in dengue patients.

 Health Care Manag Sci 2021; 24(4): 786-98.
- Day ME, Puello YC, Sang MEM, et al.

 Complete blood count values over
 time in young children during
 the dengue virus epidemic in the

- Dominican Republic from 2018 to 2020. *BioMed Res Int* 2024; 2024: 3716786.
- Du M, Jing W, Liu M, Liu J. The global trends and regional differences in incidence of dengue infection from 1990 to 2019: an analysis from the global burden of disease study 2019. *Infec Dis Ther* 2021; 10(3): 1625-43.
- Fonseca-Portilla R, Martínez-Gil M, Morgenstern-Kaplan D. Risk factors for hospitalization and mortality due to dengue fever in a Mexican population: a retrospective cohort study. *Int J Infect Dis* 2021; 110: 332-6.
- Guzmán MG, Kouri G, Bravo J, Valdes L, Susana V, Halstead SB. Effect of age on outcome of secondary dengue 2 infections. *Int J Infect Dis* 2002; 6(2): 118-24.
- Harapan H, Michie A, Mudatsir M, Sasmono RT, Imrie A. Epidemiology of dengue hemorrhagic fever in Indonesia: analysis of five decades data from the National Disease Surveillance. *BMC Res Notes* 2019; 12(1): 350.
- Hassan J, Borhany M, Abid M, Zaidi U, Fatima N, Shamsi T. Coagulation

- abnormalities in dengue and dengue haemorrhagic fever patients. Transfus Med 2020; 30(1): 46-50.
- Hernández Bautista PF, Cabrera Gaytán DA, Santacruz Tinoco CE, *et al.* Retrospective analysis of severe dengue by dengue virus serotypes in a population with social security, Mexico 2023. *Viruses* 2024; 16(5): 769.
- Khalil MAM, Tan J, Khalil MAU, Awan S, Rangasami M. Predictors of hospital stay and mortality in dengue virus infection-experience from Aga Khan University Hospital Pakistan. *BMC Res Notes* 2014; 7: 473.
- Khan NA, Azhar EI, El-Fiky S, et al. Clinical profile and outcome of hospitalized patients during first outbreak of dengue in Makkah, Saudi Arabia. Acta Trop 2008; 105(1): 39-44.
- Kunti DPSA, Bodhinatha AANP, Wirawan IMS. Dengue hemorrhagic fever in Bali: patient demographics, clinical manifestations, and laboratory findings, 2024 [cited 2025 Jun 10]. Available from: URL: https://journals.indexcopernicus.com/api/file/viewByFileId/2072016
- Li XC, Zhang YY, Zhang QY, et al. Global

- burden of viral infectious diseases of poverty based on Global Burden of Diseases Study 2021. *Infect Dis Poverty* 2024; 13(1): 71.
- Low JGH, Ong A, Tan LK, et al. The early clinical features of dengue in adults: challenges for early clinical diagnosis. *PLoS Negl Trop Dis* 2011; 5(5): e1191.
- Luh DL, Liu CC, Luo YR, Chen SC. Economic cost and burden of dengue during epidemics and non-epidemic years in Taiwan. *J Infect Public Health* 2018; 11(2): 215-23.
- Lye DC, Chan M, Lee VJ, Leo YS. Do young adults with uncomplicated dengue fever need hospitalisation? A retrospective analysis of clinical and laboratory features. *Singapore Med J* 2008; 49(6): 476-9.
- Mallhi TH, Khan AH, Sarriff A, Adnan AS, Khan YH. Determinants of mortality and prolonged hospital stay among dengue patients attending tertiary care hospital: a cross-sectional retrospective analysis. *BMJ Open* 2017; 7(7): e016805.
- Ministry of Health Republic of Indonesia. Indonesia Health Profile 2022, 2023 [cited 2025 Jun 10]. Available

from: URL: https://kemkes.go.id/app_asset/file_content_download/170295833665811500834
5c5.53299420.pdf [in Indonesian]

Nabila LS, Sulistiawati, Bramantono,
Maimunah U. Comorbid factors
and duration of illness in dengue
hemorrhagic fever patients at
Universitas Airlangga Hospital,
Surabaya, Indonesia, 2024 [cited
2025 Jun 10]. Available from:
URL: https://e-journal.unair.ac.id/JCMPHR/article/view/52966/28670

Oliveira RADS, Cordeiro MT, de Moura PMMF, et al. Serum cytokine/chemokine profiles in patients with dengue fever (DF) and dengue hemorrhagic fever (FHD) by using protein array. *J Clin Virol* 2017; 89: 39-45.

Ong A, Sandar M, Chen MI, Sin LY. Fatal dengue hemorrhagic fever in adults during a dengue epidemic in Singapore. *Int J Infect Dis* 2007; 11(3): 263-7.

Owens PL, Liang L, Barrett ML, Fingar KR. Comorbidities associated with adult inpatient stays, 2019, 2022 [cited 2025 Jun 10]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK588380/pdf/Bookshelf

NBK588380.pdf

Prattay KMR, Sarkar MR, Shafiullah AZM, Islam MS, Raihan SZ, Sharmin N. A retrospective study on the socio-demographic factors and clinical parameters of dengue disease and their effects on the clinical course and recovery of the patients in a tertiary care hospital of Bangladesh. *PLoS Negl Trop Dis* 2022; 16(4): e0010297.

Rasool F, Ahmad M, Masood I, Khan HMS. Evaluating relationship between white blood cells and platelets during recovery phase in dengue hemorrhagic fever cases in Punjab, Pakistan: a retrospective study. *Value Health* 2014; 17(7): A536-7.

Rayamajhi S, Harrison A, Yoo J. Prevalence, predictors and outcomes of prolonged length of stay among patients admitted under internal medicine in HCA Florida West Hospital: a retrospective cross-sectional study, 2024 [cited 2025 Jun 10]. Available from: URL: https://scholarlycommons.hcahealthcare.com/cgi/viewcontent.cgi?article=1034&context=northflorida2024

Recker M, Fleischmann WA, Nghia

- TH, et al. Markers of prolonged hospitalisation in severe dengue. PLoS Negl Trop Dis 2024; 18(1): e0011922.
- Ruangkriengsin D, Phisalprapa P.

 Causes of prolonged hospitalization among general internal medicine patients of a tertiary care center. *J Med Assoc Thai* 2014; 97(Suppl 3): S206-15.
- Setiati TE, Wagenaar JFP, de Kruif MD, Mairuhu ATA, van Gorp ECM, Soemantri A. Changing epidemiology of dengue haemorrhagic fever in Indonesia, 2006 [cited 2025 Jun 10]. Available from: URL: https://iris.who.int/bitstream/handle/10665/170263/db2006v30p1%20done.pdf?sequence=1&isAllowed=y
- Silalahi FES, Hidayat F, Dewi RS, Purwono N, Oktaviani N. GIS-based approaches on the accessibility of referral hospital using network analysis and the spatial distribution model of the spreading case of COVID-19 in Jakarta, Indonesia. *BMC Health Serv Res* 2020; 20(1): 1053
- Simmons CP, McPherson K, Van Vinh Chau N, et al. Recent advances in

- dengue pathogenesis and clinical management. *Vaccine* 2015; 33(50): 7061-8.
- Suwantika AA, Kautsar AP, Supadmi W, et al. Cost-effectiveness of dengue vaccination in Indonesia: considering integrated programs with Wolbachia-infected mosquitos and health education. Int J Environ Res Public Health 2020; 17(12): 4217.
- Thein TL, Gan VC, Lye DC, Yung CF, Leo YS. Utilities and limitations of the World Health Organization 2009 warning signs for adult dengue severity. *PLoS Negl Trop Dis* 2013; 7(1): e2023.
- Tissera H, Rathore APS, Leong WY, et al. Chymase level is a predictive biomarker of dengue hemorrhagic fever in pediatric and adult patients.

 J Infect Dis 2017; 216(9): 1112-21.
- Willeam Peter SS, Hassan SS, Tan VPK, et al. Admission clinicopathological factors associated with prolonged hospital stay among hospitalized patients with dengue viral infections. Vector Borne Zoonotic Dis 2019; 19(7): 549-52.
- World Health Organization (WHO).

 Dengue guidelines for diagnosis,
 treatment, prevention and control:

new edition, 2009 [cited 2025] Jun 10]. Available from: URL: https://iris.who.int/bitstream/han-dle/10665/44188/9789241547871_eng.pdf?sequence=1&isAllowed=y

World Health Organization (WHO).

Dengue haemorrhagic fever:
diagnosis, treatment, prevention
and control, 2nd edition, 1997
[cited 2025 Jun 10]. Available from:
URL: https://iris.who.int/bitstream/handle/10665/41988/9241545003
eng.pdf?sequence=1&isAllowed=y

World Health Organization Regional

Office for South-East Asia (WHO SEARO). Comprehensive guideline for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded edition, 2011 [cited 2025 Jun 10]. Available from: URL: https://iris.who.int/bitstream/handle/10665/204894/B4751. pdf?sequence=1&isAllowed=y

Yang X, Quam MBM, Zhang T, Sang S. Global burden for dengue and the evolving pattern in the past 30 years. *J Travel Med* 2021; 28(8): taab146.