



Mortality Among Dengue Infection Patients in Bandung City 2022

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Abstract

Background: Dengue infection is caused by the dengue virus. In 2021 in Indonesia, 705 mortalities were due to dengue infection, while in 2022, 1,232 mortalities. The CFR in 2019 was 0.67%, in 2020 it was 0.69%, and in 2021 it was 0.96%. Bandung City is one of the endemic areas. In 2022, found 21 reported mortality, with a CFR of 0.47% in 2020, 0.35% in 2021, and 0.19% in 2022. Risk factors for death due to dengue infection are old age, delay in treatment, platelet count, incidence of DSS, and hematocrit value. **Methods:** This is a quantitative observational study using a nested case-control research design. Uses secondary data from the Bandung City Health Service. **Results:** The results of this study confirmed association of mortality with age above 40 years (p-value: 0.008, OR: 6.320), high hematocrit value (p-value: 0.005, OR: 11.111), long gap between onset and diagnosis (p-value: 0.025, OR: 13.833), prolonged hospitalization (p-value: <0.001, OR: 8.125), and incidence of DSS (p-value <0.001, OR: 39.500). Low platelet count (p-value: 0.033, OR: 0.263) found to be protective. **Conclusions:** Age, hematocrit value, gap between onset and diagnosis, length of hospitalization, and incidence of DSS are risk factors for mortality among dengue infection patients.

Introduction

The rapid global expansion of dengue viruses poses challenges for public health officials and policymakers. Early detection and accessibility to medical services for dengue infection can reduce the death rate due to severe dengue infection from 50% to 2% (Messina *et al.*, 2019). The target for controlling dengue is to reduce the mortality rate from 0.8% in 2020 to 0% in 2030 (WHO, 2020). In 2022, there were 1290 mortality, representing an almost three-fold increase in mortality compared with 2021 (437 mortality). In early 2023, there was a surge in cases of dengue infection resulting in nearly five million cases and more than 5,000 mortality related to dengue infection reported in more than 80 countries and five WHO regions (WHO, 2023). Based on data from the World Health Organization, mortality due to

dengue in Indonesia reached 7938 (0.47%) of total deaths in 2020, with an age-adjusted death rate of 3.19 per 100,000 population, based on this data placed Indonesia in 2nd place in the world.

In the National Dengue Management Strategy, Indonesia has a target to reduce the dengue mortality rate to 0.5% by 2025 (Kementerian Kesehatan Republik Indonesia, 2019). In 2021 there were 705 mortality due to dengue infection, an increase in 2022 of 1,232 mortality (Kementerian Kesehatan Republik Indonesia, 2019). The CFR has increased, in 2019 it was 0.67%, in 2020 it was 0.69%, and in 2021 it was 0.96%. The CFR has exceeded the limit (0.7%) set in the National Dengue Control Strategy target (Kementerian Kesehatan Republik Indonesia, 2019). It can be concluded that the incidence of mortality due

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to dengue infection is still far from the target of the Ministry of Health of the Republic of Indonesia. West Java Province was ranked first as the highest incidence of mortality due to dengue with a total of 305 deaths and CFR: 0.83 (Kementerian Kesehatan Republik Indonesia, 2022).

The CFR in West Java Province in 2022 was still within the target ($<1\%$), but there are 12 regencies/cities with a mortality rate of $>1\%$ in 2022. Bandung City is one of the endemic areas for dengue infection in Indonesia because of the high number of cases and deaths every year. Bandung City has the highest dengue infection incidence in Indonesia, with 5205 cases in 2022. Although the incidence of dengue infection is not always directly related to the incidence of mortality, the existence of other variables can support the occurrence of mortality among dengue infection patients (Abualamah *et al.*, 2021) and with the availability of secondary data by the Bandung City Health Service, research can be carried out regarding the determinants of mortality in dengue infection patients in Bandung City. The government hopes to achieve the target of zero dengue in the Bandung City. In 2022, there were 21 reported mortality in Bandung City. The CFR of dengue infection in Bandung city was 0.35% in 2021, 0.19% in 2022, and 0.47% in 2023 (Dinas Kesehatan Kota Bandung, 2022). Based on the data presented by the Bandung City Health Service, it can be concluded that the incidence of mortality due to dengue infection is above the target.

The incidence of mortality due to dengue tends to be dominated by elderly patients, severe dengue infection, and subsequent secondary infections (Gauri *et al.*, 2022), these results are supported by research from Mahmood *et al.*, (2023) which concludes that for patients aged over 45 years, leukocytosis, and kidney injury acute disease can be a factor that influences the incidence of mortality due to dengue infection (Mahmood *et al.*, 2023). Other research which revealed that there is a relationship between age, delay in treatment, and the incidence of DSS with the mortality of dengue infection patients (Supangat *et al.*, 2023). Based on research by Medagama *et al.*, (2020), signs of bleeding, changes in level of consciousness,

plasma leakage, increased transaminases $>500\text{IU/L}$, and increased creatinine are signs and symptoms that lead to mortality (Medagama *et al.*, 2020). Laboratory results include significantly high total leukocyte count, absolute neutrophil count, and total platelet count, and a significantly low mean platelet volume are causes of mortality among dengue infection patients (Gauri *et al.*, 2022). Platelet monitoring during hospitalization is also important because of the association between initial platelet count and platelet changes and resulting mortality (Liu *et al.*, 2020). According to research by Freitas Carvalho Branc *et al.*, (2014), an increase in hematocrit $>20\%$ from the initial value can increase the incidence of mortality among dengue infection patients by 1.38% (Freitas *et al.*, 2014). This research aims to determine the determinants of the causes of mortality among dengue infection patients so that dengue management and treatment can be better managed to reduce the mortality rate due to dengue. Researchers have also carried out updates using calculations to predict the possibility of mortality among dengue infection patients. This research aims to determine the determinants of the causes of mortality among dengue infection patients so that dengue management and treatment can be better managed to reduce the mortality rate due to dengue. The hypothesis is that age, sex, platelets count, hematocrit value, the gap between onset and diagnosis, Length of hospital stay, and incidence of dengue shock syndrome are related to the incidence of mortality in dengue infection patients in Bandung City.

Method

This research has been approved by the Semarang State University Research Ethics Committee with number 232/KEPK/FK/KLE/2024. This research is a quantitative observational study using a nested case-control research design. The dependent variable in this study is the incidence of mortality among dengue infection patients. The independent variables in this study include age, sex, platelet count, hematocrit value, gap between onset and diagnosis, hospitalization, and incidence of DSS. Categorization of the age variable in this study uses the risk and non-risk categorize

based on previous research with the results that dengue infection patients aged ≥ 40 years had a greater risk of mortality than patients < 40 years (Sujatha *et al.*, 2021); categorization of the sex variable based on biological differences between men and women; categorization of platelet counts based on the WHO Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic fever is a risky condition is when thrombocytopenia occurs (i.e. a decrease in the platelet count $< 100,000$ cells/mm³ in dengue infection patients) and the patient's condition is not at risk (i.e. when the platelet count is $\geq 100,000$ cells/mm³); the categorization of the hematocrit value is based on the 2020 National Guidelines for Medical Services for the Management of Dengue Infection in Adults, there are $\leq 38\%$

and $> 38\%$; categorization of gap between onset and diagnosis based on CDC sources regarding Dengue Testing Guidance, there are > 7 days and ≤ 7 days; categorization of hospitalization uses patient's length of stay in hospital are > 5 days and ≤ 5 days based on previous research which stated that dengue infection patients who were hospitalized for > 5 days were at risk of mortality (Khalil *et al.*, 2014; Mallhi *et al.*, 2017); the categorization of incidence of DSS is based on the provisions of the Indonesian Ministry of Health regarding the criteria for diagnosing dengue infection, there are DF, DHF, and DSS (because no cases of DF were found so this research only discusses DHF and DSS); and the categorization of living and dead patients is based on the patient's final condition when discharge from the hospital, whether the

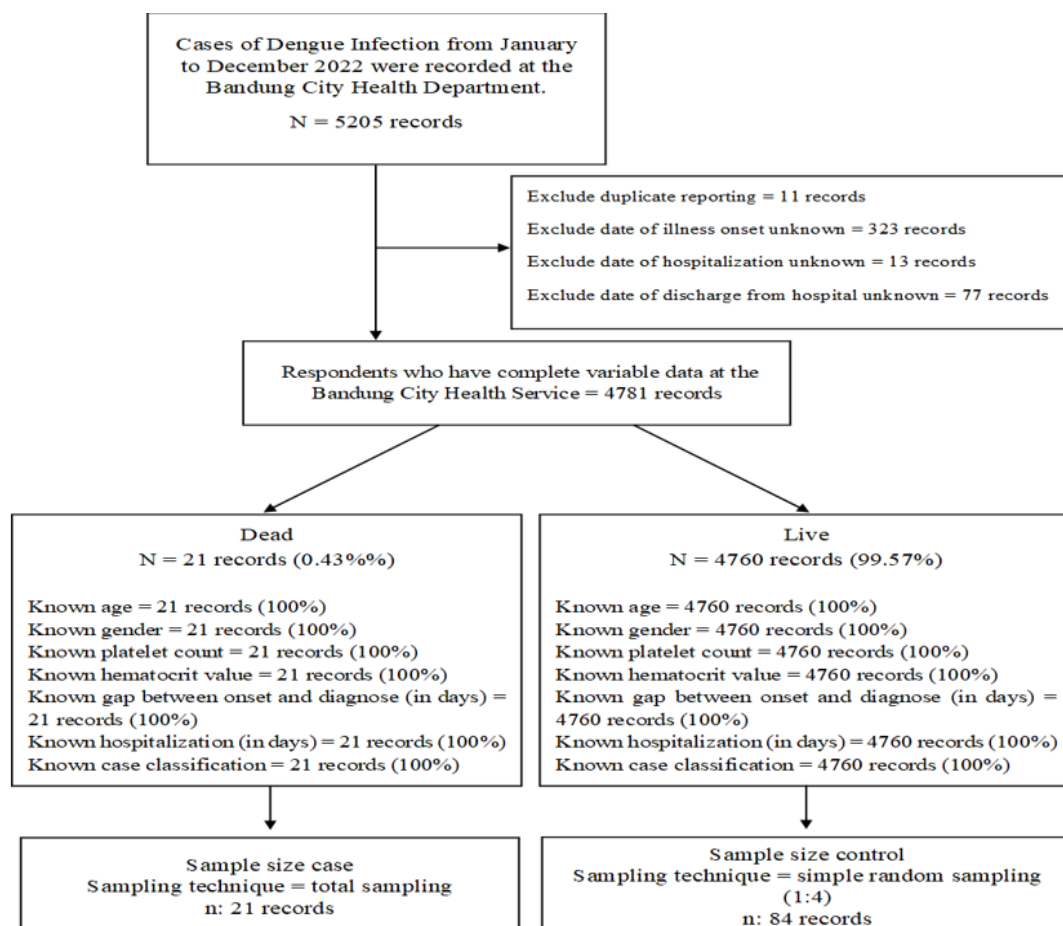


FIGURE 1. Sample Flowchart

patient is alive or dead.

The data source used in this research is obtained from the secondary data of the Bandung City Health Service from January to December 2022. The population in this study included 5205 subjects. The sample for this study was dengue infection patients in the city of Bandung from January to December 2022. The sample size used in this study was 105 subjects with 21 respondents as case subjects and 84 as control subjects. The instrument used in this research is a data collection table. Data analysis was carried out univariate, bivariate, and multivariate. Univariate analysis was carried out to obtain an overview of the frequency distribution of each variable studied. The bivariate analysis uses the Chi-Square test (or Fisher exact test as an alternative test). Multivariate analysis was carried out using a logistic regression test. Based on the sampling flow, it is known that the total data on dengue infections in the Bandung City Health Service is 5205 subjects then inclusion and exclusion criteria were identified. The inclusion criteria were 4781 records and the exclusion criteria were 424 records, resulting in a total population with complete data were 4781 records consisting of 21 case data and 4760 control data. The next stage was simple random sampling on the control group with a ratio of 1:4 to obtain a total control sample size of 84 records.

Result And Discussion

Based on the results of the univariate analysis in Table 1, out of a total of 105 patients with dengue infection, the subjects had a median age of 9 years, with a mode of 3 years. The age range spanned over 76 years, with the youngest subject being 1 year old and the oldest being 77 years old. Previous research shows that age is the dominant variable associated with the mortality of dengue infection patients in Tasikmalaya City with a p-value = 0.016 and OR = 1.873 (Supangat *et al.*, 2023). Based on analysis of various studies, it has been identified that old age (p-value <0.001) is one of the factors that can cause mortality among dengue patients in hospitals (Fonseca-Portilla *et al.*, 2021). This finding is supported by other studies that have shown that increasing age (OR 1.04, CI: 1.03–1.06) and female sex (OR 1.53,

CI: 1.01–2.33) are associated with a higher risk of mortality from dengue infection (Liew *et al.*, 2016). Patients who died had a median age of 73.9 years (interquartile range of 62 – 77 years), significantly older than those who survived, with a median age of 53.5 years (interquartile range of 37–64 years) (Lee *et al.*, 2023).

The majority of dengue infection sufferers were male with 57 patients (54.3%) while 48 patients (45.7%) were female. This result is in line with previous research, the variable independently associated with an increase in overall mortality was the male gender (HR=1.28; 95% CI: 1.23-1.34) (Msaouel *et al.*, 2014), but not in line with other previous research, reveals that women in the 30-39 year age group have a high risk of dengue infection and mortality, especially due to infection with the DEN-2 serotype (Padyana *et al.*, 2019). Laboratory tests revealed that there were 91 patients (86.7%) who had platelet counts <100,000 cells/mm³ and 14 patients (13.3%) who had platelet counts ≥100,000 cells/mm³, 74 patients (70.5%) had hematocrit values >38% and 31 patients (29.5%) had hematocrit value ≤38%. Previous research has suggested that the absolute neutrophil count and average platelet volume were predictors associated with mortality (Gauri *et al.*, 2022). Supported by research by Pinto, *et al.*, (2016) which shows that age >55 years, hematuria, gastrointestinal bleeding, and low platelet counts are factors associated with high mortality (Pinto *et al.*, 2016). Research by Gupta *et al.*, (2016) revealed that a low platelet count can be used as a predictor severity of dengue infection (Gupta *et al.*, 2016). Laboratory results indicating a significantly low platelet volume have been linked to mortality among dengue infection patients (Gauri *et al.*, 2022). Therefore important to monitor platelet levels during hospitalization due to the association between initial platelet count, platelet changes, and resulting mortality (Liu *et al.*, 2020). According to another study, patients who died had a lower platelet count (p-value: 0.017) compared to survivors when admitted to the hospital (Lee *et al.*, 2023).

Based on the diagnosis results, it was found that 20 patients (19%) experienced an incident of dengue shock syndrome, and 85

TABLE 1. Univariate Analysis Results

Variable	Median	Mode	Range	Min.	Max.
Age (year)	9	3	76	1	77

Variable	Frequency (N)	Percent (%)
Gender		
Female	48	45.7
Male	57	54.3
Total	105	100
Platelet count		
<100.000 cells/mm3	91	86.7
≥100.000 cells/mm3	14	13.3
Total	105	100
Hematocrit value		
>38%	74	70.5
≤38%	31	29.5
Total	105	100
The gap between onset and diagnosis (in days)		
>7 days	4	3.8
≤7 days	101	96.2
Total	105	100
Hospitalization		
>5 days	27	25.7
≤5 days	78	74.3
Total	105	100
Incidence of DSS		
DSS	20	19.0
DHF	85	81.0
Total	105	100
Final state		
Dead	21	20.0
Live	84	80.0
Total	105	100

patients (81%) were diagnosed with dengue hemorrhagic fever. A previous study stated that the incidence of dengue shock syndrome (DSS) was related to the mortality of dengue infection patients (Supangat *et al.*, 2023). The gap between onset and diagnosis variables was grouped based on the date of onset until diagnosis by laboratory results using IgM, IgG, or NS1 tests, while the hospitalization variable was defined

as the length of time the patient was in the hospital from admission to discharge from the hospital, whether the patient was alive or die. Among dengue infection patients, knowing that 4 patients (3.8%) were diagnosed with dengue infection more than 7 days after onset, while 101 patients (96.2%) were diagnosed in less than 7 days. During this period 27 patients (25.7%) were hospitalized for more than 5 days

while 78 patients (74.3%) were hospitalized for less than 5 days. In previous research, it was found that there was a correlation between the length of hospitalization and the incidence of patient mortality due to dengue infection (Campos *et al.*, 2015).

The bivariate analysis uses the chi-square test (or Fisher's test as an alternative) to know the relationship between variables. Found that five variables were associated with the incidence of mortality in dengue infection, including the variable age over 40 years (p-value: 0.008, OR: 6.320, CI: 1.707-23.398), high hematocrit value (p-value: 0.005, OR: 11.111, CI: 1.420-86.947), long gap between onset and diagnosis (p-value: 0.025, OR: 13.833, CI: 1.360-140.741), prolonged hospitalization (p-value: <0.001, OR: 8.125, CI: 2.840-23.245), and the incidence of DSS (p-value: <0.001, OR: 39.500, CI: 10.669-146.235). Whereas high platelet count (p-value: 0.033, OR: 0.263, CI: 0.080-0.869) was found to be a protective factor. The details of the analysis can be found in Table 2. In Table 2, it is shown that the age variable has an OR: 6.320, which means that dengue infection patients in the at-risk age category have a risk of mortality 6.320 times greater than patients at non-risk category. Previous research found a positive correlation between mortality rates and the age category over 40 years, with a p-value of 0.010 and an OR of 3.48 (Sujatha *et al.*, 2021). Several studies have shown that certain factors are associated with mortality in cases of severe dengue infection. These include older age (p-value <0.001) and lower platelet count (p-value <0.005) (Md-Sani *et al.*, 2018). Dengue infection patients have a higher risk of mortality if they are over 55 years old (OR 4.98) (Pinto *et al.*, 2016). Older age has previously been shown to cause a higher mortality rate in cases of dengue infection (Macias *et al.*, 2021).

The hematocrit value variable has an OR 11.111, this means that dengue infection patients with a hematocrit value of more than 38% have an 11.111 times greater risk of mortality (p-value: 0.005). Previous research showed that lower hematocrit levels were significantly associated with mortality in dengue infection (p-value: <0.001) (Saroch *et al.*, 2017). Supported by other research, factors associated with mortality from dengue infection are age

>40 years (p=0.004) and hematocrit value >20% (p=0.001) (Mallhi *et al.*, 2017). A previous study revealed that an increase of hematocrit >20% from the initial value can increase the incidence of mortality among dengue infection patients by 1.38% (Freitas *et al.*, 2014). The supported study that dengue infection patients who had higher hematocrit levels from day 3 to day 102 could be the main symptom of severe dengue infection and could cause a medical emergency. Regular monitoring of hematocrit values purposes to evaluate the level of plasma leakage and determine the need for therapeutic intervention in patients (Sahassananda *et al.*, 2021).

The variable gap onset and diagnosis has an OR 13.833, this means that dengue infection patients who have a time gap of more than 7 days between the onset and diagnosis of the infection have a 13.833 times greater risk of patient mortality (p-value: 0.025). Late diagnosis can cause delayed treatment and disease progression. The long time to diagnose the disease can cause severe infection and then cause respiratory failure, septic shock, and hypovolemic shock, which are reported as the main causes of mortality (Md-Sani *et al.*, 2018). Based on previous research, the average distance of a health facility from home, the time gap between the onset of symptoms and the first medical consultation in days, as well as the time gap between the onset of symptoms and the final diagnosis, were significantly related to the mortality rate. The interval between the time of onset and the time of diagnosis is associated with mortality among dengue infection patients with p-value = 0.044 and OR = 0.72 (Sujatha *et al.*, 2021).

The hospitalization variable has an OR of 8.125 (p-value: <0.001). Dengue infection can lead to prolonged hospitalization, and this may be associated with an increased risk of mortality (Shahid *et al.*, 2021). Previous research explains that duration of hospital stay is a factor associated with mortality among dengue infection patients. Length of hospital stay can be an indicator of patient care and can contribute to severe dengue infection (Fonseca-Portilla *et al.*, 2021). Supported by other research, shown a relationship between length of stay in hospital and the incidence of mortality

TABLE 2. Bivariate Analysis Results

Variable	Mortality of Dengue Infection Patients				OR (95% CI)	p-Value
	Dead (Case)		Live (Control)			
	N	%	N	%		
Age						
Risk (≥40 years)	6	28.6	5	6.0	6.320 (1.707-23.398)	0.008*
Non-Risk (<40 years)	15	71.4	79	94.0		
Total	21	100	84	100		
Gender						
Female	11	52.4	37	44.0	1.397 (0.536-3.644)	0.493
Male	10	47.6	47	56.0		
Total	21	100	84	100		
Platelet count						
<100.000 cells/mm3	15	71.4	76	90.5	0.263 (0.080-0.869)	0.033*
≥100.000 cells/mm3	6	28.6	8	9.5		
Total	21	100	84	100		
Hematocrit value						
>38%	20	95.2	54	64.3	11.111 (1.420-86.947)	0.005*
≤38%	1	4.8	30	35.7		
Total	21	100	84	100		
The gap between onset and diagnosis (in days)						
>7 days	3	14.3	1	1.2	13.833 (1.360-140.741)	0.025*
≤7 days	18	85.7	83	98.8		
Total	21	100	84	100		
Hospitalization						
>5 days	13	61.9	14	16.7	8.125 (2.840-23.245)	<0.001**
≤5 days	8	38.1	70	83.3		
Total	21	100	84	100		
Incidence of DSS						
DSS	15	71.4	5	6.0	39.500 (10.669-146.235)	<0.001**
DHF	6	28.6	79	94.0		
Total	21	100	84	100		

* = p-value < 0.05 , ** = p-value < 0.001

among dengue infection patients. The average time interval from onset of illness to hospital admission was 5 days. In patients who died, the median duration from disease onset to death was 8 days (Campos *et al.*, 2015). One of the associated factors of mortality among dengue infection patients is prolonged hospitalization (Mallhi *et al.*, 2017). In addition, time since the onset of dengue infection symptoms is one

of the most significant predictors of length of hospital stay, regardless of disease severity (Recker *et al.*, 2024).

The incidence of the dengue shock syndrome variable has an OR 39.500, which means that dengue infection patients who experienced the dengue shock syndrome (DSS) have a 39.5 times greater risk of mortality than dengue hemorrhagic fever (DHF) patients

TABLE 3. Multivariate Analysis Results

Variables	B	Wald	p-value	Adj OR (95% CI)
Incidence of DSS	3.632	20.565	<0.001**	37.806 (7.866 - 181.710)
Hospitalization	1.633	4.740	0.029*	5.118 (1.177 - 22.255)
Hematocrit value	2.653	3.825	0.050	14.197 (0.994 - 202.677)
Platelet count	-2.061	4.893	0.027*	0.127 (0.021 - 0.791)
Constant	-3.810	7.132	0.008	

* = p-value <0.05, ** = p-value <0.001

(p-value <0.001). DSS is a severe and potentially life-threatening complication of dengue infection, that is particularly challenging in children due to the high mortality rate (Armenda *et al.*, 2021). In previous research, it was known that the incidence of DSS was associated with mortality among dengue infection patients with an OR of 6.353. DSS occurs as a result of a more severe degree of infection (grade IV) (Supangat *et al.*, 2023). Supported by other research, mortality often occurs in children diagnosed with DSS. The occurrence of DSS is associated with a strong immune response (Trisasri *et al.*, 2018).

In the multivariate analysis with the logistic regression test, six variables met the requirements (p-value <0.25), including the variables age, platelet count, hematocrit value, gap between onset and diagnosis, hospitalization, and incidence of DSS. Table 3 shows that, after adjusting for other variables, the OR value obtained for the incidence of DSS is 37.806 (p-value: <0.001). The OR value for the hospitalization is 5.118 (p-value: 0.029). The Hematocrit value has an OR of 14.197 (p-value:

0.050). The platelet count has an OR of 0.127 (p-value: 0.027).

Based on the multivariate test table above, it can be concluded that after adjusting for other variables, the strongest contribution in predicting the incidence of mortality among dengue infection patients is the incidence of dengue shock syndrome. Based on previous research, revealed that DSS is a risk factor for mortality in elderly dengue infection patients (OR: 77.33, p-value <0.001) (Lee *et al.*, 2008). One of the factors associated with probable dengue mortality was shock (OR 1805.37; CI:125.44 - 25982.98) (Liew *et al.*, 2016). Supported by other research, which states that thrombocytopenia, liver dysfunction, AKI, and dengue shock syndrome (DSS) are associated with the risk of mortality (Shastri *et al.*, 2020) and in another study which stated that all DSS patients died during the study period (Jain *et al.*, 2017). Based on the results of the logistic regression analysis in the multivariate in Table 3, the logistic regression equation can be formulated as follows:

$$y = -3.810 + (3.632) (\text{DSS}) + (1.633)$$

TABLE 4. Probability of Mortality of Dengue Infection Patients in Bandung City

Respondent	Incidence of DSS	Hospitalization	Hematocrit value	Platelet count	Probability of mortality (%)
Respondent A	DSS	>5 days	>38%	<100.000 cells/mm3	93%
Respondent B	DBD	≤5 days	≤38%	≥100.000 cells/mm3	2%
Respondent C	DSS	>5 days	>38%	≥100.000 cells/mm3	98%
Respondent D	DSS	>5 days	≤38%	≥100.000 cells/mm3	81%
Respondent E	DSS	≤5 days	≤38%	<100.000 cells/mm3	9.6%
Respondent F	DSS	≤5 days	>38%	≥100.000 cells/mm3	92%
Respondent G	DBD	>5 days	≤38%	<100.000 cells/mm3	1.4%
Respondent H	DBD	≤5 days	>38%	<10.000 cells/mm3	3.8%
Respondent I	DBD	≤5 days	≤38%	<100.000 cells/mm3	0.2%
Respondent J	DBD	>5 days	>38%	≥100.000 cells/mm3	61%

(Hospitalization >5 days) + (2.653) (Hematocrit value >38%) + (-2.061) (Platelet count <100.000 cells/mm³)

The logistic regression equation above can be used to calculate the probability of mortality among dengue infection patients in Bandung City using the following formula: $p =$

Probability calculations with several scenarios are presented in the following probability table:

Based on the probability calculation table with several scenarios above, the results showed that respondent C, with the characteristics of an experience DSS, long time of hospitalization >5 days, hematocrit value >38%, and platelet count of ≥ 100.000 cells/mm³ had the highest probability of mortality among dengue infection patients, with the probability equal to 98%, while the lowest probability is respondent I with the percentage 0.2% and the characteristics of DHF, stay in hospital for ≤ 5 days, hematocrit value $\leq 38\%$, and platelet count <100.000 cells/mm³.

Conclusion

Based on the results of this study, it can be concluded that the risk factors for the incidence of death among dengue infection patients are age, hematocrit value, the gap between onset and diagnosis, hospitalization, and incidence of DSS. Platelet count was found to be a protective factor of incidence of mortality among dengue infection patients. Meanwhile, an unrelated determinant is sex. After controlling other variables, the predictor related to the incidence of death among dengue infection patients was the incidence of DSS. After adjusting for other variables, the strongest contribution in predicting the incidence of mortality among dengue infection patients is the incidence of dengue shock syndrome. This research has a limitation in that it could only consider the variables available in the Bandung City Health Service data. Moreover, many respondents had incomplete data, so missing data had to be eliminated. The recommendation for the Bandung City Health Service is to improve early detection and management of dengue to prevent critical conditions that can lead to death. The Ministry of Health is also expected to enhance existing dengue prevention programs

and increase monitoring and active surveillance activities for dengue cases. Suggestions for future researchers are expanding the research time and adding other variables.

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