

# FACTORS ASSOCIATED TO RECOVERY RATE OF DENGUE HEMORRHAGIC FEVER IN M DJAMIL HOSPITAL PADANG

Masrizal<sup>1)</sup>, Yudi Pradipta<sup>1)</sup>, Sari Laila Wahyuni<sup>1)</sup>,  
Muhammad Alfarezi<sup>2)</sup>

<sup>1)</sup>Faculty of Public Health, Andalas University

<sup>2)</sup>Program of Masters in Epidemiology, Andalas University

## ABSTRACT

**Background:** Dengue Hemorrhagic Fever (DHF) is one of the endemic diseases with the highest cases in Indonesia. The incidence of DHF has increased more than 8-fold over the past two decades by 2020, from 505,430 cases in 2000, to more than 2.4 million in 2010, and 5.2 million in 2019. This study aimed to analyze recovery rate of patients with DHF during the COVID-19 period and the associated factors.

**Subjects and Method:** This study was a retrospective cohort study conducted at Dr. M. Djamil, Padang, West Sumatera. A sample of 52 patients with DHF during the COVID-19 period (March 2020-February 2022) were selected for this study. The dependent variable was recovery. The independent variables were age, sex, duration of fever, thrombocyte level, hematocrit level, and insurance status. The data were collected from the medical record. The data were analyzed by Kaplan-Meier and Cox proportional hazard model.

**Results:** The average recovery was 10 days. The recovery rate improved with age >14 years (HR= 2.73; CI 95%= 1.05 to 7.10; p= 0.039). The recovery rate worsened with longer duration of fever (HR= 0.12; 95% CI= 0.03 to 0.54; p= 0.006), thrombocyte level <100,000 (HR= 0.88; 95% CI= 0.26 to 3.29; p= 0.006), and hematocrit level >20% (HR= 0.21; 95% CI= 0.05 to 0.93; p= 0.040). The associations between DHF and sex (HR= 1.69; CI 95%= 0.63 to 4.59; p= 0.299) and insurance status (HR= 1.29; CI 95%= 0.29 to 5.65; p= 0.739) were statistically non-significant.

**Conclusion:** The average recovery for DHF is 10 days. The recovery rate improves with age >14 years. The recovery rate worsens with longer duration of fever, thrombocyte level <100,000, and hematocrit level >20%. The associations between DHF and sex and insurance status are statistically non-significant.

**Keywords:** recovery rate, survival analysis, dengue hemorrhagic fever.

## Correspondence:

Masrizal. Faculty of Public Health, Andalas University. Email: masrizal.dtmangguang@gmail.com. Mobile: 08126733228.

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## BACKGROUND

Dengue Hemorrhagic Fever (DHF) according to the World Health Organization (WHO) is a disease caused by the bite of an Aedes mosquito infected with one of the four types of dengue virus with clinical manifestations of fever, muscle aches and joint pain accompanied by leukopenia, rash, lymphadenopathy, thrombocytopenia,

and hemorrhagic diathesis (WHO, 2020).

The *Aedes aegypti* mosquito as the main vector of DHF has a pattern of life in hot areas so that this disease develops in urban areas compared to rural areas. Risk factors for DHF transmission are rapid urban population growth, population mobilization due to improved transportation faci-

lities and infrastructure and disruption or weakening of population control so as to enable outbreaks to occur (Oroh et al., 2020).

According to WHO data in 2020, the incidence of DHF has increased more than 8-fold over the last two decades, from 505,430 cases in 2000, to more than 2.4 million in 2010, and 5.2 million in 2019. The reported deaths are between in 2000 and 2015 increased from 960 to 4032 (WHO, 2021).

Nationally, the CFR of DHF in Indonesia is 0.7%. DHF cases are also influenced by the population in an area which is described by means of incidence rate (IR). The DHF Incidence Rate in Indonesia is 40 per 100,000 population in 2020 (Ministry Health, 2020) West Sumatra is included in the top ten highest DHF Incidence Rates in Indonesia, while Sumatra Island, West Sumatra Province is the second highest after Riau Islands (Ministry Health, 2017).

Report Annually, the Padang City Health Office, the incidence of DHF fluctuates from year to year. The number of dengue cases in 2018 was 699 cases (IR= 74.3 per 100,000 population, CFR = 0.43), in 2019 there was a decrease of 430 cases) (IR= 45.2 per 100,000 population, CFR= 0), then in 2020 there were 292 cases with an increasing CFR (IR= 30.3 per 100,000 population, CFR= 0.3) (Health Department of Padang, 2022).

The health sector is currently focusing on dealing with the COVID-19 problem, thereby diverting services for cases of Dengue Hemorrhagic Fever (DHF). Diverted can be seen through the availability of space, allocation of

resources, and budget funds (refocusing). Based on the Instruction of the President of the Republic of Indonesia Number 4 of 2020 concerning Refocusing of Activities, Reallocation of Budgets, and Procurement of Goods and Services in the Context of Accelerating Handling of COVID-19. Through budget reallocation and refocusing of activities, the government can carry out programs to accelerate the handling of the pandemic, revise the budget, and program the procurement of goods and services for the purposes of handling the pandemic (Lestyowati et al., 2020).

Both DHF and COVID-19 are characterized by high fever. The similarities in symptoms between dengue fever and COVID-19 often lead to confusing diagnoses, with both infections presenting with high fever and flu-like symptoms. Likewise, routine blood tests for initial screening often show the same pattern, with the thrombocytopenia characteristic of dengue fever often appearing in COVID-19 infection as well (Kembuan, 2020).

Based on the description above, researchers are interested in researching and analyzing survival on the recovery rate of dengue hemorrhagic fever patients at Dr. M. Djamil Padang during the COVID-19 period. This study aimed to analyze recovery rate of patients with DHF during the COVID-19 period and the associated factors.

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## SUBJECTS AND METHOD

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### 1. Study Design

This was a quantitative study with an analytical approach and a retrospective cohort study design. Survival analysis is used to see factors that affect the

rate of recovery of DHF patients in Dr. M. Djamil Padang with healing as an event. This study was taken time from January to June 2022.

## 2. Population and Sample

The population of this study is all DHF patients and hospitalized in RSUP Dr. M. Djamil Padang. The number of samples was 52 patients. Sampling was carried out using simple random sampling technique based on medical record data from March 2020 until February 2022.

## 3. Study Variables

The dependent variable on this study was recovery rate of DHF. The independent variables were age, sex, trombocit level, hematocrit level, insurance status, and the duration of fever.

## 4. Definition Operational of Variable

**Recovery rate of DHF** was duration of time a person survives from the time he is diagnosed with DHF to the end of the observation event: survival status in DHF patients at the end of the observation. Measurement instrument was medical record. Recovery rate of DHF divided into: (1) Event (recover)= 0 and (2) Sensor (were still sick at the end of the observation, died, or drop out) = 1.

**Age** was the patient's life span in years from birth to the time of diagnosis of DHF. Measurement instrument was medical record. Age divided to: 0 if age  $\leq 14$  years old and 1 if age  $> 14$  years old.

**Sex** was special characteristics (reproductive organs) possessed by sufferers from birth are in accordance with those recorded on the status card. Measurement instrument was medical

record. Sex divided to: (1) Male= 0; (2) Female (1).

**The duration of fever** was the time in days between starting a fever and being admitted to the hospital. Measurement instrument was medical record. The duration of fever divided to: (1)  $\leq 4$  hari = 0; and (2)  $\geq 4$  hari = 1

**Trombocit level** was platelet count at first admission to hospital. Measurement instrument was medical record. Trombocit level divided to: (1)  $\leq 100,000 / \text{mm}^3 = 0$ ; and (2)  $> 100,000 / \text{mm}^3 = 1$ .

**Hematocrit level** was the hematocrit level when the patient was first admitted to the hospital. Measurement instrument was medical record. Hematocrit level divided to: (1)  $< 20\% = 0$ ; and (2)  $\geq 20\% = 1$ .

**Insurance status** was the type of payment used by patients, such as BPJS, JAMKESMAS, JAMKESDA, and others. Measurement instrument was medical record. Insurance status divided to: (1) without insurance= 0; and (2) with insurance= 1.

## 5. Study Instruments

This study used a medical record of DHF patients in M Djamil Hospital.

## 6. Data analysis

Univariate analysis is used to describe/describe each research variable to be studied based on the frequency distribution. The magnitude of the proportion is presented descriptively in the form of absolute numbers and percentages. Bivariate analysis is used to determine the relationship between two variables, namely the independent variable and the dependent variable. In the bivariate analysis, the Kaplan-Meier method was used to determine the probability of survival as well as

the mean and median survival. The log rank test method was used to test the mean significance between the two groups of variables. Then, the Cox regression method is used to see the relationship and the magnitude of the influence of each independent variable on the dependent variable, through the risk value in the form of the Hazard Ratio (HR), and the variable will be related if it has a  $p < 0.05$ .

### 7. Research Ethics

This study has passed an ethical test conducted by the M Djamil Hospital Health Research Ethics Protocol Team.

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## RESULTS

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Table 1 shows that of the 52 DHF patients, 17 people (32.7%) had events (cured). While those who experienced censored (died, improved, and disappeared from observation) were 35 people (67.3%) with details of 2 people (3.85%) died, 30 people (57.7%) improved or had not recovered until the end of the observation, and 3 people (5.78%) who returned home at their own request or disappeared from observation. Become a DHF patient at RSUP Dr. M. Djamil During the COVID-19 period, more experienced censored than experienced events.

The average time it takes a patient to recover from DHF at Dr. M. Djamil Padang is for 10 days with an interquartile distance of (IQR) 8-11 day. Meanwhile, the minimum and maximum recovery times were obtained for 1 and 14 days, respectively. From 52 DHF patients, 17 (32.7%)

people. While those who experienced censored (died, improved, and disappeared from observation) were 35 (67.3%) people with details as many as 2 people (3.85%) died, 30 (57.7%) people improved or had not recovered until the end of the observation, and 3 (5.78%) people who returned at their own request or disappeared from observation. So the DHF patient at the Dr. M. Djamil During the COVID-19 period, more people were censored than those who experienced events.

Table 2 shows that most of the DHF patients at RSUP Dr. M. Djamil Padang during the COVID-19 period he was  $> 14$  years old (75%), male (51.9%), had a fever for  $> 4$  days before being treated (61.5%), had a platelet level of  $\leq 100,000 \text{ mm}^3$  (84.6%), had a hematocrit level of  $> 20\%$  (75%), and used insurance (90.4%).

Table 3 showed that the average recovery was 10 days. The recovery rate improved with age  $> 14$  years (HR= 2.73; CI 95%= 1.05 to 7.10;  $p = 0.039$ ). The recovery rate worsened with longer duration of fever (HR= 0.12; 95% CI= 0.03 to 0.54;  $p = 0.006$ ), thrombocyte level  $< 100,000$  (HR= 0.88; 95% CI= 0.26 to 3.29;  $p = 0.006$ ), and hematocrit level  $> 20\%$  (HR= 0.21; 95% CI= 0.05 to 0.93;  $p = 0.040$ ). The associations between DHF and sex (HR= 1.69; CI 95%= 0.63 to 4.59;  $p = 0.299$ ) and insurance status (HR= 1.29; CI 95%= 0.29 to 5.65;  $p = 0.739$ ) were statistically non-significant.

**Table 1. Distribution and Frequencies of Survival status of DHF Patient**

Survival Status	Frequency (n)	Percentage (%)
<b>Event</b>	17	32.7
<b>Censored</b>	35	67.3
Death	2	3.85
Recovered	30	57.7
Lost to follow up (PAPS)	3	5.78
Total	52	100

**Table 2. Distribution and Frequencies of Independent Variables**

Variables	Frequency (n)	Percentage (%)
Age		
≤14 years old	13	25
> 14 years old	39	75
Sex		
Male	27	51.9
Female	25	48.1
The duration of fever		
≤ 4 days	20	38.5
≥ 4 days	32	61.5
Trombocyte level		
≤ 100.000 mm <sup>3</sup>	44	84.6
> 100.000 mm <sup>3</sup>	8	15.4
Hematocrit level		
≤ 20%	13	25
> 20%	39	75
Insurance status		
without insurance	5	9.6
with insurance	47	90.4

**Table 3. Correlation between Independent Variables and Dengue Healing Rate of Dengue Patients at RSUP Dr. M. Djamil Padang**

Variables	p-log rank	HR	(95% CI)	p
Age	0.024	2.73	1.05 to 7.10	0.039
Sex	0.269	1.69	0.63 to 4.59	0.299
The duration of fever	0.001	0.12	0.03 to 0.54	0.006
Trombocit level	0.871	0.90	0.26 to 3.19	0.877
Hematocrit level	0.011	0.21	0.05 to 0.93	0.040
Insurance Status	0.725	1.29	0.29 to 5.65	0.739

### DISCUSSION

Age is related to the rate of recovery of DHF patients. Research which states that age has a significant effect on the recovery rate of DHF patients ( $p=0.017$ ). Older patients tend to have a longer recovery rate than younger patients (Putu et al., 2012).

Gender is not related to the recovery rate of DHF patients. The results of this study are in line with the research of Mufidah and Purhadi (2016) which concluded that the time of improvement in the clinical condition of DHF patients with male and female gender was not significantly different

(Mufidah and Purhadi, 2016) Another study conducted by Like stated that gender did not have a significant relationship with the recovery rate of DHF patients ( $p= 0.763$ ) (Widyawati, 2020).

The duration of fever before being treated is related to the recovery rate of DHF patients. The results of this study are in line with the results of Putri's research, which states that DHF patients who had a long fever before being treated for  $>4$  days had a faster recovery rate than patients who had a fever before being treated for 4 days ( $p= 0.046$ ) (Hasibuan, 2018). The course of dengue fever is non-specific, patients often come to the hospital in serious condition, and many people end up not being cured. In another study, the shock phase occurred on the third to fifth day. The critical phase of dengue fever is when the body temperature drops, thrombocytopenia occurs with plasma concentrations that reflect plasma leakage. Immediate and appropriate fluid replacement with isotonic plasma solutions is a measure that can prevent shock (Hadi, 2019).

Platelets have no relationship with the healing rate of DHF patients. The results of this study are in line with the results of research conducted by Irfan, which states that platelets have no significant effect on the recovery rate of DHF patients ( $p= 0.218$ ) (Afifi Irfan, 2017). Research conducted by Mohammad also states that platelets does not have a significant relationship with recovery rate of DHF patients ( $p= 0.071$ ) (Muhammad, 2020). Dengue virus that enters the blood vessels can cause platelet cell death. be faster. This condition makes platelets quickly clot due to damage to the lini-

ng of blood vessels, and results in decreased platelet production in the bone marrow. The majority of DHF patients have quite low platelet levels.

Hematocrit has a relationship with the recovery rate of DHF patients. The results of this study are in line with the results of a study conducted by Afifi (2017), who found a significant relationship between hematocrit and the recovery rate of DHF patients ( $p= 0.004$ ) (Afifi, 2017). The same was also found from Mufidah and Purhadi (2016) research that hematocrit significantly related to the recovery rate of DHF patients. According to from Mufidah and Purhadi (2016), for every increase of one unit of hematocrit level, there is a possibility of a decrease in the patient's clinical condition improvement by 0.94 times. The data taken is the initial assessment data where the hematocrit level is indeed high.

Insurance is not related to the recovery rate of DHF patients. The results of this study are in line with the results of research conducted by Like, which stated that insurance was not significantly related to the recovery rate of DHF patients ( $p= 0.406$ ). Based on the attached Kaplan Meier curve, it can be concluded that there is no significant difference in the recovery rate between patients who use insurance or without insurance (Widyawati, 2020). In health services, patients who do not use insurance will get the same service as patients who use insurance. Patients who come to the hospital for treatment will be treated the same by health workers.

Pujiarti (2016) study found that the duration of fever before being treated  $>4$  days has a risk of developing

dengue shock syndrome (DSS) which can cause death. The duration of fever in DHF consists of three phases, namely the febrile phase, the critical phase, and the critical phase. healing. In the febrile phase, sudden fever occurs on days 1-3, the patient experiences heat with a high temperature (Pujiarti, 2016). The critical phase occurs on the 4-5th day accompanied by a sudden drop in fever and it is often thought that the patient has recovered, but at that time the patient is experiencing a critical phase. Meanwhile, the healing phase lasts more than 7 days (Yatra, 2014).

This research concludes that DHF patients at RSUP Dr. M. Djamil Padang During the COVID-19 period, there were more people who experienced censored than those who experienced events. Most of the DHF patients were >14 years old, male, had a fever > 4 days before being admitted, had platelet levels  $\leq 100,000$  mm<sup>3</sup>, had a hematocrit level >20%, and used insurance. Age, length of fever before being treated, and hematocrit affect the recovery rate of DHF patients at Dr. RSUP. M. Djamil Padang. The most dominant factor affecting the rate of recovery of DHF patients in Dr. RSUP. M. Djamil Padang was the Length of Fever Before Treatment. It is hoped that the hospital will improve the management of DHF patient services so that the patient's clinical improvement process will be faster and improve health education through the hospital health promotion program (PKM-RS) to patients, patient families, and hospital visitors related to the risk of developing dengue hemorrhagic fever. DHF.

#### **AUTHOR CONTRIBUTION**

This study conducted by team that lead by Masrizal as a Corresponding and First author. And the other author has a task such as collecting data, entry data and analyse the data.

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#### **CONFLICT OF INTEREST**

There is no conflict of interest with any person or an institution while accomplish this study.

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