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Predictive Index Using Receiver Operating Characteristic and Trend Analysis of Dengue Hemorrhagic Fever Incidence

Agung Sutriyawan[1]*, Herdianti Herdianti[2], Pandu Adi Cakranegara[3], Yosef Pandai Lolan[1], Yakobus Sinaga[1]

[1]Department of Public Health, Bhakti Kencana University, Bandung, Indonesia; [2]Department of Environmental Health, Ibnu Sina University, Batam, Indonesia; [3]Department of Management, Presidential University, Cikarang, Indonesia

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***Correspondence:** Agung Sutriyawan, Bhakti Kencana University, Bandung, Indonesia. E-mail: agung.sutriawan@bku.ac.id
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Abstract

BACKGROUND: The city of Bandung is an endemic area of dengue hemorrhagic fever (DHF). Increased cases of DHF in the area have influenced the mortality rate. The number of deaths due to DHF in 2019 was 14 people.

AIM: This study aims to analyze the epidemiological determinants and to observe the trend of analysis to project DHF cases.

MATERIALS AND METHODS: This study used a case-control design. The case population is those who have DFH, while the control population is those who do not have DHF. There were 510 respondents included in this study. Samples were taken using a purposive sampling technique. Epidemiological determinants were analyzed using the Chi-square test and logistic regression, while the trend of the disease was analyzed using exponential smooth analysis.

RESULTS: The result of this study showed that education (p = 0.036), the presence of mosquito larvae (p = 0.000), container materials (p = 0.002), water containers (p = 0.025), mosquito nets (p = 0.010), the presence of solid waste (p = 0.002), mosquito repellent plants (p = 0.041), and mobility (0.004). The most dominant epidemiological determinant was the presence of mosquito larvae (odds ratio = 3.2). The predictive index of DHF can predict people who are sick with DHF among the sick population is 68.6%.

CONCLUSION: This study concluded that the significant epidemiological determinants are education, the presence of mosquito larvae, container materials, water containers, mosquito nets, the presence of solid waste, and mosquito repellent plants. Among those determinants, the presence of mosquito larvae is the most dominant factor. This study also concluded that there will be an increase in DFH cases over the next 5 years. Hence, it is important to increase larvae free index by empowering *Kader Juru Pemantau Jentik* (*JUMANTIK*) in Bandung and conducting epidemiological surveillance.

Introduction

Dengue hemorrhagic fever (DHF) is a tropical disease that is still an international problem in public health. In recent decades, around 50 million DHF infections occurred, which causes significant morbidity and mortality worldwide [1]. DHF is an infectious disease caused by the dengue virus (DENV) through the bite of the Aedes mosquito, especially Aedes aegypti [2]. This disease is also known as the fastest-growing disease in the world [3], characterized by sudden fever and bleeding, either on the skin or elsewhere in the body which can lead to shock and death [4]

One model estimated 390 million DHF infections every year. Another study on the prevalence of dengue assessed that 3.9 billion people are at risk of infection. Despite the risk of infection in 129 countries, 70% of those originated in Asia [5]. From 2015 to 2019, DHF cases in the Southeast Asia region increased by 46% while the mortality rate decreased by 2%. One of the existent problems is the high incident rate of DHF in the Southeast Asia region, exacerbated also by the lack of effective treatment and also by the lack of a continuous comprehensive vector control program [6].

In Indonesia, there were 248,127 cases in 2019. There was a significant increase in cases from the previous year, which was 65,602 cases. In addition to the increase in incidence, there was also an increase in case fatality ration from 0.65 to 0.94 [7]. Meanwhile, until July 2020, the number of cases reached 71,633 cases. Various factors are responsible for the expansion and distribution of mosquito vectors such as high population growth rates, inadequate water supply, poor storage system, poor sewage system, poor waste management systems, increased global trade and tourism, global warming, changes in public health policy, and the development of hyperendemicity in urban areas [6]. The DHF prevention and control program has been carried out on a national scale by the Indonesian Ministry of Health (*Kemenkes*) through the *Direktorat Jenderal Pengendalian Penyakit Menular* since 1968 [8]. These programs include fogging, mass larviciding, and disease control education to the public. Despite these efforts, DHF cases have increased both in terms of incidence and geographical range over the years and have become hyperendemic with several DENV serotypes circulating together nationally [9].

Bandung is a DHF endemic city. The number of DHF cases in Bandung has not only increased over the years but also caused several deaths. In 2018, the number of cases was 2826 with 7 deaths. There was a significant increase in 2019 to 4424 cases with 14 deaths. The most effective way to reduce these breeding places is to provide basic sanitation facilities that are accessible to the entire community and also to coordinate the efforts to eradicate mosquito nests. Another effective method is to increase the ability of health workers in detecting DHF signs and symptoms and provides available treatment at health facilities. At present, guidelines for the diagnosis, treatment, prevention, and control of DHF are available in all *Puskesmas* (Community Health Center) [10]. A study uses the Poisson Kringing Model which is used to determine the level of risk of the incidence of DHF [11]. The description of DHF cases and prevention efforts has indeed been carried out, nevertheless one of the gaps in the epidemiological determinants and trends in the analysis of DHF disease in Bandung. Hence, the purpose of this study was to analyze the predictive index and observe the trend of analysis to project the number of DHF cases in Bandung.

Materials and Methods

Study design

The research method of this study is a quantitative study using an analytical observational design with a case-control approach. The data used are primary and secondary. Primary data were obtained from data collection of epidemiological determinants, while secondary data are the DHF incidence from 2016 to 2020 taken from the Bandung City Health Office which was used to determine the analysis of trends in DHF. The case population is those who have DHF in 2020 and 2021 in Bandung, while the control population is those who do not have DHF.

Sampling techniques

The sample in this study was 510 respondents, consisting of 255 case groups and 255 control groups. The determination of the minimum sample was established using the formula for hypothesis by testing the difference of two proportions. A sampling of both cases and control was carried out in thirteen Health Center (*Puskesmas)* regions throughout Bandung. The sample was taken using a purposive sampling technique with the following criteria resides in the city of Bandung, living in their own house, able to read and write, allows to have an observation both inside and outside the house. All participants agreed to the study protocol and provided written informed consent. This study has been approved by the Ethical Committee of STIK Immanuel Bandung, decisions number 054/KEPK/STIKI/VI/2021, and has followed every principle in the research process. The research instruments used were questionnaires and observation sheets.

Statistical methods

This study uses three statistical tests. First, the Chi-square test was used to observe the relationship between the characteristics of the host, agent, and environment with the incidence of DHF. Second, multiple logistic regressions were used to construct a predictive index model for the incidence of DHF. So that it will produce an odds ratio (OR) value and also the best index value can be obtained. Receiver operating characteristics (ROC) analysis was utilized also to test the performance (sensitivity and specificity) of a test within a certain range of values. The results of the ROC analysis will also produce a ROC curve that can determine the cut of point value based on the ROC curve that has been obtained. Third, an exponential smooth analysis tool with Holt's linear trend model was used to project the development of DHF cases in Bandung.

Results

This research was conducted in Bandung City. Questionnaires were distributed at thirteen Health Centers (Puskesmas). The study analyzed Host, Agent, and Environment. Those who participated in the study were 510 participants. It consisted of 255 case groups and 255 control groups. The results of the study are presented in the form of tables and figures. Table 1 shows that almost all respondents belonged to the low-risk age group; most of the respondents are female; most of the respondents are highly educated, most of the respondents are unemployed, and more than half of them have low income.

Table 1: Characteristics of respondents

Characteristics	*n* (%)
Age	
High risk	49 (9.6)
Low risk	461 (90.4)
Gender	
Male	163 (32.0)
Female	347 (68.0)
Level of education	
Low	161 (31.6)
High	349 (68.4)
Occupation	
Unmployed	312 (61.2)
Employed	198 (38.8)
Income	
Low	287 (56.3)
High	223 (43.7)
Total	510 (100.0)

Table 2 shows that the variables related to the incidence of DHF are education and the presence of mosquito larvae ($p < 0.005$). While the variables of age, gender, occupation, and income cannot be proven.

Table 2: Chi-square test of host and agent with dengue hemorrhagic fever incidence

Host and agents	DHF incidence		p	OR (95% CI)
	Cases, *n* (%)	Control, *n* (%)		
Age				
Low risk	27 (10.6)	22 (8.6)	0.548	1.254 (0.694–2.267)
High risk	228 (89.4)	233 (91.4)		
Gender				
Male	86 (33.7)	77 (30.2)	0.447	1.176 (0.810–1.708)
Female	169 (66.3)	178 (69.8)		
Level of education				
Low	92 (36.1)	69 (27.1)	0.036	1.521 (1.044–2.217)
High	163 (63.9)	186 (72.9)		
Occupation				
Unmployed	148 (58.0)	164 (64.3)	0.173	0.767 (0.537–1.097)
Employed	107 (42.0)	91 (35.7)		
Income				
Low	140 (54.9)	147 (57.6)	0.592	0.894 (0.630–1.269)
High	115 (45.1)	108 (42.4)		
Mosquito larvae				
Present	133 (52.2)	63 (24.7)	0.000	3.322 (2.281–4.839)
Not present	122 (47.8)	192 (75.3)		

DHF: Dengue hemorrhagic fever, CI: Confidence interval, OR: Odds ratio.

Table 3 shows that the environmental conditions related to the incidence of DHF are the type of container materials, water container, mosquito nets, the presence of solid waste, the presence of mosquito repellant plants, and population mobility ($p < 0.005$).

Table 3: Chi-square test of environment with dengue hemorrhagic fever incidence

Environmental	DHF incidence		p	OR (95% CI)
	Case, *n* (%)	Control, *n* (%)		
Container materials				
Ceramic/plastic	173 (67.8)	137 (53.7)	0.002	1.817 (1.268–2.605)
Cement/soil	82 (32.2)	118 (46.3)		
Water container				
Present	160 (62.7)	134 (52.5)	0.025	1.521 (1.068–2.165)
Not present	95 (37.3)	121 (47.5)		
Mosquito net				
Present	138 (54.1)	108 (42.4)	0.010	1.605 (1.132–2.278)
Not present	117 (45.9)	147 (57.6)		
Presence of solid waste				
Present	126 (49.4)	91 (35.7)	0.002	1.760 (1.234–2.510)
Not present	129 (50.6)	164 (64.3)		
Presence of mosquito repellant plants				
Present	178 (69.8)	155 (60.8)	0.041	1.491 (1.033–2.153)
Not present	77 (30.2)	100 (39.2)		
Mobility				
Yes	76 (29.8)	47 (18.4)	0.004	1.879 (1.241–2.845)
No	179 (70.2)	208 (81.6)		

DHF: Dengue hemorrhagic fever, CI: Confidence interval, OR: Odds ratio.

All independent variables that are candidates are included in multivariate analysis. Multivariate analysis aims to obtain the most dominant independent variables associated with dbd events. Table 4 depicted the result of a multiple logistic regression test which aims to determine the most dominant risk factor associated with the incidence of DHF, these results indicate that mosquito larvae are the epidemiological determinants most associated with the incidence of DHF (OR = 3.2)

Table 4: Final modeling of logistic regression epidemiological determinants of dengue hemorrhagic fever

Epidemiological determinants	*B*	p	OR (95% CI)
Mosquito larvae	1.163	0.000	3.201 (2.153–4.760)
Container materials	0.662	0.001	1.939 (1.309–2.872)
Water container	0.630	0.002	1.878 (1.258–2.803)
Mosquito nets	0.450	0.020	1.568 (1.074–2.289)
Presence of mosquito repellant plants	0.480	0.024	1.615 (1.066–2.448)
Mobility	0.680	0.005	1.974 (1.232–3.162)
Constant	−6.226	0.000	0.002

CI: Confidence interval, OR: Odds ratio.

The final results of the dual logistic regression test obtained variable drain, closing, recycling, raising fish, flick inspection, container materials, water reservoirs, mosquito wire, mosquito flicks, the presence of solid waste, the presence of parks, and mobility included in the predictive index formula.

Logistic regression equation: $Y' = a + b_1x_1 + b_2x_2 + \ldots + b_nx_n$

Predictive index formula for DHF = -10,057 + 0,639 × drain water(no) + 0,498 × close water reservoir (no) + 0,965 × recycle(no) + 0,713 × keep larvae-eating fish(no) + -0,928 × larvae inspection(no) + 0,769 × container materials(ceramic/plastic) + 0,655 × water container(yes) + 0,492 × mosquito net(not present) + 1,023 × mosquito larvae(present) + 0,444 × solid waste(present) + 0,566 × mosquito repellent plant(not present) + 0,706*mobility(yes) + 0,139 × larvicide distribution(no)

ROC analysis results will produce an ROC curve that can determine the cutoff point value. The ROC curve of DHF is shown in Figure 1.

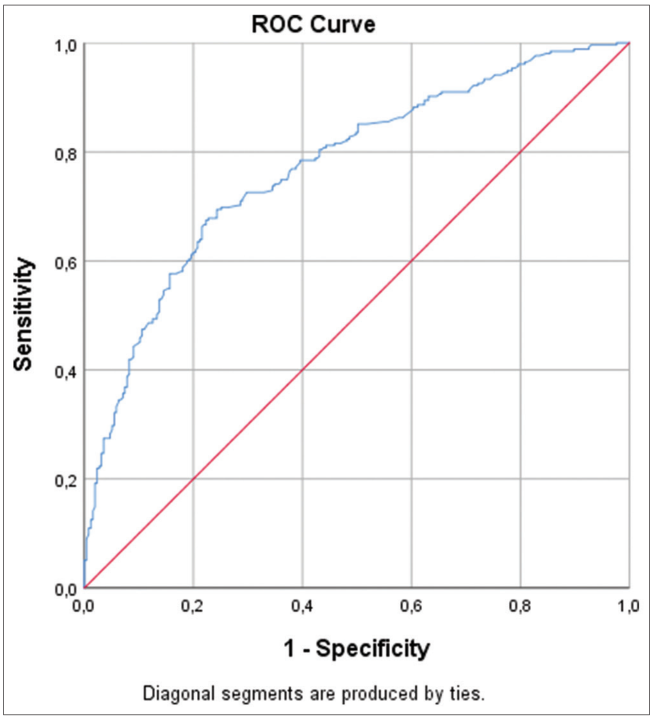

Figure 1: Receiver operating characteristics curve predictive index for dengue hemorrhagic fever

Based on the results of the ROC analysis by looking at the mid-intersection of the curve, it depicts that the formula for the incidence of DHF in this study has a sensitivity value of 68.6%. It means that the predictive index of DHF can predict people who are infected with DHF among the sick population is 68.6%. The result also shows that the value of specificity is 75.7% which means that the predictive index of DHF can predict people who are not infected with DHF among the population is 75.7%.

Trends of dengue hemorrhagic fever

The result of the projection in Figure 2 shows an increase in DFH cases in 2021–2025. This projection also depicts that in 2021 there will be 3.036 cases, this higher than DHF cases in 2020 (base year) in which there are 2790 cases. This projection also shows that there will be 3189 cases in 2025. It means that there is an increasing trend in DHF cases in Bandung in the next 5 years.

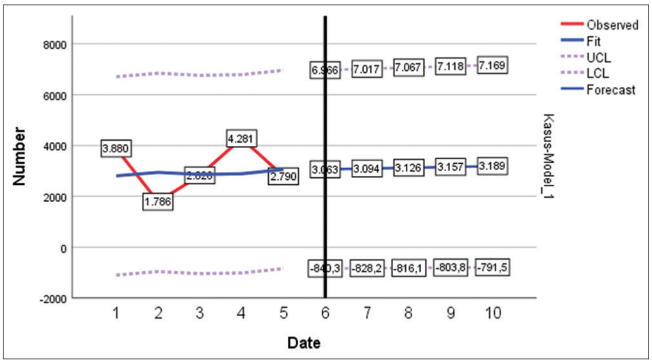

Figure 2: Graph of projected number of dengue hemorrhagic fever events for the period of 2021–2025

Discussion

The result of this study showed that the host factor associated with the incidence of DHF was education. Those with a lower level of education have a 1.5 times chance of contracting DHF. This result is in line with previous research which stated that education is one of the important risk factors for an individual to be infected with DHF. Meanwhile, another study stated that the distribution pattern of DHF tends to move in a positive direction with the variables of age, employment status, educational status, and population density [12].

This study also shows that the higher the education level of the respondent, the greater the ability to filter the information obtained. Those who have a higher level of education tend to pay more attention to their health and their families as well. Most of the respondents in this study have a high level of education in which they graduated from senior high school and college as well. However, those who have had DHF are more likely to have low education compared to those who have never had DHF.

Education is closely related to knowledge and this is expected if an individual with good education background will have better knowledge [13]. The lack of knowledge will lead to a lack of awareness about the importance of preventing and overcoming DHF [14]. Those with low educational levels tend to seek less education and are also unable to perceive it. Hence, with the respondent's lack of knowledge, they were unable to take preventive action against DHF [15].

Tabel 5: The result of the area under the receiver operating characteristic curve AQ1

Area	SE[a]	Asymptotic signifcance[b]	Asymptotic 95% CI (lower bound–upper bound)
0.772	0.021	0.000	0.732–0.813

CI: Confidence interval, SE: Standard error.

The area under the curve is 0.772 with a significance value of 0.000. This result shows that the DHF predictive Index has a good capability to predict true positive and true negative cases with a 0.0013 cut-off point. The result according to the cut off point index was 0.314 which means:

1. If the Index score is <0.0013, it means that there is a low risk for DHF.

2. If the index score is 0.0013, it means that there is a high risk for DHF

The agent factor studied in this research is the presence of mosquito larvae in the water reservoir. Observations were made in jars, drum baths, and buckets. In this study, no further identification was carried out to ensure that the larvae found were larvae of aedes aegypti or not. The results showed that the agent factor (presence of mosquito larvae) was associated with the incidence of DHF. This result is in line with the previous study which stated that the presence of mosquito larva is one of the risk factors associated with DHF[16], [17]

This study, it was observed that the case group used plastic water buckets more often even though they have permanent water containers in their lavatory. In the control group, almost all of the respondents have implemented mosquito nest eradication which in turn affected mosquito breeding. Multiple logistic regression tests showed that the presence of mosquito larvae was the most dominant factor in the incidence of DHF. Those who live in a house where there are mosquito larvae in such places as a jar, a drum tub, or a bucket have a 3.2 times chance more likely to be infected with DHF. In this study, researchers surveyed 510 houses in the city of Bandung; there were 314 houses where no mosquito larvae were found. Hence, the larva-free rate is 61.6% which is calculated by this formula: (number of houses without mosquito larvae/number of houses observed) × 100%.

Larva free rate is the percentage of houses and or public places where mosquito larvae are not found during the larval inspection. This rate is usually obtained from larvae surveys conducted by the government to determine whether an area is larva-free or not. This survey is one of the efforts to prevent the early DHF outbreak caused by the Aedes Aegypti mosquito which breeds in the form of larvae. Mosquito larvae are the forerunners of adult mosquitoes that can be seen in mosquito nets. The more mosquito larvae that are found mean more numbers of adult mosquitoes. Hence, the greater risk of DHF transmission that may occur [18].

It is possible to reduce the risks of DHF transmission by increasing the larva-free rate. Therefore, the active role of *jumantik* cadres to eradicate mosquito nests is very much needed. In addition, health workers need to carry out systematic monitoring so that the presence of mosquito larvae may be detected earlier.

Judging from physical environmental factors, water container materials are associated with the incidence of DHF. This is in line with the previous research which stated that the container material is one of the factors for the presence of Aedes aegypti mosquito larvae [19]. Through observations made by the researchers, it was found that many plastic buckets and ceramic water tubs in the lavatory were used as water containers both in the case and control group. The preferred place of the Aedes aegypti mosquito, which is the vector of DHF is a water reservoir with clear water and not exposed to direct sunlight. Aedes aegypti mosquitoes cannot live in water that is in direct contact with soil. Among the different types of water containers, the one in the lavatory is the most preferred place for the Aedes aegypti mosquito. It is suspected that this mosquito prefers the water tub in the lavatory because of its relatively larger volume and placed inside the house which is quite conducive for their breeding [20].

However, this study did not calculate the container index (CI) which is one of the indicators to determine the condition of DHV through a larva survey. A study in Jepara shows that houses with a high-risk CI score have a 5 times higher risk of contracting DHF compared to houses that have a low-risk CI score [21].

This study also proves that water reservoirs are related to the incidence of DHF. This is in line with the previous research which stated that poor environmental conditions were a risk factor for the incidence of DHF. Mosquitos will breed well if the environment is suitable to the breeding conditions, including the presence of water reservoirs that will become resting and breeding places [22].

Garbage that can hold water such as used cans, used tires, used buckets that can hold water are also suitable breeding grounds for mosquitoes. These things, if not managed properly, can become breeding ground for mosquitoes, and inadvertently the number of Aedes aegypti mosquitoes can continue to increase. Aedes aegypti mosquitoes breed in clean water; besides water containers, Aedes aegypti mosquito also prefer to breed in plastic bottles, used cans, used car tires, coconut shells, open water reservoirs, bamboo fences, coconut husks, fruits wastes, and fresh flower vase filled with water [23].

This study also shows that mosquito nets are associated with the incidence of DHF. Several other studies have stated the same facts, in which the absence of a mosquito net is a risk factor toward DHF [24]. According to the observations made by the researchers in regard to the ventilation in respondents' houses; it was found that most of the respondents in the case and control group have already used wire mesh for ventilation. Nevertheless, in most of the case group houses, the wire mesh used was not for mosquitoes.

Ventilations can be used by the mosquito to enter and exit the house. Installation of mosquito mesh is one of the effective ways to prevent transmission of DHF. The goal is to prevent mosquitoes enter the house and biting its occupants. To prevent the entry of DHF vectors, it would be better if the ventilation was in line with mosquito wire mesh and did not open doors and windows frequently to lower the possibility of mosquitoes entering the house [24].

The presence of waste can be related also the incidence of DHF. This study observed whether there are waste disposal areas and also the frequency as well. Field observation showed that in the control group most of the respondents have provided watertight waste storage area and stored the waste for no more than 2 days. In addition, the government has also provided temporary waste shelters that are placed in public places such as the market, on the side of the road, such as in the residential complexes, making it easier for the community to manage their waste.

Prevention of the spread of DHF can be done in various ways; currently, the effective way is to break the chain of transmission vector control [25] Good environmental conditions can cause mosquito breeding sites to be not optimal. DHF vectors will thrive in places where there are lots of water reservoirs, especially those that are rarely cleaned or monitored [26].

Mosquito repellant plants are associated with the incidence of DHF. In this study, the mosquito repellent plants that were used among the respondents were lemongrass, celery, geranium, and rosemary. The results of observations made by the researchers showed that most of the mosquito repellent plants owned by the respondents were lemongrass and lavender. Planting mosquito-repellant plants are one of the behavior to eradicate mosquito nests [27]. The program to eradicate mosquito nests is a main priority that can be directly implemented by the community according to local conditions and culture [28].

Population mobility is associated with the incidence of DHF. This is in line with a study done in Lampung which states that population mobility is one of the risk factors for the incidence of DHF [29]. Bandung City is one of the areas in Greater Bandung, and it is directly adjacent to several surrounding cities such as Cimahi City, Bandung Regency, and West Bandung Regency. In addition, many people living in Bandung also work in Jakarta, where they usually go back to Bandung once a week. In this study, there were 29.8% of respondents from the case group always went out of town to work every week. Thus, it provides an opportunity for DHF transmission from other areas.

High population mobility brought a negative impact also with the spread of disease from one area to another due to population movement [30]. Population mobility is one of the risk factors for the transmission of DHF. One of the main causes of DHF Extraordinary events and the increasing number of affected areas, among others, is due to the increasingly dense population and its high mobility [31].

The DHF cases in Bandung can be forecasted using the exponential smoothing method. This method was used due to limited data that can be accessed by researchers. This method is one of the most widely used methods for projecting the number of cases in the next few years. The total number of dengue cases in 2020 in 2790 cases. Based on the forecasting results, there will be an increase of 273 cases. Hence, in 2015, there will be 3189 cases. By knowing the results of forecasting, it would be possible to plan and implement appropriate prevention of DHF transmission. Another study projected the number of DHF cases in East Java and concluded that the peak of DHF cases was correlated with the rainy season [32].

Rainfall can increase the number of breeding places for aedes aegypti mosquitoes [33]. The increasing intensity of mosquito bites causes the number of DHF cases to increase every time the rainy season arrives [32] The result of the prediction obtained in this research is expected to assist the government's effort to prevent and control DHF in the city of Bandung. Early efforts to eradicate and minimize DHF cases can be taken by carrying out dengue surveillance which aims to monitor trends.

Conclusion

Epidemiological determinants that are related to the incidence of DHF are education, the presence of mosquito larvae, container materials, water containers, mosquito nets, the presence of solid waste, and mosquito repellant plants. On the other hand, age, gender, and employment status are not related. The presence of mosquito larvae is the dominant factor associated with the incidence of DHF. The predictive index of DHF can predict people who are sick with DHF among the population is 68.6%. There will be an increase in DHF cases in the next 5 years. Hence, it is necessary to increase Larva free level by optimizing *Jumantik* cadres and conducting systematic monitoring so that the presence of larvae is detected earlier. Another important matter is conducting epidemiological surveillance of DHF cases.

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