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Prediction model of dengue hemorrhagic fever transmission to enhance early warning system in Gergunung Village, Klaten District, Central Java

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ABSTRACT

The dengue virus that causes dengue hemorrhagic fever (DHF) in principle is transmitted to humans through the bites of *Aedes* sp. In Indonesia, the disease is endemic in most provinces, including in Gergunung Village in Klaten District, Central Java. The village has shown the highest incidence of DHF for the last 5 years. Changes in demographical conditions, environment, and climate condition are predictors of dengue fever. This study aimed to demonstrate the association among human behavioral variables, physical environmental factors, and climate elements with DHF transmission to develop active surveillance model of DHF outbreak by the analysis of potential predictors. The research was an observational analytic study with case control design. Study population was selected from households with DHF case in 2016 through 2017 and the controls with ratio of 1:2. In total, 34 households were labeled as case and 68 households were labeled as control. Data collection was performed by observations, direct measurements, and interviews. Data were analyzed using appropriate statistical analysis with probability value of $p<0.05$. The result showed that insecticide use, proper waste management, livestock breeding, presence of plastered floor, water-resistant walls, bedroom windows, doors, gutters, and open drainage system, all did not show association with DHF case occurrence ($p>0.05$). In contrast, houses closer to each other tended to have more DHF cases ($p<0.05$; OR: 2.96; 95% CI: 1.01–8.67). Physical environmental factors and climate elements did not demonstrate significant associations with DHF case occurrence in this study. Human behavioral variables, physical environmental factors, and climate elements may serve as potential predictors of DHF outbreak, hence should be put into the model to enhance early warning system.

ABSTRAK

Virus dengue yang menyebabkan demam berdarah dengue (DBD) pada prinsipnya ditularkan ke manusia melalui gigitan Aedes sp. Di Indonesia, penyakit ini endemik di sebagian besar provinsi, termasuk di Desa Gergunung di Kabupaten Klaten, Jawa Tengah. Desa menunjukkan insiden DBD tertinggi selama 5 tahun terakhir. Perubahan kondisi demografis, lingkungan, dan kondisi iklim adalah prediktor demam berdarah. Penelitian ini bertujuan untuk menunjukkan hubungan antara variabel perilaku manusia, faktor lingkungan fisik, dan elemen iklim dengan penularan DBD untuk mengembangkan model pengawasan aktif wabah DBD dengan analisis prediktor potensial. Penelitian ini adalah penelitian analitik observasional dengan rancangan case control. Populasi penelitian dipilih dari rumah tangga dengan kasus DBD pada tahun 2016 hingga 2017 dan kontrol dengan rasio 1: 2. Secara total, 34 rumah tangga ditandai sebagai kasus dan 68 rumah tangga ditandai sebagai kontrol. Pengumpulan data dilakukan dengan observasi, pengukuran langsung, dan

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wawancara. Data dianalisis menggunakan analisis statistik yang sesuai dengan nilai probabilitas p <0,05. Hasil penelitian menunjukkan bahwa penggunaan insektisida, pengelolaan limbah yang tepat, pembiakan ternak, keberadaan lantai plester, dinding tahan air, jendela kamar tidur, pintu, talang, dan sistem drainase terbuka, semua tidak menunjukkan hubungan dengan kejadian kasus DBD (p> 0,05). Sebaliknya, rumah yang lebih dekat satu sama lain cenderung memiliki lebih banyak kasus DBD (p <0,05; OR : 2,96; 95% CI: 1,01-8,67). Faktor lingkungan fisik dan elemen iklim tidak menunjukkan hubungan yang signifikan dengan kejadian kasus DBD dalam penelitian ini. Variabel perilaku manusia, faktor lingkungan fisik, dan elemen iklim dapat berfungsi sebagai prediktor potensial wabah DBD, oleh karena itu harus dimasukkan ke dalam model untuk meningkatkan sistem peringatan dini.

INTRODUCTION

Dengue fever is one of the most important mosquito-borne diseases in the world, particularly in the tropics.[1] The disease is caused by dengue virus, transmitted to humans through the bites of *Aedes* sp.[2] Dengue fever has a variety of clinical spectrum, and the term dengue hemorrhagic fever (DHF) is one of the severe forms of the disease.[3] About two-fifth of global population live in high-risk areas for dengue transmission, and Southeast Asia region ranks the first in the incidence of DHF.[4] Along with the increasing case fatality rate (CFR) in each year, the disease is potentially fatal, especially in young population.

In Indonesia, the disease is endemic in most provinces, including in Central Java. The Klaten District belonged to area of moderate endemicity of dengue transmission, with incidence rate (IR) of 45.2 per 100,000 population and CFR of 4.7% in year 2015.[5] The village of Gergunung in the Klaten District has been showing the highest incidence of DHF for the last 5 years, with over 50 cases reported annually.[6] Consistently high incidence of DHF may be due to changes in demographical conditions, urbanization, and insufficient clean water supply.[7] Additionally, changes in climate and transmission patterns may also contribute to high incidence of DHF.[8,9] All of these factors may form a complex group of non-homogenous, unstable predictors of DHF. As the changes of potential predictors and risk factors are not followed by improvement in DHF surveillance system, it is essential to analysis these factors in correlation with DHF outbreak occurrence to produce an effective early warning system.[10]

This study aimed to demonstrate the association among human behavioral variables, physical environmental factors, and climate elements with DHF transmission in Gergunung Village of Klaten District, Central Java. The results can be beneficial in developing an active surveillance model for DHF outbreak by the analysis of potential predictors, as well as in identifying high-risk areas for DHF outbreak so that timely management can be achieved.

MATERIALS AND METHODS

Design and study populations

The research was an observational and analytic study with case control design. Current study was conducted in the village of Gergunung, Klaten District, Central Java (E110^{0}30'–110^{0}45', S7^{0}30'–7^{0}45') from July to October 2018, during which dry season took place. Research approval has been granted by the Medical and Health Research Ethics Committee (MHREC), Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta (Ref: KE/FK/0372/EC/2018 and KE/FK/0715/EC/2018). Study population was selected from households with DHF case in 2016 through 2017 and the controls with ratio of 1:2. In total, there were 35 households with DHF case, however 1 household refused to participate in the study and was then excluded from the study. Surveyed households without DHF cases were selected within a radius of 100 m from case households.[11] Finally, total sample of the study was 34 households labeled ascase and 68 households labeled as control.

Data collections

Data of climate elements, including wind velocity, specific humidity, rainfall, and temperature, were obtained from earth data online database of the National Aeronautics and Space Administration (NASA) from year 2016.[12] On the other hand, following data related to physical environmental factors were collected by direct observation and measurements i.e. lighting, CO_2, indoor and outdoor air temperature and humidity, flooring, wall, ceiling, ventilation, drainage, residential density, and distance between houses. Additionally, behavioral variables were acquired from interviews and checklists, including insecticide use, waste management, and livestock breeding.

Statistical analysis

Data were analyzed using SPSS ver. 16.0 (SPSS Inc., USA), and were tested using Chi-square test, Fisher exact test, or student t-test, wherever appropriate. The probability value was $p<0.05$.

RESULTS

Current study was conducted in the village of Gergunung, Klaten District, Central Java. With a total area of 1.42 km^2, Gergunung Village consists of 7,827 people residing in 41 neighborhoods (*Rukun Tetangga*). The village ranked the first in DHF incidence in the last five years, with family members from 35 households positively diagnosed as DHF in year 2016-2017. As one household was excluded from the study, the total sample was 102 households: 34 case households and 68 control households. Characteristics of respondents are presented in TABLE 1.

TABLE 1. Demographic characteristics of respondents in Gergunung Village, Klaten, Central Java

Variables	Case		Control		Total	
	n	%	n	%	n	%
Gender						
• Male	32	94.1	58	85.3	90	88.2
• Female	2	5.9	10	14.7	12	11.8
Education						
• Non-educated	1	2.9	3	4.4	4	3.9
• Primary school	3	8.8	20	29.4	23	22.5
• Middle school	5	14.7	15	22.1	20	19.6
• High school	12	35.3	21	30.9	33	32.4
• College/university level	13	38.2	9	13.2	22	21.6
Occupation						
• Unemployed	3	8.8	9	13.2	12	11.8
• Public sector employee	5	14.7	4	3.9	9	8.8
• Private sector employee	5	14.7	2	2.9	7	6.9
• Self-employed	11	32.4	17	25.0	28	27.5
• Worker	9	26.5	36	53.0	45	44.1
• Retired	1	2.9	0	0	1	1.0

Households who practice the use of insecticide were more likely to have DHF case, while households that sent their wastes to landfills have lower tendency to have household members affected by DHF. However, none of the parameters showed statistical significance, as summarized in TABLE 2.

TABLE 2. Analysis of behavioral variables in study population

Variables	Case		Control		p*	OR (95% CI)
	n	%	n	%		
Insecticide use						
• Did not use	17	16.7	28	27.5	0.398	1.43 (0.62–3.27)
• Used	17	16.7	40	39.2		
Waste management						
• Burned	5	4.9	14	13.7	0.472	0.66 (0.22–2.03)
• Landfills	29	28.4	54	52.9		
Livestock breeding						
• Yes	14	13.7	28	27.5	0.999	1.00 (0.43–2.31)
• No	20	19.6	40	39.2		

*Chi-square

Observation and measurements of housing physical conditions, including flooring, wall, ceiling, ventilation, drainage, residential density, and distance between houses were made to obtain potential factors that favor mosquito breeding and dengue virus transmission. Presence of plastered floor, water-resistant walls, and bedroom windows demonstrated protective effect against dengue transmission (TABLE 3). Yet, no statistical significances were observed among those factors. On the other hand, houses with doors in every room, presence of gutter, as well as presence of open drainage system were more likely to have household members with DHF ($p>0.05$). Houses with closer distance to each other tended to have more DHF cases (OR: 2.96; 95% CI:1.01–8.67), and this parameter showed statistically significant association.

TABLE 3. Analysis of housing physical conditions in study population

Variables	Case		Control		p*	OR (95% CI)
	n	%	n	%		
Flooring						
• Plain ground	4	3.9	12	11.8	0.441	0.62 (0.18–2.09)
• Plastered/tiled/ceramics	30	29.4	56	54.9		
Wall						
• Non-water resistant	3	2.9	11	10.8	0.309	0.50 (0.13–1.93)
• Plastered, water resistant	31	30.4	57	55.9		

Ceiling						
• Non, or in several rooms	12	11.8	25	24.5	0.884	0.93 (0.39–2.21)
• Present in all rooms	22	21.6	43	42.2		
Door						
• Main door only	5	4.9	7	6.9	0.514	1.50 (0.44–5.13)
• Main door and all rooms	29	28.4	61	59.8		
Ventilation						
• No wire net	28	27.5	56	54.9	0.999	1.00 (0.34–2.94)
• Wire net installed	6	5.9	12	11.7		
Gutter						
• None	20	19.6	36	35.3	0.547	1.27 (0.55–2.92)
• Present	14	13.7	32	31.4		
Drainage						
• Closed	18	17.6	27	26.5	0.204	1.71 (0.74–3.91)
• Open	16	15.7	41	40.2		
Residential density						
• Dense (≥8 m^2/person)	25	24.5	49	48.1	0.875	1.07 (0.42–2.72)
• Sparse (<8 m^2/person)	9	8.8	19	18.6		
Distance between houses						
• Close (<5.5m)	29	28.4	45	44.1	0.041	2.96 (1.01–8.67)
• Far (5.5-10m)	5	4.9	23	22.6		

*Chi-square

Environmental factors of the home composed of lighting, CO_2, as well as indoor and outdoor air temperature and humidity in the study population were measured and are presented in TABLE 4. The intensity of light, the room CO_2 level, and the outdoor humidity, are lower, all of which show a protective effect against dengue virus transmission. Air temperatures preferred for mosquito breeding, both indoor and outdoor, did not show tendencies as to which one had more impact in dengue virus transmission among household members. None of the parameters demonstrated statistical significance (p>0.05).

TABLE 4. Analysis of environmental factors of the home in study population

Variables	Case		Control		p*	OR (95% CI)
	n	%	n	%		
Light intensity						
• Low (<60 lux)	20	19.6	42	41.2	0.774	0.88 (0.38–2.04)
• High (≥60 lux)	14	13.7	26	25.5		
Room CO_2 level						
• High (≥53%)	15	14.7	36	35.3	0.401	0.70 (0.31–1.60)
• Low (<53%)	19	18.6	32	31.4		
Indoor air temperature						
• Not preferred (<25°C or >27°C)	14	13.7	29	28.4	0.887	0.94 (0.41–2.17)
• Preferred (25–27°C)	20	19.6	39	38.3		

Outdoor air temperature						
• Not preferred (<25°C or >27°C)	18	17.6	39	38.3	0.672	1.19 (0.52–2.73)
• Preferred (25–27°C)	16	15.7	29	28.4		
Indoor humidity						
• High (≥60%)	20	19.6	39	38.3	0.887	1.06 (0.46–2.44)
• Low (<60%)	14	13.7	29	28.4		
Outdoor humidity						
• High (≥60%)	17	16.7	41	40.2	0.322	0.65 (0.28–1.50)
• Low (<60%)	17	16.7	27	26.4		

*Chi-square

According to its topography, Gergunung Village belonged to the lowlands. Available data regarding climate elements in Gergunung Village in year 2016 are presented in TABLE 5. Highest wind velocities were recorded during August to December. This is in line with lowest air temperatures that were also observed during that period. However, specific humidity did not show much difference along the year, whereas heaviest rainfall occurred in two terms: February and September. In correlation with dengue virus transmission, climate elements described did not demonstrate any association with DHF case occurrence in this study.

TABLE 5. Description of climate elements in study location in year 2016

Variables	Average**	Lowest period	Highest period
Wind velocity (m/s)	2.11 (1.7–3.0)	May	December
Specific humidity	0.021 (0.020–0.023)	August	April–May
Rainfall (mm)	264.50 (115.56–421.76)	August	February
Temperature (°C)	25.05 (24.28–25.77)	August	January

**mean (min–max)

DISCUSSION

From the preceding results, potential factors influencing occurrence of DHF in Gergunung Village were investigated further through observations made of the human behavior, housing physical environment, environmental factors, and climate elements.

Human behavior

In general, all of the respondents in both groups reported daily use of different brands of insecticide from the pyrethroid group to avoid getting mosquito bites. However, use of insecticide did not show significant association in current study. This may be due to inappropriate use of insecticide, in terms of time and frequency. Most of the respondents outlined that they used insecticide at nighttime after dusk, time not suitable for *Aedes* mosquitoes feeding. *Aedes aegypti* as principal vectors of dengue virus have peak biting activities in the morning, at 08.00 to 12.00.[13] The results showed improper practice of insecticide use due to poor knowledge on mosquito feeding habits. Additionally, the respondents also reported that they have been using the same insecticide for over 6 months. Prolonged, repeated use of insecticide from the same group may lead to development of insecticide resistance,[14] which in turn may explain non-association with DHF occurrence in this study.

There were two methods of waste management observed in the study population: burning the waste or directing the waste to landfills. Majority of households (81.3%) in current study carried out their waste management by putting the waste in landfills. Nevertheless, those households only put the waste in landfills once in every 2 weeks, which caused the waste to pile up and became favored breeding place for mosquitoes.[15] Similar concept was observed in those households that burned their waste in current study. In order to avoid piling up of solid waste to become potential mosquito breeding sites, waste management should be carried out twice weekly at the least.[16] *Aedes aegypti* are highly anthropophilic mosquitoes, which implies that this species predominantly feed on humans rather than animals.[17] The presence of livestock, especially cattle, near human houses may act as cattle barrier (zooprophylaxis).[18] However, highly anthropophilic mosquitoes will still feed on mosquitoes despite the presence of cattle, making the zooprophylaxis ineffective.[19] Furthermore, none of the households in current study breed cattle in their surroundings. These states supported current study results that showed no significant association between presence of livestock and occurrence of DHF in Gergunung Village.

Housing physical environment

Although the average residential density in Gergunung Village was 4.5 m^2/person, approximately 73% of participating households had residential density of ≥8 m^2/person, which was categorized as densely populated.[20] *Aedes aegypti* mosquitoes are much easier to transmit dengue virus in densely populated residential houses, as they are multiple biters and may bite multiple persons in short period of time.[21] Additionally, their flight range is only 50 to 100 m, which makes their vectorial capacity even better in environment with packed population and houses in close proximity with each other.[22] In present study, roughly 72.5% of surveyed households were located very close to each other, and that closer distance between houses demonstrated statistically significant association with DHF occurrence. The presence of dengue-infected mosquitoes in one house initiates dengue transmission cycles to people residing inside the house and to people surrounding the house within the flight range of the mosquitoes.[23,24]

In regard to house flooring, it is preferred to have plastered, or flooring made of tiles or ceramics in order to reduce room humidity, interrupting mosquito breeding cycle.[25] Flooring of plain ground will turn damp during rainy season, hence creating more humid environment suitable for mosquito breeding.[26] Similarly, plastered walls are also preferred so that dengue-carrying mosquitoes cannot enter the house through small holes in the walls.[27] In this study, over 80% of total surveyed households, both in case and in control groups have already owned houses with plastered flooring and walls. This may explain non-association between those factors and DHF occurrence in the study population. Current study results also showed that there were no associations between open drainage and presence of gutter with occurrence of DHF. This is in conflict with previous studies that demonstrated positive association, as gutters and open drainage served as potential mosquito breeding places.[28]

The presence of windows, doors,

ceilings, and ventilation were thought to be associated with dengue virus transmission in home environment.[29] Current study results showed that over 75% of total surveyed households had bedroom windows and doors in all of the rooms. The presence of doors and windows may result in two different outcome i.e. reduced mosquito density due to reduced humidity and increased light intensity, or increased mosquito density due to presence of more entryways for mosquitoes to enter the house when they are left opened.[23,30] However, these two factors did not demonstrate association with DHF occurrence in present study. The presence of ventilations may also have similar outcomes, if the ventilations were not installed with wire nets. In both case and control groups, ventilations with no wire nets were observed in approximately 82% of total houses. Wire nets installed in ventilations, doors, and windows may act as barriers for mosquitoes to enter the house, preventing it from resting and biting humans inside.[31] Absence of ceilings may facilitate the entry of mosquitoes in houses.[32]

Environmental factors

In present study, lower light intensity, lower room CO_2 level, and lower outdoor humidity, all indicated protective effect against dengue virus transmission, despite having no statistically significant associations. Light intensity is one of the major factors in *Aedes aegypti* bionomics. Approximately 61% of surveyed houses had generally poor lighting and therefore have an increased risk of mosquito breeding. As low levels of light penetrating rooms generate a dark environment in the house, these shaded spots will become ideal resting and breeding places for mosquitoes.[33]

The CO_2 is an important product of human respiration and is known to be an attractant for mosquitoes.[34] In houses with lack of ventilation, higher CO_2 level will be a favorable condition for mosquitoes to come and rest inside the house, thus increasing the risk of transmitting dengue virus to humans residing inside the house.[30] However, no statistically significant association was observed in current study.

Additionally, temperature and humidity affect mosquito bionomics as well, particularly feeding behavior and mosquito development. In present study, humidity and temperature indoor and outdoor were generally similar, and both did not demonstrate associations with the occurrence of DHF case. Environment with a temperature of 25-27°C is optimal for *Aedes aegypti* larvae development,[35] and the time required for mosquitoes to fully develop from egg to adult depends on this range of temperature.[36,37] Increased temperature may result in shorter time needed for mosquito development, hence increasing mosquito density and risk in transmitting dengue virus.[38] Conversely, humidity of less than 60% causes shorter mosquito life span, decreasing their vectorial capacity as dengue vectors.[39]

Climate elements

Current study showed that specific humidity remained similar throughout the year, while highest wind velocities along with lowest air temperatures were recorded during August through December. None of these parameters showed statistically significant association with DHF case in this study. Mosquitoes are responsive to changes in temperature and moisture. Humidity level of 60-80% allows mosquitoes to remain alive, as dry conditions decrease the ability of mosquitoes to survive in nature.[40,41] Measurements of humidity levels may strongly predict dengue transmission.[42]

Furthermore, two peaks of heaviest rainfall were observed in February and September. Heavy rainfall may raise humidity and provide more water reservoirs that act as breeding places for *Ae. aegypti.*[43] This is strengthened by current study results that showed slight increase of DHF case in March through August. Another study has reported similar findings.[44] However, current study results demonstrated no statistically significant association between rainfall and occurrence of DHF cases.

Formulation of prediction model does not always work by using single study in one population. Present study was conducted in smaller extend of population and data collection was done at only one time and therefore may not represent the exact condition of the whole district. Heterogenous sociodemographic condition of the study population may also alter study results. Thus, interpretation of data should be carefully performed.

CONCLUSION

Current study demonstrates that insecticide use, waste management, livestock breeding, presence of plastered floor, water-resistant walls, bedroom windows, doors, gutters, and open drainage system all does not show association with DHF case occurrence. Despite many factors showing no statistically significant association with DHF case occurrence, there are some of the elements that demonstrated tendencies to be protective factors against dengue transmission, which include far distance between houses, proper house lighting, and lower carbon dioxide levels. Periods of heavy rainfall should be carefully notified to ensure DHF outbreak preparedness. These factors may serve as potential predictors of DHF outbreak, hence should be put into the model to enhance early warning system for DHF.

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