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**META-ANALYSIS** 

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## META ANALYSIS: RISK FACTOR ANALYSIS OF DENGUE DISEASE INCIDENCE IN INDONESIA

Abstract

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Introduction: Dengue fever is endemic in over 100 countries, Africa, America, and several other European countries. Indonesia became the top of the list a few years ago. The study aimed to analyze risk factors (hanging clothes, water reservoir conditions, and jumantik cadres) with the incidence of DHF. Methods: This is quantitative research with meta-analysis. Meta-analysis has four stages: data abstraction, data analysis using JASP Version 0.18.3, and publication bias test. Conduct heterogeneity tests, funnel plots, egger tests, and forest plots. **Results and Discussion:** The heterogeneity test of hanging clothes and water reservoirs using a random effects model because p-value smaller than 0.05. Jumantik cadre using the fixed effects model is larger than p < 0.001 i.e. p = 0.303. The forest plot of hanging clothes has pooled value  $PR=e^{0.26} = 1.297$  (95% CI -0.05-0.57), pooled water reservoir value  $PR = e^{0.55} = 1.73$  (95% CI 0.30 - 0.79), and jumantik cadre pooled value  $OR = e^{0.70} = 2.01$  (95% CI 0.24 - 1.33). The highest risk factor for dengue cases is jumantik cadres with the pooled value obtained  $PR = e^{0.70} = 2.01$ (95% CI 0.24 – 1.33). Conclusion: Based on the results of the meta-analysis in this study, jumantik cadres has the greatest risk factor value compared to other variables. The second highest risk factor was in water reservoirs, followed by the next variable hanging clothes.

### INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is a significant public health problem that causes outbreaks in Indonesia. Dengue fever is transmitted to humans through the bite of an Aedes aegypti mosquito infected with the dengue virus. Dengue fever can occur yearly and affects all age groups (1). The virus disrupts the capillaries and blood coagulation system, thereby causing bleeding. Clinical manifestations of dengue virus infection may include dengue fever and dengue fever. DHF is a global health problem in developing countries. The Centers for Disease Control and Prevention reports that about 2.5 billion people, or 40 percent of the world's population, live in areas at risk for dengue transmission. The World Health Organization (WHO) estimates that 50-1-million infections occur each year, including 500,000 dengue cases and 22,000 deaths. Dengue fever is endemic in over 100 African countries, America, France, and several other European countries (2). In 2021, WHO estimates that there are around 100-400 million dengue infections globally each year. Asia ranks first in the number of dengue sufferers as much as 70% each year. It is known that dengue fever is the main cause of morbidity and mortality in Southeast Asia with 57% of the total dengue fever cases in Southeast Asia occurring in Indonesia. The number of dengue fever cases continues to hit several countries in Asia, including, the Philippines with 420,000 cases, Vietnam with 320,000 cases, Malaysia with 131,000 cases, Indonesia with 102,303 cases and Bangladesh with 101,000 cases (3).

Dengue Fever Virus is commonly found in tropical and subtropical areas, mostly in urban and suburban areas. In Indonesia, with its tropical climate, it is very suitable for the growth of animals or plants and is

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good for the development of various diseases, especially diseases carried by vectors, namely organisms that spread pathogenic agents from host to host, such as mosquitoes that transmit many diseases. Population density and dengue fever cases have an important point in its transmission, as Indonesia is a highly-populated country; Indonesia's population deploys across 34 provinces, and so do the climatic conditions. Although it is a tropical area, climatic conditions in various provinces in Indonesia are diverse (4). The population density is moderate, there are endemic dengue cases. (5). Besides population density, risk factors contributing to the spread of dengue fever in Indonesia are poor sanitation and low public awareness about dengue fever prevention and treatment (6). Dengue Hemorrhagic Fever (DHF) control to date has been more emphasised in efforts to break the chain of transmission, namely in the larval phase because the number of larvae can indicate the number of Aedes aegypti vector populations (7).

A risk factor for DHF that is directly related to behaviour and environment is the habit of hanging clothes. People who have a habit of hanging clothes are 2,778 times more likely to get sick with DHF than people who do not have the habit of hanging clothes. WHO notes that hanging clothes are one of the resting places for mosquitoes (8). A research shows that there is a significant relationship between the variable habit of hanging clothes and the incidence of DHF in the Working Area of the Martubung Health Centre, with the evidence that there are many clothes and damp towels left hanging on the clothesline of the house, this makes mosquitoes perch on clothes. People who have the habit of hanging clothes have a 4,942 times larger risk of suffering from DHF than people who do not have the habit of hanging clothes (9).

The presence of mosquito larvae is one of the risk factors for dengue disease, so the presence of Aedes aegypti mosquito larvae must be watched out for. The dwelling of these larvae is a breeding ground for mosquitoes. In the previous study, the high dengue cases in Indonesia, especially in Bandung, occurred in March. In Indonesia, March is the rainy season with high humidity, so water reservoirs are filled with rainwater (10). Draining water reservoirs is one way to prevent dengue fever by cleaning the breeding sites of *Aedes aegypti* mosquitoes. This prevention is mainly done at home but can also be done in offices and other public places. Draining the landfill at least once a week can reduce the breeding area of *Aedes aegypti* larvae (11), as it is

well known that eradicating mosquito nests by draining the landfill properly effectively reduces the incidence of dengue fever.

Community participation is a critical factor in dengue disease control because mosquito larvae of the Aedes aegypti dengue virus are found in many residential areas. Rest places for adult mosquitoes are primarily at home. In this case, the community has a role to follow PSN briefings every week regularly. PSN, done routinely, can help reduce vector density, reduce human contact with vectors, and ultimately reduce dengue cases (12). Therefore, in the community, there is a need for volunteer officers or Gender Monitors to help convey health information, especially about dengue hemorrhagic fever. Juru Pemantau Jentik (Jumantik) is a working group tasked with eradicating dengue disease at the village/sub-district level at the Village Community Resilience Institute or sub-district health forum. Jumantik is a forum for local communities whose formation and supervision of performance is entirely the responsibility of the city government. The role of health cadres as community role models is to mobilize families to prevent and eradicate dengue fever. Therefore, Jumantik has a very strategic position in eradicating dengue disease. In this regard, Jumantik's attitudes and behaviours must be strengthened to support the goal of preventing the spread of dengue fever (13). Therefore, it is necessary to design research related to the Risk Analysis of Hanging Clothes, Water Reservoir Conditions, and the Role of Jumantik Cadres with DHF Events.

#### METHODS

This research method is quantitative research with meta-analysis. Meta-analysis has four stages: data abstraction, data analysis using JASP Version 0.18.3, and publication bias test. Conducting heterogeneity tests, funnel plots, test Egger's Test, and forest plots. Summarizing technique Meta-analysis involves collecting various research results quantitatively by looking for value effect size or a data summary. This research data comes from scientific articles such as journals, theses, theses, and relevant scientific proceedings, which can be found in electronic databases from Google Scholar (2020 - 2024). Keywords used in the search included "Indonesia", "Dengue Fever", "habits that result in dengue fever", "Hanging Clothes", "Water reservoirs", and "jumantik cadres" using PICO (Population, Intervention, Comparison/Control, Outcome) method. The article was screened and sorted using the PRISMA flow chart shown in figure 1.



## Figure 1. PRISMA Flow Chart Meta-Analysis of Hanging Clothes, Water Reservoirs, and Jumantik Cadres

The results of the article search show that there are 40 articles found after the screening process. However, after being re-elimination again using inclusion criteria, the final number of articles was 25 articles. Data analysis techniques involve several stages: data abstraction, data analysis, and publication bias testing. At the data abstraction stage, information from each research article is converted into a uniform table format, including the year of publication, exposure, and results of each study. If the variation between variables is homogeneous or the p-value of heterogeneity is more significant than 0.05, then the analysis model is a fixed effect model. Conversely, if the variation between variables is heterogeneous or the p-value of heterogeneity is smaller than 0.05, then the analysis model used is a random effect model.

Data analysis was carried out using a fixed or random effect model. The software used to perform Meta-Analysis is JASP Version 0.18.3. The data processing results will be presented in funnel plots and forest plot graphs to illustrate the combined effect size of each variable. The Publication Bias Test was used to identify the possibility of publication bias in this study, which will be evaluated through funnel plots.

## RESULTS

### Heterogeneity Test for Hanging Clothes, Water Reservoirs (Containers) and Jumantik Cadres (Jumantik Cadres)

Based on Table 1, it is known that the p-value of the variable hanging clothes and water reservoirs in the heterogeneity test is smaller than 0.05, namely p =0.001, which means that the variation between studies is heterogeneous, so this analysis uses a random effects model. Jumantik cadres are known to have a p-value heterogeneity test larger than 0.05, namely p = 0.303, which means that variations between studies are homogeneous, so this analysis uses a fixed effects model. This is supported by Table 2, the results of residual heterogeneity estimates I<sup>2</sup> hanging clothes and water reservoirs above 50%, so this analysis uses a random effects model.

Table 1. Test of Heterogeneity and Residual HeterogeneityEstimates Meta-Analysis of Hanging Clothes, WaterReservoirs, and Jumantik Cadres

Variables	Q	Df	р
Hanging Clothes			
Omnibus test of Model Coefficients	2.627	1	0.105
Test of Residual Heterogeneity	40.209	10	< 0.001
Water Reservoirs			
Omnibus test of Model Coefficients	18.86	1	< 0.001
Test of Residual Heterogeneity	66.71	12	< 0.001
Jumantik Cadre			
Omnibus test of Model Coefficients	149.25	1	< 0.001
Test of Residual Heterogeneity	10.61	9	0.303

Table 2. Residual Heterogeneity EstimatesHangingClothes, Water Reservoirs, and Jumantik Cadres

Variable	I <sup>2</sup> (%)
Hanging Clothes	80.2052
Water Reservoirs	74.3961

## Funnel Plot Risk Factors for Hanging Clothes, Water Reservoirs and Jumantik Cadres

Figure 2a. Funnel Plot of hanging clothes, Figure 2b. Funnel Plot of the water reservoir and Figure 2c. Funnel Plot of jumantik cadres indicates Publication bias because there are partially black circles coming out in the triangle area.



Figure 2. (a) Funnel Plot of Hanging Clothes, (b) Funnel Plot of Water Reservoirs, (c) Funnel Plot of Jumantic Cadres

### Egger's test (Publication Bias Test) Hanging Clothes, Water Reservoirs and Jumantik Cadres

Variable hanging clothes, water reservoirs, and jumantik cadres were subjected to a publication bias test with Egger's test. These three variables have a p-value larger than 0.005, which means there is no indication of publication bias.

## Forest Plot Risk Factors for Hanging Clothes, Water Reservoirs and Jumantik Cadres

The results of the forest plot figure (3a) obtained a pooled value PR =  $e^{0.26}$  = 1.297 (95% CI -0.05-0.57), so it can be concluded that the behaviour of hanging clothes

has a risk of 1.297 times larger incidence of dengue fever than those who do not hang clothes. The results of the forest plot figure (3b) obtained a pooled value PR =  $e^{0.55}$ = 1.73 (95% CI 0.30 - 0.79), so it can be concluded that the existence of water reservoirs around the house has a risk of 1.73 times larger incidence of dengue fever than those who diligently clean water reservoirs. The forest plot image (3c) result obtained a pooled value of OR=  $e^{0.70}$ = 2.01 (95% CI 0.24 – 1.33). So, it can be concluded that houses with inactive jumantik cadres have a 2.01 times larger risk of dengue fever than those with active jumantik cadres.



Figure 3. (a) Forest Plot of Hanging Clothes, (b) Forest Plot of Water Reservoir, (c) Forest Plot of Kader Jumantik (14,19-41)

The highest risk factor for dengue cases is jumantik cadres with the pooled value obtained PR =  $e^{0.70} = 2.01 (95\% \text{ Cl } 0.24 - 1.33)$ , so it can be concluded that houses with inactive jumantic cadres have a 2.01 times larger risk of dengue fever incidence than those with active jumantik cadres.

 Table 3. Test Table of Egger's test Meta-Analysis of Hanging

 Clothes, Water Reservoirs, and Jumantik Cadres

Egger's Test	Z	p-value
Hanging Clothes	1.5896	0.112
Water Reservoirs	-1.2838	0.199
Jumantik Cadre	1.9608	0.050

Table 4. Risk Factor for the Use of Heterogeneity Test ofHanging Clothes, Four Water Reservoirs, and JumantikCadre

Variable	Pooled PR value	95% CI
Hanging Clothes	$e^{0.26} = 1.297$	-0.05-0.57
Water Reservoirs	$e^{0.55} = 1.73$	0.30 - 0.79
Jumantik Cadre	e <sup>0.70</sup> = 2.01	0.24 - 1.33

#### DISCUSSION

## Risk Analysis of Hanging Clothes Behavior on Dengue Fever Incidence

The results of the heterogeneity test of the metaanalysis were known that the habit of hanging clothes (p-value = 0.001 < 0.05), which means variation between heterogeneous studies, so it was analyzed using a random effect model that resulted in a pooled odd ratio value of 1.297 (95% CI -0.05-0.57). It is interpreted that people with the habit of hanging clothes have a 1,297 times larger risk of dengue fever. In line with the results of research that showed there are risk factors that significantly influence the occurrence of dengue hemorrhagic fever, namely the habit of hanging clothes (14). Respondents who had the habit of hanging clothes in the case group of as many as 24 people (70.6%), more than the control group of 9 people (26.5%), were shown with p values = 0.0001 < 0.05. This shows that the habit of hanging clothes is one of the risk factors for dengue hemorrhagic fever because the habit will be a resting place for mosquitoes, making mosquitoes quickly contact humans.

Based on a theory from the Indonesian Ministry of Health in 2012, hanging clothes are a preferred place for *Aedes aegypti* mosquitoes to hide (15). *Aedes aegypti* mosquitoes prefer dark and humid places, usually biting during the day in slightly dark places. *Aedes aegypti* mosquitoes also favour clothes that hang indoors to rest after sucking human blood because clothes that humans have worn will be exposed to sweat containing  $CO_2$  gas which is an attraction for dengue vectors to come to humans.

## Risk Analysis of Water Reservoirs on Dengue Fever Incidence

The residual test results of variable heterogeneity of water reservoirs are heterogeneous with p values < 0.001. These results show that the variables used are diverse and varied. The Pooled odds ratio of JASP output using the Restricted ML or Random Effect Model method is 1.73 (95% CI 0.30 - 0.79). This value can be interpreted as the condition of water reservoirs with larvae having a risk of 1.73 times larger dengue fever than water reservoirs without larvae. This is linear with research that showed almost all TPA characteristics examined affect the presence of larvae with an average odd ratio of 3.2 (16). If carried out correctly, routine landfill draining significantly reduces the chances of mosquito eggs hatching into larvae by 11,843 times more than landfills that are rarely drained.

In previous studies, natural or biological larvae eradication that was considered adequate was larvicide using ethanol solvent extraction method containing essential oils, saponins, and flavonoids (17). Water reservoirs that trigger waterlogging will have a larger chance of becoming breeding grounds for Aedes aegypti mosquitoes and causing dengue disease.

# Risk Analysis of Jumantik Air Cadres on Dengue Fever Incidence

It was found that the results of the meta-analysis heterogeneity test showed that the role of jumantik cadres (p-value = 0.303 > 0.05), which means variation between studies is homogeneous, so it was analyzed using a fixed effect model that resulted in a pooled odd ratio value of 2.01 (95% CI 0.24 - 1.33). It was interpreted that jumantik cadres who did not have a role in changing community behavior towards mosquito nest eradication had a 2.01 times larger risk of dengue fever incidence. In line with another research, that showed there is a relationship between the role of jumantik cadres and the incidence of dengue disease in cadres in the Banjarejo Health Center work area, which shows that p-value = 0.036 < 0.05 with a value of 5.727 (95% Cl 1.189 - 27, 594) (18).

Of the incidence of dengue hemorrhagic fever in the Banjarejo Health Center area, 11 respondents were sick with DHF. Although there were only 11 cases of dengue incidents, early vigilance was still carried out to prevent dengue disease. The working area of the Banjarejo Health Center still has dengue cases every year; as was the case in the last three years, the Banjarejo Puskesmas work area was ranked third in the city of Madiun, where there were dengue cases. Therefore, it is necessary to prevent dengue disease through the role of jumantik cadres and the community to suppress dengue cases.

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### **AUTHORS' CONTRIBUTION**

SK: Conceptualization, Methodology; RA: Software, Formal Analysis, Investigation; FMH: Writing -Review & Editing; JBJ: Writing - Review & Editing; ZAS: Writing - Original draft Preparation

#### CONCLUSION

Based on the results of the meta-analysis in this study, jumantik cadres have the greatest risk factor value compared to other variables. Community environments that do not have jumantik cadres have a greater risk of developing dengue fever 2.01 than community environments that have jumantik cadres. The second highest risk factor is in water reservoirs, followed by the next variable hanging clothes. The recommendation from the results of this study is to increase jumantik cadres in each household unit and to supervise the presence of mosquito larvae in each water reservoir to be destroyed so as not to become adult mosquitoes resulting in dengue fever.

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