

# The Association between Obesity and Severity of Dengue Hemorrhagic Fever in Children at Wangaya General Hospital

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## Abstract

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**Keywords:** Obesity; Children; Dengue hemorrhagic fever; Severity

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**BACKGROUND:** Dengue is a mosquito-borne disease caused by any one of four closely related Dengue virus (DENV 1-4). The clinical sign Dengue virus infection can vary from mild (mild febrile illness), Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) to Dengue Hemorrhagic Fever with shock (Dengue Shock Syndrome, DSS).

**AIM:** This study was designed to determine the relationship of obesity with the severity of Dengue Hemorrhagic Fever in children.

**METHODS:** It is a case-control study. The data of patients were retrospectively collected from the Department of Child Health at the Wangaya General Hospital between March 2019 to May 2019. It uses consecutive sampling. The total sample of 22 children with DHF with shock and 22 children with DHF without shock were investigated. Statistical analysis has been performed by SPSS Statistics 20.0 for Mac (IBM Corp., Armonk, New York, USA). DHF positive results were compared by the Chi-square test and binary logistic regression.

**RESULTS:** Prevalence of DHF with shock is fifty per cent's and DHF without shock is 50%. Prevalence of obesity is 40.9%. The result of binary logistic regression analysis of obesity in children and the severity of DHF was significantly correlated with P-value 0.004 and OR = 7.734.

**CONCLUSION:** Obesity is associated with the severity of Dengue Hemorrhagic fever in children.

## Introduction

Dengue is a mosquito-borne disease caused by any one of four closely related *Dengue virus* (DENV 1-4). The clinical sign *Dengue virus* infection can vary from mild (mild febrile illness), Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) to Dengue Hemorrhagic Fever with shock (Dengue Shock Syndrome, DSS). DHF is an infection commonly found in tropical countries such as Indonesia.

This Dengue infection usually affects children < 15 years old with a high mortality rate [1]. In 2009, Indonesia had the most case of DHF in Southeast Asia. In 2015, the top 3 provinces with a high rate of DHF were Bali (208.7 per 100 thousand population), East Kalimantan (183.12 per 100 thousand

population) and Southeast Kalimantan (120.08 per 100 thousand population) [2]. Several risk factors associated with the Dengue severity in children and one of them is obesity. In DHF, there is a plasma leakage which can lead to hypovolemic shock that causes DSS. In an obese patient, there is an increase in the production of interleukin and Tumor Necrosis Factors (TNF). One of the effects of TNF is increased capillary permeability; therefore, the increased capillary permeability was higher and eventually will lead to DSS because of massive plasma leakage [3]. From study of Devi et al., in 2015, there is a relationship between obesity and Dengue severity, and also Elmy in 2008 have found that obesity is the risk factor of DSS, but from the study of Sugiyanto et al. and study in Thailand there is no relationship between obesity and Dengue severity [3].

This study was designed to determine the

relationship of obesity with the severity of Dengue Hemorrhagic Fever in children.

## Material and Methods

### Study Design

This study is an observational study with a case-control design. The data were retrospectively collected from the Department of Child Health at the Wangaya General Hospital between March 2019 to May 2019. This study consists of 44 serum sample. This study uses consecutive sampling. Subjects were divided into two groups. First group, the control group consist of subjects with DHF without shock (grade I or grade II), positive tourniquet test, 2 – 7 days of fever, thrombocytopenia and positive signs of plasma leakage such as increased hematocrit, or having pleural effusion, or ascites. Second group, the case group included patient diagnosed with DHF with shock (grade III or grade IV), who meet the criteria of DHF grade I or grade II plus sign of shock, such as weak pulse, narrowing pulse pressure, poor tissue perfusion, clammy skin, and decreased urine output according to WHO criteria [4]. Obesity was assessed with BMI for age  $p > 85$  according to CDC growth chart [5].

### Inclusion and Exclusion Criteria

**Inclusion criteria:** All inpatient with DHF grade I–IV in the Department of Child Health at the Wangaya General Hospital.

**Exclusion criteria:** Patients with severe malnutrition and congenital heart disease.

### Statistical Analysis

Data were presented in distribution tabulation, and data analysis was performed with a computer-assisted statistical package (SPSS 20 for Mac). Bivariate data was analysed with Chi-square and multivariate analysis with binary logistic regression.

### Ethics Statement

The study was performed following the principles of the Declaration of Helsinki. Participation in the study was fully voluntary and anonymous, and was approved by the Ethics Committee for Medical Research of Wangaya General Hospital.

## Results

We included 44 children in this study which consist of 22 (50%) children of DHF without shock and 22 (50%) children of DHF with shock. The main characteristics of the children of both groups are shown in Table 1.

**Table 1: Main Characteristics of the Study**

Characteristics	Frequency, n (%)
Gender	
Male	28 (63.6%)
Female	16 (36.4%)
Obese	
Yes	18 (40.9%)
No	26 (59.1%)
Shock	
Yes	22 (50%)
No	22 (50%)
Age, years	11.11 (4.271) Min: 3, Max: 17
Body Weight	41.76 (20.050) Min: 12, Max: 99

Statistical analysis was performed to identify the association between obesity and Dengue severity (in this case, DSS). Statistical analysis revealed that there is an association between obesity and DSS with a p-value of 0.004 ( $< 0.05$ ) and OR of 7.734 meaning it is the risk factor of DSS with OR value  $> 1$ . The result of bivariate and multivariate analysis is shown in Table 2.

**Table 2: Results of the statistical analysis**

	Shock, n (%)	No Shock, n (%)	Unadjusted (bivariate analysis chi-square)			Adjusted (multivariate analysis, binary logistic regression)		
			p value	OR	CI 95%	p-value	OR	CI 95%
Obese	14 (63.6%)	4 (18.2%)	0.005	7.875	1.964-31.574	0.004	7.734	1.910-31.321
Normal	8 (36.4%)	18 (81.8%)						

## Discussion

This study found out that obesity is associated with Dengue severity (it is the risk factor of DSS). This finding was supported by the theory that obesity may affect the severity of dengue infection due to the increased production of white adipose tissue which causes increased inflammation mediator production. These inflammation mediators were TNF  $\alpha$  (*tumour necrosis factor*  $\alpha$ ) and several interleukins (IL) such as IL-1  $\beta$ , IL-6, and IL-8. In obese children, there are increasing of TNF  $\alpha$  dan IL-6. This inflammation mediator will increase the permeability of the capillaries. Subsequently, progressive plasma leakage leads to a higher risk of DSS [4]. The results of this study was also supported by previous studies such as Ridha in 2018 with p-value of 0.000 [6]; Elmy et al., in 2009 with p-value of 0.009 with OR of 4.927 [3]; and from Chuansumrit et al., that show children with  $> 50$ th percentile body weight for age were more likely to have grade III and grade IV DHF than those with lesser body weight with P-value = 0.039 [7]. Those studies above stated that obesity was associated with

severity of dengue and therefore becoming a DSS risk factor. But this study contradicted with the study from Maria et al in 2013 that result in obesity is not a risk factor or associated with the Dengue severity with P-value = 0.07 [1]. And also contradicted with the study from Tantri in 2017 with P-value = 0.309 meaning there is no association between obesity with Dengue severity [8].

From this study, we can see that obesity is associated with the severity of Dengue Hemorrhagic fever in children. Obese children have a higher risk of shock when experiencing dengue hemorrhagic fever. From this study, we can predict the prognosis of obese children when experience DHF; therefore, we can anticipate and prevent obese children from went into shock when diagnosing with DHF.

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