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Dengue Shock Syndrome with Recurrent Shock and Obesity in Children: A Case Report

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ABSTRACT

Introduction: Dengue fever remains a major global health problem that is widespread in tropical and subtropical regions. DSS is one of the dangerous clinical manifestations of dengue infection, characterized by severe plasma leakage due to increased vascular permeability leading to a progressive decrease in intravascular volume. Obesity has been proposed as a potential risk factor for the development of DSS in children. Management with proper fluid resuscitation is essential to prevent worsening in patients with Dengue Shock Syndrom.

Case Presentation: This study reports a 5-year-old obese pediatric patient with a body mass index of 31 kg/m2 who developed Dengue Shock Syndrome and recurrent shock. Vital signs examination at the initial examination obtained a pulse rate of 99x / min palpable weak, not strong lift with a temperature of 36oCand extremities acral palpable was cold with Capillary Refill Time (CRT) elongated > 2 seconds. The patient was given initial management in the ER in the form of oxygenation with a 2 lpm nasal cannula, then given lactate ringer (RL) as a fluid teraphy 10cc/kgBB, which was 310cc finished in 30 minutes. Initial complete blood hematological examination showed a leukopenia result of 3.1 x103/uL. The patient had an increased hematocrit of 51% with a haemoglobin level of 17g/dL. Platelet levels were found to be below normal levels at 60 x103/uL. The patient experienced recurrent shock during treatment. The patient was given several rounds of fluid resuscitation but worsened during treatment. The patient had seizures leading to respiratory arrest and cardiac arrest. The patient was later pronounced dead after cardiopulmonary resuscitation was unsuccessful.

Conclusion: Dengue infection with obesity has a higher risk of Dengue Shock Syndrome in children. Management with proper fluid resuscitation is important in the hope of reducing morbidity and mortality of Dengue Shock Syndrome in children.

KEYWORDS: Pediatric Dengue Shock Syndrome, Obesity, Recurrent shock, Fluid therapy

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INTRODUCTION

Dengue virus (DENV) is a flavivirus with 4 serotypes (DENV 1-4) that causes dengue fever with high morbidity and mortality globally. The Aedes mosquito is the vector of the virus.[1] Dengue fever continues to be a major global public health problem.[2] Dengue infection is widespread in tropical and subtropical regions. A total of 129 countries in Asia are at risk of dengue infection, with an estimated 390 million dengue cases occurring annually worldwide. 96 million cases have clinical symptoms and cause approximately 50,000 deaths per year.[1,2] The mortality rate of patients infected with dengue fever in hospitals can increase from 20% to 25.6% if not treated appropriately.[2]

Dengue fever usually presents with symptoms of fever lasting more than 3 days, accompanied by nausea and vomiting, headaches, joint pain, muscle pain, and bleeding. In severe conditions, it can manifest as organ damage, bleeding, and plasma leakage, causing a life-threatening shock called Dengue Shock Syndrome (DSS).[2] DSS is one of the most dangerous clinical manifestations of dengue infection,

characterized by severe plasma leakage due to increased vascular permeability that causes a progressive decrease in intravascular volume.[3]

The presence of obesity can exacerbate dengue infections.[4] Obesity has been proposed as a potential risk factor for the development of DSS. There has been a marked increase in obesity rates in all regions of the world between 1990 and 2010, associated with changes in nutrient availability dominated by processed foods high in fat, salt, and sugar. The number of overweight children younger than 5 years was estimated to be more than 42 million in 2010, with the predominance of incidence occurring in developing countries.[4] Obesity is an excessive accumulation of abnormal fat and poses a risk of health problems. Increased production of interleukins and tumor necrosis factor (TNF) is common in obese patients. TNF can cause severe plasma leakage due to the effect of increased capillary permeability, so that ultimately, dengue infection patients with obesity will be at risk of experiencing DSS.[5]

In this case report, the authors report the case of a child with dengue shock syndrome who had the comorbidity of obesity and experienced recurrent shocks. The patient received treatment for one day in the intensive care room, but the patient could not be helped after experiencing recurrent shock and dengue encephalopathy. DSS causes poor outcomes in children, especially in patients who have comorbid obesity. Management by administering appropriate fluid resuscitation is very important to prevent worsening in patients with dengue shock syndrome. This case report is made to be considered along with knowledge about the incidence of DSS and obesity in children. In addition, the provision of appropriate fluid therapy is expected to reduce the morbidity and mortality rates of DSS with obesity in children.

CASE PRESENTATION

A 5-year-old child with a body weight of 31 kg and a height of 100 cm has a body mass index of 31 kg/m2. Based on the CDC curve, the patient is above the 95th percentile, which indicates the patient is obese. The patient came to the emergency room at Sanjiwani Hospital, Gianyar, with the main complaint of a fever since 4 days before admission. The fever fluctuated with the medication. Patients also complained of nausea and a decreased appetite for eating and drinking. The patient had not wanted to eat at all since the morning before admission. The last urine was said to be 6 hours before admission. On examination, the patient appeared generally weak. The examination of the vital signs showed that the pulse was 99 x/minute with weak palpability and not strong. The temperature was 36 oC, and the extremities felt cold acral, with a capillary refill time (CRT) extending for > 2 seconds. In the initial treatment of the emergency room, the patient was given oxygenation with a 2 lpm nasal cannula, then given a loading of lactated ringer fluid (RL) of 10 cc/kgBB, which was 310 cc and finished in 30 minutes. The patient was also given an injection of 25 mg of ranitidine and 4 mg of ondansetron. The proposed supporting examinations given are a complete blood hematological examination, clinical chemistry, and electrolytes to confirm the diagnosis.

At the 30-minute post-resuscitation evaluation, the pulse was still weak and the acral extremities still felt cold. The first complete blood hematological examination result (Table 1) showed a leukopenia of 3.1 x 103/uL. The patient had an increased hematocrit of 51% with a hemoglobin level of 17 g/dL. Platelet levels were found to be below normal levels; the patient experienced thrombocytopenia with platelet levels of 60 x 103/uL. The patient was then given fluid loading again, with 300 cc of RL finished in 30 minutes. Two intravenous lines were installed, right and left, where the first line was 300 cc RL and the second line was 300 cc, for a total of 600 cc RL finished in 30 minutes. In the following physical examination evaluation, it was found that the patient's general condition was still weak, and the blood pressure examination was obtained at 122/98 mmHg. The patient's pulse rate was 150 x/min which palpably weak. The patient's acral extremities felt warm. The initial diagnosis made based on the results of the history, physical examinations, and supporting examinations was dengue shock syndrome and obesity.

The patient was admitted to the pediatric intensive care unit. The patient was given nasal cannula oxygenation at 4-5 lpm. The patient was also given intravenous fluids with a RL of 300 cc (as much as 150 cc on line 1 and 150 cc on line 2), which was finished in 1 hour. The patient was given nasal cannula oxygenation at 4-5 lpm. The patient was also given intravenous fluids with a RL of 300 cc (as much as 150 cc on line 1 and 150 cc on line 2), which was finished in 1 hour. Furthermore, the patient was given 250 cc of RL fluid again, which was 125 cc of RL on line 1 and 125 cc of RL on line 2, finished in 1 hour. Fluid resuscitation was continued by administering a total of 150 cc of RL fluid, which was 75 cc of fluid on lines 1 and 2. The patient then underwent a complete blood hematological examination for evaluation 6 hours after resuscitation. Maintenance fluid was continued with RL fluid at 90 cc/hour. The patient was given therapy in the form of ondansetron 3 x 3 mg IV, ranitidine 2 x 30 mg IV, and paracetamol 4 x 300 mg IV. Close monitoring was carried out on patients regarding fluid balance, fluid intake, fluid output, and urine production. During monitoring, the patient experienced a decrease in his condition again. The patient appears restless. A blood pressure examination showed a blood pressure of 135/128 mmHg. The patient's pulse rate was 184 x/min, which was palpably weak. Examination of the extremities showed that the acral felt cold, with CRT extending > 2 seconds. The patient was given additional resuscitation fluid in the form of a total of 600 cc of RL fluid, of which 300 cc of RL fluid in each line was finished in 1 hour.

The results of the evaluation of a complete blood hematological examination after 6 hours post-resuscitation (Table 1) showed a leukocyte result of 6.92 x 103/µL. Hematocrit was still increased at 50.4% with a hemoglobin

level of 17.3 g/dL. Platelet levels were found to be still below normal levels at 65 x 103/uL. The patient was given fluid therapy in the form of galafusal at line 1 at 300 cc/hour and RL fluid at line 2 at 90 cc/hour for 30 minutes. The patient also received 5 mcg/kgBW/minute dobutamine therapy, in which 2 ampoules of dobutamine diluted with 50 cc of 0.9% NaCl dripped at a speed of 0.9 cc/hour.

The patient underwent a complete blood hematological examination again (Table 1), where the leukocyte result was 4.8 x 103/uL and the platelet level was still below normal levels at 36 x 103/uL. Hematocrit was in the normal range of 38.4% with a hemoglobin level of 12.8 g/dL. Furthermore, the patient is given 150 cc/hour of RL fluid with 75 cc/hour each on lines 1 and 2 for 4 hours.

During monitoring, the patient's condition worsened again; the patient appeared restless. The patient's acral extremities felt cold. A blood examination showed a blood pressure of 60/43 mmHg with a pulse rate of 82 x/min and palpably weak. The patient experienced a decrease in oxygen saturation of 80% with a 5 lpm nasal cannula. The patient was given an additional 300 cc of Galafusal resuscitation fluid, which was finished in 30 minutes. The evaluation of blood pressure obtained a blood pressure of 129/70 mmHg. Pulse rate was 182x/minute, and oxygen saturation was 100% with 5 lpm nasal cannula oxygen. In the results of the following complete blood hematological examination (Table 1), leukocyte results were 4.8 x 103/µL. Platelet levels were found to be still below normal levels at 36 x 103/uL. Hematocrit was in the normal range of 38.4% with a hemoglobin level of 12.8 g/dL. The patient was given 300 cc of RL fluid on lines 1 and 2, which finished in 1 hour, followed by 125 cc of RL fluid on lines 1 and 2.

The results of the following complete blood hematological examination (Table 1) showed that leukocytes were 10.99 x 103/µL. Platelet levels were found to be still below normal levels at 33 x 103/uL. Hematocrit was 41.9% with a hemoglobin level of 14.3 g/dL. The patient was given RL fluid at 75 cc/hour on lines 1 and 2. The patient was initially planned to be referred to Prof. Ngoerah General Hospital, but during monitoring, the patient experienced a seizure. The patient was then given a phenobarbital loading of 20 mg/kgBW diluted with 30 cc of 0.9% NaCl drip in 30 minutes. On examination, the patient's blood pressure was not measured, the patient's pulse was not palpable, and the patient then experienced respiratory arrest and cardiac arrest. The patient underwent cardiopulmonary resuscitation (CPR), but it failed, and the patient was later declared dead.

Table 1. Hematological Examination Result

NAME OF TEST AND INDICATOR	RESULT					UNIT	REFERENCE VALUE
COMPLETE BLOOD COUNT	15/03/24	16/04/24					
	08.07 PM	07.59 AM	09.05AM	00.42 PM	03.11 PM		
M C V	77.3	77.7	76.4	74.4	75.2	fL	80.0 - 100.0
RDW-SD	49.7	40.1	49.4	50.4	49.7	fL	35.0 - 56.0
Trombosit (PLT)	60	65	36	25	33	10^3/uL	150 - 450
M C H	25.8	26.7	25.5	25.5	25.7	pg	27.0 - 34.0
RDW-CV	15.1	14.8	15.2	15.5	15.3	%	11.0 - 16.0
Bas%	0.8	0.0	1.1	1.0	0.6	%	0.0 - 2.0
Hematokrit (HCT)	51.0	50.4	38.4	45.2	41.9	%	37.0 - 48.0
Eritrosit (RBC)	6.59	6.49	5.03	6.07	5.57	10^6/uL	3.50 - 5.50
Mon#	0.13	0.57	0.46	0.61	0.63	10^3/uL	0.10 - 1.20
Neu#	2.29	4.43	3.26	5.29	8.70	10^3/uL	2.50 - 7.50
Neu%	73.9	64.0	68.0	62.1	79.2	%	47.0 - 80.0
PCT	0.065	0.054	0.041	0.025	0.031	%	0.108 - 0.282
Hemoglobin(HGB)	17.0	17.3	12.8	15.5	14.3	g/dL	11.0 - 16.0
Lym%	21.2	27.7	20.6	29.5	14.2	%	13.0 - 40.0
Bas#	0.02	0.00	0.05	0.08	0.07	10^3/uL	0.00 - 0.10
PDW	16.8	17.1	16.8	17.2	17.5	fL	9.0 - 17.0
Lekosit (WBC)	3.10	6.92	4.80	8.51	10.99	10^3/uL	4.00 - 10.00
MPV	10.9	8.3	11.3	9.9	9.3	fL	6.5 - 12.0

Mon%	4.0	8.2	9.5	7.1	5.7	%	2.0 - 11.0
Lym#	0.66	1.91	0.99	2.51	1.59	10^3/uL	1.00 - 4.00
M C H C	33.4	34.3	33.3	34.3	34.1	g/dL	32.0 - 36.0
Eos#	0.00	0.01	0.04	0.02	0.03	10^3/uL	0.00 - 0.50
Eos%	0.1	0.1	0.8	0.3	0.3	%	0.5 - 5.0
CLINICAL CHEMISTRY							
Glukosa Sewaktu	87					mg/dL	80 - 120
SGOT	148					U/L	< 35
SGPT	69					U/L	< 41
Ureum	24.5					mg/dL	18 - 55
Creatinin	0.12					mg/dL	0.2 - 0.7
ELECTROLITE							
Natrium	117					mmol/l	132 - 145
Kalium	4.7					mmol/l	3.5 - 5.0
Chlorida	95					mmol/l	95 - 111

DISKUSI

Cases of DSS in children with obesity often lead to poor outcomes. Dengue virus is an arbovirus that has high morbidity and mortality. The expansion of the geographical area of the Aedes mosquito vector has caused cases to increase.[1] Research in the American journal conducted in 2019 regarding dengue infections in children found that the highest number of children infected with the dengue virus were found at the age of 0–5 years (51.68%). The ratio of boys was found to be more than girls, at 55%. Research conducted in 2022 also found that the ratio of boys infected was higher than that of girls, namely 2.5:1.9. Research conducted in 2017 regarding the severity of dengue infection in children stated that children aged 0–5 years were more at risk of experiencing DSS. In contrast to other research conducted, it was found that children over 5 years old were more at risk of experiencing shock than children under 5 years old. The relationship between age and the shock that occurs in pediatric patients with DSS is still controversial. Research conducted in Surabaya in 2020 regarding the relationship between nutritional status and DSS outcomes in children found that the relationship between age and recurrent shock or death in pediatric patients with DSS was not significant.[5,6] This case report discusses a 5-year-old male patient with dengue shock syndrome and comorbid obesity who experiences recurrent shock.

In a study conducted in 2019, a sample of pediatric patients with dengue infection who had a BMI ≥ 95th percentile was 42.64% of the total sample. This study found that mortality was only found in patients who had a BMI ≥ the 95th percentile, which was 6.89% of the total sample with a BMI ≥ the 95th percentile.8 One of the risk factors for shock in children with DHF (dengue hemorrhagic fever) is obesity. In pediatric patients with obesity, the risk of shock is 2.29 times greater than in non-obese children. 4 A study conducted in 2022 regarding risk factors for severe dengue in children found that one of the risk factors for developing severe dengue in children is the nutritional status of overweight or obesity, which is statistically significant.[9] Research in Bali conducted in 2019 regarding the relationship between obesity and the severity of DHF patients in children found a statistically significant relationship between obesity and DSS. This research found a p value of 0.004 (<0.05) and an OR > 1, which means obesity is a risk factor for DSS.[7]

The main signs and symptoms of dengue infection are fever, accompanied by headaches, nausea, vomiting, joint pain, muscle pain, and bleeding. A small proportion of cases can progress to severe dengue, which manifests as organ damage, bleeding, and plasma leakage and can cause a life-threatening state of shock.[8] The most common symptom was high-temperature fever, experienced by 66.29% of the entire sample of patients who have symptoms of fever. Other symptoms that many patients experienced were nausea, vomiting, abdominal pain, bleeding symptoms such as nosebleeds and gum bleeding, and headaches.[10] Abdominal pain and vomiting were the second-most common clinical features and occurred in 77.3% of patients. Just like other reports, other studies also report the same thing, with abdominal pain as the second most common clinical picture, followed by vomiting symptoms.[10,11] Vomiting symptoms generally occur in severe dengue. The presence of mucosal bleeding symptoms and fluid accumulation is the most common clinical warning sign for severe dengue. Patients with severe dengue are at greater risk for shock, with 94 cases, or 62.7% of samples with severe dengue, experiencing shock.[11] In a 2023 study regarding the clinical manifestations and prognosis of severe dengue, it was found that the most common sign of dengue infection were positive NS1

laboratory tests in 76% of cases, with thrombocytopenia dominant in 85.5% of cases. Leukopenia was found in 42 cases, or 28%, but more normal leukocytes were found in 63.54% of cases. An increase in hematocrit of >45% was found in 40 cases, which is 26.7% of cases. Increased liver function was also quite common, where an increase in SGOT occurred in 42.7% of cases and an increase in SGPT occurred in 60% of cases.[10] This increase in SGOT was similar to another study conducted in 2019 where they found SGOT increased in 47.42% of patients when compared to SGPT, which was 30.92% of cases.[12] In this case, the patient came with a chief complaint of fever. This finding is in line with previous research, which states that fever is the most common main clinical manifestation. The findings are in line with previous research suggesting that fever is the most common major clinical manifestation. The patient also complained of nausea and a decreased appetite. On laboratory examination, it was found that the patient had leukopenia and thrombocytopenia with an increase in hematocrit >45%, especially when the patient first arrived and fluid resuscitation had not been carried out. Patients also found elevated liver function (SGOT and SGPT).

The risk of shock tends to increase in children with dengue infection due to obesity; this was stated in a 2018 study regarding the relationship between obesity and the severity of dengue infection in children.[13] Another study conducted in 2018 also found that obese patients with dengue virus infection have a higher frequency of hemoconcentration, severe thrombocytopenia, increased creatinine, elevated liver enzymes, a rapid increase in hemoconcentration, a rapid increase in platelet levels, and longer hospitalization.[14] The increased risk of shock in obesity is thought to be caused by adipose tissue that can express pro-inflammatory cytokines that play a role in the inflammatory process, namely TNF-α, IL-6, IL-8, and IL-1β, which cause more severe plasma leakage in pediatric patients with dengue infection who have excess adipose tissue. In contrast to the previous study, a study conducted in 2020 at a hospital in Surabaya stated that obesity did not have a significant relationship with the outcome of recurrent shock or death in pediatric patients with DSS, but although in this study it was found that the nutritional status of obesity did not affect the final outcome of pediatric patients with DSS, in this study there were 2 patients who died and both were obese.[6,13] A 2020 journal review article found several theories that could explain how obesity is associated with the development of severe dengue. Obesity can downregulate AMP-Protein Kinase (AMPK), which leads to the accumulation of lipids in the endoplasmic reticulum (ER) that will facilitate viral replication. Long-term production of pro-inflammatory adipokine, often found in patients with obesity, can lead to endothelial and platelet dysfunction, increasing the occurrence of severe dengue, which increases the risk of shock. In addition, obesity can also cause endothelial dysfunction through the production of reactive oxygen species (ROS) and possible damage to the glycocalyx found in the endothelium. Ultimately, obesity has some immunomodulating effects that reduce NK cell function and B and T cell responses and increase the predisposition to stronger proinflammatory cytokine responses after viral infection. Greater viral proliferation and greater tissue damage may contribute to the severity of dengue infection in children.[1] In this case, it was found that the patient was obese with a BMI of ≥ 95th percentile, so this condition contributed to the occurrence of DSS in this patient.

There is no specific therapy that can be done for DSS. Fluid therapy is the main management for patients with DSS. Management for DSS is based on the evaluation of the patient's hemodynamic status by looking at the level of hemoconcentration, dehydration, and electrolyte imbalance due to fluid movement and massive fluid administration.[1,15] The initial management that can be done for DSS is to provide oxygenation at 2-4 lpm, and then the administration of fluid therapy can be done by giving crystalloid fluids such as ringer lactate (RL) or NaCl 0.9%. In patients with DSS, initial fluid administration can be given with a crystalloid infusion of 10–20 ml/kgBB finished in 30 minutes. Evaluation after fluid resuscitation is very important, such as the evaluation of the patient's vital signs. If vital signs are found to be improving and signs of shock are resolved, namely improved consciousness, a strong palpable pulse with sufficient contents, the patient's acral is warm, and urine production is sufficient (>1 ml/kg BB/kg/hour) then fluid therapy can be reduced to 10 ml/kkg BB/hour. If there is an improvement in the patient's clinical condition, then the liquid can be done at 7–5–3 ml/kkg BB/hhour. In pediatric patients with obesity, intravenous fluid administration is given based on the patient's ideal body weight. Colloidal fluid can be considered for shock fluid therapy in pediatric patients with DSS and obesity.[16,17] In this case report, the patient was treated with appropriate initial treatment. The patient received oxygenation with a 2 lpm nasal cannula and fluid therapy in the form of ringer lactate (RL) of as much as 10 cc/kg BB in 30 minutes. Patients are also routinely monitored and evaluated for vital signs and hemodynamic status after fluid therapy. The patient in this case report had given colloidal fluid, Galafusal, which can indeed be considered to be given to DSS patients.

Obesity, as a prognostic risk factor, can influence the severity of dengue fever through inflammatory pathways. Increased white adipose tissue (WAT) deposition in obese individuals leads to increased production of interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-α). IL-6, IL-8, and TNF-a are important mediators of inflammatory pathways that increase capillary permeability. Increased capillary permeability in obese dengue patients may be progressively underlying the severe plasma leakage process. Obese pediatric patients with dengue infection have a more severe disease course risk prognosis compared to non-obese patients. Clinical findings of obesity may be useful in the identification of high-risk dengue patients. Obese patients

are at high risk of complications and death due to their stronger immune response compared to malnourished patients. Therefore, with the increasing prevalence of obesity in areas with a high risk of dengue infection and the hypothesis of a link between obesity and dengue severity, early detection of obese dengue patients is necessary for closer monitoring and early treatment.

CONCLUSION

Dengue infection with obesity has a higher risk of developing Dengue Shock Syndrome in children. DSS tends to cause poor outcomes in children, especially in patients who have obese comorbidities. The administration of fluid resuscitation management in DSS patients must be based on hemodynamic evaluations such as hemoconcentration and clinical levels of patients to avoid a lack or excess fluid in patients. Management with proper fluid resuscitation is important in the hope of reducing the morbidity and mortality of dengue shock syndrome in children. Pediatric patients with obesity who have dengue infection have a more severe prognosis for the course of the disease. Therefore, early detection of dengue patients who are obese is needed for closer monitoring and early treatment of dengue fever cases.

RESEARCH ETHICS

Before obtaining patient data through medical records, the authors provided informed consent which was approved by the patient to be reported in this case report.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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There was no funding in this study and the authors used independent funding.

AUTHORS' CONTRIBUTION

All authors contributed to the data writing process up to publication.

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