Renal Function in Childhood Dengue Hemorrhagic Fever

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Abstract

Dengue hemorrhagic fever (DHF) is the dengue virus infection characterized by plasma leakage as a result of increased vascular permeability. Consequently, it will influence renal function especially in dengue shock syndrome (DSS). The aim of this study was to assess glomerular filtration rate (GFR) in DHF and DSS. A descriptive study with cross sectional design was performed in all DHF children who were admitted to Department of Child Health Dr. Hasan Sadikin Hospital Bandung, from October 2003 to January 2004. Diagnosis of DHF was confirmed by WHO criteria. The patients were divided into DHF group (grade I and II) and DSS group (grade III and IV). Glomerular filtration rate was calculated by Schwartz formula from creatinine serum level. The distribution of sex, age, and nutritional status were using chi-square test and the proportion of GFR was used t test. From 68 subjects, 41 (60%) were diagnosed as DHF and 27 (40%) as DSS. There were no significant difference in distribution of sex, age, and nutritional status between DHF and DSS group, each p value was >0.05. Mean GFR in all subjects, DHF, and DSS group were 155.9±47.8, 152.3±49.2, and 161.3±45.9, consecutively. The proportion of GFR between DHF and DSS group was 137.50 (94.8–1318.2) vs. 155.38 (89.2–261.9), p=0.322. In conclusions, all subjects have normal GFR, there is no difference of GFR between DHF and DSS group. [MKB. 2011;43(2S):44S–7].

Key words: Dengue hemorrhagic fever (DHF), dengue shock syndrome (DSS), glomerular filtration rate (GFR)

Fungsi Ginjal pada Demam Berdarah Dengue Anak

Abstrak


Kata kunci: Laju filtrasi glomerulus (LFG), demam berdarah dengue (DBD), sindrom syok dengue (SSD)

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Introduction

Dengue virus infection clinically manifests as dengue fever (DF), dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). Dengue hemorrhagic fever (DHF) and DSS are the severe manifestation of dengue virus infection characterized by plasma leakage as a result of increased vascular permeability. Following this leakage, hypovolemic and decrease renal blood perfusion occurs as a consequence of a plasma volume loss. Consequently, it will influence glomerular filtration rate (GFR) especially in severe DHF (grade III and IV).

Dengue hemorrhagic fever is a sporadic fever disease, which is characterized by hemorrhage, tends to produce shock and might death.1-2 Capillary damage allows fluid, electrolyte, and protein to leak into extravascular spaces. This internal redistribution of fluid results in hemoconcentration and hypovolemia. Hemoconcentration in DHF patients occur more than 20%.1 Shock is the most feared complication for DHF patients.3 Shock in DHF is caused by hypovolemia, and hypovolemia will cause a decrease of cardiac output which in turn will decrease renal blood flow (RBF). This reduce in RBF from hypovolemia means that the fluid balance control system does not work well, it will lead to renal dysfunction and even acute kidney injury.4

In recent years there has been an increasing report of unusual manifestation of dengue viral infection including renal system involvement. Renal involvement in several cases has been reported usually accompanied with acute kidney injury with or without shock, hemolysis, rhabdomyolysis, and sepsis.5-6 There are a few reports about renal function in patients with dengue hemorrhagic fever (DHF). Renal dysfunction is manifested by an increase in serum creatinine concentration. Even so, the duration needed from hypovolemia to renal dysfunction is uncertain.4 This study will assess and want to know the difference renal function by examining creatinine level in patients with DHF and DSS when diagnosed for the first time.

Methods

This was an analytic descriptive study with a cross sectional design. The amount of sample was based on a confidence interval of 95% and a power test of 80%. The subject of this study were all pediatric DHF patients hospitalized at the Pediatric Department of Dr. Hasan Sadikin Hospital Bandung, from October 2003 to January 2004.

The subject of DHF was fulfilled by WHO clinical and laboratory criteria, whose parents willing to join and sign the informed consent. The exclusion criteria for this study were the patients had already received intravenous fluid therapy by the time DHF was diagnosed, children with dehydration due to diarrhea and vomiting and those with renal disease.

All subjects’ identity was filled, including the general characteristics of name, age, sex, address, and nutritional status. Dengue hemorrhagic fever patients were classified as DHF or DSS group. The serum creatinine concentration was measured by the Jaffe method on admission (from Outpatient or Pediatric Emergency Department) and then the GFR was calculated by the Schwartz formula. Ethical approval for this study was obtained from the Ethic Committee of the Faculty Medicine of Padjadjaran University/Dr. Hasan Sadikin Hospital Bandung.

The distribution of sex and nutritional status in both groups were compared using chi-square test, while the age, length of fever before admitted to hospital, and hematocrit using t test. Data analysis was conducted descriptively for mean and standard deviation. To compare GFR value means between DHF and DSS groups were used t test, and p values <0.05 were considered to indicate statistical significance. Statistic package for social sciences (SPSS) 17.0 computer program was used to analyze data from this study.

Results

A total number of 68 children with DHF and DSS fulfilled the enrollment criteria.

Statistical analysis shows there were no difference in distribution of sex, age, and nutritional status, length of fever before admitted to hospital and hematocrit using t test. The difference of platelet count in DHF and DSS was significant (Table 1). All subjects had normal GFR. There was no difference of mean GFR between DHF and DSS group (Table 2).

Discussion

The World Health Organization criteria for dengue hemorrhagic fever are fever (2–7 days), minor or major hemorrhagic manifestations, thrombocytopenia (≤100,000/mm$^3$), and objective evidence of increased capillary permeability (hematocrit increased >20%). Dengue shock syndrome should fulfill these criteria plus hypotension or narrow pulse pressure (<20 mm
All of these features were present in our described patient studies. The GFR is clinically important because it is a measurement of renal function. Measuring serum creatinine is a simple test and it is the most commonly used indicator of renal function. Creatinine, as a waste product of metabolism, is not reused by the body and is normally excreted exclusively by the kidney. Creatinine is also produced naturally by the body (creatinine is a break-down product of creatine phosphate, which is found in muscle). It is freely filtered by the glomerulus, but also actively secreted by the peritubular capillaries in very small amounts such that creatinine clearance overestimates actual GFR by 10–20%.

Serum creatinine concentration will be affected by the following variables: sex, age, weight, nutritional status, and race. In this study shows there were no difference in distribution of sex, age, and nutritional status from both DHF and DSS groups.

The results of this study found that GFR of DHF and DSS patients were within normal values according to age and sex. There was no difference in GFR between DHF and DSS patients, p=0.322 (Table 2). It was not in accordance with the theory that hypovolemia occurred in DHF and DSS patients may caused a major circulation disturbance in all organs including kidney. Hypovolemia that occurred in DHF and DSS would cause a decrease in cardiac output which in turn will decrease renal blood flow (RBF). In more severe cases when degree of plasma leakage is to greater extent, the patients will have clinical signs of shock. In contrast with our study, the previous studies from small series of patients or case reports. Tanphaichitr et al. found one case of transient azotemia and one case of acute renal failure (ARF) among 17 patients with DHF. Mendez and Gonzales found 1.6% of ARF among 617 children with DHF in Colombia. Lee et al. reported 4.9% of ARF in 81 Chinese patients suffering from DHF/DSS and Abboud reported 5% of ARF in DHF. Other studies, there were eight cases of acute kidney injury (AKI) reported in patients with DHF/DSS and DSS. More recently, there were 15 cases of nephropathy dengue has been reported. Mostly dengue infection induced renal injury accompanied with syok, rhabdomyolysis, and hypotension. Chotmongkol and Sawanyawisuth reported of dengue infection induced renal injury, there was a case of dengue infection induced glomerulonephritis without shock, hypotension, or rhabdomyolysis.

It was assumed that the hypovolemia or shock in our study was so brief that the decreased RBF does not persist, so the circulation system can function well causing no renal damages. It was probably caused by the short lived hypovolemia in DHF patients and the renal autoregulation system causing the kidney as the last organ to be affected by hemodynamic dysfunction.

According to Vogt and Avner, the time needed from hypovolemia to cause renal dysfunction is still uncertain.

There were no reduces and differences of GFR in DHF and DSS patients at the time of diagnosis.

### Table 1 Characteristics of DHF and DSS

<table>
<thead>
<tr>
<th></th>
<th>DHF</th>
<th>DSS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16</td>
<td>13</td>
<td>*0.457</td>
</tr>
<tr>
<td>Female</td>
<td>25</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Age, mean (years)</td>
<td>7.6</td>
<td>8.4</td>
<td>0.337</td>
</tr>
<tr>
<td>Nutritional status, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEM</td>
<td>13</td>
<td>8</td>
<td>*0.856</td>
</tr>
<tr>
<td>Non PEM</td>
<td>28</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Length of fever before admitted to hospital, mean (days)</td>
<td>4.0</td>
<td>4.3</td>
<td>0.329</td>
</tr>
<tr>
<td>Hematocrit, mean (%)</td>
<td>41.98</td>
<td>42.22</td>
<td>0.833</td>
</tr>
<tr>
<td>Platelet, mean/mm³</td>
<td>96517</td>
<td>69037</td>
<td>0.007</td>
</tr>
</tbody>
</table>

p = t test, *chi-square test

### Table 2 GFR in DHF and DSS

<table>
<thead>
<tr>
<th></th>
<th>DHF (n=41)</th>
<th>DSS (n=27)</th>
<th>Combination (n=68)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>152.30 (49.20)</td>
<td>161.31 (45.88)</td>
<td>155.88 (47.77)</td>
<td>0.322</td>
</tr>
<tr>
<td>Median</td>
<td>137.50</td>
<td>155.38</td>
<td>141.89</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>94.88–318.21</td>
<td>89.17–261.90</td>
<td>89.17–318.21</td>
<td></td>
</tr>
</tbody>
</table>

*p = Mann Whitney test
The affect of hypovolemia in renal function could not be determined based on serum creatinine level at the time the diagnosis of DHF was confirmed. Creatinine will not be raised above the normal range until 60% of total kidney function is lost. \(^6\) To ascertain the renal function in DHF and DSS patients, a more accurate examination is necessary and repeated that measurement during the course of the illness is needed. Further study with serial GFR and serum creatinine level evaluation is needed to make the natural history of DHF and DSS clear. We concluded that there are no increases and differences of GFR on DHF and DSS patients at the time of diagnosis.

References

Karakteristik Dengue Berat yang Dirawat di Pediatric Intensive Care Unit

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Abstrak


Kata kunci: Dengue berat, karakteristik, pediatric intensive care unit

Characteristic of Severe Dengue Hospitalized in Pediatric Intensive Care Unit

Abstract

Dengue viral infections affect all age groups and produce a spectrum of clinical illness that ranges from asymptomatic to severe and occasionally fatal disease. Severe dengue characterized by plasma leakage, hemoconcentration, and hemostatic disorder. The aim of this study was to know the characteristic of severe dengue patients admitted to Pediatric Intensive Care Unit (PICU) Dr. Hasan Sadikin Hospital Bandung during January 2009 to December 2010. This was a retrospective descriptive study based on the data collected from the medical records. Twenty-one severe dengue cases in two years was admitted 15/21 females and 6/21 males, and 5/21 of them died during hospitalization because of dengue shock syndrome (DSS) and disseminated intravascular coagulation (DIC). Most of them were 1–5 years old with good nutritional status. Hepatomegaly was found in all cases with mean hematocrit was 38%. In this research, the most manifestation of severe dengue were DSS (15/21), DIC (11/21), encephalopathy (6/21), pleural effusion (5/21), myocarditis (3/21), and acute respiratory distress syndrome (3/21). In conclusions, severe dengue more common in girls, 1–5 years old, and well-nourished children. The most common clinical manifestation of severe dengue were shock, disseminated intravascular coagulation, and encephalopathy. [MKB. 2011;43(2S):48S–52].

Key words: Characteristic, pediatric intensive care unit, severe dengue

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