Profile of Liver Function among Pediatric Patients with Dengue Infection Admitted to a Tertiary Referral Hospital during the COVID-19 Pandemic

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Abstract

Background: Dengue infection is endemic in more than 100 countries; 70% of cases occur in Asia. One of dengue infection complication is hepatic dysfunction. The COVID-19 pandemic may cause a delay in seeking treatment and affect severe case of dengue infection when admitted to the hospital. This study aimed to analyze the liver function profile in dengue pediatric patients during the COVID-19 pandemic.

Methods: All patients under 18 years old with confirmed dengue serology (NS-1 immunochromatography or IgM anti-Dengue (ELISA) test and IgG anti-Dengue (ELISA) test) in Dr. Hasan Sadikin General Hospital from 2021–2022 were included in this retrospective study. The patients were categorized based on the modified WHO classification of 2009. Data were processed with SPSS® ver. 25 and analyzed using Chi-Square and One Way-ANOVA.

Results: In total, 85 patients were tested for the liver function; most severe dengue patients had abnormal SGOT and SGPT levels (100% vs. 64%). The SGOT and SGPT levels during the initial admission were higher in the severe dengue group (634 U/l and 271 U/l) and significantly different among groups (p=0.001 and p=0.032). The elevated SGOT (1,339 U/l vs. 203 U/l vs. 87.3 U/l; p=0.014) and SGPT (438 U/l vs. 100 U/l vs. 42.8 U/l; p=0.005) levels were higher in the severe dengue group.

Conclusions: The severity of dengue is in line with the increase in SGOT and SGPT levels. During the COVID-19 pandemic, the liver dysfunction persists and may be interfered with by delays in dengue treatment. Early recognition and prompt treatment are needed to decrease morbidity and mortality.

Keywords: COVID-19, dengue, liver function test, pandemic

Introduction

Dengue is an infection caused by the dengue virus (DENV-1, DENV-2, DENV-3, and DENV-4), leading to damage to the liver and increased liver function.[1–5] Liver dysfunction varies from mild injury with an elevation of transaminases to severe hepatocyte injury that causes jaundice in patients.[1,2] Dengue is endemic in more than 100 countries, 70% in Asia, with an increase in mortality rate annualy.[6] According to the Indonesia Ministry of Health, the incidence rate of dengue in Indonesia is 27 per 100,000, and the case fatality rate is 0.96%.[7]

COVID-19 is a newly emerging viral infection that caused a pandemic.[8] After the first report in China in December 2019, the disease spread worldwide affecting more than 576 million people in 200 countries.[8,9] In Indonesia it affects more than 6 million people and causes 157,000 mortalities.[10] Due to its infectivity, the local government has decided to implement large-scale social restrictions (LSSR) to respond to COVID-19.[11] This new regulation has disrupted and impeded access to health facilities, including medical care for acute infections such as Dengue. Meanwhile, people with acute fever also delayed treatment due to fear of the misperception of being infected by COVID-19.[12,13]

A study in India has concluded that hepatic dysfunction depends on the severity of disease.[15] There were elevated liver enzymes in the severe dengue group compared to the others.[15] To date, there is a lack of studies about Dengue infection during a pandemic, whereas the COVID-19 pandemic may influence the healthcare system, including impeding health

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access for acute infection. Consequently, this study aimed to analyze the liver function profile in dengue pediatric patients, including dengue patients without warning signs, with warning signs, and severe dengue during the pandemic of COVID-19.

Methods

This retrospective study included all pediatric patients under 18 years old in the registry with confirmed dengue serology admitted to Dr. Hasan Sadikin General Hospital from March 2021 to 2022. The institutional ethics committee had approved this study with number LB.02.01/X.6.5/195/2022.

Dengue serology tests were conducted using NS-1 immunochromatography or IgM anti-Dengue test and IgG anti-Dengue test (ELISA test by Biosynex). The patients were categorized based on the modified WHO classification of 2009 into dengue with or without the warning signs and severe dengue.[16]

The following data was obtained from the hospital medical records. Patient gender, age and liver function test were retrieved, including serum glutamic pyruvic transaminase (SGPT), an enzyme found in renal, liver and skeletal (5–40 IU/L) and serum glutamic oxaloacetic transaminase (SGOT), specific liver enzyme (7–56 IU/L) (Abbott Alinity).

Patients were grouped into groups with abnormal liver enzyme levels (SGOT and SGPT tests) during hospitalization. Initial SGOT and SGPT tests were the liver enzyme result at hospital admission; elevated SGOT and SGPT tests were the highest liver enzyme level during hospitalization.

Considering the anticipated prevalence of hepatic dysfunction in dengue to be around 50%, α error 5% (Zα=1.96), β error 20% (Zβ= 0.842) and a power of 80%, with a precision of 5%, according to the following formula (p= prevalence; q=(1-p); and d=precision).[17]

$$n = \frac{[(Z_\alpha + Z_\beta)^2 + pq]}{d^2}$$

Data were analyzed using the statistical package for the social science (SPSS) version 25. The statistical method employed for data analysis was the chi-Square test for categorical outcomes. Comparison of multiple means across disease severity was made using One Way-ANOVA with post hoc analysis with a level of significant <0.05.

Results

During the observation, there were 97 data. From a total of 157 patients, 18% had dengue without warning signs, 53% had dengue with warning signs, and 29% had severe dengue (Table 1). The age of the patient varied from one month to 17 years old, with average of 5.5 years old. The majority of the patient was male (61%).

Only 85 of 157 patients were enrolled on SGOT and SGPT tests of whom the liver enzyme test was only performed in clinically severe cases, resulting in 12 patients were dengue without warning signs, 31 were dengue with warning signs, and 42 were severe dengue (Table 2).

Most of the patients had abnormal SGOT test during the first laboratory examination, 92% in dengue without warning sign group, 93.5% in dengue with warning sign group, and all patients with severe dengue group; whereas an abnormal SGPT results were only found in around 25% in dengue with or without warning sign group, and higher (64%) in patients with severe dengue group (Table 2).

The initial liver function test was significantly highest in the severe dengue group with the highest level of SGOT was 634 U/l (p=0.001) compared to others during the critical phase. The initial SGPT level was higher in the severe dengue group was also significant higher compared to other groups (p=0.032). Similarly, the elevated level of SGOT and SGPT during the critical phase of dengue infection was the highest in the severe dengue group compared to other groups as shown in Table 2.

Table 1 Characteristic of Pediatric Patients with Dengue, Period 2021–2022

Variable	Total (n=157)
Diagnose	
Dengue without warning sign	28 (18%)
Dengue with warning sign	84 (53%)
Severe Dengue	45 (29%)
Age (mean)	5.5 years old
Gender	
Male	96 (61%)
Female	61 (39%)

Table 2 Liver Function Profile in Dengue Patients

	Dengue without Warning Sign (n=12)	Dengue with Warning Sign (n=31)	Severe Dengue (n=42)	p-value
Abnormal SGOT	11 (92%)	29 (93,5%)	42 (100%)	0.209
Abnormal SGPT	3 (25%)	7 (22%)	27 (64%)	0.001
Initial SGOT test (U/l)	86.25	197	634	0.001
Initial SGPT test (U/l)	42.8	96.9	271	0.032
Elevated SGOT (U/I)	87.3	203	1,339	0.014
Elevated SGPT (U/l)	42.8	100	438	0.005

Note: SGOT= Serum glutamic pyruvic transaminase, SGPT=Serum glutamic oxaloacetic transaminase, Abnormal SGOT and SGPT test: the number of patients who had abnormal levels of the liver enzyme during hospitalization; Initial SGOT and SGPT test: the liver enzyme result at hospital admission; Elevated SGOT and SGPT test: the highest liver enzyme level during hospitalization

Discussion

This study is the first to evaluate elevated liver enzymes among dengue pediatric patients during pandemic. Our study found that the dengue with warning signs is the most prevalent with the majority of patients was males, in line with study in India.[18] However, this finding contrasts with previous systematic reviews that found females as a risk factor for severe dengue due to the higher cytokine production, increased permeability of capillary bed, and immune response among female patients.[18–20] This difference result of male-to-female ratio could be due to the lower self-reporting among female patient in Asian communities.[18]

Hepatic involvement in infections of dengue varies from an asymptomatic elevation of the liver enzyme to fatal fulminant hepatic failure.[1,21] DENV targeted hepatocytes and caused liver disfunction.[3] In our study, we found abnormal SGOT levels in 90 to 100% patients of all groups, indicating that most pediatric dengue patients had liver dysfunction.[14]

The COVID-19 pandemic has influenced society and the healthcare system, including the motivation to seek treatment for acute infetcions.[12] The local government has decided to implement large-scale social restrictions (LSSR) to respond to COVID-19.[11] This new regulation has disrupted and impeded access to health facilities, including medical care for acute infections such as dengue.[12] The study from the Philippines describes some factors that contributed to this problem, including financial constraints, mode of transportation and traffic density, location, and full hospital capacity due to COVID-19 cases during the pandemic.[12] According to a cross-sectional study in Turkey, fear of COVID-19 misperception causes avoidance of going to the hospital and delayed medical treatment.[13] The fear of COVID-19 in patients with fever, cough and weakness which are considered COVID-19 symptoms.[13] The COVID-19 pandemic adversely impacts the provision of essential health services in the South-East Asian region, particularly in managing tuberculosis, HIV and Dengue fever.[22]

Nevertheless, our study found that pediatric patients with abnormal SGPT had less than abnormal SGOT. The abnormal SGPT level was mainly found in the severe dengue group. In most studies, elevation in SGOT is more often than SGPT during the first week of infection, with a tendency to decrease to normal levels within three weeks.[1,2] This phenomenon is explained due to the release of SGOT from damaged myocytes at the earlier stage.[1,2] It was found that the level of SGPT was lower than SGOT in each classification group. In line with other studies, these findings are due to the specification of SGPT as a liver enzyme and only found in low concentrations in skeletal muscle, brain, and intestinal.[2,15,18] In contrast, SGOT is released following damage to the liver, cardiac and skeletal muscle.[2]

The higher SGOT and SGPT levels are aligned with the dengue's severity. Our study found that SGOT and SGPT levels are higher in severe dengue group compared with the other during initial test and elevated test during hospitalization. In DENV infection, high-level viremia is associated with the involvement of the liver in the severe form of the disease.[1,21] Mechanism of liver injury due to a direct effect of the virus or host immune response, circulatory compromise, and metabolic acidosis or hypoxia due to circulatory failure.[18]

The strengths of our study are that we have performed the first study in the pediatric population to estimate liver function tests in dengue patients, especially during the COVID-19 pandemic. In addition, our study analyzes the subject's disease severity and liver function profile. The limitations of our study are the subject selected from tertiary centers, which tend to find clustering of more severe cases. Further study should analyze clinical signs and symptoms, including other laboratory findings including platelet, alkaline phosphatase, total bilirubin, direct bilirubin, and albumin in Dengue patients.

In conclusion, the severity of dengue is in line with the increase in SGOT and SGPT levels. During the COVID-19 pandemic, the incidence of liver dysfunction persists and may be interfered with by delays in dengue treatment. Early recognition and prompt treatment are needed to decrease the morbidity and mortality of dengue patients.

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