Differences in Liver Impairment between Adults and Children with Dengue Infection

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Abstract. Dengue infection (DI) is a major vector-borne disease in southeast Asia and an important cause of morbidity. The complications such as hepatic impairment are common, and because the physiology of the liver differs between children and adults, the DI-associated liver impairments might be expected to differ as well. This study aims to compare the differences in liver impairment between adults and children with DI. We retrospectively studied 158 adults and 79 children with serologically confirmed DI admitted to the Bangkok Hospital for Tropical Diseases from 2008 to 2012. In total, 93% of adults and 87% of children exhibited abnormal liver enzyme levels during hospitalization. Overall, 76 (42.4%) adults and 16 (20.3%) children had dengue hemorrhagic fever (DHF). Compared with children, adults with dengue fever (DF) presented a significantly higher incidence of liver function impairment (alanine transaminase [ALT] > 2 × upper limit of normal [ULN]) (47.1% versus 25.5%), hepatitis (ALT > 4 × ULN) (29.4% versus 12.8%), and severe hepatitis (aspartate transaminase [AST]/ALT > 10 × ULN) (16.5% versus 4.3%). Children with DHF showed a significantly higher incidence of liver function impairment due to AST derangement than did adults (100% versus 73%). There were no differences in the total bilirubin, albumin, or total protein levels between adults and children. Liver enzymes normalized significantly more slowly in adults, and AST recovery was faster than ALT. In conclusion, liver function impairment was more common among adults than children with DF. As the severity progressed to DHF, liver injury became more common in children.

INTRODUCTION

Dengue is considered to be the most common arboviral disease worldwide and one of the most important emerging viral tropical diseases.¹ Dengue infection is transmitted through the bites of *Aedes* mosquitoes infected with any of the four dengue viral serotypes. Dengue infection may cause asymptomatic infection or a broad spectrum of disease ranging from a mild febrile illness known as dengue fever (DF) to a severe and life-threatening condition characterized by increased vascular permeability, thrombocytopenia, bleeding disorders, and a tendency to develop shock known as dengue hemorrhagic fever (DHF).² Although children were mainly affected with dengue virus infection during the past few decades, the age distribution has shifted to older groups in recent years.³ The prevalence of dengue infection in 2013 in Thailand was more common in patients aged 15–24 years (29.16%) followed by those aged 10–14 years (21.31%) and 5–9 years (15.72%).⁴

Atypical clinical manifestations of dengue infection have been reported and have become more common within the last few years. Such clinical manifestations include involvement of the liver, central nervous system, and heart.⁵ Even though the liver is not the major target organ, pathological findings such as hepatocellular necrosis and inflammatory cell infiltration have been identified in liver biopsy specimens of patients with DF, and derangement in liver enzymes is commonly seen.⁶ Because the anatomy and physiology of the liver differ between children and adults, DF-associated liver changes have been expected to differ as well.^{7,8} For instance, clinical jaundice was detected around 1.7–17% in adults^{9–11} while children had a higher percentage of hepatomegaly.^{12,13} Although liver dysfunction in patients with dengue infection is a common condition, few reports have compared the clinical

differences between adult and child cases in a single population.^{14,15} This makes difficulties for comparing affected age groups who come from various endemic areas in which differences in disease severity influencers such as the infecting serotypes and the previous exposure of an individual to other dengue serotypes may be encountered.¹⁶ This study aims to describe the differences in liver impairment, disease severity, and recovery of liver function between adults and children with dengue infection.

MATERIALS AND METHODS

Study design. We conducted a retrospective study involving patients diagnosed with dengue infection who were admitted to the Bangkok Hospital for Tropical Diseases from April 2008 to December 2012. All medical records of dengue-infected patients during this period were reviewed. The data were retrieved from the hospital database according to the following codes of the 10th revision of the International Classification of Diseases: A90 (DF) and A91 (DHF). Only patients with confirmed dengue infection were enrolled in this study. Confirmation was based on the presence of acute fever with clinically suspected dengue infection¹⁷ plus at least one of the following criteria: a positive nonstructural protein 1 antigen, a positive IgM, and/or a 4-fold increase in the IgG titer for dengue, or a positive polymerase chain reaction result for dengue virus.¹⁸ Patients with underlying diseases that may have interfered with the outcome (such as chronic liver, kidney, lung, heart, or hematologic diseases and/or coinfection with other infectious disease agents) were excluded. Patients who met the eligibility criteria were classified as children (age of < 15 years) or adults. Clinical data were collected from the medical records while biochemistry and screening results were taken directly from the laboratory database. After the standard of care at the hospital during this period, the patients who were diagnosed with DI were given guidance for outpatients follow-up or hospitalized after clinical evaluation. The treatment instituted for these patients

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was basically symptomatic with the use of antipyretics, analgesics, antiemetics, and venous hydration for the hospitalized patients. Routine laboratory investigations were performed and recorded, and blood cell count was performed daily. Liver function tests were obtained by clinicians within the first 3 days of admission in cases with manifestations of suspected liver dysfunction such as prominent GI symptoms, bleeding manifestation, and atypical manifestations as well as repeated during hospitalization for abnormal results. Abdominal ultrasounds and chest radiographs were performed and interpreted by experienced clinicians to collect information about pleural effusion and ascites indicating plasma leakage. After discharge, patients were followed up by performing clinical and laboratory assessments for up to 4 weeks. The ethics committee of the Faculty of Tropical Medicine, Mahidol University approved this study.

Sample size estimation. The sample size estimation was based on prior data indicating an 80.3% and 63.6% prevalence of liver function impairment among adults and children, respectively.¹⁵ The ratio of adult inpatients with dengue infection was higher than that of children in this hospital. Assuming a ratio of two adults per child at an alpha level of 0.05 and power level of 0.8, 158 adults and 79 children with dengue infection were to be included in the analysis. All medical records of patients with dengue infection from 2008 to 2012 were reviewed.

Definition of disease severity. Patients were classified as having DF or DHF upon discharge based on the World Health Organization guidelines.¹⁷ DHF was defined as presence of fever, hemorrhagic manifestations, thrombocytopenia with a platelet count of $< 100,000$ cells/mm³, and hemoconcentration (hematocrit increase of $\geq 20\%$ above the baseline value) or evidence of plasma leakage. DHF cases were further graded as I–IV following the World Health Organization guidelines. Grade I was defined by the presence of fever, thrombocytopenia, hemorrhagic manifestations (positive tourniquet test), and evidence of plasma leakage indicated by the presence of pleural effusion, ascites, and/or hemoconcentration. Grade II DHF was diagnosed as in grade I plus spontaneous bleeding. Patients who presented the above signs accompanied by circulatory failure (weak pulse, narrow pulse pressure < 20 mmHg, hypotension, or restlessness) were classified as grade III. Patients with undetectable blood pressure and pulse were classified as DHF grade IV. DHF grades III and IV were collectively classified as dengue shock syndrome (DSS). Abnormal liver function test results during hospitalization were determined by selecting the peak values from each patient's tests performed during the whole hospitalization period. Definitions for liver function impairment were from previous similar studies in the literature by Kuo and others and Wang and others.^{6,15} Liver function impairment was defined as an increase in the aspartate transaminase (AST) and/or alanine transaminase (ALT) level of at least twice higher than the upper limit of normal (ULN).¹⁵ Hepatitis was defined as an AST and/or ALT level at least four times higher than the ULN, and severe hepatitis was defined as an AST and/or ALT level of at least 10 times higher than the ULN.⁶ The ULN of ALT and AST was defined as > 40 U/L.^{6,15}

Statistical analysis. Categorical data are presented as frequency and percentage (%). Continuous data are presented as mean and standard deviation (SD) or median and interquartile range (IQR). Categorical variables between the two

groups were compared using the χ^2 test or Fisher's exact test as appropriate. Continuous variables between the two groups were compared using Student's *t* test or the Mann–Whitney *U* test as appropriate. A Kaplan–Meier curve was used to present the liver enzyme recovery times, and the log rank test was performed for statistical significance. All analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 15.0 (SPSS Inc., Chicago, IL). A two-tailed *P* value of < 0.05 was considered statistically significant.

RESULTS

Patient characteristics. In total, 201 and 129 medical records of adults and children with dengue infection, respectively, were reviewed, of which 43 adults and 50 children were excluded, and the remaining 158 adults (66.7%) and 79 children (33.3%) who met the eligibility criteria were included in the analysis (Figure 1).

Finally, 91 (57.6%) adults and 63 (79.7%) children were diagnosed with DF, whereas 67 (42.4%) adults and 16 (20.3%) children were diagnosed with DHF. Of the 67 adults with DHF, 42 (62.7%) had DHF grade I, 24 (35.8%) had DHF grade II, and one (1.5%) had DHF grade III. Of the 16 children with DHF, eight (50%), seven (43.8%), and one (6.2%) presented with DHF grade I, II, and III, respectively. None of them developed DHF IV; *P* = 0.006 (data not shown). The mean (SD) age of adults was 24.7 years (8.4), and that of children was 11.3 years (3.0). The male-to-female ratio was similar between the two groups. Adults presented to the hospital at a mean (SD) of 4.6 days (1.4) after the onset of symptoms, and children presented at a mean of 4.4 days (1.7) (Table 1).

Liver function test abnormalities on admission. Among the 121 (76.6%) adults and 44 (55.7%) children who underwent liver function tests on admission, 104 (86.0%) and 39 (88.6%) had high liver enzyme levels (AST and/or ALT of > 40 U/L).

The median (IQR) AST and ALT levels were greater in adults than in children with DF (AST in adults: 96.0 [64.5–154.5] U/L versus AST in children: 66.0 [46.5–95.5] U/L, *P* = 0.025; ALT in adults: 63.0 [32.0–134.0] U/L versus ALT in children: 27.5 [20.5–46.3] U/L, *P* = 0.001). The other differences in liver function test results on admission between adults and children with DF included a higher alkaline phosphatase (ALP) level in children (median [IQR]: 68.0 [54.0–91.5] U/L versus 140.0 [108.0–206.5] U/L, respectively, *P* < 0.001) (ALP values were not corrected for age-related laboratory norms). No statistically significant differences were found in the remaining blood chemistry results, including bilirubin, total protein, and albumin levels, in patients with DHF (Table 2).

Liver function test abnormalities during hospitalization. Liver function test results obtained during hospitalization were available for 148 (93.7%) adults and 62 (78.5%) children. A total of 137 (92.6%) adults and 54 (87.1%) children exhibited elevated liver enzyme levels. Statistically significant differences between adults and children with DF included an increased ALT level only (liver function impairment: 47.1% versus 25.5%, respectively, *P* = 0.015 and hepatitis: 29.4% versus 12.8%, respectively, *P* = 0.031) and an increased AST and/or ALT level (liver function impairment: 67.1% versus 48.9%, respectively, *P* = 0.041 and severe hepatitis: 16.5%

FIGURE 1. Patient enrollment.

versus 4.3%, respectively, $P = 0.039$) (Table 3). The median (IQR) AST and ALT levels in adults with DF were significantly higher than those in children (AST: 117.0 [73.0–247.5] U/L versus 79.0 [43.0–129.0] U/L, respectively, $P = 0.006$ and ALT: 76.0 [35.5–185.0] U/L versus 31.0 [21.0–82.0] U/L, respectively, $P < 0.001$) (Figure 2).

Significantly more children than adults with DHF showed higher AST levels (100.0% versus 73.0%, respectively; $P = 0.023$). No statistically significant differences were observed in the ALT level between the two groups (Table 3).

Liver function test recovery. An abnormal AST level was noted at discharge in 135 (91.2%) adults and 54 (87.1%) children. Among them, 69 (51.1%) adults and 23 (42.6%) children were followed up with liver function testing after discharge. At the 4-week follow-up, the AST recovery rate was significantly higher in children than in adults (82.6% versus 55.1%, respectively, $P = 0.018$). The ALT level was still high

at discharge in 109 (74.1%) adults and 31 (50.8%) children ($P = 0.001$). Among them, 56 (51.4%) adults and 17 (54.8%) children were followed up with liver function testing 4 weeks after discharge. At the 4-week follow-up, the ALT recovery rate was also significantly higher in children than in adults (58.8% versus 19.6%, respectively, $P = 0.002$).

TABLE 1

Characteristics of patients with dengue infection at study entry

	Adults	Children
	<i>N</i> = 158	<i>N</i> = 79
Percentage of patients (%)	66.7	33.3
Age in years, mean (SD)	24.7 (8.4)	11.3 (3.0)
Sex (male:female)	1.3:1.0	1.3:1.0
Days of illness at enrollment, mean (SD)	4.6 (1.4)	4.4 (1.7)
DF:DHF ratio	1.4:1.0	3.9:1.0
DHF, <i>n</i> (%)	67 (42.4)	16 (20.3)
Patients with liver enzymes above ULN at admission (%)	104 (86.0)*	39 (88.6)*

DF = dengue fever; DHF = dengue hemorrhagic fever; SD = standard deviation; ULN = upper limit of normal.

*Liver function tests available for 121 adults and 44 children.

TABLE 2

Liver function test results on admission of patients with dengue infection

Severity	Blood chemistry parameters	Adults	Children	<i>P</i> value
DF	AST (U/L)	96.0 (64.5–154.5) <i>N</i> = 69	66 (46.5–95.5) <i>N</i> = 34	0.025
	ALT (U/L)	63.0 (32.0–134.0) <i>N</i> = 67	27.5 (20.5–46.3) <i>N</i> = 34	0.001
	ALP (U/L)*	68.0 (54.0–91.5) <i>N</i> = 61	140.0 (108.0–206.5) <i>N</i> = 21	NA
	Total bilirubin (mg/dL)	0.4 (0.2–0.5) <i>N</i> = 65	0.3 (0.2–0.4) <i>N</i> = 20	0.272
	Albumin (g/dL)	4.2 (3.9–4.4) <i>N</i> = 63	4.4 (4.2–4.6) <i>N</i> = 21	0.131
	Total protein (g/dL)	7.1 (6.7–7.4) <i>N</i> = 49	7.3 (7.0–7.7) <i>N</i> = 15	0.238
DHF	AST (U/L)	96.5 (54.0–184.8) <i>N</i> = 54	162.5 (117.5–260.5) <i>N</i> = 10	0.067
	ALT (U/L)	61.0 (28.5–136.8) <i>N</i> = 54	71.0 (41.8–118.0) <i>N</i> = 10	0.731
	ALP (U/L)*	58.0 (47.0–81.8) <i>N</i> = 46	114.0 (91.5–151.0) <i>N</i> = 5	NA
	Total bilirubin (mg/dL)	0.5 (0.3–0.6) <i>N</i> = 46	0.4 (0.4–1.0) <i>N</i> = 5	0.963
	Albumin (g/dL)	4.1 (3.7–4.4) <i>N</i> = 48	4.2 (3.1–4.4) <i>N</i> = 5	0.686
	Total protein (g/dL)	6.9 (6.5–7.3) <i>N</i> = 38	7.2 (5.1–7.6) <i>N</i> = 5	0.868

ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate transaminase; DF = dengue fever; DHF = dengue hemorrhagic fever; NA = not applicable. Data are presented as median (interquartile range). Values in bold are statistically significant.

*No correction was made for age-related laboratory norms.

TABLE 3
Hepatic impairment during hospitalization in patients with DF and DHF

Severity		DF			DHF		
Liver function test	Categories	Adults	Children	P value	Adults	Children	P value
		N = 85	N = 47		N = 63	N = 15	
AST	Liver function impairment ($> 2 \times \text{ULN}$)	56 (65.9)	23 (48.9)	0.057	46 (73.0)	15 (100.0)	0.023
	Hepatitis ($> 4 \times \text{ULN}$)	28 (32.9)	10 (21.3)	0.156	32 (50.8)	10 (66.7)	0.268
	Severe hepatitis ($> 10 \times \text{ULN}$)	13 (15.3)	2 (4.3)	0.056	12 (19.0)	3 (20.0)	≥ 0.05
ALT	Liver function impairment ($> 2 \times \text{ULN}$)	40 (47.1)	12 (25.5)	0.015	39 (61.9)	10 (66.7)	0.732
	Hepatitis ($> 4 \times \text{ULN}$)	25 (29.4)	6 (12.8)	0.031	19 (30.2)	4 (26.7)	≥ 0.05
	Severe hepatitis ($> 10 \times \text{ULN}$)	5 (5.9)	1 (2.1)	0.421	2 (3.2)	2 (13.3)	0.165
AST and/or ALT	Liver function impairment ($> 2 \times \text{ULN}$)	57 (67.1)	23 (48.9)	0.041	48 (76.2)	15 (100.0)	0.035
	Hepatitis ($> 4 \times \text{ULN}$)	29 (34.1)	10 (21.3)	0.122	33 (52.4)	10 (66.7)	0.317
	Severe hepatitis ($> 10 \times \text{ULN}$)	14 (16.5)	2 (4.3)	0.039	12 (19.0)	3 (20.0)	≥ 0.05

ALT = alanine transaminase; AST = aspartate transaminase; DF = dengue fever; DHF = dengue hemorrhagic fever; ULN = upper limit of normal.
Data are presented as n (%). Values in bold are statistically significant.

When the liver enzyme recovery rate was analyzed by disease severity, significantly more children than adults with DF exhibited a return to normal AST and ALT levels within 4 weeks of follow-up (AST recovery rate: 93.8% versus 58.5%, respectively; ALT recovery rate: 72.7% versus 6.5%, respectively). There was no significant difference in the recovery rate of liver enzymes between children and adults with DHF (AST recovery rate: 57.1% versus 50.0%, respectively; ALT recovery rate: 33.3% versus 36.0%, respectively).

Patients whose transaminases returned to normal levels after 4 weeks of follow-up were included in the survival analysis (Figure 3 and 4). The AST recovery time was significantly longer in adults than in children (median time to recovery, 13.0 days [95% CI: 10.0–16.0] versus 9.0 days [95% CI: 6.9–11.1], respectively, $P = 0.016$). A similar finding was observed for ALT, which required a longer period to return to a normal level in adults than in children (median time to recovery: 18.0 days [95% CI: 10.5–25.5] versus 10.0 days [95% CI: 8.6–11.4], respectively, $P < 0.001$) (Table 4).

DISCUSSION

Our results indicate that 93% of adults and 87% of children had increased levels of liver enzymes during admission.

FIGURE 2. Median aspartate transaminase (AST) and alanine transaminase (ALT) (U/L) among patients with dengue infection during hospitalization by age group.

Adults had more predominant hepatic involvement than did children with DF. However, as the severity progressed to DHF, liver injury became more prominent in children.

The liver is one of the target organs in dengue infection, and clinical manifestations of hepatic dysfunction may appear during the course of the disease. Although the literature regarding changes in liver enzymes in patients with dengue infection is limited, mild to moderate liver involvement seems to be a common condition, particularly in patients with DHF. In this study, nearly 90% of patients who underwent liver function tests exhibited increased transaminase levels during the hospital stay; this high percentage is similar to that found in other studies, in which it ranged from 50% to 90%.^{6,11,19,20} The median AST and ALT levels were significantly greater in adults than in children with DF at hospital admission. However, while the median transaminase levels remained constant in adults with DHF, they more than doubled in children with DHF, and higher transaminase levels were observed in children with more severe infection. This finding indicates that although children and adults face the same disease, the pathogenetic mechanism in the liver seems to differ, and a distinct clinical approach in each age group is apparently necessary.

The mechanism of liver injury in patients with dengue infection remains unclear. This mechanism has been postulated may be due to a direct viral effect on hepatocytes, a dysregulated host immune response to the virus, or nonspecific

FIGURE 3. Kaplan-Meier estimates of cumulative aspartate transaminase (AST) recovery over time in adults and children with dengue infection.

TABLE 4

Median AST and ALT recovery over time (days) among children and adults with abnormal liver function

Status	Median AST	95% CI	P value*	Median ALT	95% CI	P value*
Adults	13 N = 69	10.0–16.0	0.016	18 N = 55	10.5–25.5	< 0.001
Children	9 N = 23	6.9–11.1		10 N = 17	8.6–11.4	
Overall	11 N = 92	8.3–13.7		14 N = 72	9.7–18.3	

ALT = alanine transaminase; AST = aspartate transaminase; CI = confidence interval.

*Log-rank (Mantel-Cox) test. Values in bold are statistically significant.

effects of plasma leakage, shock, and hypotension.²¹ The reason for children with DHF developing more severe liver dysfunction in this study is unclear. We suspect that children have a higher susceptibility than adults to various nonspecific factors of DHF such as plasma leakage, while liver injury in adults may be more strongly influenced by specific viral or host immune response effects on hepatocytes. For example, children with DHF were more likely than adults to develop DHF grades II and III. In addition, hepatotoxic drugs may have affected the liver dysfunction in this study. The effects of potentially hepatotoxic drugs taken during the early stage of the disease on liver dysfunction are still controversial.^{22,23} Because this study was retrospective, we could not collect data on the intake of acetaminophen or other hepatotoxic drugs in our studied population. Only five adults and three children received antibiotics, and no differences in liver dysfunction were observed.

We also confirmed that the AST levels were higher than the ALT levels in both adults and children. AST has been found to be greater than ALT in several studies.^{6,12,20} The meaning of this trend is still unclear, but a possible mechanism may be the excess release of AST from damaged myocytes during dengue infection.⁶ This phenomenon is rarely seen in patients with viral hepatitis caused by the hepatitis A, B, or C viruses, but is similar to the phenomenon in patients with alcoholic hepatitis.²⁴ This could help clinicians to differentiate between these different conditions upon a patient's first presentation. ALP was within the normal reference range values for both groups and was not notably affected throughout the course of the infection in our population.

FIGURE 4. Kaplan-Meier estimates of cumulative alanine transaminase (ALT) recovery over time in adults and children with dengue infection.

Kuo and others reported that liver enzymes increased to maximum levels around 9 days after the onset of fever.⁶ In this study, patients presented to the hospital at a median of 4 days after the onset of symptoms; therefore, an increase in the transaminase levels would be expected during hospitalization. We recorded and categorized the peak increase in liver enzymes into different severity groups. Liver function impairment and hepatitis due to an increase in ALT and severe hepatitis due to an increase in both ALT and AST were significantly more common in adults than in children with DF. Among patients with DHF, an increased AST level at least 2-fold higher than the ULN was significantly more common in children; this actually occurred in 100% of the children in this study. This finding should remind clinicians to closely monitor the development of DHF when an abnormally high transaminase level is detected, especially in pediatric patients.

Dengue infection was previously reported to be the most common cause of acute liver failure in children in different Thai studies,^{25,26} while it seemed to be a rare condition in adults.²⁷ In an evaluation of 699 adult patients with DF, Parkash and others reported a 2.7% mortality rate among adults with severe hepatitis.⁹ In contrast, another study reported a 50.0% mortality rate in a pediatric population.²⁸ In this study, although 17.6% of adults and 16.1% of children developed severe hepatitis, the disease course was self-limiting, and there were no cases of liver failure or death. This observation was also highlighted by Ahmad and others in India.²⁹

In our hospital, patients with abnormal liver enzymes were followed for up to 4 weeks after discharge. We found that the AST and ALT levels returned to the normal range within 4 weeks of follow-up in a significantly higher percentage of children than adults with DF (AST recovery rate: 93.8% versus 58.5% and ALT recovery rate: 72.7% versus 6.5%, respectively). When the disease became more severe, the difference was not significant. Liver enzyme recovery also took a significantly longer period in adults than in children. Several studies have reported a decrease in liver enzymes to the normal range within 3 weeks after the liver enzymes had increased to maximum levels.^{6,30} We observed a longer recovery time for liver enzymes. These different results may be explained by the different degrees of liver injury among the studies. Among patients in whom the liver enzymes returned to normal within 4 weeks of follow-up, we observed that AST returned to a normal level faster than did ALT and that ALT took longer to recover in adults than in children. This may be because ALT has a longer half-life and increases at a later onset than does AST.^{6,31} This may explain its later recovery.

This study adds valuable clinical information to the limited number of reports to date comparing liver impairment in adults and children in a single population.^{14,15} We observed liver involvement patterns between the two groups similar to those shown in these previous studies, but we also added a follow-up period of up to 4 weeks after discharge. This allowed us to assess the impact of these patterns on the subsequent restoration of liver function.

This study has some limitations. First, because of the retrospective nature of the study, coagulation tests results were only available for five patients during admission, not all patients underwent liver function tests at the hospital (94% of adults and 79% of children), and some of them did not undergo follow-up liver enzyme measurement during hospitalization. These issues may have caused an underestimation of the

findings of abnormal liver function. Furthermore, most patients were followed up for no more than 4 weeks, which limited the ability to accurately estimate the time required for full liver enzyme recovery. Another limitation may be the small number of children with DHF who received liver function tests. This makes generalizing from the comparison of liver enzyme levels between adults with DHF and children with DHF difficult. Because of these three limitations, further prospective studies are necessary to be studied to fully understand the dynamic changes in liver enzymes during the course of dengue infection, the correlation of these changes with disease severity, and details regarding the recovery phase as well as to increase the number of children with DHF.

CONCLUSION

Liver impairment was more common among adults than children with dengue infection and presented as various degrees of serum transaminase elevations. Among patients with DF, more adults than children developed hepatitis. Nevertheless, as the disease progressed into a more severe form, liver injury became more notable in children. Liver enzymes required a significantly longer time to return to normal in adults than in children, and the recovery rate was slower for ALT than for AST.

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