

Evaluation of Liver Functional Test (LFT) and Kidney Functional Test (KFT) in Dengue Patients

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ABSTRACT

Background: Dengue is an acute infection caused by an arbovirus in the *Flavivirus* genus, and the mosquito *Aedes aegypti* is the vector. Case fatality ratio in India is reported to be 3 to 5 percent. One of the least studied complications occurring in dengue is acute kidney injury (AKI) and liver abnormalities are few of the least studied complications of dengue. Hence, we planned the present study to assess the LFT and KFT in Dengue patients. **Methods:** The present study included assessment of 100 patients out of which 50 patients were found to be sero positive for dengue while rest 50 were found to be sero negative. Assessment of levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), the degree of hepatic involvement was done in all the patients included in the present study. AKIN definition for classification of AKI (Acute kidney injury) Stages was used for the present study. All the results were analyzed by SPSS software. **Results:** Total proteins level among dengue sero positive and negative subjects was found to be 7.01 and 7.89 g/dl. Significant results were obtained while comparing the total proteins levels among dengue positive and negative subjects. While comparing the albumin and globulin levels between dengue positive and negative subjects, significant results were obtained. Significant results were obtained while comparing the AST and ALT levels between both the study groups. 14.5 And 63.5 percent of the patients were AKI and AKIN- 1 AKI. **Conclusions:** Hepatic and renal involvement occurs in patients suffering from dengue fever.

Key words: Dengue, Kidney Functional Test, Liver Functional Test

INTRODUCTION

One of the most rapidly spreading mosquito-borne viral diseases all over the world is Dengue. It is an acute infection caused by an arbovirus in the *Flavivirus* genus, and the mosquito *Aedes aegypti* is the vector. Case fatality ratio in India is reported to be 3 to 5 percent.^[1] It has an incubation period of 4 to 8 days and is characterized by onset of fever, generalized body ache, myalgia, arthralgia, and headache.^[1] Atypical manifestations of dengue have been reported with multiple organ involvement.^[2] Hepatic

involvement is characterized by right hypochondrium pain, hepatomegaly, jaundice, and elevated aminotransferase levels peaking at ninth day and gradually running to normal within 4 weeks.^[3]

One of the least studied complication occurring in dengue is acute kidney injury (AKI) is one of the least studied complications of dengue. Proteinuria has been detected in as high as 74% of patients with Dengue hemorrhagic fever (DHF).^[4] Various types of glomerulonephritis have been reported during or shortly after dengue infection in humans and mouse models of dengue infection. On a rare occasion, dengue infection is associated with systemic autoimmune disorders involving the kidneys. In the vast majority of cases, dengue infection and associated renal disorders are self-limited.^[5] The majority of previous studies used variable definition of AKI in dengue virus infection (DVI), and included only patients with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).^[6] Hence; we planned the present study to assess the LFT and KFT in Dengue patients.

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METHODS

The present study was conducted in the department of Haematology and Renal medicine of the medical institution

and included assessment of 100 patients who reported from 2014 to 2016. Out of 100, 50 patients were found to be sero positive for dengue while rest 50 were found to be sero negative. Ethical approval was taken from the institutional ethical committee and written consent was obtained after explaining in detail the entire research protocol. Dengue was suspected when two or more of the following symptoms were present: fever, retro-orbital pain, myalgia, arthralgia, skin rash, nausea/vomiting, and hemorrhagic manifestations. Complete blood counts, renal functional tests and liver function tests were carried out. Tests for detection of anti-dengue antibodies and/or NS1 antigen test were carried out in all patients. These samples were subjected to immuno-enzymatic assay. When results of either of these tests were positive, patients were considered to be currently infected with dengue virus, while cases in which the results were negative were considered unconfirmed.

Liver functional tests

Measurement of the levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), the degree of hepatic involvement was done in all the subjects included in the present study. 40 U/L was the reference range set for the measurement of AST and ALT.

Kidney functional tests

AKIN definition for classification of AKI (Acute kidney injury) Stages was used for the present study. Stage 1 AKI was defined as an increase in serum creatinine >26.5 µmole/L (≥0.3 mg/dL) or 1.5 to 2-fold increase from baseline. Stage 2 AKI was defined as an increase in serum creatinine of >2–3-fold from baseline. Stage 3 AKI was defined as an increase in serum creatinine of >3-fold from baseline or an absolute serum creatinine of >354 µmol/L (≥4 mg/dL).^[7] All the results were analyzed by SPSS software. Chi-square test, student t test and univariate analysis were used for the assessment of level of significance.

RESULTS

Table 1 and Graph 1 shows the Liver profile of the patients. Total bilirubin value in dengue sero positive and negative subjects 1.3 and 0.8 mg/dl. Total proteins level among dengue sero positive and negative subjects was found to be 7.01 and 7.89 g/dl. Significant results were obtained while comparing the total proteins levels among dengue positive and negative subjects. While comparing the albumin and globulin levels between dengue positive and negative subjects, significant results were obtained. Significant results were obtained while comparing the AST and ALT levels between both the study groups. Table 2 and Graph 2 shows the incidence, severity and outcome of AKI at the time of discharge. 14.5 And 63.5 percent of the patients were AKI and AKIN- 1 AKI.

DISCUSSION

Dengue shock syndrome is an important cause of hospitalization among children living in dengue-endemic

areas. However, in general, severe bleeding is not a major problem in this group, despite often profound thrombocytopenia and clear evidence of a coagulopathy.^[8] In recent years, there has been a notable increase in the number of adults with dengue requiring hospitalization in Asia and South America. Dengue shock syndrome appears to be less frequent in adults than children, possibly reflecting age-dependent differences in intrinsic vascular permeability, but there is anecdotal evidence to suggest that bleeding manifestations and hepatic dysfunction are both more common in older age groups.^[9-11]

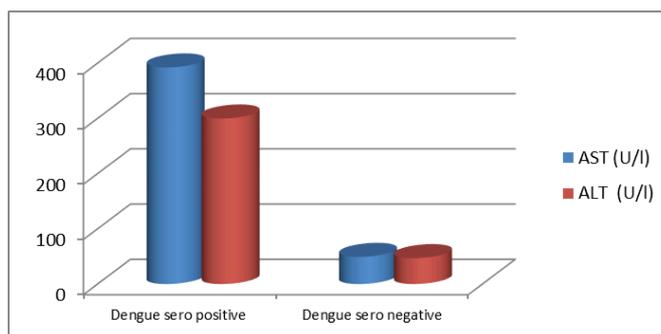
Table 1: Liver profile of the patients

Parameter	Dengue sero positive	Dengue sero negative	p-value
Total bilirubin (mg/dl)	1.3	0.8	0.32
Total proteins (g/dl)	7.01	7.89	0.03*
Albumin (g/dl)	3.92	4.52	0.02*
Globulin (g/dl)	2.93	3.02	0.03*
AST (U/l)	392.2	49.2	0.01*
ALT (U/l)	299.7	46.9	0.04*

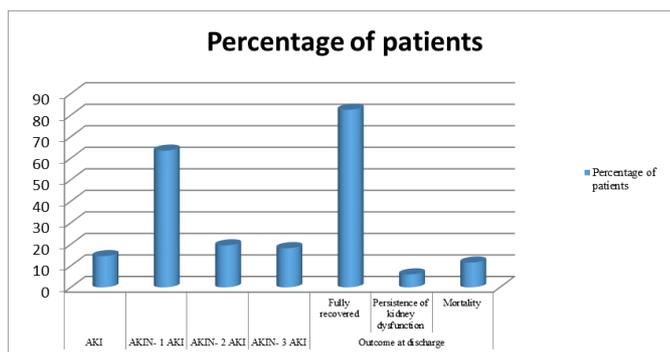
*: Significant

Table 2: Incidence, severity and outcome of AKI at the time of discharge

Parameter	Percentage of patients
AKI	14.5
AKIN- 1 AKI	63.5
AKIN- 2 AKI	19.5
AKIN- 3 AKI	18.2
Outcome at discharge	
Fully recovered	82.5
Persistence of kidney dysfunction	6
Mortality	11.5



Graph 1: Liver profile of the patients



Graph 2: Incidence, severity and outcome of AKI at the time of discharge

Hepatic dysfunction is a well-recognized feature of dengue infections, often demonstrated by hepatomegaly and mild-to-moderate increases in transaminase levels although jaundice and acute liver failure are generally uncommon.^[12]

Biopsy specimens obtained from a small number of patients with DSS who died have shown a variety of patterns including microvesicular steatosis, hepatocellular necrosis with associated councilman bodies, Kupffer cell destruction, and inflammatory infiltrates at the hepatic portal tracts.^[13] Several forms of renal involvement have been identified in patients with dengue, including elevation of the serum creatinine level, AKI, acute tubular necrosis, hemolytic uremic syndrome, proteinuria, glomerulopathy and nephrotic syndrome.^[14] AKI is a significant, albeit poorly studied, complication of dengue. The data available are heterogeneous and mostly originate from retrospective case series and case reports. The reported frequency of this association exhibits wide variation in accordance to the particular population being assessed, severity of dengue, criteria used for the diagnosis of AKI and time of evaluation.^[15,16] Hence; we planned the present study to assess the LFT and KFT in Dengue patients.

In the present study, we observed that elevated AST and ALT levels are observed in almost all the patients with serologically positivity for dengue. Similar results were reported in the past literature by Gandhi et al.^[17] We also observed higher incidence of AKI among dengue positive patients. Our results were in correlation with the results observed by Muhammad et al.^[18]

Gandhi et al conducted an analysis of 27 serologically confirmed cases of dengue infection at a tertiary care hospital was made. Patients with normal aminotransferase levels were categorized into Grade A, those with at least one of the enzymes raised to less than 3 times the reference range as Grade B, those with at least one of the enzymes elevated more than 3 times but less than 10 times as Grade C and those with elevations more than 10 times as Grade D. 89% of the cases had alterations in the aminotransferase levels, with 37% categorized into Grade B, 30% into Grade C, and 22% as Grade D or acute hepatitis ($P < 0.001$). Aspartate aminotransferase (AST) levels were higher compared to the levels of alanine aminotransferase (ALT) (mean: 390.7 U/l and 296.9 U/l, respectively). Liver damage with alteration of aminotransferases is a common complication of dengue infection and valuable marker for monitoring these patients.^[17] Muhammad et al determine the frequency, severity and predictors of AKI in patients with DVI and to study the impact of AKI on the length of hospital stay and mortality. They retrospectively reviewed medical records of patients aged ≥ 14 years hospitalized with a primary diagnosis of DVI at Aga Khan University Hospital Karachi between January 2008 and December 2010. Binary logistic regression models were constructed to identify factors associated with the development of AKI and to study the impact of AKI on hospital stays of more than 3 days. Out of 532 patients, AKI was present in 13.3% (71/532). Approximately two-thirds (64.8%) of these patients had mild AKI and a third (35.2%) had moderate to

severe AKI. Independent predictors for AKI were male gender [odds ratio (OD) 4.43; 95% CI 1.92–10.23], presence of dengue hemorrhagic and dengue shock syndrome (DSS, OD 2.14; 95% CI 1.06–4.32), neurological involvement (OD 12.08; 95% CI 2.82–51.77) and prolonged activated partial thromboplastin time (aPTT, OD 1.81; 95% CI 1.003–3.26). AKI was associated with a length of stay ≥ 3 days when compared with those who did not have AKI (OD 2.98; 95% CI 1.66–5.34). Eight patients (11.3%) with AKI died whereas there were no mortalities in patients without AKI ($P < 0.001$). Only 5 patients (7%) had persistent kidney dysfunction at discharge. AKI in DVI is associated with neurological involvement, prolongation of aPTT, greater length of hospital stay and increased mortality.^[18]

CONCLUSION

From the above results, the authors concluded that hepatic and renal involvement occurs in patients suffering from dengue fever. Hence, multidisciplinary approach should be carried out while treating such patients.

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