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Original Research Article.

A Study of Serum Electrolytes, Urea, Creatinine and Aspartate & Alanine Transaminases in Dengue Patients

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ABSTRACT

Background: In India dengue has become a growing public health problem. There have been observations of several clinical complications in the dengue patients. Electrolyte imbalance, kidney and liver involvement in dengue were reported in literature.

Objectives: To study serum electrolytes, blood urea, serum creatinine, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in control and dengue patients.

Materials and Methods: Total of 94 subjects including male 26, female 16 controls and male 34, female 18 dengue positive cases were included for the study. Fasting blood samples were collected and analyzed for blood urea, serum creatinine, Na, K, Cl, AST and ALT by semi-auto analyzer using commercial kits. Values were reported as mean ± standard deviation. The data were analyzed by student t-test and p value of < 0.05 was taken as statistically significant at 95% confidence interval.

Results: Blood urea, AST and ALT were significantly increased in both male and female dengue patients when compared to controls. Na and K were significantly decreased in both male and female dengue patients when compared to respective control groups. There was no change observed on serum creatinine and Cl concentration in dengue patients compared to respective controls.

Conclusions: The observed increased blood urea and transaminases indicates the involvement of kidney and liver respectively in dengue infection. Decreased Na and K in dengue patients indicates the importance of maintaining the electrolytes in dengue patient management.

Keywords: Dengue, Urea, Creatinine, Electrolytes, Transaminases.

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INTRODUCTION

Dengue is now endemic in over 125 countries.[1,2] According to the World Health Organization (WHO) estimates, 50 million dengue infections are recorded annually, and more than 2.5 billion people who are living in endemic areas are at risk of dengue infection.[3] Southeast Asia accounts for more than 75% of the global burden of the disease.[3,4] Dengue viruses are spread to people through the bite of an infected Aedes species (Ae. aegypti or Ae. albopictus) mosquito. Dengue is caused by one of any of four related viruses: Dengue virus 1, 2, 3, and 4. Hence there is a possibility that a person can be infected with a dengue virus as many as four times in his or her lifetime.

Dyselectrolytemia is more common in dengue fever. Dengue viral infection has been shown to be associated with electrolyte abnormalities.[5] Hyponatremia and hypokalemia are the commonest electrolyte disturbances seen in dengue fever.[6] Sodium is an essential nutrient in humans; regulates blood volume, blood pressure, osmotic equilibrium and pH. Hyponatremia is frequent in dengue, which can cause central nervous system dysfunctions. Hyponatremia could occur as a consequence of salt depletion, excess water from increased metabolism, transient inappropriate antidiuretic hormone or the influx of sodium in the cells as a result of dysfunction of sodium potassium pump.

Dengue infection also leads to mild hypokalemia due to poor intake and an increase in renal excretion due to activation of renin angiotensin and aldosterone system secondary to volume

depletion. Hypokalaemia can lead to acute neuromuscular weakness including respiratory muscle paralysis. As the occurrence of dyselectrolytemia in patients of dengue is common, it is necessary to treat the electrolyte disturbances accordingly. Serum chloride changes have also been observed in a few dengue patients.

Dengue is a major international health concern that is prevalent in tropical and subtropical countries. This disease has been found to have profound effect on multiple organ systems, the commonest being the liver. Study of dengue infection and its Liver complications are scarce from countries like India. Liver involvement in acute dengue infection has been observed frequently and sometimes leads to acute liver failure.[7,8] Many factors are thought to contribute to liver dysfunction, including hypoxic injury due to decreased perfusion, direct damage by the virus and immune mediated injury. Hepatic involvement can prolong the clinical course of this self-limiting disease and can be a major predictor of morbidity and mortality of patients with dengue fever. So, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) can be useful early markers to assess the severity of the disease which can thus lead to early recognition of high-risk cases.

Kidney involvement in dengue is not that rare.[2,9,10] The prevalence of proteinuria and hematuria has been reported in high percentage of Dengue virus infection. A correct diagnosis can be made depending on basic investigations of kidney function such as urinalysis, blood urea, serum creatinine and electrolytes. Dengue virus infection related renal involvement should be taken care of, to make an early diagnosis to prevent Acute Kidney Infection (AKI) and its complications, and if AKI does occur, dialysis may be required.

The objective was to study serum electrolytes, blood urea, serum creatinine, AST and ALT in control and dengue patients

MATERIALS AND METHODS

Samples

This study was conducted in a teaching and a private hospital from September 2018 to February 2019 for a period of 6 months. A total of 34 male and 18 female patients admitted with fever and tested positive for dengue by rapid qualitative solid phase immune-chromatographic test for the qualitative detection of dengue NS1 antigen and differential detection of IgG and IgM antibodies to dengue virus.[11] Another 26 male and 16 females were included as control groups who did not have any fever and were otherwise healthy individuals. Patient's demographic details and clinical history were noted.

Exclusion Criterion

Patients with pre-existing renal and hepatic dysfunction were excluded.

Sample Collection

Blood sample was collected from the subjects at the time of admission. About 5 ml of venous blood was drawn under aseptic precaution in a sterile plain vacutainer from selected subjects. As soon as the sample is collected, serum is separated, and estimations were done on the same day.

Assay Method

Sodium, potassium and chloride[12-14], serum creatinine[15], blood urea[16], AST and ALT[17] were estimated using Erba-chem-5 plus2 semi-automated analyzer. The quality control was checked using control sera of two levels.

Results were reported as mean ± standard deviation (SD). The data were analyzed by student t-test and p value of < 0.05 was taken as statistically significant at 95% confidence interval.

Ethical Considerations: Sample was collected after taking written/oral consent from the subjects. This project has been approved by the Ethical committee of Shadan Institute of Medical Sciences.

Table 1: Gender and age of control subjects and Dengue patients

Study groups	No of Subjects	Age range (Mean ± SD)
Male Control	26	20 – 52
Male Dengue patients	34	9 - 72
Female Control	16	18 - 45
Female Dengue patients	18	15 - 68
Total number of subjects	94	9– 72*

*Minimum and Maximum years of age

Table 2: The concentration of Blood Urea, Serum creatinine, Na, K, Cl, AST and ALT in Control and Dengue patients

	Male		Female	
	Control	Dengue patients	Control	Dengue patients
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Urea (mg/dl)	25.2 ± 3.9	29.9 ± 8.9*	24.8 ± 4.9	30.6 ± 7.3*
Creatinine (mg/dl)	1.03 ± 0.17	1.13 ± 0.37	0.98 ± 0.18	1.06 ± 0.28
Na (mmol/l)	138.9 ± 4.2	134.5 ± 3.6**	140.3 ± 4.2	133.8 ± 4.1**
K (mmol/l)	4.16 ± 0.29	3.92 ± 0.42**	4.38 ± 0.30	3.87 ± 0.29**
Cl (mmol/l)	100.4 ± 2.8	99.9 ± 6.1	101.4 ± 2.7	99.7 ± 2.8
AST (u/l)	30.8 ± 9.3	99.6 ± 55.4**	28.2 ± 7.1	85.8 ± 36.2**
ALT (u/l)	28.4 ± 8.9	64.9 ± 36.5**	26.9 ± 6.3	57.1 ± 40.7**

Statistical analysis done by student T-test

Values are Mean ± SD;

*= $p< 0.05$ and **= $p<0.001$ compared to corresponding control group

RESULTS

Table 1 gives the number and age of subjects in study groups. Male Dengue patients' group was with 34 number of subjects having 9-72 years of age and control male group was with 26 number of subjects having 20 -52 years of age. Female Dengue patients' group was with 18 number of subjects having 15-68 years of age and control female group was with 16 number of subjects having 18 - 45 years of age. Overall, the subjects were from 9 to 72 years of age.

The concentration of Blood Urea, Serum creatinine, Na, K, AST and ALT in control and dengue patients were shown in Table 2. Blood Urea, SGOT and SGPT levels clearly showed an increase in male and female dengue patients when compared to corresponding control groups. Na and K levels clearly showed a decrease in male and female dengue patients when compared to corresponding control groups. Serum creatinine and chloride were statistically not significant in male and female dengue patients when compared to corresponding control groups.

DISCUSSION

In India dengue has become a growing public health problem. There have been observations of several clinical complications in the dengue patients. The present study was done to study the effects of dengue virus on the kidney and liver function, along with serum electrolytes. In our present study, all the biochemical investigations of dengue patients were analysed on the day of admission.

Hyponatemia and Hypokalemia are the commonest electrolyte disturbances seen in dengue fever. The mean value of serum sodium observed in male and female controls was 138.4 mmol/L and 140.3mmol/L respectively. The mean values of serum potassium in male and female were 4.16 mmol /L and 4.38mmol/L respectively. There was positive and significant correlation between difference in serum sodium and potassium levels of dengue patients compared to controls. A significant decrease has been observed in serum sodium and potassium in all the male and female patients suffering from dengue compared to controls. Similar results were reported by some authors in their studies.[18-20]

This study did not observe any significant changes in serum chloride values. There were some studies which reported a change in serum chloride levels[21,22], but contrary to such results we did not find any significant changes in both male and female dengue patients. Dyselectrolytemia is more common in dengue fever. Serum electrolytes testing early is very important in dengue patients during management so that if any abnormalities are found, they can be appropriately managed as some of these abnormalities may lead to increased severity as well as mortality.

Several mechanisms have been postulated for the pathogenesis of dengue-associated kidney infection, including direct action by the virus, haemodynamic instability, rhabdomyolysis, haemolysis, and acute glomerular injury.[23] Renal involvements related to dengue virus infection have a variety of presentations, including proteinuria, glomerulonephritis, and severe acute kidney injury (AKI).[24]

AKI is a significant, albeit poorly studied, complication of dengue virus infection. The incidence of AKI in dengue virus infection has shown great discrepancy, with previous studies reporting a range from 0.83–14.40%. The prevalence of AKI of 4.8% was reported by Ajib et al.[25]

This study intended to study the effects on the kidney function, for which the levels of urea and creatinine were analysed in dengue patients. Serum creatinine levels were not very different in dengue patients compared to controls, whereas urea levels were significantly high in dengue infected patients of both males and females. This is an indication that dengue virus does effect the glomerular function, leading to acute kidney disorder.

There are few studies regarding effects of dengue virus on the liver functions. The effect of dengue virus on liver usually could be asymptomatic but can be atypical and have varied severity. Studies done in mouse models have proposed that dengue associated liver injury can be both viral induced or immune mediated. The dengue virus has been shown to readily infect hepatocytes in mouse models, and HepG2 and Huh7 hepatoma cell lines.[26-28]

As part of liver function test both AST and ALT were assayed. AST and ALT are considered as indicators of liver function as they are released into the circulation following liver cell injury.[29] Although ALT is also found in low concentrations in skeletal muscle, brain and intestinal tissue, it is predominantly considered to be a liver specific enzyme. In contrast, AST has various sources including the heart, striated muscle, erythrocytes, etc., apart from the liver, whilst ALT is hepatic in origin.

The present study observed significant increase of AST and ALT in both males and females. Similar results are observed in a few studies.[30,31] A very important observation in our study and others[30,31] was that the increase in AST was much higher compared to ALT. Therefore, rise in AST might not be a true reflection of hepatic involvement. Thus, the results observed probably suggest that sources apart from the liver could also be contributing to the rise in serum aspartate amino transferase. A few more studies are required for relating the increased AST with dengue virus. The study was concluded that the observed increased blood urea and transaminases indicates the involvement of kidney and liver respectively in dengue infection. Decreased Na and K in dengue patients indicates the importance of maintaining the electrolytes in dengue patient management.

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