Research Article

Biochemical Profile Alterations in Dengue Patients

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ABSTRACT

Dengue is an important febrile disease with wide spectrum of manifestations seen mainly in tropical countries .This study was designed to evaluate the alterations in biochemical parameters in blood of freshly diagnosed dengue patients. Routine liver and renal function markers were estimated in100 sero positive dengue patients and 50 age and sex matched normal subjects by spectrophotometric methods. Serum ferritin was evaluated as a marker of acute phase reaction to viral infection by ECLIA. Dengue patients showed hypoalbuminemia, hyper bilirubinemia with significant increase in transaminases compared to normal healthy individuals. Increase in AST was double that of ALT. Further, elevation in AST/ALT ratio was more significant than individual enzymes in these patients. Furthermore, mild metabolic acidosis was observed in dengue patients with statistically significant decrease in serum bicarbonate level. Hyperferritinemia (p= 0.001) was an outstanding feature of dengue patients. Serum ferritin positively correlated with ALT(r=0.328, p=0.03) and negatively correlated with albumin(r=-0.463. p=0.33). Serum IgM showed significant positive correlation with ferritin (r=0.299, p=0.041) and bilirubin (r=0.247, p=0.042). The results confirm the fact that liver damage is the most common complication in dengue patients with no significant effect on kidneys or pancreas as serum creatinine and amylase remained normal. Since hepatic involvement is evident from the early stages of the disease, care must be taken regarding the use of drugs which may worsen the liver damage in the treatment of dengue.

Keywords: Dengue, hyperferritinemia, liver biochemical tests, amylase, creatinine

INTRODUCTION

Dengue is an acute febrile disease with clinical features varying from mild to severe to lethal when presented as classic form to dengue hemorrhagic fever to dengue shock syndrome respectively .[1] Dengue virus is a flavi virus with four distinct serotypes primarily transmitted by Aaedesaegypti mosquito found in tropical and subtropical countries. Dengue pathology is not completely understood as it is multifactorial with acute viral injury, dysregulated immune system to hypoxic insult.[2]

Clinically hepatic involvement is demonstrated by hepatomegaly and the effects on liver can be asymptomatic, atypical and may have varied severity from mild elevation in transaminases to hepatic failure. Literature survey indicates conflicting data on various hepatic markers. Interestingly, dengue has also been implicated in worsening chronic liver disease.[3] Atypical manifestations may include cardiac myopathies and encephalitis. Hence, the present study attempts to establish the effect of dengue infection on organs like liver, pancreas and kidney.

Further, to study the acute viral injury, serum acute phase protein ferritin has also been investigated. In view of a wide range of symptoms the diagnosis of dengue should be based on both clinical and laboratory findings. Complementary lab data may help in evaluating the severity of the disease.

MATERIALS AND METHODS

Blood samples were collected from 100 freshly diagnosed serologically positive dengue patients with the age group ranging from 15-65 years,48-96 hours after the onset of fever. The data obtained was compared with that of 50 age and sex matched normal individuals. Patients with renal diseases, hepatic diseases and alcoholics were excluded from the study. Serological test for IgM was done using immune enzymatic assay IgM - Dengue-Pan Bio in accordance with the manufacturers instruction. Serum liver and renal biochemical tests were done spectrophotometrically.[4,5] Ferritin was estimated by ECLIA based on sandwich principle, amylase was determined by using ethylidene –pNP-G7 as substrate and bicarbonate by PEPCK method in Cobas 6000.Data was analyzed statistically by student t test using IBM SPSS version 20 software. Correlation analysis was done by Pearsons or Spearmans test for normal and skewed distributions respectively. $p<0.05$ was considered statistically significant.

RESULTS

Hepatic involvement in dengue was evident from the results of the present study where, total proteins and albumin decreased significantly compared to normal individuals ($p<0.001$). Total bilirubin and direct bilirubin increased significantly in dengue patients. Increase in hepatic markers ALP, AST and ALT was also statistically significant compared to controls. Further, the degree of

increase in significance of the ratio AST/ALT was more than the individual enzymes (p=0.001) (Table 1). When compared to controls, ferritin showed marked elevation and bicarbonate decreased significantly in dengue patients. However, serum renal function markers creatinine, urea and uric acid levels did not alter in dengue patients. Further, serum amylase also remained normal in these patients (Table 2).

There was a significant positive correlation between ferritin and enzymes, ALT(r=0.328 p=0.03) and ALP(r=0.445 p=0.007) (Table3).A significant negative correlation was observed between ferritin and albumin. Further, hyper ferritinemia strongly correlated with IgM (r=0.322 p=0.033). Furthermore, IgM showed significant positive correlation with total bilirubin(r= 0.247 p=0.042)(Table 4). However, other parameters studied did not show any significant correlation either with IgM or ferritin.

Table 1: Comparison of markers of liver function in patients with dengue and controls

Parameters	Dengue (n=100)	Controls (n=50)	p value
Total protein (g/dL)	6.53±0.73	7.46±0.33	<0.001
Albumin (g/dL)	3.75±0.49	4.46±0.21	<0.001
Globulin (g/dL)	2.79±0.51	3.00±0.37	0.006
Total Bilirubin (mg/dL)	1.41±3.39	0.49±0.15	0.026
Direct Bilirubin (mg/dL)	0.92±2.73	0.17±0.05	0.034
AST (IU/L)	805.81±2326.05	41.41±10.85	0.006
ALT (IU/L)	349.88±896.37	28.5±21.90	0.003
ALP (IU/L)	104.67±70.26	68.00±15.00	<0.001
AST/ALT	1.98±0.93	0.74±0.36	<0.001
Ferritin(ng/mL)	5045.05±4706.36	87.13±46.51	0.001

n= sample size

Table 2: Comparison of markers of renal function and amylase in normal and dengue patients

Parameters	Dengue (n=100)	Controls (n=50)	p
Creatinine(mg/dL)	0.97±0.78	0.86±0.17	NS
Urea (mg/dL)	28.14 ± 9.99	25.54±8.91	NS
Uric acid (mg/dL)	5 ± 0.13	4.66±0.15	NS
BUN	13.07 4.9	11.83 4.2	NS
Amylase(IU/L)	72 ± 9.89	89 ± 11.63	NS
Bicarbonate(mEq/L)	18.97 2.9	23.6 1.5	0.05

NS – Not significant

Table 3: Correlation of FERRITIN with liver function markers

Parameters	r value	p value
ALT	0.328	0.03
ALP	0.445	0.007
ALBUMIN	-0.463	0.033

Table 4: Correlation of Ig M with ferritin and total bilirubin

	r value	p value
FERRITIN	0.299	0.041
TOTAL BILIRUBIN	0.247	0.042

DISCUSSION

Dengue is an important febrile disease in India that may show asymptomatic hepatic involvement. The results of the present study showed a considerable decline in the synthetic function of liver as indicated by significant decrease in serum total protein and albumin. In one of the earlier studies, clinical jaundice was reported in less than 17% of the patients but hyper bilirubinemia in 48%.[6]Our study also justifies these findings as the dengue patients had only subclinical jaundice. The marginal increase in total bilirubin and conjugated bilirubin supported the fact that there was no significant cholestasis [7]although mild impairment in bilirubilin metabolism was seen. However, Significant increase in ALP observed in our study was similar to one of the previous studies which showed mild elevation in ALP throughout the illness.[8] In majority of the studies, elevation of AST was more than ALT[2]as seen in the present study, where AST values doubled that of ALT. The possible explanation for this increase could be the fact that AST can originate from multiple sites like heart, skeletal muscle, RBC, WBC, brain.[9]However, increase in transaminases did not vary with the severity of dengue.[10] In the present study AST/ALT ratio was significantly higher in dengue patients compared to normal. Linda et al[11] opined that this ratio was a better indicator to differentiate severe dengue from non severe dengue and from hepatitis.[12]Decline in serum bicarbonate level in dengue patients indicated metabolic acidosis following viral infection. Positive correlation between ferritin and IgM observed in the present study underlines the fact that viral replication in monocytes and macrophages can activate production of ferritin which correlates positively with the viral load.[13]However, it is likely that hepatocytes are also activated by proinflammatory cytokines to produce high amounts of ferritin, an acute phase protein leading to immune activation in dengue.[14] In vitro studies have shown that ferritin can block the release of bradykinin a potent vasoactive agent suggesting that hyperferritinemia in dengue is an effort to protect the host.[15] The present study highlights the fact that involvement of other organs like kidney or the pancreas is minimal in dengue as renal markers and serum amylase remained normal in freshly diagnosed cases. However, in

severe forms of dengue hepatic failure can lead to severe complications like encephalopathy, renal failure and bleeding.[16]

On the whole, it can be concluded that hepatic dysfunction is one of the major complications and hyperferritinemia is the characteristic biochemical alteration associated with dengue. Hence, liver biochemical tests along with ferritin may be included in the panel of tests for dengue. Since hepatic involvement is evident from the early stages of the disease, care must also be taken regarding the use of drugs which may aggravate the liver damage.

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