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Hepatic Dysfunction in Patients With Dengue Virus Infection

Medical Science

KEYWORDS : dengue infection, aminotransferase levels.

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ABSTRACT

Background- *Hepatic dysfunction in dengue infection is very common . The aim of the current study was to evaluate liver involvement in patients with dengue infection.*

Methods – *Retrospective analysis of adult patients admitted with dengue infection was conducted. Patients were grouped into 4 categories base on serum alanine and aspartate aminotransferase levels.(ALT and AST)*

Results- *Total 155 patients were included in the study. Average serum total bilirubin was 0.81 mg% . Average serum alkaline phosphotase was 85.7 U(n-71). 104(67.1%) patients had raised AST while 93 (60%) had raised ALT .Abnormal ultrasonography abdomen findings were seen 78.5% (n-65) patients.*

Conclusion- *Liver injury in the form of rise in aminotransferase levels is common in dengue infection. Hence estimation of liver enzymes is important in all patients of dengue fever.*

Introduction-

Dengue is a major public health problem in India and outbreaks are very common in monsoon months. In addition to the classical features of dengue infection like fever, myalgia, joint pain, rash, thrombocytopenia etc, hepatic dysfunction is common but usually mild and self limiting. There are isolated case reports of fulminent hepatic failure in dengue infection. Pre-existing liver disease, use of hepato toxic drugs, concomitant hepatitis virus infection are some of the contributing factors for hepatic dysfunction in dengue infection. (1) Histopathology findings in the liver in dengue include, microvesicular steatosis, hepatocellular necrosis, Kupffer cell hyperplasia, Councilman bodies and monocyte infiltration of portal tract (1,2). The aim of the current study was to evaluate liver involvement in patients admitted with dengue infection.

Materials and methods-

Retrospective analysis of all adult patients (age more than 18 years) admitted in medicine wards of Smt. Kashibai Navale Medical College and General Hospital, Pune , Mararashtra with dengue fever from January 2014 to December 2014 ,was done. Patients with positive tests for anti dengue IgM antibody and /or positive NS1 (non structural protein 1) antigen were diagnosed to have dengue infection. We included patients with dengue fever in whom liver function tests were done ,for our study. Patients with malaria, enteric fever and viral hepatitis co infection were excluded. Patients' clinical record data was used to analyse demographic profile, bleeding manifestations, complete blood count and liver function tests. Patients were grouped into 4 categories based on serum alanine and aspartate aminotransferase levels(ALT and AST) The reference value for ALT and AST was 40 IU/L. Patients with normal AST and ALT levels were grouped as A .Those with elevation of at least one of the transaminase level but less than 5 times upper limit of normal (ULN) were grouped as B. Those with elevation of either of the aminotransferase level 5-10 times ULN were grouped as C and those with elevation of either of the aminotransferase level more than 10 times ULN were grouped as D.

Results –

Total 155 patients were included in this study, with females 54 (34.8 %) and males 101(65.2 %).Age range was from 18 to 65 years with mean age 31 years. Average duration of stay was 6.4days. Bleeding manifestations were found in 21 patients (13.5 %). These patients had either mucosal or gastrointestinal bleeding. No death due to the disease occurred.

Of 155, 64(41.3 %) patients had leucopenia(Total leucocyte count<4000/cmm) and 128 (82.6 %)patients had thrombocytopenia(platelet count <1,00,000/cmm). Average serum total bilirubin was 0.81 mg% and 8 (5.1%) patients had total bilirubin more than 2 mg %. Serum alkaline phosphotase was done in 71 patients and average value was 85.7. 104(67.1%) patients had raised AST while 93 (60%) had raised ALT .

47 (30.3%) patients had normal liver function tests(group A) while 108 (69.7%) had raised aminotransferase levels .92(59.3%) patients were in group B , 10 (6.45%) in group Cand 6(3.8%) in group D. (Table 1). Duration of stay ,incidence of bleeding manifestations and leucopenia were almost similar in all groups while thrombocytopenia was seen in all patients of group C and D. (Table 1)

Ultrasonography(USG) of the abdomen was done in 65 patients, of which 51(78.5%) patients had abnormal findings. Splenomegaly and gall bladder wall edema was reported in 18 patients each (27.7 %). 17(26.1 %) patients had evidence of free fluid in the abdomen. While 14(21.5 %) and 13 (20%) patients had hepatomegaly and pleural effusion on USG, respectively. Abnormal ultrasonographic findings were noted more commonly in group C and D patients. Ascitis in all patients was mild.

Discussion-

Dengue is a common arthropod –borne viral disease. And risk of dengue fever has been increased due to rapid urbanisation and poor water management. There is lack of awareness in the general population about breeding of mosquitoes and protection from their bite.

Deranged liver function test in dengue infection is mainly attributed to direct attack of virus on hepatic cells and upregulation of host immune response.(3). Our study supports the alteration in transaminase levels in dengue fever. 67% had raised AST and 60 % had raised ALT levels in our study. But most of the other studies reported higher percentage of study population, more than 90% with abnormal AST and ALT levels.(3, 4,5) .However we report higher percentage of abnormal AST than ALT, which is

consistent with other studies. Upregulated host immune response and virulent nature of the dengue virus play a major role in determining the severity of the dengue infection. (1). Majority of the patients in our study population had mild elevation of liver enzymes and no one had fulminent hepatic failure. Souza LJ et al stated that liver damage is a common complication of dengue infection and aminotransferase levels are a valuable marker for monitoring these cases.(6)

Cause of bleeding manifestations in dengue fever is multifactorial like, thrombocytopenia, coagulopathy and hepatic dysfunction. We have found that bleeding manifestations were comparable in all groups in our study. Om Prakash et al showed the association of various complications of dengue like bleeding, encephalopathy and renal failure associated with deranged liver function tests (5).Similar finding is also supported by Khan et al(7). Kuo et al reported association of bleeding episodes with high levels of ALT, AST and GGT (gamma glutamyl transferase). Probably due to small sample size, we couldn't get the significant association.

In our study, thrombocytopenia was seen in all patients with AST and or ALT levels more than 5 times ULN and serum bilirubin and alkaline phosphotase values were higher in patients with severely deranged aminotransferase levels than in other groups.

Ultrasound findings in early , mild cases of dengue include gall bladder wall edema, minimal free fluid in the abdomen, hepato-splenomegaly and pleural effusion. While in severe forms, in addition to these findings, ultrasound may reveal hepatic and splenic subcapsular fluid , pericardial effusion, pancreatic involvement.(8,9) . In our study, we found that USG abnormalities are more common in patients with severe hepatic dysfunction, more over features like hepatomegaly, free fluid in the abdomen and pleural effusion are more common. Santhosh et al states that USG abdomen is helpful in the diagnosis of dengue fever and it also helps in estimating the severity of the disease.

Due to small sample size and relatively short duration of study period, exact correlation between serum aminotransferase levels and severity of dengue could not be ascertained.

In conclusion liver involvement in the form of mild rise in aminotransferase level is common in dengue infection. Hence estimation of liver enzymes is important in all patients of dengue fever. Avoidance of hepato-toxic drugs in such patients will help to prevent further liver damage and assist in early recovery.

Table-1 Profile of patients in four groups, based on serum aminotransferase levels.

	A (n-47)30.3%	B (n-92) 59.4%	C (n-10) 6.5%	D(n-6) 3.8%
Female	18 (38.3%)	31(33.7%)	4(40%)	1(16.7%)
Male	29(61.7%)	61(66.3%)	6(60%)	5(83.3%)
Age in years	18-62	18-65	18-65	22-43
Duration of stay in days (avg)	6.19	6.5	6.5	6.8
bleeding manifestations	5(10.3%)	15(16.3%)	1(10%)	1(16.7%)
Leucopenia	19(40.4%)	39(42.4%)	4(40%)	2(33.3%)
Thrombocytopenia	36(76.6%)	76(82.^%)	10(100%)	6(100%)
SrTotal Bilirubin (Avg)	0.9	0.78	0.4	1.1
Sr Alk.PO4 (Avg)	97.35(n-14)	82.19(n-46)	69.5 (n-6)	104.6(n-5)
USG abdomen findings	n-14	n-41	n-5	n-5
Hepatomegaly	2(14.3%)	8(19.5%)	1(20%)	3(60%)
Splenomegaly	3(21.4%)	12(29.3%)	2(40%)	1(20%)
free fluid in the abdomen	5(35.7%)	8(19.5%)	2(40%)	2(40%)
Gall bladder wall edema	2(14.3%)	13(31.7%)	2(40%)	1(20%)
Pleural effusion	1(7.1%)	8(19.5%)	2(40%)	2(40%)
Normal USG	3(21.4%)	10(24.4%)	1(20%)	0(0%)

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