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Original Research Article

Hepatic Enzymes Derangement in Dengue Viral Infection

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Abstract

Background: *Hepatic enzymes derangement is common in Dengue viral infection. The degree of derangement may be from mild rise in serum Aminotransferase level to acute fulminant hepatitis. The degree of derangement is evaluated by measuring the serum Aminotransferase and serum bilirubin level in dengue patients. The hepatic enzyme derangement can be categorised on the basis of serum Aminotransferase and bilirubin level.*

Objective: *The objective of this study is to evaluate the effect of Dengue virus infection on hepatic enzymes. This effect is studied by measuring the Aminotransferase and bilirubin level.*

Material and Methods: *This study was conducted for a period of two years at the department of Microbiology, Nalanda Medical College, Patna, Bihar. The degree of hepatic dysfunction is categorised into category A- in which there is normal or near normal serum Aminotransferase and bilirubin level; category B- in which the rise in Aminotransferase level is up to five times of normal value but normal serum bilirubin level; category C- the rise in serum Aminotransferase level is greater than five times but less than ten times of normal value with or without rise in serum bilirubin level; category D- patient with acute hepatitis and rise in serum Aminotransferase level greater than ten times of the normal with or without rise in serum bilirubin level.*

Result: *There are 240 confirmed patients of dengue virus infection. Patients are grouped into Group A, B, C & D depending on the level of serum Aminotransferase. The number of patients belonging to Group A are 144(60.2%), belonging to Group B are 60(24.8%), Group C are 29(12.4%) and Group D are 07(2.6%). Thrombocyte count varies from 11,000 to 170,000. Mean AST level varies from 48.3 to 1900.5 and mean ALT level varies from 45.8 to 1800.6 in Group A to D.*

Discussion and Conclusion: *Hepatic dysfunction is common complication of Dengue infection. Although mild hepatic dysfunction with rise in hepatic enzymes is common in Dengue infection but fulminant hepatitis is rare. The diagnosis of hepatic enzymes derangement can be easily done by AST and ALT measurement.*

Keywords: *Dengue fever, NS1 antigen, IgM antibody, AST, ALT, ALP, Hepatitis, Fulminant, Aminotransferase, Dengue hemorrhagic fever.*

Background

Dengue is a arthropod-born viral disease caused by Dengue virus and transmitted by its vector, Aedes aegypti[1]. It is a major epidemic as well as endemic health problem in South-East Asia[2]. In Asian countries Dengue infection is very common about 50 million of severe Dengue infection occurs every year but case fatality rate is less than 5%[3]. Dengue virus is an Arbovirus which belongs to family flaviviridae and genus flavivirus. There are 4 serotypes of the Dengue viurus DENV1, DENV2, DENV3, and DENV4. All these Dengue serotypes are serologically related but antigenically different from each other. The classical form of Dengue fever is self limiting and usually associated with high fever, joints pain, myalgias, headache, nausea-vomiting, retroorbital pain[4] etc. Atypical form of Dengue infection can also occur which may manifest as Dengue haemorrhagic fever or Dengue shock syndrom. In last few years the incidenc of atypical form of Dengue infection i.e DHF and DSS have increased significantly[5]. Dengue infection is confirmed by ELISA for NS1 (Non structural protein1) Antigen, & MAC ELISA (IgM capture enzyme- linked immunosorbent assay). Then the Dengue infected patients are studied for hepatic dysfunction. Although Dengue virus is not Hepatotropic but hepatic involvement is not so uncommon and it has been described since long time[6]. The degree of hepatic dysfunction varies from mild hepatitis with elevation of hepatic enzymes to acute fulminant hepatic failure. Liver is not the major involved organ in Dengue infection but the pathological findings may include Centrilobular necrosis, kupffer cell hyperplasia, fatty changes, acidophilic bodies, monocytic infilteration of the portal tracts[7]. Although liver involvement shows such pathological changes but major liver functional abnormality is seldom[8]. These changes may take place in association with or without DHF/DSS. The exact cause of hepatic injury whether it is a direct effect of virus load or due to response of host against the viral infection is not clear[9]. The immunoregulatory T lymphocytes are activated more in case of Dengue Haemorrhagic fever than dengue fever Activated T Lymphocytes are supposed to be responsible for severe Thrombocytopenia and capillary leakage in DHF and DSS[10]. Thus these activaed cells may suppose to cause Hepatic dysfunction that is seen in case of DHF and DSS. The Hepatic enzyme AST may be elevated in hepatic as well as other organ involvement such as Heart, Kidney, Pancreas, Skeletal muscle. ALT is mostly found in liver and to some extent in Kidney, Heart, Pancreas and Skeletal muscle but in low concentration. Hence high rise in serum ALT level is diagnostic for Toxic hepatitis, Infective hepatitis, cirrhosis of liver, hepatocellular carcinoma and sever form of Dengue infection. Hepatic involvement is more common in children than adults in Dengue infection[11]. Although fulminant hepatic involvement in adult dengue patients is rare but its early detection and management is worthwhile.

Aims and Objectives

The aim of this study is to determine the extent of hepatic dysfunction in Dengue infection. The extent of hepatic damage is estimated by the estimation of hepatic enzymes as AST (aspartate aminotransferase), and ALT (alanine aminotransferase). The correlation of hepatic dysfunction with severity of Dengue infection and its early management.

Materials and Methods

The present study is conducted in Department of Microbiology, Nalanda Medical College & Hospital, Patna. Blood samples are collected from patients visited to the Microbiology laboratory at Nalanda Medical College, Patna. Total 240 Dengue confirmed patients of different age groups, with clinically suspected hepatic dysfunction are studied prospectively. This study is conducted between June to September 2016. The written informed consent is taken from the guardian of all the patients regarding this study and the Ethical committee of institute have also

given their clearance for the study. Patients who are included in this study are serologically confirmed Dengue patients, and are confirmed by ELISA for NS1 (Non structural protein1) Antigen, & MAC ELISA (IgM capture enzyme- linked immunosorbent assay). Those patients are excluded from this study who have Dengue like symptoms but serologically IgM negative or who are ≤ 14 years of age. Those patients are also excluded who have pre-existing liver diseases such as Viral Hepatitis and other causes of liver involvement such as Malaria, Typhoid, and Alcoholic hepatitis. Those patients are also excluded who are not willing to participate in the study.

First clinically suspected cases of Dengue infection i.e patients with high grade fever, retroorbital pain, arthralgia, myalgia, hemorrhagic manifestation, nausea vomiting are tested for CBC, Dengue IgM capture ELISA, NS1 Antigen. The confirmed Dengue patients are tested for serum bilirubin, Serum alanin transaminase (ALT/SGPT), Serum aspartate transaminase, serum alkaline Phosphatase (AST/SGOT). Total 240 Dengue infected patients are tested for serum AST and ALT. The patients are classified into four groups on the basis of degree of hepatic damage by measuring the level of AST (aspartate aminotransferase) and ALT (alanine aminotransferase). The reference normal level of AST and ALT are 0-40. Those patients with normal or very mild enzymatic dysfunction of AST and ALT level are classified as Group-A, Those patients whom the level of one of the aminotransferase is raised but not greater than 5 times the normal are classified as Group-B, when the value of at least one of the aminotransferase is raised greater than 5 times but less than 10 times the normal value are classified as Group-C. Those patients whom one or both of the Aminotransferase level is raised greater than 10 times of normal value are classified as Group-D. Those patients whom the rise of enzymes level are greater than 5 times of normal are also tested for other causes of hepatitis.

Results

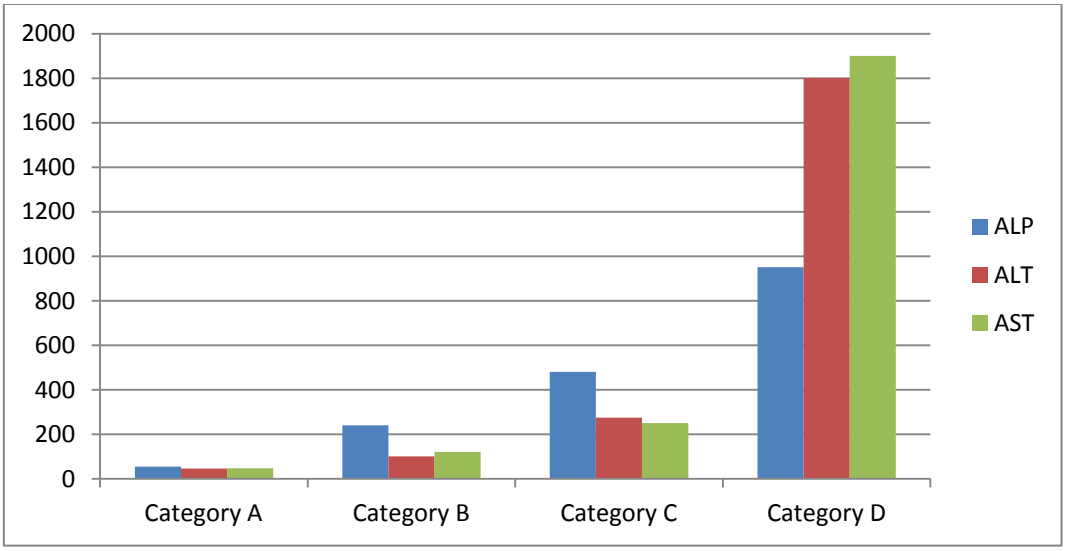
Among total 240 confirmed cases 190(79.1%) were classified as simple Dengue fever, 42 (17.5%) as Dengue haemorrhagic fever (DHF) and 08(03.3%) as Dengue shock syndrome (DSS). of dengue 127(52.91%) patients were male and 113 (47.08%) patients were female. The age group of 15years to 80 years were included in the study in which 168(70%) were between 15years to 50 years and 72(30%) were between 51 year to 80 years. Among total Dengue confirmed patients 184(76.6%) patients were from urban background and 56(23.3%) patients were from rural areas. The clinical features and epidemiological detail have been summarized in Table-1. As serum Aminotransferase level is concerned (144)60.2% patients belong to Group A, (60) 24.8% to Group B, (29) 12.4% to Group C, and (07)2.6% to Group D. As far as clinical features are concerned fever is present in all group of patients 240 (100%), body ache in 06(85.71%), 20(68.96%), 40(66.66%), and 48(33.33%) of group D, C, B and A respectively. Abdominal pain in 6 (85.71%), 21(72.41%), 31(51.66), 60(41.66%) of group D, C, B and A respectively. Nausea /vomiting in 07(57.14%), 25(86.20%), 43(71.66%), 47(32.63%) of group D, C, B and A respectively. Mucosal bleeding in 04(57.14%), 13(44.82%), 08(13.33%), 02(01.38%) of group D, C, B, and A respectively. Hepatomegaly in 06(85.71%), 13(44.82%), 02(3.33%), and nil in group D, C, B, and A respectively. Hepatic encephalopathy in 02(28.57%), 03(10.34%), group D, C, and nil in group B and A. Splenomegaly is present in 03(42.85%) in group D and 04(13.79%) in group C but none in group B and A. Thrombocytopenia is present in most of the patients (90%) with minimum count of 11,000 and maximum count is 1,70,000. Liver function tests are significantly deranged in group C and D. The comparison of laboratory findings i.e level of serum bilirubin, ALT, AST, ALP, serum albumin, globulin, total protein, between these groups have been summarized in Table-2.

Table-1

Associated factors	Category-A Normal Aminotransferase level (n=144)	Category-B Aminotransferase level up to 5 times of normal value (n=60)	Category-C Aminotransferase level > 5 but <10 times of normal value (n=29)	Category-D Aminotransferase level >10 times of normal value (n=07)
Age (years)	40 - 60	20 - 40	50 - 70	(15-30)&(60-80).
Sex (male :female)	88:56	26:34	10:19	03:04
Symptoms				
• Fever (%)	(144) (100%)	(60) (100%)	(29) (100%)	(07) (100%)
• Body ache (%)	48 (33.33%)	40 (66.66%)	(20) 68.96%	(06) 85.71%
• Vomiting (%)	47 (32.63%)	43 (71.66%)	25 (86.20%)	07 (100%)
• Abdominal pain	60 (41.66%)	31 (51.66%)	21 (72.41%)	6(85.71%)
• Rashes (%)	12 (08%)	18 (03%)	21 (72.41%)	07 (100%)
• Bleeding (%)	02 (01.38%)	08 (13.33%)	13 (44.82%)	04 (57.14%)
Clinical features				
• Jaundice (%)	11 (07%)	13 (21%)	19 (65%)	07 (100%)
• Hepatomegaly	Nil	02 (03.33%)	13 (44.82%)	06 (85.71%)
• Ascitis (%)	Nil	01 (01%)	11 (38%)	07 (100%)
• Hepatic encephalopathy	Nil	Nil	03 (10.34%)	02 28.57%)
• Splenomegaly	Nil	Nil	04(13.79)	03(42.85%)

Table-2

Laboratory parameter	Category–A n=144 (%)	Category–B n=60 (%)	Category –C n=29 (%)	Category –D n=07 (%)
Thrombocyte count (x1000/cmm)	1,10,000- 1,70,000	70,000-1,05,000	40,000-85000	11,000-60,000
Serum bilirubin (>2.0 mg/dl)	11 (7.6)	10 (16.6)	15(51.7)	07(100)
Serum albumin (Mean)	3.58±0.52	3.43±0.86	2.85±0.66	1.87±0.56
Serum globulin (Mean)	2.98±0.58	2.76±.48	3.44±0.52	3.56±0.43
Total protein (Mean)	7.4±0.4	6.8±1.2	6.4±0.8	5.6±0.6
Range(IU) ALT/SGPT(raised) mean (Average)	40-50 62.5(90%) 45.8	50-199 60(100%) 100.8	200-399 29(100%) 275.4	400-3000 07(100%) 1800.6
Range(IU) AST/SGOT(elevated) Mean (Average)	38-50 59(85%) 48.3	50-199 60(100%) 120.7	200-399 29(100%) 250.5	400-3000 07(100%) 1900.5
Range Elevated ALP Mean (Average)	40-175 76(52.77) 55.4	110-450 50(83.33) 240.8	145-800 27(93.10) 480.2	175-1550 07(100) 950.5



Comparative bar diagram of hepatic enzymes, ALP, AST and ALT.

Discussion

The present study shows that most of the patients with dengue viral infection have some degree of hepatic involvement. This can be either in the form of Hepatomegaly or hepatic enzymes derangement specially the AST and ALT level. Acute hepatitis in dengue is usually presented with jaundice. The fulminant hepatic failure or sever hepatic impairment is present in complicated form of dengue infection and it is associated with increased mortality. Mild increase in serum AST and ALT level is found in 90% and 85% respectively in Category A patients. Although in Category B, C and D there are 100% rise in serum AST and ALT level. Similar reports have been found in different studies, Souza L.J, *et al*[12]. in 2007. Hepatomegaly is found in 85.71%, 44.82%, 3.33%, and nil in group D, C, B, and A respectively. Similar reports have been published by Fadilah *et al*[13]. in 2000. It shows that the severity of Dengue infection is directly related with Hepatomegaly and hepatic enzyme derangement. Similarly the serum globulin level , platelet count are significantly reduced with severity of Dengue infection but the rise in serum Albumin, Alkaline phosphatise, Bilirubin and prothrombin level are not related with severity of disease. Similar reports have been published by Kuo C.H. *et al.* in 1992. Bleeding manifestation in the form of rashes were common in Group C and D but mucosal or other major bleeding was not so common Burke T *et al.*[14].

Conclusion

Dengue is usually associated with mild to moderate rise in Aminotransferase level, fulminant hepatic failure or acute hepatitis is less common. In the present study the hepatic damage is more common in female than male. Among 240 cases only 07 cases were suffering from acute hepatitis or fulminant hepatic failure. The extremes of ages are more prone for severe hepatitis. Acute hepatitis is more common in patients with DHF and DSS. The rise of serum Aminotransferase level may vary from normal to more than 10 fold of normal value. Therefore to evaluate the extent of hepatic damage the evaluation of Aminotransferase level is of great importance.

References

1. Halstead SB., Dengue. Curr Opin Infect Dis. 2002; 15:471-476.
2. WHO, Dengue; Guidelines for the Diagnosis, Treatment, Prevention and control. Geneva: WHO; 2009.
3. Lanciotti, R.S., D.J. Gubler, and D.W. Trent, *Molecular evolution and phylogeny of dengue-4 viruses.* Journal of General Virology, 1997.78(9): p. 2279-2284.
4. WHO; Dengue guidelines for diagnosis, treatment and prevention Geneva; WHO publishers; 2009; page 4-6.
5. Seneviratne SL, Malavige GN, deSilva HJ. Pathogenesis of hepatic involvement during DENV infections. Trans R Soc Trop Med Hyg. 2006; 100:608-14.
6. George R. D.H.F in Malaysia:a review. South-East Asian J Trop Med Public Health 1987; 18:278-283.
7. Burke T. DHF: pathological study. Trans R Sac Tropical Medicine Hyg. 1968; 62(5); 682-692.
8. lum LC, Georege R, Devi S. Acute Fulminant hepatitis in Dengue infection. Southesat Asian Journal Tropical Medicine Public Health.1993; 24(3): 467-71.
9. Bhamarapravati N. Toochinda P, Boonyapaknavik V. Pathology of Thailand hemorrhagic fever; A study of 100 autopsy cases, Ann Tropical Medicine Parasiol 1967; 61:500-510.
10. Kurane I, Nimmannitya S, Innis BL. Activation of T Lymphocytes in dengue virus infection. J Clin Invest 1991;88;1473-1480.
11. Anand VK, Patwri AK, Mohan B. Liver Dysfunction in childhood Dengue infection. J Tropical Paediatrics. 2000; 46:40-3.

12. Souza L.J. , Ribeiro Nogueira R M *et al.* the impact of Dengue on Liver Function as Evaluated by Aminotransferase Levels, BJID 2007;11(4):407-410.
13. Fadilah S, Abdul Wahid S, et al. A comparison of the pattern of liver involvement in Dengue Hemorrhagic fever with classic Dengue fever, Southeast Asian j Trop Med Public Health 2000; vol. 31(2):259-263.
14. Burke T. dengue haemorrhagic fever; a pathological study. Trans R Soc Trop Med Hyg. 2006 Jul; 100(7):608-14.

Abbreviations

DSS, (Dengue shock syndrome)
DHF, (Dengue Haemorrhagic Fever),
ALT (Alanine Aminotransferase),
AST (Aspartate Aminotransferase),
ALP (Alkaline Phosphatase),
ELISA (Enzyme linked Immunosorbent assay),
DENV (Dengue virus).