Original Article

ISSN (0): 2347-3398; ISSN (P): 2277-7253

Liver Dysfunction in Dengue Fever: A Prospective Study

Gautam Chand Jingar[1], Dinesh Parmar[2], A.K. Jain[3], Nishant Kamble[4], Ramesh Jakhar[4], Sudhir[4]

[1]Senior Resident, Department of Medicine, Government Medical College, Barmer, Rajasthan, India, [2]Associate Professor, Department of Medicine, Government Medical College, Barmer, Rajasthan, India, [3]Senior Professor & Unit Head, Department of Medicine, Dr. S. N. Medical College, Jodhpur, Rajasthan, India, [4]Resident, Department of Medicine, Dr. S. N. Medical College, Jodhpur, Rajasthan, India.

Abstract

Background: Dengue has emerged as an important arbovirus disease with significant impact on the disease burden in population residing in tropical countries. The virus seems to have some hepatotoxic effects. The aim of this study to rule out extent of liver dysfunction in Dengue fever. **Subjects and Methods:** A total of ninety six (n=96) serologically confirmed patients who were hospitalised were included in the study. NS1 and IgM anti dengue antibodies using the IgM antibody capture – enzyme linked immunosorbent assay (MAC – ELISA) for diagnosis of dengue fever were done. Detailed clinical examination was performed on admission, blood sample were collected, and all haematological, coagulation profile and biochemical investigations for renal and hepatic function were studied. **Results:** The study group consisted of 96 patients with male to female ratio was 2.3:1 and age ranging from 12 to 75 years (27.68 years). Common clinical features were fever (100%), persistent vomiting (79.17%), rash (33.33%) and bleeding manifestation (10.42%) hypotension was observed in 2 patients (2.63%) without involving particular age group. Our study showed that the leucopenia (WBC <4000/µl) was found in 58.33% of cases followed by platelet count <1000/µl found in 35.41% of cases. Among liver function tests hepatomegaly (non tender) was present in about 58.3% patients and 91% patients had raised transaminase level ,very high >25 times increase was found in 20.8% patients. S. Alkaline Phosphatase was normal in 70% and only 11% patients showed abnormal echotexture on ultrasound. **Conclusion:** The pattern of hepatic involvement of liver in dengue fever varies as per the severity of disease. In milder case of dengue fever liver function test was normal but there was hepatomegaly was present commonly but in severe form of disease pattern of hepatic involvement varies from tender hepatomegaly to significant increase in liver enzyme.

Keywords: Dengue, Liver, Viral Hepatitis, Acute Liver Failure, Transaminases.

Corresponding Author: Dr. Dinesh Parmar, Associate Professor, Department of Medicine, Government Medical College, Barmer, Rajasthan, India.

Received: June 2019
Accepted: July 2019

Introduction

Dengue is the widespread arbovirus infection worldwide. Clinical presentation of dengue virus infection varies widely from no symptoms to dengue shock syndrome, but this infection more commonly causes dengue fever (DF) and dengue haemorrhagic fever (DHF).Dengue or "break bone fever" has gradually evolved as one of the important causes of febrile illness in the tropical and subtropical region. Second only to malaria, dengue is a common mosquito-transmitted disease, and currently, it is the most common cause of arbovirus disease globally. Around 2.5 billion people in 100 endemic countries are believed to be susceptible, so are the equally significant number of travellers to these tropical and subtropical regions.[1,2]

Presenting with a wide range of severity, "severe" dengue (Group C) as categorized by World Health Organization (WHO) in 2009 includes the dengue hemorrhagic fever (DHF) and dengue shock syndrome(DSS).[3] Despite the inadequate surveillance ofcases from the underdeveloped tropical countries, the average number being reported per year has increased drastically.[1,4] A host of factors including the relentless urbanization with poor hygiene, dilapidated health systems to increasing international travel fuel the spread of this disease geographically and increase the disease burden of tropics significantly.[1,2]

This disease has been found to have profound effect on multiple organ systems, the commonest being the liver. Starting from asymptomatic elevated transaminase levels to acute liver failure (ALF), dengue has all the properties of a hepatic illness.[5] The aim of this study to find out extent of liver dysfunction in Dengue fever.

Subjects and Methods

A total of ninety six (n=96) serologically confirmed patients who were hospitalised were included in the study. NS1 and IgM anti dengue antibodies using the IgM antibody capture – enzyme linked immunosorbent assay (MAC – ELISA) for diagnosis of dengue fever were done. Patients were followed-up from the date of admission until recovery or death. Patients with fever with negative serology of dengue infection, malaria, alcoholic liver disease, viral hepatitis, septicemia and patients with any other cause identified for

deranged liver profile were excluded. The criteria for admission were acute febrile illness of 2-7 days duration with positive serology for dengue infection presenting with fever, arthralgia, myalgia, haemorrhagic manifestation like petechiae, purpura, bleeding from GI tract, dehydration, persistent vomiting and thrombocytopenia.

Detailed clinical examination was done at admission, blood sample were collected, and all haematological, coagulation profile and biochemical investigations for renal and hepatic function were done Ultrasound of abdomen was also performed in all cases.

Results

The study group consisted of 96 patients with male to female ratio was 2.3:1 and age ranging from 12 to 75 years (27.68 years). Common clinical features were fever (100%), persistent vomiting (79.17%), rash (33.33%) and bleeding manifestation (10.42%) shock was observed in 2 patients (2.63%) with no specific age prediction during the critical phase, i.e., 2 to 7 days after onset of fever [Table 1]. In bleeding manifestation, epistaxis was more common feature (4.16%) [Table 2].

Our study showed that the WBC <4000/µl were found in 58.33% of cases followed by platelet count <10000/µl occurred in 35.41% of cases [Table 3]. We observed hepatic dysfunction in 88(91.67%) patients out of 96 in form of deranged Transaminases levels. Liver enzymes, i.e., SGOT (AST) increase <3times in 19 (19.79%) patients &>3times in 69 (71.87%) patients out of 96. SGPT (ALT) increase <3times in 32 (33.33%)patients &>3times in 56 (58.33%) patients out of 96. 2 patient out of 96 presented with shock. 32(33.33%) patients out of 96 had >10times(400IU/L) elevated in serum transaminase. Out of which 20 (20.83%) patients had >1000IU/L (>25times) level of serum transaminase (SGOT & SGPT) and 7 (7.29%) patients had >2000IU/L (>50times) level of serum transaminase(SGOT &SGPT) [Table 4]. S. Alkaline Phosphatase was normal in 70% and increased levels are not very high, no patient showed decrease in SAP and only 11% patients showed abnormal echotexture on ultrasound however hepatomegaly was found in 76% patients on ultrasound study.

Table 1: Clinical features of patients with dengue.

Clinical feature	No. of cases	%
Fever	96	100
Vomiting	76	79.17
Retro-orbital pain	18	18.75
Rash	25	26.04
Mucosal/gingival bleeding	8	8.33
GI bleeding	2	2.08
Menorrhagia	3	3.12

Table 2: Bleeding manifestations seen in patients

Bleeding manifestations	Patients	%
Subconjunctivalhemorrhage	1	1.04
Epistaxis	4	4.16
Gingival bleeding	2	2.08
Hemetemesis	1	1.04
Hematuria	1	1.04
Malena	1	1.04
Menorrhagia	3	3.12

Table 3: Hematological profile at admission

Investigation(parameter)	No. of cases	Percentage (%)
Anemia	7	7.29
Hematocrit>50%	2	2.08
WBC <4000/µl	56	58.33
Platelet count >50000/µL	1	1.04
20000 - 50000/µL	32	33.33
10000 – 20000/µL	29	30.20
<10000/µL	34	35.41

Table 4: Comparison of liver function test

Investigation (parameter)	No. of cases	Percentage (%)
Elevated liver transaminase	88	91.66
SGOT (AST) <3times(120IU/L)	19	19.79
>3times(120IU/L)	69	71.87
>25 times(1000IU/L)	20	20.83
S. Alkaline Phosphatase	15	15.62
S. Albumin	18	18.75

Discussion

Clinical evidence of liver involvement in dengue infections includes the presence of hepatomegaly and increased serum liver enzymes. Several studies document raised serum transaminase levels in dengue infection. Transaminase levels are also higher in DF and tend to return to normal 14—21 d after infection. Kuo et al. (1992)6reported abnormal aspartate transaminase (AST) and alanineamino transaminase (ALT) levels in 93.3 and 82.2%, respectively. Nimmannitya (1987)7 found ALT levels elevated in 26%of patients. Wahid et al. (2000)8 found serum AST and ALT levels to be significantly higher in patients with DHF.

Mohan Kashinkunti et al (2013),[9] study shows52 patients out of 100 had complications of which most common were hepatic dysfunction 34%, renal failure 26%, multi organ failure 18%, encephalopathy13% and ARDS in 12%. Deaths reported were 11%.Varying abnormalities in liver enzymes appear to be present in most patients with symptomatic dengue infections, but they tend to recover soon (Pancharoen et al.,2002).[10] There does not appear to be chronic liver damage as with the hepatitis B and C viruses. In a subgroup of predominantly DHF/DSS patients, severe liver dysfunction occurs and is a marker of poor prognosis. During some dengue epidemics, greater degrees of liver damage are seen (Ehrenkranz et al., 1971).[11] Although this may be a consequence of different dengue serotypes having varying tissue trophism, this has not been widely studied.

In dengue infections, our study shows elevations in serum AST appear to be greater than ALT levels. This differs from the pattern inviral hepatitis, this result is matched with study of Gholson et al., 1990,[12] but it is similar to that seen with alcoholic hepatitis. The exact significanceof this pattern seen in dengue is uncertain. It has been suggested that it may be due to excess release of AST from damaged myocytes during dengue infections (Chung et al.,1992),[13] but this has not been formally tested. Simultaneous

measurement of muscle isoforms of lactate dehydrogenase and creatinine kinase may help further clarify this observation. The elevated AST levels tend to return to normal more rapidly than ALT levels. This is possibly because AST (12.5—22 h) has a shorter half-life than ALT (32—43 h)(Hawker, 1991).[14]

Dengue virus antigen is found in Kupfer cells and sinusoidal lining cells in the liver. Isolation of dengue virus type I from the liver was made by Nogueira et al. (1988),[15] in Rio de Janeiro during the 1986 epidemic. Detection of dengue antigen virus in hepatocytes suggests that such cells can support viral replication (Miagostovich et al. 2002).[16] Hepatic manifestations can be characterized by manifestations of acute hepatitis with pain in the hypochondrium, hepatomegaly, jaundice and raised aminotransferase levels. In hepatitis the levels of these enzymes peak on the ninth day after onset of symptoms and gradually return to normal levels within 3 weeks. Histopathological findings include centrilobular necrosis, fatty alterations, hyperplasia of the Kupfer cells, acidophil bodies and monocyte alteration of the portal tracts. In most cases hepatic involvement prolongs the clinical course of this self limiting viral infection but it does not constitute a sign of worse prognosis.

Conclusion

The pattern of hepatic involvement of liver in dengue fever varies as per the severity of disease. In milder case of dengue fever liver function test was normal but there was hepatomegaly was present commonly but in severe form of disease pattern of hepatic involvement varies from tender hepatomegaly to significant increase in liver enzyme. The diagnosis of Dengue can be kept in mind whenever patient presents with altered LFT and febrile illness.

References

1. Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ, Hunsperger E, Kroeger A, Margolis HS, Martínez E, Nathan MB, Pelegrino JL, Simmons C, Yoksan S, Peeling RW. Dengue: a continuing global threat. Nat Rev Microbiol2010; 8: S7-16
2. Guzmán MG, Kourí G. Dengue: an update. Lancet Infect Dis 2002; 2: 33-42.
3. WHO. Dengue: guidelines for diagnosis, treatment, prevention and control, Geneva, 2009. Available from: URL: http: //www.who.int/tdr/publications/documents/dengue-diagnosis.pdf
4. Thomas SJ, Strickman D, Vaughn DW. Dengue epidemiology: virus epidemiology, ecology, and emergence. Adv Virus Res 2003; 61: 235-89.
5. JayantaSamanta, Vishal Sharma; Dengue and its effects on liverWorld J Clin Cases 2015 February 16; 3(2): 125-31.
6. Kuo CH, Tai DI, Chang-Chien CS et al. (1992) Liver biochemical tests and dengue fever. American Journal of Tropical Medicine and Hygiene 47, 265–70.
7. Nimmannitya S. (1987) Clinical spectrum and management ofdengue haemorrhagic fever. Southeast Asian Journal of TropicalMedicine and Public Health 18, 392–397.
8. Wahid, S.F., Sanusi, S., Zawawi, M.M., Ali, R.A., 2000. A comparisonof the pattern of liver involvement in dengue hemorrhagic feverwith classic dengue fever. Southeast Asian J. Trop. Med. PublicHealth 31, 259—263.
9. Dr. Mohan D Kashinkunti ,Dr.Shiddappa, Dr.Dhananjaya M. A Study of Clinical Profile of Dengue Fever in a Tertiary Care Teaching Hospital Sch. J. App. Med. Sci., 2013; 1(4):280-82.
10. Pancharoen, C., Rungsarannont, A., Tisyakorn, U., 2002. Hepaticdysfunction in dengue patients with various severity. J. Med.Assoc. Thai. 85 (Suppl.), 298—301.
11. Ehrenkranz, N.J., Ventura, A.K., Cuadrado, R.R., Pond,W.L., Porter,J.E., 1971. Pandemic dengue in Caribbean countries and thesouthern United States — past, present and potential problems. N. Engl. J. Med. 285, 1460—69.
12. Gholson, C.F., Provenza, J.M., Bacon, B.R., 1990. Hepatologic considerationsin patients with parenchymal liver disease undergoingsurgery. Am. J. Gastroenterol. 85, 487—96.
13. Chung, H.K., Dar, I.T., Chi, S.C., Chi, K.L., Shue, S.C., Yun, F.L.,1992. Liver biochemical tests and dengue fever. Am. J. Trop. Med. Hyg. 47, 265—70.
14. Hawker, F., 1991. Liver dysfunction in critical illness. Anaesth. IntensiveCare 19, 165—181.
15. Nogueira RMR, Miagostovich MP, Schatzmayr HG et al. (1988) Virological study of a dengue type 1 epidemic in Rio de Janeiro. Memorias do InstitutoOswaldo Cruz 83, 219–25.
16. Miagostovich MP, Ramos RG, Nicol AF et al. (1997) Retrospective study on dengue fatal cases. Clinical Neuropathology 16, 204–08.

How to cite this article: Jingar GC, Parmar D, Jain AK, Kamble N, Jakhar R, Sudhir. Liver Dysfunction in Dengue Fever: A Prospective Study. Asian J. Med. Res. 2019;8(3):ME07-ME09.
DOI: dx.doi.org/10.21276/ajmr.2019.8.3.ME3

Source of Support: Nil, **Conflict of Interest:** None declared.