Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

A Study of Hepatic Involvement in Dengue Fever Along with Other Biological Changes in Relevance with Severity of Dengue Fever

Rajkumar Sangiri, Arpan Mandal, Amitabha Banerjee, Arka Chakravarty

Department of Medicine, Burdwan Medical College, West Bengal, India

Abstract

Introduction: Dengue is the most important arthropod-borne viral infection of humans. Worldwide, an estimated 2.5 billion people are at risk of infection, approximately 975 million of whom live in urban areas in tropical and sub-tropical countries in Southeast Asia, the Pacific and the Americas. Dengue viral infections are known to present a diverse clinical spectrum, ranging from asymptomatic illness to fatal dengue shock syndrome. Symptoms usually begin about four to 7 days after the initial infection. In many cases, symptoms will be mild. They may be mistaken for symptoms of the flu or another infection.

Aims: The aims of this study were to know the demographic profile of dengue patients, to know the incidence of liver involvement in dengue fever, to measure aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), serum albumin, platelet count, prothrombin time, and International Normalized Ratio, to find out the correlation between alteration of these biochemical parameters with severity of the disease, and to find out the morbidity and mortality along with hospital stay of the dengue patients with the severity of hepatic involvement.

Materials and Methods: The study was conducted in Burdwan Medical College and Hospital situated in Burdwan district (West Bengal) from March 2016 to February 2017. A total number of 102 patients diagnosed as cases of dengue fever were taken for this study.

Results: In our study, hepatomegaly in dengue infection is reported to be seen more frequently in complicated dengue in comparison to classical dengue fever. In the present study, 100% of cases in DSS group had hepatomegaly, whereas 88% in DHF group presented with hepatomegaly and only 25% cases of DF had hepatomegaly indicating that hepatomegaly may be used as a predictor for assessing the severity of the disease.

Conclusion: This study showed that dengue fever was seen in all age groups and that AST and ALT levels were raised in the majority of these patients. It was also found that AST levels were more than ALT levels, which were commonly observed in all those patients who developed complications such as DHF, DSS, ARDS, renal failure, and septicemia.

Key words: Dengue, Hepatomegaly, Jaundice and ARDS

INTRODUCTION

Dengue is the most important arthropod-borne viral infection of humans. Worldwide, an estimated 2.5 billion people are at risk of infection, approximately 975 million of whom live in urban areas in tropical and sub-tropical countries in Southeast Asia, the Pacific, and the Americas.[1] Transmission also occurs in Africa and the Eastern Mediterranean, and rural communities are increasingly being affected. It is estimated that more than 50 million infections occur each year, including 500,000 hospitalizations for dengue hemorrhagic fever, mainly among children, with the case fatality rate exceeding 5% in some areas.[2]

Access this article online

www.ijss-sn.com

Month of Submission : 05-2022
Month of Peer Review : 06-2022
Month of Acceptance : 06-2022
Month of Publishing : 07-2022

Dengue is a mosquito-borne viral disease that has rapidly spread in all regions of the WHO in recent years. Dengue virus is transmitted by female mosquitoes mainly of the species *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*. This mosquito also transmits chikungunya, yellow fever

Corresponding Author: Rajkumar Sangiri, Department of Medicine, Burdwan Medical College, West Bengal, India.

and Zika infection. Dengue is widespread throughout the tropics, with local variations in risk influenced by rainfall, temperature, and unplanned rapid urbanization. Severe dengue (also known as Dengue Hemorrhagic Fever) was first recognized in the 1950s during dengue epidemics in the Philippines and Thailand. Today, severe dengue affects most Asian and Latin American countries and has become a leading cause of hospitalization and death among children and adults in these regions.

Dengue viral infections are known to present a diverse clinical spectrum, ranging from asymptomatic illness to fatal dengue shock syndrome.[3] Symptoms usually begin about 4 to 7 days after the initial infection. In many cases, symptoms will be mild. They may be mistaken for symptoms of the flu or another infection. Young children and people who have never experienced infection may have a milder illness than older children and adults. Symptoms generally last for about 10 days and can include:

- Sudden, high-grade biphasic fever (up to 40°C)
- Severe headache
- Retro orbital pain
- Swollen lymph glands
- Severe joint and muscle pains (break bone fever)
- Skin rash (appearing between 2 and 5 days after the initial fever)
- Mild-to-severe nausea
- Mild–to-severe vomiting
- Mild bleeding from the nose or gums
- Mild bruising on the skin
- Febrile convulsions.[4]

Jaundice in dengue infection has been associated with fulminant liver failure and by itself is a poor prognostic factor.[5] However, there are only a few studies concerning liver dysfunction in children with liver dysfunction.

Although the number of patients affected by the virus is increasing each year, little work has been done in the studied area (regarding the pathogenicity, the liver changes, and the complication of dengue infection). Hence, it is with this objective that this present study was undertaken.

Aims and Objectives

This study aims to evaluate the effects of dengue fever, dengue hemorrhagic fever, as well as dengue shock syndrome on the hepatobiliary system in cases of dengue infections admitted to a tertiary setup in Burdwan, West Bengal, India. In this prospective observational cross-sectional study, I hereby intend to assess the frequency and degree of hepatobiliary dysfunction in adult patients with 26 dengue infections presenting to a tertiary care medical facility, as evident by the clinical manifestations, radiologic findings, and different laboratory workups. It will also aim to compare their outcome (mortality, length of stay, and complications) between patients with classical dengue fever and dengue hemorrhagic fever/dengue shock syndrome, with respect to their overall prognosis, morbidities, and mortality.

Specific Objective of the Study

The objectives of this study were as follows:

1. To know the demographic profile of dengue patients.
2. To know the incidence of liver involvement in dengue fever.
3. To measure aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), serum albumin, platelet count, prothrombin time, and International Normalized Ratio.
4. To find out the correlation between alteration of these biochemical parameters with severity of the disease.
5. To find out the morbidity and mortality along with hospital stay of the dengue patients with the severity of hepatic involvement.

MATERIALS AND METHODS

Study Area

The study was conducted in Burdwan Medical College and Hospital situated in Burdwan district (West Bengal).The Institution serves as the only tertiary care teaching Hospital encompassing the whole Burdwan, Birbhum, some parts of Bankura district and parts of adjoining Jharkhand state.

Study Population

Patients had been admitted in Medicine indoor of our hospital, diagnosed as having dengue fever, clinically and by serological tests, selected as cases for this study satisfying both the inclusion criteria and exclusion criteria designed to be appropriate for this study.

Study Period

This study was March 2016–February 2017.

Sample Size

A total number of 102 patients diagnosed as cases of dengue fever were taken for this study.

Inclusion Criteria

Patients more than 12 year age admitted in Medicine ward in Burdwan Medical College and diagnosed as dengue fever clinically and confirmed serologically with the help of either dengue IgM or NS1 positive or both were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

1. Patient suffering from hep B, C, E, or A.

AQ6 **Table 1: Dengue classification**

Parameters	Petechial rash		Statistic	*P* value at df 2
	Present (%)	Absent (%)		
Dengue classification				
DF (n_1=60)	0 (0)	60 (100)		
DHF (n_2=33)	31 (94)	2 (6)	χ_2=110.07	0.00
DSS (n_3=9)	7 (78)	2 (22)		
Parameters	**Tourniquet test**		**Statistic**	***P* value at df 2**
	Positive (%)	**Negative (%)**		
Dengue classification				
DF (n_1=60)	0 (0)	60 (100)		
DHF (n_2=33)	28 (84)	6 (15)	χ_2=93.58	0.00
DSS (n_3=9)	7 (78)	2 (22)		

2. Patient suffering from malaria or typhoid.
3. Patient is with chronic liver disease.
4. Patient with bleeding disorder.
5. Patient received any blood or blood product recently.
6. Patient receiving hepato toxic drugs.

Study Design

This study was prospective, observational cross-sectional study.

RESULTS AND DISCUSSION

Our data show that liver injury was almost universally present in a predominantly adult group of patients with DI. In most patients, liver dysfunction was mild-to-moderate, presenting primarily as elevation of serum aminotransferases. However, some patients had clinical manifestations of liver disease, namely, jaundice, hepatomegaly, and ascites.

Recent studies suggest that there is an upsurge of complicated dengue infections, especially in South East and South Asia. Recognition of varied presentations of dengue infections is important so as not to miss the diagnosis. Clinical features suggesting dengue-related hepatic involvement are the presence of liver enlargement and elevated transaminases.[6]

Hepatomegaly in dengue infection is reported to be seen more frequently in complicated dengue in comparison to classical dengue fever. In the present study, 100% of cases in DSS group had hepatomegaly, whereas 88% in DHF group presented with hepatomegaly and only 25% cases of DF had hepatomegaly indicating that hepatomegaly may be used as an predictor for assessing the severity of the disease.

The WHO guidelines of 1997 state that enlarged liver is observed more frequently in dengue shock than in non-shock cases.[7] Senevinatne *et al.* observed a higher incidence of hepatomegaly with DHF than DF. A similar study performed by Wallace *et al.* concluded 21% of cases in DF group with hepatomegaly and 48% in DHF group presented with hepatomegaly. Study by Chairrulfatah *et al.* concluded that number of patients with hepatomegaly was significantly higher in DSS as compared to non DSS cases.[8] Fadilah *et al.* showed hepatomegaly in 40% cases of DF and 60% of DHF cases.

In our study, hepatomegaly in dengue infection is reported to be seen more frequently in complicated dengue in comparison to classical dengue fever. In the present study, 100% of cases in DSS group had hepatomegaly, whereas 88% in DHF group presented with hepatomegaly and only 25% cases of DF had hepatomegaly indicating that hepatomegaly may be used as a predictor for assessing the severity of the disease.

de Souza *et al.* found that 45% of cases had raised ALT levels with mean value of 100.2 U/L in DHF and 84.6 U/L in DF. In the present study, it was observed that hepatic dysfunction in the form of elevated liver enzymes was seen more in DSS as compared to non DSS cases suggesting that apart from dengue virus, hypoxemia as a result of hypovolemic shock or hosts response to infection remains to be to be determined as it may contribute to the adverse effects on the liver. Kuo *et al.* have reported that 82.2% of cases of dengue infection had elevated ALT levels. Parkash *et al.* reported 86% cases with raise AST level. Lee *et al.*, Trung *et al.*, and Wong *et al.* reported 86%, 97%, and 90.60% cases with raised AST.

Our study showed that AST levels were elevated in more number of patients in all the three groups compared to ALT values. Similar study done by Kuo *et al.* reported similar results with elevation of AST and ALT in 93.3% and 82.2% patients, respectively.[9] Like other studies in the present study, majority of our patients had elevated liver

enzymes, with AST being more elevated than ALT values. Patients with severe and complicated dengue had higher level of hepatic enzyme dysfunction.

Study by Mohan *et al.* also observed deranged AST levels frequently in DSS cases in comparison to non-shock cases. de Souza *et al.* found that mean value of AST in DHF was 127.1U/L and in DF was 89.8 U/L. Souza *et al.* have reported an incidence of 63.4%cases with elevated AST. Kuo *et al.* have reported that 93.3% of cases of dengue infection had elevated AST levels. Parkash *et al.* reported 95% cases with raise AST level. Lee *et al.*, Trung *et al.*, and Wrong *et al.* reported 86%, 97%, and 90.60% cases with raised AST.[10]

We observed that the maximum value of AST shown is 1326 and the mean AST amng DF cases 59.81, DHF cases 216.12, and DSS cases is 455.55.

Patwari *et al.* reported higher incidence of 25% 66 as compared to 16% by Itha *et al.* Ding The Thrung *et al.* reported an incidence of <2% 78, whereas none of the patients had jaundice in a study by W.Petedachai.[11]

We examined that among them two patients of DHF and eight patients of DSS show hyper bilirubinemia. The mean serum bilirubin among DSS group is 2.91 and the highest measured bilirubin is 5.1 mg/dl.

Study by Fadilah *et al.* showed that the mean percentage of T (CD3) cells was significantly lower in DHF compared to DF patients. Similarly, the mean percentage of B (CD19), CD4, CD8, and CD5 cells was also significantly lower in DHF patients compared to DF patients and controls. This study confirmed the significance of decrease in T, CD4, and CD8 cells in DHF and demonstrated that these lymphocyte subsets were of some value in differentiating DHF from DF. Marked activation of immunoregulatory T lymphocyte subsets may contribute to the severe complications seen in DHF/DSS including fulminant hepatitis.[12]

Platelet Count

It was also observed that the median lowest platelet count was lowest in DHF and DSS as compared to DF ($P = 0.000$). About 22.22% DF cases and 100% of DHF and DSS cases shown low platelet count. The mean platelet count among DF, DHF, and DSS group were 138,870, 49,560, and 43,077/μl accordingly. Wichmann *et al.* also inferred that patients with DHF had significantly lower platelet values than DF.[13]

Clinical Outcome

Out of 102 serology confirmed cases of dengue infection with 60 cases in dengue fever group, 33 being in DHF group and nine presented to us in dengue shock syndrome. There were ten cases with clinical evident jaundice with deranged liver function parameters. Six of our patients had ARDS and were shifted and treated in the ICU. Among those six patients, two patients died who require ventilatory support for severe respiratory distress and very low blood oxygen saturation. Another one patient expired secondary to DIC, multiorgan involvement, renal failure, dengue shock, coagulopathy, and deranged hepatic function profile. His liver enzymes were elevated above 5 fold the normal values. He had altered coagulation profile with prolonged PT and APTT values and thrombocytopenia. All those three patients referred from local health center with fever, severe respiratory distress, hemorrhagic manifestation, bilateral pedal edema, ascites, and pleural effusion. Other 99 cases were treated and cured completely and discharged from the hospital with stable hemodynamics.

CONCLUSION

This study showed that dengue fever was seen in all age groups and that AST and ALT levels were raised in the majority of these patients. It was also found that AST levels were more than ALT levels, which was commonly observed in all those patients who developed complications such as DHF, DSS, ARDS, renal failure, and septicaemia, proving he fact that severity of hepatic involvement can be a major contributing factor in morbidity and mortality of such patients with dengue fever. Hence, AST and ALT can be a useful early marker to assess the severity of the disease which can thus lead to early recognition of high-risk cases.

REFERENCES

1. World Health Organization. Scientific Working Group Report on Dengue. Geneva: World Health Organization; 2007. Available from: https://www.apps.who.int/tdr/publications/tdr-researchpublications/swg-report-dengue/pdf/swg_dengue_2.pdf [Last accessed on 2022 Mar 23].
2. Gubler DJ. The changing epidemiology of yellow fever and dengue, 1900 to 2003: Full circle? Comp Immunol Microbiol Infect Dis 2004;27:319-30.
3. Kumar R, Tripathi P, Tripathi S, Kanodia A, Venkatesh V. Prevalence of dengue infection in North Indian children with acute hepatic failure. Ann Hepatol 2008;7:59-62.
4. Available from: https://www.healthline.com/health/dengue-fever#overview1 [Last accessed on 2022 Mar 25].
5. Chhina RS, Goyal O, Chhina DK, Goyal P, Kumar R, Puri S. Liver function tests in patients with dengue viral infection. Dengue Bull 2008;32:110-7.
6. Giri S, Agarwal MP, Sharma V, Singh A. Acute hepatic failure due to dengue: A case report. Cases J 2008;1:204.
7. World Health Organization. Dengue Haemorrhagic Fever: Diagnosis, Treatment, Prevention and Control. 2nd ed. Geneva: World Health Organization; 1997.
8. Chairulfatah A, Setibudi D, Ridad A, Colebunders R. Clinical manifestations of dengue haemorrhagic fever in children in Bandung, Indonesia. Ann Soc Belg Med Trop 1995;75:291-5.
9. Kuo CH, Tai DI, Chang-Chien CS, Lan CK, Chiou SS, Liaw YF. Liver

biochemical tests and dengue fever. Am J Trop Med Hyg 1992;47:265-70.
10. Lee LK, Gan VC, Lee VJ, Tan AS, Leo YS, Lye DC. Clinical relevance and discriminatory value of elevated liver aminotransferase levels for dengue severity. PLoS Negl Trop Dis 2012;6:e1676.
11. Petedachai W. Hepatic dysfunction in children with dengue shock syndrome. Dengue Bull 2005;29:112-8.
12. Kalayanarooj S. Clinical manifestations and management of dengue/DHF/DSS. Trop Med Health 2011;39:83-7.
13. Wichmann O, Hongsiriwon S, Bowonwatanuwong C, Chotivanich K, Sukthana Y, Pukrittayakamee S. Risk factors and clinical features associated with severe dengue infection in adults and children during the 2001 epidemic in Chonburi, Thailand. Trop Med Int Health 2004;9:1022-9.

How to cite this article: Sangiri R, Mandal A, Banerjee A, Chakravarty A. A Study of Hepatic Involvement in Dengue Fever Along with Other Biological Changes in Relevance with Severity of Dengue Fever. Int J Sci Stud 2022;10(4):39-43.

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

Author Queries???
AQ6: Kindly cite table 1 in the text part