ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2020; 6(1): 157-160
www.allresearchjournal.com
Received: 22-11-2019
Accepted: 24-12-2019

Dr. Neelesh Mehrotra
PG Student, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Dr. RS Maniram
Associate Professor, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Dr. Anil Sejwar
Associate Professor, Department of Medicine, Gandhi Medical College, Bhopal, MP, India

Dr. KK Kawre
Professor, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Dr. TN Dube
Professor, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Correspondence Author:
Dr. RS Maniram
Associate Professor, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Study of hepatic involvement in dengue: A prospective single centre study

Dr. Neelesh Mehrotra, Dr. RS Maniram, Dr. Anil Sejwar, Dr. KK Kawre and Dr. TN Dube

Abstract
Background: Dengue viral infection has become one of the major public health issue worldwide affecting 50-100 million people each year. There are there forms of dengue fever (DF) based on the severity. Early detection and differentiation is the key to prevent the infection.
Aims and Objectives: To assess the hepatic and biliary involvement with severity in Dengue.
Materials and Methods: Hundred patients were studied at the department of Medicine Gandhi Medical College and Hamidia Hospital, Bhopal after dividing in to Dengue Fever (DF; n=74), Dengue Haemorrhagic Fever (DHF, n=13) and Dengue Shock Syndrome (DSS, n=13). All patients were subjected to detailed clinical history, systemic examination, routine investigations along with liver function test (LFT) as well ultrasonography of abdomen.
Results: Dengue was more prevalent in young working age group (61%) females (75%). DF (73.4%) was more prevalent. Fever, rashes and bleeding tendency were more common in severe form of dengue. Majority of patients had elevated liver enzymes, with AST being more elevated than ALT. Patients with hepatomegaly had high total serum bilirubin (1.50±0.90, p=0.005), there were significant elevations in ALT, ALP and Hypoalbuminemia in patients who had hepatomegaly.
Conclusion: GB; gall bladder. derangement is seen more commonly in severe case of dengue infection. Early recognition of these parameters can also be used as a predictor for assessing the disease severity.

Keywords: Liver function test, dengue fever, hepatomegaly, hepatic involvement in dengue

Introduction
Dengue viral infection is a major public health issue worldwide, approximations 50-100 million cases of dengue infection occurs each year. More than 3 lakh cases of dengue hemorrhagic fever (DHF) are diagnosed each year, with the case mortality rate varying from 1% to 5% [1].

Liver involvement in DI is often demonstrated by hepatomegaly and mild-to-moderate increases in Transaminases levels; although, jaundice and acute liver failure are generally uncommon. Transaminase levels are higher in DHF/DSS than in DF and tend to return to normal 14-21 days after infection. Of late, there have been reports of fulminant hepatitis with high mortality in patients with DI [2]. Current study is an attempt to study the hepatic involvement and severity in dengue.

Materials and Methods
A observational, cross sectional and hospital based study was performed on 100 patients at the department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal from 2017 to 2019. After approval of the study protocol by the Institutional Ethics Committee, written informed consent was obtained from each patient.

All patients who were either NS1 positive by Kit method or Dengue antigen positive by ELISA having age more than 14 years were subjected to detail clinical history, systemic examination, routine investigations along with liver function test (LFT) as well ultrasonography of abdomen.

Previously known or newly detected patients of chronic liver disease of any aetiology (As evident by the clinic-radiological and biochemical parameters), patients with known recent history of intake of any hepatotoxic or similar drugs causing derangements of liver functions, having other known infections causing hepatitis as Viral hepatitis A and E, Falciparum

malaria etc., and with altered liver functions secondary to sepsis or as a part of Multiple Organ Dysfunction Syndrome unrelated to DI were excluded.

Patients were divided in to Dengue Fever (DF; n=74), Dengue Haemorrhagic Fever (DHF, n=13) and Dengue Shock Syndrome (DSS, n=13).

All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was performed to prepare the tables. PRISM and Microsoft excel was used to prepare the tables. Quantitative data was expressed as mean and standard deviation whereas categorical data was expressed as number and percentage. ANOVA using simple mean and was performed to compare the mean whereas chi square test was used to compare the categorical data. Level of significance was assessed at 5%.

Results

Majority of the patients had age between 14- 29 years (61%) followed by 30-45 years (26%). Females' preponderance was found in DF (75%) and DSS (13.9%). Majority of the males had DF (73.4%) followed by DHF (14.1%).

Fever was the most common symptoms. Rashes were more prevalent in DSS and DHF. Bleeding tendency was more prevalent in DHF (100%) and DSS (100%), however none of the patients in DF group had bleeding tendency. Abdominal pain was more common in DSS (76.9%) followed by DHF group (61.5%) then less common in DF (5.4%). Nausea/Vomiting was more prevalent in DSS (76.9%) followed by DHF (53.8%). Decrease appetite was less prevalent in DF (28.3%), then DHF (53.8%) followed by more common in DSS patients (100%) and Jaundice was mainly reported in all the cases of DSS patients (100%).

Table 1: Comparing liver function test parameters between groups

LFT	DF(n=74)	DHF(n=13)	DSS(n=13)	P value
Total serum bilirubin	0.93±0.44	1.31±0.63	1.54±0.87	<0.001
Elevated AST	54 (72.9%)	10(76.9%)	13(100%)	0.002
Elevated ALT	37(50%)	8(61.5)	13(100%)	0.021
Elevated ALP	13(17.5%)	7(53.8%)	10(76.9%)	<0.001
Hypoalbuminemia	36(48.6%)	7(53.8%)	13(100%)	0.001
Mean Serum Protein (Albumin)	2.84±0.43	2.48±0.42	2.32±0.29	<0.001
Mean Serum Protein (Globulin)	3.31±0.66	2.90±0.43	3.31±0.51	0.094

Data is expressed as mean and standard deviation and no of patients (%), LFT; liver function test, AST; aspartate aminotransferase, ALT; alanine transaminase, ALP; alkaline phosphatase, DF; Dengue Fever, DHF; Dengue Hemorrhagic Fever, DSS; Dengue Shock Syndrome. P value of <0.05 is considered as significant.

Table 2: Comparison of USG findings in Groups

USB Abdomen	Group			P value
	DF(n=74)	DHF(n=13)	DSS(n=13)	
Ascites	2 (2.7%)	7(53.8%)	10(76.9%)	<0.001
Mild Fatty liver	1 (1.35%)	1(7.6%)	2(15.3%)	
Hepatomegaly	2(2.7%)	3(23.0%)	7(53.8%)	

DF: Dengue Fever, DHF; Dengue Hemorrhagic Fever, DSS; Dengue Shock Syndrome; P value of <0.05 is considered as significant.

Table 3: Comparison of LFT in dengue infection with or without Hepatomegaly involvement

LFT	Hepatomegaly involvement		P value
	No (n=87)	Yes(n=13)	
Total serum bilirubin	1.00±0.50	1.50±0.90	0.005
Elevated AST	62(71.2%)	11(84.6%)	0.351
Elevated ALT	46(52.8%)	11(84.6%)	0.397
Elevated ALP	21(24.1%)	9(69.2%)	0.003
Hypoalbuminemia	41(47.1%)	10(76.9%)	0.598
Mean Serum Protein (Albumin)	2.76±0.46	2.54±0.37	0.030
Mean Serum Protein (Globulin)	3.26±0.64	3.20±0.52	0.722

Data is expressed as mean and standard deviation and no of patients (%), LFT; liver function test, AST; aspartate aminotransferase, ALT; alanine transaminase, ALP; alkaline phosphatase, P value of <0.05 is considered as significant.

Table 4: Comparison of total serum bilirubin and SGOT in DF, DHF and DSS groups

Parameters	Groups	Range				P value
		0-0.9	1.0-1.5	1.6-2.0	>2.0	
Total serum bilirubin	DF (n=74)	55	17	1	1	0.022
	DHF (n=13)	5	5	2	1	
	DSS (n=13)	0	2	4	7	
AST	Groups	0-45	46-200	201-400	401-600	P value
	DF (n=74)	20	50	3	1	0.034
	DHF (n=13)	6	6	1	0	
	DSS (n=13)	0	2	10	1	

Data is expressed as mean and standard deviation and no of patients (%), AST; aspartate aminotransferase, DF: Dengue Fever, DHF; Dengue Hemorrhagic Fever, DSS; Dengue Shock Syndrome. P value of <0.05 is considered as significant.

Comparing the mean value of LFT in cases with normal USG abdomen findings in Groups revealed that there was a significant difference in total serum bilirubin [0.89±0.37 (DF), 1.0±0.0 (DHF) and DSS (1.0±0.0) (p<0.001)], AST[50.83±22.43 (DF), 63.91±10.46 (DHF) and DSS (107.50±84.14) (p<0.001)], ALT [[43.0±11.52 (DF), 56.50±17.67 (DHF) and DSS (92.22±23.45) (p<0.001)], ALP [98.83±27.21 (DF), 104.67±39.98 (DHF) and DSS (98.0±18.23) (p<0.001)] and Serum Albumin [2.75±0.36 (DF), 2.60±0.40 (DHF) and DSS (2.60±0.56) (p<0.001)].

Discussion

The manifestations of DI are protean from being asymptomatic to undifferentiated fever, severe dengue infections and unusual complications. Recent studies suggest that there is an upsurge of complicated dengue infections especially in South East and South Asia [3].

It was observed that majority of the patients were of the young working age group. Bandyopadhyay *et al* found that maximum cases had age between 46 years to 61 years [4]. Sharma *et al* showed that patients below 20 years of age were more commonly affected [5]. Similarly Mehta *et al* found DF to be more common below 30 years of age, which also support present study like the others [6].

Fever was common to all the three groups, rashes, bleeding tendancy, abdominal pain and nausea and vomiting was more prevalent with DSS and DHF. Previous study revealed that pain in abdomen and vomiting were the commonest presenting complaints next to fever which was present in all the cases [4].

The appearance of jaundice in cases of DF/DHF/DSS may be multifactorial. It can be due to hepatic injury caused by the dengue virus and or hypoxia and tissue ischemia in cases of dengue shock [7]. Jaundice occur more in complicated than in uncomplicated cases. (Paula M 2004) In present study jaundice was mainly reported in DSS patients (100%). Trung DT *et al*., reported an incidence of jaundice <2% [2] One previous study reported similar findings [4].

Transaminases levels, particularly AST levels, have been suggested as a potential marker for differentiating dengue from other viral infections during the early febrile phase [2]. In present study on comparing liver function test parameters between groups it was found that total serum bilirubin was significantly increases in DSS as compared to DHF and DF.

Most of the studies showed that unlike other viral infections, in dengue the rise of AST is usually more than ALT [2, 8]. Similar trend was observed in the present study. Study by BrijMohan *et al*., also observed deranged AST levels frequently in DSS cases in comparison to non-shock cases and 100% of cases in DSS and DHF group had elevated ALT enzyme levels in comparison to 81% in dengue fever patients [9]. Kuo *et al*., have reported that 82.2% of cases of dengue infection had elevated ALT levels [10].

Serum ALP levels also showed similar trend. This means hepatic dysfunction in the form of marked elevated enzymes was higher in severe and complicated dengue in comparison to classical dengue fever. In previous study reported that elevated ALP was seen in 56% of total cases in this study [4]. Fadilah *et al*., had reported that mean levels of ALP were higher in DHF as compared to DF [11].

Hypoalbuminemia in dengue infection probably is the result of capillary leakage induced by dengue infection. Previous study reported similar findings as that of present study where they found that Hypoalbuminemia was observed in majority of the cases [4].

In a hospital-based study from Amalapuram, Andhra Pradesh including 126 clinically and serologically positive patients reported deranged liver enzyme in severe form of dengue and compared to DF [12]. findings are in line with the present study. This means the pattern of hepatic involvement of liver in dengue fever varies as per the severity of disease. In milder case of DF liver function test was normal but there hepatomegaly was present commonly but in severe form of disease pattern of hepatic involvement varies from tender hepatomegaly to significant increase in liver enzyme.

Bandopadhyay *et al*. found that plasma leakage such as ascites on USG were seen more frequently in patients with DHF (76.9%) followed by DSS (72%) and DF (33.9%), Also thrombocytopenia were seen more commonly in both DSS and Dengue Hemorrhagic Fever (DHF) [4]. Findings are in line with present study USG findings.

Hepatomegaly is frequent and is commoner in patients with DSS than in those with DF [2]. In present study prevalence of hepatomegaly was more in DSS patients (53.8%) then DHF (23.0%). The lower percentage may be due to the availability of better treatment option at our centre. Senevinatne *et al*., observed a higher incidence of hepatomegaly with DHF than DF [7]. Maria Paulo *et al*., showed 30% of cases who presented in DSS to be having tender hepatomegaly [13]. On comparing the LFT in dengue infection with or without Hepatomegaly involvement, it was found that patients with Hepatomegaly involved had high Total serum bilirubin, elevated ALT and Hypoalbuminemia.

Small sample size and cross sectional nature are the main limitation of the study. Due to that present study findings cannot be applied to large population. There is a need of a large randomized clinical trial which can provide strength to present study findings.

Conclusion

It was found that dengue was more prevalent in young working age group females. Out of three dengue type, DF was more prevalent in present study. Symptoms of dengue are more common in severe cases of dengue. Hepatic involvement in dengue is proved and supported by the previous series. 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. As the hepatic damage in dengue infections at majority of times is transient and reversible it is the responsibility of the clinician to identify early the hepatic dysfunction associated with the disease in order to avoid life threatening complications. This will decrease the mortality and morbidity due to dengue infections.

References

1. Parkash O, Almas A, Jafri SM, Hamid S, Akhtar J, Alishah H. Severity of acute hepatitis and its outcome in patients with dengue fever in a tertiary care hospital Karachi, Pakistan (South Asia). BMC Gastroenterol. 2010; 10:43.
2. Trung DT, Thao le TT, Hien TT, Hung NT, Vinh NN, Hien PT *et al*. Liver involvement associated with dengue infection in adults in Vietnam. Am J Trop Med Hyg. 2010; 83:774-80.

3. De Souza LJ *et al*. The impact of Dengue on liver function as evaluated by aminotransferase levels. The Brazilian Journal of Infectious Diseases. 2007; 11(4):407-10.
4. Gurugama P, Garg P, Perera J, Wijewickrama A, Seneviratne SL. IJD SYMPOSIUM. Indian Journal of Dermatology. 2010; 55(1):68-78.
5. Bandyopadhyay D, Chattaraj S, Hajra A, Mukhopadhyay S, Ganesan V. A Study on Spectrum of Hepatobiliary Dysfunctions and Pattern of Liver Involvement in Dengue Infection. J Clin Diagn Res. 2016; 10(5):OC21-OC26.
6. Sharma Y, Kaur M, Singh S, Pant L, Kudesia M, Jain S. Seroprevalence and trend of dengue cases admitted to a government hospital, Delhi–5-year study (2006-2010): A look into the age shift. Int J Prev Med. 2012; 3(8):537-43.
7. Mehta KD, Gelotar PS, Vachhani SC, Makwana N, Sinha M. Profile of dengue infection in Jamnagar city and district, west India. WHO South-East Asia J Public Health. 2014; 3(1):72.
8. Seneviratne SL, Malavige GN, de Silva HJ. Pathogenesis of liver involvement during dengue viral infections. Trans R Soc Trop Med Hyg. 2006; 100:608-14.
9. Shukla V, Chandra A. A study of hepatic dysfunction in dengue. J Assoc Phyis India. 2013; 16:24-25 12.
10. Mohan B, Patwari AK, Anand VK. Hepatic dysfunction in childhood dengue infection. J Trop Pediatr. 2000; 46:40-43.
11. Kuo CH, Tai DI, Chang-Chien CS, Lan CK, Chiou SS, Liaw YF *et al*. Liver biochemical tests and dengue fever. Am J Trop Med Hyg. 1992; 47:265-70.
12. Fadilah S, Wahid SA, Sansui S, Zawari MM, Ali RA. A Comparison of the pattern of Liver Involvement in Dengue Haemorrhagic fever with classic Dengue fever. South East Asian J Trop Med Public Health. 2000; 31(2):259-63.
13. Acharya A, Satyanarayana PVV, Subrahmanyam V. A prospective study of pattern of hepatic dysfunction in dengue fever patient in coastal Andhra Pradesh, India. Int J Adv Med. 2018; 5:663-7.
14. Paula M, Mourao G, Vinicius M, Lacerda G, Bastos MS, Claudio B *et al*. Dengue haemorrhagic fever and acute hepatitis: a case report. Brazillian Journal of Infectious Disease, 2004, 8(6).