International Journal of Advances in Medicine
Rajaih VN et al. Int J Adv Med. 2019 Apr;6(2):464-468
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20191160

Original Research Article

A study of hepatobiliary manifestations in dengue viral infection

Venkata Rajaih N., R. Thirunadhar*, Nikitha Dasari

Department of Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India

Received: 19 December 2018
Accepted: 29 January 2019

***Correspondence:**
Dr. R. Thirunadhar,
E-mail: drtirunadharomc@gmail.com

ABSTRACT

Background: Dengue viral infection is a major and important public health problem in many South East Asian (SEA) countries and also in more than 100 countries of tropical and subtropical region. The aim of study was to assess the frequency and degree of hepatobiliary dysfunction in adults with dengue infection presenting to our tertiary hospital, Karimnagar.
Methods: The study was a prospective observational study conducted on 120 adult patients of serological proven dengue infection with hepatic and biliary manifestations, admitted during the period of from June 2016 to June 2017. Investigations included complete blood count, liver function test, viral serology, sepsis screen, ultrasound abdomen.
Results: Majority of cases in age group of 20-56 years with male: female ration of 1.7:1. Of all the cases, 53% patients were categorized into dengue fever group, 25% into dengue hemorrhagic fever group, and 27.7% into dengue shock syndrome group in accordance to WHO guidelines.
Conclusions: This study was showed that a significant hepatobiliary derangement is seen in severe cases of dengue. Early recognition of such perturbations helps guide further management to prevent mortality.

Keywords: Dengue virus infections, Hepatic and biliary manifestations, Liver function tests

INTRODUCTION

Dengue viral infection is a major and important public health problem in many South East Asian (SEA) countries and also in more than 100 countries of tropical and subtropical region.[1,2] Dengue infections are caused by four antigenically distinct dengue virus serotypes (DENV1, DENV2, DENV3, DENV4) of family Flaviviridae. The infection is transmitted from person to person by Aedes mosquitoes. It is characterized by fever, headache, retro orbital pain, muscle and joint pains, skin rash, nausea and vomiting.

An estimated 3.97 billion people are at risk in 128 tropical and subtropical countries worldwide.[3] Some studies about hepatobiliary dysfunction are done in pediatric population but studies done in the adult population are not adequate to boast about. Infection by any one of the four serotypes could cause multiple spectra of disease including dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). India is one of the seven identified countries in SEA region regularly reporting incidence of dengue fever/dengue hemorrhagic fever.

Typically, people infected with dengue virus are asymptomatic (80%). Dengue viral infections are known to present with a diverse clinical spectrum, ranging from asymptomatic illness to fatal dengue shock syndrome. Unusual manifestations of dengue infections such as encephalitis, myocarditis, guillian barre syndrome, hemolytic uremic syndrome and hepato-biliary dysfunction are being recognized.

Hepatic injury with dengue infection has been described since 1967.[4] Liver dysfunction in patients with dengue varies from mild injury with elevation of transaminase activity to fulminant hepatic failure and hepatic encephalopathy. Acute acalculous cholecystitis, a rare and atypical presentation of dengue is also being increasing reported in the recent years. Elevation of liver enzymes is an early marker of dengue infection. It is also a predictor for assessing the disease severity.[5]

The purpose of this study was to assess the frequency and degree of severity of hepatobiliary dysfunction in patients of dengue hemorrhagic fever and dengue shock syndrome in comparison to classic dengue fever in tertiary care hospital, Karimnagar district.

METHODS

The study design was a prospective cross-sectional study. A total of 120 patients fulfilling the below criteria were studied.

Study centre and duration

The present study was conducted in the Department of General Medicine, Chalmeda AnandRao Institute of Medical Sciences, Karimnagar on patients who presented with serologically proven Dengue infection and who developed Hepatobiliary derangements during presentation or during the course of hospital stay from January 2016 to December 2016.

Patients of confirmed dengue infection with evidence of clinical, serological or radiologically proven hepatobiliary dysfunction admitted in the wards of Medicine Department were included in the study.

Inclusion criteria

- Age ≥14 years.
- Clinically as well as serologically proven dengue infection with either Hepatic and/or Biliary derangements.

Exclusion criteria

- Chronic liver disease
- Viral hepatitis A and E, leptospirosis, falciparum malaria,
- Multiple organ dysfunction syndrome
- Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steato-hepatitis.

The patients were evaluated for clinical profile based on symptoms at presentations (fever, arthralgia, retro-orbital pain, melaena, right Upper Quadrant pain abdomen and rash). General physical examination findings (heart rate and blood pressure) and systemic examination findings (cardiovascular, respiratory, central nervous system and per abdomen).

Outcome variables

The cases were isolated according to the WHO Case definitions and were divided into 3 groups: Dengue Fever (DF), Dengue hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS).

The following investigations were done for diagnosis and management of dengue fever including dengue serology, complete blood count, total bilirubin, direct bilirubin, total proteins, serum albumin, serum globulin, ALT and AST, alkaline phophastase.

The liver profile was assessed by evaluating bilirubin (total, direct and indirect), ALT and AST, alkaline phosphatase levels, total serum proteins, serum albumin, and serum globulin. The haematological profile was assessed and abnormalities like anaemia, leucopenia and thrombocytopenia were looked for based on haemoglobin levels, total count and platelet count.

Ethics approval

This study was approved by Institute ethics committee, CAIMS, Karimnagar. Patients fulfilling the selection criteria were explained about the nature of study and with their consent enrolled in the study.

Statistical analysis

The data obtained was coded and entered into Microsoft Excel Worksheet. The continuous data was expressed as mean ± standard deviation (SD). In case of more than three means, one way ANOVA test was used for the comparison. A probability value ('p'-value) of less than or equal to 0.05 at 95% CI was considered as statistically significant.

RESULTS

A prospective study was done on 120 individuals of confirmed Dengue infection with Hepatobiliary derangements (evidenced by clinical, laboratory or imaging modalities) and were categorized based on WHO defined case criteria for dengue who were admitted in CAIMS, Karimnagar, Telangana State during January 2016 to December 2016.

Table 1: Demographic data.

Age	Number of cases
<= 19 years	11 (9.16%)
20-39 years	54 (45%)
40-59 years	36 (30%)
>=60 years	19 (15.83%)

Table 1 shows the maximum number of cases were seen in the age group between 20-59 years of age i.e., 90 cases (75%). In the present study, male predominance is noted.

62.5% of cases were ma le while rests 37.5% were females with M:F ratio of 1.67:1.

Table 2: Frequency of clinical symptoms.

Parameter	Number of cases	Percentage (%)
Fever	120	100%
Pain abdomen	70	58.8%
Nausea / vomiting	69	57.5%
Myalgias	63	52.5%
Headache	93	77.5%
Arthralgia	58	48.3%
Retro orbital pain	68	56.7%
Skin rash	22	18.3%
Facial puffiness/pedal oedema	26	21.6%
Bleeding manifestations	40	33.3%

Of the total 120 cases, 64 patients categorized into DF group (53.3%), 30 patients (25%) into DHF group, 26 patients (21.67%) in to DSS group.

Table 2 shows hepatomegaly was observed more frequently in DHF patients (50%). Hepatic tenderness also was a frequent finding in DSS patients (65.3%) followed by DHF patients (60%) compare to DF patients (32.8%).

This difference in no. of patients having hepatic tenderness without hepatomegaly could be explained by mild hepatomegaly not appreciable clinically or due to geographic variations or biliary involvement like acalculous cholecystitis in those patients.

Total 14 patients had clinical jaundice, of which 8 were of DHF cases and 6 belonged to DSS. Ascites, which was of exudative type occurred more among the patients of DSS (30.4%), followed by DHF (20%) and DF patients (10.8%).

Table 3: Comparison of liver function tests (LFT).

Parameter	DF	DHF	DSS	p-value
Total serum bilirubin	2 (3.1%)	10 (33.3%)	6 (23%)	0.001
Elevated ALT	55 (86%)	29 (97%)	26 (100%)	0.047
Elevated AST	60 (94%)	30 (100%)	25 (96%)	0.012
Elevated ALP	26 (40.6%)	24 (80%)	19 (73%)	0.001
Hypo albuminemia	20 (31.2%)	22 (73.3%)	21 (80.7%)	0.001
Low sr. globulin	17 (26.6%)	3 (10%)	4 (15.4%)	0.13

As per Table 3 on comparing the liver function parameters of DF, DHF, DSS cases, it was observed that elevated levels of AST, ALT and ALP were significantly higher in Dengue shock syndrome as compared to Non-shock cases ($p<0.05$). Hypoalbuminemia was also predominantly higher in DSS followed by DHF cases. While low levels of serum globulin were seen more in DF patients than DHF or DSS patients in this study, however this difference is not statistically significant ($p=0.13$).

Bleeding tendencies like Petechiae, purpura or Ecchymosis were seen in DSS patients (46%) and DHF patients (33.3%) but none of DF patients had this sign. Further, 61.5% DSS cases and 16.6% of DHF cases had altered sensorium either at presentation or during the course of hospital stay. None of DF patients ever had this finding.

Table 4: Comparison of mean values of LFT.

Parameter	DF	DHF	DSS	p-value
Mean total Sr. bilirubin (SD value)	1.05 (0.45)	2.51 (2.8)	1.63 (1.04)	0.0002
Mean ALT (SD value)	105.5 (62.43)	145.6 (74.9)	237.38 (128.8)	0.0001
Mean AST	124.7 (77.4)	175.8 (99.83)	275.1 (147.9)	0.0001
Mean ALP	125 (36.49)	169.67 (70.85)	211.76 (98.37)	0.0001
Mean albumin	3.63 (0.42)	3.14 (0.36)	3.3 (0.48)	0.0001
Mean globulin	2.7 (0.52)	2.83 (0.36)	2.71 (0.38)	0.465
Mean total proteins	6.33 (0.66)	5.97 (0.57)	5.88 (0.54)	0.002

As per Table 4 the mean total serum bilirubin is significantly more in the cases of DHF compared to other groups. Alkaline phosphatase is significantly greater in DSS followed by DHF and DF groups.

Mean albumin value is high in DF patients implying that hypoalbuminemia is a feature seen in severe cases of Dengue. Mean Globulin value is high among DHF patients but is not statistically significant in this study. Mean total proteins are high among DF patients implying that Hypoproteinemia is also a feature increasingly seen severe case of Dengue-DHF and DSS.

Table 5 shows the transaminase levels of patients without hepatomegaly is higher than those with hepatomegaly. While, the mean total sr. bilirubin is higher in those with hepatomegaly.

Table 6 In this study, elevated levels of ALP were observed in all the three groups with highest frequency in DHF (80%) followed by DSS (73%) and DF (40.6%).

Table 5: Comparison of LFTs between with and without hepatomegaly.

Parameter	Hepatomegaly present (N= 44)	Hepatomegaly absent (N=76)	P value
Mean total sr. bilirubin (SD)	1.98 (2.45)	1.28 (0.81)	0.02
Mean AST	136.25 (94.57)	189.65 (124.85)	0.007
Mean ALT	116.95 (79.89)	159.88 (104.5)	0.02
Mean ALP	139.38 (51.59)	164 (80.62)	0.04
Albumin	3.39 (0.45)	3.42 (0.45)	0.73
Globulin	2.66 (0.47)	2.78 (0.45)	0.19

Table 6: Comparison of ALP levels.

	Normal ALP	Elevated ALP
Dengue fever	38 (59.3%)	26 (40.6%)
Dengue hemorrhagic fever	6 (20%)	24 (80%)
Dengue shock syndrome	7 (26.9%)	19 (73%)

Table 7: Comparison of ALP levels.

Parameter	DF	DHF	DSS
Thrombocytopenia	55 (85.9%)	30 (100%)	26 (100%)
Minimum platelet count (Median)	60,000	25,000	15,000
Hematocrit >38%	40 (62.5%)	25 (83.3%)	20 (71.4%)
Mean hematocrit (SD)	41 (5.3)	44.7 (6)	43.7 (7.2)

As per Table 7 shows thrombocytopenia is a prominent feature in DHF (100%) group and DSS group (100%) in comparison DF group (85.2%) in the present study. The median of the minimum platelet count during the course of hospital stay was least in DSS group. Increased hematocrit was observed more frequently in DHF & DSS patients than in DF patients. Also, the mean hematocrit was comparatively higher in DHF and DSS group of patients.

DISCUSSION

The study revealed majority of cases were in the age below 40 years constituting more than half of the study population (54.16%). These findings were similar to the study by Sharma S et al.[6] All series indicate that the most commonly affected age group is between 20 to 40 years. The present study also confirms these findings.

In the present study, based on case definitions by WHO, cases were grouped into DHF (25%), DSS (22%) and rest (53%) in to classic dengue fever. Similar pattern of frequency was noted by Bandyopadhyay et al, study, in the present study fever was the universal symptom present in 100% of the cases.[7] Similar findings were reported in other Indian studies by Chaturvedi et al, who found fever in all the patients.[8]

Hepatomegaly (36.7%) was observed less frequently in the present study as compared to other studies like Kuo et al, (75%).[9] In this study, highest frequencies of hepatomegaly among patients were observed in DHF group (50% of patients) followed by almost similar frequencies in DF and DSS group of patients. In 2012 dengue epidemic in Kolkata studied by Saha et al, Hepatomegaly was found in both DF and DHF but more common in DF.[10]

Hepatic tenderness was observed in 46.7% of total patients with highest among DSS group of patients (65.3%) comparable to Karoli et al, who reported in 63% of patients. 11 This disparity in frequency of Hepatomegaly (36.7%) and Hepatic Tenderness (46.7%) is probably because early hepatic involvement begins with RUQ pain and Tenderness before the development of manifest organomegaly and also probably due to RUQ tenderness manifested in patients having gall bladder wall thickening with or without acaculous cholecystitis in the present study.

Also, in the present study, Hypoalbuminemia was found in 52.5% of cases. Albumin levels was found to be least in DSS patients (80.7%) followed by DHF patients (73.3%). However, this difference is not statistically significant (p=0.13). Concluding these findings, higher levels of transaminases and alkaline phosphatase; and low levels of albumin were found in severely ill patients in the present study.

Early intervention with fluid therapy, continuous medical support and sequential laboratory exams. It is important to consider acute cases of hepatitis associated with Dengue because treatment of any of the classical symptoms may require the use of hepatotoxic drugs, such as acetaminophen.

In present study showed that, almost all the cases, 118 of 120 (98.3%) were completely recovered. The mortality was very low i.e., 2 case; both of whom belonged to the DSS category.

CONCLUSION

It provides long lasting and virtually permanent solution due to its non-dependence on hardware and implants. Cost of equipment and availability of surgical expertise are the only impediments to this promising treatment modality.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. 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(1):59-62.
2. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, et al. Refining the Global Spatial limits of Dengue virus transmission by Evidence-Based Consensus. PLoS Negl Trop Dis. 2012;6:e1760.
3. Martina BEE, Koraka P, OsteMunasinghe DR, Rajasuriya K. Hepatitis in Dengue fever. Ceylon Med J. 1967;12(4):222-23.
4. Wiwanitkit V. Liver dysfunction in Dengue infection, an analysis of previously published Thai cases. J Ayub Med Coll Abbottabad. 2007;19(1):10-12.
5. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, Moyes CL, Farlow AW, Scott TW, Hay SI. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis. 2012 Aug 7;6(8):e1760.
6. Sharma S, Sharma SK, Mohan A, Wadhwa J, Dar L, Thulkar S, et al. Clinical profile of dengue hemorrhagic fever in adults during 1996-outbreak in Delhi, India. Dengue Bull. 1998; 22:20-7.
7. 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 Diag Res. 2016 May;10(5):OC21.
8. Chaturvedi UC, Nagar R. Dengue and dengue haemorrhagic fever: Indian perspective. J Biosc. 2008 Nov 1;33(4):429-41.
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(3):265–70.
10. Saha AK, Maitra S, Hazra SC. Spectrum of hepatic dysfunction in 2012 dengue epidemic in Kolkata, West Bengal. Indian J Gastroenterol. 2013 Nov 1;32(6):400-3.
11. Karoli R, Fatima J, Siddiqi Z, Kazmi K, Sultania A. Clinical profile of dengue infection at a teaching hospital in North India. J Infect Dev Ctries. 2012;6(7):551-4.

Cite this article as: Rajaih VN, Thirunadhar R, Dasari N. A study of hepatobiliary manifestations in dengue viral infection. Int J Adv Med 2019;6:464-8.