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RESEARCH ARTICLE

A PROSPECTIVE STUDY OF EXTENT OF HEPATIC INVOLVEMENT IN PATIENTS OF DENGUE INFECTION PRESENTING AT A TERTIARY CARE HOSPITAL IN ROHILKHAND REGION

¹Mowar, A. B., ^{2*}Himanshu, V., ³Smita, G., ⁴Mirinda, J. and ⁵Ashita, M.

^{1,3}Department of General Medicine, SRMS-IMS, Bareilly

^{2,5}Department of Anaesthesia and Critical Care, SRMS-IMS, Bareilly

⁴Department of Pulmonary Medicine, SRMS-IMS, Bareilly

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ABSTRACT

Dengue is one of the most commonly occurring epidemic, particularly in rohilkhand region of Uttar Pradesh. The clinical manifestation ranges from being asymptomatic (in upto 80% patients) to mild illness (fever, thrombocytopenia, hepatic/renal dysfunction) to severe form (DHF/DSS – dengue haemorrhagic syndrome/dengue shock syndrome, DIC, MODS). Also it has been observed that the clinical and biochemical profile of dengue infection varies from epidemic to epidemic. We in this prospective study aim to study the epidemiological pattern, clinical profile and incidence and extent of hepatic complications in cases of Dengue fever in patients admitted at SRMS-IMS, Bareilly. We found that males were predominantly affected (73.3%). Most patients belonged to 15-45yr age group (85.5%). The incidence of DF, DHF, DSS were 64.4%, 26.7% and 8.9% respectively. Fever (100%) followed by headache (68.8%) was most common symptom. Malena (17.8%) followed by petechial rash (12.2%) and hematuria (3.3%) was most common hemorrhagic manifestation. Thrombocytopenia (platelet < 1lac/mm³) was present in 79% of patients. IgM antibody positive was seen in 40% patients and IgM was weekly positive in 15.5% patients. Raised bilirubin was present in 28.9% patients. Raised SGOT, raised SGPT, raised PT and raised APTT was present in 62.2%, 68.9%, 83.4% and 90% patients respectively. The most common finding on abdominal ultrasonography was ascitis (24.4%) followed by pleural effusion (18.9%), splenomegaly (14.4%) and hepatomegaly (6.6%).

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INTRODUCTION

Dengue viruses belong to Flaviviridae family & four serotypes (1 to 4) are reported. They are transmitted mainly by the *Aedes aegypti* mosquito. Dengue viruses produces clinical manifestations ranging from subclinical infection to a mild self limiting disease, the dengue fever (DF) and a severe disease that may be fatal (the dengue haemorrhagic fever/ dengue shock syndrome - DHF/DSS) (DENGUE, 2009). Dengue has been predominantly an urban disease but now has spread to rural areas of India as well. The factors considered responsible for resurgence of DF/DHF in India are unprecedented population growth, unplanned and uncontrolled urbanization, increased air travel, absence of an effective mosquito control programme and deterioration of Public Health infrastructure (Dash et al., 2005). Epidemic of dengue is a regular and recurrent occurrence in rohilkhand region affecting vast population and requiring admission to hospital and need for multiple blood product transfusions. It represents a major healthcare burden for people of this region.

The present study on epidemiology and clinical profile of dengue, is probably the first of its kind in rohilkhand region. We also intend to assess the impact of dengue infection on hepatic profile of patient.

MATERIALS AND METHODS

All the patients of either sex in the age group of 18-65yrs admitted in medicine department of SRMS IMS, Bareilly during the period from 01-01-2013 to 01-01-2014 who consented to be a part of our study were included. Patients with pre-existing liver disease (alcoholic liver disease or chronic liver disease), patients with HBV positive or HCV positive or malaria or widal positive and patients on antiplatelets or anticoagulants were excluded. Using the WHO criteria, patients were grouped into dengue fever (DF), dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). DF was defined as fever accompanied by constitutional symptoms, the only haemorrhagic manifestation being a positive tourniquet test. DHF was defined as spontaneous bleeding in addition to manifestations of DF and DSS was defined as circulatory collapse manifested by a rapid and weak pulse, narrowing of pulse pressure to < 20 mmHg, or

*Corresponding author: Himanshu, V.,
Department of Anaesthesia and Critical Care, SRMS-IMS, Bareilly

hypotension (Systolic Blood Pressure < 90 mm Hg) with a cold, clammy skin. A detailed history was taken in all patients and a detailed clinical examination was done. In addition, complete blood counts (haemoglobin, total leukocyte count and platelet count), liver function tests (total bilirubin – direct/indirect bilirubin, alanine aminotransferase [SGPT - ALT], aspartate aminotransferase [SGOT - AST]), coagulation profile (prothrombin time [PT] and activated partial thromboplastin time [APTT]), chest X-ray & abdominal ultrasonography were done. Patients sera were tested for IgM anti-dengue virus antibodies using a commercially available IgM capture ELISA assay.

OBSERVATIONS AND TABLE

1. SEX DISTRIBUTION

SEX	TOTAL (90)	%
MALE	66	73.3 %
FEMALE	24	26.7 %

2. AGE DISTRIBUTION :

AGE GROUP	TOTAL (90)	%
15 - 25 yrs	38	42.2%
26 - 35 yrs	18	20%
36 - 45 yrs	21	23.3%
46 - 55 yrs	07	7.9%
56 - 65 yrs	03	3.3%
66 - 75 yrs	03	3.3 %

3. SYMPTOMATOLOGY :

SYMPTOMS	TOTAL (90)	%
1.Fever	90	100%
2.Headache	62	68.8%
3.Bodyache/Joint Pain	56	62.2%
4.Petechial Rash	11	12.2%
5.Abdominal		
A.Pain Abdomen	31	34.4%
B.Vomiting	18	20%
C.Loose Stool	5	5.6%
D.Jaundice	2	2.2%
E.Malena	16	17.8%
6.Urinary		
A.Burning Micturition	11	12.2%
B.Hematuria	3	3.3%
7.High Coloured Urine	8	8.9%
8.Palpitation	1	1.1%

4. SYSTOLIC BLOOD PRESSURE :

SYSTOLIC BP	TOTAL (90)	%
< 90 mmHg	8	8.9%
90-100 mmHg	14	15.6%
100-110 mmHg	16	17.9%
110-120 mmHg	28	31.1%
120-140 mmHg	8	8.9%
140-150 mmHg	8	8.9%
>150 mmHg	8	8.9%

5. DIASTOLIC BLOOD PRESSURE

DIASTOLIC BP	TOTAL (90)	%
< 60 mmHg	8	8.9%
60-70 mmHg	42	46.6%
70-80 mmHg	34	37.7%
80-90 mmHg	6	6.8%
>90mmHg	0	0%

6. INCIDENCE OF DF/DHF/DSS :

	TOTAL (90)	%
1.DENGUE FEVER	58	64.4%
2.DENGUE HEMORRHAGIC FEVER	24	26.7%
3.DENGUE SHOCK SYNDROME	8	8.9%

7. PER ABDOMEN FINDING :

CLINICAL FINDING	TOTAL (90)	%
1.Finding Present	30	33.3%
A.Hepatomegaly	13	14.4%
B.Splenomegaly	4	4.4%
C.Hepatosplenomegaly	9	10%
D.Ascites	4	4.4%
2.Finding Absent	60	66.7%

8. HEMOGLOBIN :

HEMOGLOBIN	TOTAL	%
1.<6 g/dl	1	1.1%
2.6-8 g/dl	2	2.2%
3.8-10 g/dl	6	6.7%
4.10-12 g/dl	25	27.7%
5.12-14 g/dl	45	50%
6.14-16 g/dl	11	12.3%

9. TOTAL LEUCOCYTE COUNT :

TLC Count	TOTAL	%
1.<1500/mm ³	2	2.2%
2.1500 - 3000/ mm ³	24	26.6%
3.3000 - 4000/ mm ³	14	15.4%
4.4000 - 11000/ mm ³	40	44.4%
5.11000 - 15000/ mm ³	9	10%
6.>15000/ mm ³	1	1.1%

10. PLATELETS :

Platelet count	TOTAL	%
1.<10,000/mm ³	4	4.5%
2.10,000 - 20,000/mm ³	7	7.8%
3.20,000 - 50,000/mm ³	36	40%
4.50,000 - 1 lac/mm ³	24	26.7%
5.1-1.5 lac/mm ³	14	15.5%
6.>1.5 lac/mm ³	5	5.6%

11. DENGUE SEROLOGY (ELISA – 7 to 14 days) :

ELISA	TOTAL	%
1.IgM +	36	40%
2.IgM weakly +	14	15.5%
3.IgM -	40	44.5%

12. TOTAL BILIRUBIN :

Total Bilirubin	Total (90)	%
1.< 1.2	64	71.1%
2.1.2-2	21	23.3%
3.> 2	5	5.6%

13. DIRECT BILIRUBIN :

Direct Bilirubin	Total (90)	%
1.< 0.2	61	67.8%
2.0.2-1	26	28.9%
3.> 1	3	3.3%

14. INDIRECT BILIRUBIN :

Indirect bilirubin	Total (90)	%
1.<0.8	75	83.3%
2.0.8-1.5	13	14.5%
3.>1.5	2	2.2%

15. SGOT (AST) :

SGOT	Total (90)	%
1.Normal	25	27.8%
2.Mildly increased (1- 2times N)	18	20%
3.Moderately increased (2 - 5 times N)	22	24.4%
4.Severely increased (> 5 times N)	25	27.8%

16. SGPT (ALT) :

SGPT	Total (90)	%
1.Normal	28	31.1%
2.Mildly increased (1- 2times N)	23	25.5%
3.Moderately increased (2 - 5times N)	24	26.7%
4.Severely increased (> 5times N)	15	16.7%

17. PROTHROMBIN TIME :

PT	Total (90)	%
1.Normal (13s)	15	16.6%
2.Mildly raised (1-2times N)	69	76.7%
3.Moderately raised (2-5 times N)	6	6.7%
4.Severely raised (>5times N)	0	0%

18. APTT :

APTT	Total (90)	%
1.Normal (25s)	9	10%
2.Mildly raised (1- 2times N)	50	55.5%
3.Moderately raised (2-5times N)	31	34.5%
4.Severely raised (>5times N)	0	0

19. USG (WHOLE ABDOMEN) FINDINGS :

USG (W/A) Findings	Total (90)	%
1.Hepatomegaly	6	6.6%
2.Splenomegaly	13	14.4%
3.Ascitis	22	24.4%
4.Pleural Effusion	17	18.9%
5.Fatty Liver	5	5.6%
6.Hepatosplenomegaly	4	4.4%
7.Prostatomegaly	3	3.3%
8.WNL	20	22.2%

20. OUTCOME :

OUTCOME	Number	%
1.SURVIVED	87	96.7%
2.EXPIRED	3	3.3%

DISCUSSION

From Table 1, we observe that males (73.3%) were predominantly affected with dengue. The ratio of female: male was 1:2.7. From Table 2, we can see that majority of the patients affected belonged to 15-45 yr age group (85.5%). The most commonly involved age group was 15-25yr (42.2%) followed by 36-45yrs (23.3%) and 26-35yrs (20%). The least

commonly involved age group was elderly age group. From the Table 3, almost all the patients had fever (100%). Other major complaints of the patients were headache (68.8%) and bodyache (62.2%). Abdominal complaints were predominantly pain abdomen (34.4%), vomiting (20%) and malena (17.8%). Urinary symptoms were burning micturition (12.2%) and high coloured urine (8.9%). Farhan Fazal, Sangram Biradar (2015) in there study on Clinical and Laboratory Profile of Dengue Fever. Out of 100 cases in this study, all the cases had fever (100%). Other common symptoms noted were myalgia (61%), joint pain (54%), headache (66%), vomiting (55%), pain abdomen (48%), rash (41%), hepatomegaly (20%), bleeding (21%) and shock (8%) (Farhan Fazal and Sangram Biradar, 2015). Jain *et al.* in there study noted generalized body ache in 84%, headache in 77%, high grade fever in 73%, joint pain in 42%, symptomatic bleed in 32%, malaise in 27% and apparent jaundice in 15% of the dengue positive cases. Atypical complication seen in dengue fever was ascites in 10% and pleural effusion in 32% (Jain *et al.*, 2011).

The hemorrhagic manifestations were mainly malena (17.8%) followed by petechial rash (12.2%) and hematuria (3.3%). Respiratory and cardiovascular manifestations were rarely complained off and constituted only 3.3 % and 1.1% respectively. Jain *et al.* in there study of, found bleeding manifestations occurred in 32% cases (20) and out of which 65% was presented as having malena (13 patients), 20% as hematuria (4 patients), 10% as epistaxis (2 patients) and remaining 5% as hematemesis (1patient)⁴. Chandrakanta *et al.* (2008) reported the incidence of bleeding in dengue fever to be 38.8% out of which 23.7% cases had gastrointestinal tract bleeding (61%) (Chandrakanta *et al.*, 2008). From the Table 4, we observe that shock was present in 8 out of 90 patients (8.9%) and these constituted our patients with dengue shock syndrome. From the Table 5, we observe that diastolic BP < 60 mm Hg was present in 8 out of 90 patients (8.9%). All others had diastolic blood pressure within range of 60-90 mm Hg (91.1%).

From the Table 6, it is evident that the incidence of dengue fever was maximum with 64.4% (58 out of 90) followed by dengue hemorrhagic fever (26.7%) and dengue shock syndrome (8.9%). Farhan Fazal, Sangram Biradar (2015) in there study on Clinical and Laboratory Profile of Dengue Fever. Out of 100 cases in this study 70 cases belongs to DF, 23 cases to DHF and 7 cases to DSS based on WHO criteria³. From the Table 7, we can make out that the most common per abdomen finding clinically was hepatomegaly (14.4%) followed by hepatosplenomegaly (10%). No per abdomen finding was present in 60% of the patients. From the table 8, we observe that anemia (Hb < 10g/dl) was present in 10% of the patients. Severe anemia (Hb < 6g/dl) was found in 1 case. From table 9, we observe that TLC was within normal limits (4,000-11,000/mm³) in 44.4% of the cases. Leukopenia (< 4,000/mm³) was found in 44.4% patients and leukocytosis present in 11.1% patients. In there study observed the incidence of leucopenia in 31% while leucocytosis was found in 17% only (Jain *et al.*, 2011). Lin *et al.* (1989) reported the incidence of leucopenia in 76% of there patients. From the table 10, we found that thrombocytopenia (platelet count < 1lac/mm³) was present in 79% of cases.

The incidence of platelet count $<10,000/\text{mm}^3$ was found in 4 patients (4.5%). Majority of patients (40%) had platelets in $20,000-50,000/\text{mm}^3$ followed by $0.5-1 \text{ lac}/\text{mm}^3$ (26.7%). Chandrakanta et al. (2008) reported the incidence of thrombocytopenia to be 60%. Jain et al. (2011) in their study noted the incidence of thrombocytopenia was found to be 92%. Farhan Fazal, Sangram Biradar (2015) in their study on Clinical and Laboratory Profile of Dengue Fever. Out of 100 cases in this study, low platelet count of less than 100,000/cu mm according to WHO criteria was present in 73% patients. From the above Table 11, it is evident that IgM antibody was positive in 40% of the patients. IgM weakly + was seen in 15.5% of patients. From table 12, we can observe that normal bilirubin was present in 71.1% of patients. Mildly increased bilirubin (1.2 - 2) was seen in 23.3% patients. Only 5 patients (5.6%) had total bilirubin $> 2 \text{ mg/dl}$.

Ludhiana reported in 2006, the incidence of jaundice in dengue fever to be 19.5% (Chhina et al., 2008). While Mohan et al. (2000) reported the incidence of jaundice in dengue fever to be 25%. Jain et al. (2011) found that liver dysfunction was present in the form of jaundice in 15% cases; of which one third cases were of direct hyperbilirubinemia and two third were those of indirect hyperbilirubinemia. From table 13, we can observe that normal direct bilirubin was present in 67.8% of patients. Mildly increased direct bilirubin (0.2 - 1) was seen in 28.9% patients. Only 3 patients (3.3%) had total bilirubin $> 1 \text{ mg/dl}$. From table 14, we can observe that normal indirect bilirubin was present in 83.3% of patients. Mildly increased indirect bilirubin (0.8 - 1.5) was seen in 14.5% patients. Only 2 patients (2.2%) had indirect bilirubin $> 1.5 \text{ mg/dl}$. From Table 15, SGOT was normal in 27.8% patients. Mildly increased (1-2times normal), moderately increased (2-5times normal) and severely increased (> 5 times normal) SGOT was noted in 20%, 24.4% and 27.8% of the patients. From Table 16, SGPT was normal in 31.1% patients. Mildly increased (1-2times normal), moderately increased (2-5times normal) and severely increased (> 5 times normal) SGPT was noted in 25.5%, 26.7% and 16.7% of the patients.

Jain et al reported elevation of serum transaminases (SGOT and SGPT) in 68 and 71% of the cases. Severe degree of hepatic dysfunction that is SGOT and SGPT $> 200 \text{ IU/L}$ were present in 13-16% of total dengue positive cases (Jain et al., 2011). Chhina et al. (2008) described the incidence of rise in SGOT and SGPT to be 97.7 and 93.9% respectively. Souza et al. (2004) observed SGOT and SGPT were deranged only in 63.4 and 45% patients respectively. Mohan et al. (2000) reported the incidence of rise in serum transaminases to be between 81-87%. Farhan Fazal, Sangram Biradar (2015) in their study on Clinical and Laboratory Profile of Dengue Fever. Out of 100 cases in this study, deranged liver function test was seen in 26 patients. From Table 17, PT was normal in 16.6% patients. Mildly increased (1-2 times normal), moderately increased (2-5 times normal) and severely increased (>5 times normal) PT was noted in 76.7%, 6.7% and 0% of the patients. From Table 18, APTT was normal in 10% patients. Mildly increased (1-2 times normal), moderately increased (2-5 times normal) and severely increased (> 5 times normal) APTT was noted in 55.5%, 34.5% and 0% of the patients.

From Table 19, the most common ultrasound finding was ascitis which was present in 24.4% of the patients followed by splenomegaly (14.4%), hepatomegaly (6.6%). Other major finding was of pleural effusion (18.9%). Jain et al in their study noted the incidence of pleural effusion as 32% while that of ascites as 10% (Jain et al., 2011). Thulkar et al. (1999) reported the incidence of pleural effusion and ascites in grade III DHF to be 53 and 15%, respectively. From Table 20, most of our patients survived (86.7%). Only 3 (3.3%) patients expired.

Conclusion

We in this first ever study of its kind in rohilkhand region on epidemiology and clinical profile of dengue fever found that males were predominantly affected. The most common age group affected was 15-45yrs. The most common complain was fever followed by headache. Liver involvement was very common as seen by jaundice in 28.9% of patients. Derangement in liver enzymes was also commonly noted with elevated SGOT & SGPT seen in 62.2% and 68.9% patients respectively. Severely elevated SGOT & SGPT was seen in 27.8% and 16.7% patients. Deranged coagulation profile was also seen with elevated PT & APTT in 83.4% & 90% patients but mostly the elevation was only mild (76.7% & 53.5%). The mortality rate was 3.3% and was seen in those patients who presented late with multiorgan dysfunction. Further studies in future are needed to study the effect of dengue infection on liver profile and evaluate its impact on outcome.

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