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A study of various hepatic manifestations in dengue fever and their correlation with severity of dengue fever

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ABSTRACT

Background: Hepatic involvement in Dengue is known with protean of manifestations ranging from hepatomegaly, elevated liver enzymes to fulminant hepatic failure. Aim of the study was to study the hepatic manifestations in children with dengue illness.

Methods: This is a prospective Study with 60 Patients hospitalized with Dengue infection (Seropositive for Dengue). Dengue Seropositive patients are selected and examined for Hepatomegaly and Jaundice and subjected to complete blood count and Liver function tests were analysed.

Results: Of 60 serologically confirmed cases hospitalized with dengue, were classified into (i)(DF), (ii) DHF I (iii) DHF II (iv) DHF III and (v) DHF IV. In our study, upon 60 seropositive cases were reported at our hospital during the study period of which 18 were DF, 12 were DHF I, 15 were DHFII, 8 were DHF III and 7 were DHF IV respectively. The Hematocrit levels were raised 20% from the baseline in four classes of Dengue and not raised in DF. Most commonly occurred in age group of 5-7 years. Hepatomegaly was the commonest clinical sign seen. Thrombocytopenia was seen in 88% of all cases. Serum total bilirubin was raised in 10% of subjects with severe dengue infection in DHF III and DHF IV. Serum SGOT and SGPT was raised in 63.3% and 56.7% of patients with dengue of all classes including DF respectively. Thrombocytopenia occurred in 75% of patients with dengue fever, 98% with warning signs and 100% in severe dengue.

Conclusions: In developing country like India, incidence of dengue outbreaks is increasing. Hepatic involvement of varying degrees have been reported. As hepatic dysfunction in dengue is transient and reversible, early identification of the same would help to reduce life threatening complications. The role of hepato protective drugs in reducing morbidity and mortality should be analysed by further studies.

Keywords: Dengue infection, Hepatomegaly, Haematocrit, Thrombocytopenia

INTRODUCTION

Dengue is the most important of the arboviral infections of humans. Global incidence of Dengue fever (DF) and Dengue hemorrhagic fever (DHF) has increased dramatically in the recent decades. In India, epidemics are becoming more frequent. Involvement of younger age group and increase in the frequency of epidemics are indicators of higher incidence of infection. If untreated,

mortality from complications of DF is as high as 20%, whereas if recognized early and managed properly, mortality is less than 1%. Early diagnosis is essential and clinical suspicion is based on the frequency of symptoms in the population. Additional data about the disease lead to implementation or alteration of public health programs. Thus, there is a need to keep track of various manifestations and gather descriptive data of the disease in each epidemic. There are at least 4 distinct antigenic

types of dengue virus DEN 1, DEN 2, DEN 3, DEN 4 which is a member of family Flaviviridae.

Factors for dengue's spread include uncontrolled population growth, uncontrolled urbanization, overcrowding, inadequate health facilities, increased travel to epidemic areas, poor vector control, climate change and lack of awareness among people. Dengue infections are known to present with a diverse clinical spectrum, ranging from asymptomatic illness to fatal outcome.

Unusual manifestations have become more common. These include encephalitis, Guillian-Barre Syndrome, dengue hepatitis, myocarditis and acute respiratory distress syndrome. Hepatic dysfunction varies from mild injury with elevation of transaminase activity, hepatomegaly to severe damage with jaundice and fulminant hepatic failure. The severity of hepatic dysfunction varies with clinical presentation. The cause for hepatic dysfunction may be due to inadequate perfusion, metabolic acidosis and disseminated intravascular coagulation.

This in turn leads to ischaemia causing severe hepatic dysfunction. Presence of fever, jaundice, hepatomegaly in endemic areas should arouse the suspicion of dengue hepatitis. Awareness of these manifestations of hepatic involvement in dengue may be helpful in arriving at early diagnosis and avoiding morbidity and mortality. However only less number of studies have been reported regarding hepatic dysfunction in dengue. Hence it is with this objective this present study has been undertaken.

Aim of the study was to study the hepatic manifestations in children with dengue illness.

METHODS

This prospective study was done on cases of DF/DHF reporting at department of Pediatrics, Narayana Medical College, Nellore between January 2018 and June 2019. A total of 100 children identified as probable cases by clinical suspicion (any acute febrile illness with one of the following: myalgia, headache, retro-orbital pain, bleeding, altered sensorium, shock or low platelet count) were registered in the study and detailed clinical history was taken.

For all cases, the rapid IgM-IgG and ELISA test, which has become the standard for serological diagnosis of dengue fever was done. Children positive for IgM alone or both IgM and IgG were followed up for clinical profile.

Inclusion criteria

Children less than 15 years of age, dengue IgM positive were included.

Exclusion criteria

Cases of typhoid and leptospirosis were excluded by serological tests. Cases where malaria parasite was seen in peripheral smear were also excluded.

The number of cases included based on the above criteria was 60, who satisfied WHO criteria for the diagnosis of DHF but expired before serodiagnosis. Children who were dengue seropositive were classified on basis of WHO criteria3 as follows: (i) DF; (ii) DHF I; (iii) DHF II; (iv) DHF III and (v) DHF IV.

Laboratory investigations carried out in these patients included hemoglobin, total and differential leukocyte count, hematocrit, platelet count, liver function tests and urine examination. Complete blood counts including hematocrit were repeated daily during the acute phase of the illness and chest X-ray was taken to demonstrate pleural effusion in all cases.

The clinical manifestations and laboratory findings of each group of illness were compared using chi-square or fisher's exact test for proportions and analysis of variance (ANOVA) for continuous data. The SPSS version 20 for windows used for analysis. Cases were managed according to the WHO protocol and outcome was analyzed.

RESULTS

Statistically 60 seropositive cases were reported at our hospital during the study period of which 18 were DF, 12 were DHF I, 15 were DHFII, 8 were DHF III and 7 were DHF IV. The age group of the affected children was between 1 year to 12 years (5.9±3.9) (Table 1), with a modal age group of 5-6 years. DSS occurred at lower age group than other complications of dengue fever.

Most common presentations were fever (100%), vomiting (91.5%), bleeding manifestations (45%), myalgia (66.6%), Headache (41%), retro-orbital pain (20%), abdominal pain (36.6%), and Jaundice (10%). Fever, vomiting and body pain was the commonest combination of symptoms on presentation. Fever was high grade, intermittent, and associated with rigors.

On clinical examination the most consistent finding was hepatomegaly. Hepatomegaly was seen in 66.6% of patients. Other findings included epigastric tenderness in 16.6%. Laboratory investigations revealed a large proportion of mildly anemic patients among our cases. The mean hematocrit levels were observed as 32.1. Platelet counts were also significantly lower in DHF III and DHF IV group.

Liver enzymes were markedly elevated (SGOT- 56.7% and SGPT- 63.3%) of the children who were dengue seropositive (Table 2).

Table 1: Symptoms and signs of dengue cases.

Feature		Dengue infection	DF	DHF I	DHF II	DHF III	DHF IV	p value
Number of cases		60	18	12	15	8	7	0.91
Mean age, y(SD)		5.9±3.9	6.9 ± 5.2	6.5±3.5	7.2 ± 4.2	5.2 ± 2.2		-
Gender	Male	40(60.6%)	15	8	7	5	5	0.902
	Female	20(40%)	3	4	8	3	2	0.924
Symptoms	Fever, no. (%)	60(100%)	18	12	15	10	5	0.922
	Mean duration of fever days:(SD)	5.2±1.9	4.2±1.9	5.5±2.7	4.9±1.2	4.0±2.0	-	-
	Vomiting, no.	55(91.5%)	12	15	15	8	5	0.935
	Jaundice	6(10%)	-	-	-	3	3	-
	Body pain, no.	40(66.6%)	18	10	12	-	-	0.793
	Headache, no.	25(41.6%)	10	10	5	-	-	0.894
	Drowsiness, no	10(16.6%)	-	-	-	6	4	-
	Abdominal pain, no	22(36.6%)	6	9	4	3	-	0.899
	Retro-orbital pain, no.	12(20%)	4	6	1	1	-	0.752
	Bleeding manifestations	27(45%)	-	-	14	7	-	0.825
Signs	Hepatomegaly, no	40(66.6%)	8	12	12	5	3	0.865
	Epigastric tenderness	10(16.6%)	2	4	3	1	-	-
	Shock, no.	10(16.6%)	-	-	-	3	7	-
	Rashes, no.	15(25%)	5	3	2	3	2	0.978

Table 2: Investigations and management of dengue seropositive cases.

Feature	Dengue infection	DF	DHF I	DHF II	DHF III	DHF IV	p value
Mean hemoglobin, g/dL	10.5±1.1	10.4 ± 0.4	11.0 ± 0.4	10.5 ± 1.2	11.3±1.5	11.5 ± 2.8	0.37
Bilirubin (mg/dl)	0.68 ± 0.45	0.59 ± 0.45	0.65 ± 0.52	0.78 ± 0.6	1.08 ± 0.89	1.2 ± 0.9	0.05
Haematocrit, mean (SD)	32.1±2.9	31.9±1.9	32.2±2.1	34.9±4.8	36.4±2.2	37.5±2.5	0.01
Platelet count cells/ cumm, mean	89559	96440	108712	60919	35250	25450	0.004
Platelet count >100000/cumm, no (%)	15	5	5	3	1	1	0.45
Platelet count 50001- 100000/cumm, no (%)	25(41.6%)	6	10	4	3	2	0.12
Platelet count less than 50000/cumm, no (%)	20(33.3%	10	4	2	3	1	0.35
AST(SGOT) >50 IU/L, no	38(63.3%)	10	12	8	6	2	0.19
ALT >50 IU/L, no. (SGPT)	34(56.7%)	10	8	8	6	2	0.33
S. Alkaline Phosphatase >200 IU/L, no	20(33.3%)	3	4	2	1	-	0.21

DISCUSSION

Dengue infection is one of the most common mosquito borne disease of the world. The age group affected by dengue fever and its complications is lower in this study compared to previous Indian studies. This supports the view that endemicity of dengue fever is increasing in India. Among the subgroups of dengue there is a distinct tendency for DSS to occur at lower age.⁴⁻⁷

Fever and vomiting were the most frequent symptoms and hepatomegaly was the most frequent sign in these

children, as observed in earlier studies.^{8,9} Vomiting and retro-orbital pain are slightly more common in DSS and DHF II group than the others, though the difference is not statistically significant. Hepatomegaly is a less frequent finding among adults as reported in Philippines and Delhi.^{10,11} We found hepatomegaly to be more in DHF II and DSS groups than others, in contrast to previous studies.¹² Hematemesis is the most common bleeding manifestation in our cases as reported in other studies on Indian children.^{5,9,12}

There is a low proportion of children with evidence for hemoconcentration in our study group. If this was not taken as an essential criteria for DHF as in Aggarwal et al, nine more cases could have been included in DHF group and three more in DSS group.⁹ The overall mean hematocrit value in the non DSS group was only 36%.

Other findings of the laboratory was the rise in serum levels of liver enzymes (LFTs) as reported in various studies. 4,10,12 The high incidence of vomiting, hepatomegaly and elevated liver enzymes can serve as markers for suspicion of dengue during an epidemic. Subclinical hepatitis may contribute to the abdominal pain and vomiting in these children. Higher is the level of liver enzymes, poorer is the prognosis SGPT is primarily associated with hepatocytes and is raised due to liver damage. SGPT is found in cardiac and skeletal muscle, hepatocytes, renal and brain tissue and is raised due to damage to these structures. Liver enzymes can be a potential marker for dengue during early febrile phase.

Serum SGOT was raised in 63.3 % of patients with dengue. When compared between the groups, rise in SGPT occurred in 56.7% of patients with DF, 98% with warning signs and 100% in severe dengue.

Study by M Narayanan et al, SrivenuItha et al, and Brij Mohan et al, also observed deranged liver enzyme levels. ¹³⁻¹⁵ Souza et al, reported elevation of SGOT in 63.4% cases and Kuo et al, observed rise in SGOT in 56.7% of cases. ¹¹

When compared between the groups, rise in SGPT occurred in almost patients with a study by M Narayanan et al, SrivenuItha et al, and Brij Mohan et al, also observed elevation in SGPT. Luiz Jose Souza et al, found rise in ALT in 45% of cases. MMA Faridi et al, reported 64.6% rise in ALT levels. Patients with severe dengue had higher level of enzymes.

When compared between the groups, rise in ALP occurred in 33.3% of patients with dengue fever of all types.

Jaundice is associated with poor prognosis. It is associated with fulminant hepatic failure. Serum total bilirubin was raised in 10% of subjects with DHF III and DHF IV. 18

Thrombocytopenia occurred in 75% of patients with dengue fever, 98% with warning signs and 100% in severe dengue.

Of 60 seropositive cases were reported at our hospital during the study period of which 18 were DF, 12 were DHF I, 15 were DHFII, 8 were DHF III and 7 were DHF IV. No mortality was observed in this study. The mortality in our series was comparable with other Indian studies.^{5,9,19}

To conclude, this study shows that DF is becoming more prevalent in India. In children, importance should be given to symptoms like fever, vomiting, bleeding and musculoskeletal pain. If these are associated with hepatomegaly and elevated liver enzymes in context of a low platelet count, a strong possibility of DF.

CONCLUSION

In developing country like India, incidence of dengue outbreaks is increasing. Hepatic involvement of varying degrees have been reported. As hepatic dysfunction in dengue is transient and reversible, early identification of the same would help to reduce life threatening complications. This can help to reduce the severity of dengue infection. The role of hepato protective drugs in reducing morbidity and mortality should be analysed by further studies.

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