

A Study on Clinical Correlation and Outcome of Dengue Fever with Hepatic Dysfunction in Children

Dr. Z. Havila Monalisa

Abstract: ***Objective:** To study hepatic dysfunction in childhood dengue infection and to study clinical co - relation like severity, clinical features, and outcome. **Methods:** 70 Dengue seropositive patients were admitted during the study period and examined for hepatomegaly and jaundice and subjected to complete blood count, liver function tests, ultrasound abdomen, PT, APTT, HBsAg, HCV, widal and analysed. **Results:** All patients presented with fever, most commonly occurred in age group of 5 to 7years, hepatomegaly was the commonest clinical sign seen, thrombocytopenia was seen in 88% of cases, Serum total bilirubin was raised in 10% of subjects with severe dengue infection. Serum SGOT was raised in 72.8 % of patients with dengue. When compared between the groups, rise in SGOT occurred in 58.6%, 78.8 % and 100% of patients with dengue without warning signs, with warning signs and in severe dengue respectively. SGPT was raised in 58% of patients with dengue infection. When compared between the groups, rise in SGPT occurred in 44.8%, 66.6% and 75% of patients with dengue without warning signs, with warning signs and in severe dengue respectively. Prothrombintime was raised in 11% of patients with dengue infection. When compared between the groups, rise in PT occurred in 9% with warning signs and 62.5% in severe dengue. Activated Partial Thromboplastin Time was raised in 11% of patients with dengue infection. When compared between the groups, rise in APTT occurred in 9% of patients with warning signs and 62.5% in severe dengue. Serum total protein was reduced in 12% of patients with dengue infection. When compared between the groups fall in serum protein occurred in 15% with warning signs and 50% in severe dengue. Serum Albumin was reduced in 3% of patients with dengue infection. In our study 2 cases suffering from severe dengue expired, in which the enzyme levels were highly elevated. **Conclusion:** Significant rise of liver enzymes helps in recognition of severe forms of dengue infection. As hepatic dysfunction in Dengue is transient and reversible, early identification of the same should help to reduce life threatening complications. Serial liver function tests can help in early detection of fulminant hepatic failure. This can help to reduce the morbidity and mortality.*

Keywords: Hepatic dysfunction, Dengue infection, Prothrombintime

1. Introduction

Dengue infection is a major public health problem in most of the tropical areas of the world with the greatest risk occurring in Indian sub - continent and other South East Asian countries. [1]. Dengue is the most common arbo viral disease transmitted globally. There are atleast 4 distinct antigenic types of dengue virus DEN 1, DEN 2, DEN 3, DEN 4 which is a member of family Flaviviridae.

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, Guillain - 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 cause for hepatic dysfunction may be due to inadequate perfusion, metabolic acidosis and disseminated intravascular coagulation. This in turn leads to ischemia causing severe hepatic dysfunction. [2]

In recent studies from India and Thailand, dengue infection was the most important cause of acute hepatic failure in children contributing to 18.5% and 34.3% of the cases respectively [3, 4].

Early recognition and prompt initiation of appropriate supportive treatment can decrease the morbidity and mortality. Most data reported on abnormal liver functions in dengue are retrospective [5 - 7]. Therefore this cross sectional study with new data was undertaken to assess the spectrum of hepatic involvement in children with dengue infection at a tertiary care center.

2. Materials and Methods

This prospective observational study was conducted in Department of Paediatrics, Government General Hospital, Ananthapur from September to November 2021. All serologically proven cases of dengue were included in the study. Any child with associated infections known to cause hepatic involvement like malaria, enteric fever, hepatitis, leptospirosis were excluded. Dengue seropositive patients are selected and examined clinically for hepatomegaly and jaundice and subjected to complete blood count, liver function tests, ultrasound abdomen, PT, APTT, Widal, HBsAg, HCV and analysed.

3. Results

This study was conducted on 70 serologically IgM dengue antibody positive cases between age group 2 months to 12 years of age fulfilling the WHO criteria for the diagnosis of dengue infection.

Of the 70 patients hospitalized with dengue infection, 29 were classified as having Dengue without warning signs, 33 were with Warning Signs and 8 were suffering from Severe Dengue.

Dengue mainly affected children of age group 5 to 7 years i. e. in 45% among 70. Dengue affected male and female children almost equally.

Table 1: Comparison of changes in Liver Function Tests and Platelet Count

	Normal		Decreased		Increased		Total
	N	%	N	%	N	%	
PLATELET	9	12	61	88	-	-	70
SBR - TOTAL	63	90	-	-	7	10	70
SGOT	18	26	-	-	52	74	70
SGPT	30	42	-	-	40	58	70
ALP	50	72	-	-	20	28	70
PT	62	89	-	-	8	11	70
APTT	62	89	-	-	8	11	70
S. PROTEIN	61	88	9	12	-	-	70
ALBUMIN	68	97	2	3	-	-	70

Hepatomegaly was seen in 55% of patients. When compared between the groups, 90% in patients with warning signs and 100% in seen severe dengue.

Table 2: Comparison between groups with respect to hepatomegaly

Liver span	Diagnosis						Chi square	p
	D - WS		D+WS		SD			
	N	%	N	%	N	%		
Normal	29	100	3	10	-	-	88.65	0.001**
Increased	-	-	30	90	8	100		
Total	29	100	33	100	8	100		

** Significant (Highly significant)

Thrombocytopenia occurred in 73% of patients with dengue without warning signs, 97% with warning signs and 100% in severe dengue

Table 3: Comparison between groups with respect to platelet count

Platelet	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	8	27.6	1	3.1	-	-	9	13.85	0.001**
Decreased	21	72.4	32	96.9	8	100.0	61		
Total	29	100.0	33	100.0	8	100.0	70	-	-

** Significant (Highly significant)

In this study, serum total bilirubin was raised in 10% of subjects with severe dengue infection.

Table 4: Comparison between groups with respect to Serum Bilirubin

SBR – Total	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	29	100.0	33	100.0	1	9.1	63	89.90	< 0.001**
Increased	-	-	-	-	7	90.9	7		
Total	29	100.0	33	100.0	8	100.0	70		

** Significant (Highly significant)

Serum SGOT was raised in 73 % of patients with dengue. When compared between the groups, rise in SGOT occurred in 58.6% of patients with dengue without warning signs, 78.8% with warning signs and 100% in severe dengue.

Table 5: Comparison between groups with respect to serum SGOT:

SGOT	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	12	41.4	7	21.2	-	-	19	9.59	0.008**
Increased	17	58.6	26	78.8	8	100.0	51		
Total	29	100.0	33	100.0	8	100.0	70		

** Significant (Highly significant)

- SGPT was raised in 58% of patients with dengue infection. When compared between the groups, rise in SGPT occurred in 44.8% of patients with dengue without warning signs, 66.6% with warning signs and 75% in severe dengue.
- Serum Alkaline Phosphatase was raised in 28% of patients with dengue infection. When compared between the groups, rise in ALP occurred in 10.3% of patients with dengue without warning signs, 33.3% with warning signs and 75% in severe dengue.

Table 6: Comparison between groups with respect to serum SGPT

SGPT	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	16	55.2	11	33.4	2	25	29	7.74	0.021*
Increased	13	44.8	22	66.6	6	75	41		
Total	29	100.0	33	100.0	8	100.0	70		

** Significant (Highly significant)

Table 7: Comparison between Groups with Respect to Serum Alkaline Phosphatase

ALP	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	26	89.7	22	66.7	2	25	50	23.27	< 0.001**
Increased	3	10.3	11	33.3	6	75	20		
Total	29	100.0	33	100.0	8	100.0	70		

** Significant (Highly significant)

- Prothrombin time was raised in 11% of patients with dengue infection. When compared between the groups, rise in PT occurred in 9% with warning signs and 62.5% in severe dengue.

Table 8: Comparison between groups with respect to prothrombin time

PT	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	29	100.0	30	91	3	37.5	62	49.03	< 0.001**
Increased	-	-	3	9	5	62.5	8		
Total	29	100.0	33	100.0	8	100.0	70		

** Significant (Highly significant)

- Activated Partial Thromboplastin Time was raised in 11% of patients with dengue infection. When compared between the groups, rise in APTT occurred in 9% of patients with warning signs and 62.5% in severe dengue.

Table 9: Comparison between Groups with respect to APTT

APTT	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	29	100.0	30	91	3	37.5	62	49.03	< 0.001**
Increased	-	-	3	9	5	62.5	8		
Total	29	100.0	33	100.0	8	100.0	70		

** Significant (Highly significant)

- Serum total protein was reduced in 12% of patients with dengue infection. When compared between the groups fall in serum protein occurred in 15% with warning signs and 50% in severe dengue. Serum Albumin was reduced in 3% of patients with dengue infection. When compared between the groups, fall in serum albumin occurred in 4.3% with warning signs and 9% with severe dengue.

Table 10: Comparison between groups with respect to serum total protein:

S. Protein	Diagnosis						Total	Chi square	p
	D - WS		D+WS		SD				
	N	%	N	%	N	%			
Normal	29	100.0	28	85	4	50	61	24.61	< 0.001**
Decreased	-	-	5	15	4	50	9		
Total	29	100.0	33	100.0	8	100.0	70		

** Significant at 1 % (Highly significant)

In our study 2 cases suffering from severe dengue expired. In these two cases, the enzymes levels were very high.

bilirubin was raised in 10% of subjects with severe dengue infection.

Table 11: Outcome

Outcome	Diagnosis			Total	Chi square	P
	D - WS	D+WS	SD			
Expired	-	-	2	2	16.51	< 0.001**
Recovered	29	33	6	68		
Total	29	33	8	70		

** Significant (Highly significant)

4. Discussion

Dengue infection is one of the most common mosquito borne disease of the world. The causative agent is dengue virus, mainly of four serotypes DEN 1, DEN 2, DEN 3, DEN 4. It has a protean of manifestations ranging from asymptomatic to life threatening complications. Hepatomegaly in dengue occurred more commonly in patients with severe dengue and those with warning signs. In present study, 90% with warning signs and 100% with severe dengue had hepatomegaly. Thus hepatomegaly may be used as a tool to indicate the severity of the disease.

Hypoalbuminemia may be due to liver injury and capillary leakage. In current study 12% had hypoalbuminemia. In another study by Jagadishwar et. al, hypoalbuminemia was observed in 66% of the cases [8].

Serum SGOT was raised in 72.8 % of patients with dengue. When compared between the groups, rise in SGOT occurred in 58.6% of patients with dengue without warning signs, 78.8% with warning signs and 100% in severe dengue. Elevation of SGOT was more compared to SGPT in the present study and similar observations was made by others also [9, 10].

SGPT was raised in 58% of patients with dengue infection. When compared between the groups, rise in SGPT occurred in 44.8% of patients with dengue without warning signs, 66.6% with warning signs and 75% in severe dengue. SGOT rise more than SGPT in dengue may be due to involvement of myocyte. This differs from the pattern seen in viral hepatitis, in which SGPT levels are usually higher than or equal to SGOT levels.

Jaundice is associated with poor prognosis. It is associated with fulminant hepatic failure. In this study, serum total

Prothrombin time was raised in 11% of patients with dengue

infection. When compared between the groups, rise in PT occurred in 9% with warning signs and 62.5% in severe dengue. Wong et al reported low globulin level in 14.2% and low albumin level in 16.5%, derangements in PT and APTT in 42.5% of his adult cases [6].

Reports have demonstrated a high affinity of the dengue virus for human liver cells and dengue virus has been isolated from the liver of fatal cases. Shivbalan et al found SGPT, tender hepatomegaly and abdominal pain to be significant predictors for bleeding in dengue children [11].

Thrombocytopenia occurred in 74% of patients with dengue without warning signs, 98% with warning signs and 100% in severe dengue.

Of 70 serologically confirmed cases hospitalized with dengue, 29 were classified as having Dengue without warning signs, 33 were with Warning Signs and 8 were suffering from Severe Dengue. Two cases of severe dengue expired secondary to DIC. Injection vitamin K was given to the children who had elevated PT and APTT. Fresh whole blood transfusion was required in 4 children in view of falling hematocrit. Elevated transaminase levels have been suggested as a potential marker to help differentiate dengue from other viral infections during the early febrile phase.

5. Conclusion

Elevation of liver enzymes can occur with or without hepatomegaly. Significant rise of liver enzymes helps in recognition of severe forms of dengue infection. Early interventions could prevent life threatening complications like massive haemorrhage. The role of hepato - protective drugs in dengue could be tried for early recovery and thereby decreasing morbidity and mortality in future studies.

References

- [1] World health Organization. Dengue guidelines for diagnosis, treatment, prevention and control. Geneva: World health Organization; 2009. [Online] Available from: http://www.who.int/tdr/publications/documents/dengue_diagnosis.pdf [Accessed on 27th October, 2015]
- [2] Wiwanitkit V. Liver dysfunction in dengue infection: an analysis of previously published Thai cases. J Ayub Med Coll Abbottabad 2007; 19 (1): 10 - 2.
- [3] Kumar R, Tripathi P, Tripathi S, et al. Prevalence of dengue infection in north Indian children with acute hepatic failure. Ann Hepatol.2008; 7 (1): 59–62.
- [4] Poovorawan Y, Hutagalung Y, Chongsrisawat V, et al. Dengue virus infection: a major cause of acute hepatic failure in Thai children. Ann Trop Pediatric.2006; 26 (1): 17–2
- [5] Wahid SF, Sanusi S, Zawawi MM, Ali RA. A comparison of the pattern of liver involvement in dengue hemorrhagic fever with classic dengue fever. Southeast Asian J Trop Med Pub Health.2000; 31 (2): 259–63.
- [6] Wong M, Shen E. The Utility of liver function tests in Dengue. Ann Acad Med.2008; 37 (1): 82–3.

- [7] Kamath SR, Ranjith S. Clinical Features, complications and atypical manifestations of children with severe forms of Dengue hemorrhagic fever in south India. Indian J Pediatr.2006; 73 (10): 889–95.
- [8] Jagadishkumar K, Jain P, Manjunath VG, Umesh L. Hepatic involvement in dengue fever in children. Iranian journal of pediatrics.2012 Jun; 22 (2): 231.
- [9] Nimmannitya S, Thisyakorn U, Hemsrichart V. Dengue hemorrhagic fever with unusual manifestations. Southeast Asian J Trop Med Public Health.1987; 18 (3): 398–405.
- [10] Trung DT, Thu Thao LT, Hien TT, et al. Liver involvement associated with dengue infection in adults in Vietnam. Am J Trop Med Hyg.2010; 83 (4): 774–80.
- [11] Shivbalan S, Anandnathan K, Balasubramanian S, et al. Predictors of spontaneous bleeding in Dengue. Indian J Pediatr.2004; 71 (1): 33–62.