

LIVER ENZYMES AS AN EARLY PREDICTOR OF SEVERE DENGUE FEVER

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Abstract

Background: Elevated liver enzymes is seen commonly in early stages of dengue infection and there are several studies showing the increase in transaminases. **Aim:** To evaluate if elevated liver enzymes can be used as an early predictor of severe dengue fever. **Material & Methods:** The present study is a Hospital based observational study including Children in the age group of 1month to 12years who are admitted in king George hospital Visakhapatnam, from Aug 2021 to July 2022. All patients from 1 month to 12 years admitted with fever with IgM antibody or NS1Ag positive for dengue. **Results:** In the present study,120 dengue positive(NS1/IgM) children admitted in Paediatric ward, KGH were enrolled. The age group of the majority of children in this study was 6 to 12 years (71.66%). 67 (55.8%) were male children and 53 (44.2%) were females. 70.83 % of the children had dengue fever with warning signs. The mean AST value in children with dengue infection was 228U/L whereas the mean ALT was 148U/L. So, the elevation of AST level is more compared to that of ALT level (p-value of <0.05). Most of the children (50.58%) with warning signs had 2-5 times rise in AST levels. Most of the children (80%) with severe dengue infection had >5 times AST elevation, indicating that AST levels are proportional to the severity of the dengue. Most of the children (40%) with mild dengue infection had < 2 times rise in ALT levels. Most of the children (50%) with severe forms of dengue infection had >5 times rise in the ALT values. Mean AST values in the 3 categories of severity of dengue infection (DF, DFWS and SD) were 125, 240 and 400 U/L respectively. Mean ALT values in the 3 categories of severity of dengue infection (DF, DFWS and SD) were 107, 140 and 320 U/L respectively. (P value of <0.05). Both elevated ALT and AST are early predictors of severity of dengue infection. ALT and AST elevation of 2-5 times and >5 times respectively was seen with platelet counts of 20,000-50,000/mm³ and <20,000/mm³ The children with severe forms of dengue had longer duration of hospital stay(13.5days), whereas duration of hospital stay was shorter (6.4days & 7.4days) with milder forms of dengue infection (DF and DFWS). (p-value of <0.05). **Conclusion:** Hepatic dysfunction is common in dengue fever and elevation of transaminases early in course of illness help in predicting severity of illness. This helps in close monitoring of those who are likely to go into severe forms and initiate appropriate treatment.

INTRODUCTION

Dengue fever is caused by arthropod borne flavivirus and has clinical presentation ranging from mild fever, haemorrhage to shock. Dengue infection

can occur in all groups, it is observed that outbreaks with significant mortality were seen in all over the world.

As per the WHO reports, the dengue infection cases increased from 2.4 million in 2010 to 5.2 million in 2019.^[2] The death due to dengue increased from 960 in 2010 to 4032 in 2015, mostly affecting the younger age group. Liver is a commonly involved organ in dengue and dengue associated liver injury was first reported in 1967.^[3]

Hepatomegaly is one of the warning signs in dengue. Hepatic dysfunction in dengue may range from mild elevation of transaminases to acute liver cell failure. The pathogenesis of liver function is not exactly known. It is either due to the direct effect of virus or because of dysregulated immunological host response.^[4]

The clinical picture of Dengue fever is highly variable,^[5] and it is difficult to assess which child is likely to progress to severe dengue infection particularly in the early stages. Drop in platelets and rise in haematocrit,^[6] marks the onset of leaky phase and appears late, so they cannot be used as prognostic markers.

Elevated liver enzymes is seen commonly in early stages of dengue infection and there are several studies showing that the increase in transaminases,^[7] at admission can be used to assess the severity of dengue infection. Hence the study is undertaken to assess the usefulness of liver enzymes as early markers of severity of dengue and their role in predicting the prognosis.

MATERIALS AND METHODS

The present study is a Hospital based observational study including Children in the age group of 1 month to 12 years who are admitted in king George hospital Visakhapatnam, from Aug 2021 to July 2022.

Inclusion Criteria

All patients from 1 month to 12 years admitted with fever with IgM antibody or NS1Ag positive for dengue.

Exclusion Criteria

Children with pre-existing liver disease

Methodology

120 children between 1 month to 12 years of age attending Paediatric department with fever who are IgM antibody or NS1 antigen positive for dengue and who fulfil the inclusion criteria are enrolled in the study. Demographic details like age, sex, and residence of enrolled children are noted. History regarding fever, vomiting, rash, any bleeding tendencies, etc. are noted. Detailed general and systemic examination is done to note the warning

signs. The enrolled children are given protocol treatment and followed daily during their hospital stay for any complications. Investigations like CBC, AST, ALT are done for all children.

RESULTS

Out of 120 children enrolled 67 (55.8%) were male children and 53 (44.2%) were female children. The male to female ratio was 1.26:1. Most of them were between 6-12 years of age (71.66%). 16 children were less than 1 year of age and 18 children were between 1-5 years of age. Out of 120 patients with dengue, 25 (20.83%) had dengue fever, 85 (70.83%) had dengue fever with warning signs and 10 (8.33%) had severe dengue fever. [Table 1]

The mean AST value is 228 in children. The mean ALT value is 146.9 in children. This difference is statistically significant with p value of <0.05. [Table 2]

The mean AST in children with DF, DFWS and SD was 125, 240 and 400

respectively. The p value is 0.00051. The mean ALT in children with DF, DFWS and SD was 107, 140, and 320 respectively. The p value is 0.000275.

This difference is statistically significant with p value of < 0.05. [Table 3]

Out of 25 children with Dengue fever with no warning signs, the values of ALT were found to be normal in 36% of children and < 2 times in 40 % of the children, 2 to 5 times in 16%, and > 5 times in 8 %.

Among 85 children with warning signs, 17.65% had normal ALT levels, 35.29 % had < 2 times, 34.12 with 2-5 times and 12.94% with >5 times rise in ALT values.

Rise in ALT values of 2-5 times the normal were seen in 34.15% of children with warning signs and 40 % children with Severe Dengue infection. More than 5 times increase in ALT values was seen in 12.94% cases of Dengue infection with warning signs and in 50% cases of Severe Dengue infection. [Table 4]

16% of children with DF and 7.05% of children with DFWS had normal levels of AST, 36% and 20% of children with DF and DFWS respectively had AST elevation of <2 times.

40%, 50.58% and 20% of children with DF, DFWS and SD respectively had 2 to 5 times elevation of AST. 8%, 22.35% and 80% of children with DF, DFWS and SD respectively had >5 times rise in AST. [Table 5]

Table 1: Age and Gender Distribution of Study Population

Age	Male	Female	Total	Percentage
< 1 Year	10	6	16	13.33%
1-5 Years	11	7	18	15%
6-12 Years	46	40	86	71.66%
Total	67	53	120	100%
Percentage	55.8%	44.2%		

Table 2: Clinical Classification of Study Population

Clinical diagnosis	Number	Percentage
Dengue fever	25	20.83%
Dengue fever with warning sign	85	70.83%
Severe dengue fever	10	8.33%

Table 3: Mean Transaminase Value in Dengue

	Mean	P value
AST	228	0.025594
ALT	148	

Table 4: Severity of Dengue Vs. Mean Transaminases

	DF	DFWS	SD	P Values
Mean AST	125	240	400	0.00051
Mean ALT	107	140	320	0.000275

Table 5: Alt Vs. Severity of Dengue

ALT	Dengue fever	Dengue fever with warning sign	Severe dengue	Total
Normal	9 (36%)	15 (17.65%)	0	24
< 2 times	10 (40%)	30 (35.29%)	1 (10%)	41
2-5 times	4 (16%)	29 (34.12%)	4 (40%)	37
>5 times	2 (8%)	11 (12.94%)	5 (50%)	18
Total	25	85	10	120

Table 6: AST Vs. Severity of Dengue

AST	Dengue fever	Dengue fever with warning sign	Severe dengue	Total
Normal	4 (16%)	6 (7.05%)	0	9
< 2 times	9 (36%)	17 (20%)	0	26
2-5 times	10 (40%)	43 (50.58%)	2 (20%)	56
>5 times	2 (8%)	19 (22.35%)	8 (80%)	29
Total	25	85	10	120

DISCUSSION

In this study majority (71.66%) of children affected with dengue were in the age group of above 6 years. In the studies done by Dr. Siddappa F.D et al,^[8] and Dr. Lakshmanaswamy. A et al,^[9] 55.77% and 69% of children affected were above 6 years respectively. This is due to the reason that children above 6 years spend more time outside the house like in schools and parks and are more exposed to mosquito bites. In all the above studies infants are least affected by dengue. This may be explained by protected home environment they live in.

In this study, 55.8% of the study population were males and 44.2% were females. Studies done by Dr. Lakshmanaswamy. A et al,^[9] Amrita Roy et al and Manohar et al also found equal distribution of cases among males and females. In the study done by Dr. Siddappa F.D et al,^[6] 63.38% were males and 34.6% were females. There is male preponderance in their study with male to female ratio of 1.7:1.

In this study, majority of dengue cases belong to clinical category of dengue fever with warning signs (70.83%). In the studies done by Dr. Lakshmanaswamy. A et al,^[9] and Manohar et al,^[10] also more number of cases belong to DFWS. 20.83%, 29% and 21% of cases belong to dengue fever without warning signs in this study, Dr. Lakshmanaswamy. A et al study and Manohar et al,^[10] study respectively. This is due to fact that all these studies were conducted in tertiary care centres where more serious cases are admitted. In Dr.

Siddappa F.D et al,^[8] study majority of study population (50%) belonged to DF without warning signs whereas in study done by Amrita Roy et al,^[11] majority of cases (60.83%) belonged to severe dengue category.

Liver is the most common organ involved in dengue & the hepatic dysfunction ranges from mild elevation of transaminases to acute fulminant hepatic failure and hepatic encephalopathy.

In the present study, AST was elevated in 92.5% of children with dengue infection whereas ALT is elevated in 80% children. In Dr. Siddappa F.D et al study,^[8] AST & ALT elevation was seen in 51.42 % & 40% of children with dengue respectively which is in contrast to the present study. Dr. Lakshmanaswamy. A et al,^[9] (elevation of AST in 87% cases, ALT in 61% cases) and Amrita Roy et al,^[11] (elevation of AST in 94.1% cases & ALT in 89.1% cases) also showed elevation of AST & ALT in majority of cases. In all the above studies, AST is elevated in a greater number of cases than ALT.

In this study, AST is elevated >2 times in most of the cases (2-5 times in 46.66% cases and >5 times in 24.16% cases) whereas ALT is elevated >2 times in 50% of cases. AST was normal in only 7.5% of cases with dengue, whereas ALT was normal in 20% of cases with dengue. Dr. Lakshmanaswamy. A et al,^[9] study showed similar results in their study where AST was normal in 13% cases and ALT was normal in 39% of cases with dengue.

In this study, mean values of AST and ALT in the study population were 228 and 148 U/L respectively. The mean ALT in the study by Fatima Ayaz et al study was 201.4. Ambreen et al,^[12] and Manohar et al,^[10] reported the mean AST values as 234.17 & 231.31 respectively and their Mean ALT values were 100.29 and 201.14 respectively.

Unlike viral hepatitis, AST was more elevated than ALT in children with dengue fever in all these studies.

ALT is primarily hepatic in origin whereas AST has various sources including heart, striated muscle, erythrocytes etc. Injury in dengue infection to non-hepatic tissues could be the cause for more raise in AST. ALT is higher in infections caused by hepatotropic viruses like in viral hepatitis. Hepatic involvement is more common among children with dengue compared to adults.

In the present study, mean ALT was 107, 140 & 320 U/L in patients with the three categories of dengue infection (DF, DFWS and SD). This difference is statistically significant with P value of <0.05. The mean value of AST was 125, 240,400 dL in patients with DF, DWS and SD respectively. This difference is significant with P value <0.05. Dr. Siddappa F.D et al,^[8] Amrita Roy et al,^[11] and Manohar et al,^[10] also showed positive correlation between increase in transaminases and severity of dengue.

CONCLUSION

In the present study,120 dengue positive(NS1/IgM) children admitted in Paediatric ward, KGH were enrolled. ALT and AST elevation of 2-5 times and >5 times respectively was seen with platelet counts of 20,000- 50,000/mm³ and <20,000/mm³. The children with severe forms of dengue had longer duration of hospital stay(13.5days), whereas duration of hospital stay was shorter (6.4days & 7.4days) with milder forms of dengue infection (DF and DFWS). (p-value of <0.05). Hepatic dysfunction is common in dengue fever and elevation of transaminases early in course of illness

help in predicting severity of illness. This helps in close monitoring of those who are likely to go into severe forms and initiate appropriate treatment.

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