European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 03, 2022

ORIGINAL RESEARCH

A SIGNIFICANCE OF LIVER FUNCTION TESTS TO PREDICT THE SEVERITY OF DENGUE FEVER IN SEROLOGICALLY POSITIVE CHILDREN BELOW 18 YEARS OF AGE

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ABSTRACT:

Background: Liver dysfunction in dengue varies from mild injury with elevation of transaminases to severe hepatocyte injury. Despite hepatocytes are not a major target, hepatic dysfunction is the recurrent feature. Predictive hepatic serum markers represent a solution for the dynamic care of serious dengue and predicting disease prognosis. In the present study we pursued to mold the mode of hepatic involvement in children with dengue and its association with seriousness of disease.

Materials and Methods: This was a cross sectional analytical study conducted at Department of Pediatrics, Govt Medical College &hospital during the period of 18 months from October 2019 April 2021 on 120 children under 18 years of age diagnosed with dengue positive and similar age and sex matched controls were included in this study. After obtaining informed consent, Patient demographics, presenting symptoms, clinical signs, laboratory parameters such as complete blood count, serum AST, serum ALT, ALP, total and direct bilirubin; serum albumin levels were collected. P-value <0.05 and CI 95% were considered significant in all correlation analyses between transaminases and platelet count.

Results: The mean age of the study population was 8.65 years with male preponderance. The mean total bilirubin, serum albumin, SGOT, SGPT, ALP, PT and INR were 0.76 mg/dl, 3.8g/dl, 233.18U/L, 118.15U/L, 200.65 U/L, 12.9s and 1.09 respectively. The mean SGOT was significantly higher than SGPT. The degree of deranged LFTs was significantly more in SDF group than DNWS and DWWS groups. Serum albumin was significantly decreased in children with SDF group correlating with disease severity, prognosis and outcome.

Conclusion: Hepatic dysfunction was present in all forms of dengue infection, with SGOT rising significantly more than SGPT. All biochemical liver parameters were significantly

deranged in patients with severe dengue fever indicating prolonged illness and poor prognosis**.**

Keywords: Dengue fever; Liver dysfunction; Severe dengue fever.

INTRODUCTION:

Dengue is endemic worldwide and is the leading cause of hospitalization. The disease had a predominant urban distribution a few decades earlier but is now also reported from peri-urban as well as rural areas.[1,2] Hepatic injury with dengue infection has been described since 1967.[3] Liver dysfunction varies from mild injury with elevation of transaminases to severe hepatocyte injury, resulting in jaundice. Although dengue virus is a non- hepatotropic virus, hepatomegaly is commonly seen in dengue along with a rise in serum hepatic markers. Direct hepatotoxicity as well as deranged host immune response against the virus is responsible for the hepatic dysfunction. Though there have been isolated cases of fulminant hepatic failure, the derangements in the transaminases are usually self-limiting and may serve as a predictor for assessing the disease severity.[4] Limited studies are available in our geographic location to understand the pattern of liver involvement in dengue patients based on 2009 WHO categorization.[5] We have sought to address this gap in the literature by conducting a study in coastal Indian population. Our aim of the study was to assess the prevalence of hepatic dysfunction in patients with dengue and to correlate between the severity of the disease with the extent of hepatic dysfunction. An awareness regarding the hepatic manifestations in dengue may be helpful in arriving at an early diagnosis and help avoid morbidity and mortality.[6-11] However, there are no large clinical studies documenting hepatic involvement in dengue infection, especially in children and liver functions tests are not routinely done to assess severity of dengue infection.[12] Dengue viruses cause symptomatic infections or asymptomatic seroconversion. Symptomatic dengue infection is a dynamic systemic disease. It has a wide clinical spectrum that includes both severe and non-severe clinical manifestations. Hence this study was taken up to Department of Pediatrics Govt Medical College& hospital, in Nalgonda to assess the severity of dengue viral infection in Children through Liver function tests.

Objectives

To assess the significance of Liver Function Tests (LFTs) to predict the severity of Dengue fever in serologically positive children.

MATERIALS & METHODS:

Children aged below 18 years who were diagnosed with dengue fever (NS1 Antigen positive and IgM positive) admitted to Department of Pediatrics, Govt Medical College & Hospital, in Nalgonda, Telangana, India.

Method of collection of the data:

All serologically confirmed dengue fever patients admitted to the Paediatric Department of Pediatrics, Govt Medical College & Hospital during the study period of 18 months from October 2019 April 2021 on 120 samples.

Inclusion Criteria:

- Serologically confirmed (NS1 Antigen Positive and IgM Reactive) dengue fever patients admitted To Govt Medical college &hospital, Nalgonda.
- Children<18years irrespective of the sex.

Exclusion Criteria:

- NS1 Antigen negative and IgM non-reactive Dengue like illness.
- Children with history of pre-existing liver diseases

RESULTS:

Out of 120 children enrolled in the study group, based on the clinical manifestations, as per WHO classification, 26.66% belonged to the group dengue fever with no warning signs (DFNWS), 50% belonged to the group dengue fever with warning signs(DFWS) and 23.33% belonged to the group severe dengue fever (SDF, [Table 1]).

Table 1: Distribution of study population as per WHO classification of Dengue fever

Groups	**Dengue fever with no warning signs (DFNWS)**	**Dengue fever with warning signs (DFWS)**	**Severe Dengue fever (SDF)**
No of cases	32 (26.66%)	60 (50%)	28 (23.33%)

Gender Distribution

Out of 120 children, majority 68.33% were males among which 59.75% categorised into dengue fever with warning signs. 20.73% were categorized into dengue fever with no warning signs and 19.51% belonged to severe dengue.

Table 2: Gender distribution of the study population

Sex	**Dengue fever withnowarning signs(DNWS)**	**Dengue fever with warning signs(DWWS)**	**Severe Dengue fever(SDF)**	**Total n=120**
Male	17(20.73%)	49(59.75%)	16(19.51%)	82(68.33%)
Female	15(39.47%)	11(28.94%)	12(31.57%)	38(31.66%)
Total	32 (26.66%)	60(50%)	28(23.33%)	120(100%)

Edema was seen in 14.28% children with SDF and 13.33% child with DWWS. Lymphadenopathy was seen in 3.57% child with SDF, 18.33% children with DWWS and 18.75% child with DNWS. Petechiae was seen only in 1.66% of children with DWWS and 28.57% in SDF. Icterus was also seen in 3.33% children with DWWS and only 17.85% in children with SDF. Hepatomegaly was seen in 46.66% of children withDWWS and 32.14% of children in SDF. Right hypochondriac tenderness was seen in 16.66%, 3.57% of children with DWWS and SDF respectively.

Table 3: Distribution of cases with varying severity of dengue fever based on clinical signs.

Signs	Dengue fever with no warning signs(n=32)	Dengue feverwith warning signs(n=60)	Severe dengue fever(n=2 8)	p value
No visible symptoms	25(78.12)	0(0%)	0(0%)	0
Edema	1(3.12%)	8 (13.33%)	4(14.28%)	0.213
Lymphadenopathy	6(18.75%)	11(18.33%)	1(3.57%)	0.327
Petechiae	0(0.0%)	1(1.66%)	8(28.57%)	0.009
Icterus	0(0.0%)	2(3.33%)	5(17.85%)	0.045
Hepatomegaly	0(0.0%)	28(46.66%)	9(32.14%)	0.008
Right hypochondriac tenderness	0(0.00%)	10(16.66%)	1(3.57%)	0.000

Laboratory parameters:

The mean ±SD leukocyte count in children with DNWS was 5954.26±3665.83cells/µL, in DWWS was 4985.15±3470.79cells/µL and in children with SDF was 5210.00±2916.41 cells/µL (p=0.002). The mean±SD platelet count in DNWS group was 129988.13±35414.17cells/µL; DWWS was 80985.45±41287.98cells/µL; SDF group was 43288.00±22871.cells/µL(p=0.001). The mean HCT was 40.12±5.23%, 38.25±5.90%, 39.66±8.11% in DNWS, DWWS and SDF

group respectively (p=0.005). The mean SGOT was 112.15±91.62, 184.12±122.21U/L, 466.66±147.79U/L in DNWS, DWWS and SDF group respectively (p=0.001). The mean SGPT was 89.33±21.80U/L, 99.16±39.41U/L, and 188.72±124.54U/L in DNWS. DWWS and

SDF group respectively (p=0.001). The mean±SD total bilirubin in DNWS, DWWS, SDF groups were 0.98±0.27mg/dl, 0.78±0.71mg/dl and 1.17±0.95mg/dl respectively (p=0.005). The mean±SD serum total proteins in DNWS, DWWS, SDF was 6.15±0.41g/dl, 6.89±0.94g/dl and 3.81±1.45g/dl respectively (p=0.001). The mean±SD serum albumin in DNWS, DWWS and SDF was 5.31±0.47g/dl, 5.28±0.71g/dl and 2.47±1.11g/dl respectively (p=0.001). The mean±SD PT was 13.11±1.13s, 12.17±1.92s, 15.16±4.99s in DNWS, DWWS and SDF groups respectively(p=0.005). The mean±SD INR was 1.19±0.078, 1.09±0.18, 1.15±0.17in DNWS, DWWS and SDFgroups respectively (p=0.002).

Table 4: Distribution of mean values of laboratory parameters in comparison with WHO classification of dengue fever.

Measurement	DNWS (n=32)	DWWS(n=60)	SDF(n=28)	p value
	Mean±SD	Mean±SD	Mean±SD	
Total leukocyte	5954.26±3665.83	4985.15±3470.79	5210.00±2916.41	0.722

count (cells/µL)				
Plateletcount (cells/µL)	129988.13±35414.17	80985.45±41287.98	43288.00±22871.21	0.00
HCT%	40.12±5.23	38.25±5.90	39.66±8.11	0.863
SGOT (U/L)	112.15±91.62	184.12±122.21	466.66±147.79	0.00
SGPT(U/L)	89.33±21.80	99.16±39.41	188.72±124.54	0.00
Totalbilirubin (mg/dl)	0.98±0.27	0.78±0.71	1.17±0.95	0.072
Serum proteins (g/dl)	6.15±0.41	6.89±0.94	3.81±1.45	0.00
Albumin (g/dl)	5.31±0.47	5.28±0.71	2.47±1.11	0.00
PT (Seconds)	13.11±1.13	12.17±1.92	15.16±4.99	0.005
aPTT (seconds)	34.58±0.76	43.72±1.96	36.80±3.96	0.267
INR	1.19±0.078	1.09±0.18	1.15±0.17	0.018

Children with higher SGOT levels had prolonged hospital stay ($p<0.05$). 8.33% of children who had <3 times elevation of SGOT had <3 days of hospital stay. 12.5% of children who had <3times elevation of SGOT had 4 to 5 days of hospital stay and 6.66% of children who had SGOT elevation <3times had >10 days of hospital stay 4.16%. 13.33% of children who had SGOT elevation between 4 to 5times had hospital stay between 4 to 5 days. 3.33% of children who had SGOT elevation between 4 to 5 times had hospital duration between 6 to 10 days. 2.5% and 5% in > 10d stay. 6.66% of children who had SGOT elevation between 6 to 10 times the normal value had hospital stay between 4 to 5 days and 6 to 10 days respectively. 5% of children who had SGOT elevation >10 times normal had >10 days of hospital stay.

Table 5: SGOT levels in comparison with Duration of hospital stay.

SGOTLevels		**Duration of the hospital stay**					**p Value**
		0-3d	**4-5d**	**6-10d**	**>10d**		
(<3)N*	No. of children	10	15	8	5	38	0.001
	% of children within clinical diagnosis	8.33%	12.5%	6.66%	4.16%	31.65%	
(4-5)N*	No. of children	16	4	7	6	33	
	% of children within clinical diagnosis	13.33%	3.33%	5.83%	5%	27.50%	
(6-10)N*	No. of children	8	6	3	6	23	
	% of children within clinical diagnosis	6.66%	5%	2.5%	5%	19.16%	

(>10)N*	No. of children	6	8	4	8	26	
	% of children within clinical diagnosis	5%	6.66%	3.33%	6.66%	21.66%	

*(N= SGOT value of 40U/L)

One children who expired of severe dengue fever in our study, one of them had SGOT level more than 5 times elevated and another had more than ten times elevation of SGOT.

Table 6: SGOT levels in comparison with outcome of children in dengue fever.

SGOT levels		**Improved**	**Death**	**Total**
(<3)N*	No. of children	37	1	38
	% of children within clinical diagnosis	31.66%	0.833%	32.5%
(4-5)N*	No. of children	33	0	33
	% of children within clinical diagnosis	15%	0.0%	15%
(6-10)N*	No. of children	22	1	23
	% of children within clinical diagnosis	24.16%	0.833%	25%
(>10)N*	No. of children	15	11	26
	% of children within clinical diagnosis	12.5%	15%	27.5%

*(N= SGOT value of 40 U/L)

60% of children with severe dengue fever had SGPT elevations more than 6 times (p=0.00). 14(31.1%), 17(37.8%), 13(28.9%), 1(2.2%) of children who had SGPT level <3 times the normal value had stayed in the hospital for duration of 0-3 days, 4-5days, 6-10days and >10 days respectively. 2(20%), 6(60%), 2(20%) of children who had SGPT elevations between 4-5 times the normal values had stayed in the hospital for duration of 4-5days, 6-10days and >10 days respectively.

Table 7: SGPT levels in comparison with duration of hospital stay.

SGPT levels		**Duration of the hospital stay**				**p value**
		0-3d	**4-5d**	**6-10d**	**>10d**	
(<3)N*	No. of children	10	15	8	5	
	% of children within clinical diagnosis	8.33%	12.5%	6.66%	4.16%	
(4-5)N*	No. of children	16	4	7	6	
	%ofchildrenwithin clinical diagnosis	13.33 %	3.33%	5.83%	5%	0.001
(6-10)N*	No. of children	8	6	3	6	
	%ofchildrenwithin clinical	6.66%	5%	2.5%	5%	

	diagnosis					
(>10)N*	No. of children	6	8	4	8	
	%ofchildrenwithin clinical diagnosis	5%	6.66%	3.33%	6.66%	

*(N= SGPT value of 40 U/L)

Among two children who expired with dengue fever, one patient had SGPT levels elevated >6 times the normal and another patient had elevation of SGPT more than 3 times the normal value.

Table 8: SGPT levels in comparison with outcome of dengue fever.

SGPT levels		**Improved**	**Death**	**Total**
(<3)N*	No. of children	37	1	38
	% of children within clinical diagnosis	31.66%	0.833%	32.5%
(4-5)N*	No. of children	33	0	33
	% of children within clinical diagnosis	15%	0.0%	15%
(6-10)N*	No. of children	22	1	23
	% of children within clinical diagnosis	24.16%	0.833%	25%
(>10)N*	No. of children	15	11	26
	% of children within clinical diagnosis	12.5%	15%	27.5%

*(N= SGPT value of 40 U/L)

DISCUSSION:

Author	**Year**	**Sample size**	**Conclusion**
Anusha Mruthyunjaya Swamy,[16]	2021	120	liver involvement in the form of elevated transaminases was found in 74.2% dengue patients. Serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase level increases with increase in dengue severity which is indicated by fall in platelet count as they are negatively correlated with each other. Liver damage is one of the common complications of dengue and transaminitis, hypoalbuminemia and reversal of A: G ratio should be used as biochemical markers in dengue patients todetect and monitor hepatic dysfunction.
Yashwanth Raju H. N,[17]	2019	60	Hepatic dysfunction was present in all forms of dengue infection, with SGOT rising significantly more than SGPT. All biochemical liver

			parameters were significantly deranged in patients with severe dengue fever indicating prolongedillness and poor prognosis.
JanardhanReddy Pulluru,[18]	2022	50	Hepatic dysfunction was present in all forms of dengue infection, withSGOT rising significantly more than SGPT. All biochemical liver parameters weresignificantly deranged in patients with severe dengue fever indicating prolonged illnessand poor prognosis.
Tran Quang Thach,[19]	2021	80	The findings suggest that alterations of platelet count and AST level—in the first 72 hours offever onset—are independent markers predicting the development of severedengue.
Present study	2021	120	Hepatic dysfunction was present in all forms of dengue infection, with SGOT rising significantly more than SGPT. All biochemical liver parameters were significantly deranged in patients with severe dengue fever indicating prolonged illness and poor prognosis.

Dengue fever is a disease caused by an arbovirus, which has four related virus serotypes (DENV- 1, DENV-2, DENV-3 and DENV-4). It is one of the most important arthropod transmitted viral disease in humans and constitutes an important worldwide health problem. It is estimated that 3 billion people live in endemic regions and 390 million infections (96 million symptomatic) and 20,000 deaths occur due to dengue fever annually.[13-18] Dengue infection has varied clinical presentations, ranging from a non-specific febrile illness to a severe dengue fever. The viruses can affect many cell types with diverse clinical and pathological effects. Liver involvement is known in dengue fever since 1950s. Hepatic involvement in dengue can occur in the form of hepatomegaly, elevated liver enzymes to fulminant hepatic failure. Thorough knowledge about these hepatic manifestations in dengue fever will certainly help in arriving at an early diagnosis and help avoid morbidity and mortality.[19,20] Our results were very much consistant with the previous works as shown in [Table].

CONCLUSION:

In this study, attempt has been made to understand the profile of hepatic involvement in dengue fever to predict disease severity. LFT derangement was seen in all forms of dengue fever and was significantly more common in severe dengue fever group. Higher SGOT and SGPT levels (SGOT>SGPT) predicts the disease severity, prolonged hospital stay and fatal outcomes.

Low serum albumin serves as an indicator of vascular permeability alteration and correlates with disease severity, prognosis and outcome.

Acknowledgment:

The author is Thankful to Department of Pediatrics for providng all the facilities to carry out this work.

REFERENCES:

1. NVDCP. National Guidelines for Clinical Management of Dengue Fever.2014 Dec;20(3).
2. Rigau-Perez JG. The Early Use of Break-Bone Fever (Quebranta Huesos, 1771) and Dengue (1801) in Spanish. Am J Trop Med Hyg 1998;59(2):272- 4.
3. Who. Handbook of Clinical Management Of Dengue Infection, Dengue Bulletin Southeast Region, Dec 2012;36(1).
4. Itha S, Kashyap R, Krishnani N, Sararswat Va, Choudhari G, Agarwal R. Profile Of Liver Involvement In Dengue Virus Infection. Natl Med J India 2005;18(3):127-30.
5. Sabin AB. Research on Dengue During World War II. Am J Trop Med Hyg 1973;22:82-91.
6. Hammon WM, Rudnick A, Sather GE. Viruses Associated With Epidemic Hemorrhagic Fevers Of The Philippines And Thailand. Science 1960;1102- 3.
7. Tun B. Hospital Universitikebangsaan Malaysia, Kuala Lumpur, Malaysia.A Comparison Of The Pattern Of Liver Involvement In Dengue Hemorrhagic
8. Fever With Classic Dengue Fever. The Southeast Asian Journal Of Tropical Medicine And Public Health (Impact Factor:0.72) 2000;31(2):63-259.
9. Mohan B, Patwari AK, Anand VK. Hepatic Dysfunction in Childhood Dengue Infection. J Trop Pediatr 2000 Feb;46(1):3-40.
10. Itha S, Kashyap R, Krishnani N, Sararswat VA, Choudhari G, Agarwal R. Profile Of Liver Involvement In Dengue Virus Infection. Natl Med J India 2005;18(3):127-30.
11. Seneviratnea SL, Malavige GN, De Silva C. Pathogenesis Of Liver Involvement During Dengue Viral Infections Transactions Of The Royal Society Of Tropical Medicine And Hygiene, Mar 2006;100(3):608-14.
12. Ranjit S, Kissoon N. Dengue Hemorrhagic Fever and Shock Syndromes. Pediatr Crit Care Med 2011;12(1):90-100.
13. Narayanan M, Arvind M A, Ambikapathy P. Dengue Fever-Clinical and Lab Parameters Associated With Complications. Dengue Bulletin; 2003. p27.
14. Kabilan L, Balasubramanian S, Keshava S M, Satyanarayana K. The 2001 Dengue Epidemic in Chennai. Indian J Pediatr 2005;72(11):919-23.
15. Jadhav R, Lohiya S, Agarkhedkar S, Lohakare A, Salunkhe S. Study of Dengue fever with special reference to predictors of spontaneous bleeding in
16. Dengue Infection. J Pharm Biomed Sci 2015;5(11):851-6.
17. Anusha Mruthyunjaya Swamy, Prasanth Yelkana Mahesh, Sujith Tumkur Rajashekar; Liver function in dengue and its correlation with disease severity: a retrospective cross-sectional observational study in a tertiary care center in Coastal India; PAMJ - 40(261). 23 Dec 2021

18. Yashwanth Raju H. N., Rajendra Kumar*, Sudha Rudrappa; Liver function tests to predict the severity of dengue fever in serologically positive children below 18 years of age; Int J Contemp Pediatr. 2019 Mar;6(2):358-364
19. Janardhan Reddy Pulluru, Suraboina Satishkumar, Gajula Ravi; Liver Function Tests to Predict the Severity of Dengue Fever in Serologically Positive Children Below 18 Years of Age; European Journal of Molecular & Clinical Medicine Volume 09, Issue 03, 2022.
20. Tran Quang Thach et al; Predictive markers for the early prognosis of dengue severity: A systematic review and meta-analysis; | https://doi.org/10.1371/journal.pntd.0009808 October 5, 2021.