



An Observational Study on Effect of Dengue Fever on Liver Function in Patients Admitted to a Tertiary Care Centre in Rural South Kerala

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Background

Dengue is an important mosquito borne disease in the tropical and subtropical countries. It is often self limited and presents with arthralgia, myalgia, head ache and fever. Though not a hepatotropic virus, liver injury is not un common in dengue infection⁽¹⁾. The degree of liver dysfunction varies from mild to severe.^(2,3) The exact mechanism of the liver dysfunction is not known, but is postulated to be either a direct effect of the virus or a dysregulated host immune response⁽²⁾.

The present study aims at finding the effects of dengue virus on the liver function and its effect on the severity and outcome of the disease in patients admitted in a tertiary care centre in south Kerala.

Aims and Objectives

- A. To study the pattern of liver function abnormalities in patients admitted with dengue.
- B. To study the effects of liver function abnormality on the severity and the outcome of dengue.

Materials and Methods

Study Population

Patients admitted with the diagnosis of Dengue fever from the June – December 2018 in a tertiary care centre in rural south Kerala.

Study Design: Observational study

Inclusion Criteria

- a. Age more than or equal to 13 years of both the sexes.
- b. Patients satisfying the WHO definition for Dengue.

Exclusion Criteria

- a. Those who are not willing to give consent.
- b. Those with known pre existing chronic liver disease or acute hepatitis of other etiology.

Methods

Among the patients presenting to the outpatient department or emergency department of the institution who satisfied the inclusion criteria were enrolled in the study.

After history taking and physical examination the following investigations will be performed.

1. Blood Samples for: Complete Blood Counts, Erythrocyte Sedimentation Rate, Blood Urea, Serum Creatinine
2. Daily Liver function tests
3. Ultrasound abdomen in relevant cases.

The patients will be hospitalized according to the institutional protocol and managed as per the WHO guidelines. Patients will be monitored clinically for the development of Dengue Shock Syndrome/ Dengue Hemorrhagic Fever. Daily CBC will be measured for the evidence of hemoconcentration.

Liver function abnormalities were classified as mild (up to two fold elevation of liver enzymes-ALP, ALT and AST), Moderate (3-4 fold elevation) and severe (> 5 fold). The serum bilirubin and the albumin levels were also observed. The INR value of prothrombin time were also measured.

The hospital course, the development of complications and its relationship with liver function abnormality were studied. The final outcome was measured as died or survived.

Definitions

WHO 2009 definitions of Dengue fever

1. Probable Dengue fever

An acute febrile illness with 2 or more of the following:

- Retro orbital pain
- Myalgia and arthralgia
- Nausea and vomiting a
- Skin rash
- Hemorrhagic manifestations.

AND

Supportive serology OR

Occurrence at the same location and time as other confirmed cases of Dengue fever

2. Confirmed case of Dengue fever: Confirmation of Dengue fever is based on laboratory criteria
Isolation of virus from serum or tissue sample

OR

Demonstration of 4 fold or more rise in Ig G and Ig M antibody titres to the dengue antigens in paired serum samples

OR

Demonstration of dengue antigens in tissue, serum, CSF by immunohistochemistry, immunofluorescence or ELISA

OR

Detection of genomic sequences by PCR

Dengue Hemorrhagic Fever: Requires all 4 of the following to be satisfied:

- a. Acute fever lasting 2-7 days occasionally biphasic.
- b. Hemorrhagic tendencies as evidenced by at least one of the following: a positive tourniquet test, petechiae, ecchymosis purpura, bleeding from mucosa, hematemesis or melena
- c. Thrombocytopenia <100000/mm³
- d. Plasma leakage as evidenced by at least one of the following: Rise in hematocrit > 20%, Fall in hematocrit >20% after IV fluids, Pleural effusion, ascites or hypoalbuminemia.

Dengue Shock Syndrome

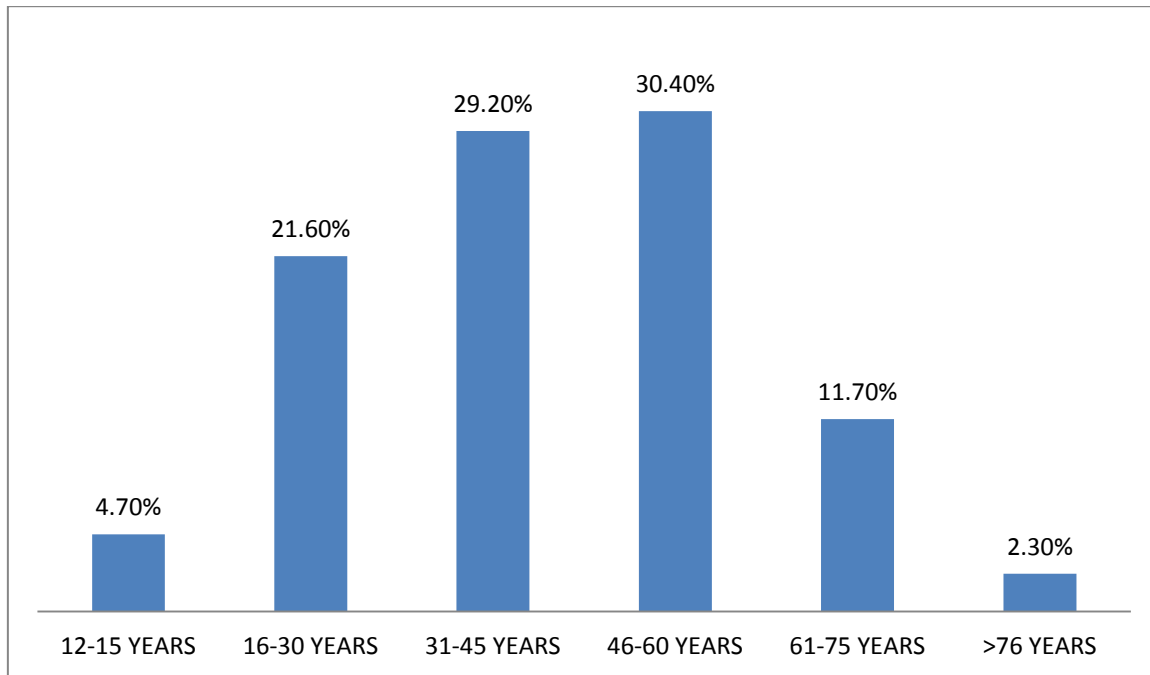
The identification of Dengue shock syndrome requires all 4 of the dengue hemorrhagic fever criteria and evidence of circulatory failure as manifested by:

1. Rapid and weak pulse
2. Narrow pulse pressure (< 20mm Hg)
3. Hypotension for age (<90mm Hg for age > 5 years)
4. Cold clammy skin, restlessness.

Observations

342 cases satisfied the inclusion criteria and were enrolled after obtaining an informed consent.

Figure 1: Age Distribution of Cases



Most of the patients were in the age group of 16-60 years of age, which represents the most productive of the age groups.

31% of the cases were females and 69% were males.

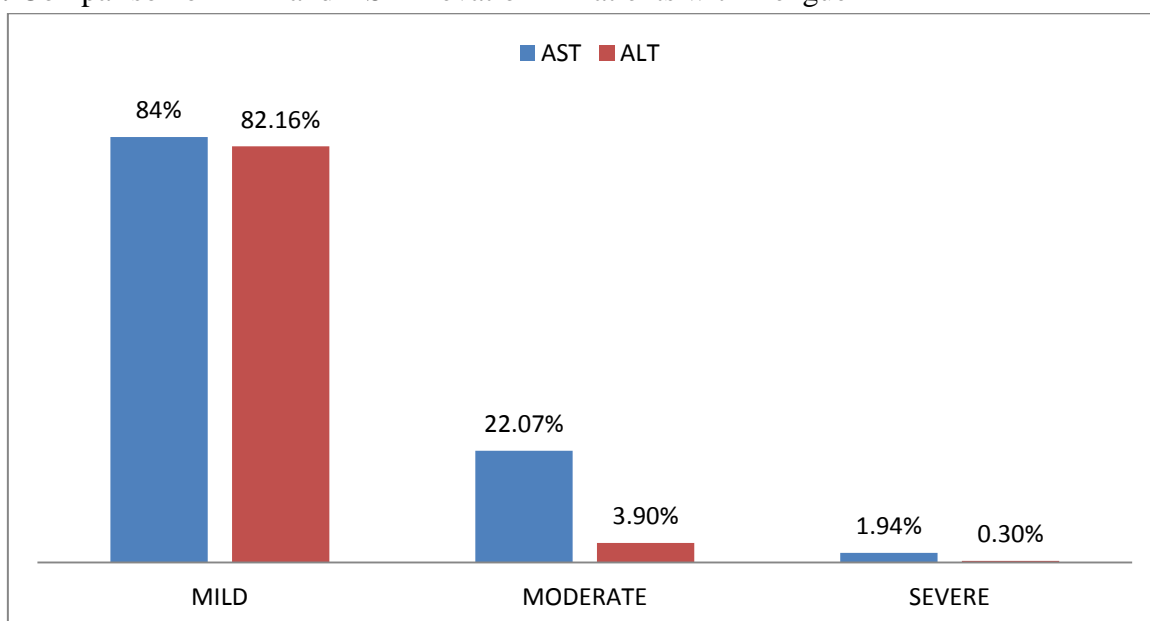
Of the 342 cases, 75.4% were classified as having Dengue Fever, 23% as Dengue Hemorrhagic fever and 1.5% as Dengue Shock Syndrome, according to the WHO definitions.

88.88% were having NS1 antigen positivity, 69.8% had IgM antibody and 20.7% had IgG

antibody against dengue virus. Of the patients with Dengue Shock Syndrome, 60% were positive for the IgG antibody, signifying a re infection.

Hepatic dysfunction in the form of deranged bilirubin, AST, ALT, Albumin and PT/INR were seen in 4.3 %, 97.07%, 80.7%, 6.4%, and 11.1% respectively.

Figure 2: Comparison of ALT and AST Elevation in Patients with Dengue



The mean AST was more than the mean ALT in the patients.

Among the cases, 75.4% had Dengue fever, 23.1% had Dengue Hemorrhagic Fever and 1.5% had

dengue shock syndrome. 0.9% succumbed to the illness, whereas, 99.1% survived.

Figure 3: Pattern of AST Elevation among Various Class of Dengue

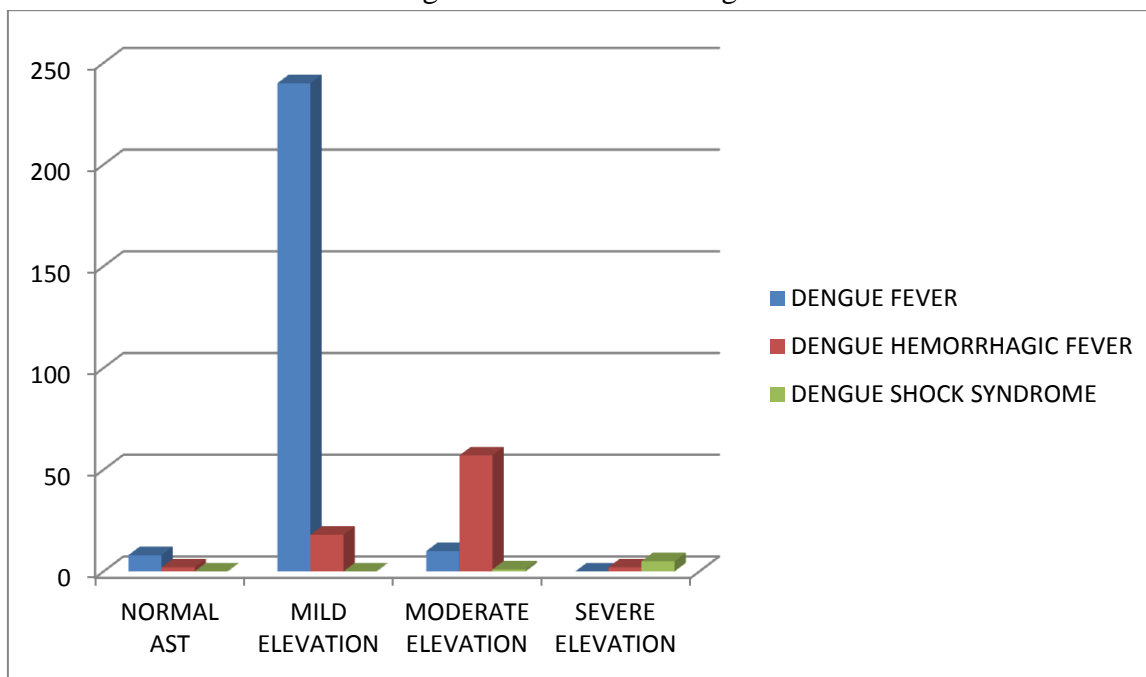
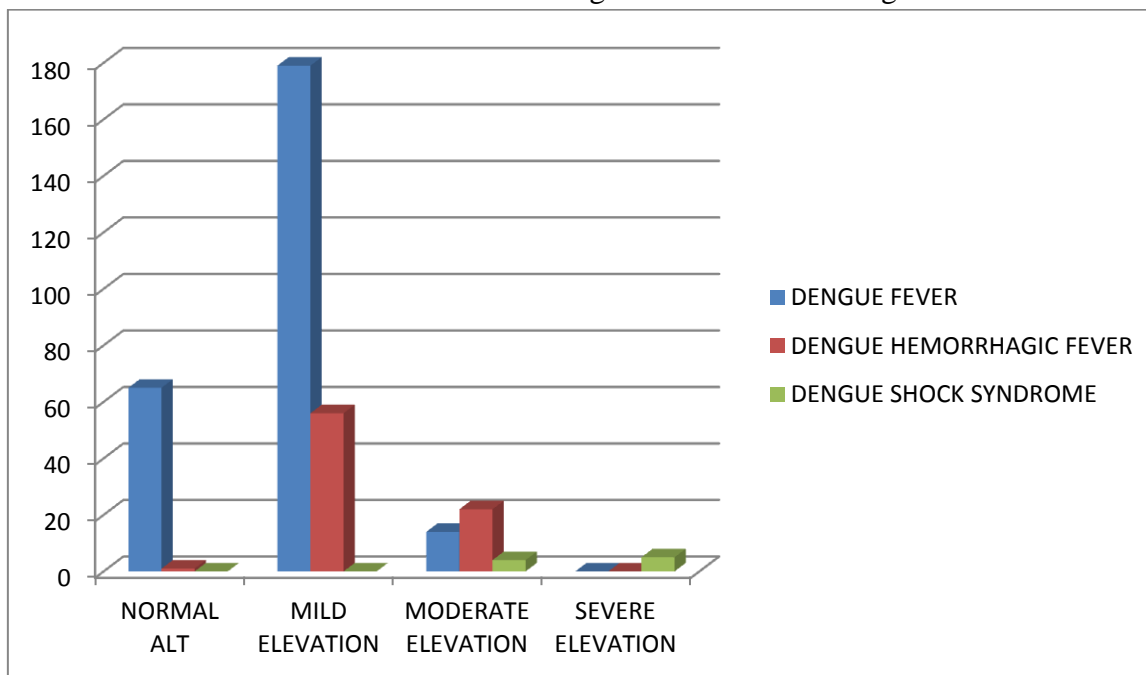


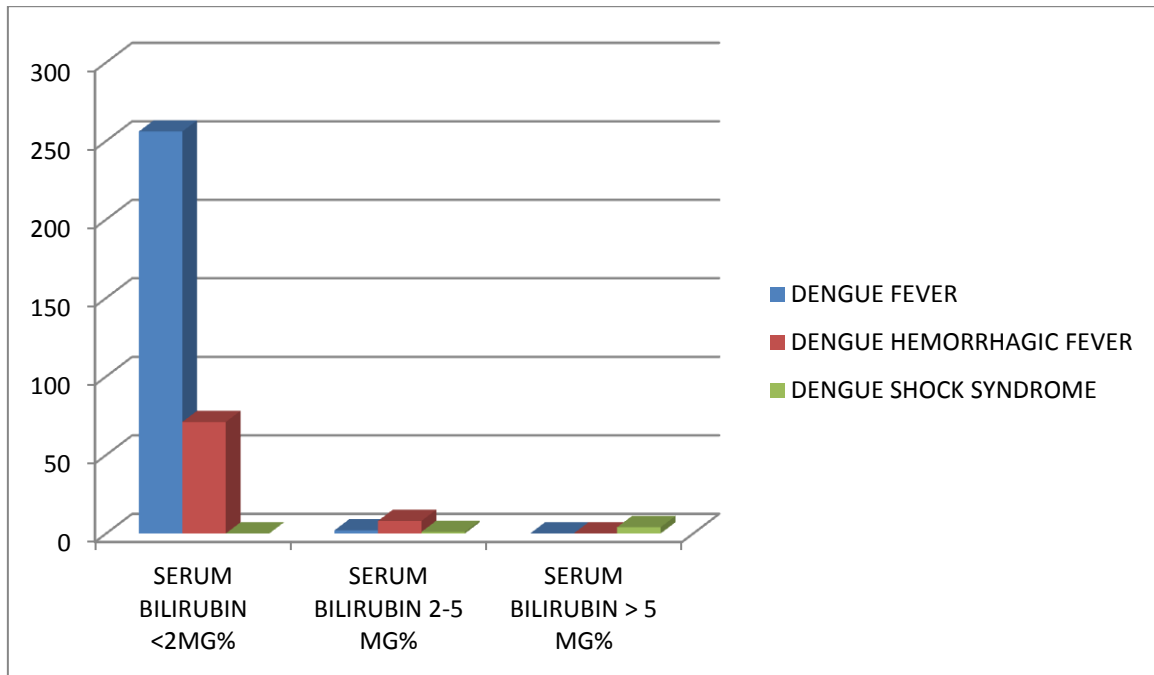
Figure 4: Pattern of Elevation of ALT Elevation among various Class of Dengue



There was significant association between the level of rise of aminotransferases and

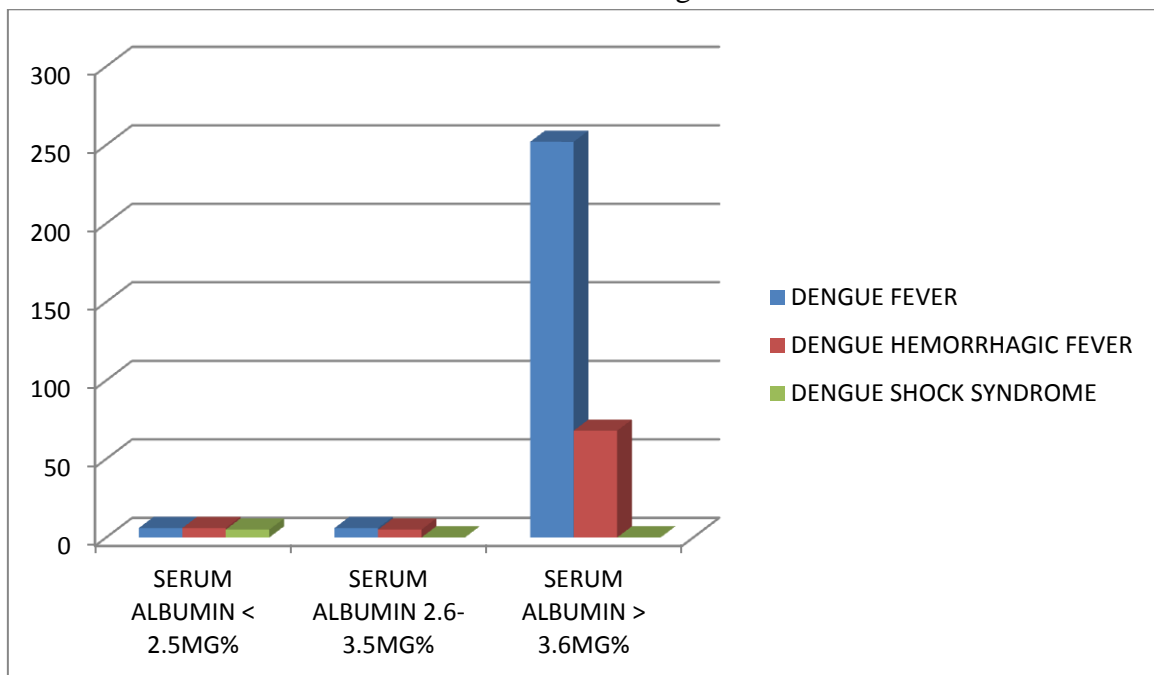
complications, like DHF and DSS. (p Value 0.000).

Figure 5: Pattern of Elevation of Serum Bilirubin in Various Class of Dengue



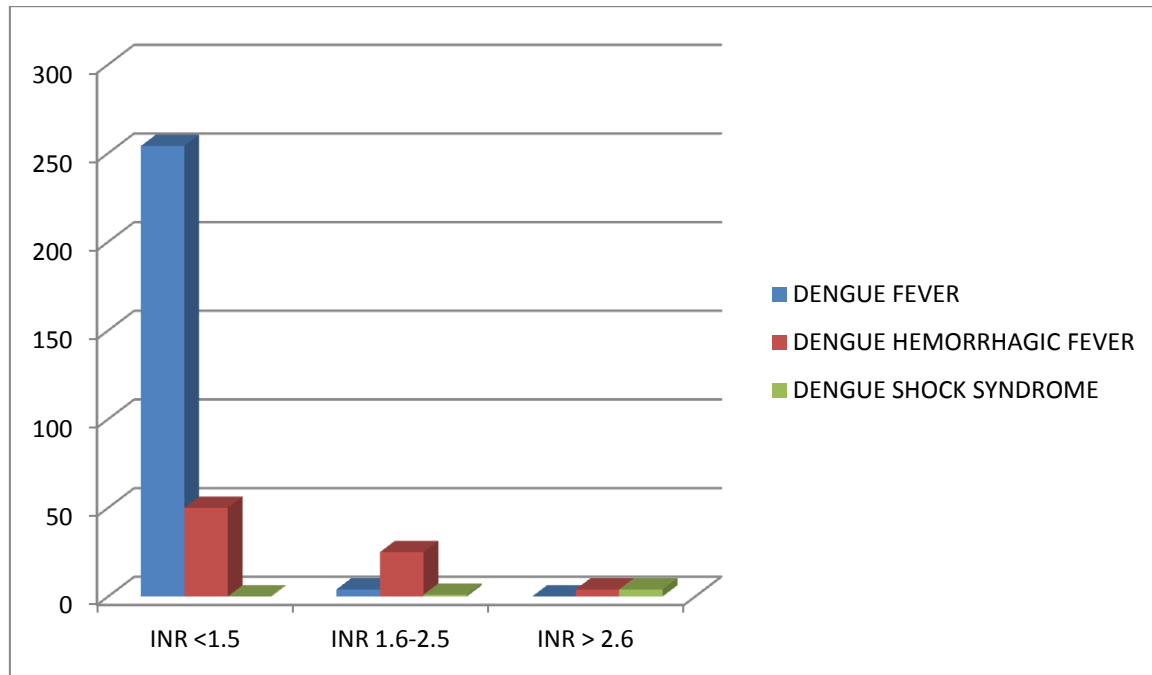
There was a significant relation between rise in serum bilirubin and occurrence of DHF and DSS. (p value 0.00)

Figure 6: Pattern of Albumin Levels in Various Class of Dengue



An association was noted between low albumin levels and occurrence of severe forms of dengue.

Figure 7: Prothrombin Time with INR Levels among Various Classes of Dengue



There was no significant association between elevated INR values and occurrence of severe forms of dengue. (p value > 0.05)

Table 1: Relationship between ALT Levels and Occurrence of Dengue Shock

VARIABLE		DENGUE SHOCK SYNDROME		P VALUE
		YES	NO	
ALANINE AMINO TRANSFERRASE LEVELS	NORMAL	0	66	0.270
	ELEVATED	5	271	

Table 2: Relationship between AST Levels and Occurrence of Dengue Shock

VARIABLE		DENGUE SHOCK SYNDROME		P VALUE
		YES	NO	
ASPARTATE AMINO TRANSFERRASE LEVELS	NORMAL	0	10	0.000
	ELEVATED	5	327	

Table 3: Relationship of Bilirubin Levels and Occurrence of Dengue Shock

VARIABLE		DENGUE SHOCK SYNDROME		P VALUE
		YES	NO	
BILIRUBIN LEVELS	<2 MG%	0	327	0.000
	>2 MG%	5	10	

Table 4: Relation between Serum Albumin Levels and Occurrence of Dengue Shock

VARIABLE		DENGUE SHOCK SYNDROME		P VALUE
		YES	NO	
ALBUMIN LEVELS	<3.5 MG%	0	17	0.000
	>3.5 MG%	5	320	

Table 5: Relationship between Prothrombin Times INR with Occurrence of Dengue Shock

VARIABLE		DENGUE SHOCK SYNDROME		P VALUE
		YES	NO	
PROTHROMBIN TIME INR LEVELS	<1.5	0	304	1.87
	>1.5	5	33	

Table 6: Relationship of Various Variables to the in Hospital Outcome

VARIABLE			IN HOSPITAL OUTCOME		P VALUE
			DIED	SURVIVED	
ALANINE AMINO TRANSFERASE	NORMAL		0	66	0.300
	ELEVATED		3	273	
ASPARTATE AMINOTRANSFERASE	NORMAL		0	10	0.76
	ELEVATED		3	329	
SERUM BILIRUBIN	<2MG%		1	326	1.12
	>2MG%		2	13	
SERUM ALBUMIN	<3.5MG%		3	19	3.2
	>3.5MG%		0	320	
PROTHROMBIN TIME INR LEVELS	<1.5		0	304	1.87
	>1.5		5	33	

There was no significant relation between the occurrence of bleeding manifestation to the level of aminotransferases, albumin, bilirubin or INR levels.

Discussion

The clinical and biochemical impact of dengue virus on the liver function during an outbreak in south kerala was studied. Total 342 cases were included in this study.

The occurrence of abnormal liver function test in the form of abnormal AST (97.07%) and ALT (80.07%) seen in our study was comparable to previous studies.^(4,5,6)

Rise in bilirubin was seen only in a small proportion.⁽⁶⁾

The aspartate aminotransferase levels in dengue tends to be greater than alanine amino transferase. This differs from the usual pattern of viral hepatitis. The exact cause of this is not known but is thought to be due to the release of AST from monocytes. This can be used as an indicator of Dengue infection at the early stages itself.^(7,8,9)

In our study, the degree of liver dysfunction had a correlation with the severity of dengue infection. This is in accordance with the observations made in a previous study.⁽⁹⁾

A high serum bilirubin and a low serum albumin had an association with the occurrence of shock in dengue, in our study.

Our study failed to identify a positive correlation between the various liver function parameters and the occurrence of bleeding.^(10,11)

Our study failed to identify any correlation between mortality and liver function abnormality, though liver dysfunction was more in non survivors than survivors.

This study thus throws light into the fact that liver function can be used as a predictor of development of severe forms of dengue, though mortality in dengue may not be related to the liver function abnormalities alone.

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