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A Study of Hepatic Dysfunction with Severity of Dengue Fever

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Abstract **Original Research Article**

Background: Dengue viruses belong to flavivirus, which include four serotypes 1,2,3 and 4. Dengue virus infection manifestations vary from asymptomatic to severe dengue with shock. An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries. Liver is affected in the form of derangements of liver function tests. ***Objectives:*** 1. to study the frequency and pattern of hepatic dysfunction in dengue fever 2. To find out the correlation of Hepatic dysfunction with severity of Dengue fever**.** ***Methods:*** An observational cross-sectional study done on patients admitted in hospitals attached to Bangalore Medical College and Research Institute, Bangalore, Karnataka, between June 2019-November 2019. Confirmed Dengue patients are included after meeting inclusion and exclusion criteria. Complete Blood count, liver function tests are estimated at the time of admission. ***Results:*** Out of 100 patients, 27 developed Dengue fever with warning signs and 10 patients developed severe Dengue. Multivariate analysis showed that low albumin of <3.5 gm/dl was associated with severe dengue, which was statistically significant (p value 0.028). ***Conclusions:*** Early changes in liver enzymes and serum albumin may be detected in patients with dengue fever. Low serum albumin levels if present may be a marker of the critical phase of the disease and an early indicator of plasma leakage due to altered vascular permeability and a useful predictor of severity of dengue fever.

Keywords: Dengue fever, Severe Dengue, Serum albumin, Liver Function Test, Hepatic dysfunction.

INTRODUCTION

Dengue is one of the most important emerging infectious diseases in the world. The dengue virus (DENV), belongs to genus Flavivirus in the family Flaviviridae. It is a single-stranded enveloped RNA virus, with four distinct, but related, serotypes (DENV1–4) [1]. In India Dengue virus first isolated in 1945. In 2010, 28,292 cases of Dengue were reported in India which increased to 50,222 in 2012 and 75,808 in 2013.[2] World Health Organization (WHO) estimates 50-100 million Dengue infections occur every year with 22,000 deaths [2]. Among the millions of dengue virus 1-4 infections, around 5, 00,000 cases of severe dengue occur annually, with a lethality rate of around 2.5% [3].

Dengue fever is benign in its classical form and serious in dengue hemorrhagic fever and dengue shock syndrome. Severe dengue is characterized by thrombocytopenia, spontaneous hemorrhages, and gradual plasma leakage that can lead to shock [3-5]. There have been reports of dengue fever involving heart, nervous system and liver, leading to myocarditis, encephalitis and hepatitis respectively. Degree of liver damage ranges from mild injury with mild elevation of serum transaminases to severe injury with acute fulminant hepatitis.

Acute dengue infection is often unrecognized until the appearance of the more severe forms of the disease. This variation in clinical presentation leads to inadequate or delay in treatment of a potentially lethal medical condition. Many studies have found relation between severe dengue and albumin levels [6, 7]. Very few studies have been done to show the degree of liver damage and severity of Dengue fever.

OBJECTIVES

- To study the frequency and pattern of hepatic dysfunction in dengue fever
- To find out the correlation of Hepatic dysfunction with severity of Dengue fever

MATERIALS AND METHODS

An observational cross-sectional study done between June 2019-November 2019 on patients admitted in hospitals attached to Bangalore Medical

College and Research Institute, Bangalore, Karnataka. Ethical committee permission taken.

Inclusion criteria

- Patients more than 18 years of age
- Confirmed dengue fever cases with Dengue NS1 Ag / IgM positive or both
- Fulfilling WHO Criteria for Dengue fever
- Patients willing to give consent

Exclusion criteria

- Patients with preexisting liver disease
- Alcoholics
- Patients with Drug induced Liver injury

Method of collection of data

- Informed and written consent was obtained from all patients.
- The following investigations are done in all cases: Hemoglobin (Hb%), Packed cell volume (PCV), platelet count, Dengue serology NS1 Ag & IgM, and Liver Function Tests (LFT).

The sample size was calculated using the following formula assuming an error 5% (Za = 1.96) and b error 20% (Zb = 0.842) and a power of 80%, with a precision of 5% from previous studies.

$$n = \frac{(Za + Zb)2 + p\,q}{d\,2}$$

p = prevalence
q = 1 - p
d = precision

Statistical analysis was done using SPSS (Statistical Package for Social Sciences) version 20. Data was entered in the excel sheet. Descriptive statistics was analyzed by mean and standard deviation for quantitative variable. Frequency and proportions were used for qualitative variables. Inferential statistics was done by Chi square test to assess significance between qualitative variables.

RESULTS

Majority of patients (54%) were in the age group of 18-30 years in our study (Fig. 1). Mean age group was 35.22 years. Male preponderance was seen with 74% being males (Fig. 2). In our study most common presentation was fever which was present in all patients followed by myalgia (28%), vomiting (21%), and bleeding manifestations (20%) (Fig 3). Out of 100 patients, 63 patients had Dengue fever without warning signs, 27 had dengue fever with warning signs and 10 patients had severe dengue (Table 3). Total protein was low in 53% and Globulin was high in 45% of patients. Bilirubin was high in 30% of patients. Aspartate Transaminase (AST) was raised in 73%, Alanine Transaminase (ALT) was raised in 55% and ALP was raised in 31% of patients. Out of 100 patients 29 (29%) patients had serum albumin <3.5gm/dl. Out of 29 patients with serum albumin of <3.5gm/dl, 12 (44.4%) had Dengue with warning signs and multivariate analysis showed that out of 10 patient who developed severe Dengue, 9 (90%) patients had low serum albumin which was statistically significant with P value- 0.028 (Table 3).

Table-1: Age distribution among cases

Age in years	Frequency	Percent
18-30	54	54.0
31-45	25	25.0
46-60	13	13.0
>60	8	8.0
Total	100	100.0

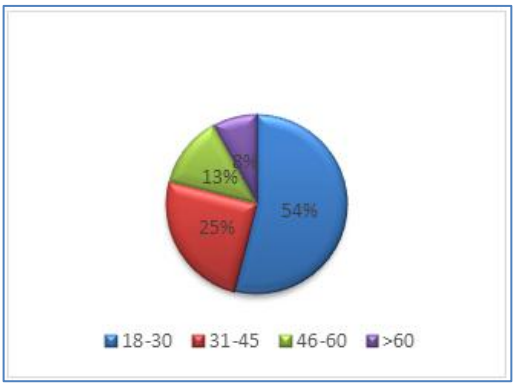

Fig-1: Age wise distribution

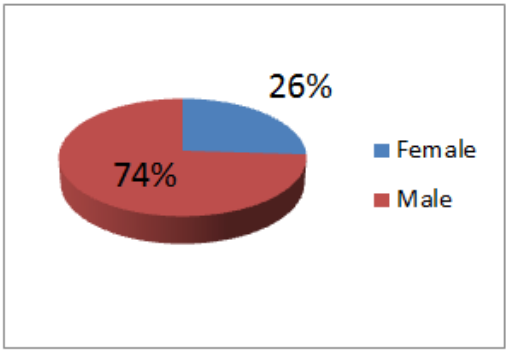

Fig-2: Gender-Wise Distribution of the Subjects

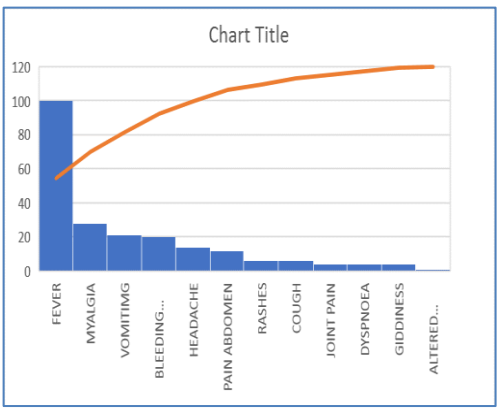

Fig-3: Clinical presentation of cases

Table-2: Distribution of the Subjects Based on WHO Criteria

	Frequency	Percent
Dengue Fever without warning signs	63	63.0
Dengue Fever with warning signs	27	27.0
Severe Dengue	10	10.0
Total	100	100.0

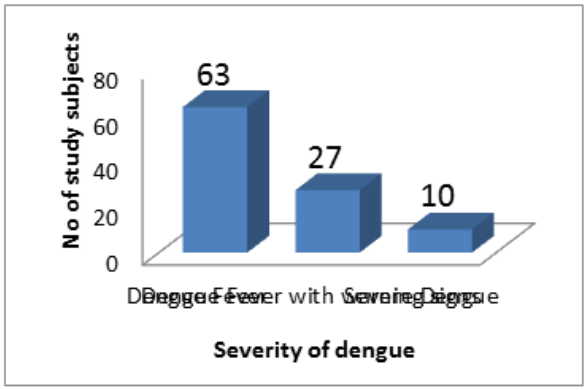

Fig-4: Distribution of the Subjects Based on WHO Criteria

Table-3: Cross-Tabulation of Albumin and WHO Criteria

Albumin		WHO CRITERIA			Total
		Dengue Fever	Dengue Fever with warning signs	Severe Dengue	
Low	Count	29	12	9	50
	Percent	46.0%	44.4%	90.0%	50.0%
Normal	Count	34	15	1	50
	Percent	54.0%	55.6%	10.0%	50.0%
Total	Count	63	27	10	100
	Percent	100.0%	100.0%	100.0%	100.0%
Chi-square value- 7.13					
P value- 0.028*					

*significant

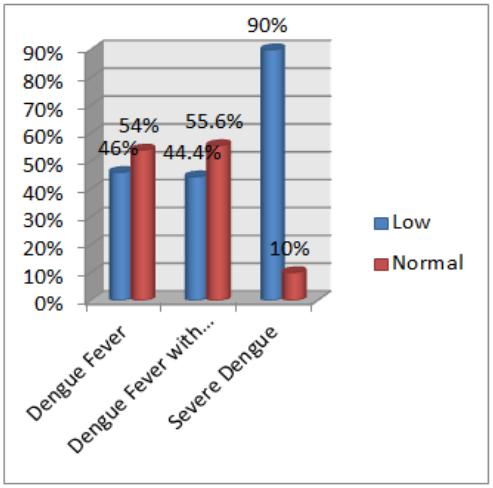

Fig-5: Cross-Tabulation of Serum Albumin and WHO Criteria

DISCUSSION

In our study, serum albumin of <3.5 g/dl was associated with higher incidence of severe Dengue which was statistically significant (p value-0.028). Total protein was low in 53% and Globulin was high in 45% of patients. Bilirubin was high in 30% of patients. Aspartate Transaminase (AST) was raised in 73%, Alanine Transaminase (ALT) was raised in 55% and ALP was raised in 31% of patients.

In a study done by Narasimhan D, Ponnusamy P and Sathish, out of 100 patients, 92% had elevated SGOT while 82% had elevated SGPT. 5% patients had elevated bilirubin, 25% had elevated ALP, and serum proteins were low in 43% and serum albumin was low in 31% of cases and concluded the fact that spectrum of liver involvement can vary from asymptomatic biochemical involvement to severe acute liver cell injury. Low albumin levels may be a marker of critical phase of the disease [8].

A study by Rajoo Singh Chinna, Omesh Goyal *et al.* out of 214 serologically positive Dengue, deranged total bilirubin, AST, ALT, ALP, albumin and PT INR was present in 19.5% (29/143), 97.7% (209/214), 93.9% (199/214), 32.6% (47/144), 29.1% (44/151) and 15.5% (22/156) patients respectively. Concluded the fact that hepatic dysfunction was very common in all forms of dengue infection, with AST rising significantly more than ALT. Serum bilirubin, ALT and ALP were significantly higher in patients with DSS, hemorrhage, sequential infection and non-survivors. While preferentially high AST may serve as an early indicator of dengue infection, high bilirubin, ALT and ALP may act as poor prognostic markers [9].

A study by Luiz Jose de Souza, Carlos Eduardo *et al.* found that in 169 serologically confirmed cases of dengue 65.1% had abnormal aminotransferase levels and concluded that aminotransferase levels are a valuable marker for monitoring these cases [10].

An analysis of th previously published Cases by Viroj Wiwanitkit found that the overall rate of liver dysfunction among 191 subjects is 34.6 % (66/191). The rate of liver dysfunction among the patients without shock (36/120) is not significantly different from those with shock. 8% (5/66) the patients with liver dysfunction developed hepatic encephalopathy [11].

A study by Srivenu Itha, Rajesh Kashyap *et al*. found that out of 45 patients, LFTs revealed ALT and AST elevation in 96% of patients each, hyperbilirubinaemia (>2 mg/dl) in 30% patients and hypoalbuminemia (<3.5 g/dl) in 76% patients [12].

Albumin helps in the integrity of the vascular endothelium, when albumin levels falls below 3.5 g/dl may lead to alteration of vascular permeability causing plasma leakage. Many variables, like inflammation, are known to affect serum protein markers [13]. Serum proteins are affected by capillary permeability, drugs, impaired liver function and inflammation [14, 15]. Serum proteins are involved in repair and maintenance of immune system along with other body tissues. Albumin is an established indicator of morbidity and mortality [15, 16]. Hence serum albumin may be used as an early indicator of plasma leakage and severity of dengue fever and may serve as a useful prognostic marker [14].

CONCLUSION

The spectrum of hepatic involvement in dengue fever can vary from asymptomatic biochemical involvement to severe acute liver cell injury. Decreased serum albumin levels may be present and can cause plasma leakage due alteration of vascular endothelium in dengue and may serve as a marker of the critical phase of the disease and an indicator of severity.

LIMITATIONS

Sample size was small; a larger sample size is needed to generalize the results.

Declarations
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Conflict of interest: None
Ethical approval: Approved by Institutional Ethical Committee

REFERENCES

1. Kuhn RJ, Zhang W, Rossmann MG, Pletnev SV, Corver J, Lenches E, Jones CT, Mukhopadhyay S, Chipman PR, Strauss EG, Baker TS. Structure of dengue virus: implications for flavivirus organization, maturation, and fusion. Cell. 2002 Mar 8;108(5):717-25.
2. Ministry of Health and Family Welfare (India). Status note on dengue fever and dengue hemorrhagic fever. In: National vector borne disease control programme. 2009. Available at: www. nvbdcp.gov.in/Doc/DenStatusNote.pdf. Accessed June.
3. Lee MS, Hwang KP, Chen TC, Lu PL, Chen TP. Clinical characteristics of dengue and dengue hemorrhagic fever in a medical center of southern Taiwan during the 2002 epidemic. Journal of microbiology, immunology, and infection= Wei mian yu gan ran za zhi. 2006 Apr;39(2):121-9.
4. Gubler DJ. Dengue and dengue hemorrhagic fever. Clinical microbiology reviews. 1998 Jul 1;11(3):480-96.
5. Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S, Kunentrasai N, Viramitrachai W, Ratanachu-Eke S, Kiatpolpoj S, Innis BL, Rothman AL. Early clinical and laboratory indicators of acute dengue illness. Journal of Infectious Diseases. 1997 Aug 1;176(2):313-21.
6. Siqueira Jr JB, Martelli CM, Coelho GE, da Rocha Simplício AC, Hatch DL. Dengue and dengue hemorrhagic fever, Brazil, 1981–2002. Emerging infectious diseases. 2005 Jan;11(1):48.
7. Rigau-Pérez JG, Clark GG, Gubler DJ, Reiter P, Sanders EJ, Vorndam AV. Dengue and dengue haemorrhagic fever. The Lancet. 1998 Sep 19;352(9132):971-7.
8. Narasimhan D, Ponnusamy P, M Sathish. Analysis of liver function tests in dengue fever. Int J Adv Med. 2018;5;47-9.
9. Rajoo Singh Chinna, Omesh Goyal Deepinder Gaur Chhina, Prerna Goyal, Raj Kumar, Sandeep Puri. LFT in Dengue infections. Dengue Bulletin. 32, 2008.
10. Luiz Jose de Souza, Carlos Eduardo, Rita Maria, Felipe Pinto Alves, Leandro Codreiro Soares, Bruno Ribas. Impact of Dengue on liver function as evaluated by Serum transaminases. The Brazilian Journal of Infectious Diseases. 2007;11(4):407-410.
11. Viroj Wiwanitkit. Liver dysfunction in Dengue, An analysis of the previously published THAI Cases. J Ayub Med Coll Abbottabad. 2007;19(1).
12. Srivenu Itha, Rajesh Kashyap Narendra Krishnani, Vivek A. Saraswat, Gourdas Choudhuri, Rakesh Aggarwal. Profile of liver involvement in dengue virus infection. National Medical Journal India. 2005; 18:127–30.
13. CR Parrish, J Krenitsky and S McCray. University of Virginia Health System Nutrition Support Traineeship Syllabus. University of Virginia Health System Nutrition Support Traineeship; 2003.
14. C Mueller. True or false: Serum hepatic proteins concentration measure nutritional status. Suppor. Lin. 2004; 26, 8-16.
15. DS Seres. Surrogate nutrition markers, malnutrition, and adequacy of nutrition support. Nutr. Clin. Pract. 2005; 20, 308-13.
16. Biochemical Alterations as Markers of Dengue Hemorrhagic Fever. Luis Angel Villar-Centeno, Fredi Alexander Díaz-Quijano, and Ruth Aralí Martínez Vega School of Medicine, and Centro de Investigaciones Epidemiológicas, Universidad Industrial de Santander, Bucaramanga, Colombia. Am J Trop Med Hyg. 2008;78(3):370-4.