

# Serum Albumin Levels in Patients with Dengue Fever – A Longitudinal Study

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## Abstract

**Background and Objectives:** Dengue is an arboviral disease that is a major public health threat globally. In the past 50 years, the incidence of dengue has increased about 30-fold. Clinical manifestations may range from asymptomatic patients to dengue shock syndrome. It is very important to know early, which patient will go on to develop complications for planning management. Like any other disease, dengue also has various biomarkers which are used to find out dengue infection and severity of dengue infection. Serum albumin is a negative acute-phase reactant whose level decreases during many infections. Serum albumin was found to be an independent factor associated with severe dengue and dengue mortality in various studies. The aim of this study is to compare serum albumin levels among severe and non-severe cases of dengue and to find any association.

**Materials and Methods:** This study was done on 120 dengue patients admitted in Government Medical College Ernakulam from January 2017 to December 2017. The clinical features and investigations results were noted. Serum albumin was done on the day of admission and the 3<sup>rd</sup> day of admission. Patients were classified into mild, moderate, and severe based on the severity of dengue. Serum albumin levels were compared with the different severity groups.

**Results and Discussion:** Of the 120 patients studied, 84 were male and 36 were female. The mean serum albumin of dengue patients on the day of admission was 3.61 g/dl and on the 3<sup>rd</sup> day of admission was 3.48 g/dl. The mean albumin on the day of admission was 3.71 g/dl, 3.60 g/dl, and 3.34 g/dl for mild, moderate, and severe dengue, respectively ( $P = 0.005$ ). The mean albumin on the 3<sup>rd</sup> day of admission was 3.62 g/dl, 3.47 g/dl, and 3.19 g/dl for mild, moderate, and severe dengue patients, respectively ( $P = 0.001$ ). As the severity of dengue increases, the mean day 1 and day 3 albumin levels decrease, which is statistically significant. Hypoalbuminemia ( $<3.5$  g/dl) was seen on day 1 in 34.8%, 34%, and 57.1% among mild, moderate, and severe dengue patients, respectively ( $P = 0.148$ ). There was no significant association of hypoalbuminemia on day 1 with the severity of dengue. Hypoalbuminemia was seen on day 3 in 26.1%, 47.2%, and 81% of mild, moderate, and severe dengue patients. There is a significant association between hypoalbuminemia on day 3 and severity of dengue. On 3<sup>rd</sup> day of admission, hypoalbuminemia was seen more as the severity of dengue increased.

**Conclusions:** As the severity of dengue increased, there was a fall in serum albumin levels and it was statistically significant. Serum albumin can be used as a prognostic marker for dengue.

**Key words:** Dengue fever, Serum albumin, Severe dengue

## INTRODUCTION

Dengue is an arboviral disease that is a major public health threat globally. At present, dengue fever (DF) causes more illness and death than any other arboviral disease

of humans. Dengue belongs to the family Flaviviridae, genus *Flavivirus*, and species dengue virus (DENV). There are four serologically distinct types of DENV, DENV-1, DENV-2, DENV-3, and DENV-4. These viruses are transmitted to human beings by *Aedes* mosquitoes such as *Aedes aegypti* and *Aedes albopictus*. In the past 50 years, the incidence of dengue has increased about 30-fold.<sup>[1]</sup> In India, dengue was first reported in Madras (now Chennai) in 1780, and the first outbreak of dengue occurred in Calcutta (now Kolkata) in 1963. Thereafter, outbreaks occurred in different parts of India. Even though dengue was previously restricted to urban areas, now, it has spread

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to rural areas also.<sup>[2]</sup> In 2017, Kerala had the maximum number of dengue patients in India.<sup>[3]</sup>

### Objectives

The objectives of this study were to estimate serum albumin levels in dengue patients admitted in wards of Government Medical College, Ernakulam, and to compare serum albumin levels among severe and non-severe cases of dengue.

## MATERIALS AND METHODS

This was a longitudinal study conducted in patients admitted with dengue in the medical wards of Government Medical College, Ernakulam. The study was conducted for 1 year. All patients who fulfilled the inclusion criteria were recruited to the study with informed consent.

Once the patient got admitted history was taken and data collected in prestructured pro forma. Details of history, examinations, and laboratory and technical investigations reports were noted from time to time. Patients were treated specifically and symptomatically.

DF was confirmed by immunochromatographic method identifying the antibodies against DENV – immunoglobulin M (IgM) and dengue viral antigen – nonstructural protein 1 (NS1). Five milliliters of venous blood was taken to a plain bottle for estimation of serum albumin. Serum albumin was measured using ALB slide method using VITROS ALB slides. Serum albumin levels were measured on day 1 and day 3 of admission. Patients were followed up clinically during the hospital stay until discharge. DF was classified based on criteria by DHS Kerala [Table 1].

### Inclusion Criteria

The following criteria were included in the study:

1. Age more than 13 years
2. Dengue confirmed by NS1Ag test or IgM dengue or both NS1Ag and IgM.

### Exclusion Criteria

The following criteria were excluded from the study:

1. All other cases of acute febrile illness
2. Patients with bleeding disorders
3. Patients with cardiac/liver/respiratory diseases
4. Patients already having severe dengue
5. Malnourished patients.

### Data Management and Statistical Analysis

Data were coded and entered into Microsoft Excel. The analysis was done using SPSS software. Quantitative variables were summarized using mean and standard deviation. Association between quantitative variables was tested using *t*-test and ANOVA.

### Ethical Issues

Only the patients who gave consent were included in the study. Ethical clearance was obtained from the ethical committee.

## OBSERVATIONS AND RESULTS

Of the 120 patients studied, 84 were male and 36 were female [Table 2]. DF was seen more among males. The age range of patients was 14–83 years, and the mean age was 33.52 years. Moderate dengue was seen more compared to mild and severe dengue [Table 3]. The mean serum albumin of dengue patients on the day of admission was 3.61 g/dl and on the 3<sup>rd</sup> day of admission was 3.48 g/dl [Table 4]. The mean albumin on the day of admission was 3.71 g/dl, 3.60 g/dl, and 3.34 g/dl for mild, moderate, and severe dengue, respectively [Table 5]. The mean albumin on the 3<sup>rd</sup> day of admission was 3.62 g/dl, 3.47 g/dl, and 3.19 g/dl for mild, moderate, and severe dengue patients, respectively [Graph 1]. As the severity of dengue increased, the mean day 1 and day 3 albumin levels decreased and were statistically significant [Tables 6 and 7]. Hypoalbuminemia (<3.5 g/dl) was seen on day 1 in 34.8%, 34%, and 57.1% among mild, moderate, and severe dengue patients, respectively ( $P = 0.148$ ). There was no significant association of hypoalbuminemia on day 1 with the severity of dengue [Table 8]. Hypoalbuminemia was seen on day 3 in 26.1%, 47.2%, and 81% of mild, moderate, and severe dengue patients. On day 3, the proportion of hypoalbuminemia increased as the severity of dengue increased and was statistically significant [Table 9]. There was no association between the outcome of the patients and dengue severity. There were no deaths in the study population.

## DISCUSSION

Male preponderance was seen in this study. It was similar to a study conducted by Shiji *et al.* in Kerala, where 72% of the patients were males.<sup>[4]</sup> This could be due to the fact that males predominantly go out in the day time when the carrier *A. aegypti* bites them. Males outnumbered females in the majority of the reports of dengue outbreaks in India, and in a few studies, all from Delhi, the male-to-female ratio was as high as 3–5:1. The significance of this finding is unclear.<sup>[5-9]</sup>

Hypoalbuminemia has been described with dengue infections and is an indicator of severity.<sup>[10]</sup> The mean serum albumin concentration in the present study was 3.61 g/dl on the day of admission. Bhagyamma *et al.* showed that the mean serum albumin levels among dengue patients were 3.13 g/dl.<sup>[11]</sup> A study by Singh *et al.*, on 214 dengue patients in a tertiary hospital in Punjab,

**Table 1: Dengue case classification**

Mild	Moderate	Severe
Nausea, vomiting	Abdominal pain or tenderness	Severe plasma leakage leading to: Shock (dengue shock syndrome)
Rash	Persistent vomiting	Fluid accumulation with respiratory distress
Aches and pains	Mucosal bleed	Severe bleeding
Tourniquet test positive	Lethargy, restlessness	Severe organ involvement
Leukopenia	Liver enlargement >2 cm	Liver: AST or ALT ≥1000
	Increase in Hematocrit	CNS: Impaired consciousness
	Concurrent with rapid decrease In platelet count	Heart and other organs
	Clinical fluid accumulation	
	With comorbid conditions such as old age, diabetes, hypertension, pregnancy, CAD, hemoglobinopathies, immunocompromised patients, patients on steroids, anticoagulants, or immunosuppressants	

**Table 2: Percentage distribution of the sample according to sex**

Sex	Frequency	Percentage
Male	84	70
Female	36	30
Total	120	100

**Table 3: Percentage distribution of the sample according to dengue severity**

Severity	Frequency	Percentage
Mild	46	38.3
Moderate	53	44.2
Severe	21	17.5
Total	120	100.0

**Table 4: Descriptive of day 1 and day 3 albumin among the study subjects**

Day	Mean albumin (g/dl)	Standard deviation	95% Confidence interval
Day 1	3.61	0.4363	3.522–3.680
Day 3	3.48	0.4170	3.405–3.555

India, showed that the mean serum albumin was 3.2 g/dl. The mean albumin levels in DF, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) were 3.3 g/dl, 3 g/dl, and 2.7 g/dl, respectively. There was also a significant fall in serum albumin levels in DSS patients compared to DHF patients.<sup>[12]</sup>

Another study by Jnaneshwari *et al.* among 166 patients in Bangalore also showed that the mean serum albumin was 3.52 g/dl, and there was also a significant fall in serum albumin levels as the severity of dengue increased. The mean serum albumin levels in different groups were 3.61 g/dl, 3.31 g/dl, and 2.71 g/dl in DF, DHF, and DSS, respectively.<sup>[13]</sup>

**Table 5: Descriptive of day 1 and day 3 albumin according to the severity of dengue**

Severity	n	Mean	Standard deviation	95% Confidence interval
Day 1 albumin				
Mild	46	3.711	0.4478	3.578–3.844
Moderate	53	3.608	0.3736	3.505–3.711
Severe	21	3.343	0.4697	3.129–3.557
Day 3 albumin				
Mild	46	3.622	0.3988	3.503–3.740
Moderate	53	3.472	0.4059	3.360–3.584
Severe	21	3.190	0.3375	3.037–3.344

**Table 6: Comparison of mean day 1 albumin according to dengue severity**

Severity	n	Mean albumin day 1 (g/dl)	F	P-value
Mild	46	3.71	5.5	0.005
Moderate	53	3.60		
Severe	21	3.34		

**Table 7: Comparison of mean day 3 albumin according to dengue severity**

Severity	n	Mean albumin day 3	F	P-value
Mild	46	3.62	8.73	0.001
Moderate	53	3.47		
Severe	21	3.19		

However, a study by Reddy and Roshan, on 100 dengue patients attending a Tertiary Care Hospital in Mangalore, India, showed that even though serum albumin was low in severe dengue compared to non-severe dengue, it was not statistically significant. The mean serum albumin was 3.76 g/dl in the total population with 3.55 g/dl and 3.77 g/dl for severe and non-severe dengue patients, respectively.<sup>[14]</sup> Villar-Centeno *et al.* showed that albuminemia >4 g/dl was associated with a lower risk of DHF.<sup>[15]</sup>

**Table 8: Hypoalbuminemia on day 1 in dengue patients**

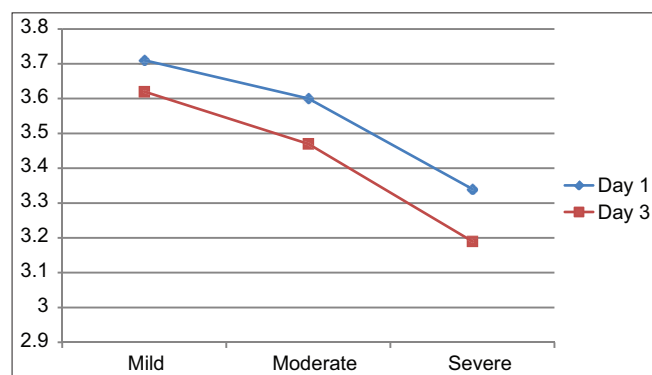
Dengue type	Hypoalbuminemia	Normal	Total
Mild			
Count	16	30	46
Percent	34.8%	65.2%	100.0%
Moderate			
Count	18	35	53
Percent	34.0%	66.0%	100.0%
Severe			
Count	12	9	21
Percent	57.1%	42.9%	100.0%
Total			
Count	46	74	120
Percent	38.3%	61.7%	100.0%

$\chi^2=3.817, P=0.148$

**Table 9: Hypoalbuminemia on day 3 in dengue patients**

Dengue type	Hypoalbuminemia	Normal	Total
Mild			
Count	12	34	46
Percent	26.1%	73.9%	100.0%
Moderate			
Count	25	28	53
Percent	47.2%	52.8%	100.0%
Severe			
Count	17	4	21
Percent	81.0%	19.0%	100.0%
Total			
Count	54	66	120
Percent	45.0%	55.0%	100.0%

$\chi^2=17.716, P\leq 0.001$



**Graph 1: Comparison of mean day 1 and day 3 albumin according to dengue severity**

## CONCLUSIONS

It was seen that as the severity of dengue increased, there was a fall in serum albumin levels and it was statistically significant. The fall in albumin levels was seen even on

the day of admission and persisted on day 3 as well. The mean albumin levels on day 3 of admission were lower than admission day albumin levels for mild, moderate, and severe dengue patients. Serum albumin is a cheap and easily available laboratory test, and its measurement can be used in the peripheral hospitals as a prognostic marker of dengue severity. This helps in early referral to the higher center if the albumin levels are low.

## Limitations of the Study

- The study was 1 year only
- Small sample size
- There was no mortality in the cases studied because the study was done in a tertiary care center with adequate facilities
- Being a tertiary care center in a metro city, the study might not always represent an actual situation in the community.

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