



A STUDY ON CORRELATION OF SERUM CALCIUM WITH SEVERITY OF DENGUE FEVER – A CROSS-SECTIONAL STUDY

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ABSTRACT

Introduction: Since 1780, people have been aware of the existence of the Aedes mosquito-borne disease known as dengue. The fastest-emerging viral illness carried by a vector is dengue. In tropical areas, dengue fever is a leading cause of morbidity and mortality. It is well recognised that serum calcium plays a crucial role in heart and circulation health. We assessed the relationship between the level of serum calcium and the severity of dengue along with the length of hospital stay. **Materials and methods:** The patient who satisfies the inclusion criteria will be enrolled for the study after receiving informed permission and approval from the institutional ethical committee. A total of 140 patients with dengue fever diagnoses will be counted as cases. Dengue was classified according to World Health Organization criteria and confirmed by either IgM antibody or NS1 antigen detection. **Results:** Majority of them were aged between 21 to 30 years (37.1%), were males (77.1%) and had fever from 3 to 5 days (62.1%). We had 35% without warning signs, 17.1% with warning signs and 47.9% with severe dengue. The mean serum calcium was significantly higher in dengue without warning signs (9.1 ± 0.69 mg/dl) compared to dengue with warning signs (8.4 ± 0.83 mg/dl) and severe dengue (7.8 ± 0.94 mg/dl) compared to non-severe dengue cases ($785.9 \pm 193.1 \mu\text{g/l}$) ($p < 0.001$). Similarly platelet count, albumin and corrected calcium also decreased with increased severity ($p < 0.05$). **Conclusion:** Serum calcium levels significantly correlated with dengue severity and severe dengue manifestations.

KEYWORDS : Dengue, Dengue haemorrhagic fever, Dengue shock syndrome, Serum Calcium

INTRODUCTION:

The flavivirus member known as the dengue virus is the cause of the vector-borne disease dengue.¹ Due to its potential to place a significant burden on the public health system and the fact that it spreads quickly through mosquito bites, dengue is a disease of great concern around the world. According to World Health Organization data, there are between 50 and 100 million new dengue infections each year, and the number of nations reporting the disease is steadily rising.²

Clinical symptoms of dengue infection ranged from asymptomatic infection or a straightforward viral sickness to dengue shock syndrome. Dengue can result in fatal haemorrhage, vascular shock, and more. Thus, the cornerstone of care is early identification and recognition of severe dengue illnesses such as dengue haemorrhagic fever and dengue shock syndrome. Although paediatric dengue infections are common, adult admissions have surged recently, particularly in India. Unfortunately, there is a lack of information regarding dengue infections in adults; this study aims to fill that gap.^{3,4}

In recent years, dengue has been a serious health problem in India, notably in the state of Karnataka, which has contributed significantly to mortality and morbidity. The severe type of dengue infection and its side effects, including shock syndrome, hemorrhagic symptoms, and severe thrombocytopenia, are the main causes of this death. So, we must pinpoint the patients who will all experience these issues. With the commencement of plasma leakage, multiple serum biochemical parameter abnormalities take place in patients with severe dengue infection; these derangements are not seen in patients with non-severe dengue. This investigation examined the relationship between serum calcium levels and the severity of dengue infection.

METHODOLOGY

After receiving approval from the institutional ethical committee, a cross-sectional study was conducted in the department of general medicine of a tertiary care centre.

Openepi software version 2.3.1 was used to estimate sample size. 80% of the study's power and a 95% degree of

confidence. According to the investigation made by Constantine GR et al.⁵ The proportion of Dengue Hemorrhagic fever patients who had hypocalcemia $86.9\% = p$ At 10%, Relative precision, Sample size estimated is $69 = 70$ considering the design effect of 2, the estimated sample size was 140.

Formula used $n = \frac{[DEFF * Np(1-p)]}{[(d^2/Z^2(1-\alpha)/2 * (N-1) + p * (1-p)]}$

The study was conducted for 2 months among confirmed cases of dengue IgM positive or NS1 Ag positive, aged > 18 years. We excluded patients' hypertension, diabetes, and cardiac disease, malaria, on calcium supplements, those on antihypertensive / anti-arrhythmic agents or any drugs affecting calcium homeostasis, those with malabsorption syndrome or renal dysfunction.

Following a thorough history and clinical examination to determine the severity and consequences of the patient's condition. Positive serological tests for dengue confirmed that every patient in this investigation was a case of the disease. Before the treatment began, all the investigations were sent. Following a diagnosis of dengue, the patient had fluid therapy and symptomatic treatment in accordance with the most recent WHO recommendations.

According to the patient's conditions, additional supportive care was provided. Individuals with dengue fever are admitted to the medical wards. ELISA was used to measure the serum ferritin levels on the first day of admission to the hospital. All data were entered in Microsoft excel and statistical analysis was performed using the statistical software SPSS version 21.0.

RESULTS

We studied total of 140 subjects with dengue. Table 1 shows baseline characteristics of our study subjects. Majority of them were aged between 21 to 30 years (37.1%), were males (77.1%) and had fever from 3 to 5 days (62.1%). We had 35% without warning signs, 17.1% with warning signs and 47.9% with severe dengue.

Table 1: Baseline characteristics

Baseline characteristics		Frequency (%)
Age	<20 years	29 (20.7%)
	21 to 30 years	52 (37.1%)
	31 to 40 years	27 (19.3%)
	41 to 50 years	14 (10%)
	>50 years	18 (12.9%)
Gender	Male	108 (77.1%)
	Female	32 (22.9%)
Duration of fever	<2 days	17 (12.1%)
	3 to 5 days	87 (62.1%)
	6 to 10 days	36 (25.7%)
Dengue diagnosis	NS1 positive	53 (37.9%)
	IgM positive	87 (62.1%)
Dengue severity	Dengue without warning signs	49 (35%)
	Dengue with warning signs	24 (17.1%)
	Severe dengue	67 (47.9%)
Severe dengue manifestations	Bleeding manifestations	39 (27.9%)
	Pleural effusion	25 (17.9%)
	Ascites	25 (17.9%)
	GB wall edema	37 (26.4%)
Transfusions	Blood transfusion	2 (1.4%)
	FFP transfusion	1 (0.7%)
	Platelet transfusion	14 (10%)
Duration of hospitalization	1-2 days	36 (25.7%)
	3-4 days	65 (46.4%)
	5-6 days	21 (15%)
	7-8 days	18 (12.9%)

Table 2 shows the mean serum laboratory values in dengue severity. The mean serum calcium was significantly higher in dengue without warning signs (9.1 ± 0.69 mg/dl) compared to dengue with warning signs (8.4 ± 0.83 mg/dl) and severe dengue (7.8 ± 0.94 mg/dl) compared to non-severe dengue cases ($785.9 \pm 193.1 \mu\text{g/l}$) ($p < 0.001$). Similarly platelet count, albumin and corrected calcium also decreased with increased severity ($p < 0.05$)

Table 2: Association of laboratory parameters and severity of dengue

	Dengue without warning signs	Dengue with warning signs	Severe Dengue	P value
Serum calcium (mg/dl)	9.1 ± 0.69	8.4 ± 0.83	7.8 ± 0.94	<0.001
Hemoglobin	11.2 ± 1.65	11.4 ± 1.92	12.1 ± 4.15	0.321
Platelet count	1.32 ± 0.32	1.06 ± 0.53	0.64 ± 0.54	<0.001
Hematocrit	34.04 ± 5.2	33.67 ± 5.5	36.2 ± 6.3	0.064
Albumin (g/dl)	4.17 ± 0.36	4.07 ± 0.23	3.98 ± 0.24	0.006
Corrected calcium (mg/dl)	8.96 ± 0.64	8.35 ± 0.79	7.78 ± 0.94	<0.001

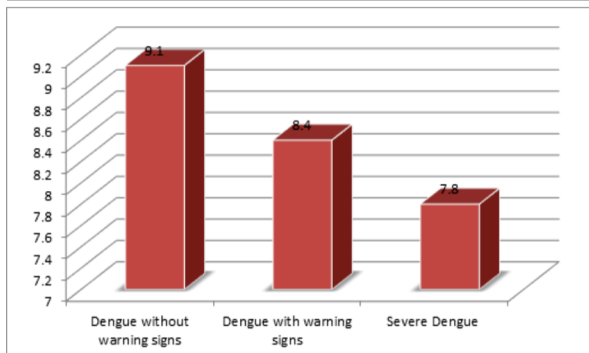


Figure 1: Bar graph showing serum calcium and severity of dengue

Table 3 shows the baseline characteristics comparison with serum calcium levels. We found that gender, dengue severity and severe dengue manifestations was associated with serum calcium levels on admission ($p < 0.05$).

Table 3: Association of baseline characteristics with serum calcium levels on admission

Baseline characteristics		Serum calcium (mg/dl)		P value
		Normal (8.5 to 10.5)	Low (<8.5)	
Age	<20 years	11 (17.5%)	18 (23.4%)	0.786
	21 to 30 years	25 (39.7%)	27 (35.1%)	
	31 to 40 years	14 (22.2%)	13 (16.9%)	
	41 to 50 years	5 (7.9%)	9 (11.7%)	
	>50 years	8 (12.7%)	10 (13%)	
Gender	Male	54 (85.7%)	54 (70.1%)	0.042
	Female	9 (14.3%)	23 (29.9%)	
Duration of fever	<2 days	10 (15.9%)	7 (9.2%)	0.121
	3 to 5 days	42 (66.7%)	45 (59.2%)	
	6 to 10 days	11 (17.5%)	24 (31.6%)	
Dengue diagnosis	NS1 positive	23 (36.5%)	30 (39%)	0.765
	IgM positive	40 (63.5%)	47 (61%)	
Dengue severity	Dengue without warning signs	41 (65.1%)	8 (10.4%)	<0.001
	Dengue with warning signs	9 (14.3%)	15 (19.5%)	
	Severe Dengue	13 (20.6%)	54 (70.1%)	
Severe dengue manifestations	Bleeding manifestations	5 (7.9%)	34 (44.2%)	<0.001
	Pleural effusion	2 (3.2%)	23 (29.9%)	
	Ascites	1 (1.6%)	24 (31.2%)	
	GB wall edema	6 (9.5%)	31 (40.3%)	
Transfusions	Blood transfusion	1 (1.6%)	1 (1.3%)	1
	FFP transfusion	0	1 (1.3%)	
	Platelet transfusion	4 (6.4%)	10 (13%)	

DISCUSSION

Dengue is a major arboviral infection spread by mosquitoes. Due to plasma leakage, certain serum biochemical parameters change in severe dengue infection. Analyzing the connection between serum calcium and its link to a severe dengue infection may therefore be useful for enhancing the effectiveness of treatment.

We found that the mean serum calcium was significantly higher in dengue without warning signs (9.1 ± 0.69 mg/dl) compared to dengue with warning signs (8.4 ± 0.83 mg/dl) and severe dengue (7.8 ± 0.94 mg/dl) compared to non-severe dengue cases ($785.9 \pm 193.1 \mu\text{g/l}$) ($p < 0.001$). Similarly platelet count, albumin and corrected calcium also decreased with increased severity ($p < 0.05$)

Similar to this, Habbu et al.⁶ observed that the calcium level in dengue patients ranged from 6.0 to 11 gm/dl and 10.0 to 15.0 gm/dl in healthy controls, while it dropped in controls and ranged from 5.5 to 10 mg/dl in DF. Calcium level decreased in DF range from 5.5-10mg/dl and 8-11 mg/dl among the controls. Our study findings were comparable to studies by Jayachandra et al.⁷, N J Dahanayaka et al.⁸, Constantine GR et al.⁵ and Adikari M et al.⁹

Serum ionised calcium and hematocrit were found to be statistically significantly correlated (p value 0.001), according

to Mahajan et al.¹⁰ Moreover, a statistically significant correlation between serum ionised calcium levels and ALT levels was discovered (p value 0.001).

Our study results are in line with the study by Kavita et al.¹¹ where they observed that low serum calcium levels correlated significantly with severity of dengue illness and increased risk of bleeding manifestations.

According to Castilla-Guerra et. al.¹² and Sara Syed et al.¹³, acute hypocalcemia is the primary cause of increased neuromuscular excitability and tetany is usually linked to dengue virus infection. The substantial calcium levels seen in dengue patients are consistent with their findings.

CONCLUSION

Serum calcium levels show significant correlation with dengue fever severity, severe dengue manifestations and gender. In patients with severe dengue infection and dengue fever with warning signs compared to those with dengue fever without warning signs, the mean serum calcium levels were considerably lower.

Serum calcium levels can also be utilized as a prognostic indicator and a possible biomarker to determine the severity of a dengue illness. However further research is required to back this up.

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