

An Association between serum calcium level and severity of dengue virus infection in a tertiary care hospital

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Abstract

Background: Dengue is a disease of major concern throughout the world due to its ability to cause huge burden on public health system since it is rapidly transmitted by mosquito. Dengue infection presented with variety of clinical manifestations ranging from asymptomatic infection or simple viral illness to dengue shock syndrome. In patients with severe dengue infection numerous serum bio chemical parameter changes occur with the onset of plasma leakage, these derangements are not apparent in non severe dengue patients. The various biochemical markers has been measured to identify the

severe form of dengue infection like AST, ALT, platelet count, PCV and electrolytes especially calcium levels.

Materials and Methods: The present observational study was conducted in tertiary care institute located in Hyderabad, Telangana state over a period of 1 year from June 2021 to June 2022 including 100 cases admitted of dengue fever.

Results: Serum calcium levels has an significant correlation in terms of severity of dengue fever and it was observed in the study that patients with dengue with warning signs and severe dengue there is significant hypocalcemia that corresponds to the correlation with the serum calcium levels and to the severity of dengue

illness and help in prognosticating the patient with dengue fever. .

Conclusion: It was observed that serum calcium levels shows significant correlation with dengue fever severity. The Mean serum calcium levels was significantly lower in cases with severe dengue infection and dengue fever with warning signs than in patients with dengue fever without warning signs. Furthermore, the serum calcium levels can be used as a potential biomarker to predict the severity of dengue infection and can be used a prognostic marker as well.

Keywords: Dengue fever, serum calcium, hypocalcemia, severe dengue,

Introduction

Dengue is a disease of major concern through the world due to its ability to cause huge burden on public health system since it is rapidly transmitted by mosquito. Based on (WHO) World Health Organization reports, about 50 to 100 million new dengue infections are estimated to occur annually, with a steady increase in the number of countries reporting the disease. [1] Dengue infection presented with variety of clinical manifestations ranging from asymptomatic infection or simple viral illness to dengue shock syndrome. Dengue causes severe bleeding, circulatory shock and even death. So early diagnosis and recognition of severe form of dengue infections like dengue hemorrhagic fever, dengue shock syndrome is cornerstone in management. Though dengue infections are common in paediatric age group, adult admissions has been increased in recent years especially in India. However, the data of adult dengue infections are limited; this study is to get additional data on dengue infections among adults. In India, particularly in Tamilnadu state in recent years dengue has been a major health issue contributing to significant mortality and morbidity. The

major factors contributing to this mortality is severe form of dengue infection and its complications like shock syndrome, hemorrhagic manifestations and severe thrombocytopenia. So we need to identify the patients who are all going to these complications. In patients with severe dengue infection numerous serum bio chemical parameter changes occur with the onset of plasma leakage, these derangements are not apparent in non severe dengue patients. The various biochemical markers has been measured to identify the severe form of dengue infection like AST, ALT, platelet count, PCV and electrolytes especially calcium levels.

Materials and methods

The present prospective study was undertaken over 100 patients admitted with dengue fever for period of 1 year from June 2021 to June 2022 at general medicine department in kamineni academy of medical sciences and research Centre, Hyderabad. All Patients after obtaining a detailed medical history and physical examination the following investigations are done CBP, SERUM ELECTROLYTES, SERUM CALCIUM, DENGUE NS1 ANTIGEN, DENGUE SEROLOGY, PERIPHERAL SMEAR, CUE, other relevant markers are done.

Inclusion criteria

AGE: 15-50 yrs. Either sex. Patients with hypotension. Patients with third space fluid collection like ascites pleural effusion, gallbladder edema evidenced by USG. Patients with severe thrombocytopenia, Patients with bleeding manifestations.

Exclusion criteria

Patient refusal. Patient with comorbid conditions like diabetes, liver diseases, cardiac failure, CKD. Patients with fever associated with other illness like URI, LRI, and UTI.

Results

Table 1: Age Distribution among all fever cases

Age	Frequency	Percentage
15-20	36	36.0
20-29	38	38.0
30-39	18	18.0
>=40	8	8.0
Total	100	100.0

Different age groups of subjects were studied in the study and has been correlated and segregated into different groups based on their clinical and laboratory considerations and further co-related with the serum calcium levels.

Table 2: Comparison of Sr. Calcium within study groups

	N	Mean	Standard Deviation
No Dengue	38	8.95	0.70
Dengue Without Warning	21	9.27	0.51
Dengue With Warning	24	7.95	0.96
Severe Dengue	17	7.60	1.21

P value was 0.0005 which was highly significant

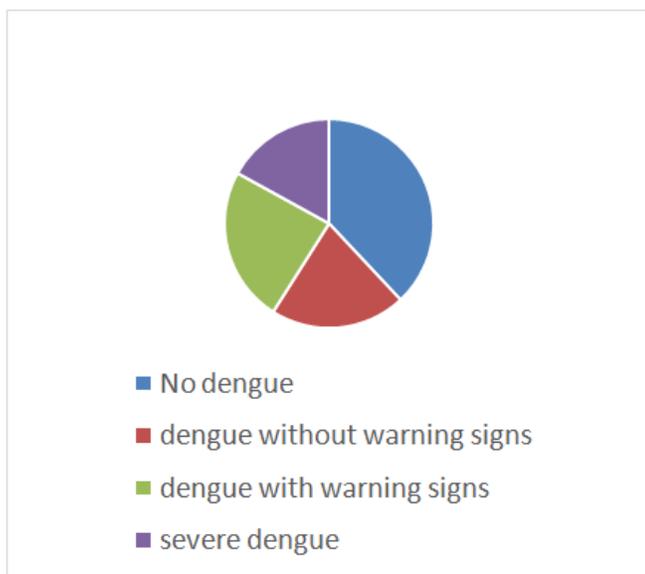


Figure 1: Pie diagram showing frequency of subjects among different groups of dengue

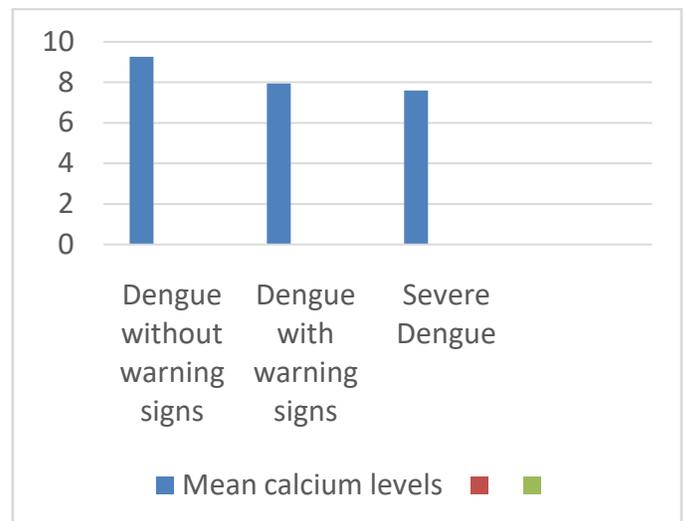


Figure 2: Bar Diagram Showing Mean Calcium Levels Within Dengue Groups

The mean serum calcium levels in dengue patient without warning signs is 9.27meq/l, in dengue patients with warning signs is 7.95 meq/l, in patients with severe dengue infection 7.60 meq/l. There is no statistical significance in serum calcium levels between dengue negative with dengue positive without warning signs (p=0.580). There is no statistical significance in serum calcium levels between dengue with warning signs and severe dengue infection (p=0.541). There is high statistical significance in serum calcium levels between dengue negative and dengue positive with warning signs (p=0.0005). There is high statistical significance in serum calcium levels between dengue positive without warning signs and severe dengue infection (p=0.0005). There is high statistical significance in serum calcium levels between dengue positive without warning signs and dengue with warning signs (p=0.0005)

Discussion

Dengue is a major arboviral infection spread by mosquitoes. In Southeast Asia, the Pacific, and the Americas every year, there are around 50 million dengue infections and around 500,000 individuals hospitalized

with DHF. Dengue is a rapidly emerging disease in India and it has been prevalent for about 230 years here. India recorded 99913 cases and 220 deaths during a major outbreak in 2015 according to the NVBDCP. In severe dengue infection various serum biochemical parameter changes occur due to plasma leakage. Thus analyzing the relation between serum free calcium and its association with severe dengue infection may prove helpful in improving treatment outcomes. Hypocalcaemia is known to be associated with plasma leakage during severe dengue and this insists the need for studies on this area so as to improve the treatment outcomes. In view of the above said we did a study titled “an association between serum calcium level and severity of dengue virus infection in Kamineni Academy of Medical Sciences And Research Center ,hyderabad” to assess the correlation between serum ionized calcium as a biochemical marker of severity of dengue infection. In dengue fever various biochemical parameters altered with the onset of plasma leakage, particularly in hematocrit, platelet count, elevation of liver enzymes, hyponatremia, and hypocalcemia Etc. These changes are not apparent in non severe dengue cases. The relationship between serum calcium levels and dengue fever was analyzed by various studies across the world and observed that calcium level is reduced in severe form of dengue infection. The calcium ion plays an important role in normal cellular function and myocardial contractility. [3]. Hypocalcemia may also be commonly seen in other illness like severe sepsis, traumatic injury. So, it has a relationship to mortality in severely ill patients. The exact cause for this relation is not defined. The following possible mechanisms may be the cause for hypocalcemia, parathyroid insufficiency, defective vitamin D3 synthesis, reduced dietary intake

during illness. The measurement of serum calcium is routinely not done in clinical practice for dengue infection. it's postulated that hypocalcaemia in dengue fever could be due to the influx of calcium ions and calcium replacement could enhance the dengue virus activity by increasing the concentration of intracellular calcium ions. This can be supported by in vitro studies showing that calcium channel blockers inhibiting the activity of the influx of calcium ions in to T cells and macrophages and reducing the disease activity of dengue. However, there is only very limited supportive evidence on calcium supplementation in the management of dengue fever. Padmini Prakash Habbu et al ., at Ashwini Rural Medical College, Hospital and Research Centre, Sholapur over the period of 6 month with sampling of 70 individuals studied Hb, SGOT and SGPT, creatinine and calcium estimations of Healthy control and Dengue patients and found that in dengue patients Calcium level decreased in DF range from 5.5-10 mg/dl and 8-11 mg/dl among the controls the Hb values are low as compared to Healthy controls it's ranging from 6.0 - 11gm/dl in dengue patients and 10.0-15.0gm/dl in Healthy controls. SGOT and SGPT values are raised in dengue as compared to healthy controls it's ranging between 56 - 532 IU/L among dengue patients and 19-60 IU/L among healthy control groups. The creatinine values are almost same in control and patients ranging between 0.5- 2.8 mg/dl. Calcium level decreased in DF range from 5.5-10 mg/dl and 8-11 mg/dl among the controls [6] Jayachandra et al., of Department of Medicine, BMC, Bangalore conducted a study using 145 patients and concluded that hypocalcemia is associated with severe dengue infection compared with dengue fever patients without warning signs. [7] Mitrakrishnan C Shivanthan et al., of University of Colombo,

Department of Medicine, Sri Lanka studied the relation between dengue infection and serum calcium levels and found that dengue related Myocarditis has a relationship with alteration in intracellular calcium level. They also observed that there is increased mortality in severe dengue with hypocalcemia. [8] N J Dahanayaka et al., studied the significance of detecting hypocalcaemia to predict severity of dengue infection .Using 36 probable cases of dengue conducted a cross sectional study at University Medical Unit (UMU), Teaching Hospital Anuradhapura and found that Positive and negative predictive values of hypocalcaemia predicting TSFA was 29% and 100% respectively with a positive likelihood ratio of 2.17 (95% CI 1.84-2.551). Mean SIC (lowest) among patients with TSFA (Third space fluid accumulation) was 0.97 (SD 0.1) mmol/l compared to

Conclusion

It was observed that serum calcium levels shows significant correlation with dengue fever severity. The Mean serum calcium levels was significantly lower in cases with severe dengue infection and dengue fever with warning signs than in patients with dengue fever without warning signs. Furthermore, the serum calcium levels can be used as a potential biomarker to predict the severity of dengue infection and can be used a prognostic marker as well. But further studies are needed to support this.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate consent forms. In the form the patients have given their consent for the images and other clinical information to be reported in the journal.

1.12 (SD 0.14) mmol/l among those without TSFA ($p=0.035$). Patients with hypocalcaemia had significantly lower platelet count and serum albumin levels (Table 3). All five patients with platelet countmajor reduction in serum calcium level within the first 24 hours of the onset of severe dengue clinical criteria. [9] Dr. Aditya Mahajan et al ., of Department Of General Medicine, A J Institute Of Medical Sciences / Rajeev Gandhi University Of Health Sciences, India conducted a study over 2 years on Correlation between Serum Ionized Calcium and Severity of Dengue Infection using a cross-sectional study done at A.J Institute of Medical Sciences in Mangalore, Karnataka with 50 probable cases and found that a statistically significant association was found between serum ionized calcium and dengue severity(p value-0.0001)

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