

CORRELATION BETWEEN HYPOCALCEMIA AND SEVERITY OF DENGUE FEVER IN CHILDREN

Dr. Thulasi ¹, Dr. Kishore. N ^{2*}, Dr. Syed Mohammed ³ and
Dr. Santhosh Kumar T ⁴

^{1,2,3,4} Department of Paediatrics, Saveetha Medical College and Hospital SIMATS,
Saveetha University.

*Corresponding Author Email: kishore.ssp@gmail.com

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Abstract

Background: Dengue fever remains a significant public health challenge worldwide, with children being particularly vulnerable to its severe forms. Recent evidence suggests a potential link between electrolyte imbalances, such as hypocalcemia, and the severity of dengue infection. This study aims to explore the correlation between hypocalcemia and the severity of dengue fever in pediatric patients. **Methods:** This cross-sectional study included 200 children diagnosed with dengue fever, admitted to a tertiary care hospital over a period of one year. Patients were categorized into two groups based on the severity of dengue fever: severe and non-severe, as defined by WHO criteria. Serum calcium levels were measured within 24 hours of admission. Statistical analysis was performed to identify the correlation between serum calcium levels and the severity of dengue fever, using Pearson's correlation coefficient and chi-square tests. **Results:** Out of the 200 children with dengue fever, 120 were classified with non-severe dengue, and 80 with severe dengue. Hypocalcemia was observed in 60% of the severe dengue cases compared to 30% in non-severe cases. A statistically significant inverse correlation was found between serum calcium levels and the severity of dengue fever ($p < 0.05$). Children with severe dengue fever had significantly lower mean serum calcium levels than those with non-severe dengue fever. **Conclusion:** The study found a significant correlation between hypocalcemia and the severity of dengue fever in children, suggesting that hypocalcemia may serve as a useful biomarker for predicting the severity of dengue infection. These findings underscore the importance of monitoring electrolyte levels as part of the management of children with dengue fever, potentially guiding more targeted interventions to mitigate the risk of severe complications.

Keywords: Dengue Fever, Hypocalcemia, Children, Severity, Electrolyte Imbalance.

INTRODUCTION

Dengue fever, a mosquito-borne viral infection, has emerged as a significant public health challenge globally, particularly in tropical and subtropical regions. Characterized by high fever, severe headache, pain behind the eyes, muscle and joint pains, rash, and mild bleeding manifestation, dengue fever can progress to more severe forms such as dengue hemorrhagic fever and dengue shock syndrome. Among the various complications associated with dengue fever, hypocalcemia, or low calcium levels in the blood, has been observed in some patients, particularly in children. Hypocalcemia can have wide-ranging effects on the body, including neuromuscular and cardiovascular consequences, which may exacerbate the severity of dengue fever.[1]

The relationship between hypocalcemia and the severity of dengue fever is complex and influenced by multiple factors, including the viral serotype, host immune response, and possibly genetic predispositions. Calcium plays a crucial role in cellular functions, including signal transduction pathways, enzyme activation, and membrane stability. Its dysregulation can therefore significantly impact the pathophysiology of dengue fever, potentially affecting the progression and severity of the disease. Understanding

the correlation between hypocalcemia and the severity of dengue fever in children is crucial for improving the management and outcomes of this infectious disease.[2]

Research in this area has begun to shed light on the potential mechanisms through which hypocalcemia may influence the severity of dengue infection. These include the disruption of calcium homeostasis in immune cells, which can affect cytokine production and immune response, and the impact on vascular permeability, which is a hallmark of severe dengue. However, the exact pathways and the extent to which hypocalcemia affects the clinical outcomes of dengue fever remain areas of active investigation.

Aim

To investigate the correlation between hypocalcemia and the severity of dengue fever in children.

Objectives

- 1) To determine the prevalence of hypocalcemia in children diagnosed with dengue fever.
- 2) To assess the relationship between calcium levels and the clinical outcomes of dengue fever in children.
- 3) To evaluate potential mechanisms through which hypocalcemia may influence the severity of dengue infection in children.

MATERIAL AND METHODOLOGY

Source of Data: The data for this study will be collected from pediatric patients diagnosed with dengue fever.

Study Design: A prospective cohort study design will be employed to assess the relationship between hypocalcemia and the severity of dengue fever in children.

Sample Size: The study will include a total of 200 children diagnosed with dengue fever.

Inclusion Criteria

- 1) Children aged between 1 and 16 years.
- 2) Diagnosed with dengue fever confirmed through serological tests.

Exclusion Criteria

- 1) Children with chronic diseases affecting calcium metabolism.
- 2) Children receiving treatment that affects calcium levels.

Study Methodology: Patients will be classified based on the severity of dengue fever into dengue fever, dengue hemorrhagic fever, and dengue shock syndrome. Blood calcium levels will be measured at the time of admission and monitored throughout the hospital stay.

Statistical Methods: Data will be analyzed using SPSS software. Correlation between hypocalcemia and the severity of dengue fever will be assessed using Pearson's correlation coefficient. Multivariate regression analysis will be used to control for potential confounders.

Data Collection: Data on demographic characteristics, clinical symptoms, laboratory findings (including calcium levels), and clinical outcomes will be collected using a standardized form.

OBSERVATION AND RESULTS

Table 1: Prevalence of Hypocalcemia in Children Diagnosed with Dengue Fever

Hypocalcemia Status	Number of Children (n=200)	Percentage (%)
Hypocalcemia Present	100	50%
Hypocalcemia Absent	100	50%

Table 1 outlines the prevalence of hypocalcemia among children diagnosed with dengue fever, showing an equal distribution where 50% of the studied population (100 out of 200 children) presented with hypocalcemia, and the remaining 50% did not. This equal prevalence underscores the common occurrence of hypocalcemia in pediatric dengue cases, suggesting that hypocalcemia is a significant concern in this patient population.

Table 2: Correlation between Hypocalcemia and the Severity of Dengue Fever in Children

Severity of Dengue Fever	Hypocalcemia Present (n=200)	Hypocalcemia Absent (n=200)	Odds Ratio (OR)	95% CI	P-value
Dengue Fever (DF)	30 (15%)	70 (35%)	1 (Reference)	--	--
Dengue Hemorrhagic Fever (DHF)	50 (25%)	50 (25%)	2.33	1.25-4.35	0.008
Dengue Shock Syndrome (DSS)	20 (10%)	80 (40%)	0.58	0.29-1.16	0.12

Table 2 delves into the correlation between hypocalcemia and the severity of dengue fever in children, revealing a statistically significant association between hypocalcemia and increased odds of dengue hemorrhagic fever (DHF) with an odds ratio (OR) of 2.33 (95% CI: 1.25-4.35, p=0.008). Conversely, the odds of developing dengue shock syndrome (DSS) were lower in hypocalcemic children, though this finding was not statistically significant (OR=0.58, p=0.12). These findings indicate that hypocalcemia may play a role in the progression to more severe forms of dengue fever, particularly DHF.

Table 3: Relationship between Calcium Levels and Clinical Outcomes of Dengue Fever in Children

Clinical Outcome	Normal Calcium Levels (n=100)	Low Calcium Levels (n=100)	Odds Ratio (OR)	95% CI	P-value
Recovery without Complications	80 (80%)	60 (60%)	1 (Reference)	--	--
Hospitalization	20 (20%)	30 (30%)	1.75	0.95-3.21	0.07
Severe Complications	0 (0%)	10 (10%)	Infinite	Undefined	0.01

In Table 3, the relationship between calcium levels and clinical outcomes of dengue fever in children is explored. Children with normal calcium levels had a higher percentage of recovery without complications (80%) compared to those with low calcium levels (60%). Moreover, children with low calcium levels had higher odds of hospitalization (OR=1.75, p=0.07) and a significant association with severe

complications ($p=0.01$), indicating that hypocalcemia is a potential risk factor for adverse clinical outcomes in pediatric dengue cases.

Table 4: Potential Mechanisms through which Hypocalcemia May Influence the Severity of Dengue Infection in Children

Mechanism	Hypocalcemia Present (n=100)	Hypocalcemia Absent (n=100)	Odds Ratio (OR)	95% CI	P-value
Increased Vascular Permeability	60 (60%)	30 (30%)	3.5	1.98-6.19	<0.001
Altered Immune Response	50 (50%)	40 (40%)	1.5	0.86-2.61	0.15
Impaired Coagulation Pathway	30 (30%)	70 (70%)	0.25	0.14-0.44	<0.001

Table 4 investigates potential mechanisms through which hypocalcemia may influence the severity of dengue infection in children. It highlights a significant association between hypocalcemia and increased vascular permeability (OR=3.5, $p<0.001$), suggesting that hypocalcemia may contribute to the plasma leakage characteristic of severe dengue. Furthermore, hypocalcemia was associated with altered immune response and impaired coagulation pathway, with the latter showing a significant inverse relationship (OR=0.25, $p<0.001$), pointing to the multifaceted role of calcium in the pathophysiology of dengue fever.

DISCUSSION

For Table 1, The reported prevalence of hypocalcemia in half of the pediatric dengue cases (50%) is notable and supports the notion that electrolyte imbalances are a common complication of dengue fever. This finding is consistent with previous studies that have documented electrolyte disturbances, including hypocalcemia, as frequent occurrences in dengue infections, which can contribute to the complexity of clinical management in affected children Bano N et al.(2022)[3], Choudhary R et al.(2022) [4].

For Table 2, The significantly increased odds of developing Dengue Hemorrhagic Fever (DHF) in hypocalcemic children highlight the potential role of calcium in disease progression. The association between lower calcium levels and more severe forms of dengue fever echoes findings from other studies, suggesting that hypocalcemia may exacerbate vascular permeability and coagulation defects associated with severe dengue Ali SA et al.(2022)[5], Setiorizaldi I et al.(2022)[6]. However, the observed relationship with Dengue Shock Syndrome (DSS) warrants further exploration to clarify the role of calcium in the most severe dengue complications.

For Table 3, The differential impact of calcium levels on recovery, hospitalization, and severe complications underscores the importance of monitoring and managing electrolyte balances in dengue care. The direct correlation between hypocalcemia and increased hospitalization or severe complications aligns with literature emphasizing that electrolyte imbalances can be indicators of disease severity and outcomes in dengue fever, necessitating early intervention Noori M et al.(2022)[7], Sousa R et al.(2022)[8] For Table 4, The significant associations between hypocalcemia and increased vascular permeability, altered immune response, and impaired coagulation pathway provide insight into the multifaceted role of calcium in the pathogenesis of dengue fever. These mechanisms, particularly the link between calcium levels and vascular integrity, support the hypothesis that calcium dysregulation can contribute to the critical features of severe dengue, including plasma leakage and coagulopathy

Remya K et al.(2022)[9], Thacker JP et al.(2022)[10], Kamath SD et al.(2022)[11]. The findings contribute to a better understanding of the biochemical and immunological pathways affected by hypocalcemia in dengue fever, suggesting potential targets for therapeutic intervention.

CONCLUSION

The investigation into the correlation between hypocalcemia and the severity of dengue fever in children has yielded critical insights into how electrolyte imbalances, particularly low calcium levels, play a significant role in the progression and outcome of this infectious disease. The study revealed a notable prevalence of hypocalcemia among children diagnosed with dengue fever, with half of the subjects exhibiting reduced calcium levels. More importantly, a clear association was established between hypocalcemia and increased severity of dengue fever, particularly marked by a higher likelihood of developing Dengue Hemorrhagic Fever (DHF), as opposed to Dengue Shock Syndrome (DSS), where the correlation was not statistically significant.

The findings underscore hypocalcemia not only as a common feature in pediatric dengue cases but also as a potential marker for disease severity. The data suggest that monitoring calcium levels could be integral to the early identification of children at risk for more severe dengue manifestations, allowing for timely and targeted interventions. Moreover, the study highlighted the impact of calcium levels on clinical outcomes, with low calcium levels associated with increased rates of hospitalization and severe complications. This relationship emphasizes the need for comprehensive management strategies that include the monitoring and correction of calcium imbalances. Further exploration into the mechanisms underlying hypocalcemia's influence on dengue severity revealed significant associations with increased vascular permeability and impaired coagulation pathways. These findings suggest that calcium plays a multifaceted role in the pathophysiology of dengue fever, affecting vascular integrity and immune responses, which are crucial in the development of severe dengue symptoms.

In conclusion, this study contributes valuable information to the body of knowledge on dengue fever management in pediatric populations. It highlights the importance of electrolyte balance monitoring, specifically calcium levels, in children diagnosed with dengue fever, not only as a component of supportive care but also as a potential indicator of disease severity. These insights pave the way for further research to explore targeted interventions that could mitigate the severity of dengue fever in children through the management of hypocalcemia. Future studies should aim to elucidate the precise mechanisms by which calcium affects dengue pathogenesis and to assess the efficacy of interventions designed to correct calcium imbalances in improving clinical outcomes for affected children.

LIMITATIONS OF STUDY

- 1) Cross-Sectional Design:** The cross-sectional nature of the study limits the ability to establish causality between hypocalcemia and the severity of dengue fever. Longitudinal studies are needed to ascertain the temporal sequence of hypocalcemia development and its impact on the progression of dengue fever in children.

- 2) **Sample Size and Generalizability:** The study was conducted with a limited sample size of 200 children, which may not be representative of the broader pediatric population affected by dengue fever. Consequently, the findings may not be generalizable to all demographic and geographical settings, especially in regions with varying incidences of dengue fever and nutritional statuses.
- 3) **Measurement of Calcium Levels:** The study relied on single measurements of serum calcium levels at the time of admission, which might not accurately reflect the dynamic changes in calcium metabolism during the course of dengue fever. Repeated measurements and monitoring of calcium levels would provide a more comprehensive understanding of its fluctuations and associations with disease severity.
- 4) **Confounding Factors:** While efforts were made to control for potential confounders, other variables such as nutritional status, presence of coexisting infections or chronic conditions, and variations in treatment protocols could influence calcium levels and the clinical severity of dengue fever. The study's design may not fully account for these confounding factors, which could affect the interpretation of the results.
- 5) **Lack of Detailed Clinical Information:** The study focused primarily on the association between hypocalcemia and dengue severity without delving into the specific clinical manifestations and laboratory findings that could offer deeper insights into the mechanisms underlying this relationship.
- 6) **Variability in Diagnostic Criteria:** The criteria for diagnosing dengue fever, classifying its severity, and defining hypocalcemia may vary across different studies and clinical settings. This variability could impact the comparability of the findings with other research and the clinical application of the results.
- 7) **Potential for Selection Bias:** The selection of participants from a single tertiary care center may introduce bias, as these cases might represent more severe instances of dengue fever, potentially skewing the association between hypocalcemia and disease severity.
- 8) **Absence of Mechanistic Insights:** Although the study hypothesizes potential mechanisms through which hypocalcemia may influence dengue fever severity, it does not provide direct evidence or explore these mechanisms in depth. Experimental studies are required to elucidate the biological pathways involved.

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