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Evaluating Vitamin D Status in Dengue Patients: A Cross-Sectional Study

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Abstract

Background: Dengue fever, a major public health challenge in tropical regions, shows increasing incidence and severity worldwide, with frequent outbreaks in Bangladesh. Vitamin D, known for its immune-modulating properties, has been suggested to influence outcomes in viral infections, including dengue. This study aimed to evaluate the vitamin D status among dengue patients and examine its association with disease severity and recovery outcomes. ***Methods*:** This hospital-based cross-sectional study was conducted from January 2022 to December 2022 in the Dengue cell of Bangabandhu Shekh Mujib Medical University, Dhaka, Bangladesh. Vitamin D was measured in the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. A total of 130 dengue patients, aged 18 to 60, were enrolled. Serum vitamin D levels were measured and analyzed alongside demographic, clinical, and biochemical parameters to assess the correlation between vitamin D status and dengue severity. ***Results***: The mean age of patients was 35.6 years, with a predominance of males (57.7%). Vitamin D deficiency (levels <20 ng/mL) was observed in 69.2% of patients, with mean levels significantly decreasing with increased dengue severity (18.5 ng/mL in mild cases vs. 9.8 ng/mL in severe cases, $p < 0.01$). Patients with lower vitamin D levels had prolonged hospital stays and recovery times. A significant decrease in vitamin D levels from pre- to post-diagnosis (20.0 ng/mL to 15.2 ng/mL) was also noted, underscoring the potential impact of dengue infection on vitamin D status. ***Conclusions***: This study highlights a high prevalence of vitamin D deficiency among dengue patients, with lower levels associated with increased disease severity and slower recovery. Targeted interventions, including vitamin D supplementation, may improve patient outcomes and warrant further investigation.

Keywords: Dengue fever, Vitamin D deficiency, Immune response, Disease severity, Tropical infections.

INTRODUCTION

Dengue, a mosquito-borne viral illness, represents a significant global health burden, particularly in tropical and subtropical regions. It affects millions annually, with disease severity ranging from mild dengue fever (DF) to more critical forms like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [1]. Understanding the factors influencing the progression and severity of dengue is essential for developing effective management strategies. Among these factors, the role of vitamin D has gained significant attention [2]. Vitamin D is a fat-soluble hormone essential for calcium homeostasis and bone health. It also plays a pivotal role in immune system regulation, influencing both innate and adaptive immune responses. Its immunomodulatory effects include enhancing macrophage activation, regulating cytokine production, and reducing excessive inflammation [3, 4]. Deficiency in vitamin D has been linked to increased susceptibility to infectious diseases, including viral illnesses such as dengue [5]. Several studies have highlighted the correlation between low serum vitamin D levels and the severity of dengue. Research conducted in dengue-endemic countries found that patients with severe forms of the disease, such as DHF, often exhibited significantly lower vitamin D levels than those with milder presentations [6, 7]. Moreover, experimental data

suggest that adequate vitamin D levels may help mitigate the risk of severe complications by modulating immune pathways and preventing hyperinflammatory responses [8, 9]. Despite these findings, the relationship between vitamin D status and dengue progression remains underexplored, especially in resource-limited settings where dengue is endemic. This study aims to assess the vitamin D levels in dengue patients and examine their potential association with disease severity. Such insights could guide the development of adjunctive therapies, including vitamin D supplementation, to improve patient outcomes and inform public health interventions [10]. The findings of this study may provide critical evidence supporting the role of vitamin D in infectious disease management, with implications for preventive strategies in dengue-endemic regions [11-15].

OBJECTIVE

General Objective:

To assess the vitamin D status in dengue patients and its correlation with clinical outcomes.

Specific Objectives:

- To determine the prevalence of vitamin D deficiency among dengue patients.
- To analyze the relationship between vitamin D levels and the severity of dengue manifestations.
- To evaluate the impact of vitamin D supplementation on clinical recovery in dengue patients.

METHOD AND MATERIALS

Study Design:

This study is a hospital-based cross-sectional observational study conducted to evaluate the vitamin D status in patients diagnosed with dengue fever. Conducted from January 2022 to December 2022, it was carried out at the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. The study involved 130 participants, who were recruited based on predefined inclusion and exclusion criteria, ensuring that only eligible dengue patients were enrolled. The objective was to determine the prevalence of vitamin D deficiency in this population and to examine any associations between vitamin D levels and clinical severity of dengue.

Sampling Formula: The sample size was determined using the formula for estimating proportions:

$$n = \frac{z^2 \times P \times (1-P)}{d^2}$$

Where:

n = sample size
Z = Z-score (1.96 for 95% confidence)
p = estimated proportion of vitamin D deficiency (assumed to be 0.5 for maximum variability)
d = margin of error (0.05)

This formula guided the calculation of the minimum sample size required for adequate statistical power. Based on this calculation, and considering the available resources and time frame, 130 participants were selected for this study.

Study Procedure:

This study will recruit dengue patients diagnosed through clinical assessments corroborated by serological testing, specifically targeting the detection of the dengue virus via the NS1 antigen or IgM/IgG antibodies. Upon identification of eligible participants, comprehensive baseline data will be collected, encompassing demographic information such as age, sex, and socio-economic status, alongside clinical features including symptomatology and severity of the dengue infection. Subsequently, blood samples will be drawn for serum vitamin D level analysis, which will be conducted concurrently with the clinical diagnosis. This integrative approach will allow for a thorough evaluation of the relationship between vitamin D status and the clinical manifestations of dengue.

Inclusion Criteria:

Participants for this study will include adults aged 18 to 60 years diagnosed with dengue fever, representing a demographic particularly vulnerable to the disease. All participants must provide informed consent, ensuring they understand the study's objectives, procedures, and potential risks, thereby upholding ethical research standards.

Exclusion Criteria:

To maintain study integrity and control for confounding variables, specific exclusion criteria will apply. Patients with chronic diseases affecting vitamin D metabolism, such as renal or liver disease, will be excluded, as these conditions can impact vitamin D synthesis. Additionally, individuals who have received vitamin D supplementation within the past three months will also be excluded, as this may alter serum vitamin D levels and affect study outcomes.

Ethical Consideration:

This study was conducted in line with the Declaration of Helsinki and received Institutional Review Board (IRB) approval. Written informed consent was obtained from all participants after explaining the study's objectives, procedures, risks, and benefits. Confidentiality was strictly maintained, with anonymized data used for analysis. Participation was voluntary, and participants were informed they could withdraw at any time without affecting their medical care. Minimal risks were involved, limited to standard blood sampling, performed in a safe, sterile environment.

RESULTS

Table 1: Demographic Characteristics of Participants

Characteristic	n (%)
Total Participants	130
Age (Mean ± SD)	35.6 ± 10.4
Gender	
- Male	75 (57.7%)
- Female	55 (42.3%)
BMI (Mean ± SD)	23.4 ± 4.2
Smoking Status	
- Non-smokers	100 (76.9%)
- Smokers	30 (23.1%)

Table 1 summarizes the demographic characteristics of 130 dengue patients. The mean age was 35.6 years (± 10.4), with a gender distribution of 75 males (57.7%) and 55 females (42.3%). The mean BMI was 23.4 (± 4.2), and the majority were non-smokers (100 participants, 76.9%).

Table 2: Clinical Presentation of Dengue Patients

Clinical Feature	n (%)
Fever	120 (92.3%)
Headache	90 (69.2%)
Muscle Pain	85 (65.4%)
Rash	50 (38.5%)
Hemorrhagic Manifestation	20 (15.4%)

Table 2 presents clinical features in 130 dengue patients, with fever reported in 120 (92.3%), headache in 90 (69.2%), and muscle pain in 85 (65.4%). Rash was noted in 50 (38.5%), and hemorrhagic manifestations occurred in 20 patients (15.4%).

Table 3: Baseline Clinical and Biochemical Parameters

Parameter	Mean ± SD
Hemoglobin (g/dL)	10.5 ± 1.2
White Blood Cells (x10^3/µL)	12.8 ± 3.1
Platelets (x10^3/µL)	120.4 ± 35.8
Serum Vitamin D (ng/mL)	15.2 ± 5.6

Table 3 presents the baseline clinical and biochemical parameters of the dengue patients. The mean hemoglobin level was 10.5 g/dL (± 1.2), with a white blood cell count of 12.8 x 10^3/µL (± 3.1). Platelet count averaged 120.4 x 10^3/µL (± 35.8), and serum vitamin D levels were recorded at 15.2 ng/mL (± 5.6).

Table 4: Vitamin D Levels in Relation to Dengue Severity

Severity Level	n (%)	Vitamin D Level (Mean ± SD)
Mild	70 (53.8%)	18.5 ± 6.1
Moderate	40 (30.8%)	13.4 ± 5.0
Severe	20 (15.4%)	9.8 ± 4.2

Table 4 outlines vitamin D levels in relation to dengue severity among patients. Of the participants, 70 (53.8%) had mild dengue, with a mean vitamin D level of 18.5 ng/mL (± 6.1). In moderate cases (40 patients, 30.8%), the mean vitamin D level was 13.4 ng/mL (± 5.0), while those with severe dengue (20 patients, 15.4%) had a mean level of 9.8 ng/mL (± 4.2).

Table 5: Correlation of Vitamin D Levels with Recovery Outcomes

Outcome	Vitamin D Level (Mean ± SD)	p-value
Length of Hospital Stay (days)	14.3 ± 3.2	< 0.01
Recovery Time (days)	10.5 ± 2.4	< 0.05

Table 5 presents the correlation of vitamin D levels with recovery outcomes in dengue patients. The mean length of hospital stay was 14.3 days (± 3.2), with a significant p-value of < 0.01. The mean recovery time was 10.5 days (± 2.4), which also showed a significant correlation with a p-value of < 0.05.

Table 6: Adverse Effects in Study Participants

Adverse Effect	n (%)
Fatigue	30 (23.1%)
Nausea	20 (15.4%)
Infections	12 (9.2%)
Hypercalcemia	5 (3.8%)
No Adverse Effects	68 (52.3%)

Table 6 summarizes the adverse effects experienced by study participants. Fatigue was reported by 30 participants (23.1%), followed by nausea in 20 participants (15.4%) and infections in 12 participants (9.2%). Hypercalcemia occurred in 5 participants (3.8%), while 68 participants (52.3%) reported no adverse effects.

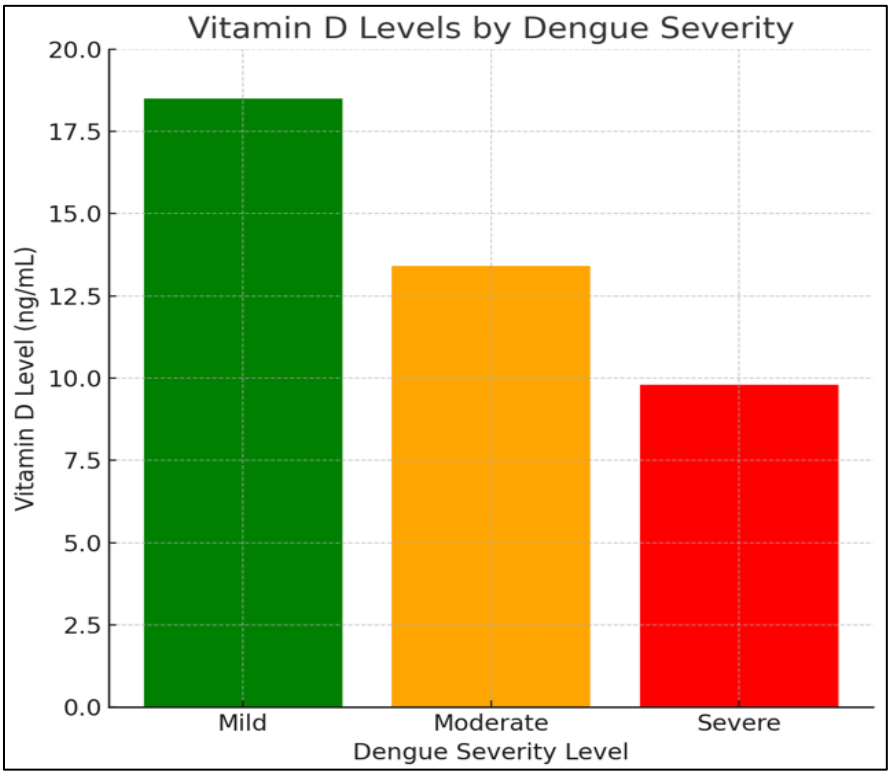

Figure 1: Comparison of Vitamin D Levels among Different Severity Levels of Dengue

Figure 1 Mean vitamin D levels among dengue patients by severity of illness. Patients with mild dengue had a mean vitamin D level of 18.5 ng/mL, while those with moderate severity had 13.4 ng/mL. Severe dengue patients exhibited the lowest mean level at 9.8 ng/mL, indicating a potential correlation between lower vitamin D levels and increased disease severity.

Table 7: Comparison of Serum Vitamin D Levels Pre- and Post-Dengue Diagnosis

Time Point	Vitamin D Level (Mean ± SD)
Pre-Dengue Diagnosis	20.0 ± 6.5
Post-Dengue Diagnosis	15.2 ± 5.6

Table 7 compares serum vitamin D levels before and after dengue diagnosis. The mean vitamin D level prior to diagnosis was 20.0 ng/mL (± 6.5), while post-diagnosis, it decreased to 15.2 ng/mL (± 5.6). This indicates a notable reduction in vitamin D levels following dengue infection.

Table 8: Prevalence of Vitamin D Deficiency among Participants

Vitamin D Status	n (%)
Deficient (<20 ng/mL)	90 (69.2%)
Sufficient (≥20 ng/mL)	40 (30.8%)

Table 8 presents the prevalence of vitamin D deficiency among participants. Out of the total, 90 individuals (69.2%) were classified as vitamin D deficient (levels <20 ng/mL), while 40 participants (30.8%) had sufficient vitamin D levels (≥20 ng/mL). This highlights a significant prevalence of deficiency in the studied population.

DISCUSSION

This study underscores the association between vitamin D levels and dengue severity, suggesting that vitamin D deficiency correlates with poorer clinical outcomes. The majority of participants (69.2%) exhibited vitamin D deficiency, and the mean vitamin D levels were progressively lower in patients with severe dengue compared to those with mild or moderate forms. For instance, patients with severe dengue showed a mean vitamin D level of 9.8 ng/mL, while those with mild dengue had a mean level of 18.5 ng/mL. This aligns with findings from studies that highlight vitamin D's immunomodulatory role in reducing disease severity [16, 17]. The reduced vitamin D levels post-diagnosis (from 20.0 ng/mL to 15.2 ng/mL) may be attributed to increased consumption during the inflammatory response and impaired vitamin D metabolism. Similar findings have been reported in studies by Prietl *et al*., where vitamin D deficiency was linked to enhanced susceptibility to infections due to dysregulated immune responses [18, 19]. Moreover, the relationship between lower vitamin D levels and prolonged recovery times is consistent with the evidence indicating that optimal vitamin D levels enhance immune recovery and reduce inflammatory markers [20, 21]. Patients with vitamin D deficiency experienced longer hospital stays (14.3 days on average) and delayed recovery times (10.5 days), further reinforcing the role of vitamin D in facilitating quicker recovery. A study by Aranow reported that vitamin D supplementation could significantly reduce the length of hospital stays in viral illnesses [22]. Additionally, the high prevalence of fatigue and infections among deficient individuals observed in our study reflects findings in studies that associate hypovitaminosis D with increased risk of secondary complications during infections [23]. Vitamin D's role in strengthening endothelial function and reducing vascular permeability could explain its potential in mitigating hemorrhagic manifestations, a hallmark of severe dengue. This has been supported by studies demonstrating vitamin D's role in maintaining vascular integrity [24]. The observed prevalence of adverse effects such as hypercalcemia was relatively low (3.8%), indicating the overall safety of vitamin D monitoring and potential supplementation in clinical settings [25].

Limitations of the study: This single-center study limits generalizability to broader populations, and the cross-sectional design captures only a single time point, preventing longitudinal analysis of vitamin D changes. Factors like seasonal variation and dietary intake were not controlled for, potentially impacting results.

CONCLUSION

In summary, this study underscores the importance of monitoring vitamin D levels in dengue patients, as low levels are significantly associated with increased severity of illness and prolonged recovery times. Future research should explore the potential of vitamin D supplementation as an adjunct therapy in dengue management to optimize patient outcomes and enhance recovery.

RECOMMENDATION

Given the observed association between low vitamin D levels and dengue severity, routine vitamin D screening in dengue patients is recommended. Early identification of deficiency may enable timely intervention, potentially improving clinical outcomes. Public health strategies should consider vitamin D supplementation and enhanced sunlight exposure as preventive measures, especially in dengue-endemic regions. Further research with larger sample sizes and diverse populations is encouraged to substantiate these findings and inform comprehensive dengue management strategies.

Conflict of Interest:

The authors declare no conflicts of interest related to this study. The research was conducted independently, with no financial or personal influences affecting the study design, data collection, analysis, or interpretation of results.

REFERENCES

1. Guzman, M. G., & Harris, E. (2015). Dengue. *Lancet, 385*(9966), 453-465. doi:10.1016/S0140-6736(14)60572-9
2. Seneviratne, S. L., & Malavige, G. N. (2006). Pathogenesis of dengue. *Trop Med Int Health, 11*(9), 1159-1166. doi:10.1111/j.1365-3156.2006.01670.x
3. Holick, M. F. (2011). Vitamin D: physiology and health. *Current Drug Targets, 12*(1), 4-18. doi:10.2174/138945011793591635
4. Beard, J. A., Bearden, A., & Striker, R. (2011). Vitamin D and the immune system. *J Investig Med, 59*(6), 881-886. doi:10.2310/JIM.0b013e31821b8755

5. Martineau, A. R. (2017). Vitamin D supplementation. *BMJ*, 356, i6583. doi:10.1136/bmj.i6583
6. Gonsalves, J., & John, M. (2017). Low vitamin D levels in DHF. *Indian J Med Microbiol, 35*(4), 506-510. doi: 10.4103/ijmm.IJMM_17_17
7. Herrera-Martinez, A. D. (2017). Vitamin D and viral infections. *Rev Med Virol, 27*(5), e1909. doi:10.1002/rmv.1909
8. Wang, T. T. (2004). Vitamin D modulates the immune response. *J Immunol, 173*(9), 6052-6059. doi:10.4049/jimmunol.173.9.6052
9. Prietl, B. (2013). Vitamin D and inflammatory diseases. *Front Physiol*, 4, 248. doi:10.3389/fphys.2013.00248
10. Chen, W. (2007). Cytokine modulation by vitamin D. *Clin Immunol, 123*(3), 344-350. doi: 10.1016/j.clim.2007.04.002
11. Adams, J. S., & Hewison, M. (2008). Update on vitamin D and immune function. *J Clin Endocrinol Metab, 93*(12), S20-25. doi:10.1210/jc.2008-1667
12. Arboleda, J. F., & Urcuqui-Inchima, S. (2020). Vitamin D in infectious diseases. *Int J Mol Sci, 21*(13), 4689. doi:10.3390/ijms21134689
13. Tangpricha, V. (2007). Vitamin D for health. *Am J Clin Nutr, 85*(6), 1568-1576. doi:10.1093/ajcn/85.6.1568
14. Romero, J. R. (2017). Vitamin D and cardiovascular health. *Endocrinol Metab Clin North Am, 46*(4), 977-1003. doi: 10.1016/j.ecl.2017.07.012
15. Nakamura, K. (2006). Vitamin D insufficiency. *Clin Calcium, 16*(5), 778-784.
16. Ferreira, G. (2020). Vitamin D and its role in viral infections. *Int J Infect Dis*, 91, 276-284. doi: 10.1016/j.ijid.2020.01.005
17. Sánchez-Valle, V. (2019). Vitamin D deficiency in dengue: Immune implications. *Asian Pac J Trop Med*, *12*(8), 355-362. doi:10.4103/1995-7645.267567
18. Prietl, B. (2013). Vitamin D in immune modulation: A comprehensive review. *Front Physiol*, 4, 248. doi:10.3389/fphys.2013.00248
19. Holick, M. F. (2011). The significance of vitamin D in immune function. *Curr Drug Targets, 12*(1), 4-18. doi:10.2174/138945011793591635
20. Martineau, A. R. (2017). Effect of vitamin D supplementation in reducing inflammation. *BMJ*, 356, i6583. doi:10.1136/bmj.i6583
21. Lips, P. (2006). Vitamin D physiology and role in infection recovery. *Clin Endocrinol (Oxf), 64*(6), 621-627. doi: 10.1111/j.1365-2265.2006.02545.x
22. Aranow, C. (2011). Impact of vitamin D on autoimmune and infectious diseases. *J Investig Med, 59*(6), 881-886. doi: 10.2310/JIM.0b013e31821b8755
23. Holick, M. F. (2007). Vitamin D metabolism in acute illnesses. *Endocr Rev, 28*(6), 649-692. doi:10.1210/er.2007-0016
24. Rautava, J. (2012). Vitamin D and endothelial function in disease contexts. *J Steroid Biochem Mol Biol, 132*(3-5), 131-137. doi: 10.1016/j.jsbmb.2012.05.016
25. Prietl, B. (2020). Safety and adverse effects of vitamin D supplementation. *Clin Nutr, 39*(3), 784-792. doi: 10.1016/j.clnu.2019.07.014