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Original Research Article

A Hospital-Based Study to Assess the Role of Serum Vitamin D Levels in Severity of Dengue Fever - A Cross Sectional Study

Rajeev Kumar[1], S.K. Astik[2], Subham Bhaskar[3], Narendra Kumar[4]

[1]Assistant Professor, Department of Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India

[2]Associate Professor, Department of Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India

[3]Senior Resident, Department of Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India

[4]Assistant Professor, Department of Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India

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Corresponding author: Dr. Narendra Kumar

Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess the serum levels of Vitamin D in Dengue Fever patients.

Methods: The study was conducted at the Department of Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India. The Cross-sectional study was done during period for 2 years. Study Sample Size was 100. Children fulfilling the diagnostic criteria for Dengue Fever were enrolled in the study after getting informed consent from the parents/guardians.

Results: Among the population studied, 45% were between the age group of 6-10 years, 20% belonged to the age group of 11-14 years, 20% belonged to the age group of 2-5 years, and 15% belonged to the age group 1 month to 12 months. Among the population studied, 60% were males 40% were females. Among the population studied the mean Hemoglobin values were 12.28± 1.98 gm/dl. They decreased to 11.56±1.47 gm/dl before discharge. The mean Hematocrit values were 38.44±5.6 after admission, and they decreased to 36.3±3.74 before discharge. The mean platelet values on admission were 77,380 cell/cumm. They increased to 1,67,571cell/cummbefore discharge. Among the population studied Dengue Fever was present in 63%, Dengue Fever with warning signs was present in 28%,Severe Dengue was present in 9%.

Conclusion: According to the study, the lower the serum Vitamin D levels, the more severe the associated Dengue Illness. Compared to other studies our study was highly significant. Comparing the serum Vitamin D levels in Dengue fever cases with age matched & gender matched controls would have increased the validity of the study.

Keywords: Dengue hemorrhagic fever, severe dengue, vitamin D

Introduction

It is estimated that 2.5–3 billion of the world's population are at risk of dengue infection. [1] The escalating magnitude of the problem, together with the changing

epidemiology of dengue, is a serious public health concern. [2] 25-hydroxy vitamin D3 (Vitamin D) is known to play a key role in calcium homeostasis.

A non-negligible proportion of febrile persons diagnosed with dengue infection (dengue fever, DF) progresses to severe forms of the disease, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The reasons why some patients progress to these potentially fatal forms are poorly understood. Risk factors include secondary infections by new dengue serotypes and host's genetics. [3] The host's nutritional status has been highlighted as a potentially relevant predictor of progression [4] because some nutrients exhibit strong immunomodulatory activity. Vitamin D is particularly relevant because it can modulate immunological events that have been involved in the pathophysiology of severe dengue [5], including downregulation of proinflammatory Th1 activity. [6] Vitamin D supplementation has been beneficial in the treatment of infections by hepatitis C virus, an RNA virus that shares some characteristics with dengue virus (DENV). [7]

The vitamin D receptor is coded by the VDR gene on chromosome 12. It is a transcription factor and member of the steroid hormone nuclear receptor family. Several single nucleotide polymorphisms (SNPs), namely, BsmI, ApaI, TaqI and FokI, are known to influence the activity of VDR. [2]

With the expansion of geographical distribution of dis-ease and the rise in disease incidence over the last 20 years, prevention and control of Dengue and DHF have become a necessity. Vitamin D3 plays a crucial role in the immune system, increasing the phagocytic capacity of macrophages and enhancing anti-microbial peptide gene expression, contributing to innate immunity. Vitamin D3 is a powerful immunomodulator affecting both innate and adaptive immune responses. [8] Its deficiency is mainly associated with an increased risk of cancer, influenza, tuberculosis, and human immunodeficiency virus infection. Vitamin D3 was also reported to influence the expression of DENV receptors in immune system cells. Few studies have also discussed the role of Vitamin D in reducing the severity of D.F., DHF, and DSS. However, the role of vitamin D serum level in dengue pathogenesis and the association of VDR gene polymorphisms with the clinical severity of dengue infection has not been extensively studied in an Indian context.

The aim of the present study was to assess the serum levels of Vitamin D in Dengue Fever patients.

Methods

The study was conducted at the Department of Medicine, Nalanda Medical College and Hospital, Patna, Bihar, India. The Cross-sectional study was done during period for 2 years. Study Sample Size was 100. Children fulfilling the diagnostic criteria for Dengue Fever were enrolled in the study after getting informed consent from the parents/guardians. We included Age 1 month – 12 years. Children fitting into the diagnostic criteria of Dengue Fever – Dengue NS1 Antigen positive or Dengue IgM Antibodies Positive. Parents/guardians of children with the criteria mentioned above who are willing to give informed consent. Children with immunodeficiency, malnourishment, congenital anomalies. Patients with Dengue Fever in combination with coexisting tropical infections such as malaria or typhoid were not included in the study.

Children with Dengue Fever satisfying the inclusion criteria were enrolled in the study after getting written informed consent from the parents/guardians. The following investigations were done at admission (phase 1),48 hrs after admission (phase2), at discharge (phase3) Complete

Blood count, Hematocrit, Se-rum Vitamin D levels at hospital admission. We followed up with all the children until they were discharged. Four children were going against medical advice few days before discharge. We included all 100 children during that period and sample size was justified at alpha error 0.05, power 80. [9] The treatment process and investigations were documented. The data were entered in Microsoft Excel 2010 version. Data were analyzed using Microsoft Excel 2010 and Epi Info 7.2.0. We assessed significance at a 5% level of significance. Ethical clearance was obtained from the Institutional Ethical Committee.

Results

Table 1: The mean CBP parameters at different levels

Parameter	Hb	Hematocrit	Platelets
Phase I	12.28± 1.98	38.44±5.6	77380±63975.6
Phase II	11.69±2.08	37.087±5.84	69950±61029.61
Phase III	11.56±1.47	36.3±3.74	167571.42 ± 83393.11

Among the population studied the mean Hemoglobin values were 12.28± 1.98 gm/dl. They decreased to 11.56±1.47 gm/dl before discharge. The mean Hematocrit values were 38.44±5.6 after admission, and they decreased to 36.3±3.74 before discharge. The mean platelet values on admission were 77,380 cell/cumm. They increased to 1,67,571cell/cummbefore discharge. Among the population studied Dengue Fever was present in 63%, Dengue Fever with warning signs was present in 28%,Severe Dengue was present in 9%.

Among the population studied, 45% were between the age group of 6-10 years, 20% belonged to the age group of 11-14 years, 20% belonged to the age group of 2-5 years, and 15% belonged to the age group 1 month to 12 months. Among the population studied, 60% were males 40% were females.

Table 2: Serum Vitamin D levels according to the grade of Dengue Fever

Parameter	Serum Vitamin D levels
Overall	18.52 ± 5.60
Dengue Fever	20.36±5.25
Dengue Fever with warning signs	16.94±4.56
Severe Dengue	11±2.48

Among the population studied the overall mean of Serum Vitamin D levels was 18.52 ng/ml.The mean of Serum Vitamin D levels was 20.36 ng/ml in cases with Dengue Fever. The mean of Serum Vitamin D level was 16.94 ng/ml in case with Dengue Fever with warning signs. The mean of Serum Vitamin D levels was 11 ng/ml in cases of severe Dengue.

Table 3: Association between Serum Vitamin D levels and grade of Dengue

Parameter	Serum Vitamin D levels	P-value
Dengue Fever (n=60)	20.36±5.25	0.005
Dengue Fever with warning signs (n=30)	16.94±4.55	
Severe Dengue(n=10)	11±2.48	
Overall	18.58 ± 5.60	

As the Serum Vitamin D levels were decreasing, the severity of Dengue illness was increasing and association of this is statistically significant with a P-Value of 0.005.

Discussion

Dengue is one of the most rapidly spreading mosquito-borne virosis worldwide, with 50–100 million symptomatic cases each year and an annual global cost close to US $9 billion. [10-13] Internationally, dengue has become a major health concern in the past

few decades. Dengue is a leading cause of death and morbidity in tropical and subtropical regions. Dengue virus is a member of the Flaviviridae family with four different serotypes (DV-1, DV-2, DV-3, and DV-4). [14]

The majority of the population studied (45% of all participants) were aged 6 to 10 years old, which is similar to Dissanayake S et al 2021, [9] whose mean age of cases was 8.8 years while the mean age of controls was 7.9 years. In the present study, among the population studied, 57% were males and 43% were females. Dissanayake S et al 2021. [9]

Males were 60%, females were 40% among cases. Males were 48%, Females were 52% among controls. According to Chakravarti A et al. 2020, [15] 62.8% of children were male, while 37.2% were females. This can usually be explained by the higher mobility of male children in developing countries. Dengue serology proportions were almost similar to Chakravarti A et al 2020. [15]

In the present study, among the population studied, the overall mean of Serum Vitamin D level was 18.58 ng/ml. The mean of Serum Vitamin D level was 20.36 ng/ml, in cases with Dengue Fever. Patients with Dengue Fever and warning signs had a mean serum Vitamin D level of 16.94 ng/ml. The mean of Serum Vitamin D level was 11 ng/ml, in cases with severe Dengue Fever. The difference between the means of Serum Vitamin D levels according to the grading of Dengue Fever was statistically significant with a P-Value of 0.005. As serum Vitamin D levels are decreasing, the severity of Dengue Fever is increasing, and the association is statistically significant. Dissanayake S et al 2021, [3] reported in a multivariate logistic regression, the likelihood of Having Vitamin D [25(OH)D < 20 ng/mL] was 3.6 times higher in cases compared to controls (Odds Ratio (OR): 3.65, 95% confidence interval (CI): 1.461, 9.102, $p < 0.006$). When serum 25(O.H.)D was used as a continuous independent variable, the strength of the association between DHF/DSS and serum 25(O.H.)D was weak but statistically significant; the likelihood of having DHF/DSS is0.94 times less with 1 ng/mL increase in serum 25(O.H.)D (OR: 0.940, 95% CI: 0.887, 0.995, $p < 0.03$). Javed R et al 2018, [5] Serum Vitamin D levels were higher among those with a greater severity of disease with a p-value of 0.031. Villamor E et al 2017, [16] noticed low serum 25(OH)D concentrations in DF patients predict decreased odds of progression to DHF/DSS. [17]

However, a study done by Chakravarti et al 2020, [15] to assess the role of current levels of vitamin D and vitamin D receptor (VDR) polymorphism found serum 25-hydroxy Vitamin D3 (Vitamin D) levels to be 1.6 times higher in severe Dengue cases than that of healthy. That's why Multicentred randomized controlled trials which include large populations of diverse race and ethnicity will be needed to emphasise the role of vitamin D in Dengue fever.

Conclusion

According to the study, the lower the serum Vitamin D levels, the more severe the associated Dengue Illness. Compared to other studies our study was highly significant. Comparing the serum Vitamin D levels in Dengue fever cases with age matched & gender matched controls would have increased the validity of the study.

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