Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Microbiology Research

Journal homepage: www.ijmronline.org

Original Research Article

# Prognostic value of mannose binding lectin and vitamin D in dengue: Study from a tertiary care centre from southern India

**Sabeeha Naaz[1], Mohd Ansaruddin Zoheb[2], Thrilok Chander Bingi[3*]**

[1]Dept. of Neurology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India
[2]Dept. of Nephrology, Star Hospital, Hyderabad, Telangana, India
[3]Dept. of General Medicine, Gandhi Medical College, Secunderabad, Telangana, India

## Abstract

**Background:** Dengue disease severity is related to dysregulated immune response. Mannose binding lectin and vitamin D alter innate and adaptive immune responses. Hence, we wanted to assess the predictive value of these early serum biomarkers for reducing mortality and morbidity.
**Aim and Objectives:** To determine serum mannose binding lectin and vitamin D levels in patients diagnosed with Dengue and to correlate with Dengue severity.
**Results:** The study patients were divided into three groups, dengue without warning signs (group 1), dengue with warning signs (group 2), and severe dengue (group 3). Mannose binding lectin levels were found to have significant P values between group 1 and group 3 (p=0.002), and group 2 and group 3 (p=0.005). Vitamin- D levels showed a significant p-value between Group 1 and Group 2 (p=0.008), group 1 and Group 3 (p=0.000), and Group 2 and 3 (p=0.000). Hence lower levels of mannose binding lectin are associated with severe dengue and patients with low normal levels of vitamin D had severe dengue.
**Conclusions:** This study highlights the immunomodulator role of Mannose binding lectin and vitamin D in shifting immune responses from Th-1 to Th-2 resulting in dengue severity. The role of vitamin D is always thought to be protective but it may act as a double-edged sword. This study also opens new doors of therapeutics for treating dengue infection.

**Keywords:** Cytokines, T cells, Molecular biology, Dengue, MBL, Vitamin D.

**Received:** 18-10-2024; **Accepted:** 16-12-2024; **Available Online**: 29-03-2025



## 1. Introduction

Dengue burden amplified 30-fold over the last 50 years. The dengue cases have increased up to 50-100 million annually worldwide.[1,2] The virus, host genetics, and host immune factors play a vital role in the severity and complications of dengue, depending on individual, epidemiologic, and ecologic conditions.[3]

High viral loads and the mechanisms that regulate cytokine production lead to impairment in the control of dengue virus (DENV) leading to the overproduction of pro-inflammatory cytokines and hence dengue severity.[4]

After a mosquito bite, DENV replicates in the dermal dendritic cells (DC) and macrophages, these cells enable further propagation to peripheral tissue and a proinflammatory cytokine storm secondary to exuberant activation of poorly lytic cross-reactive T cells, and excessive complement activation occurs.[5]

Opsonization and lysis of the pathogen, production of potent proinflammatory molecules, and generation of the classical inflammatory response occur by activation of complement cascade.[6] Commencement of the complement system occurs via three convergent pathways referred to as the classical, lectin, and alternative pathways. Mannose-binding lectin (MBL) or ficolin initiates the lectin pathway.

Mannose-binding lectin (MBL) is a pattern-recognition molecule of liver origin that recognizes specific sugar moieties present on the surface of microorganisms, including DENV. It functions as a first line of defense in the innate

*Corresponding author: Thrilok Chander Bingi
Email: thrilok73@gmail.com

https://doi.org/10.18231/j.ijmr.2025.009

immune response.[7] In addition, it can induce cytokine production as well.

Therefore, MBL is important in host defense, especially in infancy, when the acquired immunity has not fully developed. Individuals lacking this protein may develop severe episodes of bacterial infections from early life.[8] MBL is also important when the immune system of an individual is compromised, such as when a patient is under immunosuppressive therapy, or receiving chemotherapies or a bone marrow transplant.[9]

In young children and immunocompromised patients enhanced susceptibility to infections was observed with low MBL serum levels. In adults HIV, hepatitis B, hepatitis C, and herpes simplex virus disease progression is influenced by low serum MBL concentrations.[10,11]

Additionally, vitamin D3 being an immunomodulator, enhances immunoregulatory mechanisms that avoid damage to the host and acts as a key factor in governing immune responses that arise from excessive inflammatory responses to several pathogens, as in dengue disease.[12,13]

1, 25(OH) 2D3 inhibits IL-12 production by macrophages and DC by suppressing transcriptional activation of the p35 and p40 genes. Importantly, this inhibition is dependent, at least in part, on the downregulation of NF-kB activation and binding to a kB sequence identified within the p40 promoter.[14]

The inhibitory effect of 1, 25-(OH) 2D3 on DC maturation and differentiation is very similar to that of IL-10, an anti-inflammatory cytokine, and to that of glucocorticoids.[15]

Interleukin 12 is an important immunoregulatory cytokine that is produced mainly by antigen-presenting cells, it bridges the early nonspecific innate resistance and the subsequent antigen-specific adaptive immunity.[16] The type of adaptive immune responses decided by the host are determined by the expression of IL-12, which regulates innate response. IL-12 induces interferon-γ (IFN-γ) production and triggers CD4+ T cells to differentiate into type 1 T helper (Th1) cells and help in the elimination of pathogens.[17]

The Antiviral function and immunomodulatory role of MBL and vitamin D in dengue virus infection have not been investigated precisely. Hence, we plan to assess the levels of vitamin D and MBL and correlate them with dengue severity.

## 2. Materials and Methods

### *2.1. Study design*

Observational study.

### *2.2. Duration of study*

26th July 2018 to 31st JULY 2019.

### *2.3. Methodology*

All Patients who presented to the Medicine clinic during 1 year with fever and were dengue positive were enrolled in this study based on inclusion and exclusion criteria after obtaining written informed consent from the subjects. An Institutional Ethical Committee approval was granted for this study through a letter numbered (Rc. No. IEC/GMC/2017) and dated (30/12/2017).

### *2.4. Inclusion criteria*

Patients above 18 years, confirmed as Dengue by either NS1

Ag/ IgM/IgG were included.

### *2.5. Exclusion criteria*

Patients suffering from the following disorders have been excluded

1. Haematological disorders with bleeding manifestation.
2. Documented autoimmune diseases and immune-compromised states.
3. Other bacterial, viral, and parasitic infections.
4. Drug-induced thrombocytopenia and malignancies.
5. Previous heparin usage in the last 100 days.
6. Rheumatological diseases.
7. Pregnant woman.

All patients were confirmed to have dengue by detection of DENV antigen via NS1 assay (Pan-E dengue early ELISA kit) or DENV-specific antibodies via in-house capture IgM/IgG Enzyme-Linked Immunosorbent Assay (ELISA). Patients were divided into three groups based on the WHO 2009 criteria as dengue without warning signs (Group 1), with warning signs (Group 2), and severe dengue (Group 3). Detailed history regarding clinical features was taken and laboratory investigations were performed.

Blood from the patients was collected within 24-48 hours of fever onset. Serum samples were separated into two aliquots and were stored at -80ºC. The MBL levels in the serum of all patients were analyzed using ELISA (Human-MBP/MBL QY-E03418) kits. Raw data was initially measured as the relative fluorescence intensity and then converted to MBL concentration based on the standard curve generated from the reference concentrations supplied in the kit. Levels less than 500ng/ml were used to define patients as MBL deficient.[27] Vitamin D levels were estimated by CLIA-ADVIA Centaur XPT immunoassay system, using ADVIA Centaur vitamin D ready pack reagents (REF 10699201). Analytical measuring range (4.2-150ng/ml).

*2.6. Statistical analysis*

The parameters were recorded and systematically analyzed with a chi-square test to discover the relationship between two categorical variables. One-way ANOVA was used to evaluate differences between raw MBL levels among three groups of dengue patients. To establish the correlation between MBL, vitamin D, and clinical parameters/findings, Pearson's two-tailed correlation was applied.

Results are given as correlation coefficient, r (ranges from -1 to +1). A two-tailed P value of less than 0.05 was considered to be significant for all tests performed. All three statistical analyses performed were done using IBM SPSS Version 22.0.

## 3. Results

A total of 100 patients who met the inclusion and exclusion criteria were included in this study. Patients were divided into three groups based on the 2009 WHO classification to determine independent predictors of severity and morbidity. 38 patients fell into dengue without warning signs (Group 1), 40 patients into dengue with warning signs (Group 2), and 22 patients in severe dengue (Group 3). Male preponderance was noted as 62 were males and 38 were females. The Mean Age among groups is not significant. Clinical symptoms like Gum bleeding, Rash, Petechiae, Malena, Epistaxis, Joint pains, Retro orbital pain, and abdominal pain had a significantly higher frequency in the severe dengue group (**Table 1**).

The co-morbid conditions like Diabetes, Hypertension, and Asthma were insignificantly associated with dengue fever with p values of 0.520, 0.169, and 0.439 respectively in groups.

Clinical signs like subconjunctival haemorrhage, pallor, pleural effusion, gallbladder edema, conjunctival congestion, and ascites had a P value <0.05 among three categories of patients (**Table 2**).

Haemoglobin, white blood cell counts, serum electrolytes, Creatinine, calcium, and bilirubin were not found significant among three categories of patients, with p-values >0.100. (**Table 3**).

Platelet counts have dropped significantly in group 3 compared to other groups with a mean of 53078.9474 ± 6321.336 in group 1, 36900.00±5508.594 in group 2, and 24904.761±6014.2310 in group 3 with p-value significant between group 1 and group 2 (p=0.045) and group 1 and group 3 (p=0.004). Thrombocytopenia is observed to be more common in severe dengue compared to other groups. (**Figure 1**)

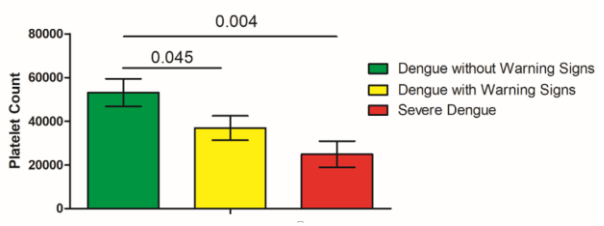


**Figure 1**: Bar diagram of platelet count and dengue types. Data is shown in Mean with standard error

The MBL levels are statistically significant among groups. (**Figure 2**). MBL levels are 43.022± 1.976 in group 1, 41.89± 1.944 in group 2, and 33.131± 2.078 in group 3 with P value significant between group 1 and group 3 (p=0.002) and group 2 and group 3 (p=0.005).

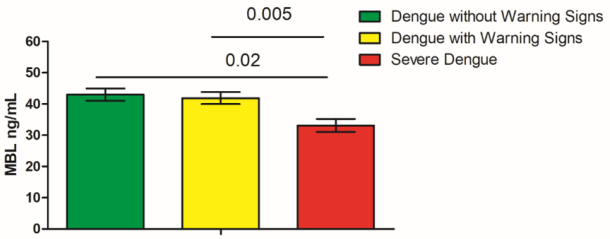


**Figure 2:** Bar diagram of MBL and dengue severity. Data is shown in Mean with standard error

Vitamin- D value is 14.508± 0.995 in group 1, 19.811± 1.199 in group 2, and 32.568± 2.813 in group 3 with p-value significant between group 1 and group 2 (p=0.008), group 1 and group 3 (p=0.000), group 2 and group 3 (p=0.000) (**Figure 3**)

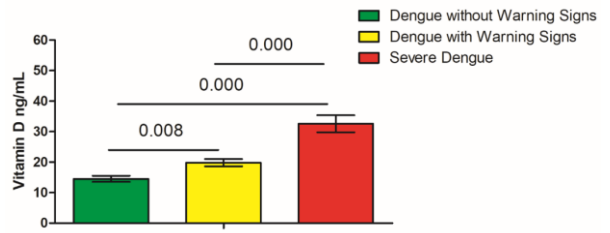


**Figure 3**: Bar diagram of vitamin D and dengue severity. Data is shown in Mean with standard error

There is a negative correlation between MBL and vitamin D with r=-0.270 with a p-value of 0.007. (**Figure 4**)

Markers for hepatocellular damage like ALT and AST were elevated significantly in group 3 compared to the other two groups and these enzymes showed a negative correlation with MBL, values being r = -0.202, p-value 0.044 and r =-0.278, p-value 0.005 for ALT and AST respectively.

Vitamin D showed a significant positive correlation with the markers for Liver injury with values as r=0.483, p-value 0.000 and r=0.401, p-value 0.000 for ALT and AST respectively (**Figure 5**)

**Table 1**: Showing clinical symptoms of dengue patients in the study

| Clinical Symptoms | Groups | | | | | | Total Cases | | Chi-square | p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | Group 1 | | Group 2 | | Group 3 | | Yes | No | | |
| | Yes | No | Yes | No | Yes | No | | | | |
| Headache | 16 | 22 | 15 | 25 | 12 | 10 | 43 | 57 | 1.703 | 0.427 |
| Retroorbital Pain | 12 | 26 | 3 | 37 | 10 | 12 | 25 | 75 | 12.32 | 0.002 |
| Myalgia | 23 | 15 | 32 | 8 | 19 | 3 | 74 | 26 | 6.082 | 0.048 |
| Joint Pains | 10 | 28 | 13 | 27 | 13 | 9 | 36 | 64 | 6.851 | 0.033 |
| Rash | 3 | 35 | 3 | 37 | 9 | 13 | 15 | 85 | 14.852 | 0.001 |
| Petechiae | 1 | 37 | 3 | 37 | 7 | 15 | 11 | 89 | 12.958 | 0.002 |
| Purpura /Ecchymosis | 0 | 38 | 0 | 40 | 2 | 20 | 2 | 98 | 7.236 | 0.027 |
| Hematemesis | 0 | 38 | 2 | 38 | 0 | 22 | 2 | 98 | 3.061 | 0.216 |
| Melena | 0 | 38 | 28 | 12 | 11 | 11 | 39 | 61 | 41.572 | 0 |
| Epistaxis | 0 | 38 | 3 | 37 | 4 | 18 | 7 | 93 | 7.101 | 0.029 |
| Haemoptysis | 0 | 38 | 1 | 39 | 1 | 21 | 2 | 98 | 1.554 | 0.46 |
| Bleeding Gums | 0 | 38 | 2 | 38 | 9 | 13 | 11 | 89 | 26.27 | 0 |
| Haematuria | 0 | 38 | 1 | 39 | 1 | 21 | 2 | 98 | 1.554 | 0.46 |
| Vaginal Bleeding | 0 | 38 | 3 | 37 | 5 | 17 | 8 | 92 | 9.801 | 0.007 |
| Abdominal Pain | 0 | 38 | 17 | 23 | 12 | 10 | 29 | 71 | 26.034 | 0 |
| Edema | 0 | 38 | 1 | 39 | 3 | 19 | 4 | 96 | 7.138 | 0.028 |
| Restlessness | 0 | 38 | 2 | 38 | 6 | 16 | 8 | 92 | 14.896 | 0.001 |
| Breathlessness | 0 | 38 | 2 | 38 | 5 | 17 | 7 | 93 | 11.465 | 0.003 |
| Altered Sensorium | 0 | 38 | 0 | 40 | 2 | 20 | 2 | 98 | 7.236 | 0.027 |
| Seizures | 0 | 38 | 1 | 39 | 4 | 18 | 5 | 95 | 10.574 | 0.005 |
| Chest Pain | 0 | 38 | 0 | 40 | 2 | 20 | 2 | 98 | 7.236 | 0.027 |

**Table 2:** Showing clinical signs of dengue patients in the study

| Signs | Groups | | | | | | Total Cases | | Chi Square Test | p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | Group-1 | | Group-2 | | Group-3 | | Yes | No | | |
| | Yes | No | Yes | No | Yes | No | | | | |
| Pallor | 0 | 38 | 1 | 39 | 3 | 19 | 4 | 96 | 7.138 | 0.028 |
| Conjunctival Congestion | 0 | 38 | 2 | 38 | 5 | 17 | 7 | 93 | 11.465 | 0.003 |
| Subconjunctival Haemorrhage | 0 | 38 | 3 | 37 | 6 | 16 | 9 | 91 | 12.837 | 0.002 |
| Pleural Effusion | 0 | 38 | 4 | 36 | 11 | 11 | 15 | 85 | 28.627 | 0 |
| GB Edema | 0 | 38 | 2 | 38 | 10 | 12 | 12 | 88 | 30.355 | 0 |
| Ascites | 0 | 38 | 4 | 36 | 7 | 15 | 11 | 89 | 14.477 | 0.001 |
| IC Bleed | 0 | 38 | 0 | 40 | 2 | 20 | 2 | 98 | 7.236 | 0.027 |

**Table 3:** Showing laboratory parameters of dengue patients in the study

| | | Dengue without warning signs Group 1 | Dengue with warning signs Group 2 | Severe Dengue Group 3 | p-value |
|---|---|---|---|---|---|
| **HB** | Mean± | 12.528 | 13.125 | 11.977 | 0.197 |
| | SE | 0.415 | 0.359 | 0.527 | |
| **WBC** | Mean± | 4383.95 | 5035.5 | 4280 | 0.301 |
| | SE | 357.297 | 366.576 | 395.222 | |
| **HCT** | Mean± | 37.994 | 38.715 | 42.386 | 0.02 |
| | SE | 1.012 | 0.912 | 1.22 | |
| **Sodium** | Mean± | 136.21 | 137.28 | 137.86 | 0.586 |
| | SE | 1.26 | 0.748 | 1.3 | |
| **Potassium** | Mean± | 3.908 | 3.775 | 3.909 | 0.476 |
| | SE | 0.077 | 0.073 | 0.155 | |
| **Chloride** | Mean± | 99.11 | 101.5 | 100.95 | 0.063 |
| | SE | 0.981 | 0.544 | 0.66 | |
| **Creatinine** | Mean± | 0.74 | 0.771 | 0.757 | |
| | SE | 0.022 | 0.026 | 0.032 | 0.666 |
| **ALT** | Mean± | 70.752 | 123.74 | 170.263 | 0 |
| | SE | 3.842 | 3.626 | 7.023 | |
| **AST** | Mean± | 69.542 | 101.772 | 350.44 | 0 |
| | SE | 10.666 | 3.559 | 27.818 | |
| **Bilirubin** | Mean± | 0.856 | 1.081 | 1.369 | 0.236 |
| | SE | 0.065 | 0.109 | 0.46 | |
| **ALP** | Mean± | 118.742 | 207.742 | 224.518 | 0.044 |
| | SE | 5.668 | 45.256 | 5.582 | |
| **PT** | Mean± | 12.186 | 16.902 | 16.304 | 0.223 |
| | SE | 0.563 | 3.085 | 0.409 | |
| **INR** | Mean± | 0.778 | 1.194 | 1.39 | 0 |
| | SE | 0.03 | 0.019 | 0.045 | |
| **APTT** | Mean± | 35.15 | 52.415 | 76.66 | 0 |
| | SE | 0.951 | 1.954 | 2.387 | |
| **ESR** | Mean± | 9.84 | 13.7 | 15.73 | 0 |
| | SE | 0.429 | 0.273 | 0.596 | |
| **BT** | Mean± | 4.58 | 6.35 | 8.09 | 0 |
| | SE | 0.171 | 0.222 | 0.286 | |
| **CT** | Mean± | 9.68 | 10.68 | 13.77 | 0 |
| | SE | 0.329 | 0.236 | 0.436 | |
| **Calcium** | Mean± | 8.936 | 8.7 | 8.727 | 0.178 |
| | SE | 0.093 | 0.101 | 0.109 | |

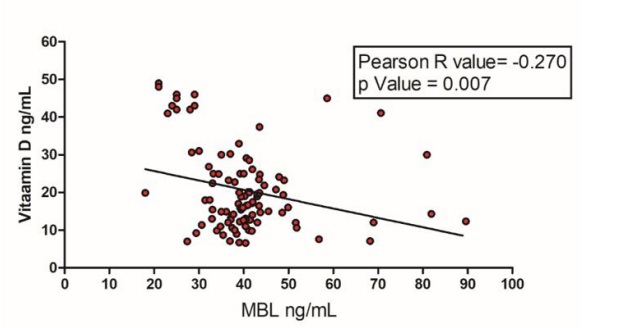


**Figure 4**: Correlation graph between MBL and Vitamin D

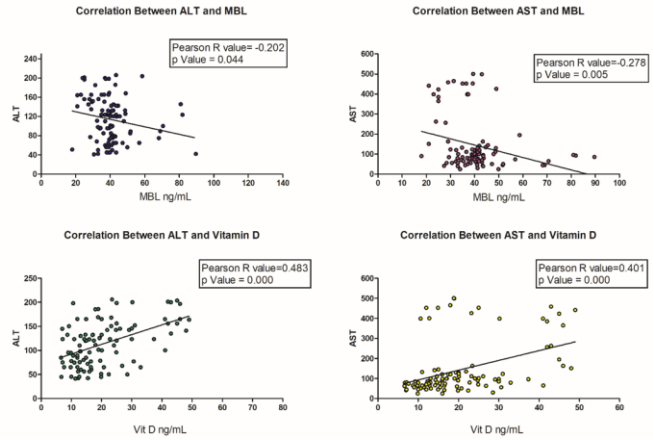


**Figure 5**: Figure label showing correlation graphs between liver enzymes (ALT, AST) and MBL & liver enzymes (ALT, AST) and Vitamin D

## 4. Discussion

The most common presenting symptoms in this study were Myalgias, Headache, Malena, joint pains, and abdominal pain. The observed frequencies of symptoms in this study are similar to the previous studies but with some notable differences.[2] Age and gender did not affect the severity of dengue fever as all the age groups of both genders are equally affected. In this study, the mean platelet count in the Severe Dengue group was significantly lower than other Dengue groups similar to other studies.[18]

In this study all the dengue patients were found to have MBL deficiency and patients with severe dengue had lower levels compared to patients without warning signs and with warning signs. These findings are in concordance with the study done by Kalichamy Alagarasu *et al.*[24]

Human MBL inhibits infection of all DENV serotypes by both complement-dependent and complement-independent mechanisms. Lectin pathway-mediated neutralization of DENV-2 is by direct opsonization, regulation of cytokine production, and amplification of adaptive immunity which depends on MBL concentration.[19] Another explanation is that MBL deficiency may impact dendritic cell (DC) function hence low concentrations of MBL lead to increased secretion of the proinflammatory cytokines interleukin- 6, interleukin -1β, and tumor necrosis factor α Which in turn shifts the immune response towards Th-2 and thereby subsequent disease progression.[20]

Low MBL concentrations have been associated with increased susceptibility to infections in both animal models and humans, as well as with poor disease prognosis.[10,11,21] The modulation of disease severity is partly thought to be through a complex, dose-dependent influence on cytokine production.

Patients with severe dengue had near-normal Vitamin D values compared to the other groups. Vitamin D is known for its beneficial effects rather than deleterious effects. A Positive association between a total of 25(OH)D concentrations and severe dengue is an interesting finding. This association may be attributed to the inducing effect of vitamin D on Fcγ receptor expression which might subsequently lead to higher viral load in dengue cases and development of severe dengue.[22] This association is further strengthened by our finding that normal levels of vitamin D are associated with clinical features of rash, petechiae, ecchymosis, epistaxis, bleeding gums, vaginal bleeding, pain abdomen, subconjunctival hemorrhage, pleural effusion, GB edema, ascites, and all these findings are statistically significant with $p<0.05$.[23] A study done by Kalichamy Alagarasu et al[24] has shown that elevated levels of vitamin D were associated with dengue severity unlike in our study where severe dengue patients had near normal vitamin D levels compared to other groups. Similar findings were noted in a study done by Bharara T *et al.*[29] Explanatory mechanisms remain speculative. When 1α,25-(OH)2D3 is added to mitogen-stimulated human peripheral blood lymphocytes in vitro, it inhibits their proliferation, Ig synthesis, and accumulation of transcripts for IL-1, IL-2, IL-6, TNF-a, and -b and IFN-gamma.[12] Further studies are required to confirm this hypothesis. A study by Iqtadar S et al[28] and Sadarangani SP et al[30] have shown that vitamin D Deficiency is associated with severe Dengue. Hence further studies are needed to know the exact role of Vitamin D.

Deranged liver function in dengue infection can result from the virus's direct effect on hepatocytes or an unregulated host immune response against the virus.[25] Both AST and ALT were significantly raised in patients with Severe Dengue and the increase in AST was higher than the increase in ALT.[26]

In the present study too, the difference in both AST and ALT levels among the groups was significant, suggestive of dengue hepatopathy. Further, AST, ALT, and ALP showed a strong positive correlation with vitamin D and a strong negative correlation with MBL (**Figure 5**) which reinforces that dysregulated immune response is the major contributor to organ damage during severe dengue.

Finally, the th1/th2 paradigm can provide the basis for the severity of dengue disease which is mediated by complement cascade and vitamin D-induced immune

modulation.[21,23] This study emphasizes the importance of serum MBL and vitamin D levels as prognostic markers in assessing the severity of dengue and the potential role of therapeutic MBL replacement in the management of severe dengue.

## 5. Limitations

1. MBL genotypes were not determined.
2. Larger studies are needed to confirm our results and elucidate the underlying mechanisms.
3. The study needs to be validated in larger samples to understand the role of Vitamin D in dengue severity.

## 6. Conclusions

In our study Levels of vitamin D were found to be low in patients of group 1 compared to groups 2 and 3, indicating that patients with low normal levels of Vitamin D had less severe dengue. MBL levels were found to be low in all patients with dengue (<500ng/ml) but MBL levels in patients with severe dengue were further less compared to group 2 and group 1. Hence low serum levels of MBL are associated with severe dengue.

## 7. Abbreviations

DSS: Dengue shock syndrome; D.F: Dengue fever; DHF: Dengue haemorrhagic fever; DENV/DEN/DV: Dengue virus; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; WHO: World Health Organization; ELISA: Enzyme-Linked immunosorbent assay; NS1Ag: Non-structural antigen; IgM: Immunoglobulin M; IgG: Immunoglobulin G; TNF: Tumor necrosis factor; NF kβ: Nuclear Factor kβ; IL: Interleukin; VDR: Vitamin D receptor; MBL: Mannose binding lectin; MASP: MBL associated serine protease; GlcNAc: N Acetyl glucosamine; SNP: Single nucleotide polymorphism; DC: Dendritic cells; CLEC5A: C-Type lectin domain family 5, member A; MR: Mannose receptor; PRP: Pattern recognition receptor; RIG 1: Retinoic acid inducible gene 1; MDA 5: Melanoma differentiation associated protein 5; IRF: Interferon regulator factors; DBP: Dengue binding protein; HSP: Heat shock protein; RXR: Retinoid x receptor; VDRE: Vitamin D response elements; HRP: Horse radish peroxidase; OD: Optical density; ROC: Receiver operative characteristic; SOB: Shortness of breath; DM: Diabetes mellitus; HTN: Hypertension; BA: Bronchial asthma; GB edema: Gall bladder edema; GBS: Guillain barre syndrome; MODS: Multiple organ dysfunction syndrome.

## 8. Ethical Approval

This study was approved by Institute Ethical review committee with ref. no. IEC/GMC/2017() dated 30/12/2017.

## 9. Source of Funding

This work has been partially Funded by ICMR as a part of MD PG Thesis Grant vide reference letter No.3/2/June-2017/PG Thesis-HRD (20) from ICMR.

## 10. Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

1. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature*. 2013;496(7446):504–7.
2. Mutheneni SR, Morse AP, Caminade C, Upadhyayula SM. Dengue burden in India: recent trends and importance of climatic parameters. *Emerg Microbes Infect*. 2017;6(8):e70.
3. Martina BEE, Koraka P, Osterhaus ADME. Dengue virus pathogenesis: an integrated view. *Clin Microbiol Rev.* 2009;22(4):564–81.
4. Chaturvedi UC, Nagar R, Shrivastava R. Dengue and dengue hemorrhagic fever: implications of host genetics. FEMS Immunol Med Microbiol. 2006;47(2):155–66.
5. Dunkelberger JR, Song WC. Complement and its role in innate and adaptive immune responses. *Cell Res*. 2010;20(1):34–50.
6. Kulkarni HS, Liszewski MK, Brody SL, Atkinson JP. The complement system in the airway epithelium: An overlooked host defense mechanism and therapeutic target? *J Allergy Clin Immunol*. 2018;141(5):1582–6.
7. Takahashi K, Ip WE, Michelow IC, Ezekowitz RA. The mannose-binding lectin: a prototypic pattern recognition molecule. *Curr Opin Immunol*. 2006;18(1):16–23.
8. Gupta GS. Animal lectins: form, function and clinical applications. Springer Science & Business Media; 2012.
9. Turner MW. The role of mannose-binding lectin in health and disease. *Mol Immunol*. 2003;40(7):423–9.
10. Pana ZD, Samarah F, Papi R, Antachopoulos C, Papageorgiou T, Farmaki E, et al. Mannose-binding lectin and ficolin-2 polymorphisms are associated with increased risk for bacterial infections in children with B acute lymphoblastic leukemia. *Pediatr Blood Cancer*. 2014;61(6):1017–22.
11. Eisen DP, Minchinton RM. Impact of mannose-binding lectin on susceptibility to infectious diseases. *Clin Infect Dis*. 2003;37(11):1496-505.
12. Beard JA, Bearden A, Striker R. Vitamin D, and the anti-viral state. *J Clin Virol*. 2011;50(3):194-200.
13. van Etten E, Mathieu C. Immunoregulation by 1, 25-dihydroxyvitamin D3: basic concepts. *J Steroid Biochem Mol Biol*. 2005;97(1-2):93–101.
14. D'Ambrosio D, Cippitelli M, Cocciolo MG, Mazzeo D, Di Lucia P, Lang R, et al. Inhibition of IL-12 production by 1, 25-dihydroxyvitamin D3. Involvement of NF-kappaB downregulation in transcriptional repression of the p40 gene. *J Clin Invest.* 1998;101(1):252–62.
15. Heine G, Niesner U, Chang HD, Steinmeyer A, Zügel U, Zuberbier T, et al. 1, 25-dihydroxyvitamin D3 promotes IL-10 production in human B cells. *Eur J Immunol*. 2008;38(8):2210–8.
16. Trinchieri G. Interleukin-12 and the regulation of innate resistance and adaptive immunity. *Nat Rev Immunol*. 2003;3(2):133–46.
17. Trinchieri G. Interleukin-12: a proinflammatory cytokine with immunoregulatory functions that bridge innate resistance and antigen-specific adaptive immunity. *Ann Rev Immunol*. 1995;13(1):251–76.
18. Kumar A, Rao CR, Pandit V, Shetty S, Bammigatti C, Samarasinghe CM. Clinical manifestations and trend of dengue cases admitted in

a tertiary care hospital, Udupi district, Karnataka. *Indian J Community Med*. 2010;35(3):386–90.
19. Thiel S, Frederiksen PD, Jensenius JC. Clinical manifestations of mannan-binding lectin deficiency. *Mol Immunol*. 2006;43(1-2):86–96.
20. Ling MT, Tu W, Han Y, Mao H, Chong WP, Guan J, et al. Mannose-binding lectin contributes to deleterious inflammatory response in pandemic H1N1 and avian H9N2 infection. *J Infect Dis*. 2012;205(1):44–53.
21. Swale A, Miyajima F, Kolamunnage-Dona R, Roberts P, Little M, Beeching NJ, et al. Serum mannose-binding lectin concentration, but not genotype, is associated with Clostridium difficile infection recurrence: a prospective cohort study. *Clin Infect Dis*. 2014;59(10):1429–36.
22. Berber A, Stöckl J, Majdic O, Wagner T, Kollars M, Lechner K, et al. 1, 25-Dihydroxyvitamin D3 inhibits dendritic cell differentiation and maturation in vitro. *Exp Hematol*. 2000;28(5):575–83.
23. Villamor E, Villar LA, Lozano A, Herrera VM, Herran OF. Vitamin D serostatus and dengue fever progression to dengue hemorrhagic fever/dengue shock syndrome. *Epidemiol Infect.* 2017;145(14):2961–70.
24. Alagarasu K, Bachal RV, Bhagat AB, Shah PS, Dayaraj C. Elevated levels of vitamin D and deficiency of mannose binding lectin in dengue hemorrhagic fever. *Virol J.* 2012;9:86.
25. Rachman A, Rinaldi I. Coagulopathy in dengue infection and the role of interleukin-6. *Acta Med Indones*. 2006;38(2):105–8.
26. Pongpan S, Wisitwong A, Tawichasri C, Patumanond J. Prognostic indicators for dengue infection severity. *Int J Clin Pediatr.* 2013;2(1):12–8.
27. Auriti C, Prencipe G, Moriondo M, Bersani I, Bertaina C, Mondì V, et al. Mannose-binding lectin: biologic characteristics and role in the susceptibility to infections and ischemia-reperfusion related injury in critically ill neonates. *J Immunol Res*. 2017;2017(1):7045630.
28. Iqtadar S, Khan A, Mumtaz SU, Livingstone S, Chaudhry MN, Raza N, et al. Vitamin D Deficiency (VDD) and Susceptibility towards Severe Dengue Fever—A Prospective Cross-Sectional Study of Hospitalized Dengue Fever Patients from Lahore, Pakistan. *Trop Med Infect Dis.* 2023;8(1):43.
29. Bharara T, Chakravarti A, Kapoor N. Correlation of 25-hydroxy vitamin D3 levels with dengue disease severity–Can vitamin D levels predict dengue prognosis?. *Int J Infect Dis*. 2020;101:260.
30. Sadarangani SP, Htun HL, Ling W, Hawkins R, Yeo TW, Rivino L, et al. Association of systemic vitamin D on the course of dengue virus infection in adults: A single-centre dengue cohort study at a large institution in Singapore. *Singapore Med J*. 2024;65(6):332–9.

**Cite this article:** Naaz S, Zoheb MA, Bingi TC. Prognostic value of mannose binding lectin and vitamin D in dengue: Study from a tertiary care centre from southern India. *Indian J Microbiol Res*. 2025;12(1):63–70.