



RESEARCH ARTICLE

Association of Dengue Serotypes with Hematological Parameters, Hypoalbuminemia, and Severe Clinical Outcomes in Patients Admitted to a Tertiary Care Hospital

Sreejith Sreedharan Panicker*

¹Dept of Microbiology, Mahavir
Institute of medical Sciences,
Telangana, Vikarabad

Abstract

Introduction: The following study discusses dengue, which is a major mosquito-borne viral disease. It is caused by four serotypes (DEN-1 to DEN-4), with varying clinical severity. Differences in serotype virulence may influence hematological abnormalities, hypoalbuminemia, and disease outcomes. The aim of this study is to evaluate the relationship between dengue serotypes, hematological parameters, serum albumin levels, and severe clinical outcomes among hospitalized dengue patients. **Methods:** This is a hospital-based observational study which was conducted among 95 laboratory-confirmed dengue patients who were admitted to a tertiary care hospital over one year. Dengue serotypes were identified using RT-PCR. Clinical, hematological, and biochemical parameters, including serum albumin levels, were collected and analyzed. Associations between serotypes, hypoalbuminemia, hematological changes, and clinical outcomes were evaluated using appropriate statistical tests. **Results:** Among the dengue serotypes, DEN-2 exhibited the lowest mean serum albumin level (2.84 ± 1.16 g/dL), significantly lower than DEN-1 (3.42 ± 0.69 g/dL), DEN-3 (3.51 ± 0.78 g/dL), and DEN-4 (3.58 ± 0.67 g/dL) ($p < 0.05$). Severe dengue occurred in 11 patients (17.2%), with a mean albumin level of 2.62 ± 0.71 g/dL, while plasma leakage was observed in 45.5% of these cases. The majority of patients were aged 19–34 years (49.5%). DEN-2 also showed the lowest platelet count (1.36 ± 0.59 lakh/mm³), whereas DEN-3 had the highest (1.69 ± 0.70 lakh/mm³). **Conclusion:** The study has concluded that a significant association between dengue serotypes and variations in serum albumin levels, with DEN-2 infection showing the greatest degree of hypoalbuminemia and thrombocytopenia.

Keywords: Assistant Professor, Dept of Microbiology, Mahavir Institute of medical Sciences, Vikarabad, Telangana

Copyright : © 2019 The Authors. Published by Publisher. This is an open access article under the CC BY-NC-ND license (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).

1 | INTRODUCTION

Dengue, or dengue fever, is an acute febrile disease that is transmitted by mosquitos and caused by the dengue virus (DENV). The dengue virus has four distinct serological types (DENV-1 - DENV-4) (1, 2). While people affected by a primary infection typically experience self-limiting febrile episodes as their only symptom of dengue, those who experience a secondary heterologous infection are at increased risk of developing severe forms of dengue, characterized by serious plasma leakage, hemorrhage, and shock (1, 2). DENV transmission has reached epidemic levels worldwide, with more than 6.5 million people diagnosed with dengue in 2022, and increases of four times the amount of dengue-infected mosquito vectors in Latin America in 2024 (1, 2). India has become hyper-endemic for dengue and currently exhibits all four serotypes co-circulating throughout the country, with a significant and dynamic shift of predominant serotypes in many areas of India (for example: New Delhi has shifted from predominantly DENV-2 to DENV-3) (1, 2). Changes in the predominant serotypes negatively impact the clinical management and treatment of dengue due to the occurrence of antibody-dependent enhancement (1, 2). Infection from the dengue virus causes changes in blood cells and blood vessels throughout the body due to two reasons: 1.) Damaged bone marrow function will reduce the number of red blood cells and white blood cells; 2.) The immune system destroys more white blood cells than normal because of the presence of large amounts of plastic waste products created by the infection and pre-existing inflammation (3, 4). The acute loss of both red blood cell (thrombocytopenia) and white blood cell (leukopenia) can be seen as symptoms of dengue. Circulating large amounts of viral proteins found in dengue can also trigger the immune system to destroy endothelial cells, which leads to increased blood permeation out of the blood vessel (plasma leakage), causing the following symptoms: hemoconcentration, and clear symptoms of severe dengue disease (3, 4).

Dengue virus (DENV) serotypes differ from each other in terms of virulence and the tissues they

infect (tissue tropism), with DENV-2 and DENV-3 associated historically with aggressive clinical courses and severe plasma leakage (5, 6). Historical data from tertiary-care hospitals in North India and Pune show that changes in the dominance of DENV serotypes and the return of previously suppressed strains (e.g., DENV-4) correlate with increased severe cases and higher mortality rates (5, 6). Heterologous secondary infections are often worsened due to antibody-dependent enhancement (ADE), where antibodies created during the first infection facilitate the entry of the virus during the second infection, even though these antibodies are not neutralizing and do not stop virions from entering cells (5, 6). Although these are well-established epidemiological observations, there is limited published data on the relationship between DENV serotypes and precise biochemical traits, such as changes in serum albumin levels or defined immediate triage variables that stratify DENV serotypes in the Indian population (5, 6).

The purpose of this research is to analyze how certain strains of circulating dengue virus can be linked with blood-based changes, low blood protein levels and serious illnesses for the purposes of better identifying patients at risk and helping physicians make treatment decisions for patients treated in a tertiary care hospital.

2 | METHOD

Research design

This is a hospital-based observational study which evaluated the association of the serotypes of dengue with the Haematological Parameters, Hypoalbuminemia and other patient outcome. The study was

Supplementary information The online version of this article (<https://doi.org/xx.xxx/xxx.xx>) contains supplementary material, which is available to authorized users.

Corresponding Author: *Sreejith Sreedharan Panicker*

Assistant Professor, Dept of Microbiology, Mahavir Institute of medical Sciences, Vikarabad, Telangana

ASSOCIATION OF DENGUE SEROTYPES WITH HEMATOLOGICAL PARAMETERS, HYPOALBUMINEMIA, AND SEVERE CLINICAL OUTCOMES

conducted in Icare Institute of Medical Sciences And Research and Dr. Bidhan Chandra Roy Hospital, Haldia, during the period of one year. Total 95 patients were selected for the study those who had confirmed the dengue patients admitted. Clinical and laboratory information were collected from the hospital dataset and the laboratory assessments. The dengue serotype was conducted by the use of real-time polymerase chain reaction (RT-PCR) techniques. All of the patients were categorised according to the World Health Organization (WHO) dengue severity guidelines, and the association between the hematological parameters, hypoalbuminemia, dengue serotypes and the clinical outcome were evaluated.

Inclusion criteria

- Patients with any age and gender were selected for the study.
- Those who were laboratory confirmed the infection of dengue
- Patients of any age and gender with laboratory-confirmed dengue infection (NS1 positive)

Exclusion Criteria

- Patients with the other febrile illnesses, or the chronic hematological disorders were excluded.
- Patients those who have received the immunosuppressive therapy
- Irrelevant or missed clinical information were excluded

Procedure

The ethical approval as obtained from all of the patient, which showed that 95 laboratory-confirmed dengue patients were enrolled. The proper structured proforma was utilised for the collection of the demographic details, clinical symptoms, vital signs, and laboratory findings. Laboratory investigations were performed such as NS1 antigen status, dengue serotyping, complete blood count, hematocrit, liver function tests, platelet count trends, and serum albumin levels. All of the patients were categorised a severity of the disease and the association between the serotypes of dengue, hematological parameters, hypoalbuminemia and various clinical outcome were evaluated.

Statistical analysis

SPSS version 27 was used for the data entry and analysis. The mean $\pm$ standard deviation was used for the expression of the categorical variables. The combination of the dengue serotypes and clinical or laboratory parameters were evaluated. The frequencies and percentages were represented by mean $\pm$ standard deviation. The association between the serotype and the Chi-square test or Fisher's exact test were used. The p value was considered to be as 0.05 for statistical significance.

3 | RESULT

howed the level of mean serum albumin among patients those who were infected with dengue serotypes. DEN-2 showed the lowest level of the mean albumin (2.84 ± 1.16 g/dL), which revealed the highest degree of the hypoalbuminemia rather than the DEN-1, DEN-3, and DEN-4. The highest level of mean value of the albumin was noted in DEN-4 (3.58 ± 0.67 g/dL).

howed that severe dengue had developed among 11 patients (17.2%), with their mean value of the serum albumin was 2.62 ± 0.71 g/dL, which indicated the hypoalbuminemia. 5 patients (45.5%) represented the leakage of the plasma. The relationship between the low level of albumin and the severe form of dengue along with the plasma leakage was significant, which indicated that hypoalbuminemia may be significant as a marker of the severity of the disease for the infection of the dengue infection.

howed the distribution of age of about 95 dengue patients, which indicated that majorly patients were in the age group of 19–34 years, which accounted for 47 patients (49.5%). This was followed by those patients of age <18 years (25.3%). Patients of age 35–50 years included 14.7%, while those patients of age >50 years, which presented small proportion of people of 10.5%. These study findings indicated that the young adults were mostly affected by the group of age among the study population.

represented the mean value of the platelet counts among patients. The highest mean value was noted for the N-3 (1.69 ± 0.70 lakh/mm³), which was fol-

TABLE 1:

Biochemical Parameter	DEN-1 Mean $\pm$ SD	DEN-2 Mean $\pm$ SD	DEN-3 Mean $\pm$ SD	DEN-4 Mean $\pm$ SD	p-value
Albumin (g/dL)	3.42 $\pm$ 0.69	2.84 $\pm$ 1.16	3.51 $\pm$ 0.78	3.58 $\pm$ 0.67	<0.05*

TABLE 2: The association of the level of the Serum Albumin along with the severe dengue with the leakage of plasma

Parameter	Total Severe Dengue Cases	Mean $\pm$ SD	Patients Presenting with Plasma Leakage	p-value
Albumin (g/dL)	11 (17.2%)	2.62 $\pm$ 0.71	5 (45.5%)	<0.05*

TABLE 3: The distribution of dengue patients according to age

Age (Years)	Number (n)	Percentage (%)
<18	24	25.3
19–34	47	49.5
35–50	14	14.7
>50	10	10.5
Total	95	100

TABLE 4: The comparison of the count of platelet among study population

Hematological Parameter	DEN-1 (Mean $\pm$ SD)	DEN-2 (Mean $\pm$ SD)	DEN-3 (Mean $\pm$ SD)	DEN-4 (Mean $\pm$ SD)
Platelets (lakh/mm ³)	1.52 $\pm$ 0.45	1.36 $\pm$ 0.59	1.69 $\pm$ 0.70	1.43 $\pm$ 0.40

lowed by the DEN-1 (1.52 $\pm$ 0.45 lakh/mm³). Low count of platelet was noted for the DEN-4 (1.43 $\pm$ 0.40 lakh/mm³) and DEN-2 (1.36 $\pm$ 0.59 lakh/mm³), which indicated the high thrombocytopenia.

4 | DISCUSSION

Multicenter observational and epidemiological data from Indian intensive care units (ICUs) demonstrate that severe forms of dengue and clinical outcomes are more influenced by dysfunction of non-hematological organs and dynamics of specific serotypes than by localised cytopenias (1, 7). Among adults in the ICU (N=42) with Dengue haemorrhagic fever or Dengue shock syndrome, mortality was 19% with nonsurvivors having a significantly lower mean baseline serum albumin (2.9 $\pm$ 0.3 g/dL vs 3.4 $\pm$ 0.7 g/dL) and a higher average 72-h cumulative fluid balance (6.2 L vs 3.5 L) than survivors (7). Multiple

organ failure including cardiovascular, respiratory and neurological failure was highly associated with mortality while isolated hematologic failure was not associated with mortality (7). A similar pattern was observed in the 2009 Delhi Dengue Outbreak (N=107) where positive RT-PCR testing from both DENV-2 and DENV-4 was seen (1). Although the presentation of patients at the Delhi outbreak was less severe in terms of overt bleeding, many patients had severe atypical manifestations of plasma leakage such as ascites, pleural effusion and cholecystitis that did not correlate statistically with nadir platelet counts or with clinical bleeding severity (1, 7).

According to epidemiology studies carried out on the 2006 dengue outbreak in New Delhi, it was found that the annual cycles of dengue virus transmission remain a serious public health problem, being characterized by differing serotypes being the dominant serotype, and significant changes in the hematological and biochemical profiles of affected

patients (8, 9). An analysis of the different hospital cohorts from the local patients showed a shift in demographics toward adult males with a large number of cases presenting atypically, such as with diarrhea, menorrhagia, seizures, and biochemical abnormalities affecting their ability to clot (8, 9). There were also documented instances of widespread cytopenia, but upon comparative analysis, it was found that there was no statistical correlation between absolute platelet counts and different bleeding manifestations, until counts dropped below 20,000/ μ L (8). Also, the presence of florid clinical symptoms prior to laboratory determined seroconversion suggests that acute phase pathogenesis places a greater burden on the hematologic kinetics of patients than initial humoral immunologic profile (8, 9).

It is critical for managing severe dengue phenotypes (type of dengue virus) that longitudinal serological evaluations track long-term trends and confirm the condition called plasma leakage (10, 11). In a comparative cohort study (N=65), 57.14% of cases of dengue hemorrhagic fever (severe form of dengue fever) had standard World Health Organization-defined hemoconcentration (>20%) while area-specific hematocrit cut-off values or using ultrasound were 91.42% effective for diagnosis; with ultrasound producing an 84.21% negative predictive value for occult plasma leakage (evidence of a leak) (10). A longitudinal five-year retrospective analysis of 1,426 suspected cases found an overall rate of IgM seropositivity (immunoglobulin M; a type of protein produced by the body after it has been infected by a type of virus or bacterium) increasing to 29.7%, with only children displaying a statistically significant rise ($P<0.001$) (11). Also, there was a considerable burden of secondary heterotypic infections in 41% of seropositive patients, who were dual IgM and IgG positive (11). This proliferation of seroprevalence indicates an increase risk to develop imminent endemically severe epidemics in hyper-endemic areas (occurring at higher-than-normal rates) where multiple serotypes are co-circulating (10, 11).

Future efforts need to realign clinical paradigms to move away from using traditional diagnostic markers of severity, and instead start using population-specific, objective threshold values to allow earlier

risk stratification of severe dengue phenotypes (12, 13). Therefore, data show that the conventional tourniquet test has only very low clinical sensitivity when assessing the severity of isolated thrombocytopenia, and that the severity of isolated thrombocytopenia does not correlate well with hemorrhagic manifestations such as epistaxis or hematemesis (12, 13). As a result, future protocols should focus more on high-resolution diagnostic metrics and not merely on the use of fluctuating platelet nadirs for this purpose (12). Utilising local baseline "cut-off" values for haematocrit status via discriminant analysis for use in specific populations serves to identify hemoconcentration and occult plasma leakage much more accurately than other methods (12). In the long term, the incorporation of these precise hematological metrics with quantifiable markers of endothelial dysfunction and severe hypoproteinaemia into large-scale clinical frameworks will permit early detection of multi-organ failure, improve intensive care triage, and decrease mortality rates within tertiary care settings (12, 13).

5 | CONCLUSION

The study has concluded that a significant association between dengue serotypes and variations in serum albumin levels, with DEN-2 infection showing the greatest degree of hypoalbuminemia and thrombocytopenia. Lower serum albumin levels were significantly associated with severe dengue and plasma leakage, highlighting hypoalbuminemia as a potential marker of disease severity. Additionally, young adults (19–34 years) constituted the most affected age group, emphasizing the need for early monitoring of serum albumin and platelet counts to identify patients at risk of severe clinical outcomes.

REFERENCES

1. Chakravarti A, Arora R, Luxemburger C. Fifty years of dengue in India. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2012;106(5):273–282.

2. Ganeshkumar P, Murhekar MV, Poornima V, Saravanakumar V, Sukumaran K, Anandaselvasankar A, et al. Dengue infection in India: A systematic review and meta-analysis. *PLoS neglected tropical diseases*. 2018;12(7).
3. Srichaikul T, Nimmannitya S. Haematology in dengue and dengue haemorrhagic fever. *Bailliere's best practice & research. Clinical haematology*. 2000;13(2):261–276.
4. Malavige GN, Ogg GS. Pathogenesis of vascular leak in dengue virus infection. *Immunology*. 2017;151(3):261–269.
5. Prakash O, Singh DD, Mishra G, Prakash S, Singh A, Gupta S, et al. Observation on dengue cases from a virus diagnostic laboratory of a tertiary care hospital in North India. *The Indian journal of medical research*. 2015;142(1):7–11.
6. Cecilia D, Kakade MB, Bhagat AB, Vallentyne J, Singh A, Patil JA, et al. Detection of dengue-4 virus in pune, western india after an absence of 30 years—its association with two severe cases. *Virology journal*. 2011;8.
7. Schmitz L, Prayag S, Varghese S, Jog S, Bhargav-Patil P, Yadav A, et al. Nonhematological organ dysfunction and positive fluid balance are important determinants of outcome in adults with severe dengue infection: a multicenter study from India. *Journal of critical care*. 2011;26(5):441–448.
8. Rai S, Chakravarti A, Matlani M, Bhalla P, Aggarwal V, Singh N, et al. Clinico-laboratory findings of patients during dengue outbreak from a tertiary care hospital in Delhi. *Tropical doctor*. 2008;38(3):175–177.
9. Sinha N, Gupta N, Jhamb R, Gulati S, Ajit VK. The 2006 dengue outbreak in Delhi. *India The Journal of communicable diseases*. 2008;40(4):243–248.
10. Balasubramanian S, Janakiraman L, Kumar SS, Muralinath S, Shivbalan S. A reappraisal of the criteria to diagnose plasma leakage in dengue hemorrhagic fever. *Indian pediatrics*. 2006;43(4):334–339.
11. Vijayakumar TS, Chandy S, Sathish N, Abraham M, Abraham P, Sridharan G. Is dengue emerging as a major public health problem. *The Indian journal of medical research*. 2005;121(2):100–107.
12. Gomber S, Ramachandran VG, Kumar S, Agarwal KN, Gupta P, Gupta P, et al. Hematological observations as diagnostic markers in dengue hemorrhagic fever—a reappraisal. *Indian pediatrics*. 2001;38(5):477–481.
13. Anuradha S, Singh NP, Rizvi SN, Agarwal SK, Gur R, Mathur MD; 1998.

How to cite this article: Sreedharan Panicker S. **Association of Dengue Serotypes with Hematological Parameters, Hypoalbuminemia , and Severe Clinical Outcomes in Patients Admitted to a Tertiary Care Hospital .** *Innovative Journal of Medical and Health Science*. 2019;1765–1769. <https://doi.org/10.15550/ijmhs/2019-7-99>