



Circulating Dengue Serotypes and their Correlation with Severity of Disease at a Tertiary Care Hospital in Jaipur, Rajasthan

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ABSTRACT

Introduction: Dengue is a major health threat with epidemic potential and is prevalent in tropical and subtropical regions of the world. This study was aimed at analyzing the circulating dengue serotypes in our region and their correlation with the severity of disease presenting to our hospital.

Materials and methods: A hospital-based retrospective study was done on 100 patients with dengue infection who fulfilled the inclusion and exclusion criteria, admitted under the Department of General Medicine of Mahatma Gandhi Medical College and Hospital, Jaipur. Dengue serotype was confirmed by RT-PCR.

Results: A total of 100 patients were included in the data analysis. Adult age group (82%) and male gender (54%) were the most commonly affected group. The most common serotypes in circulation were DENV-2 and DENV-3 (60% cases). Severe dengue was maximum in patients with DENV-2 (20.6%). Concurrent infection with two serotypes was present in four cases. The mean duration of hospital stay was maximum in DENV-4 (5.33 ± 2.09 days). The maximum percentage of DENV-1 cases required platelet transfusion.

Conclusion: At our hospital, adult age group and male gender are most commonly affected, with DENV-2 being the most common serotype and having maximum severity. Initial serotyping of dengue patients can help monitor the epidemiological and clinical trends of the different serotypes of dengue infection. Co-infection with two serotypes can also occur.

Keywords: Dengue, Dengue virus, DENV, RT-PCR, Serotype, Thrombocytopenia.

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INTRODUCTION

In recent decades, with increasing geographic expansion to new countries, the global incidence of dengue virus (DENV) infection has increased.¹ As mosquitoes are widely distributed in India and can serve as vectors of the dengue virus, combined with the rapid growth of population, unplanned urbanization, and increased international travel, it has increased the epidemic risk.

Dengue is caused by four serologically and genetically distinct viruses (DENV-1, DENV-2, DENV-3, and DENV-4 serotypes). Infection with any one serotype confers the host's lifelong homotypic immunity to that serotype. Dengue has distinct epidemiological patterns, associated with the four serotypes of the virus. These can cocirculate within a region, and indeed many countries are hyperendemic for all the four serotypes. Dengue has an alarming impact on both human health and the global and national economies.

In this study, we evaluated the patients admitted with dengue at our tertiary care hospital, in an urban setting for their serotype, and the correlation of the infecting serotype with the disease severity.

AIMS AND OBJECTIVES

- To study the frequency of the four dengue serotypes.
- To correlate the infecting serotype with the disease severity, duration of hospital stay, and platelet transfusion requirement.

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MATERIALS AND METHODS

This retrospective study was conducted in the Department of General Medicine of Mahatma Gandhi Medical College and Hospital, Jaipur. A total of 100 patients (in-patient) admitted to the department with dengue fever were selected for the study from the period of January 2019 to June 2020.

Inclusion Criteria

- Patients over 12 years of age.
- Test positive for dengue by RT-PCR.
- Informed consent.

Exclusion Criteria

- Patients aged less than 12 years.
- Patients with comorbidities—diabetes mellitus, hypertension, hypothyroidism, and chronic renal failure.
- Patients with other underlying malignancy, hematological disorder, or use of any drug which may cause thrombocytopenia.
- Patients with a documented cause of thrombocytopenia other than dengue.

Investigations Required

Patients admitted with suspected dengue fever underwent a detailed medical history and a thorough physical examination.

- All routine blood parameters were sent.
- The dengue serotype was confirmed by RNA amplification by ABI 7500 Fast Dx Real Time Polymerase Chain Reaction.
- Patients were classified into nonsevere dengue without warning signs/nonsevere dengue with warning signs/severe dengue as per the WHO classification (Flowchart 1).

Data Analysis

- For descriptive analyses, numbers and percentages were used to express categorical variables. Means with standard deviations were used to express continuous variables.
- Analysis was performed using IBM SPSS Statistics 26.
- The Pearson's Chi-square test for independence and the Kruskal–Wallis nonparametric test for ordinal variables and the One-way ANOVA test for continuous variables were applied. A p -value <0.05 was considered statistically significant.

RESULTS

Table 1 shows the distribution of patients according to age groups. There was no statistically significant difference in the distribution of

age groups between the different serotypes of infection (Pearson's Chi-square 32.681).

Table 2 shows the distribution of patients on the basis of gender. There was no statistically significant difference in the distribution of gender between the different serotypes of infection (Pearson's Chi-square 3.710).

Table 3 shows the distribution of serotype and the severity of the disease. There was no statistically significant difference in the distribution of severity between the different serotypes of infection (independent samples Kruskal–Wallis test, p -value-0.491).

Table 4 shows the mean duration of hospital stay in patients affected by the various serotypes. There was a statistically nonsignificant difference in the duration of hospital stay between the different serotypes of infection (one-way ANOVA, p -value 0.888).

Table 5 shows the platelet transfusion requirement for different serotypes. There was a statistically significant difference in the distribution of platelet transfusion between the different serotypes of infection (independent samples Kruskal–Wallis test, p -value 0.025).

DISCUSSION

In India, the resurgence of an epidemic of dengue activity poses a major public health challenge nowadays. This upsurge has been associated with the geographical expansion of both the mosquito vectors and the viruses. Dengue infections have spread throughout the country without clear geographical distribution, and with all serotypes in circulation.² Serotyping of dengue is not performed routinely; therefore, data on circulation of different serotypes in various parts of the country are very limited. To the best of our knowledge, research articles on serotyping of dengue from Rajasthan are not available from recent past. In this context, the present study was conducted to know about the circulating serotypes of dengue in Jaipur, Rajasthan.

Flowchart 1: Classification of dengue disease progression and severity. Adapted from World Health Organization guidelines

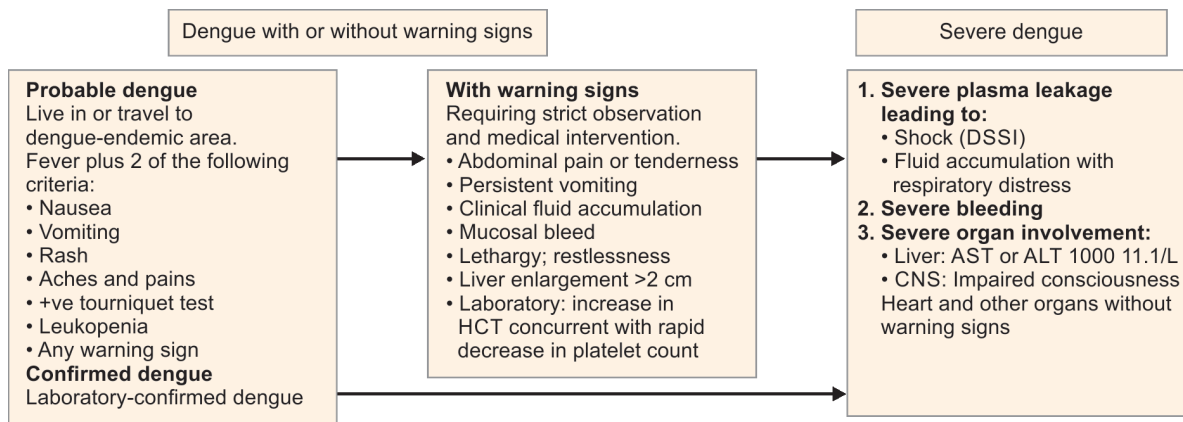


Table 1: Distribution of patients on the basis of age

Age group (years)	No. of cases (n)/%
12–18 years	18
19–45 years	58
46–75 years	19
>75 years	05

Table 2: Distribution of patients on the basis of gender

Group	Male		Females	
	(n)	%	(n)	%
Children (n = 18)	11	61.1	07	38.9
Adults (n = 82)	43	52.4	39	47.6
All patients (n = 100)	54	54	46	46

Table 3: Distribution of patients on the basis of serotype and severity of disease

Serotype	Total (n)	NS without W n (%)	NS with W n (%)	Severe n (%)
DENV 1	21	08 (38.1)	10 (47.6)	03 (14.3)
DENV 2	34	18 (52.9)	09 (26.5)	07 (20.6)
DENV 3	26	14 (53.8)	10 (38.5)	02 (7.7)
DENV 4	15	04 (26.7)	08 (53.3)	03 (20)
Co-infection (1 + 3)	03	02 (66.7)	01 (33.3)	–
Co-infection (2 + 3)	01	–	01 (100)	–
Total (n)	100	46	39	15

NS without W, nonsevere dengue without warning signs; NS with W, nonsevere dengue with warning signs

Table 4: Mean duration of hospital stay on the basis of serotype

Serotype	No. of cases (n)	Hospital stay (days)
DENV 1	21	4.71 ± 2.15
DENV 2	34	5.06 ± 1.82
DENV 3	26	4.69 ± 1.35
DENV 4	15	5.33 ± 2.09
Co-infection (1 + 3)	03	4.67 ± 1.53
Co-infection (2 + 3)	01	5.00

Table 5: Platelet transfusion requirement on the basis of serotype

Serotype	Platelet transfusion YES	Platelet transfusion NO
DENV 1 (n = 21) (%)	15 (71.4)	06 (28.6)
DENV 2 (n = 34) (%)	14 (41.2)	20 (58.8)
DENV 3 (n = 26) (%)	09 (34.6)	17 (65.4)
DENV 4 (n = 15) (%)	10 (66.7)	05 (33.3)
Co-infection (1 + 3) (n = 03) (%)	00 (0)	03 (100)
Co-infection (2 + 3) (n = 01) (%)	01 (100)	00 (0)

A total of 100 cases were included in this study. Adult age group was the most affected (82% of all cases) among all the age groups (Table 1). Males (54%) were more affected in comparison to females (46%) in our study (Table 2). The male–female ratio was 1.17:1. There was no statistically significant difference in the distribution of age groups and gender between the different serotypes of infection (Pearson's Chi-square 32.681 and 3.710, respectively). These results were in concordance with other studies.^{2–7} This age group comprises of working and student population. As dengue is mainly spread through *Aedes* mosquitoes which are day-biters, crowded areas such as workplaces and colleges may facilitate the spread of infection.

We found that 60% of the cases were infected with DENV-2 and DENV-3 (Table 3). Maximum cases (34%) of DENV-2, followed by 26% cases of DENV-3. This is in concordance with other studies from Delhi,⁶ Uttar Pradesh,⁵ and Mumbai.³ Racherla et al.⁸ in 2018 conducted a similar study and they also found that out of 60 cases, 25 cases were of DENV-2 (which were maximum in their study). Wardhani et al.⁹ in 2017 found different results, as they found maximum cases of DENV-1 and least cases of DENV-3.

In our study, four patients had concurrent infection with two types of dengue serotype. Three patients had co-infection with serotypes 1 and 3, and one patient had co-infection with serotypes 2 and 3. Previously, a study from Delhi⁶ reported the first concurrent infections by different dengue serotypes. Study at Ernakulum, Kerala,¹⁰ reported an approximate rate of 56.8% of concurrent infections with the association of DENV-1, 2, and 3.

The prevalence of each serotype has changed through the years. In 2009, DENV-3 was the dominant serotype, but in 2010 and 2011, DENV-2 became predominant, which was later replaced by DENV-1.⁵ In eastern parts of India, studies from Odisha and Kolkata reported DENV-2 and DENV-3 as the dominants circulating, with no sign of DENV-4.² A 9 year (2007–2015) study from Mumbai,³ Western India, reported all serotypes, with DENV-2 as the predominant serotype, whereas DENV-3 was more common during 2012–2015. Co-circulation of DENV-1, 2, and 3 was reported from Pune¹¹ during 2002–2008 with additional detection of DENV-4 serotype among others during 2009–2010. Although circulation of all four dengue virus serotypes is reported, the dominant subtypes and epidemiology of dengue viruses keep on fluctuating.

When we distributed the serotypes according to severity (Table 3), we found maximum cases of severe dengue in DENV-2 (20.6%) and DENV-4 (20%), but the difference in the distribution of severity between the serotypes of infection was statistically nonsignificant (p -value-0.49). According to Racherla et al.⁸ in 2018, although DENV-2 was the predominant serotype in their study, the severity of infection was high in infections with DENV-3 and DENV-4.

Mean hospital stay was longer in patients affected with DENV-4 and DENV-2, most probably because these were also the serotypes with the most cases of severe dengue (Table 4, statistically nonsignificant, p -value 0.888). The maximum duration of hospital stay (11 days) was in a patient infected with DENV-4.

Out of 100 patients, a total of 49 patients required platelet transfusion and a significantly higher percentage of patients with DENV-1 infection (71.4%) required platelet transfusion (Table 5, statistically significant, p -value 0.025). A similar study by Makroo et al.¹² in 2007, found out of 97 patients, 47 received platelet transfusion. The reason why more cases with DENV-1 infection required platelet transfusion in our study is not clear.

No mortality occurred in our study.

CONCLUSION

The maximum percentage of cases of dengue, in our study, occurred in the age group of 19–45 years, and in males, putting this population at the highest risk of morbidity and mortality associated with dengue. All four serotypes were present from January 2019 to June 2020 in this region of India, and DENV-2 and DENV-3 were the predominant serotypes. Co-infection is also not uncommon with dengue and we found four cases with concurrent infection with two dengue serotypes. The mean duration of hospital stay was the longest in DENV-4 and DENV-2 infections, which correlates with the highest percentage of severe dengue cases in these serotypes (statistically nonsignificant). It highlights the importance of monitoring patients with DENV-2 or DENV-4 infection for signs of severe dengue (severe plasma leakage, severe hemorrhage, or severe organ impairment) and for nonsevere dengue with warning signs which can progress to severe dengue. The maximum percentage of DENV-1 cases required platelet transfusion in our study.

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