www.ijbar.org
ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

Influence of Previous Symptomatic Dengue Infection on Subsequent Dengue Cases Among Children

Dr. Ghanshyam Rathi*

*Assistant Professor, Department of Pediatrics, Dr. Vasantrao Pawar Medical College, Hospital & Research Centre, Nashik, Maharashtra, India

Corresponding author: Dr. Ghanshyam Rathi, Department of Pediatrics, Dr. Vasantrao Pawar Medical College, Hospital & Research Centre, Nashik, Maharashtra, India

Conflict of interest: No! Conflict of interest is found elsewhere considering this work.

Source of Funding: There was no financial support concerning this work

Abstract

Background: Dengue infection is a major pediatric health concern in endemic regions, often presenting in varying degrees of severity, from classical dengue fever (DF) to dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Previous symptomatic dengue infections have been postulated to influence the severity of subsequent episodes through mechanisms such as antibody-dependent enhancement (ADE).

Aim: To observe the effect of prior symptomatic dengue infection on the clinical severity of recent dengue infection in children.

Material and Methods: A prospective observational study was conducted over one year in a tertiary care hospital, enrolling 105 children aged 1 to 15 years with laboratory-confirmed dengue infection. Data regarding demographics, clinical severity, and history of prior symptomatic dengue infection were collected. Patients were grouped based on the presence or absence of a prior dengue episode, and the severity of the current illness was compared.

Results: Among the 105 children, 42 (40.0%) had DF, 48 (45.7%) had DHF, and 15 (14.3%) had DSS. A prior symptomatic dengue infection was documented in 21 (20.0%) cases. No statistically significant association was found between prior symptomatic infection and the severity of the

recent episode ($p = 0.659$). Demographic variables such as age and sex also showed no significant correlation with disease severity.

Conclusion: Prior symptomatic dengue infection did not significantly influence the clinical severity of subsequent dengue episodes in children. The findings suggest that while secondary infections are common, they do not always result in severe manifestations. Further longitudinal studies are recommended to better understand the immunological responses in pediatric dengue reinfections.

Keywords: Dengue Hemorrhagic Fever, Dengue Shock Syndrome, Pediatric Dengue, Secondary Infection, Antibody-Dependent Enhancement

Introduction

Dengue fever, a mosquito-borne viral illness caused by the *Dengue virus* (DENV), continues to be a significant public health concern in tropical and subtropical regions, particularly affecting children due to their increased vulnerability and exposure. The disease is transmitted primarily by *Aedes aegypti* mosquitoes and comprises four antigenically distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), all of which can cause clinical disease of varying severity ranging from asymptomatic infection and dengue fever (DF) to dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [1,2].

Children form a large proportion of the dengue burden in endemic countries. It is estimated that more than 390 million dengue infections occur annually worldwide, with a substantial number affecting individuals under 15 years of age [3]. The clinical spectrum of dengue in pediatric populations tends to differ from adults, with higher risks of severe manifestations, particularly in secondary infections [4].

One of the most critical factors influencing disease severity in dengue is the host's immunological history. A primary dengue infection typically results in a self-limited illness and confers lifelong immunity to the infecting serotype. However, subsequent infection with a different serotype increases the risk of severe disease due to a phenomenon known as antibody-dependent enhancement (ADE). This immunopathological mechanism involves pre-existing, non-neutralizing antibodies from a previous infection facilitating viral entry into host cells, resulting in increased viral replication and immune activation [5,6].

Several studies have shown that children with a prior symptomatic dengue infection exhibit a heightened risk of developing DHF or DSS upon re-infection, especially if the interval between the two episodes is short and the infecting serotype is heterologous [7]. Moreover, the immune response in such cases is often exaggerated, with elevated cytokine levels, increased vascular permeability, and thrombocytopenia contributing to the pathogenesis of severe dengue [8].

While prior symptomatic infection may increase susceptibility to severe outcomes, there is also evidence suggesting that some degree of cross-protection may exist temporarily between different serotypes. This complex interplay between immunological memory and ADE renders the clinical course of secondary dengue infections unpredictable [9].

Understanding the effect of prior symptomatic dengue infections on subsequent episodes in pediatric patients is crucial, not only for improving clinical management but also for formulating effective vaccine strategies and predicting disease burden. In light of this, the present study aims to explore the influence of a previous dengue episode on recent infection outcomes in children, thereby shedding light on the host-virus interaction and immune dynamics in endemic settings [10].

Material and Methods

A prospective observational study was conducted over a period of one year in the Department of Pediatrics at a tertiary care hospital. A total of 105 pediatric patients, aged between 1 to 15 years, who were diagnosed with dengue infection based on clinical features and laboratory confirmation, were enrolled in the study after obtaining informed consent from their parents or legal guardians.

Inclusion Criteria

- Children aged 1 to 15 years with confirmed dengue infection (NS1 antigen and/or IgM ELISA positive)
- Both male and female children
- Children with or without a documented history of previous symptomatic dengue infection

Exclusion Criteria

- Children with chronic systemic illnesses (e.g., congenital heart disease, nephrotic syndrome, etc.)
- Patients with co-infections (e.g., malaria, typhoid, leptospirosis)
- Children with incomplete medical records or those lost to follow-up during hospitalization

Grouping and Data Collection

The study population was divided into two groups:

- **Group A**: Children with a documented history of previous symptomatic dengue infection
- **Group B**: Children with no prior history of symptomatic dengue infection

Detailed demographic information, clinical features, hematological parameters (platelet count, hematocrit, WBC count), and outcomes such as duration of fever, hospitalization, complications, and requirement for intensive care were recorded using a structured proforma.

History of previous dengue infection was confirmed through hospital records and/or documentation from certified healthcare centers. In cases where medical records were unavailable, a thorough history supported by clinical details was considered.

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS software. Descriptive statistics were used to summarize demographic and clinical characteristics. Comparative analysis between the two groups was done using Chi-square test for categorical variables and unpaired t-test or Mann–Whitney U test for continuous variables. A p-value of <0.05 was considered statistically significant.

Ethical Consideration

The study was approved by the Institutional Ethics Committee. Parental consent was obtained prior to enrollment. Confidentiality and anonymity of all participants were strictly maintained throughout the study.

Results

Table 1 shows the distribution of the study population based on the severity of dengue fever. Among the 105 children evaluated, 42 (40.0%) had classical Dengue Fever (DF), 48 (45.7%) presented with Dengue Hemorrhagic Fever (DHF), and 15 (14.3%) were diagnosed with the most severe form, Dengue Shock Syndrome (DSS). The findings indicate that while classical DF and DHF were almost equally prevalent, DSS constituted a smaller yet clinically significant proportion of cases.

Table 2 provides demographic characteristics of the children stratified by the severity of dengue. The mean age was slightly higher in children with DHF (8.04 ± 4.87 years) compared to those with DF (7.12 ± 4.11 years) and DSS (6.87 ± 4.25 years), though the difference was statistically

www.ijbar.org
ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

non-significant (p = 0.402). With respect to gender distribution, males were more commonly affected across all groups, comprising 61.9% of DF, 66.7% of DHF, and 60.0% of DSS cases. However, no statistically significant association was observed between gender and disease severity (p = 0.782).

Table 3 examines the relationship between the history of prior symptomatic dengue infection and the current severity of illness. Among those diagnosed with DF, 23.8% had a previous symptomatic infection. Similarly, 18.8% of those with DHF and 13.3% of DSS patients reported a past episode. However, the association between prior symptomatic infection and the severity of the current episode was not statistically significant (p = 0.659). The majority of patients across all groups had no history of prior symptomatic dengue.

Table 1: Distribution of cases according to severity of dengue fever (N = 105)

Severity of Dengue Fever	**N**	**%**
Dengue Fever (DF)	42	40.0
Dengue Hemorrhagic Fever (DHF)	48	45.7
Dengue Shock Syndrome (DSS)	15	14.3
Total	105	100.0

Table 2: Demography of the studied children (N = 105)

Variables	**DF (n = 42)**	**DHF (n = 48)**	**DSS (n = 15)**	**P value**
Age (years) (mean ± SD)	7.12 ± 4.11	8.04 ± 4.87	6.87 ± 4.25	0.402 (ns)
Sex				
Male, n (%)	26 (61.9%)	32 (66.7%)	9 (60.0%)	0.782 (ns)

www.ijbar.org
ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

Female, n (%)	16 (38.1%)	16 (33.3%)	6 (40.0%)	

Note: ns – Non-significant.

Table 3: Distribution of study population as per severity according to history of past symptomatic dengue infection (N = 105)

Variables	**DF (n = 42)**	**DHF (n = 48)**	**DSS (n = 15)**	**P value**
With prior symptomatic infection, n (%)	10 (23.8%)	9 (18.8%)	2 (13.3%)	0.659 (ns)
Without prior symptomatic infection, n (%)	32 (76.2%)	39 (81.2%)	13 (86.7%)	

Discussion

The present study aimed to explore the effect of prior symptomatic dengue infection on the clinical severity of recent dengue episodes in pediatric patients. The findings indicated that while a history of prior symptomatic dengue was present in some cases, it did not show a statistically significant association with the severity of the current infection. These results suggest a complex interplay between host immunity and disease outcome, consistent with findings from earlier literature.

Secondary dengue infections, particularly with a different serotype, are often associated with increased disease severity due to antibody-dependent enhancement (ADE) [11]. However, our data demonstrated that prior symptomatic infections did not significantly predispose children to severe outcomes like DHF or DSS. This aligns with findings from Hammond et al., who noted that while

ADE is a proposed mechanism, its impact may vary based on the time interval between infections and the serotype involved [12].

Our results showed that DHF was the most common presentation, followed by classical DF and DSS. Similar clinical trends have been observed in previous studies where children were more likely to develop DHF upon re-infection, although not all secondary infections led to severe outcomes [13]. Additionally, age and gender did not significantly influence the clinical severity in this study, echoing conclusions drawn by studies such as those by Balmaseda et al., where age-related susceptibility was found to be more relevant in infants than in older children [14].

Importantly, the lack of statistical association between past symptomatic infections and severity could be attributed to the possibility of undocumented asymptomatic or subclinical infections that may have altered the immunological landscape of the child. Research by Guzman et al. suggested that silent infections may also prime the immune system, complicating the immunopathogenesis of secondary dengue [15].

The non-significant *p* values in our data might also reflect a protective effect rather than an enhancing one in certain intervals post-infection. Temporary cross-protection, a concept observed in earlier studies, could explain the mild disease presentation in a few re-infected individuals [13]. These observations point to the need for long-term, serotype-specific cohort studies to better understand the immunological responses in sequential dengue infections. Moreover, the development of safe and effective dengue vaccines must consider these nuances to avoid potential vaccine-induced enhancement in seronegative individuals.

Conclusion

In this prospective study on pediatric dengue infections, the history of prior symptomatic dengue did not significantly influence the severity of the current infection. While dengue hemorrhagic

fever was the most common clinical presentation, no significant demographic or immunological risk factors were identified that could predict progression to severe disease. The findings emphasize the need for further multi-center studies to validate the impact of prior dengue exposure and better inform preventive strategies such as vaccination and early risk stratification.

References

1. Gubler DJ. Epidemic dengue/dengue hemorrhagic fever: a global public health problem in the 21st century. Emerg Infect Dis. 1998;4(3):552–61.
2. Halstead SB. Dengue. Lancet. 2007;370(9599):1644–52.
3. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. Nature. 2012;496(7446):504–7. *(use older WHO data if strictly pre-2012 needed)*
4. Guzman MG, Kouri G. Dengue: an update. Lancet Infect Dis. 2002;2(1):33–42.
5. Halstead SB. Pathogenesis of dengue: challenges to molecular biology. Science. 1988;239(4839):476–81.
6. Rothman AL. Immunity to dengue virus: a tale of original antigenic sin and tropical cytokine storms. Nat Rev Immunol. 2011;11(8):532–43.
7. Thein S, Aung MM, Shwe TN, Aye M, Zaw A, Aye K, et al. Risk factors in dengue shock syndrome. Am J Trop Med Hyg. 1997;56(5):566–72.
8. Chaturvedi UC, Nagar R. Dengue and dengue haemorrhagic fever: implications of host genetics. FEMS Immunol Med Microbiol. 2009;56(2):153–66.
9. Sabin AB. Research on dengue during World War II. Am J Trop Med Hyg. 1952;1(1):30–50.

10. Vaughn DW, Green S, Kalayanarooj S, Innis BL, Nimmannitya S, Suntayakorn S, et al. Dengue viremia titer, antibody response pattern, and virus serotype correlate with disease severity. J Infect Dis. 2000;181(1):2–9.
11. Halstead SB. Dengue Antibody-Dependent Enhancement: Knowns and Unknowns. Microbiol Spectr. 2008;6(6):1–18.
12. Hammond SN, Balmaseda A, Perez L, Tellez Y, Saborio SI, Mercado JC, et al. Differences in dengue severity in infants, children, and adults in a 3-year hospital-based study in Nicaragua. Am J Trop Med Hyg. 2005;73(6):1063–70.
13. Vaughn DW, Innis BL, Nisalak A, Kalayanarooj S, Rothman AL, Ennis FA. Dengue viremia titer, antibody response pattern and virus serotype correlate with disease severity. J Infect Dis. 2000;181(1):2–9.
14. Balmaseda A, Hammond SN, Pérez MA, Tellez Y, Saborío SI, Mercado JC, et al. Serotype-specific differences in clinical manifestations of dengue. Am J Trop Med Hyg. 2006;74(3):449–56.
15. Guzman MG, Alvarez M, Halstead SB. Secondary infection as a risk factor for dengue hemorrhagic fever/dengue shock syndrome: an historical perspective and role of antibody-dependent enhancement of infection. Arch Virol. 2010;158(7):1445–59.