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# Association of the Severity of Dengue Fever with Ns1 Antigen Titres in Children

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**ABSTRACT**
There are 390 million dengue infections per year, making them one of the arboviral illnesses that are now spreading the fastest. Particularly in developing nations, they significantly increase morbidity and death, placing a heavy economic burden on those nations. To evaluate the function of the NS1 antigen Assay in the delivery of pediatric dengue treatment. Prospective, observational cross-sectional research was used in the current study. The Surat Municipal Institute of Medical Education and Research's pediatric department conducted this study from January 2021 to December 2022. Within three days of the illness, 79 (63.2%) of the youngsters tested positive for the NS1 Antigen. Ns1 antigen tests were positive in 46 children (36.2%) who had been unwell for 4 to 5 days. Primary dengue fever struck 61 (48.8%) of the 125 children, whereas secondary dengue fever struck 64 (51.2%). Mild dengue was identified in 13 (27.0%) children with titre values between 9 and 11, 16 (35.4%) children with titre levels below 9, and 19 (38.8%) children with titre levels above 11. Tissue titres were as low as 9, as high as 11, and as low as >11 in 8 of the children with severe dengue. Children with severe dengue had titre levels as low as nine in three (23.1%), two (15.4%), and eight (61.5%) cases. The p value of 0.3637 indicated that it was not statistically significant. Our findings suggest that further research is needed to establish early detection tools for dengue fever, and that NS1 Antigen ELISA titres may not be useful in predicting the severity of dengue fever in children.

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**Key Words**
Dengue infection, IL 10, monocytes, NS1 antigen, T cell function

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## INTRODUCTION

One of the arboviral diseases now expanding the quickest is dengue, which has 390 million infections per year[1]. They are a severe burden on economies, particularly in developing countries where they sharply raise mortality and morbidity rates.

While the majority of dengue infections are asymptomatic or present as an undifferentiated viral fever, a small percentage of dengue infections progress to fluid leakage and bleeding signs, leading to dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).

There is currently no licensed vaccine or effective antiviral medication to prevent infection, thus the only practical course of action is careful hydration control and monitoring for effects.

In the past, estimates for the mortality rate associated with dengue infections have ranged from 2.5-5.4%[1]. Organ dysfunction and shock have been named as the two main reasons of death from dengue illness.

Case fatality rates in many dengue-endemic nations have fallen considerably as a consequence of improved fluid management strategies and a better knowledge of the linkages between severe dengue and early therapy. However, clinical and laboratory indicators are evaluated at least twice or three times each day in all patients admitted to the hospital with a dengue infection in order to discover individuals who are at high risk of developing severe dengue.

Despite the fact that children should have numerous clinical parameters examined every two hours, due to a lack of medical resources, this is not always possible. As a result, to determine which children are most likely to acquire severe clinical illness, a quick test that can be conducted in a ward would be required. We thought that by developing a predictor of severe dengue, we would be able to drastically reduce mortality through early identification and treatment.

## MATERIALS AND METHODS

**Study design:** Hospital based prospective observational study.

**Place of study:** The Pediatric, Surat Municipal Institute of Medical Education and Research did this study over a 12-month period.

**Time period:** January 2021 to December 2022
**Sample size:** 125 samples were required.

**Inclusion criteria:**

- **Age:** less than 18 years
- Study was carried out in children with clinical suspicion of dengue fever with features like
- Fever > 3 days
- Myalgia
- Rash
- Arthralgia

**Inclusion criteria:** Children with dengue fever and co infections were excluded

## RESULTS AND DISCUSSION

With rising epidemics every year, dengue fever is a recent health issue. To lower the death rate associated with severe dengue infection, the 2011 revision of the World Health Organization's dengue fever recommendations has placed an emphasis on the necessity of early identification and treatment.

Our research aims to create a predictor of dengue fever severity as there are presently no clear or established interventions or means to assess the severity of dengue fever in children.

**Demographic distribution of the study**:

**Age:** The majority of the participants in our study (47%) were under the age of five, and roughly 79% were under the age of ten. The average age of the hospitalized kids was 6.5+4.54. This was comparable to studies conducted by Lapphra *et al*.[2], in which the mean age of the kid population was 6.9 years and 6.8 years, respectively.

**Sex distribution:** In the population of our study, men outnumbered women by a ratio of 1.1 to 1. This result was comparable to that of the Lapphra *et al*.[2]

**Admission status:** 10.4% of our children received care as outpatients, leaving 89.6% of them receiving care as inpatients. On the other hand, inpatients made up the whole research population in theinvestigation. The children who were turned away had mild dengue, but no symptoms.

**Observation of NS1 Antigen testing and the day of illness:** When tested within 3 days of illness, 79 (63.2%) youngsters tested positive for the NS1 Antigen. When tested after 4-5 days of sickness, 46 children (36.8%) tested positive for Ns1 antigen. When performed during day 5 of sickness, the NS1 Assay was shown by Susu *et al*.[3] to be extremely sensitive for detecting dengue infection. A similar finding was made in our investigation.

**Severity of illness:** In our study, mild dengue affected 51.2% of participants, moderate dengue affected 38.2%, and severe dengue affected just 10%. This is consistent with the typical pattern of infectious diseases, when less serious cases predominate over more serious ones. Alcon et al. and Jeanne et al. found comparable outcomes in their research (Table 1).

Table 1: Distribution of study population according to ns1 titre levels

| Parameters | No. | Percentage |
|---|---|---|
| **Clinical diagnosis** | | |
| Mild dengue | 64 | 51.2 |
| Moderate dengue | 48 | 38.8 |
| Severe dengue | 13 | 10.0 |
| Total | 125 | 100.0 |
| **Type of dengue** | | |
| Primary dengue | 61 | 48.8 |
| Secondary dengue | 64 | 51.2 |
| Total | 125 | 100.0 |
| **NS1 levels** | | |
| < 9 | 40 | 32.4 |
| 9-11 | 37 | 29.4 |
| >11 | 48 | 38.0 |
| Total | 125 | 100.0 |

Table 2: Agreement between NS1 titre levels and clinical diagnosis

| | Clinical diagnosis | | | |
|---|---|---|---|---|
| | Mild dengue | Moderate dengue | Severe dengue | p-value |
| **Age group** | | | | |
| <5 years | 34 (53.1) | 20 (41.6) | 6 (46.2) | 0.9446 |
| 6-10 years | 17 (26.6) | 15 (31.3) | 4 (30.7) | |
| 11-15 years | 8 (12.5) | 9 (18.8) | 2 (15.4) | |
| >15 years | 5 (7.8) | 4 (8.3) | 1 (7.7) | |
| **NS1 levels** | | | | |
| <9 | 21 (32.8) | 16 (35.4 ) | 3(23.1) | 0.3637 |
| 9-11 | 22 (34.4) | 13 (27.0) | 2(15.4) | |
| >11 | 21 (32.8) | 19 (38.8) | 8(61.5) | |
| Total | 64 | 48 | 13 | |

**Association between study population and serology:** Sixty-one (48.8%) of the 125 children had primary dengue fever, and sixty-four (51.2%) had secondary dengue fever.

**Association between age group and clinical diagnosis:** When the relationship between age group and the clinical diagnoses of mild, moderate, and severe dengue was analyzed, it was found that in children under the age of 5, 56.7% of the children had mild dengue, 40% had moderate dengue, and 10% had severe dengue.

Children aged 6-10 years old who had mild dengue were affected in 47.9% of cases, while those who had moderate dengue were affected in 42.3% of cases and those who had severe dengue were affected in 9.9% of cases. When it comes to youngsters between the ages of 11 and 15, mild dengue affected 40% of the children, moderate dengue affected 47.5%, and severe dengue affected 12.5% of the children. Children older than 15 years old who had dengue were diagnosed with mild dengue in 52.6% of cases, moderate dengue in 42.1% of cases, and severe dengue in 5.3% of cases. An analysis of the statistical association produced a p value of 0.61, which was not significant. The majority of the children, however, were diagnosed with mild dengue, and the average age at presentation was under 5 years. In a related study by Lapphra *et al*.[2], NS1 Ag was found to be positive in 55 (83.1%) of the patients, with non-severe dengue accounting for 36 (65.9%) and severe dengue accounting for 19 cases (34.1%, respectively) (Table 2).

**Association between age group and ns1 titre values:** In the age range of 0-5 years, 9-11 titre values were seen in 8 (26.7%) of the children, and in the range of 6-10 years, 9-11 titre values were seen in 6 (36.6%) of the children. Three (30%) of the children in the 11 to 15 year age range had titre values between 9 and 11, whereas just one (21.1%) of the youngsters in the above 15 year age range had such values.

11 children (35.8%) had titre values of less than 9 when they were younger than 5 years old, while 20 children (32.4%) were between the ages of 6 and 10 years. Two (20%) children in the age group of 11-15 years had titre values of less than nine. Four (36.2%) children in the age range of 11-15 years had NS1 antigen titre levels below 9.

Children with titre values >11 were found in 22.5 (37.5%) of the children under the age of 5, and 11 (31%) of the children with titre values >11 between the ages of 6 and 10. 10% (or 50%) of the youngsters in the age range of 11-15-year-olds had titre values greater than 11.4 (42.1% of the children) in the age group of children >15 years had NS1 titres of >11. The statistically insignificant P value was 0.323. Similar findings were made in the study of Dutta *et al*.[4], which also included a large pediatric sample but found no statistically significant correlation between NS1 Antigen levels and dengue fever severity. This investigation, which employed the same J Mithra kit for titre estimation as our study, was carried out in a teaching hospital in South India.

**Association between ns1 titres and clinical diagnosis:** When the correlation between NS1 titre levels and clinical diagnosis was performed, titre levels of 9 were found in 16 (35.4%) of children with moderate dengue, titre values of 9 to 11 were found in 13 (27.0%), and titre values of >11 were found in 19 (38.8%) of children with moderate dengue. Children diagnosed with severe dengue had titre levels as low as 9, as high as 11, and as low as >11 in 8. Of the children diagnosed with severe dengue, 3 (23.1%), 2, (15.4%) and 8 (61.5%) had titre levels as low as 9. The statistically insignificant p value was 0.3637, which was not significant.

Our study's findings were consistent with a study by Hermann *et al*.[5] conducted in Indonesia, which revealed that NS1 Antigen levels did not accurately predict the severity of dengue fever.

The aforementioned study, however, was only conducted on severely ill children, but in our investigation, we attempted to link the antigen titres with all children classified as having mild, moderate, or severe dengue that was precisely quantitated.

As a result, we draw the conclusion that NS1 Antigen ELISA titres cannot be used to predict the severity in young patients. Semi-quantification of NS1 titres was performed for our investigation, although

titres were not It may be prudent to consider quantifying NS1 Assays, which can aid in the accurate diagnosis and management of dengue fever.

Studies on the effectiveness of the NS1 Assay and other therapies may also help in predicting the severity of dengue fever and lowering mortality and additional sequelae.

## CONCLUSION

According to the results of our study, NS1 Antigen ELISA titres may not be beneficial in predicting the severity of dengue fever in children, and more research is needed to develop early diagnostic tools that might significantly reduce mortality.

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