

ABSTRACT

CORRELATION OF NS1 ANTIGEN TITRES WITH THE SEVERITY OF DENGUE FEVER IN CHILDREN

INTRODUCTION

Dengue infections are currently one of the most rapidly emerging arboviral infections in the world, which result in 390 million infections every year. They cause significant morbidity and mortality especially in developing countries and is a huge burden on their economies. Although the majority of dengue infections result in asymptomatic infection or manifest as undifferentiated viral fever, some develop fluid leakage and bleeding manifestations which result in dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS.)

As there is no effective antiviral treatment or a licensed vaccine to prevent infection, meticulous fluid management and monitoring for complications is currently the only option available. Earlier case fatalities due to dengue infection have been reported to be around 2.5% to 5.4%. Shock and organ impairment have been shown to be the most important factors that lead to fatalities in dengue infection. As a result of better fluid management regimens and greater awareness of associations of severe dengue and early interventions, the case fatality rates have significantly dropped in many dengue endemic countries. However, in order for early detection of those who are likely to develop severe dengue, the clinical and laboratory parameters are measured at least two or three times a day in all patients admitted to the hospital with dengue infection.

Although ideal management of children includes monitoring of many clinical parameters at least every 2 hours, this is sometimes impossible due to limited health resources. Therefore, a simple test that can be done in a ward would be of utmost importance to determine the children who are most likely to develop severe clinical disease. Early diagnosis and prompt treatment can help in reducing significant mortality and our study has attempted to identify a predictor of severe dengue.

AIM

To assess the role of NS1 antigen Assay in the management of dengue fever in children

OBJECTIVE

To assess the utility of NS1 antigen assay in predicting severity of dengue fever in children by estimating titres.

MATERIALS AND METHODOLOGY

STUDY DESIGN

Hospital based prospective observational study

Place of study - PSG Hospitals, PSGI MS&R, Coimbatore

Time period - January 2016 to May 2017

SAMPLE SIZE: 250 samples were required based on the formula $4p9/d2$ considering the prevalence of dengue fever.

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

Exclusion Criteria

Children with dengue fever and co infections were excluded .

METHODOLOGY

Ethical committee approval was obtained and Prospective collection of data was done in children who fulfilled the inclusion criteria in the Pediatrics department at tertiary care centre, PSGIMSR, Coimbatore where systematic computer coding for registry is used. NS1 Antigen ELISA was done in all children between day 1 to 5 illness who fulfilled the inclusion criteria and 2ml of blood was drawn and collected in EDTA container. NS1 Antigen ELISA was tested using (J-Mithra kit)India at the Serology lab in our hospital. Qualitative and semi Quantitative analysis was done. Titre of >11 was considered strongly positive, 9-11 as equivocal and titre value of 9 was mild positive. Dengue Serology for IgG antibodies for secondary infection and IgM antibodies for primary infection were performed on the same children using ELISA Assay. All other relevant and additional investigations were done as per the course of illness. Data was entered in structured proforma and case definition, diagnosis and management used for dengue fever were categorized into Mild, Moderate and Severe dengue as per revised NVBDCP guidelines. All other relevant clinical data were collected.

DENGUE CASE CLASSIFICATION:

Mild dengue – Fever and any two of the following-	Moderate dengue	Severe Dengue
<ul style="list-style-type: none"> -Nausea, vomiting -Rash -Aches and pains -Leukopenia -Positive tourniquet Test 	<ul style="list-style-type: none"> -Abdominalpain/Tenderness -Persistant vomiting -Ascites/ pleural effusion -Mucosal bleeding -Lethargy, restlessness -Liver Enlargement >2 cm Laboratory : Increase in HCT concurrent with rapid decrease in Platelet count 	<ul style="list-style-type: none"> Severe plasma leakage leading to- -Shock -Fluid accumulation with respiratory distress -Severe Bleeding Severe organ Involvement -Liver AST or ALT \geq 1000 CNS:Impaired Consciousness

RESULTS:

Demographic distribution of the study

Age

Majority of our study population (48%) were less than 5 years of age and nearly 75% of our study population was less than 10 years. The mean age of children admitted was 6.8 + 4.93years.

Sex distribution

Our study population had slightly male predominance, the male:female ratio were 1.1: 1.

Admission status

Most of our children were treated as inpatients (89.6%) and the remaining 10.4% were treated as out patients. The children who were not admitted were mild dengue children without any warning signs.

Observation of NS1 Antigen testing and the day of illness

NS1 Antigen was found to be positive in 158(63.2%) children when done in less than 3 days of illness. NS1 antigen was positive in 92 children (36.8%) when done on 4 to 5 days of illness.

Severity of illness

In our study there were 51.2% of mild dengue, 38.2% of moderate dengue and only 10% were severe dengue. This can be attributed to the normal pattern of infectious diseases, where milder illnesses are more common than severe forms of the disease.

Association between study population and serology

Out of 250 children included 122(48.8%) had primary dengue and 128(51.2%) had secondary dengue fever.

Association between age group and clinical diagnosis

When the association between age group and clinical diagnosis of mild, moderate and severe dengue was analysed it was observed that in children less than 5 years of age, Mild dengue was seen in 56.7% of the children, Moderate dengue was seen in 40% of the children and 10% of the children had severe dengue. In the age group of children from 6 to 10 years mild dengue was seen in 47.9% of the children, moderate dengue was seen in 42.3% of the children and severe dengue was seen in 9.9% of the children. In children between age group of 11 to 15 years mild dengue was seen in 40% of the children, moderate dengue was seen in 47.5% of the children and severe dengue was seen in 12.5% of the children. In children more than 15 years, mild dengue was seen in 52.6% of the children, 42.1% of the children had moderate dengue and severe dengue was seen in 5.3% of the children. Statistical correlation was done which showed a p value of 0.61 which was not significant. However majority of the children were categorized as mild dengue and the common age of presentation was less than 5 years.

Association between age group and ns1 titre values

In the age group of less than 5 years titre values of 9 to 11 was seen in 32(26.7%) of the children, in the age group of 6 to 10 years titre values of 9 to 11 was seen in 26(36.6%) of the children. In the age group of 11 to 15 years titre values of 9 to 11 was seen in 12(30%) of the children, in age group of > 15 years titre values of 9 to 11 was seen in 4 (21.1%) children. In age group of less than 5 years titres titre values of less than 9 was seen in 43 children(35.8%) and in age group of 6 to 10 years titre values of less than 9 was seen in 23 children(32.4%). In children with age group of 11 to 15 years titre values of <9 was seen in 8 (20%) children. Children with age group of 11 to 15 years NS1 antigen titre values of <9 was seen in 7(36.8%) children.

In the age group of children <5 years titre values of > 11 was seen in 45(37.5%) children, in children with age group of 6 to 10 years titre values > 11 was seen in 22(31%) of the children. In age group of children between 11 to 15 years titre values of > 11 was seen in 20(50%) of the children . In age group of children > 15 years NS1 titres of > 11 was seen in 8(42.1%) of the children. P value was 0.323 which was not statistically significant.

Association between ns1 titres and clinical diagnosis

When the association between NS1 titre levels and clinical diagnosis was correlated, Titre levels of <9 was seen in 33(40.7%) of children with moderate dengue, titre values of 9 to 11 was seen in 27(36.5%) of the children diagnosed with moderate dengue, titre values of > 11 was seen in 37(38.9%) of children diagnosed with moderate dengue Titre levels of < 9 was seen in 6 children(7.4%) of children diagnosed with severe dengue, titre values of 9 to 11 was seen in 4 (5.4%) children diagnosed with severe dengue, titre values of > 11 was seen in children 15 (15.8%) of children diagnosed with severe dengue. The p value was 0.525 which was not statistically significant.

CONCLUSION:

In our study we conclude that NS1 Antigen ELISA titres may not be useful in predicting the severity of dengue fever in children and further research is warranted for early identification of severity of dengue which can help in significant reduction in mortality.

LIMITATIONS

However our study had few limitations that NS1 antigen Assay was not quantitated and NS1 Assay was not performed uniformly on one particular day of illness which would have warranted more clinical significance.

KEYWORDS: Antigen Titres, Dengue, Myalgia, Arthralgia