

# NS1 Antigen Titre as a Predictor of Severity of Dengue Illness in Children of 1-18 Years Age

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## Abstract

**Objective:** To study NS1antigen titre as a predictor of severity of dengue illness in children of 1-18 years age.

**Keywords:** NS1antigen; dengue illness; plasma leakage

## Methods

Patients between the ages of 1 to 18 years with clinical features of probable dengue fever as per revised WHO criteria formed the study subjects ,NS 1 antigen titre levels were estimated at admission with in 6 days of onset of illness by NS1 dengue early ELISA and correlated with the clinical severity and final outcome. Severity was categorised as per WHO criteria for severe dengue. Probable dengue and dengue with warning signs were categorised into non severe dengue, Severe dengue is defined by one or more of the following: (i) severe plasma leakage that may lead to shock (dengue shock) and/or fluid accumulation, with respiratory distress, and/or (ii) severe bleeding, and/or (iii) severe organ impairment [1-3].

The study was carried out in the year 2013, at the Colombo South Teaching Hospital, which is a tertiary care hospital in Colombo with a bed strength of over 1000. 186 adult patients, who were admitted with a suspected acute dengue infection, were recruited following informed written consent. The study was approved by the Ethics Review Committee of the Faculty of Medical Sciences University of Sri Jayawardenapura. All patients who were aged over 18 years, with features of a possible dengue infection were included following written consent. Those who had a febrile illness due to other infections such as pneumonia, urinary tract infection were excluded. All clinical features such as fever, blood pressure, presence of any bleeding manifestations and presence of any possible fluid accumulation in the pleural cavity and abdomen were monitored several times a day from the time of admission to hospital, until they were discharged. Bleeding manifestations were defined as the presence of petechiae, ecchymoses, epistaxis, haematemesis, melaena or the presence of per vaginal bleeding in the absence of the monthly period in women. Serial recordings of laboratory

investigations such as full blood counts were made for entire duration of the illness. Serum alanine transaminase (ALT) and aspartate transaminase (AST) levels were performed on admission in all patients. Based on the 2011 WHO diagnostic criteria, shock was defined as lowering of pulse pressure to 20 mmHg or less or the presence of signs of poor capillary perfusion (cold extremities, poor capillary refill or a rapid pulse rate) [4-5]. None of the patients had shock before admission or during admission.

In order to determine the usefulness of the NS1 antigen positivity as a marker of severe disease we classified severe disease if the patients had any one of the following clinical or laboratory features. These were evidence of fluid leakage (clinical and/or radiological or a rise in haematocrit of >20% of the baseline) or a narrow pulse pressure (>20 mmHg) or platelet count of <25000 cells/mm<sup>3</sup> or liver enzyme levels of >500 IU or the presence of bleeding manifestations or any evidence of myocarditis or encephalopathy. Those who did not have even one of the above criteria were categorized to the non-severe dengue group [6-8].

## Results

The median NS1 antigen titre level of non severe dengue group was 25 pan bio units ,where as the severe dengue group had higher median NS1 antigen titre level of 65.80 panbio units, The NS1 antigen titre cut off value above 64.25 panbio units within 6 days of illness was associated with 58.7% sensitivity and 87.92% specificity for developing severe dengue.

The subjects with higher median NS1 antigen titre levels developed complications like hypotension(median NS1 Ag titre : 52.6 ),shock (66.6),respiratory distress (64.16) and bleeding manifestations (62.5) and association was found to be statistically significant (p value<0.001).It was also found that higher NS1 antigen titre levels (with Spearman's rho of .152 and p value of .02) were associated with longer duration of hospital stay and subjects with median NS1 antigen titre level above 58 panbio units required ICU stay.(p value<0.001).Higher NS1 antigen titre is correlating with the lower platelet count with a significant correlation coefficient(spearman's rho of -.274 and p value< 0.001.

## Discussion

In this study we have evaluated the use of the NS1 antigen test as a marker of severe dengue infection. We found that NS1 antigen positivity especially beyond day 5 of illness, was associated with a higher risk of developing severe dengue (odds ratio 3.0). In this study in order to evaluate the usefulness of the NS1 antigen positivity as a marker of severe clinical disease, we have used different criteria for the definition of severe clinical disease. This is due to the fact that many patients with an acute dengue infection who has evidence of fluid leakage, bleeding manifestations, platelet counts of <25,000 cells/mm<sup>3</sup> or liver transaminase levels of >12 times the upper limit of normal are very much at a higher risk of developing shock or organ impairment. In our study the NS1 antigen was positive in 64% of those who went on to develop shock on date of admission when compared to those who did not develop shock (47.2%).

## Conclusion

NS1 antigen titre level >64.25 panbio units with in 6 days of onset of illness is an early predictor of severity of dengue illness. Patients with higher NS1 antigen titres require longer duration of hospital stay and ICU admission and have comparatively low platelet count.

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