Clinical and Laboratory Parameters Predicting Severity of Dengue Infection

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A B S T R A C T

Dengue infections are currently one of the most rapidly emerging arboviral infections in the world. There is high mortality associated with severe dengue infection so we conducted study to predict various factors indicating severity of dengue infection. This cross- sectional study conducted in tertiary care hospital of central India. Data associated with various clinical features of dengue infection collected in predesigned questionnaire. Patient tested for complete blood count, serum alanine transaminase (ALT), aspartate transaminase (AST) levels, early dengue NS1 capture ELISA (Panbio, Brisbane, Australia) and commercial capture-IgM and IgG ELISA (Panbio, Brisbane, Australia). Total 678 suspected patients for dengue infection included in the study, 128(18.9%) patients were diagnosed as dengue positive, 58(45.3%) patients showed severe dengue infection, 66(51.6%) patients had thrombocytopenia, 38(29.7%) had raised liver enzymes,62 (48.4%) patients had decreased total leukocyte counts. Our study demonstrated various clinical and laboratory parameters to predict severity of the dengue infection which can be used to categorize the patients in resource poor country like India for the management of dengue infection.

Introduction

Dengue infections are currently one of the most rapidly emerging arboviral infections in the world,[1] which result in 390 million infections every year.[2] It causes significant morbidity and mortality in developing nations.[3] There are different spectrum of dengue infections like asymptomatic, simple undifferentiated viral fever to clinical complications like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[4] As there is no effective antiviral treatment or a licensed vaccine to prevent infection, early case detection of complicated dengue infection and its 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%.[5, 6] Shock

and organ impairment have been shown to be the most important factors that lead to fatalities in dengue infection.[7,8] Early interventions in sever dengue infection significantly decreases the case fatality rate. [9] There are different clinical and laboratory parameters which can help in early detection of sever dengue. So the current study is planned to predict various factors indicating severity of dengue infection.

Materials and Methods

The cross-sectional study was carried out from the month of 1st June 18 to 30th November 2018 at department of Microbiology the Shri Vasantrao Naik Govt Medical College Yavatmal, which is a teaching tertiary care hospital in Yavatmal, Maharashtra India, with the bed strength of over 780. All patients, who were admitted with suspected acute dengue infection, were recruited after obtaining informed written consent. The study was approved by the Institutional Ethics Committee. Patients who had a febrile illness due to other infections were excluded. All clinical features such as fever, low blood pressure, presence of any bleeding manifestations and presence of any possible fluid accumulation in the pleural cavity and abdomen were mentioned in predesigned questionnaire for each patients. Presence of petechiae, ecchymoses, epistaxis, haematemesis, melaena noted (bleeding manifestations). Recordings of laboratory investigations such as complete blood counts, Serum alanine transaminase (ALT) and aspartate transaminase (AST) levels done.[10] 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).[3] Suspected dengue infection was confirmed by testing the serum samples which were collected on the day of admission

with the early dengue NS1 capture ELISA (Panbio, Brisbane, Australia) and commercial capture-IgM and IgG ELISA (Panbio, Brisbane, Australia). Positive and negative controls were included as a part of the assessment. In order to determine the usefulness of the NS1 antigen positivity as a marker of severe disease, we classified into severe dengue infection and non-severe dengue infection, if the patients had bleeding manifestations or other clinical complications and any one of the following laboratory features such as platelet count of $<1,50,000$ cells/mm^3 or liver enzyme levels of >40 IU considered as severe dengue infection. Those who did not have even one of the above criteria were categorized to the non-severe dengue infection. Data was entered and tabulated in Microsoft excel sheet and analyzed by statistical software EpiInfo^{TM} Version 7 (Atlanta, Georgia, USA) for frequencies, percentages and scatter diagram.

Results and Discussion

Thus total 678 suspected dengue patients referred for laboratory diagnosis. Of 678, total 128(18.9%) patients were diagnosed as dengue positive by dengue NS1 pan bio ELISA, dengue IgM pan bio ELISA, dengue IgG pan bio ELISA. Of 128 positive patients, 72 (56.2%) were males and 56 (43.8%) were females. About the age distribution of 128 positive patients, 45(35.2%) patients were in the age group of 1 to 12 years, 71 (55.5%) patients were in the age group of 13 to 48 years and 12 (9%) patients were in the age group of 49 to 72 years. Regarding the history of fever among dengue positive patients, 80 (62.5%) patients had the history of 1 to 5 days of fever, 48 (37.6%) patients had the history of 6 to 8 days of fever. In view of severity of dengue infection, 58 (45.3%) patients showed dengue infection. Of 58 (45.3%), severe dengue infection, hypotension 27(21.1%), petechiae rash 12(7.6%), meningitis

4(3.12%), ascitis 2(1.6%), maleana 1(0.8%) encephalitis 2(1.6%), pulmonary haemorrhage 1(0.8%) were the clinical complication observed in the patients (Table 1).

Of 128 positive dengue infection, 29 (22.7%) patients only NS1 pan bio ELISA positive, 74 (57.8%) only IgM positive, 15 (11.7%) patients both NS1 and IgM Elisa positive, 8(6.25%) patients both IgM positive and IgG positive, 2 (1.6%) patients all NS1, IgM and IgG positive.

With respective to platelet count, total WBC count, ALT and AST in 128 positive dengue infection, 66 (51.6%) patients had platelets count <1,50,000 and 62 (48.4%) patients had platelets count >1,50,000. The 61(47.7%) patients had total WBC count less than 5,000, 52(40.6%) patients were in the range of 5,000 to 10,000 and 15(11.7%) patients had > 10,000. The 38 (29.7%) patients had ALT in the range of 1- 40 IU/ml and 90 (70.3%) patients were >41 IU/ml. The 34 (26.6%) patients had AST in the range of 1-40 IU/ml and 94 (73.4%) patients were >41 IU/ml. The

39(30.5%) patients had severe dengue infection and thrombocytopenia, 16(12.5%) patients had severe dengue infection and normal platelet count, 13(10.6%) patients had non-severe dengue infection with thrombocytopenia and 60 (46.9%) patients had non-severe dengue infection with normal platelets (Table 2).

Of 46 NS1 ELISA positive patients, 44 (91.3%) had panbiounites >20, and 4 (8.7%) patients had panbiounits in range of 11-20 panbiounits.

We applied the chi-square test to test association between NS1 positivity in patients and severe dengue infection, NS1 positivity in patients and raised liver enzymes. We observed significant association between NS1 positivity in patients and severe dengue infection (P< 0.001) and also with raised liver enzymes (P< 0.001)

We found inverse correlation between NS1 Panbio Unit and level of platelet count (Figure 1) and also with total WBC count.

Table.1 Showing dengue complications

Dengue complication	No. patients
Petechiae rash	12(7.6%)
Hypotension	27(21.1%)
Pleural effusion	9 (7.03%)
Meningitis	4 (3.12%)
Ascitis	2 (1.6%)
Maleana	1 (0.8%)
Encephalitis	2(1.6%)
Pulmonary haemorrhage	1(0.8%)
Total	58(45.31%)

Table.2 Association between complicated dengue infection and thrombocytopenia

Patients with severe dengue infection and thrombocytopenia	39(30.5%)
Patients with severe dengue infection and normal platelets	16(12.5%)
Clinically non-severe dengue patients with thrombocytopenia	13(10.6%)
Clinically non-severe dengue patients with normal platelets	60 (46.9%)

Fig.1 Association between NS1 positivity and thrombocytopenia
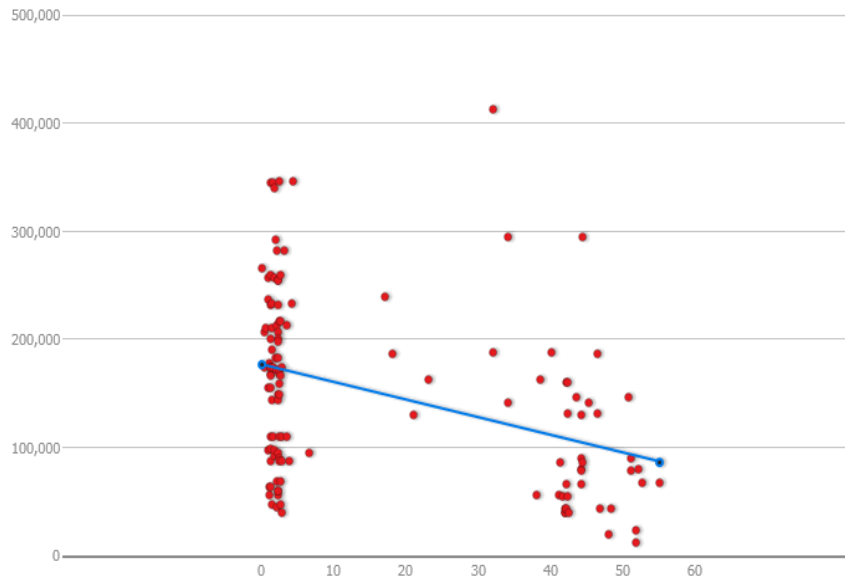
Dengue is an important infection affecting many lives in India. In our region, maximum numbers of patients we get followed by the rainy season as there is increase in the growth of mosquitoes. In these periods, extrinsic incubation period of dengue is short [11].

In our study, all age groups and both sexes were equally affected by dengue infection. Fever is the predominate symptom of dengue infection. Maximum number of patients had history of fever from 1-5days. Paranavitane A [10] *et al.,* study also demonstrated the similar findings in their study.

In our study, hypotension and petechial rashes were predominant clinical complications and other clinical complications were pleural effusion, meningitis, ascitis, maleana, encephalitis, pulmonary haemorrhage. Paranavitane *et al.,* [10] demonstrated similar complications in dengue patients. In the present study, thrombocytopenia, total WBC count and raised liver enzymes were important laboratory parameters to predict severity of dengue infection.

In the current study, there was positive correlation between NS1 positivity in patients

and clinical features of severe dengue infection like thromobocytopenia and total WBC count. We had evaluated NS1 antigen positivity in terms of its panbiounits parameter to predict the severity of dengue infections as it indicates viremia in the dengue patients. Hence the qualitative reporting like 'NS1 positive' or 'NS1 Negative' is not enough. It should be reported in the terms of panbiounits because the raised levels of panbiounts predict the severity of dengue infection.

Many studies reported the usefulness of liver transaminase levels, platelet counts, other clinical and laboratory parameters to predict severity of dengue infection and also suggested that none of these parameters can be used alone to predict severe dengue infection.[12-16.] We also found that positive correlation between liver transaminase levels with NS1 panbiounits and inverse correlation of NS1 panbiounts with total WBC count. Libraty *et al.,*[17] had showed that NS1 levels were higher in patients with DHF throughout the illness.

The present study demonstrated that history of 1-5 days of fever, bleeding manifestations, NS1 antigen positivity, increased NS1 panbiounits >20 units, thrombocytopenia, raised liver enzymes and decreased total WBC counts were clinical and laboratory parameters to predict severity of the dengue infection which can be used to categorize the patients in resource poor country like India for the management of dengue infections.

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