Original Research Paper

General Medicine

PREDICTING THE SEVERITY OF DENGUE BASED ON A FEW CLINICAL AND LABORATORY INDICATORS: A RETROSPECTIVE ANALYSIS

Dr. Purwa Doke	Department of Medicine, Bharati Hospital and Research Centre, Pune Satara Road, Pune 411043
Dr. Bharat Purandare*	Department of Medicine, Bharati Hospital and Research Centre, Pune Satara Road, Pune 411043 *Corresponding Author

ABSTRACT
Background: Dengue has acquired an important place amongst the febrile illnesses, for three reasons. Firstly, for its increasing incidence in an epidemic form; secondly, it's diverse severity. And lastly, for a near absence of an indicator system predicting its severity/mortality. Although there have been some attempts like identifying the molecular indicators to predict the severity of Dengue fever; yet a well acknowledged and a simple investigations based system is sought after.
Aim: The aim of the study was to measure the association between some laboratory investigations and clinical findings with the outcomes especially admission to ICU, among the admitted Dengue patients.
Materials and methods: The study was carried out in a teaching hospital located in Pune Municipal Corporation area. It is a 850 bedded hospital having basic and super-speciality services. Secondary data from the hospital records section was collected. Diagnosis confirmed by either NS1 antigen or IgM antibodies was accepted. Patients discharged from 1st July to 31st December 2015 were first enlisted. Their relevant details were coded and entered in an excel sheet and analysed. Pearson correlation coefficient between quantitative variables and ICU admission were calculated and χ^2 test for qualitative variables was applied. A simple system having a maximum score of 10 was developed, based on five variables.
Results: During the study duration, 370 patients were admitted. There was a seasonal variation showing a peak in the month of November. The mean platelet count was 61,165. Few patients having platelet count less than 50,000 had some bleeding tendency. Diabetes was the commonest (13%) comorbidity. The association between a higher total score and ICU admission was observed.
Conclusions: The scoring system is easy and its predictability is satisfactory.

KEYWORDS : Seasonal variation, age, bleeding tendency, comorbidity, SGPT

INTRODUCTION:

Dengue is the commonest arthropod borne viral illness. The diverse spectrum of disease poses difficulties in estimation of morbidity and mortality. Globally approximately 58.4 million cases and 576,900 deaths /year are reported. [] One recent estimate indicates 390 million Dengue infections per year, of which 96 million manifest clinically. [] A study estimates that 3.9 billion people, in 128 countries, are at risk of infection with Dengue viruses. [] In 2016 to 2018 in India 101,192 to 188,401 cases and 172 to 325 deaths have been officially reported. [] All four serotypes are prevalent in India; and the principal vector is Aedes aegypti. [] It causes outbreaks of varied magnitude. Although it is a mild disease, when bleeding occurs or shock sets in, Dengue can cause death. Many others develop complications and need careful management like blood transfusions, platelet transfusions and admissions in critical care units. Dengue has hence sought attention both from the medical fraternity as well from the community because of the mortality, the rising prevalence and unavailability of a specific therapy or vaccine. Recently one vaccine against Dengue has been marketed in a few countries. Control of Dengue is a real challenge due to the bionomics of Aedes aegypti together with the quality of environmental hygiene. Reduction in mortality is also challenging because of the varied progress of the disease. There is a paucity of information about the outcome predicting conditions and this is a sought need.

Pune is one the highly affected cities in Maharashtra State having many tertiary care hospitals. The patients admitted in these hospitals are thoroughly investigated and diagnosed. Complications like respiratory distress syndrome, bleeding diathesis, hypotension, hepatic failure and acute renal failure lead to a fatal outcome. [] The study was carried out to measure the association between the laboratory investigations and clinical findings with outcome/course particularly with regard to admission in ICU.

MATERIAL AND METHODS:

Study location

The study was carried out in Pune, Maharashtra. This study was carried out in a major tertiary care teaching hospital having 850 beds. It was an analysis of secondary data retrieved from the medical records section, pertaining to Dengue cases discharged from hospital from 1st July to 31st December 2015. The hospital uses a combined rapid diagnostic test kit having NS1, IgM and IgG tests with controls.

Usually patients going into/having shock, ARDS are admitted in ICU. The study was carried out in 2016.

Inclusion criteria

All patients 14 years or older having a positive test by the presence of NS1 and/or IgM antibodies were included.

Exclusion criteria

Patients having concomitant acute diseases like malaria, typhoid, leptospirosis etc. and patients having alcoholic hepatitis and acute viral hepatitis were excluded.

Need to admission to ICU was considered as a proxy of severity of Dengue. A simple scoring system was designed which consisted of the following variables - age, bleeding tendency, platelet count, co-morbid conditions and SGPT levels, for anticipating admission in ICU. Each variable was given a maximum of two marks. Thus maximum possible score was ten. The details of scoring system are given in table 1.

Table 1: Scoring system for assessment of severity of dengue

Variable	Score	
	1	2
Age	14-59	60 and above
Bleeding tendency	No	Yes
Platelet count	50,000 or more	<50,000
Comorbidity	No	Yes
SGPT	Up to 120	121 or more

Data included a few demographical variables, method of diagnosis, presence of co-morbid conditions, duration of hospital stay, results of laboratory investigations and the clinical outcome. All the data from case records was coded and entered in Microsoft Excel. Data cleaning was performed. Using Excel, regression analysis and Chi Square tests were carried out. The significance level was set at $P<0.05$.

Institutional ethics committee approval was obtained before starting the study.

RESULTS:

General

In the six months, 370 Dengue patients were admitted. Almost all (98.38%) patients were from Pune district. The age and sex

distribution of the patients is given in table 2.

Table 2: Dengue patients in Bharati Hospital in 2015

Age group	Male	Female	Total	Per cent
-20	37	14	51	13.78
21-30	116	58	174	47.03
31-40	48	40	88	23.78
41-50	20	12	32	8.65
51-60	10	6	16	4.32
61-70	4	1	5	1.35
71+	4	0	4	1.08
Total	239	131	370	100.00

The mean age of patients was 30.68 years (S.D. =11.49; S.E. Mean=0.60). Sex distribution among the age groups was similar (χ^2=8.43; P=0.21). The month wise number of admitted patients is given in figure 1.

Figure 1 : Seasonal variation of Dengue patients in Bharati Hospital, Pune , 2015
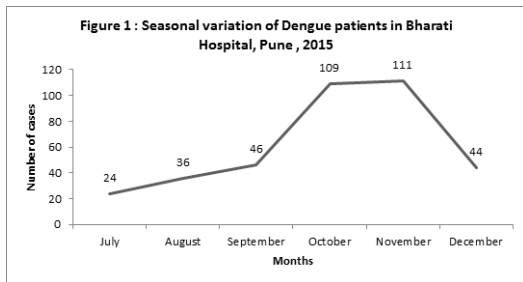
Maximum number of cases (60%) occurred in the month of October and November 2015.The diagnosis was confirmed by NS1 in 289 cases out of 370. The details of diagnosed patients by different methods is given in figure 2.

Figure 2: Dengue patients diagnosed by different methods (%) in Bharati Hospital, Pune, 2015
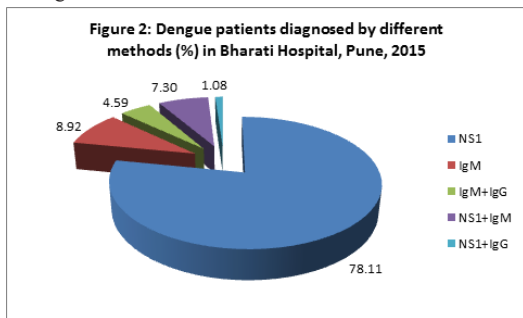
One patient died in the hospital. The patient was a 60 years old female with shock who also required mechanical ventilation.

Laboratory investigations and symptoms
The mean platelet count was 64,165 (S.D. = 53,771). Only one patient had a platelet count of 3.50 lakhs. Thrombocytopenia (platelets <100,000) was observed in 277 cases (74.86%) cases, among them eight had severe thrombocytopenia (platelets < 10,000).

A total of 184 patients had a platelet count of < 50,000. Out of these 43 (23.37%) patients had some form of bleeding. Among patients having a platelet count 50,000 or more, only 11 cases (5.98%) had bleeding tendencies. This difference was highly significant (χ^2=22.42; P<0.001).Out of the 54 cases, 10 had exclusive haematuria, two patients had haematuria and melaena, and 15 cases had only melaena. Total cases with melaena were 21 while those with haematuria were 15. Eight patients had exclusive PV bleeding, two patients had exclusive gum bleeding, and four had gum bleed alongwith some other form of bleeding tendency.

The mean of serum albumin was 3.61 (S.D. = 0.37). There was a negative correlation between age and the serum albumin levels (r=-0.27; 95% CI=-0.15 to -0.38); but a positive correlation between platelet count and the serum albumin levels (r=0.32; 95% CI=0.21 to 0.43).

Comorbidities
Amongst the female patients, five were pregnant at the time of admission. None of them had any bleeding tendency. Only one patient had severe thrombocytopenia and was transfused with six RDP. A total of 41 patients has some comorbid condition and out of them 13 cases were diabetic. Only three among them had bleeding tendencies with a

mean platelet count of 44,461.

Complications
A total of 38 cases developed some complication. No patient had encephalopathy. Myocarditis was suspected in 27 patients; however 20 had a normal echocardiogram. Only one case had a positive echo for myocarditis with raised cardiac enzymes and abnormal ECG. Only two patients had mild pulmonary hypertension. Three patients had global LV hypokinesia and one had a dilated LA. A total of five patients had elevated CPK levels and ten had elevated CPK MB levels. ECG was abnormal in five patients.

ARDS occurred in four total cases needing ventilatory support. Their platelet count range was 12,000 to 1.70 L. One patient had a bleeding tendency with a platelet count of 1.70 L. Blood and blood product transfusions were given in three patients. Two cases also developed VAP, one had CAUTI. Two patients went into shock. It was seen that once ARDS occurred, there was also some form of complication.

LRTI was seen in four patients, URTI in six patients, UTI in four patients, CNS complications in six patients and other complications in five patients were observed. Hyperglycaemia was observed in 15 patients. Out of these, four were detected to have DM. Half of the patients having diabetes and hypertension needed ICU admission.

Out of the 38 cases with complications, nine required ICU admission. Mean stay was 5.89 days in ICU and mean stay in wards was 4.27 days.

Overall length of stay in ICU and wards
Average length of stay was 3.96 days (SD 2.59). Out of the total 370 cases, 23 patients required ICU admission. Mean stay in ICU was 3.6 days. Four were discharged from ICU and rest were transferred to wards staying additionally for 3.78 days. A total of 14 cases without complications also needed ICU admission. Their mean stay was 2.1 days. Mean stay in wards of 329 patients without complications was 3.69 days. Patients who were not admitted in ICU had a mean age of 29.94 years (SD=10.70) while the patients admitted in ICU had a mean age of 41.87 years (SD=16.51) Z=3.49; P<0.01

Information of all five selected criteria required for scoring for predicting ICU admission was available from 348 patients. The association between score and ICU admission is given in table 3 and shown graphically in figure 3.

Table 3: Scoring system implications

Score	Patients needed ICU (%)	Patients not needed ICU	Total
5	1 (0.81)	123	124
6	6 (4.76)	120	126
7	8 (11.27)	63	71
8	5 (19.23)	21	26
9	1 (100.00)	0	1
	21 (6.03)	327	348

Figure 3: Score and prediction of need in ICU
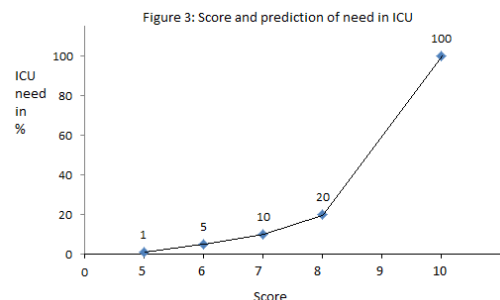
DISCUSSION:
Predicting severity in a case of Dengue is always a challenge to any physician. His/her opinion is mostly based on the results of investigations. Although many investigation reports are presented here; the main focus of this study was to establish a system of prediction of severity in a diagnosed Dengue patient. The World Health Organization has given three conceptual criteria for identifying a severe Dengue case. [7]WHO has also recommended monitoring of seven warning signs. [7]But studies attempting establishment of such a system are remarkably rare. Before the month of July and after

December there were very few cases; hence they were not considered for analysis. This is in consonance with the known transmission season in India and is matching with other studies. [,89]Patients in this study were younger than in one study in Odisha, in which male preponderance was more than this present study; [8]but it may not be universal. In Sri Lanka, female patients outnumbered males. [10] This difference may be due to more gender discrimination in India than in Sri Lanka. Higher bleeding tendency particularly gum bleeding was observed in the Sri Lankan study than this present study. [10] Some risk factors like secondary infection, extremes of age, pregnancy, under nutrition or over nutrition and comorbidities are well known risk factors. [11,12]A comparable study of haematocrit, Glasgow Coma Score, urine protein, creatinine, and platelet count was used to predict severe Dengue among children. [13]Predicting severity based exclusively on WHO recommended warning signals has also been attempted. [14]The highest recorded sensitivity itself was very low to the tune of 59%. [14] Mucosal bleeding had highest odds ratio. [14]In a study, a scoring system using simple parameters like signs/symptoms along with basic information was developed but it was to confirm diagnosis of Dengue in small health care institutions. [15]In one study, a simple peripheral blood count was attempted to predict the severity of Dengue; significant difference was observed in platelet count and haemoglobin and later even in white blood cells. [16]In children such blood count was used to create a diagnostic algorithm, was proved to be quite sensitive. [17]Although correlation between platelet count and bleeding is not universally observed; vascular leakage is acknowledged. [18]A meta-analysis showed that among the 11 signs/symptoms studied; five confirmed an increased risk for severe disease. Among bleeding conditions, only hematemesis and melaena were significantly associated with severity of disease. [19]In the context of many potential prognostic viral, immunological, endothelial activation or micro vascular disruption, biomarkers are being tried.[15]It is also known that patients having concomitant bacterial infection have higher CRP and APTT levels as well as a higher mortality. [20]Encephalopathy as well encephalitis is known to occur, [21]although we did not observe it in our study. Like our study; nonspecific self-resolving signs of neurological involvement have been observed in some patients. [22]Despite raised SGPT levels in many patients, severe liver involvement may not be observed. [23] In this study, myocarditis as a complication was suspected to a lesser extent than the known rate of 11.2%. [24]Comorbidities in general[25] and diabetes and hypertension specifically are known to lead to haemorrhagic manifestations, [24] in this study these two were important contributors to ICU admission. In almost all hospitals, critically ill patients are admitted in ICU. Therefore need of admission to ICU may be considered a valid proxy for the severity of Dengue. Many variables were analysed but the selected five had some predictive value for ICU admission. Findings from table 3 clearly indicate that more the score, higher is the chance of getting admitted in ICU. There was only one patient having a score of nine and none having ten. Conceptually 100% admission is anticipated for a score of ten. The best estimation for a score of nine will be about 60%. The scoring system is easy to calculate and may be used to take actions which will reduce case fatality rate substantially.

LIMITATIONS:

Important information of some patients was incomplete. Acute kidney injury could not be defined properly.

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