

Predictors of dengue-related mortality in young adults in a tertiary care centre in North India

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ABSTRACT

Background: Outbreaks of dengue fever cause widespread mortality. There is a paucity of studies on predictors of morbidity and mortality in dengue. This observational study was performed to study the factors predicting adverse outcomes caused due to dengue fever thereby optimally manage the patient's to reduce mortality. **Methods:** The study included a 1-year retrospective and 1-year prospective period were clinical, laboratory and outcome data of patients between 18-30 years of age, having serology proven (NS1/dengue IgM) dengue fever were recorded and analysed. **Results:** Out of 418 patients, 404 (96.64%) recovered and 14 (3.35%) expired, resulting in a 3.35% mortality rate. Platelet count did not determine the outcome in dengue patients. The shock factor was present in 45 (11.1%) patients who recovered and 10 out of 14 patients who expired (71.4%), *P* value was statistically significant. Mean value of SGOT and SGPT in dengue patients who expired were 2865.43 and 1510.07 IU/L, respectively, which were significantly higher than the mean values of SGOT and SGPT in those who survived. Bleeding was present in 39 (9.7%) patients who recovered. Out of the 14 expired patients, bleeding was present in 5 (35.7%) which is statistically significant. Hence, on multivariate logistics analysis, bleeding, a higher SGOT and SGPT value and shock were found to be significant risk factors for mortality in dengue fever patients. **Conclusion:** Bleeding, shock and raised SGOT and SGPT levels were identified as predictors of adverse outcomes and mortality in dengue fever. Timely identification of these risk factors and active management is important to reduce dengue-related mortality.

Keywords: Dengue, mortality, predictor, shock

Background

Dengue, the second most common arthropod related disease, poses a worldwide threat and is a major source of public health concern.^[1] Recent decades have witnessed an emergence and re-emergence of dengue, with more frequent and severe outbreaks, in previously unaffected areas.^[2] There are four closely related serotypes of dengue (DENV1 to DENV4) and a fifth serotype was reported in 2013 from the forests of Malaysia but

it has not yet been reported from India.^[3-5] Infection with one serotype of DENV provides lifelong immunity to that serotype but results only in partial and transient protection against subsequent infection by the other three serotypes.^[6]

There has been a significant debate over the utility of the original 1997 and the revised 2009 classification criteria for dengue proposed by the WHO.^[7,8] Although the 2009 classification is easier to apply from a public health point of view and has higher sensitivity and specificity, it is relatively broad in its context and has limited usefulness in a research setting where more stringent definitions of severity are required.^[9,10]

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Knowledge of factors that predict worse prognosis can help the health workers in primary care centres to identify the patients requiring intensive medical management. Such patients need to be admitted to intensive care units in tertiary care centres so that mortality due to dengue can be controlled. As dengue commonly infects the young adult population which is more productive socially, saving the life of the young earning member can save the entire family from sustaining a financial loss. Losing precious lives because of dengue fever has proven to be a significant economic burden to society.

Under the gleaming light of a sudden upsurge of this vector-borne disease, the identification of certain reliable predictors of disease severity and mortality is central to the reduction of morbidity and mortality associated with it. Studies in this direction have been limited and have yielded varied combinations of clinical and biochemical predictors of disease severity. In an attempt to understand the same, this observational study was undertaken, wherein certain clinical and laboratory features of adult dengue patients hospitalised during a period of 2 years were studied and were correlated with the disease outcome.

Material and Methods

This observational study included young adults (18 to 30 years) suffering from dengue fever, admitted in the department of medicine over a period of 2 years, prospectively from January 1, 2014, to December 31, 2014, and retrospectively from January 1, 2013, to December 31, 2013. The study design was approved by the institutional ethics committee (30-08-2013). Informed consent was taken from all patients prior to their inclusion in the study. The data (demographic/clinical/laboratory/outcome) of retrospective cases were obtained from the records office and for prospective cases, it was noted from the files of the admitted patients.

This study included patients suffering from serology proven (NS1 and/or IgM) dengue fever fulfilling the criteria of acute fever more than 2 days, thrombocytopenia (100000 cells per cu. mm. or less at any time either at admission or during course of hospital stay), haemorrhagic tendencies (in patients with dengue haemorrhagic fever evidenced by petechiae, ecchymosis or purpura, bleeding in mucosa, gastrointestinal tract, injection site or haematemesis or melena), plasma leakage due to increased vascular permeability (manifested by rise in haematocrit greater than 20% above average for age, sex and population), or signs of plasma leakage such as pleural effusion, ascites, hypoproteinemia and shock (in dengue shock syndrome). Patients with thrombocytopenia due to chronic liver disease, idiopathic thrombocytopenic purpura and leukaemia or antiplatelet drugs were excluded from the study.

The outcome of the study was in the form of an analysis of the varied clinical profile of dengue fever and the end result of treatment resulting in either discharge on recovery, discharge on request and discharge against medical advice or death of the patient. The statistical analysis was carried out using mean (range and standard deviation). A *P* value of <0.05 was taken as statistically significant.

Results

The study included 418 cases, a majority of whom (45.69%) belonged to the age group of 20–25 years. The male to female ratio was 3.2:1.

Fever was present in 417 patients followed by vomiting and pain abdomen in 29.43% and 17.94% patients, respectively. Petechial rash, myalgias and bleeding were seen in 12.92%, 13.16% and 10.29% of patients, respectively. Headache, diarrhoea, abdominal distension, breathlessness and melena were present in 7.89%, 4.78%, 4.78%, 3.83% and 3.83% of patients, respectively. Retro-orbital pain, the classical feature of dengue fever was present in only 1.67% of patients. Other less common complaints of dengue fever patients were joint pains, weakness, jaundice, urinary disturbances, seizure, loss of consciousness, palpitations and altered sensorium. Around 404 (96.64%) patients were discharged and 14 (3.35%) expired. So the mortality rate was 3.35%. In our study, bleeding was found to be a statistically significant risk factor for mortality as 5 out of 14 expired patients had bleeding [Table 1].

High SGOT and SGPT values were found to be a risk factor for mortality as the mean values of SGOT and SGPT were significantly higher in dengue patients who expired. [Table 2].

Shock, another ominous sign, was present in 45 (11.1%) out of 404 patients who recovered and 10 (71.4%) out of 14 patients who expired; *P* value was statistically significant. [Table 3].

Table 1: Distribution of bleeding in dengue patients

Outcome	Bleeding		Total	<i>P</i>
	No	Yes		
Expired	9	5	14	0.010
Expired	64.3%	35.7%	100.0%	
Recovery	365	39	404	
Recovery	90.3%	9.7%	100.0%	
Total	374	44	418	
	89.5%	10.5%	100.0%	

Table 2: Distribution of SGOT and SGPT in dengue patients

	EXPIRED		RECOVERED		<i>P</i>
	Mean	SD	Mean	SD	
SGOT	2865.43	3780.07	193.95	263.61	0.000
SGPT	1510.07	1506.57	125.81	210.48	0.000

Table 3: Distribution of shock in dengue fever patients

Outcome	Shock		Total	<i>P</i>
	No	Yes		
Expired	4	10	14	0.000
Expired	28.6%	71.4%	100.0%	
Recovery	359	45	404	
Recovery	88.9%	11.1%	100.0%	
Total	363	55	418	
	86.8%	13.2%	100.0%	

The commonest underlying cause of death was multiorgan failure following shock, which was seen in 11 out of 14 patients, all of whom developed metabolic acidosis as the terminal event. Other causes of death were dengue encephalopathy, ARDS and intracranial haemorrhage occurring in 1 (7.1%) patient each.

Discussion

Dengue is a self-limiting, vector-borne disease caused by the dengue virus (DENV). The steady increase in the number of dengue patients in the past few years can be attributed to rapid urbanisation and unplanned construction activities.^[1-4] People who go out to work and children playing in public places are exposed to bite of the *Aedes aegypti* mosquito which serves as a vector for this flavivirus. Whether dengue affects adults, who are generally more economically productive members of the families, or whether it affects children, who are more susceptible to dehydration and shock; dengue causes increased mortality and have proven to be a socioeconomic burden resulting in loss of many productive working hours. Treatment and management of dengue are also costly especially in face of complications like bleeding or shock which may require transfusions.

With male to female ratio of 3.2:1, males are more commonly affected than the females in accordance with their outdoor working ethics, as also reflected in other studies.^[11-18] The study population included adults in the age group of 18–30 years and the majority belonged to the age group of 20–25 years, as also observed by Kauser *et al.*^[12]

Bleeding was present in 10.29% of patients and the most common site was from the gums (30.3%) while Daniel *et al.* reported gastrointestinal tract (GIT) as the commonest site of bleeding.^[16] Bleeding episodes were attributable to vasculopathy, thrombocytopenia, prothrombin complex deficiency and platelet dysfunction. Presence of bleeding in our study held statistical significance in having a worse outcome than those who did not. According to Shah *et al.*, PTT is more deranged in cases of dengue shock syndrome (DSS) as compared to cases of dengue hemorrhagic fever (DHF).^[17] Acharya *et al.* also found a bleeding tendency, severe thrombocytopenia and prolonged prothrombin time (PT) are independent markers of increased mortality.^[18]

The maximum and mean haematocrit at the day of admission were 56.2 and 42.2, respectively. Higher haematocrit is related to increased severity and is explained by the increased plasma permeability which is the basic pathophysiological alteration in dengue. In our study, higher haematocrit was related to severe dengue infection. However, hemoconcentration was not found to be a statistically significant marker of mortality by Shah *et al.*^[17]

In our study, patients with elevated transaminases had a worse outcome, which was also reported by Daniel *et al.*, Acharya *et al.*, Fujimoto *et al.* and Bhushan and Parkash *et al.*^[16-21] SGOT elevation was found to be more than SGPT. Similar findings have also been reported by other studies.^[20,22] This finding can

be explained by the fact that SGOT is also secreted by heart, muscles and erythrocytes while SGPT is only secreted by the hepatocytes.^[20] Acharya *et al.* reported raised SGOT in 67.4% and SGPT in 47.6% of their patients.^[18] Kauser *et al.* found elevated SGOT and SGPT in 27.39% and 24.65% of patients, respectively while Mandal *et al.* found raised SGOT in 83.78% and SGPT in 70.27% of their patients.^[12,23] Sharma *et al.* reported elevated transaminases in 90% of patients.^[24] In the present study mean SGOT and SGPT values in patients who survived were 193.95 and 125.81 IU/L while the same values in expired patients were 2865.43 and 1510.07 IU/L, respectively. Similar observations were made by Bhushan, Acharya *et al.*, Parkash *et al.* and Daniel *et al.*^[16,18,20,21] SGOT was elevated (>250 IU/L) in 84% of patients who died, thereby associating abnormal SGOT with the worse outcome; as also observed by Fujimoto *et al.*^[19] A lower transaminase cut-off value of 250 U/L needs to be examined in subsequent studies as a 'predictor' of severe disease, in tandem with the WHO cut-off the value of 1000 U/L for 'defining' severe disease.^[8] In a study of pediatric dengue cases, SGPT was found to be more commonly elevated in patients of DSS as compared to patients having DHF but this SGPT elevation was not statistically significant.^[17]

Dengue encephalopathy was also a cause of death in our study. These findings are in corroboration with those of Shah *et al.* and Acharya *et al.* who have also reported increased mortality in patients having altered sensorium and abnormal reflexes which signify the central nervous system (CNS) involvement.^[17,18]

ARDS was another cause of mortality in our study. Acharya *et al.* have also reported ARDS in 45% of dengue-related deaths in their study.^[18] Capillary leak syndrome causes ARDS.

The shock was present in 71.4% of patients who succumbed during the course of hospitalisation further concluding that shock in patients with dengue is an ominous sign and is another predictor of mortality, as also observed by Shah *et al.* and Acharya *et al.*^[17,18]

Conclusion

Bleeding tendency, elevated transaminases and presence of DSS predict the worse outcome. These patients require strict monitoring and prompt supportive management to reduce mortality. Early diagnosis, identifying the risk factors through appropriate investigations and intensive medical management is the cornerstone of treatment which is mainly symptomatic and based on adequate hydration, haematocrit monitoring and looking out for the warning signs. These measures can go a long way in reducing mortality caused due to dengue. Dengue results in a great economic burden on society and also has a negative impact on the health indices by causing increased mortality if not managed appropriately and timely. Hence, all the health workers, especially in primary and community health centres need to be aware of warning signs that herald a severe course of this disease.

Prevention of dengue is imperative to reduce morbidity and mortality. The dengue infection needs to be controlled by reducing the transmission of this virus by a mosquito. This requires proper water sanitation and awareness in the masses about cleanliness and vector control. Strict measures are required to control this endemic disease which acquires epidemic proportions with seasonal variation.

Limitation of study

This was an observational study on hospitalised patients between 18–30 years of age.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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