

Study of clinical and laboratory predictors of in hospital outcome in dengue fever in Mumbai city

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Abstract

Objective: Dengue fever is one of the most common arboviral mediated outbreaks reported with increased prevalence year after year with considerable morbidity and mortality. This study was designed to assess the clinical and biochemical parameters of dengue fever patients. **Methods:** Prospective observational study was undertaken among adult patients in 1500 bedded Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai. Two hundred patients were studied and analysed. All patients who were NS1 antigen/IgM dengue positive were included in the study. Clinical features, haematological and biochemical parameters were noted. **Results:** Of the 200 patients studied, majority of the patients (80%) were in the age group of 15-35 years. There were 63% male patients and 37% female patients. Fever was the major symptom (100%) followed by bodyache (84%), rash (44%), abdominal pain (39.5%), pleural effusion (36.5%) and ascites (17%). Significant derangements in platelet (94%), raised PT/a PTT (39.5%), leucocytosis (23%) and raised serum transaminases (40%) were noted. About 50% of patients were diagnosed as classical dengue fever and the remaining 50% of the patients were diagnosed as dengue haemorrhagic fever. In this study 19% cases developed Dengue shock syndrome i.e. dengue haemorrhagic fever grade III and IV. Significant derangements in platelet was seen in 94%, and platelet count of < 10000 was seen in 17% of patients. Increased PT/a PTT was seen in 39.5%, leucocytosis in 23% and raised serum transaminases was seen in 40% of the patients. Mortality rate was 2%. **Conclusion:** Fever associated with headache, retroorbital pain, erythematous morbilliform rash, conjunctival suffusion and itching in palms and soles along with thrombocytopenia, leucopenia, elevated liver transaminases should prompt a clinician on the possibility of dengue infection. Platelet transfusions have little role in management of dengue patients. Mortality in DHF was mainly related to the complications of the DHF, so early recognition of the disease and prevention of complications is most important for the favourable outcome of the disease.

Keywords: Dengue fever, in hospital outcome, clinical and laboratory predictors.

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INTRODUCTION

Infection with dengue virus is witnessing a global resurgence over last 1 to 2 decades. Of the estimated 50 to 100 million cases occurring annually, about 5,00,000 cases require hospitalization. Among children of South

East Asian Region Countries, these infections including dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) are the leading causes of hospitalization and death was preceded in prevalence by diarrhoeal disease and acute respiratory infections only. The resurgence of infections is attributed to decay in public health infrastructure, lack of mosquito control, unplanned urbanization and global population explosion. Increase in air travel and excellent mode of transport of pathogens also contributes spread. A total of 2500 million people worldwide are at risk of dengue virus infection. Dengue affects more than 100 countries in all continents except Europe. Dengue fever and dengue haemorrhagic fevers are self limiting mosquito born, viral diseases caused by the bite of female Anophele, Aedes aegypti mosquito. Dengue fever has been known for more than a century in the tropical countries. Dengue fever has

emerged as one of the most important arthropod tropical infections in the recent years with an estimated 2.5 billion people at risk all over the world. Initial dengue infection may be asymptomatic (50-90%)¹, may result in a nonspecific febrile illness, or may produce the symptom complex of classic dengue fever (DF). Classic dengue fever is marked by rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation, and a centrifugal maculopapular rash, among other manifestations. A small percentage of persons who have previously been infected by one dengue serotype develop bleeding and endothelial leak upon infection with another dengue serotype. This syndrome is termed dengue hemorrhagic fever (DHF). Dengue as a disease has been poorly studied and important lacunae remain in the understanding of the presentations, the complications and the treatment of the disease. The exact clinical and laboratory profile is crucial for diagnosis as well as successful management of the patients. This study is an attempt to elucidate the clinical and laboratory profile of serologically confirmed cases of dengue fever in our hospital and to identify clinical and laboratory predictors of in hospital outcome of dengue fever with respect to mortality and system morbidity.

MATERIALS AND METHODS

The study was approved by the Ethical and Research Committee of our hospital. This prospective observational study was carried out in a 1500 bedded Lokmanya Tilak Municipal Medical college and General hospital, Sion, Mumbai from January 2013 to December 2015. All indoor admissions with history of fever (approximately 10000 patients) were screened for diagnosis of fever with serological and pathological tests for malaria, leptospirosis and dengue. Patients above 12 years with confirmed dengue, who were either hospitalized or managed as outdoor patients with NS1 (non-structural protein) antigen and/or IgM dengue antibody positivity were included in the study. The patients with concomitant malaria, typhoid, leptospirosis etc were excluded from the study. At admission detailed history was taken in every patient and thorough general and systemic examinations were carried out with special attention to the symptoms of the patient, conscious level, temperature, pulse, blood pressure, pallor, citrus, skin lesion bleeding manifestations, hepatosplenomegaly, ascites and pleural effusion. Laboratory investigations done were hemoglobin, total and differential leucocyte counts, platelet count, hematocrit, liver function tests, blood urea and serum creatinine, chest radiograph and ultrasound scan of abdomen. Haematocrit was monitored every 12 hourly in Dengue Haemorrhagic fever Grade III and

Grade IV Blood counts were monitored periodically as and when required till resolution. Other differential diagnosis was excluded by appropriate tests. SOFA score was calculated for all patients as given below. Following statistical tests of significance are used as per distribution of data (Normal or non-normal) Un-paired t test, Chi square test.

Criteria	Point Value
PaO ₂ /FiO ₂ (mmHg)	
<400	+1
<300	+2
<200 and mechanically ventilated	+3
<100 and mechanically ventilated	+4
Platelets (×10 ³ /μl)	
<150	+1
<100	+2
<50	+3
<20	+4
Glasgow Coma Scale	
13-14	+1
10-12	+2
6-9	+3
<6	+4
Bilirubin (mg/dl) [μmol/L]	
1.2-1.9 [20-32]	+1
2.0-5.9 [33-101]	+2
6.0-11.9 [102-204]	+3
>12.0 [204]	+4
Mean Arterial Pressure OR administration of vasopressors required	
No Hypotension	0
MAP <70 mm/Hg	+1
dop ≤5 or dob (any dose)	+2
dop >5 OR epi ≤0.1 OR nor ≤0.1	+3
dop >15 OR epi >0.1 OR nor >0.1	+4
Creatinine (mg/dl) [μmol/L] (or urine output)	
<1.2 [106]	0
1.2-1.9 [106-168]	+1
2.0-3.4 [177-301]	+2
3.5-4.9 [309-433] (or < 500 ml/d)	+3
>5.0 [442] (or <200 ml/d)	+4

RESULTS

A total of 200 patients who reported between January 2013 and December 2014 were studied and analysed. Majority of these cases reported to our hospital coinciding with rainy season, showing the breeding of mosquitoes during the said period. Majority of the patients were males 126 (63%). Females formed 74 (37%) of the cohort. Maximum patients were in 15-25 age group (49.5%) (Table 1). Fever was universal followed by other symptoms like bodyache (84%) (in the form of arthralgia, myalgia, headache, backache, retro-

orbital pain), vomiting (45%) and abdominal pain (diffuse) (39.5%). (Table-2) In our study, out of 200 patients, majority that is 110 (55%) cases were classical DF, 24 (12%) cases were DHF Grade – I, 24 (12%) were DHF Grade – II and 39 (19%) cases were DSS (DHF Grade – III and Grade IV).(Table3) On clinical examination 44% had petechiae/ echymosis, 36.5% had pleural effusion, 36% had hepatomegaly, 25.5% had bradycardia, 17% had ascites, 14.5% had subconjunctival haemorrhage, 10% percent had icterus and 7.5% had splenomegaly.(Table-4) Eighty nine patients (45%) had one or the other evidence of haemorrhagic manifestations. Amongst them 26 (13%) cases were gastrointestinal tract bleed in the form of hematemesis or melena was present. Platelet count at presentation was less than 1,00,000/cumm in around 94% of cases, though it kept on falling further during hospitalization/observation. Minimum platelet count noted was 8,000/cumm. Thirty four patients i.e. 17% had thrombocytopenia of <10,100/cmm. Leucopenia was noticed in around 23% of cases. Raised liver serum transaminases were noted in 40% of patients. Raised hematocrit (>45%) was noted in 25% of patients at presentation and raised PT/aPTT (raised PT/aPTT when values raised more than 1.5 times of the normal values) was seen in 79 (39.5%) patients.(Table-5) In the present study, out of 200 patients, 18 (9%) cases had evidence of circulatory failure who required vasopressor support, and out of which 2 patients had non recordable blood pressure. Our study reveals that 95.0% cases had sofa score < 9 followed by 3.0% cases had sofa score between 9 – 11 and 2.0% cases had sofa score > 11.(Table-6) There is no specific treatment indicated for dengue fever. All the patients were managed with careful monitoring of blood pressure, hematocrit, platelet counts on as and when required basis. Antipyretics (paracetamol) were used along with intravenous fluids (normal saline and ringer lactate) on as required basis. Despite majority (54%) of the patients with the platelet count being less than 20,000 /mm³ improved with single donor platelet and combination with FFP. Out of 90 patients with DHF, 74 (37.0%) had deranged aPTT and 20 Of them required FFP for stabilization of bleeding manifestations apart from fluid therapy. Total mortality was 4 (2%). Dengue shock syndrome was seen in two patients as cause of death and two patients has DSS. There was no mortality in DF and DHF Grade I and Grade II.

36-45	12	06.0
46-55	12	06.0
56-65	12	06.0
66 above	04	02.0

Table 2: Profile of symptoms wise distribution

Symptoms	No. of Cases (N=200)	Percentage (%)
Fever	200	100.0
Arthralgia	03	01.5
Vomitting	90	45.0
Headache	80	40.0
Abdominal pain	79	39.5
Backache	72	36.0
Diarrhea	55	27.5
Malaena	29	14.5
Altered sensorium	10	05.0
Seizures	03	01.5

Table 3: Profile of grading of dengue fever

Grading	No. of Cases (N=200)	Percentage (%)
Classical DF	110	55.0
DHF Grade – I	24	12.0
DHF Grade – II	27	14.0
DHF Grade – III	31	16.0
DHF – IV	08	03.0

Table 4: Profile of signs wise distribution

Signs	No. of Cases (N=200)	Percentage (%)
Petechiae / Echymosis	88	44.0
Pleural effusion	73	36.5
Hepatomegaly	72	36.0
Bradycardia	51	25.5
Ascites	34	17.0
Subconjunctival haemorrhage	29	14.5
Icterus	20	10.0
Splenomegaly	15	07.5

Table 5: lab parameres (N=200)

Parameter	No of patients (%)
Thrombocytopenia(<1,00,000/cmm)	188 (94%)
Raised PT/aPTT (1.5 times normal)	79(39.5%)
Leucopenia (<4000/cmm)	46(23%)
Raised AST,ALT >45IU/L	80(40%)
Raised hematocrit(>45%)	50(25%)

Table 6: Profile of sofa score

Sofa score	No. of Cases (N=200)	Percentage (%)
< 9	190	95.0
9-11	06	03.0
> 11	04	02.0

Table 1: Profile of age distribution

Age group (years)	No. of Cases (N=200)	Percentage (%)
15-25	99	49.5
26-35	61	30.5

Table 7: Association between thrombocytopenia and bleeding

Platelet count	No. of cases	% of cases with Bleeding
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		Yes No %	NoNo %
<10,000	34	*28 82.4	06 17.6
10,000 - 20,000	42	21 50.0	21 50.0
20,000 - 50,000	68	34 50.0	34 50.0
50,000 - 1,00,000	44	07 15.9	37 84.1
>1,00,000	12	--	12 100.0

By Chi Square Test P = *0.001 * Significant

Table 8: Profile of mean platelet count trend during hospital stay among study cases

Duration In Days	Mean Platelet count (/cmm) ($\bar{X} \pm SD$)			
	N	≤ 5 (N=118)	N	> 5 (N=82)
1	118	*61690.68 \pm 58772.47	82	30743.90 \pm 22527.09
2	88	65863.64 \pm 32063.22	81	67000.00 \pm 32063.22
3	99	105505.05 \pm 53744.17	76	97447.37 \pm 53744.17
4	62	*121483.87 \pm 36824.24	57	125778.95 \pm 36824.24
5	29	192896.55 \pm 227427.44	31	143838.71 \pm 227427.4
6	07	*100000.00 \pm 0.00	16	160500.00 \pm 96434.43
7	00	-	10	162900.00 \pm 104796.6

By Student t Test * Significant

DISCUSSION

Increase in the number of dengue cases over the past few years has been attributed to rapid unplanned urbanization with unchecked construction activities and poor sanitation facilities contributing fertile breeding areas for mosquitoes, it is also seen that increase in alertness among medical personnel following the epidemics and availability of diagnostic tools in the hospitals have contributed to the increased detection of cases² Male to female ratio in our study was 1.7: 1. Slightly higher number of males is primarily because males are working outdoor and are exposed to mosquito bites. Fever was the most common presentation (100%), which is in unison with other similar studies from India and South East Asia³⁻⁶ Headache and myalgia were seen in majority of cases. Altered sensorium or history of convulsion due to intracranial bleed, or hypoxia of brain due to hypotension were present in four (5%) cases. Conjunctival injection was documented in 35% of all cases and diffuse erythematous skin rash in 44%. Mandal *et al* in a similar study have documented headache in 62.16% and rash in 37.84% of cases⁽⁷⁾ Thrombocytopenia may not be the sole causative factor for development of these rashes as they developed in patients with platelet counts above 50,000/cumm. Dengue virus interacts with host cells, causing release of cytokines and stimulation of immunologic mechanism causing vascular endothelial changes, infiltration of mononuclear cells and perivascular edema⁸ Munde *et al* in their series of patients have shown myalgia in 50% and headache in 25% of all patients⁶ Muniraja *et al* documented conjunctival congestion in 2.6 to 7.3% of cases which is much less than our study patients⁹ Positive tourniquet test was seen in 16.50% and bleeding in form of petechiae in

around 6.7% of patients which was less than some other similar studies and in line with Shabid *et al* from Karachi¹⁰ Bleeding diathesis is a known feature of dengue fever because of low platelet count and leakage from blood vessels. Bone marrow suppression, Immune-mediated clearance and spontaneous aggregation of platelets to virus infected endothelium may be responsible for such thrombocytopenia. This study shows that, 82.4% cases with <10,000 platelet count had bleeding which was significantly more as compared to other groups of platelet counts (Table-7). Raised liver transaminases were documented in 40% of cases. In study by Kularatne *et al*, 88% patients showed elevated ALT and AST, with 122 of them having a two-fold increase¹¹ Mandal *et al* documented elevated transaminases in 83.78% of cases⁽⁷⁾ A study from Brazil by Silva *et al* 17, C1q has found an interacting partner between NS1 protein and liver proteins in the causation of hepatic dysfunction in dengue fever¹² Pleural effusion documented in 36.5% on chest radiography and ascites seen in 17% of patients on ultrasound scan of abdomen was marginally higher from other similar studies¹³ The above result states that at Day 1 mean Platelet count was 61690.68 whose duration of hospital stays ≤ 5 which was significantly more as compared to 30743.90 whose duration of hospital stay > 5 . (Table-8) The overall mortality in our study population was 2% which is in sync with fatality rates in South-East Asian countries. Higher mortality rates shown in other studies could be due to re-infection and late presentation to the hospital. In DSS, 4 (2.0%) patients died, due to acute respiratory distress, fulminant hepatic failure, dengue encephalitis. Sofa score in all the 4 patients who died was more than 11.

CONCLUSION

Dengue infection is increasing proportional to increased urbanization and compromised sanitation measures. Fever associated with headache, retroorbital pain, erythematous morbilliform rash, conjunctival suffusion and itching in palms and soles along with thrombocytopenia, leucopenia, elevated liver transaminases should prompt a clinician on the possibility of dengue infection. Platelet transfusions have little role in management of dengue patients. Early diagnosis, careful monitoring and proper fluid management goes a long way in reducing the mortality due to dengue hemorrhagic fever and shock syndrome.

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