Research Article

Dengue: multicentre clinical profile of patients admitted in intensive care unit

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ABSTRACT

Background: Dengue with 2.5 billion people at risk and 50 million new cases every year is one of the most rapidly spreading vectors borne disease in world. We aimed to analyse the clinical profile of dengue patients requiring ICU admission.
Methods: In a cross-sectional, observational, multicenter case study 105randomly selected laboratory positive dengue subjects were randomly selected from four tertiary care centers ICU's. Socio-demographical, clinical, therapeutic & laboratory parameters were evaluated. Statistical analysis was done using SPSS version 14.0.
Results: The main cause of ICU admission was shock or hypotension due to sepsis (20%). Most patients presenting complaint was fever (93.33%), bodyache (84.76%) and retro-orbital pain (34.3%). Most prevalent warning sign indicating severe dengue was abdominal pain (37.4%). Mucosal bleed (20.9%) was the most common haemorrhagic manifestation. 37.14% with warning signs and 62.86% patients with severe dengue required ICU care.
Conclusions: A rapid assessment of clinical profile, presenting symptoms and warning signs can aid in early decision for requirement of ICU admission & may go a long way in decreasing mortality.

Keywords: Dengue, ICU, Clinical profile

INTRODUCTION

Dengue is a mosquito-borne viral disease caused by Dengue virus (DEN). Dengue virus (DEN) is a small single-stranded RNA virus. Four distinct serotypes, (DEN 1-4) are transmitted to humans through the bites of infected *Aedes* mosquitoes, mainly *Aedes aegypti*. World Health Organization (WHO) estimates 2.5 billion people to be at risk, with 50 million new cases every year and twenty thousand deaths from dengue every year.[1,2] National Vector Borne Disease Control Programme of India,[2] reports rapid increase in cases from 3306 in 2001 to 75,454 in 2013; and also an increase in mortality. India is endemic for dengue, with prevalent four serotypes. Several epidemics have occurred, one in 2012 having

thrice the cases as 1996, many requiring intensive care facilities. In developing countries, like India with limited ICU availability, understanding the clinical presentation, causes of dengue admissions can go a long way in decreasing disease morbidity & mortality.

METHODS

Study design and subjects

In a cross-sectional, observational, multicenter case study 105 subjects were randomly selected from four tertiary care center ICU's. Adult (≥18 years) laboratory-confirmed cases of dengue were evaluated. Laboratory-confirmed dengue cases included those with at least one

of the following positive laboratory results: dengue immunoglobulin-G (IgG), immunoglobulin-M, (IgM), nonstructural protein 1 (NS1) antigen test.

Data collection

Apart from socio-demographic data, information was collected pertaining to cause of ICU admission, comorbidity, presenting symptomatology, clinical & laboratory parameters.

According to the WHO 2009 criteria 3, following "warning signs" were noted during study; abdominal pain or tenderness, vomiting, clinical fluid accumulation, mucosal bleeding, lethargy or restlessness, hepatomegaly and a rise in hematocrit concurrent with a rapid drop in platelet count. "Severe dengue" comprised of (1) severe plasma leakage leading to shock or fluid accumulation with respiratory distress, (2) severe bleeding, (3) severe organ involvement or (4) transaminase levels 1000 units/L.

Statistical Analysis

Statistical analysis was done using SPSS, version 14.0.

RESULTS

In 105 laboratories confirmed dengue patients studied, mean age was 38.6±18.4 years (Table 1), with 46.51% being males. The main cause of ICU admission was shock or hypotension due to sepsis (20%), closely followed by severe thrombocytopenia (19.05%) and respiratory failure (18.1%). Most of the studied subjects gave history of comorbid hypertension (22.86%), COPD (17.14%) and diabetes (16.2%).

Table 1: General characteristics at time of admission.

Characteristics	Dengue patients n=105 (%)
Age (years), mean (SD)	38.6 (18.4)
Male sex, n (%)	40 (46.51)
Cause ICU Admission	
Shock or Hypotension due to sepsis	21 (20)
Severe thrombocytopenia with or without bleeding	20 (19.05)
Cardiac Failure	10 (9.52)
Respiratory Failure	22 (20.95)
Renal Failure	10 (9.52)
Gastrointestinal bleeding	8 (7.62)
Neurological	8 (7.62)
Comorbidity, n (%)	
Hypertension	24 (22.86)
Chronic Renal Failure	8 (3.81)
Diabetes	17 (16.2)
COPD	18 (17.14)

Most of the subjects presented with complaint of fever 98 (93.33%), whereas body ache (84.76%), retro orbital pain (34.3%) & arthralgia (30.5%) were the commonest complaints at time of admission in ICU. Only 30.5% patients had a rise in their hematocrit values. Most common site of plasma leakage was pleural space (32.4%) followed by pedal edema (13.33%) and ascites (11.4%) (Table 2).

Table 2: Clinical profile, severity & admission details.

Signs & Symptoms, n (%)	Dengue patients n=105 (%)
Fever	98 (93.33)
Body ache	89 (84.76)
Arthralgia	32 (30.5)
Rash	22 (20.95)
Retro-orbital pain	36 (34.3)
Cough	17 (16.2)
Diarrhoea	21 (20)
Signs of Plasma Leakage	
Pleural effusion	34 (32.4)
Ascites	12 (11.4)
Oedema	14 (13.33)
Haematocrit increased	32 (30.5)
Warning/Red Flag Signs	
Abdominal Pain & tenderness	39 (37.14)
Vomiting	37 (35.2)
Hypotension	21 (20)
Dyspnoea	27 (25.7)
Hepatomegaly	22 (20.95)
Lethargy or restlessness	36 (34.3)
Oliguria	26 (24.8)
Haemorrhagic Manifestation (Any)	61 (58.1)
GI Bleed	20 (19.05)
Mucosal bleed	24 (22.9)
Spontaneous bleed from skin	17 (16.2)
Duration ICU Stay (days), median (IR)	2.0 (1.0-4.0)
Duration Hospital Stay (days), median (IR)	4.0 (2.0-10.5)
Time From symptom onset to hospitalization (days), median (IR)	3.0 (2.0-7.0)
WHO 2009 criteria at admission, n (%)	
Dengue with Warning Signs	39 (37.14)
Severe Dengue	66 (62.86)

SD, standard deviation; IR, interquartile range; ICU, intensive care unit; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WHO, World Health Organization; ICU, intensive care unit.

Among the warning signs, abdominal pain was seen in thirty nine patients (37.4%). Vomiting (35.2%) and restlessness (34.3%) were other common warning signs associated. 61 (58.1) patients had hemorrhagic manifestations, commonest being mucosal bleed (20.9%)

followed by gastrointestinal bleed (19.05%). Many patients had bleeding from multiple sites, among 24 patients with mucosal bleed, hematuria was present in 16 (15.24%), gum bleeding in 11 (10.5%) and epistaxis in 6 (5.7%) subjects. Laboratory parameters for total sample (like albumin, platelets, total leucocytes, hemoglobin hematocrit, AST, ALT and creatinine) are shown in Table 3. Sixty six (62.86%) dengue patients admitted in ICU suffered from severe dengue. Only 39 (37.14%) dengue positive patients with warning signs were admitted in ICU, mainly for associated complications or comorbidities.

Table 3: Laboratory parameters.

Laboratory values	Dengue patients n=105 (%)
Albumin (g/dl), mean ± SD	3.0 ± 0.8
Platelet count, mean ± SD	78500±54000
TLC, mean ± SD	7814±5916
Haematocrit, mean ± SD	36.4±7.3
Hemoglobin (g/dl), mean ± SD	11.8±3.2
Creatinine (g/dl), median (IR)	1.1 (0.7-1.5)
AST (U/L), median (IR)	62 (30-184)
ALT (U/L), median (IR)	47 (32-116)

SD, standard deviation; IR, interquartile range; ICU, intensive care unit; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 4: Intensive care therapeutics interventions.

Inpatient therapy	Dengue patients n=105 (%)
Vasopressor/ionotropic support before ICU, n (%)	8 (7.6)
Mechanical ventilation before ICU, n (%)	12 (11.43)
Mechanical ventilation during ICU, n (%)	36 (34.3)
Vasopressor/ionotropic support during ICU stay, n (%)	34 (32.4)
Hemodialysis, n (%)	18 (17.14)
PRBC transfusion, n (%)	19 (18.1)
Platelet transfusion, n (%)	56 (53.33)
FFP transfusion, n (%)	16 (15.23)
Septic shock during ICU stay, n (%)	28 (26.7)
Steroid use, n (%)	8 (7.6)
Antibiotic treatment, n (%)	84 (80)

Antibiotics were employed in 84 (80%) patients; 37 due to lower respiratory tract infections, 28 due to unspecific sepsis, 11 due to urinary infection, 8 due to upper respiratory tract infection. 8 (7.6%) were given steroids as an adjuvant to septic shock therapy during their ICU stay. Thirty four required vasopressor support (32.4%) and thirty six subjects required mechanical ventilation (34.3%) during ICU stay. 8 (7.6%) and 12 (11.43%) subjects were already on vasopressor and ventilator support respectively before ICU stay at hospitals studied.

DISCUSSION

Among studied dengue patients, 37.14% patients had abdominal pain, which was comparable to 38% reported by Sharma et al during 1996 dengue epidemic in Delhi.[4] This is attributed to early leak phase, hepatomegaly and serosal inflammation. Bleeding manifestation from various sites in present study (58.1%), were similar to finding of Horvath et al from Australia[5] and Sharma et al from India[4]; 63% and 69% respectively. Mucosal bleeding (22.9%) followed by gastrointestinal (19.05%) were the common sites of bleeding in present study. Similarly bleeding from various gastrointestinal sites is commonly reported in several studies.[4,6] Median AST & ALT were 62 and 47 U/L. Dengue virus-induced hepatocytes damage, shock, hypoxia are the postulated causes associated with transaminitis. No case of fulminant hepatic failure was encountered in our study. 20.95 % of studied subjects showed hepatomegaly which was slightly more than several previous studies.[4,7]

In this study, 84 patients received antibiotics, and 49 were treated for septic shock. 21 presented with septic shock whereas 28 developed sepsis during ICU stay. The clinical spectrum of severe sepsis or septic shock resembles that of severe dengue patients making it an extremely difficult choice to decide between bacterial sepsis and dengue with organ dysfunction.[8-10] The clinical dilemma stems from fact that delaying antibiotics increases the mortality risk in co-infected patients, indiscriminate rampant use may increase the resistance among microbes, causing multi-resistant infections. The risk benefit approach must be used at clinician's judgment to serve patient's best interest.

Similarly another point for debate is the use of steroids. Use of stress dose of corticosteroids, is recommended in Surviving sepsis protocols,[11] whereas its contraindicated in dengue fever shock 3. Subjects with sepsis and comorbid dengue infection pose a clinical challenge in terms of presentation and therapy. Some studies have tried to address this issue, [9,10] but further investigations are still needed in this direction. The management of fluid therapy in comorbid hypertension and chronic renal disease; makes dengue management extremely challenging.[3,12]

CONCLUSION

Understanding the complexities among presenting symptoms, associated clinical & laboratory profile of dengue can go a long way in early diagnosis, treatment & deciding need for critical care.

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