

## Dengue hemorrhagic fever—epidemic in Karachi, Pakistan (2006-2016) experience at a tertiary care centre

M. Rasheed Durrani, Muhammad Danial Iqbal, Nadia Munir, Anum Jamal

### Abstract

**Objective:** To document cases of Dengue hemorrhagic fever (DHF) seen in a major tertiary care center in Karachi in an epidemic of dengue fever.

**Methods:** A retrospective study of all patients admitted during the epidemics who fulfilled the criteria for DHF.

**Results:** A total of 1,602 patients during the epidemic period 2006 to 2016 were included. Mean age was 34 years. The overwhelming majority of the patients were males. Nearly all cases were seen during the months of July to November. Most of patient in our study survived. Despite developing DHF only 03 patients developed D.S.S and all of them died. Patients mostly presented with fever, headache, rashes, severe general weakness and bleeding from different sites.

**Conclusion:** Early diagnosis and treatment is essential. There are desperate need for effective steps to prevent and control the infection.

**Keywords:** Dengue virus, dengue fever, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), Epidemic, thrombocytopenia, Aedes Aegypti mosquito

### Introduction:

Dengue is one of the mosquito borne disease which is transmitted by Aedes aegypti mosquito or less frequently A albopictus. It is flavivirus.<sup>1</sup> Dengue virus is a single stranded RNA virus. There are 4 serotypes (1,2,3,4) which result in spectrum of disease with simple DF on one extreme and DSS on another. Flaviviridae and is most commonly found in tropical and subtropical countries especially in urban areas.<sup>2</sup> The primary vector is the Aedes Aegypti mosquito.<sup>3</sup> An estimated 50 to 100 million cases report worldwide every year and over 50,000 patients require admission to hospital. Ninety percent patients are under 15 years of age.<sup>4</sup> Travelers to the endemic area are at risk for infection. Dengue virus infection is a common cause of fever in travel-

ers to the endemic areas.<sup>5</sup> Dengue infection is now more prevalent than ever and this is due to the global climate changes. In spite of its low mortality rate, it is source of huge miseries to peoples and also of large burden on health care resources.<sup>6</sup> Its complications are Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The A.A mosquito is unique type of mosquito because in favourable conditions its life cycle is started with smaller size mosquito and they are produced at faster rate. Also one mosquito can bite several host (in one family mostly) for his dietary fulfillment on one occasion. So it is important to take measures during the outbreak. The virus infects the mosquito in its early life and when the mosquito bites a human, the disease is transferred to them. The fe-

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**Jinnah Post Graduate  
Medical Centre, Karachi**  
M.R.Durrani  
M.D. Iqbal  
N. Munir  
A. Jamal

**Correspondence:**  
Dr. M.Rasheed Durrani  
National Poison Centre,  
Medical Unit II, (Ward  
6), Jinnah Post Graduate  
Medical Centre, Karachi  
Cell:+92 3312913458  
Email: drrasheeddurrani@  
gmail.com

male mosquitoes are responsible for spread of disease to humans normally during day time and they are generally resistant to insecticides. They prefer indoor activity and are highly infective. This can be explained on two facts first they lay 100 eggs per feed every one to two weeks and second that it can transform in to small size mosquito with shorter half life but same virulence.<sup>7</sup>

Clinically presents as acute febrile illness to bleeding diathesis. It can ultimately decay to DSS in small number of patient. Spectrum of presentation range from simple anti-febrile illness to severe bleeding diathesis.

Bimodal (Saddle back) fever is diagnostic of DF other symptoms like severe musculo skeletal pain, headache rash and exhaustion are the main features.

There is no specific treatment and only symptomatic treatment can be offered. Preventive measure remain main stay.

For the past few years, urban areas of Pakistan have faced a severe outbreak of dengue fever, especially during the hot, humid and rainy summer season, when the mosquitoes are able to breed in large amounts. Uncontrolled population growth and urbanization and poor sanitary conditions have aggravated the situation. Over the past 2 to 3 years, innumerable deaths occurred in urban areas of Pakistan. Dengue fever presented as a mostly mild to moderate disease in this study cohort. Out-patient treatment was adequate for the majority of patients.<sup>10</sup>

Karachi in South Pakistan was also in the grip of a dengue fever epidemic in the last decade of the new millennium. However, unlike central Pakistan, the severity of the disease was mild and very few deaths occurred. This study documents the cases we studied admitted at the largest government hospital in Karachi during this period.<sup>11</sup>

A retrospective study comprising all patients admitted in Medical Unit-II Jinnah Postgraduate Medical Centre (JPMC), Karachi during the

period 2006 to 2016 who fulfilled the criteria for D.H.F.

Currently, the criteria for DHF include the following diagnostic components; fever, hemorrhagic manifestations, including skin bleeding (petechiae or ecchymosis), mucosal bleeding (epistaxis, gastrointestinal bleeding menorrhagia etc), thrombocytopenia (platelet count < 100,000 mm<sup>3</sup>), positive tourniquet test; and evidence of plasma leakage (pleural effusion, ascites, hemoconcentration, hypoproteinemia etc.).

The criteria for DSS includes criteria for DHF plus pulse pressure <20 mmHg and blood pressure <80 mmHg in patients below 50 years of age, and <90 mmHg in patients above 50 years of age.<sup>10</sup>

All patients were assigned grades according to the WHO grading system for DHF and DSS.

- Grade-1 Positive tourniquet test
- Grade-2 Spontaneous bleeding
- Grade-3\* Circulatory failure
- Grade-4\* Undetectable blood pressure and pulse

\*Grades 3 & 4 are associated with DSS.

All patients had regular complete blood counts (CBC) and hematocrit, along with liver and renal function tests, blood gases, dengue serology test, blood culture, x-rays chest and ultrasound etc. infection with dengue type 2 (DEN-2) virus in individuals previously infected with a different serotype of the virus is a major risk factor for dengue haemorrhagic fever and dengue shock syndrome.<sup>12</sup>

The prognosis of DF is generally good and worst symptoms usually last 1-2 weeks mostly recovery may take several months. It fatal in 1% of population. If DHF is not treated it can lead to mortality of 20-50% mortality.<sup>13,14</sup>

Table 1: Haematological manifestations of DHF in our study (1602)

S.No	Bleeding site*	No of patients	Percentage %
1.	Petechiae	486	30.33
2.	G.I. bleeding	888	55.43
3.	Gum bleeding	670	41.82
4.	Hemoptysis	430	26.84
5.	Hematuria	70	4.37
6.	Retinal bleeding	04	0.25
7.	Subconjunctival bleeding	638	39.82
8.	Vaginal bleeding	10	0.62
9.	Epistaxis	512	31.96
10.	Maena	49	03.05
11.	Ascites	12	00.74
12.	Pleural effusion	14	00.87

Individual patient may be bleeding from more than one site.

Table 2: Laboratory findings in our patients (n=1602)

S.No	Investigation	No. of Patients	Percentage
1.	WBC count	1602	100
2.	Platelet count >150 ( X 1000)	1602	100
	> 40 (X 1000)	1266	79.02
3.	Haemoglobin >12 G%	1497	93.44
	Hematocrit >30%	1497	93.44
	>38%	5	0.31
4.	S. ALT >40	414	25.84
5.	S. Creatinine >1.1mg/dl	43	2.68
6.	PT, APTT	987	42.88
7.	S. AST	85	5.30
8.	S. Albumin <3 mg/dl	41	2.55

Table 3: Demographic and clinical features

S.No	Clinical features	No of Patients	Percentage
1	Gender		
	Male	1414	88.26
	Female	188	11.73
2	Medium age (years)	34	-
3	Hospital stay 1-7 days	average-3 days	-
4	Dengue shock syndrome	3	0.18
5	Death	3	0.18
6	Concurrent bacteremia	117	7.30
7	Concurrent plasmodium vivax	85	5.30
8	Fever	1602	100
9	Bone pain	140	8.74
10	Abdominal pain	650	40.57
11	Hemoptysis	714	44.57
12	Cough	76	4.74
13	Skin rashes	1180	73.65
14	Arthralgia	86	5.37
15	Malgia	1020	63.67
16	Headache	920	57.43
17	General weakness	1478	92.26

## Material and method:

The study is carried out at JPMC, Karachi, a tertiary care centre in Karachi. Record is generated in Medical Unit.II from June 2006 to June 2016. Data is generated regarding presentation, biochemical and prognosis aspects. All patients were having fever and they all were positive for Dengue Serology (ELISA positive IgM).

### Inclusion Criteria:

- i. Febrile patient
- ii. Elisa positive patient.

### Exclusion Criteria:

- i. Other haemorrhagic diathesis
- ii. Enteric fever
- iii. Malaria
- iv. Laptospirosis.
- v. Alcoholic liver disease.

Data generated is recorded on SPSS. The record especially thrombocytopenia is described in percentage and averages.

## Results:

A total of 1602 patients who fulfilled the criteria for DHF and were admitted in our hospital during 2005 to 2016 were included in the study. Of these, 1441 (88.26%) were males, while 188 (11.73%) were females. Mean age was 34 years. Average duration of hospital stay was 03 days (range 1 to 7 days).

An interesting finding was that nearly all cases were seen during July and November; the disease was almost non-existent in the winter months.

Main symptoms included fever, headache, general weakness, rashes and bleeding from different sites. Pleural effusion and ascites were rarely seen. Out of 1,602 patients, only 03 (0.18%) developed DSS. These patients died and represented the only deaths during the study pe-

Table 4: Common features seen in our patients (1602)

S.No.	Clinical features	No of patients	Percentage
1	Fever	1602	100
2	Abdominal pain	650	40.57
3	Hemoptysis	714	44.57
4	Skin rashes	1180	73.65
5	Myalgia	1020	63.67
6	Headache	920	57.43
7	General weakness	1478	92.26

Table 5: Complications of DHF

Clinical feature	No of Patients	Percentage
Liver Dysfunction (ALT)	70	4.36
Significant Bleeding	1275	79.58
Altered Sensorium	5	0.31
Renal Dysfunction (>3mg/dl)	22	1.37
Respiratory Failure	9	0.56
ARDS	2	0.12
DIC	15	0.93

Table 6: Total number of patients (2006 - 2010): (n=1602)

2006		2007		2008		2009		2010	
Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
16	18	16	18	16	18	16	18	16	18

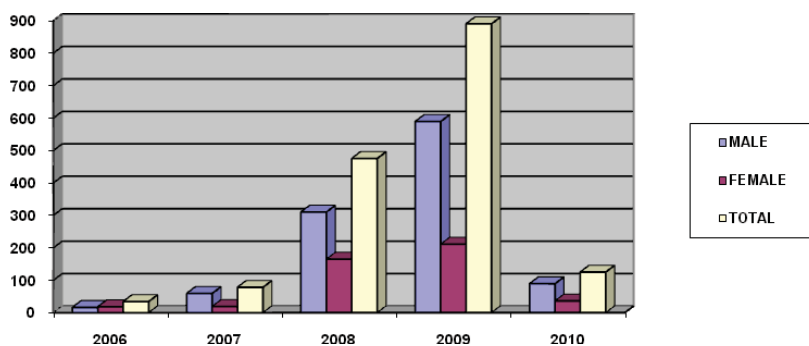


Figure 1: Total number of patients (n=1602)

riod. Mortality rate, therefore was extremely low(0.18%).

Laboratory investigations classically showed decreased leukocyte count in early stage in almost all patients. Similarly, thrombocytopenia was common to all and few patients. Platelet transfusion remained important part of treatment in patient with bleeding rashes and in patient with platelet count < 100,000 in our case. Platelet count was > 40,000 mm<sup>3</sup> in 79%

patients. Prothombin time (PT) and Activated Partial Thromboplastin Time [APTT] were deranged in 987 (48.22%), serum Albumin was low (<3mg/dl) in 570 patients (35.5%). Serum Alanine Amino Transferase (ALT) was raised in 704 (36%) patients. The details of our findings are shown in table 1 to 4. Total 1,602 patient enrolled in the study which is an anterospective. These all patient fulfill the inclusion criteria. Median age is 34 with 88.2% to 11.7% male to female ratio. As per criteria 100% patient had thrombocytopenia.

### Discussion:

Dengue fever is an infectious disease which one end of spectrum is symptomfree to severe complications of bleeding and multi-organ dysfunction and death. In general itself limiting febrile disease which during the very critical phase of defervescence may follow devastating course of severe disease with possible fatal outcome. Severe disease is situation of hemodynamic disturbances, increased vascular permeability hypovolemia, (DSS) hypotension and shock.<sup>15</sup> These have thrombocytopenia and platelet dysfunction these demographic data are describe by different studies. Average age is 34 which is also documented by contemporary 16 studies.<sup>16</sup>

In the present study there were 88.2% male and 11.7% which is comparable to study

Thrombocytopenia is seen in 100% of our study in which significant bleeding and rashes are seen 79% of patient and these patient had platelets less 40,000/uL. There finding close mentioned by contemporary studies.

Since D.H.F is associated with multi-organ dysfunction, it is associated with mild derangement in major organ of body which is self limiting with recovery disease.<sup>17,18</sup>

We examined all proven cases which has glaring features of thrombocytopenia. These features mention is great stress and source of apprehension and concern for people especially patients community and health department. This study also proves that thrombocytopenia is main con-

cern.<sup>19</sup>

DHF is an unpleasant and painful disease which still affects a large number of people around the world. In spite of improvements in management, deaths still occur. Dengue virus infection is prevalent in the tropical and subtropical regions, including South East Asia and South America. Infection with the dengue virus can easily transform into DHF and DSS and cause death.

An epidemic of dengue fever affected Karachi from 2001 to 2010 reaching a peak in 2006 – 2007. Most patients in our study were in their thirties and forties with a mean age of 34 years. These patients were usually students, factory workers and housewives. However, it was observed that adults were more commonly affected.

The viral serology has good or also been considered to have a role in causing severe DHF and DSS leading to a worse outcome accordingly. The epidemic in Karachi in spite of the high rate of DHF fortunately mild. But the epidemic in central Pakistan, especially other urban areas of low mortality rate for last three to four years has claim a heavy toll of human lives. Due to poverty, malnutrition, overcrowding, high population growth and poor hygienic conditions, especially in urban areas, there is a heavy burden of disease. There is a lack of facilities for prevention, tests and management of the disease. Peoples generally has no access to investigations and proper management. All these factors have compounded the increase in of the people suffering from not just dengue fever, but from other diseases as well. Also in our country, the high morbidity and mortality seen in DHF may be due to secondary or concurrent infections. Patients usually present late due to non-affordability. They only seek medical attention when symptoms become severe. But by that time, complications often already occurred. As mentioned above, the epidemic in Karachi was mild, otherwise it would almost have caused as much havoc as the one that struck central Pakistan. Early diagnosis and prompt, effective management are essential.

### Conclusion:

Fatal Dengue Hemorrhagic Fever or Dengue Shock Syndrome is rare in adults. A small amount of patients may develop DHF, DSS or intractable coagulopathy and this occurs despite treatment. Therefore, there is a need of close monitoring and due management, especially in the presence of recent development in the management of disease.

### Limitation:

Elisa kit is not easily available. This is hospital based study

**Conflict of interest:** None

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### Role and contribution of authors:

Dr. M. Rasheed Durrani, MCPS, FCPS Associate Professor of Medicine at Medical unit II Jinnah Post Graduate Medical Centre, Karachi, concieve the idea and wrote the article

Dr. Muhammad Danial Iqbal, MBBS, House Officer at Medical unit II Jinnah Post Graduate Medical Centre, Karachi, did data collection and computer work

Dr. Nadia Munir, MBBS, resident of medicine FCPS part II at Medical unit II Jinnah Post Graduate Medical Centre, Karachi, peer research

Dr. Anum Jamal, MBBS, resident of medicine FCPS part II at Medical unit II Jinnah Post Graduate Medical Centre, Karachi, peer research

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