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Original Research Article

An Observational assessment of Clinical and Hematological Profile of Patients with Dengue Fever

Chandra Shekhar Das[1], Chirag Agrawal[2], Rajeshwer Kumar Ranjan[3]

[1]Senior Resident, Department of General Medicine, Nalanda Medical College & Hospital, Patna, Bihar, India

[2]Junior Resident, Department of General Medicine, Nalanda Medical College & Hospital, Patna, Bihar, India

[3]Assistant Professor, Department of General Medicine, Medini Rai Medical College and Hospital, Palamu, Jharkhand, India

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Corresponding author: Dr. Chirag Agrawal
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Abstract

Objectives: To study the clinical and hematological profile of dengue fever cases presenting to a hospital.

Methods: A total of 450 patients were examined during a period of 6 months. Patients with fever and other signs of dengue with either positive NS1 antigen test or IgM or IgG antibody were included.

Results: NS1 was positive in 109 patients (24.2%), IgM antibody test was positive in 302 patients (67.1%) while in 33 patients (7.3%) the IgM antibody was negative, but they showed positivity for IgG antibody. Mild dehydration was noted in 164 patients of DF (40%) who were treated with oral rehydration therapy, while 51 cases of DFWS (12.4%) required intravenous fluid therapy. Twelve patients (2.9%) had severe dehydration requiring IV fluid resuscitation.

Conclusion: This study highlights the most common clinical and laboratory profiles of dengue viral infections that could alert physicians to the likelihood of dengue virus infections in the study area.

Keywords: Dengue, Clinical features, Hematological tests, Biochemical parameters.

Introduction

Dengue is a mosquito-borne arboviral disease and is a major global public health threat that is prevalent in tropical and sub-tropical regions of the world, mostly in urban and semi-urban areas [1]. The WHO estimates, more than 2.5 billion individuals live at risk of dengue transmission in more than 100 countries and approximately 50-100 million individuals have infected with dengue annually[2]. of these, 500,000 severe dengue cases are diagnosed each year resulting in 24,000 deaths per year [3–6]. Dengue is endemic in the WHO regions of Africa, the Americas, the Eastern Mediterranean, South-East Asia, and the Western Pacific regions and the Caribbean [7]. In the recent decades, the global

incidence of dengue virus (DENV) infection has increased with increasing geographic expansion to new countries [8].

In 2005, the World Health Assembly, through WHA Resolution 58.3, in a review of the International Health Regulation (IHR), included dengue fever as an emergent public health disease, with implications for health safety due to the spread of the epidemic beyond national boundaries [9].

The clinical presentation of DF is triphasic with the febrile phase typically characterized by high fever, headache, myalgia, body ache, vomiting, joint pain, transient rash and mild bleeding manifestations such as petichiae, ecchymosis at pressure sites and bleeding from venipunctures [10] In the next critical phase there is a heightened risk of progression of the patient to severe dengue which is defined by presence of plasma leakage that may lead to shock and/or fluid accumulation such as ascites or pleural effusion with or without respiratory distress, severe bleeding, and/or severe organ impairment. [11] The risk of severe bleeding in dengue is much higher with a secondary infection and is seen in about 2-4% of cases having secondary infection. [12-14]

In this study we evaluated patients with dengue presenting to the outpatient or emergency departments of a tertiary care hospital in an urban setting for their clinical and hematological profile, management and outcomes.

Material and Methods:

This was an observational prospective study conducted at a Nmch, Patna, Bihar over a period of 06 months during the dengue fever seasons. Patients presenting to the emergency department, outpatient department (OPD) or pediatric OPD with complaints of fever and clinical features of dengue with positive NS1 antigen test or dengue antibody serology IgM or IgG or both were included in the study.

Institutional ethical committee clearance was obtained and written informed consent was taken from all patients.

Methodology:

Age, gender, clinical presentation, duration of fever, dehydration, hemodynamic status, urine output, hepatomegaly, ascites, pleural effusion, presence of petechiae, positive tourniquet test, other bleeding manifestations, hematocrit and platelet count were recorded at presentation. Increased hematocrit was taken as a value > 45% while thrombocytopenia was defined a platelet count < 1 lac/cu.mm. Patients were categorized as dengue fever without warning signs (DF), dengue fever with warning signs (DFWS), or severe dengue (SD) based on presence of abdominal pain, vomiting, pleural effusion, ascites, lethargy and restlessness, hepatomegaly, severe bleeding, respiratory distress, and other organ involvement as per the World Health Organization (WHO) classification. [11]

Diagnosis of dengue was made on the basis of NS1 antigen positivity and/or detection of IgM and IgG antibodies using a commercially available one-step immunochromographic assay (SD Bioline Dengue Duo, Alere, Germany). NS1 antigen test was done in all patients with clinical features suggestive of dengue infection presenting within 5 days of onset of the symptoms. In patients with clinical features suggestive of dengue infection who presented beyond 5 days of onset of symptoms IgM and IgG antibody test was done. All patients with bleeding manifestations, thrombocytopenia with platelet count < 30,000 cu/mm were admitted. All pregnant patients and infants irrespective of their platelet counts were admitted.

Paracetamol was given for fever and pain relief with complete avoidance of any other non-steroidal analgesic (NSAID). Patients

were treated with oral rehydration therapy, intravenous (IV) fluid therapy, packed red blood cell (PRBC) transfusion, platelet concentrates depending upon the clinical condition. Patients with DF were managed with oral rehydration salt (ORS) solution, oral paracetamol and advised review every 3 days.

Patients with warning signs including a rising hematocrit (>20% increase over baseline) and falling platelet count were managed with 0.9% Normal Saline (NS) infusion started at 5-7 ml/kg/hour for 1-2 hours, 3-5 ml/kg/hour for the next 2-4 hours and finally 2-3 ml/kg/hour maintaining the urine output at 0.5-1 ml/kg/hour and monitoring the hematocrit for rise. Patients with SD with severe plasma leakage or severe bleeding were given fluid resuscitation with IV NS bolus of 20 ml/kg over 1-2 hours, repeated under close supervision. The intake-output charting was done meticulously realizing fully that the input to output ratio was not adequate for judging fluid requirement during this period. Fluid resuscitation was considered adequate with decreasing tachycardia, improving blood pressure, pulse volume, warm extremities, capillary refill time (CRT) < 2 seconds, urine output ≥ 0.5 ml/kg/hour, decreasing metabolic acidosis and normal sensorium. Patients were discharged once there were no signs of dehydration, adequate urine output and platelet count > 50,000 cu/mm.

Demographic and clinical characteristics were described as proportions. Data was analyzed using SPSS 17.

Results:

There were 390 adult patients and 60 children who were diagnosed to have the various dengue syndromes over the 6-month period of observation. Of the 390 adult patients, 210 were males and 240 were females. There were 36 boys and 24 girls in the pediatric population. Patients' age varied from 6 months to 77 years.

NS1 was positive in 109 patients (24.2%), IgM antibody test was positive in 302 patients (67.1%) while in 33 patients (7.3%) the IgM antibody was negative, but they showed positivity for IgG antibody. The commonest presenting complaint was fever (99.1%) with severe arthralgia and myalgia (98.2%). Other symptoms were loose motions (15.1%), rashes (54.6%), vomiting (13.1%), breathlessness (2.8%), headache (64.2%), retro-orbital pain (71.3%) and abdominal pain (13.7%). (Table 1)

Mild dehydration was noted in 164 patients of DF (40%) who were treated with oral rehydration therapy, while 51 cases of DFWS (12.4%) required intravenous fluid therapy. Twelve patients (2.9%) had severe dehydration requiring IV fluid resuscitation. (Table 2).

Thrombocytopenia was seen in 372 (82.6%) patients while increased hematocrit was seen in 78 (17.3%) patients at the time of presentation (Table 1).

Bleeding manifestations were seen in 32 patients of DFWS. Out of these 21 patients had petechiae, 6 patients had epistaxis, 1 had hematemesis and 3 had melena. (Table 3).

Platelet transfusions were given in all 36 cases. PRBC transfusion was required in 3 patients with DFWS with hemoglobin < 8.5 gm/dl and 10 patients with SD with severe bleeding.

Table 1: Demographic and clinical characteristics of patients enrolled in the study

Age group	N	%
< 1 year	02	0.4
1-5 years	08	1.7
6-12 years	35	7.7

13-18 years	78	17.3
19-45 years	296	65.7
46-75 years	51	11.3
> 75 years	30	6.6
Dengue fever		
Primary	408	90.6
Secondary	42	9.3
Clinical features		
Fever	446	99.1
Body ache	442	98.2
Headache	289	64.2
Retro-orbital pain	321	71.3
Abdominal pain	62	13.7
Loose stools	68	15.1
Vomiting	59	13.1
Skin rash	246	54.6
Breathlessness	13	2.8
Bleeding manifestations	50	11.1
Dehydration at presentation		
No dehydration	230	51.1
Mild	134	29.7
Moderate	56	12.4
Severe	12	2.6
Shock	9	2.0
Clinical syndrome		
DF without warning signs	388	86.2
DF with warning signs	43	9.5
SD with severe plasma leak	9	2
SD with severe bleeding	10	2.2
Diagnosis, n Diagnosis		
NS1 antigen test positive	109	24.2
IgM positive ± IgG positive	302	67.1
IgG positive only	33	7.3
NS1 negative & IgM positive	6	1.3
Hematological findings		
Thrombocytopenia	372	82.6
Increased hematocrit	78	17.3

Table 2: Treatment and outcome details of the admitted patients.

Treatment and outcome	N	%
Treatment, n = 450		
OPD	360	80
IP	90	20
Duration of hospitalization, n = 90		
< 7 days	10	11.1
7 – 14 days	52	57.7
> 14 days	28	31.1

Fluid therapy, n = 410		
Oral rehydration	164	40
IV fluid therapy	51	12.4
IV fluid resuscitation	12	2.9
Not required	223	54.3
Blood component, n = 450		
Platelet concentrate	60	13.3
Packed RBC	21	4.6
Fresh whole blood	0	0
Mortality, n = 450		
SD with severe bleeding	3	0.6
SD with severe plasma leak	5	1.1
DF with/without warning signs	0	0

DF = Dengue fever; IP = In-patient; OPD = Outpatient department; SD = Severe dengue; RBC = Red blood cell.

Table 3: Correlation of thrombocytopenia with bleeding manifestation and number of cases in Dengue fever patients (n=32)

Bleeding manifestation	**Platelet count (per cu.mm)**						
	< 10,000	11-20,000	21-30,000	31-40,000	41-50,000	51000-1 lac	>1 lac
Epistaxis	5	1	0	0	0	0	0
Melena	0	3	0	0	0	0	0
Hematemesis	1	0	0	0	0	0	0
Petechiae	2	18	1	0	0	0	0
Total number with platelet count, n (%)	8 (25%)	22 (68.7)	1 (3.1)	0	0	0	0

Table 4: Duration of hospitalization with different indications

Indication for admission	**Number of cases, n = 90**	**Duration of hospitalization**		
		< 7 days	**7 – 14 days**	**> 14 days**
SD with severe bleeding	11	3*****	0	7
SD with severe plasma leak	6	3#	0	3
DF with bleeding	41	0	27	11
DF with other warning signs	16	1	9	5
Pregnancy	6	0	3	3
Pediatric age group	10	5	8	0

Discussion:

In recent decades, the global prevalence of dengue has increased dramatically due to the limitation of currently available control strategies, such as vaccines and pesticides [15,16]. Hence early diagnosis and proper medical management are of prime importance. As dengue is a recently known problem in Ethiopia [17,18] the knowledge regarding its clinical presentations along with laboratory tests is vital for patient management.

The frequency of dengue fever in the study was higher in the group aged 15 years old or over. These results are similar to those of

Rocha & Tauil [19] in an epidemiological study conducted in Manaus, AM. The correlation between gender and the clinical form showed a significant difference for SD, with a predominance of women, a result that is in disagreement with the literature. [20, 21]

Appropriate timing of NS1 antigen test is important. We performed NS1 antigen testing in patients presenting within 5 days of onset of symptoms in order to reliably identify cases of primary dengue infection as well as secondary dengue infection also in which the NS1 antigen test remains positive for a shorter time frame.[22] There were 6 (1.3%) patients in whom the NS1 antigen test turned out to be negative but were later confirmed to be dengue IgM antibody test positive. We used the one-step immunochromographic assay for IgM and IgG antibody testing which identifies acute as well as past dengue infections with excellent sensitivity and specificity.[23]

The use of NS1 antigen test, IgM and IgG antibody testing for diagnosis of dengue infection can show false positivity due to cross reaction with other flaviviral infections.[24] We did not use real-time polymerase chain reaction (RT-PCR) for viral RNA detection for diagnosis due to feasibility issues and these are the limitations of our study.

Conclusion:

Our findings show that majority of DF cases can be managed on OPD basis, NS1 antigen test maybe false negative if done too early in the course of the illness, patients with DFWS require admission of up to 7-14 days, thrombocytopenia is common but very few patients will require platelet transfusion.

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