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A hospital-based study to investigate the clinical and haematological characteristics of patients with dengue fever

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Abstract
Aim: The aim of the present study was to assess the clinical and hematological profile of dengue fever cases presenting to a tertiary care hospital.
Methods: This was an observational prospective study conducted at a tertiary care hospital over a period of 6 months. Patients presenting to the emergency department, outpatient departments of Medicine and Pediatrics 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. 200 patients were included in the study.
Results: Out of the total 200 patients, there were 110 men and 90 female. Out of the 90 female patients, four were pregnancy positive. The most frequent reported symptom was fever (99%) accompanied by intense joint pain and muscle pain (96%). The other symptoms reported were diarrhea (13%), skin eruptions (45%), emesis (10%), dyspnea (1.6%), cephalalgia (48%), pain behind the eyes (65%), and stomach discomfort (12%). 72 patients with DF (36%) had mild dehydration and were managed with oral rehydration treatment, whereas 20 instances with DFWS (10%) need IV fluid therapy. Out of the total 200 patients, six individuals (3%) had severe dehydration that required intravenous fluid resuscitation, petechiae in 12 cases, epistaxis in 2 cases, hematemesis in 1 case, and melena in 1 case. 5 patients had a platelet count below 10,000/cu.mm, 10 patients had a platelet count ranging from 11,000 to 20,000/cu.mm, and in 1 patient the platelet count was between 21,000 and 30,000/cu.mm.
Conclusion: The results of our study indicate that most cases of dengue fever (DF) can be effectively treated on an outpatient basis. It is important to note that the NS1 antigen test may yield false negative results if performed too early in the course of the illness. Patients with dengue fever with warning signs (DFWS) may need to be admitted to the hospital for a period of 7-14 days. While thrombocytopenia (low platelet count) is a common occurrence, only limited number of patients will require platelet transfusion. On average, patients with DFWS and severe dengue (SD) will require 3 and 12 units of platelet concentrates, respectively. Spontaneous dissection (SD) accompanied by plasma leakage and bleeding is associated with a significant risk of death.

Keywords: Dengue fever, dengue hemorrhagic fever, dengue shock syndrome, thrombocytopenia

Introduction
Dengue is a short-term, quickly spreading disease that lasts around 5-7 days. It is characterized by symptoms such as fever, weakness, headache, muscle pain, skin rash, swollen lymph nodes, and low white blood cell count. The disease is caused by four different types of dengue viruses that are closely related but distinct from each other. These viruses are transmitted to humans through mosquito bites, primarily by mosquitoes of the Aedes genus, including Aedes aegypti, Aedes albopictus, and Aedes polynesiensis. It manifests both in epidemic and sporadic occurrences in India, Japan, West Africa, and Southeast Asia [1].
Approximately 50 million cases of dengue occur globally each year, with almost 2.5 billion people, or 40% of the world's population in tropical and subtropical nations, being at risk. The documented mortality rate in India is estimated to be between 3 and 5% [2, 3]. Many underdeveloped nations have widespread outbreaks of febrile diseases such as typhoid, measles, leptospirosis, and severe acute respiratory distress syndrome. These infections might

be mistaken for dengue because they share similar clinical characteristics [4]. Human transmission of the virus occurs by the bite of an infected female Aedes aegypti mosquito carrying one of four serotypes of the virus. The primary carrier is this urban-adapted domestic mosquito [5].

The time of transmission from people to mosquitoes starts one day before to the onset of fever and extends until the sixth day of sickness, which corresponds to the viremia phase. Following a bite from a female mosquito during the viremia phase, the viral replication process (known as extrinsic incubation) commences in the vector during a span of eight to twelve days. The incubation time in humans varies from 3 to 15 days, with an average of 5 days [5, 6]. According to the World Health Organisation (WHO), over 50 million cases of dengue fever occur each year globally, and 2.5 billion people reside in regions with a high risk of infection [7]. In 2005, the World Health Assembly, in WHA Resolution 58.3, recognized dengue fever as a newly emerging public health illness. This decision was made during a review of the International Health Regulation (IHR). The inclusion of dengue fever as an emergent disease highlights its potential to spread over national borders, posing risks to global health safety [8].

The predominant clinical manifestation of dengue fever (DF) is an acute febrile viral illness characterized by headaches, bone, joint, and muscle pains, rash, and leucopenia. It is often referred to as break bone fever because of the intense bone aches it causes [9]. Dengue hemorrhagic fever (DHF) is distinguished by four primary clinical manifestations: a high fever of significant intensity, bleeding occurrences, often accompanied by an enlarged liver, and, in severe instances, indications of inadequate blood circulation. The occurrence of significant plasma leakage in these individuals might result in hypovolemic shock and circulatory failure. The medical term for this condition is dengue shock syndrome (DSS), which has the potential to result in fatality [10]. Theclinical diagnosis of early dengue patients, is difficult due to the presence of nonspecific symptoms such as fever, headache, and myalgia. Given the presence of other infectious illnesses with comparable clinical characteristics, a blend of clinical and laboratory indicators in cases of sudden fever might serve as diagnostic markers for early detection of dengue infection.

The objective of the current investigation was to evaluate the clinical and haematological characteristics of patients with dengue fever who sought medical attention at a hospital.

Materials and Methods

This was an observational prospective study conducted at a tertiary care hospital over a period of 6 months (June-December) in the year 2023.

Patients presenting to the emergency department, outpatient department of Medicine & Pediatrics in coordination with central laboratory of the hospital. All the patients 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. 200 patients were included in the study.

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 immunochromatographic assay (SD Bioline Dengue Duo, Alere, Germany).

All individuals exhibiting clinical symptoms indicative of dengue infection within 5 days of symptom onset underwent an NS1 antigen test. IgM and IgG antibody tests were performed on individuals exhibiting clinical characteristics indicative of dengue infection, who sought medical attention more than 5 days after the beginning of symptoms. Admission was granted to all patients exhibiting bleeding symptoms and thrombocytopenia, with a platelet count below 30,000 cu/mm. All pregnant patients and babies, regardless of their platelet levels, were hospitalized. The primary focus of treatment included ensuring enough hydration and promptly identifying instances of plasma loss and shock. The patients were managed rigorously in accordance with the clinical care guidelines for dengue. A total of 5 Paracetamol tablets were administered to alleviate fever and provide pain relief, while strictly refraining from the use of any other non-steroidal analgesic (NSAID). Patients received oral rehydration treatment, intravenous (IV) fluid therapy, packed red blood cell (PRBC) transfusion, and platelet concentrates as needed based on their clinical status. Patients diagnosed with DF were treated with oral rehydration salt (ORS) solution and oral paracetamol. They were also instructed to schedule a follow-up appointment every 3 days. Patients exhibiting warning indications such as a significant rise (>20%) in hematocrit levels compared to their baseline, as well as a decrease in platelet count, were treated with a 0.9% solution. The administration of Normal Saline (NS) begins at a rate of 5-7 ml per kilogramme per hour for 1-2 hours, followed by a rate of 3-5 ml per kilogramme per hour for the subsequent 2-4 hours. Finally, the rate is adjusted to 2-3 ml per kilogramme per hour to maintain a urine output of 0.5-1 ml per kilogram per hour. Throughout this process, the hematocrit is monitored for any increase. If, despite this, the hematocrit continues to exhibit an upward trajectory, a bolus of normal saline (NS) measuring 10 ml per kilogramme of body weight is administered, followed by a further infusion of NS as previously indicated. Intravenous fluids were administered until the patient's clinical condition reached a stable state and their oral intake was sufficient. Patients diagnosed with SD and experiencing significant plasma leakage or excessive bleeding were given fluid resuscitation by an intravenous normal saline bolus of 20 ml per kilogramme of body weight, delivered over a period of 1-2 hours. This procedure was repeated while closely monitoring the patient's condition.

The intake-output charting was monitored with great attention, acknowledging that the input to output ratio was insufficient for accurately assessing fluid needs at this time. The fluid resuscitation was deemed sufficient based on the following criteria: lowering heart rate, increasing blood pressure, increased pulse volume, warm extremities, capillary

refill time (CRT) less than 2 seconds, urine output of at least 0.5 ml/kg/hour, reducing metabolic acidosis, and normal mental state. Patients were released upon exhibiting absence of dehydration, sufficient urine production, and a platelet count above 50,000 cubic millimeters. Administration of oxygen treatment via a face mask was provided as needed. Patients who exhibited clinical bleeding and had substantial blood loss (6-8 ml/kg) or showed signs of hemolysis received a PRBC transfusion. Approval was acquired from the institutional ethics committee and signed informed permission was collected from all patients. The demographic and clinical variables were expressed as proportions. The data obtained from this study was spread in a excel sheet. The analysis was expressed in form of percentage and chi square was used wherever feasible. Data was analyzed using SPSS 17.

Results

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

Patients' characteristic	N	%
Adult Gender Distribution		
Males	110	55
Females	90	45
Age Groups in years		
< 1 year	2	1
1-5 years	4	2
6-12 years	20	10
13-18 years	24	12
19-45 years	110	55
46-75 years	22	11
> 75 years	18	9
Dengue Fever		
Primary	180	90
Secondary	20	10
Clinical features	198	99
Fever	192	96
Body ache Headache	96	48
Retro-orbital pain	130	65
Abdominal pain	24	12
Loose stools	26	13
Vomiting	20	10
Skin rash	90	45
Breathlessness	4	2
Bleeding manifestations	20	10
Dehydration at presentation		
No dehydration	104	52
Mild	72	36
Moderate	20	10
Severe	2	1
Shock	2	1
Clinical Syndrome		
DF without warning signs	170	85
DF with warning signs	20	10
SD with severe plasma leak	4	2
SD with severe bleeding	6	3
Diagnosis		
NS1 antigen test positive	48	24
IgM positive ± IgG positive	132	66
IgG positive only	14	7
NS1negative & IgM positive	6	3

Of the 200 patients, 110 were males and 90 were females. Among the females 4 patients were pregnant. The commonest presenting complaint was fever (99%) with severe arthralgia and myalgia (96%). Other symptoms were loose motions (13%), rashes (45%), vomiting (10%), breathlessness (1.6%), headache (48%), retro- orbital pain (65%) and abdominal pain (12%). Breathlessness was seen in 4 patients (2%) all of whom had serositis. DF was diagnosed in 170 cases (85%), DFWS in 20 cases (10%), SD with severe bleeding in 6 (3%) and SD with severe plasma leakage in 4 cases (2%).

Table 2: Treatment and outcome details of the admitted patients

Treatment and Outcome	N	%
Treatment		
OP	160	80
DIP	40	20
Duration of hospitalization		

<7 days	30	15
7 –14 days	110	55
>14 days	60	30
Fluid therapy		
Oral	72	36
Rehydration IV fluid therapy	20	10
IV fluid	10	5
Resuscitation Not required	98	49
Blood component	20	10
Platelet concentrate Packed RBC	6	3
Fresh whole blood	0	0
Mortality		
SD with severe bleeding	1	0.5
SD with severe plasma leak	2	1
DF with/without warning signs	0	0

160 cases (80%) were treated as outpatients while 40 patients (20%) required admission. Mild dehydration was noted in 72 patients of DF (36%) who were treated with oral rehydration therapy, while 20 cases of DFWS (10%) required intravenous fluid therapy. Six patients (3%) had severe dehydration requiring IV fluid resuscitation.

Table 3: Correlation of thrombocytopenia with bleeding manifestation and number of cases in Dengue fever patients

Bleeding manifestation	Platelet count (percu.mm)						
	<10,000	**11-20,000**	**21-30,000**	**31-40,000**	**41-50,000**	**51-1 lac**	**>1 lac**
Epistaxis	1	1	0	0	0	0	0
Melena	0	1	0	0	0	0	0
Hematemesis	1	0	0	0	0	0	0
Petechiae	3	8	1	0	0	0	0
Total number with platelet count <30,000	5	10	1	0	0	0	0

Out of these 12 patients all the 12 had petechiae, 2 patients had epistaxis, 1 had hematemesis and 1 had melena. Amongst these, 5 patients had platelet count < 10,000/cu.mm, 10 patients had platelet count was between 11-20,000/cu.mm while in 1 patient the platelet count was between 21-30,000/cu mm. Platelet transfusions were given in all 16 cases.

Discussion

Dengue is a viral illness caused by the dengue virus, which is part of the flaviviridae family. It is a self-limited and acute systemic infection.The prevalence of dengue fever (DF) has been steadily rising in recent years, making it a significant worldwide issue [13]. Dengue fever with warning symptoms (DFWS) and severe dengue (SD) with significant plasma leakage, excessive bleeding, or serious organ involvement have become significant public health concerns in metropolitan settings. This phenomenon may be attributed to the movement of people to cities, which leads to excessive population density and the creation of infrastructure in these regions, creating ideal conditions for the vector to breed without obstacles [14]. There is a temporary increase in the number of patients, particularly from May to September, that are seen in the emergency and outpatient departments. This puts further strain on an already overwhelmed system, particularly in terms of personnel, laboratory resources, and admissions to acute wards. The clinical manifestation of DF follows a three-phase pattern. The febrile phase is often marked by elevated body temperature, intense headache, muscle pain, general discomfort, vomiting, joint pain, temporary skin rash, and modest bleeding symptoms such as small red spots, bruising at pressure points, and bleeding from needle punctures [15].

Out of the total of 200 patients, 110 were male and 90 were female. Out of the female patients, four of them were pregnant. Deshwal *et al* [16] and Vibha *et al* [17] also reported a higher proportion of male patients in their trials, with 72.8% and 70% male patients respectively. The most often reported symptom was fever (99%) accompanied by severe joint pain and muscle pain (96%). The other symptoms reported include diarrhoea (13%), skin eruptions (45%), emesis (10%), dyspnea (1.6%), cephalalgia (48%), retro-orbital discomfort (65%), and stomach discomfort (12%). Four individuals (2%) exhibited breathlessness, all of whom presented with serositis. The results were similar to those reported by others, however there were minor differences in the frequency of the symptoms. Our investigation observed itching, particularly in the palms and soles, in 01% of patients, which aligns with the findings of a similar study conducted by Deshwal *et al* [16]. Out of the total number of cases, 16 individuals were diagnosed with DF (dengue fever), accounting for 85% of the cases. DFWS (dengue fever with warning signs) was seen in 20 instances, making up 10% of the cases. Additionally, 6 cases (3%) exhibited SD (severe dengue) with severe bleeding, while 4 cases (2%) showed SD with significant plasma leakage. Out of the total number of cases, 80% were managed as outpatients, while the remaining 20% need hospital hospitalization.

72 patients with DF (36%) had mild dehydration and were managed with oral rehydration treatment, whereas 20 instances with DFWS (10%) need IV fluid therapy. Out of the total number of patients, six individuals (3%) had severe dehydration that required intravenous fluid resuscitation. Among the 12 patients, petechiae were seen in 12 cases, epistaxis in 2 cases, hematemesis in 1 case, and melena in 1 case. Out of them, 5 patients had a platelet count below 10,000/cu.mm, 10 patients had a platelet count ranging from 11,000 to 20,000/cu.mm, and in 1 patient the platelet count was between 21,000 and 30,000/cu.mm. Platelet transfusions were administered to all 16 instances. Several research

conducted in different regions of the nation have observed notable variations in the occurrence of unusual symptoms such as neurological indications or serositis [18, 19]. Some studies have documented considerable discrepancies, while others have found identical results [20]. These variations might be attributed to the presence of additional pathogens during infection or subsequent infections with different types of dengue virus [21]. The incidence of dengue in our nation is significantly underestimated [22]. According to the World Health Organization (WHO), over 500,000 individuals are hospitalized with dengue fever in our nation every year, and India represents approximately 20% of all cases in the south-east Asian region (SEAR) [23].

Conclusion

The results of our study indicate that most cases of DF can be effectively treated on an outpatient basis. It is important to note that the NS1 antigen test may yield a false negative result if performed too early in the course of the illness. Patients with DFWS (Dengue Fever with Warning Signs) typically need to be admitted to the hospital for a period of 7-14 days. While thrombocytopenia (low platelet count) is a common occurrence, only a small number of patients will require platelet transfusion. On average, patients with DFWS and SD (Severe Dengue) will require 3 and 12 units of platelet concentrates, respectively. Severe dengue (SD) accompanied by plasma leakage and bleeding is associated with a significant risk of death.

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