

Clinico-Heamatological Study of Dengue in Adults and the Significance of Total Leukocyte Count in Management of Dengue

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ABSTRACT

Background: *Dengue is the most rapidly spreading mosquito borne viral disease in the world. There is an increase in incidence of dengue in adult population in South Asian countries in recent years.*

Objective: *To study the pattern of dengue in adults and the significance of total leukocyte count in assessing the clinical course of dengue.*

Materials & Methods: *All adult patients admitted with fever and features suggestive of dengue infection were included in the study. Serological testing for dengue virus specific antigen and antibody was done for the diagnosis of dengue fever. The demographic data, clinical features, hematological and biochemical parameters were collected. The World Health Organization classification and case definitions 2009 was used to categorize the dengue patients. The variable pattern of the disease and the importance of total leukocyte count in the monitoring of the natural course of the illness were studied.*

Results: *Of the total 169 patients admitted with suspected dengue infection, 74 were diagnosed with dengue serologically. Of these 74 patients, 31(41.9%) had primary dengue infection and 43 (58.1%) had secondary dengue infection. Number of patients who had probable dengue, dengue +warning signs and severe dengue were 39 (52.7%), 24 (32.4%) and 11 (14.9%) respectively. Petechiae were seen in 22 (29.7%) patients, tender hepatomegaly in 18 (24.3%). A very low total leukocyte count and a very low*

platelet count along with a drop in haematocrit were seen in 11 (14.9%) patients. The leukopenia preceded the fall in platelet count by 24 ± 12 hours and the recovery of platelet count was also preceded by the recovery of total leukocyte count by 24 ± 12 hours.

Conclusion: *This study highlights the pattern and the natural course of dengue in South India. It is evident that the total leukocyte count plays a significant role in predicting the natural course of the dengue in both critical as well as the recovery phase of the illness. There is increased association of severe leukopenia with severe thrombocytopenia and severe dengue.*

Keywords: *Dengue, leukocyte count, platelet count, haematocrit*

INTRODUCTION

Dengue is the most rapidly spreading mosquito borne viral disease in the world ^[1]. The incidence of dengue has increased by 30 fold over the last 50 years ^[1]. There is an increasing incidence of dengue in adult population in South Asian, South-East Asian and Latin American countries in recent years ^{[2],[3],[4]}. The dengue virus (DEN) comprises four distinct serotypes ^[1] (DEN 1-4) and DEN-3 is frequently associated with severe disease ^[2]. Majority of dengue patients have a mild self-limiting illness and a few progress to a severe disease ^[1]. Intravenous rehydration is the treatment of choice, which can reduce the mortality in dengue to less than 1% of severe cases ^[1]. Identifying the group of dengue patients progressing from mild to severe illness is difficult, but this is important as early and appropriate treatment may reduce morbidity and mortality in dengue fever. The earliest hematological abnormality is a progressive decline in total leukocyte count and it alerts a high probability of dengue infection ^[7]. Progressive leukopenia followed by a rapid decrease in platelet count ^{[1],[7]} usually precedes plasma leakage. Total leukocyte count usually starts to recover soon after the

febrile phase of dengue and it precedes the recovery of platelet count ^[1]. Monitoring the total leukocyte count will help the treating physician about the course of platelet count, plasma leakage and bleeding tendencies, which in turn will help in identifying the patients progressing into the severe form of dengue.

MATERIALS AND METHODS

The study was done at the time of an outbreak of dengue in Tamilnadu and Puducherry, India. The study was done after obtaining proper ethics committee clearance from the Institutional ethics committee. All the patients of age > 18 years, who presented with fever and features suggestive of dengue were included in the study. The demographic data, detailed history, clinical features, complete blood count, liver function test, renal function test were recorded on admission and were repeated serially as required till discharge. Diagnosis of dengue was made by detection of dengue virus specific NS 1 antigen and IgM, IgG antibody using ELISA method ^{[1],[8],[9]}. The World Health Organisation classification and case definitions, 2009 was used

to categorize the patients as having either Dengue \pm warning signs and severe dengue ^[1]. Patients with detectable dengue virus specific IgM antibody was diagnosed with primary dengue infection and patients with both IgM and IgG dengue antibodies was diagnosed with secondary dengue ^{[1][8][9]} infection. The clinical presentation was correlated with the hematological and biochemical parameters at various phases ^[1] of dengue fever, namely febrile, critical and the recovery phase.

RESULTS

Of the total 169 patients admitted with suspected dengue infection, 74 were diagnosed with dengue serologically. Of these 41(55.4%) were males and 33 (45%) were females. The age of the patients ranged from 19-59 years. All the 74 patients had fever with a temperature between 99°F-103.4 °F during the initial 1-6 days of the illness. Malaise/generalized body pain was the commonest symptom present in 56 (75.7%) patients (Table/Figure No.1). Of the total 74 patients, 31(41.9%) had primary dengue infection and 43 (58.1%) had secondary dengue infection. Number of patients who had probable dengue, dengue +warning signs and severe dengue were 39 (52.7%), 24 (32.4%) and 11 (14.9%) respectively. Petechiae was seen in 22 (29.7%) patients, respiratory distress in 05 (06.7%), gall bladder edema in ultrasonogram in 32 (43.2%) patients (Table/Figure No.1). Total leucocyte count of less than 4000/mm³ was seen in 60 (80.0%) patients and a platelet count < 100,000/mm³ was seen in 52 (70.2%) patients. A

very low platelet count less than 20000/mm³ was seen in 11(14.9%) patients (Table/Figure No.2). Renal function test was normal in all the patients. Of the 63 patients diagnosed to have probable dengue and dengue+ warning signs, 42 (66.6%) presented with hemoconcentration along with thrombocytopenia and leukopenia (Table/Figure No.3) and 11(14.9%) patients with severe dengue had a drop in haematocrit along with a very low total leukocyte count and a very low platelet count (Table/Figure No.4) . These 11 patients also had clinical features of severe dengue (Table/Figure No.1).

DISCUSSION

The study done at the time of outbreak of dengue in October to January coincided with the monsoon and post monsoon season ^{[3][10][12]}. All the patients in our study, had a temperature between 99°F-103.4 °F during the initial 1-6 days of the illness ^{[1-2][11]}. During this febrile phase most of the patients had generalized body ache, malaise, arthralgia, headache and skin rash ^{[1][2][11][13]}. All the patients presented with variable grades of leukopenia and thrombocytopenia ^{[5][13-17]}. Patients who presented with features suggestive of plasma leakage ^{[1][17-18]} like peripheral edema, pleural effusion, ascites had thrombocytopenia (platelet count < 100,000/mm³) along with hemoconcentration ^{[1][11-14][17]} (elevated hematocrit \geq 20% for age and gender or equivalent drop in hematocrit from baseline after volume replacement therapy) at day 5 to 8 ^{[11][15]} from the onset of the illness. Patients who presented with major bleeding manifestations like

heamatemesis, malena had a drop in heamatocrit¹ along with severe thrombocytopenia and leucopenia at day 5 to 8^{[11][15]}. Total leukocyte count less than 2500/mm³, a platelet count < 20000/mm³ and a heamatocrit < 35 % was associated with severe dengue manifestations. During the critical phase of dengue fever, increase in the severity^{[16][17]} of skin rash , petechiae, ecchymosis, mucosal bleeding, vomiting, abdominal pain coincided with a sudden fall in platelet count and haemoconcentration or a drop in heamatocrit^[1]. This phase of clinical worsening and drop in platelet count was preceded by 24 ± 12 hours by a fall in total leukocyte count^{[1][7]}. The recovery in platelet count was preceded by the recovery of the total leukocyte count by 24

± 12 hours^[1] in our patients at day 7-9 from the onset of the illness. Serial monitoring of the total leukocyte count helps us in predicting the critical phase of dengue by at least one day earlier and this in turn will help us in initiating early and appropriate treatment^{[1][5-6][13]} of dengue. Central nervous system manifestations like restlessness, convulsions or coma was not seen in any of our patients. All the patients were treated with supportive care with intravenous rehydration therapy^{[1][5][6]} and ten patients who presented with severe dengue needed transfusion with fresh whole blood^[1]. There was no mortality in our study.

Table No.1: Clinical presentation of Dengue (n=74)

Malaise/Generalised body pain	56 (75.7%)
Headache	50 (67.5%)
Arthralgia	43 (58.1%)
Low back pain	39 (52.7%)
Skin rash	28 (37.8%)
Petechiae	22 (29.7%)
Ecchymosis	08 (10.8%)
Gum bleeding	09 (12.6%)
Vaginal bleeding	04 (05.4%)
Haematuria	05 (06.7%)
Abdominal pain	28 (37.8%)
Persistent vomiting	13 (17.5%)
Haematemesis	03 (04.0%)
Hepatomegaly(>2 cms and tender)	18 (24.3%)
Ascites	19 (25.6%)
Pleural effusion	14 (18.9%)

Peripheral odema	28 (37.8%)
Facial puffiness	13 (17.5%)
Respiratory distress	05 (06.7%)
Dengue Shock Syndrome	02 (02.7%)

Table No. 2: Thrombocytopenia in dengue fever

Platelet count/mm ³	No. of patients (n=74)
500000-150000	36 (48.6%)
20000-50000	27 (36.5%)
<20000	11 (14.9%)

Table No.3: Hematological parameters in dengue ±warning signs (n=42)

Parameters	Day 0-5	Day 5-8	Day 7-9
	Febrile phase	Critical phase	Recovery phase
Heamatocrit %	40-45	46-65	40-45
Platelet count/mm ³	90000-160000	50000-120000	90000-180000
Total leukocyte count//mm ³	5000-7000	2800-4500	4500-6000

Table No.4: Hematological parameters in severe dengue (n=11)

Parameters	Day 0-5	Day 5-8	Day 7-9
	Febrile phase	Critical phase	Recovery phase
Heamatocrit %	40-45	25-35	40-45
Platelet count/mm ³	70000-100000	9000-20000	90000-140000
Total leukocyte /mm ³ count	3500-5000	1300-2500	4500-6000

CONCLUSION

This study highlights the pattern and the natural course of dengue in adults. The alterations in total leukocyte count precedes that of platelet count in both critical and recovery phase of dengue. There is also a increased association of severe

leukopenia with severe thrombocytopenia and severe dengue. The study highlights the role of total leukocyte count in predicting the natural course of the dengue and its significance in the early diagnosis and treatment of dengue.

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