

Clinical Profile and Role of Haematological Parameters in the Prognosis of Dengue Fever Patients Admitted in a Tertiary Hospital

Virgin Joena¹, Ananda Xavier Pragasam R²

ABSTRACT

Introduction: Even after the discovery of vaccines for dengue fever, it remains a major public health problem in developing tropical and subtropical countries, especially in India. The dengue fever has a varied clinical spectrum ranging from a mild headache to severe organ impairment or bleeding, depending on the virulence and susceptibility of the individual. The current study investigated the clinical profile of laboratory-confirmed dengue patients. A secondary objective was to find the role of haematological parameters in prognosis.

Material and Methods: This was a retrospective study conducted in a tertiary care hospital at Madurai following a dengue fever outbreak between August 2017 to November 2017 among laboratory-confirmed dengue patients older than 16 years. All the relevant clinical and laboratory investigation details of the patients were obtained from the medical records of the hospital.

Results: Fever was present in all the cases with an average duration of 4.86 ± 1.59 days followed by myalgia (57.39%), vomiting (46.96%), headache (30.43%) and abdominal pain (20%). Bleeding and hepatic complication was presented by 22.16% and 50.43%. The mean platelet recovery duration was 8.42 ± 1.74 days. A strong positive correlation between day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery (r_s value: 0.0.713, P value: <0.001) was observed.

Conclusion: Dengue fever patients have varied clinical features varying from fever to severe hepatic complication. For assessing the prognosis of dengue fever, along with the continuous monitoring of clinical profile and platelet count, evaluation of WBC recovery is also recommended.

Keywords: Dengue Fever, Thrombocytopenia, Leukopenia.

INTRODUCTION

Dengue fever (DF), a vector-borne disease caused by dengue virus (DENV) infection has increased gradually over the past 10 years in India.¹ World Health Organisation has reported that around 390 million dengue infections occur per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease).² India is one of the seven identified countries in the South-East Asia region regularly reporting the incidence of dengue fever outbreaks and may soon transform into a major niche for dengue infection in the near future.³

Dengue fever has a wide clinical spectrum. This ranges from asymptomatic disease to undifferentiated fever (or viral syndromes), classical dengue fever (DF), dengue haemorrhagic fever (DHF), or dengue shock syndrome (DSS) and expanded dengue syndrome (EDS).⁴ This is

often characterised by high fever, headache, myalgia, body ache, vomiting, joint pain, transient rash and mild bleeding manifestations such as petechiae, ecchymosis at pressure sites and bleeding from venipunctures.⁵ In the advanced severe dengue stage, patients may present with ascites or pleural effusion with or without respiratory distress, severe bleeding, and/or severe organ impairment.² 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.^{6,7} Atypical presentations are also encountered with acute liver failure, encephalopathy with seizures, renal dysfunction, lower gastrointestinal bleeding.⁸

During the course of dengue, the peripheral blood parameters changes. DF is characterised by leucopenia (White Blood Cells (WBC) < 5000 cells/mm³), thrombocytopenia (< 150,000 cells/mm³), rising haematocrit (5–10%) and there can be evidence of plasma leakage.⁹ The platelets usually drop to below 100,000/mm³ in the febrile phase or around defervescence and may remain low for the first few days of recovery.¹⁰ One study has observed that there is a progressive decline in white cell counts with sudden platelet drop which precedes plasma leakage and hence it could be the earliest prognosticator of severe dengue.¹¹ Leucopenia and the duration for recovery from it during dengue infection should be considered seriously since it increases one's susceptibility to various infection.

Most of the dengue cases are either underreported or misclassified,² or reported in an advanced stage. The most common reason being an underestimation of the clinical profile. Hence it is important to monitor the clinical profile of dengue fever properly. The present study aimed at presenting the clinical profile of laboratory-confirmed Dengue patients in a tertiary care hospital at Madurai. A secondary objective was to find the role of haematological parameters in prognosis.

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MATERIAL AND METHODS

This was a retrospective study done in tertiary care hospital at Madurai on patients suffering from dengue fever during an outbreak of the disease in August 2017 to November 2017.

Inclusion criteria

Patients admitted with the clinical suspicion of dengue fever and with NS1 antigen and IgM antibody positive for DF

Exclusion Criteria

Patients with fever positive due to other infections.
Patients who less than 16 years.

Study tools

Data was collected in a structured perform, and all the relevant clinical and laboratory investigation details of the patients were obtained from the medical records of the hospital.

Ethical considerations

Informed written consent in the mother tongue of the participants was obtained from the respondents before recruitment in the study. Confidentiality of the respondents was maintained. Respondents were given the option of quitting from the study if so desired by them. No element of compulsion was exerted.

STATISTICAL ANALYSIS

Data were collected in a structured perform, and all the relevant clinical and laboratory investigation details of the patients were obtained from the medical records of the hospital.

RESULTS

A total of 155 patients with a mean age of 30.53 ± 12.75 years with diagnosed DF constituted the study population. Equal male, the female proportion was observed. (Table 1) The prevalence of secondary dengue infection was 53.3%. Fever was the presenting complaint of all patients (100%), followed by myalgia (57.39%), vomiting (46.96%) and headache (30.43%). Half of the study population has (50.43%) had a hepatic complication. Only 1 (0.8%) patient had a shock. Twenty-nine (25.22%) patients required a blood transfusion. (Table 2)

The fever lasted for an average of 4.86 ± 1.59 days, and DF patients took 8.42 ± 1.74 days (mean \pm SD) for recovery from the onset of fever. The mean number of units of platelets transfused was 1.03 ± 1.97 . The platelet level started declining at 4.95 ± 1.4 (mean \pm SD) from the onset of fever. (Table 3)

There was a strong positive correlation between days needed for recovery (increasing trend of platelet) from the onset of fever and WBC recovery (Rs value: 0.713, P value: <0.001) (Table 4 and figure 1)

The mean days for recovery from the onset of fever and mean WBC recovery days do not significantly differ (p value= 0.050; p value=0.367) with receiving a blood transfusion or not. However, a significantly a greater number of days (p value <0.05) was needed for MPV recovery among patients

receiving blood transfusion compared to not receiving a blood transfusion. (Table 5)

Parameter	Summary
Age (Mean \pm SD)	30.53 \pm 12.75
Age group	
up to 20	28 (24.35%)
21 to 30	38 (33.04%)
31 to 40	29 (25.22%)
41 to 50	11 (9.57%)
51 to 60	6 (5.22%)
61 and above	3 (2.61%)
Gender	
Male	57 (49.57%)
Female	58 (50.43%)
Table-1: Baseline characteristics and clinical presentation (N=115)	

Parameter	n (%)
Primary	49 (46.67%)
Secondary	56 (53.33%)
Symptoms	
Fever	115 (100%)
Myalgia	66 (57.39%)
Vomiting	54 (46.96%)
Headache	35 (30.43%)
Pain abdomen	23 (20.00%)
Oliguria	6 (5.2%)
Giddiness	1 (0.87%)
Diarrhoea	1 (0.87%)
Signs	
Bleeding	26 (22.61%)
Complications	
Hepatic	58 (50.43%)
Shock	1 (0.87%)
Received Blood transfusion	
Yes	29 (25.22%)
No	86 974.78%)
Table-2: Clinical presentation of the dengue in the study population	

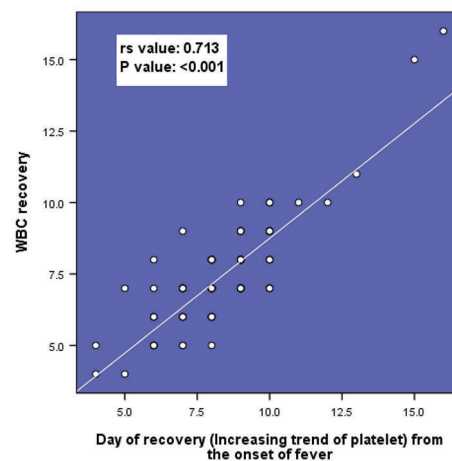


Figure-1: Scatterplot diagram of the correlation between day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery

Parameter	Mean \pm SD	Minimum	Maximum
No. of days of requiring IVF	0.44 \pm 0.85	0	4
No. of unit's platelet transfused	1.03 \pm 1.97	0	10
Day of fever requiring platelet transfusion	1.8 \pm 2.95	0	10
Day of fever when platelet start falling	4.95 \pm 1.4	0	8
No. of days the patient had a fever	4.86 \pm 1.59	0	9
Day of recovery (Increasing trend of platelet) from the onset of fever	8.42 \pm 1.74	4	16
Day of Fever when Liver Involvement	5.16 \pm 1.31	3	9
WBC Recovery	7.48 \pm 1.69	4	16
MPV Recovery	7.62 \pm 1.42	3	12

Table-3: Summary of treatment and recovery in dengue fever patients (N=115)

Parameter	Spearman rank correlation	P value
WBC recovery	0.713	<0.001

Table-4: Correlation between the day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery (N=115)

Parameter	Blood transfusion		P value
	Yes (N=29) (Mean \pm SD)	No (N=86) (Mean \pm SD)	
Day of recovery (Increasing trend of platelet) from the onset of fever	8.97 \pm 1.5	8.23 \pm 1.79	0.050
WBC recovery	7.72 \pm 1.36	7.4 \pm 1.78	0.367
MPV recovery	8.21 \pm 1.57	7.41 \pm 1.31	0.009

Table-5: Comparison of mean CBC parameters between the blood day of transfusion group (N=115)

DISCUSSION

Dengue fever is a major public health problem causing significant morbidity and mortality in the general population, especially in tropical and subtropical countries.¹² The clinical profile of patients with DF varies from mild fever to severe organ impairment and blood loss. We evaluated the clinical profile of patients with dengue fever admitted to a tertiary hospital in Madurai, India.

In the present acute infection was present in 46.67 % and secondary infection in 53.3%. Primary dengue infection was defined as an acute infection, as indicated by qualitative detection of NS1 antigen, and IgM or HI antibodies or RT-PCR positivity and absence of IgG antibodies against dengue virus.¹³

Secondary dengue causes more severe disease than the primary.¹⁴ Secondary dengue infection is indicated by NS1 Ag positive with IgM + IgG positive. The prevalence of secondary dengue infection varied in different studies. Two studies by Sidique O et al¹⁵ and Changal K et al¹⁴ reported the prevalence of secondary dengue infection as 68.4 % and 66.7% respectively, which was higher compared to our study results. However, Kumar et al¹⁶ reported the prevalence of secondary dengue infection as 50%. According to a meta-analysis by Ganesh Kumar P et al¹³ of DF infection in India, the overall proportion of secondary dengue infection among laboratory-confirmed patients was 42.9% (95%CI: 33.7–52.6).

The clinical profile of dengue revealed that fever was the most common presenting symptom (100%) with an average duration of 4.86 \pm 1.59 days. Many studies have reported fever as the foremost complaint of patients with dengue fever.^{3,4,12,17-21} Other common presenting symptoms present

were myalgia (57.39%), vomiting (46.96%) and headache (30.43%). This was in agreement with the study done by Agarwal VK et al¹⁷, were the most common symptoms were fever (100%), followed by myalgia in 88%, chills in 74.5% nausea/ vomiting 65.5% and headache in 38% of patients. In the study by Laul A et al⁴, headache was the chief complaint about 87% of patients, and 41% had typical retro-orbital pain. Mandal S. et al²² reported headache in 62.16% of the patients. Matta L et al²¹ reported the most common symptoms were fever (287;100%) followed by myalgia (223;78%), and headache (183;64%) similar to our study. The haemorrhagic manifestation was presented by 26 (22.16%) patients. This was far high compared to the study done by Rajesh et al¹⁹, were only 5% of the patients presented with bleeding. Twenty-four per cent of the patients presented bleeding in the study by Laul A et al.⁴ Bleeding is a known manifestation of dengue fever, due to thrombocytopenia. The various reasons for thrombocytopenia include bone marrow suppression, immune-mediated clearance and spontaneous aggregation of platelets to virus-infected endothelium.¹⁹

The hepatic complication was found in half of the study population (50.43%). Agarwal VK et al¹⁷ documented hepatic tenderness in 35.9% of patients. Twenty-five percentage had hepatomegaly in the study by Laul A et al.⁴ DF has a profound effect on multiple organ systems, the commonest being the liver.²³ It is the major site for NS1 protein accumulation, and preincubation of hepatocytes with soluble NS1 enhances subsequent infection by a homologous strain of DENV.²⁴

The average number of days required for the fever to subside was 4.86 \pm 1.59 day (mean \pm SD). However, 8.42 \pm 1.74 days (mean \pm SD) was required for the recovery to normal platelet level. This can be explained based on thrombopoiesis. The mean days for recovery from the onset of fever and mean

WBC recovery days do not significantly differ (p value=0.050; p value=0.367) with receiving a blood transfusion or not. However, there was a strong positive correlation between day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery (R_s value: 0.0.713, P value: <0.001). Leukopenia is usually observed in the course of dengue fever.^{9,25} It is caused by virus-induced destruction or inhibition of myeloid progenitor cells.²⁶ Increased duration for the WBC to recover increase one's susceptibility to various infections. In the study by Joshi AA et al²⁷, 47 cases of leucopenia (36%) out of 132 total cases were associated with thrombocytopenia. They reported that leucopenia is an early marker of dengue and association of leucopenia with thrombocytopenia suggests that it could be one of the prognosticators of severe dengue.²⁷ Verdeal JC et al¹¹ reported that leukopenia could be a marker of severe dengue. This points to the importance of evaluating WBC count also in the prognosis of dengue fever and should be explored in further research.

A significant number of days (p value <0.05) was needed for MPV recovery among patients receiving blood transfusion compared to not receiving a blood transfusion. This can be explained by the fact that blood transfusion is usually done in patients with severe thrombocytopenia or hemodynamically unstable patients and therefore requires more time for recovery.

There were several limitations to the current study. First of all, due to the lack of data, we could not assess the baseline and post-treatment value of various haematological parameters. However, we considered the standard value to assess the days required for recovery. Secondly, our study did not assess the relationship between baseline platelet level with recovery duration or requirement of blood transfusion. This might have biased our study results. Even though our study raised the need for monitoring WBC count in DF patients, we couldn't assess the relationship of WBC recovery with the severity of DF, due to the retrospective nature of the study.

CONCLUSION

Dengue fever patients present with varied clinical features varying from fever to severe hepatic complication in the current study. Continuous monitoring of clinical profile along with haematological parameters is recommended

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