

CHANGING CLINICAL SPECTRUM AND CORRELATION BETWEEN PLATELET COUNT AND BLEEDING TENDENCIES IN DENGUE PATIENTS AT A TERTIARY CARE CENTRE.

Raveendra K.R¹, Prakash Kikkeri Gowdaiah², Prashanth Basavanna³, Sonali Appaiah⁴,
Chandra Mohan G⁵

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ABSTRACT: INTRODUCTION: Dengue infection is recognized worldwide as the most important arthropod vector borne disease in the last four decades and a major public health problem, assuming epidemic proportion in urban areas of tropical countries in South east Asia. It is caused by one of the four dengue virus serotypes DEN-1, DEN-2, DEN-3 and DEN-4. *Aedes aegypti* is the main mosquito vector. Dengue infection can be asymptomatic or can cause two clinical entities: dengue fever (DF) and dengue haemorrhagic fever/ dengue shock syndrome (DHF/DSS). Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome. Thrombocytopenia may be frequently observed in DF, but is a constant feature and one of the diagnostic criteria of DHF/DSS. There is a need to identify various clinical presentations, complications and treatment outcome of Dengue patients. Hence, this study was undertaken to ascertain all the above mentioned clinical parameters in proven dengue patients who were admitted to this tertiary care hospital, with a special emphasis on correlation between platelet count and bleeding manifestations. **MATERIALS AND METHODS:** This cross sectional study was conducted for a period of 2 years from October 2010 to September 2012. 100 hospitalized and confirmed dengue cases were included and they were classified as having dengue fever (DF), dengue hemorrhagic fever (DHF)/ dengue shock syndrome (DSS) as per WHO criteria. A detailed clinical evaluation with appropriate laboratory investigations were done. All the patients were treated and followed up with clinical assessment and serial platelet counts. Data was analyzed with suitable software and appropriate statistical methods. **RESULTS:** There were 57 males and 43 females, with majority in the age group 21 to 40 years. Fever was the most common symptom present in all the patients (100%), followed by vomiting (24%), myalgia (23%), headache (21%), and pain abdomen (20%). Bleeding manifestation were noted in 18 patients (18%), out of which 5 patients had platelet count <20,000, 4 patients had 21,000-30,000, 2 patients 31,000-40,000, 5 patients 41,000-50,000 and 2 patients had >61,000 platelet count. There was no correlation between platelet count and bleeding manifestations (p value > 0.05). **CONCLUSION:** Dengue remains an important differential diagnosis for all acute fevers in India. Dengue should be suspected even in patients without classical presentation of dengue as many Dengue patients present with atypical manifestations. Due to lack of direct correlation between low platelet count and bleeding tendencies, low platelet count alone is not an indication for platelet transfusion and a close monitoring for bleeding manifestation and hemodynamic stability with reasonable judgment should be exercised in deciding the need for transfusion in Dengue patients. Prevention of uncomplicated Dengue fever going on for DHS and DSS will be crucial and will decrease the overall mortality and morbidity.

KEY WORDS: Dengue fever (DF), Dengue hemorrhagic fever (DHF), Thrombocytopenia.

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INTRODUCTION: There has been an increasing incidence of Dengue in recent past, due to population growth, rapid urbanization with poor public infrastructure like inadequate water supply and improper solid waste management favoring multiplication of the main vector, *Aedes aegypti*.¹ An estimated 50 million Dengue infections occur annually and approximately 2.5 billion people live in Dengue endemic countries.² Dengue has spread to more than 100 countries in Asia, the Pacific, the Americas, Africa and the Caribbean.³

Expert consensus group in Latin America (Havana, Cuba, 2007) South East Asia (Kuala Lumpur, Malaysia, 2007) and WHO (Geneva, 2008) agreed that –Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome.⁴ Hence there is a need to identify various clinical presentations, complications and treatment outcome of Dengue patients. Platelet transfusion at appropriate time remains the corner stone step in Dengue management along with the symptomatic and supportive treatment.

AIM OF THE STUDY:

- To study the various clinical manifestations, complications and treatment outcome in hospitalized confirmed Dengue patients.
- To study the correlation between the platelet count and bleeding tendencies.

MATERIALS AND METHODS: This cross sectional clinical study was conducted on 100 confirmed Dengue cases (symptoms with laboratory confirmation of IgM sero- conversion in paired sera) admitted and treated at Victoria and Bowring and Lady Curzon hospitals under the department of Medicine, Bangalore medical college and research institute, Bangalore, India, from October 2010 to September 2012, for a period of 2 years.

Prior approval for the study was obtained by the institutional Ethical committee at Bangalore medical college and research institute. All the 100 IgM Dengue antibody positive patients who were included in this study were classified as Dengue fever (DF), Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DHS) according to WHO criteria. A detailed clinical evaluation with appropriate investigations (full battery profile for fever and Dengue serology with chest X ray, ultrasound scanning of abdomen, 2D ECHO, RFT, LFT etc.) were done to all patients. All the patients were treated and followed up with clinical assessment and serial platelet counts.

Statistical method: Descriptive and inferential statistical analysis has been carried out and the statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, Medcalc 9.0, Systat 12.0 and R environment version 2.11.1 were used for the analyses of the data.

RESULTS: This cross sectional clinical study was conducted on 100 IgM antibody positive Dengue fever patients, who were hospitalized, treated and evaluated for various clinical presentations and to establish a relation (if any) between the platelet counts and bleeding tendencies. There were 57 males and 43 females with majority of patients in the age group 21 to 40 years, contributing to 60% of all cases. 42% of all cases were from rural area, and 66% of cases were referred as febrile thrombocytopenia from various hospitals.

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Symptom	Number of patients	Percentage
Fever	100	100%
Vomiting	24	24%
Myalgia	23	23%
Head ache	21	21%
Pain abdomen	20	20%
Bleeding tendency	18	18%
Joint pain	07	7%
Easy fatiguability	07	7%
Cough	05	5%
Convulsions	01	1%

Table 1: Showing various symptoms at admission.

The most common symptom at admission was fever, present in all the 100 patients. Fever duration was less than 5 days in 50% cases, 6-10 days in 42%, 11-15 days in 5% and >15 days in 3% cases. Continuous fever was seen in 6, while 94 patients had intermittent fever. High degree fever was seen in 88 patients while 11 had moderate and 1 patient had mild fever. Fever was associated with chills and rigors in 79 patients. Other symptoms noted at the time of admission were as shown in Table 1.

The different sites of clinical bleeding manifestations included –Gum bleeding in 5, epistaxis 4, hematemesis 4, purpura 3, hematuria 3 and bleeding PR in 1 patient. Important physical examination findings noted were as shown in Table 2.

Physical examination finding	Number of patients
Right hypochondrial tenderness	59
Hepatomegaly	25
Splenomegaly	11
Icterus	05
Ascites	04
Pleural effusion	03
Conjunctival suffusion	02
Consolidation	01

Table 2: Showing physical examination findings

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Platelet count	Number of patients	Number (percentage) Of patients with bleeding	P value
≤ 20,000	23	5 (21.7%)	0.664
21,000 – 30,000	24	4 (16.7%)	0.868
31,000 – 40,000	15	2 (13.3%)	0.635
41,000 – 50,000	17	5 (29.4%)	0.221
51,000 – 60,000	6	0	-
>60,000	15	2 (13.3%)	0.635
Total	100	18	-

Table 3: Showing correlation of platelet count to bleeding manifestations

All 100 patients had varying thrombocytopenia with platelet count >60,000 were noted in 15 patients, 51,000-60,000 in 6, 41,000-50,000 in 17, 31,000 to 40,000 in 15, 21,000 to 30,000 in 24 and <20,000 in 23 patients. Bleeding manifestation were noted in 18 patients, out of which 5 patients had platelet count <20,000, 4 patients had 21,000-30,000, 2 patients 31,000-40,000, 5 patients 41,000-50,000 and 2 patients had >61,000 platelet count. This data is depicted in Table 3. And there was no correlation between platelet numbers and bleeding tendencies (p value > 0.05).

Symptomatic and supportive line of treatment was given to all the patients and platelet transfusion was given to 35 patients – 23 patients received <5 units, 9 patients 6-10 units, 2 patients 11-15 units and 1 patient received >15 units of platelets.

Clinical presentation	Number of patients			Percentage
	Males	Females	Total	
Dengue fever	45	31	76	76%
Dengue Hemorrhagic fever (DHF)	9	9	18	18%
Dengue Shock Syndrome (DSS)	3	3	6	6%

Table 4: Showing various clinical presentations.

Out of 100 patients 76 had Dengue fever, 18 had Dengue hemorrhagic fever (DHF) and 6 had Dengue shock syndrome (DSS) (Table 4). DHF and DSS patients were treated as per protocol at medicine ICU, and these Patients developed many complications and important were ascites in 4, LFT abnormalities 4, Anemia 3, pleural effusion 2, meningoencephalitis 2, consolidation1, RFT abnormalities in 1 patient.

98 patients recovered from illness and were discharged– 16 patients in <3 days, 55 patients between 3-5 days, 27 patients between 6-10 days, 2 deaths occurred in this study and both patients had Dengue shock syndrome (DSS).

DISCUSSION: This cross sectional study conducted over a period of 2 years included 57 males and 43 females in the age group 18-65 years. Mean age at presentation for males was 30.09 ± 11.55 years and 34.51 ± 13.44 years for females which was statistically significant with a p value of 0.080. Rachiel Danicel et al⁵ have reported the incidence of fever in Dengue patients as 96.8% with mean age of presentation being 42.6 years and mean duration and symptoms as 6 days. In this study, fever

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was the commonest presentation, seen in all 100 patients. 49.1% males and 51.2% females had fever <5 days and the most common type of fever was intermittent both in males (92.9%) and females (95.3%). Most patients had a high grade fever- 84.2% in males, 93.1% females and was statistically significant with a 'P' value of 0.078.

The classical features of Dengue fever include - abrupt onset of fever with facial flushing, skin erythema, arthralgia, sore throat, backache, conjunctival suffusion, headache and retro orbital pain.^{6,7} In our study classical symptoms were not commonly seen as only 9% had joint pain and 21% had headache, myalgia and conjunctival suffusion were seen in 1% of cases. Important physical findings were Right hypochondrial tenderness in 59% patients, hepatomegaly 25%, pallor 15%, splenomegaly 11%, icterus 5%, Ascites 4% pleural effusion 3%, conjunctival suffusion 1% which are on par with the other studies like Rachel Daniel et al.⁵

Bleeding manifestations were noted in 18 patients and the most common bleeding sites were gum bleeding in 5, epistaxis in 4 patients, hematemesis 4, skin bleeding 3, hematuria 3, bleeding Per Rectum in 1 patient. A positive tourniquet test in early phase of febrile illness increases the probability of Dengue diagnosis⁸. As shown in Table 3, 5 patients out of 17 (29.4%) in the higher category platelet count (41000 to 50,000) had bleeding manifestations, so also 5 patients out of 23 (21.7%) in the lowest category platelet count (< 20,000) had bleeding manifestations with p value > 0.05 in both categories. Altogether, 63.33% of bleeding manifestations were noted in patients with platelet counts > 20,000. These findings illustrate that there is no correlation between absolute platelet numbers and bleeding tendencies in dengue patients. Which explains the complex nature of the hemorrhagic diathesis in dengue fever reflecting the combination of cytokine action, vascular injury, reduced platelet number and function with mild consumptive coagulopathy.⁹⁻¹²

35% of patients received platelet transfusion and majority of them i.e 65.71% received <5 units of platelets. 71 % of patients stayed for <5 days in the hospital and only 18% had required a long duration of stay i.e 6-10 days. Lee VJ et al¹³ has reported the incidence of DHF as 6% in his 1973 Dengue patients services at Singapore and Rai et al ¹⁴ has reported the incidence of DHF and DSS as 32% and 7.94% in their studies on 399 serologically confirmed Dengue patients. In our study DHF was seen in 18% of Dengue patients as ours is a tertiary care center receiving all seriously ill patients from small centers nearby.

CONCLUSION: Today Dengue remains an important differential diagnosis for all acute fevers especially in this part of the world. Dengue should be suspected even in patients without classical presentation of dengue as many Dengue patients present with atypical manifestations. Due to lack of direct correlation between low platelet count and bleeding tendencies, low platelet count alone is not an indication for platelet transfusion and a close monitoring for bleeding manifestation and hemodynamic stability with reasonable judgment should be exercised in deciding the need for transfusion in Dengue patients. Prevention of uncomplicated Dengue fever going on for DHS and DSS will be crucial and will decrease the overall mortality and morbidity.

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AUTHORS:

1. Raveendra K.R.
2. Prakash Kikkeri Gowdaiah
3. Prashanth Basavanna
4. Sonali Appaiah
5. Chandra Mohan G.

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Medicine, Bangalore Medical College and Research Institute, Bangalore.
2. Associate Professor, Department of Medicine, Bangalore Medical College and Research Institute, Bangalore.
3. Assistant Professor, Department of Medicine, Raja Rajeshwari Medical College, Bangalore.

4. Postgraduate, Department of Medicine, Bangalore Medical College and Research Institute, Bangalore.

5. Postgraduate, Department of Medicine, Bangalore Medical College and Research Institute, Bangalore.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Prakash Kikkeri Gowdaiah,
Associate Professor, Department of Medicine,
Bangalore Medical College and Research Institute,
Bangalore – 2.
Email – kikkeri47@yahoo.com

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