

Original Research Article

Systemic evaluation of febrile thrombocytopenia

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ABSTRACT

Background: Febrile patient with thrombocytopenia is commonly encountered by physicians especially during monsoon and perimonsoon period. Infections with protozoa, bacteria and viruses can cause thrombocytopenia with or without disseminated intravascular coagulation. Commonly dengue, malaria, scrub typhus and other rickettsial infections, meningococci, leptospira and certain viral infections present as fever with thrombocytopenia. Occasionally these patients can go on to develop a stormy course with multiorgan dysfunction requiring intensive care unit admission associated with high morbidity and mortality. Though thrombocytopenia is encountered in various diseases, it is for sure that potentially fatal bleeding due to thrombocytopenia is rare. The study was intended to know the underlying etiology of febrile thrombocytopenia in our community, the various presentations and relationship between platelet level and severity of disease and prognosis.

Methods: This study was carried out in 218 adult patients (age above 18 years) presenting with fever having thrombocytopenia (platelet count $<1,50,000/\text{mm}^3$) in Dept. of medicine in IIMS and R Lucknow UP.

Results: Dengue was the commonest cause of fever with thrombocytopenia (58.71%) followed by *P. falciparum* malaria 8.71% and *P. vivax* malaria 6.88%. Bleeding manifestations were seen in 24.31% of patients. 58.49% of patients had petechiae/purpura as the commonest bleeding manifestation followed by hematuria in 16.98%.

Conclusions: Fever with thrombocytopenia consists of occult presentations of common diseases rather than rare disease. Infection is the commonest cause of fever with thrombocytopenia. Among infections, dengue was the commonest cause. Treatment of underlying condition will lead to rapid improvement in platelet count with complete clinical recovery.

Keywords: Dengue, Febrile thrombocytopenia, Fever, Hematuria, Platelet count

INTRODUCTION

Depicted in the Sumerian pictographs as flaming brazier, fever was recognized as a cardinal feature of disease.¹ Sir William Osler stated, "Humanity has three great enemies: Fever, famine and war; of these, by far the greatest, by far the most terrible is fever". Like Osler, physicians since antiquity have viewed fever as an entity worthy of unremitting attention. Febrile patient with thrombocytopenia is commonly encountered by

physicians especially during monsoon and perimonsoon period. Infections with protozoa, bacteria and viruses can cause thrombocytopenia with or without disseminated intravascular coagulation. Commonly dengue, malaria, scrub typhus and other rickettsial infections, meningococci, leptospira and certain viral infections present as fever with thrombocytopenia. Occasionally these patients can go on to develop a stormy course with multiorgan dysfunction requiring intensive care unit admission associated with high morbidity and mortality.^{2,3} Though thrombocytopenia is encountered in

various diseases, it is for sure that potentially fatal bleeding due to thrombocytopenia is rare.⁴ The causes of thrombocytopenia are impaired platelet production, accelerated platelet destruction or dilution and/or splenic sequestration.⁵ Even though there is no absolute relation between platelet counts and bleeding, certain broad generalizations can be made, with counts less than 10,000/ μ L, bleeding is usual and may be severe.⁶

Infections cause decrease in platelet count both due to effects on platelet production and platelet survival.⁷ Thrombocytopenia in bacterial infections can occur as a part of sepsis with disseminated intravascular coagulation. Patients with sepsis may also develop hemophagocytic histiocytosis with phagocytosis of platelets and leucocytes in the bone marrow histiocytes. Viruses produce thrombocytopenia by various mechanisms like impaired platelet production as a result of direct viral invasion, toxic effect of viral proteins on thrombopoiesis, virus induced hemophagocytosis and increased platelet destruction caused by binding of virus-induced autoantibodies or viral antigen antibody complexes. Thrombocytopenia in dengue infection raises concern about bleeding risk. Bone marrow suppression by virus and peripheral destruction of platelets have been implicated.⁸ Thrombocytopenia during malarial infection may appear even before fever, anemia and splenomegaly become manifest.⁹ Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in marrow with diminished platelet production have all been postulated. During early stages of malaria, platelet agglutination as a result of endothelial cell activation and release of activated von Willebrand factor occurs which may cause thrombocytopenia.¹⁰ Occasionally platelets can be invaded by malarial parasites. Thrombocytopenia in malaria is rarely severe and treatment is focussed on eradication of malarial parasite.¹¹ The study was intended to know the underlying etiology of febrile thrombocytopenia in our community, the various presentations and relationship between platelet level and severity of disease and prognosis.

METHODS

This study was carried out in 218 adult patients (age above 18years) presenting with fever having thrombocytopenia (platelet count $<1,50,000/\text{mm}^3$ in Dept. of medicine in IIMS and R Lucknow, UP. Detailed history was taken. Presenting complaints and haemorrhagic manifestation were noted. The bleeding manifestations that the patients presented with or developed during their course in hospital were recorded. All the patients were subjected to routine haematological investigation like haemoglobin, total leukocyte count, platelet count, peripheral smear study, peripheral smear for malarial parasites, MCV (mean corpuscular volume), Dengue NS1 antigen, Dengue IgM and IgG, Prothrombin time with INR, Activated partial thromboplastin time, renal function test and liver function test. Baseline platelet counts were done on the day of presentation.

Repeat platelet counts were done in subjects with marked thrombocytopenia until normal or near-normal values were reached. Other investigations as necessary were done to achieve diagnosis such as bone marrow trephine biopsy, serological study for HIV infection, TSH, S. Widal, D-Dimer, Serum vitamin B12 level, Anti-Nuclear Antibody (ANA).

Inclusion criteria

Patients with fever and thrombocytopenia above 18 years of age.

Exclusion criteria

Patients with fever and no thrombocytopenia were excluded. Patients with thrombocytopenia and no fever were also excluded from study. Previously diagnosed conditions which can lead to thrombocytopenia such as ITP, cirrhosis, chronic liver disease, patients on drugs (aminosalicylic acid, linezolid, amiodarone carbamazepine, captopril, methyl dopa) causing thrombocytopenia were excluded.

RESULTS

Dengue was the commonest cause of fever with thrombocytopenia (58.71%) followed by *P. falciparum* malaria 8.71% (19/218) and *P. vivax* malaria 6.88% (15/218). Bleeding manifestations were seen in 24.31% (53/218) of patients. 58.49% of patients had patchie/purpura as the commonest bleeding manifestation followed by hematuria in 16.98 %.

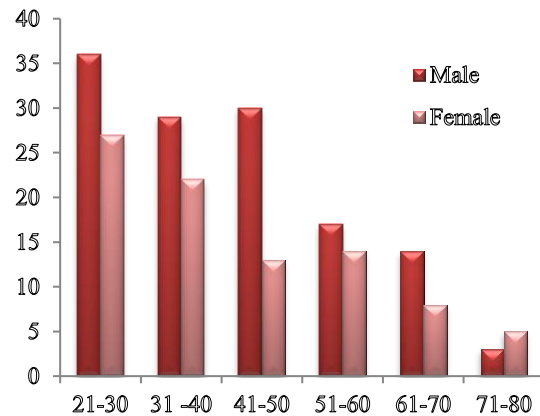


Figure 1: Age and sex distribution.

In this study a total of 218 cases were selected satisfying the inclusion criteria. Out of the total cases 129(59%) were male and 89 (41%) female. More than 50% cases were less than 50yrs of age. Maximum Number of cases 63 (29%) were in 21-30 age group as shown in Figure 2.

Dengue fever was present in 58.71% of cases presenting with febrile thrombocytopenia followed by malaria in 16.97% cases as shown in Figure 3.

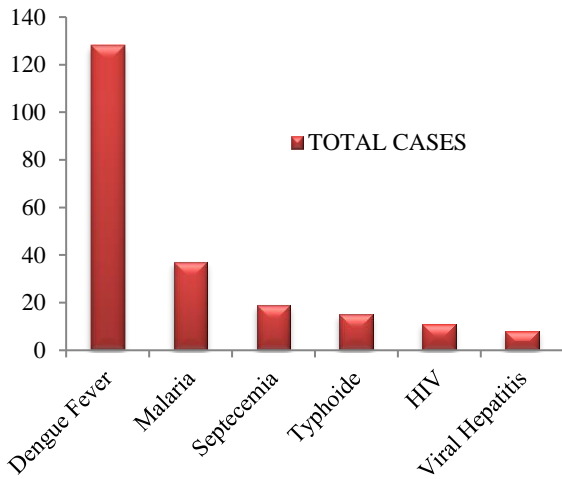


Figure 2: Etiological distribution.

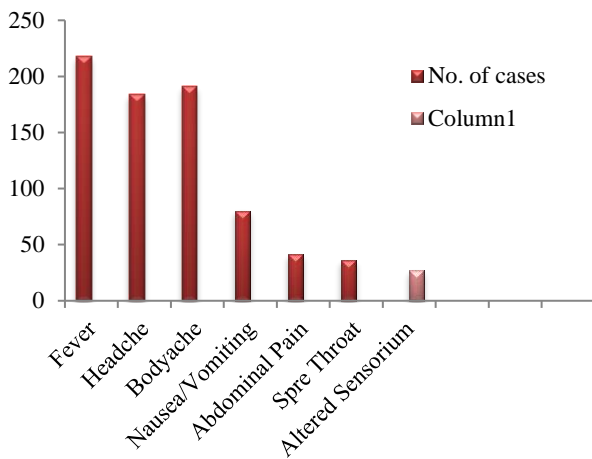


Figure 3: Distribution on basis of symptomatic manifestations.

Among the 218 cases included in this study all presented with fever. Body ache was present in 191 cases and 181 complained of headache. 80 cases had nausea/vomiting, 41cases had abdominal pain and 36 had sore throat. Only 29 cases had altered sensorium as shown in Figure 4.

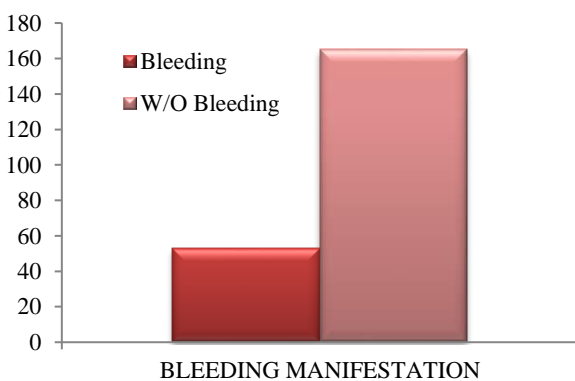


Figure 4: Distribution on the basis of Bleeding manifestation.

Out of the 218 cases of febrile thrombocytopenia only 53(24.31%) manifested any type of bleeding rest of the 165(75.68%) cases were without any bleeding.

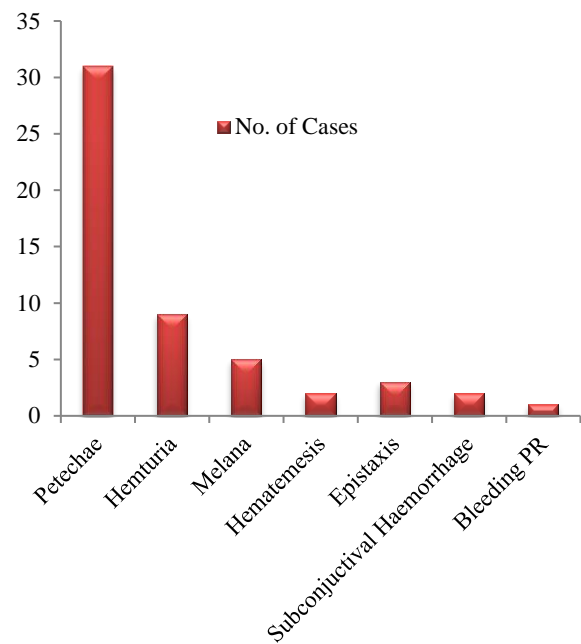


Figure 5: Distribution on basis of pattern of bleeding tendency.

Among the cases which had a bleeding manifestation, petechiae/purpura, was the most common presentation with 31 (14%) followed by haematuria 9 (4%), 5 (2%) had malena, 3 (1.3%) had epistaxis, 2 (0.9%) had subconjunctival haemorrhage, 2 (0.9%) had haematemesis, 1 (0.4%) had bleeding per rectum as shown in Figure 5.

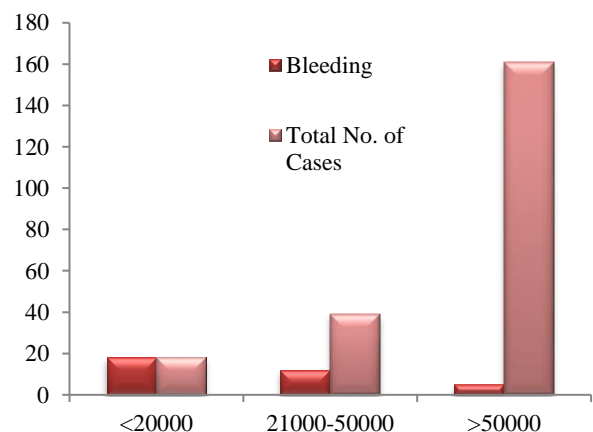


Figure 6: Distribution on the basis of platelet count and bleeding manifestations.

Out of the 35 cases who had bleeding manifestations, 18 patients had platelet count below 20000/ μ L, 12 patients had platelet count between 21000/ μ L to 50000/ μ L, 5 had platelet count above 50000/ μ L as shown in Figure 6.

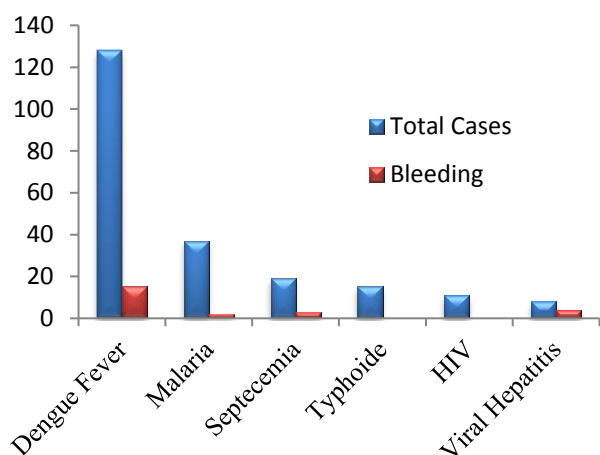


Figure 7: Distribution according to etiology and bleeding tendency.

Out of the 128 cases of dengue fever 15 (11.7%) developed bleeding. Out of the 37 cases of malaria 2 (5.4%) developed bleeding. Bleeding was there in 5 (26.3%) out of 19 cases of septicemia and 3 (37.5%) out of 8 cases of viral hepatitis as shown Figure 7.

DISCUSSION

In this study, the most common aetiology responsible for newly diagnosed thrombocytopenia in adult patients was found to be dengue fever (58.71%). The two mechanisms probably involved in dengue-induced thrombocytopenia are impaired thrombopoiesis and peripheral platelet destruction.¹² Malaria was the second most common cause accounting for 16.97% (37/218) cases. *P. falciparum* infection was present in 8.71% (19/218) followed by *P. vivax* in 6.88% (15/218). Mixed infection was present in 1.37% (3/218) patients. Both nonimmunological destruction and immune mechanism involving specific platelet-associated IgG antibodies that bind directly to malarial antigen in the platelets have been reported to play a role in the lysis of platelets.¹³ Dengue and malaria were the common causes due to the higher prevalence of these infections during the rainy season, which may be the reason for variation between different studies. Megaloblastic anemia was found in 5.36% patients due to vitamin B12 and folic acid deficiency as a result of ineffective thrombocytopenia.¹⁴

In our study distribution of platelet count in the range of $>50000-150000/\text{mm}^3$ was seen in 73.85% (161/218). Platelet count in the range of $20-50000/\text{mm}^3$ was seen in 17.88% (39/218) and platelet count in the range of $0-20000/\text{mm}^3$ was seen in 8.25% (18/218). Severe thrombocytopenia was seen more with *P. falciparum* malaria compare to *P. vivax* malaria.

CONCLUSION

Febrile thrombocytopenia is one of the most challenging problems in the field of medicine. It commonly manifests

as symptom/signs of underlying condition and sometime with bleeding manifestation. Fever with thrombocytopenia consists of occult presentations of common diseases rather than rare disease. Infection is the commonest cause of fever with thrombocytopenia. Among infections, dengue was the commonest cause. Treatment of underlying condition will lead to rapid improvement in platelet count with complete clinical recovery. Mortality in febrile thrombocytopenia is not directly associated with degree of thrombocytopenia but with concomitant involvement of other organs leading to multiorgan dysfunction.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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