

Clinical and etiological profile of thrombocytopenia in adults: A tertiary-care hospital-based cross-sectional study

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Abstract

Background: The etiologies of thrombocytopenia are diverse. Various studies on thrombocytopenia are done in the past have related to specific etiologies.

Objectives: This study attempts to determine the common etiologies of thrombocytopenia in adult patients admitted to Civil Hospital, Ahmedabad.

Material and Methods: A cross-sectional study was carried out at Civil Hospital, Ahmedabad. Patients with thrombocytopenia more than 18 years of age at admission between 1 October and 31 October 2013 were followed up during their stay in hospital, diagnosis were made, and bleeding manifestations and requirement of platelet transfusion were recorded.

Results: From the 412 patients studied, dengue was diagnosed in 28.6% of patients followed by malaria in 22.8%, chronic liver disease in 15.2%, hypersplenism in 12.3%, septicemia in 6.3%, gestational thrombocytopenia and disseminated intravascular coagulation in 5.5%, immune thrombocytopenic purpura (ITP) in 3.1%, megaloblastic anemia in 1.9%, human immunodeficiency virus in 1.4%, drug-induced thrombocytopenia in 1.2%, leukemia in 0.7%, and aplastic anemia in 0.48%. Bleeding secondary to thrombocytopenia was seen in 46 (11.2%) patients; of them, 28 were diagnosed with dengue fever, 4 with chronic liver disease, 3 with sepsis, 2 with hematological malignancies, and 9 with ITP. The common bleeding manifestations were gum bleed, purpura, petechial rash, and bruising. All the cases with platelet count $< 5,000/\mu\text{L}$ had bleeding manifestations secondary to thrombocytopenia. From the patients studied, 79.3% had fever associated with thrombocytopenia. Platelet transfusion was given to 87 patients: of these, 46 (52.8%) were transfused because of bleeding and 41 (47.1%) were given prophylactic transfusion.

Conclusion: Dengue fever was the most common cause of thrombocytopenia and the most common etiology found in patients who had bleeding secondary to thrombocytopenia with gum bleed as a common manifestation. There was no definitive trigger value of platelet for platelet transfusion, and transfusion because of bleeding and prophylactic transfusion were given in almost similar proportions of patients.

KEY WORDS: Thrombocytopenia, etiology, platelets, dengue

Introduction

Three major pathophysiological mechanisms in thrombocytopenia are decreased platelet production, increased platelet destruction or consumption, or increased splenic sequestration

(capturing of circulating platelets in the spleen). In adults, thrombocytopenia is a condition in which the platelet count falls below $1,50,000/\mu\text{L}$. Cases are considered mild if counts are between $60,000$ and $1,50,000/\mu\text{L}$, moderate if between $20,000$ and $60,000/\mu\text{L}$, and severe if less than $20,000/\mu\text{L}$. Patients with a platelet count greater than $50,000/\mu\text{L}$ often are asymptomatic. Patients with a platelet count from $30,000$ to $50,000/\mu\text{L}$ rarely present with purpura, although they may have excessive bleeding with trauma. However, counts from $10,000$ to $30,000/\mu\text{L}$ may cause bleeding with minimal trauma, and those less than $10,000/\mu\text{L}$ increase the risk of spontaneous bleeding, petechiae, and bruising. Spontaneous bleeding (i.e., mucosal, intracranial, gastrointestinal, and genitourinary bleeding) is more likely in patients with platelet counts less than $5,000/\mu\text{L}$, and is considered a hematologic emergency.

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Nair et al.,^[1] St. Stephen's Hospital, New Delhi, carried out a study of fever associated with thrombocytopenia and found out that the most common manifestation was purpura, followed by gum bleed and epistaxis. The leading causes of febrile thrombocytopenia were found to be septicemia followed by typhoid and dengue.

Recently fever with thrombocytopenia is common clinical presentation in tertiary-care hospitals. Established infective causes such as dengue are well known for fever with thrombocytopenia. There are not many studies elucidating other infections for thrombocytopenia. Thrombocytopenia is not a disease but is a diagnosis. The detailed knowledge must be acquired from patients who have thrombocytopenia. Detailed examination and laboratory tests should be done, which are related to etiology. Recent new drugs or drugs that are only taken intermittently, recent infection, previously diagnosed hematologic disease, nonhematologic diseases known to decrease platelet counts [e.g., eclampsia, sepsis, disseminated intravascular coagulation (DIC), anaphylactic shock, hypothermia, massive transfusions], positive family history of bleeding and/or thrombocytopenia, recent live virus vaccination, pregnancy, history pertaining to alcohol consumption, and human immunodeficiency virus (HIV) risk factors should be obtained.

This study aims to determine the relative frequency of different disease conditions presenting as newly found thrombocytopenia in adult patients, to determine the proportions of patients who had bleeding manifestations and the different bleeding manifestations in order of their commonness of occurring, and to determine whether a low platelet count or presence of bleeding manifestation was considered more often as indicator for platelet transfusion.

Materials and Methods

This study was carried out in 412 adult patients (age > 18 years) presenting with thrombocytopenia (platelet count <

1,50,000/ μ L) at Civil Hospital, Ahmedabad, from 1 October to 31 October 2013. All patients included in the study were followed up during their course in the hospital.

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. The bleeding manifestations that the patients presented with or developed during their course in hospital were recorded. The diagnosis made in each of these cases was noted down.

Proportion of patients receiving platelet transfusion because of presence of bleeding manifestations and those requiring prophylactic platelet transfusion were determined.

Results

During the period of 1 October to 31 October 2013, 412 patients were included in the study. There were 236 men and 176 women in the study population.

Of 412 cases of thrombocytopenia, 128 (31%) had only thrombocytopenia, 245 (59.4%) had bicytopenia, and 39 (9.4%) had pancytopenia [Table 1].

Malaria was found in 94 (22.8%) patients in which 59.5% patients had *Plasmodium falciparum* infection followed by *Plasmodium vivax* in 37.2% and mixed infection in 3.2%. Moderate thrombocytopenia was more common among all types of malaria whereas severe thrombocytopenia was more common in *P. falciparum* infection [Table 2; Figure 1].

Bleeding secondary to thrombocytopenia was seen in 46 patients with dengue (60.8%) as the most common etiology followed by chronic liver disease, sepsis, hematological malignancy, and ITP [Table 3].

Of the 412 patients studied, fever associated with thrombocytopenia was found in 327 (79.3%) [Table 4].

Table 1: Various causes of thrombocytopenia, bicytopenia, and pancytopenia in the study group

Causes	Only thrombocytopenia	Bicytopenia (thrombocytopenia + leukopenia/anemia)	Pancytopenia	Total
Dengue	23	86	9	118 (28.6%)
Malaria	37	49	8	94 (22.8%)
Chronic liver disease	16	41	6	63 (15.2%)
Hypersplenism	20	23	8	51 (12.3%)
Septicemia	9	16	1	26 (6.3%)
Gestational thrombocytopenia, DIC	6	16	1	23 (5.5%)
Immune thrombocytopenic purpura	13	0	0	13 (3.1%)
Megaloblastic anemia	0	4	4	8 (1.9%)
PLHA	0	6	0	6 (1.4%)
Drug-induced thrombocytopenia	4	1	0	5 (1.2%)
Leukemia	0	3	0	3 (0.7%)
Aplastic anemia	0	0	2	2 (0.48%)
Total	128 (31%)	245 (59.4%)	39 (9.4%)	412

Table 2: Correlation of type of malaria with severity of thrombocytopenia

Type of malaria	Mild thrombocytopenia	Moderate thrombocytopenia	Severe thrombocytopenia	Total
<i>P. vivax</i>	10 (28.5%)	21 (60%)	4 (11.4%)	35 (37.3%)
<i>P. falciparum</i>	13 (23.2%)	33 (58.9%)	10 (17.8%)	56 (59.5%)
Mixed Infection	1 (33.3%)	2 (66.6%)	0	3 (3.2%)
Total	24 (25.5%)	56 (59.5%)	14 (14.8%)	94

Discussion

In this study, the most common etiology responsible for newly diagnosed thrombocytopenia in adult patients was found to be dengue/dengue-like fever (28.6%). Dengue virus has been isolated from polymorphonuclear (PMN) leukocytes, monocyte/macrophages, dendritic cells, and others.^[2] It has also been detected in megakaryocyte progenitors and circulating platelets.^[3-5] The two mechanisms probably involved in dengue-induced thrombocytopenia are impaired thrombopoiesis and peripheral platelet destruction. Malaria was the second common etiology found in 94 (22.8%) patients in which 59.5% had *P. falciparum* infection followed by *P. vivax* in 37.2% and mixed infection in 3.2%. Moderate thrombocytopenia was more common among all types of malaria, whereas severe thrombocytopenia was more common in *P. falciparum* infection. Both nonimmunological destruction and immune mechanism involving specific platelet-associated IgG antibodies that bind directly to malarial antigen in the platelets have been recently reported to play a role in the lysis of platelets.^[6] Chronic liver disease was found in 63 (15.2%) patients, which causes persistent thrombocytopenia and manifests as cirrhosis, fibrosis, and portal hypertension. Moderate thrombocytopenia was found in 51 (12.3%) patients with hypersplenism. Septicemia (6.3%) was another cause of infections with common viruses including hepatitis B and C, HIV, Epstein-Barr virus, cytomegalovirus, varicella-zoster virus, rubella, and mumps. Gestational thrombocytopenia and DIC were found in 5.5% patients. DIC can result from severe infections, as a complication of pregnancy or labor, high blood pressure, and preeclampsia.

Thirteen (3.1%) patients with ITP had antiplatelet antibodies in plasma. Antibody of antiplatelet IgG, stick to the membrane of platelets are kept through the macrophage Fc receptors in spleen. So platelet counts decreases in circulation.^[7] Megaloblastic anemia was found in 1.9% patients due to vitamin B12 and folic acid deficiency as a result of ineffective thrombocytopoiesis. In patients with HIV (1.4%), thrombocytopenia may be related directly to HIV infection, adverse effect of drug therapy, or secondary malignancy or myelodysplasia. Five patients had drug-induced thrombocytopenia with a history of medications such as heparin, quinine, and penicillin, which can cause immunological thrombocytopenia. Patients with leukemia (0.7%) comprise two groups: (1) acute leukemia (myeloid, lymphoid) and (2) chronic leukemia. Particularly in acute leukemia, one-third of patients have petechiae, ecchymosis, and nose bleeding associated with thrombocytopenia because of bone marrow infiltration.^[8] Bleeding secondary to thrombocytopenia was seen in 46 patients. Though dengue (60.8%) was the most common etiology diagnosed followed by ITP (19.5%) in patients with bleeding secondary to thrombocytopenia, the proportion of patients with ITP (69.2%) who had bleeding manifestations was higher than the proportion of patients with dengue (23.7%) who developed bleeding manifestations. Platelet transfusion was given to 87 patients; of these cases, 46 (52.8%) patients were transfused because of bleeding and 41 (47.1%) were prophylactic.

A study was conducted by Nair et al.^[11] at St. Stephen's Hospital, New Delhi, for one and half years. A total of 109 cases (76 male and 33 female patients) were studied with the criteria of febrile thrombocytopenia. Septicemia with 29 cases

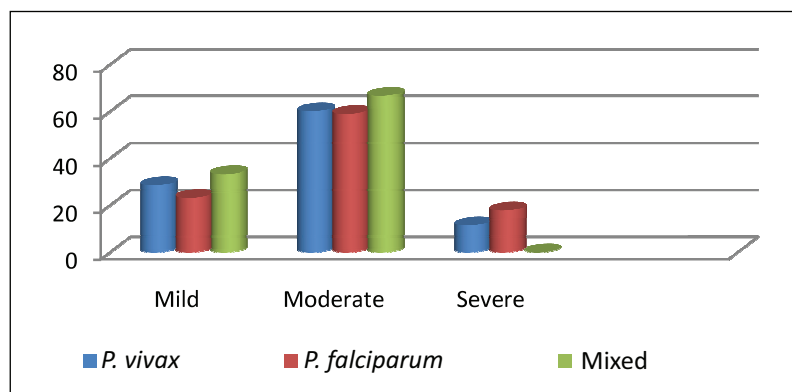


Figure 1: Graphic representation of the platelet count range in correlation with the type of malaria

Table 3: Etiologies responsible for bleeding manifestations in the study group

Dengue/dengue-like fever	28 (60.8%)
Chronic liver disease	4 (8.6%)
Sepsis	3 (6.5%)
Hematological malignancy	2 (4.3%)
Immune thrombocytopenic purpura	9 (19.5%)
Total	46

Table 4: Fever-associated thrombocytopenia in different platelet count ranges: Comparison between different studies

Platelet count range (per μL)	Nair et al. ^[1]	Present study
1,00,000–1,50,000	–	103 (31.4%)
50,000–1,00,000	62 (56.8%)	93 (28.4%)
20,000–50,000	28 (25.7%)	77 (23.5%)
10,000–20,000	10 (9.2%)	32 (9.7%)
5,000–10,000	6 (5.5%)	16 (4.8%)
< 5,000	3 (2.7%)	6 (1.8%)
Total	109	327

was the leading cause of fever-associated thrombocytopenia followed by dengue, megaloblastic anemia, malaria, and hematological malignancy. Of 109 patients, 62 (56.8%) had platelet count between 50,000 and 1,00,000, followed by 28 (25.7%) patients who had count between 20,000 and 50,000. In this study the leading causes were dengue followed by malaria, chronic liver disease, hypersplenism, and septicemia. Dengue and malaria were the common causes due to the higher prevalence of these infections during the study period (October), which may be the reason for variation between different studies. In this study, of 412 cases (236 male and 176 female patients), 93 (28.4%) had platelet count between 50,000 and 1,00,000, followed by 77 (23.5%) who had count between 20,000 and 50,000. In the study by Nair *et al.*^[1], the most common bleeding manifestation was purpura, followed by gum bleed and epistaxis. However in this study, gum bleed was the most common bleeding manifestation followed by purpura.

This study aimed to know the modes of clinical presentations and possible causes of thrombocytopenia. This study might help us to correlate the clinical features and laboratory findings to come to conclusion regarding the possible infective causes for thrombocytopenia and thus diagnosis and management. Transfusion of platelet may not be required in all thrombocytopenias. Treatment of the underlying disease may be sufficient. There is no matched control group, which is one of the limitations of this study.

Conclusion

This study shows that dengue/dengue-like fever is the most common diagnosis made in adult patients who are newly

detected to have thrombocytopenia at admission followed by malaria and chronic liver diseases. Hypersplenism, septicemia, and gestational thrombocytopenia/DIC were the other common causes. In malaria, *P. falciparum* infection was common followed by *P. vivax* and mixed infection. Fever associated with thrombocytopenia was found in 79.3% patients. Forty-six patients with thrombocytopenia tend to have bleeding manifestations, most common being the gum bleed. Dengue (60.8%) was the most common etiology diagnosed followed by ITP (19.5%) in patients with bleeding secondary to thrombocytopenia. The proportion of patients with ITP (69.2%) who had bleeding manifestations was higher than the proportion of patients with dengue (23.7%) who developed bleeding manifestations. Majority of bleeding manifestations occurred in patients with platelet count less than 10,000/ μL . No definitive trigger value of platelet was found for platelet transfusion and transfusion because of bleeding and prophylactic transfusion were given in almost similar proportions of patients.

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