

Clinico-Etiological Evaluation of Acute Febrile Illness with Thrombocytopenia: An Observational StudyAmit Kumar Nirmal¹, Rajeev Kumar², Abilesh Kumar³¹Senior Resident, Department of General Medicine, JLN Medical College and Hospital, Bhagalpur, Bihar, India²Senior Resident, Department of General Medicine, JLN Medical College and Hospital, Bhagalpur, Bihar, India³Professor and HOD, Department of General Medicine, JLN Medical College and Hospital, Bhagalpur, Bihar, India

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Conflict of interest: Nil

Abstract**Aim:** The aim of the present study was to determine the clinical and etiological profile of acute febrile illness with thrombocytopenia.**Material & methods:** This was a hospital-based prospective observational study conducted in the JLN Medical College and Hospital, Bhagalpur, Bihar, India. The study included 100 consecutive patients who were admitted during the period of one year.**Results:** Majority of the patients (65%) were from the age group of 18-40 years followed by 25% from the age group of 41-60 years, 10% from the age groups >60 years. The mean age of the patients was 38.22±10.20 years. In this study 60 (60%) patients were male while female patients constituted 40% of the study group. The causes of febrile thrombocytopenia were dengue (62%), Septicemia (15%), Malaria (9%), Enteric fever (4%), Kala azar (3%), Scrub typhus (2%), other viral fever (5%). Among 20 (20%) patients had bleeding manifestations. Petechiae was the most common site of bleeding manifestation (40%) followed by Epistaxis (20%), Malena (15%), Haematuria (15%), Haematemesis (5%) and Gum bleed (5%). In this study 67 (67%) patients had platelet count of >50,000/ μ Followed by 20 (20%) patients with platelet count of 21,000-50,000/ μ L, 8 (8%) patients with platelet count of 11,000-20,000/ μ L and 5 (5%) patients with platelet count of \leq 10,000/ μ L.**Conclusion:** The study showed that acute febrile thrombocytopenia is an important seasonal syndrome. The common causes are dengue fever and malaria. Early identification of these diseases and prompt treatment decreases complications and reduces mortality. Special consideration should be given to patients having bleeding manifestations, hepatic and renal dysfunction to reduce mortality.**Keywords:** Acute febrile illness, Clinical, etiological ThrombocytopeniaThis is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Acute febrile illness (AFI) is a common cause of patients seeking healthcare in India, especially between June and September. [1] The aetiologies of acute febrile illness can be diverse and may be dependent on geographic location. [2] The infectious causes and epidemiology of acute febrile illness (AFI), defined as illness of < 1 week duration with no identified source, remain poorly characterized in many parts of the world. [3] Common causes of acute febrile illness include upper and lower respiratory tract infections, gastroenteritis, genitourinary infections, soft tissue infections, bacteraemia, malaria, typhoid, meningitis or viral exanthems. [4]

Thrombocytopenia is defined as an abnormal decrease in platelet count below the lower limit of normal which is taken as 150,000 lac/microliter (mcL). [5,6] Infections being the commonest cause of thrombocytopenia. [7] Commonly dengue, malaria, scrub typhus and other rickettsial infections, meningococci, leptospira and certain viral infections present as fever with thrombocytopenia. [8] 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. [9,10]

The symptomatology of thrombocytopenia may range from being asymptomatic and incidentally

discovered to severe life threatening gastrointestinal or central nervous system bleed. [11] The decrease in platelet count is directly related to the risk of severe bleeding and further complications. Thrombocytopenia is not a disease but is condition caused by the underlying illness, hence it is important to acquire details regarding the underlying etiology. Detailed examination and laboratory tests should be done, which are related to etiology. This calls for a detailed history taking for 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). [12]

The climatic conditions in tropical countries like India are favourable for the transmission of most of these infections and every year, with onset of monsoons, a rising trend has been observed in the number of cases admitted into wards and intensive care units with febrile thrombocytopenia with a variable clinical course and an unpredictable outcome. [13]

Hence, it is of utmost importance to serially monitor the platelet count and to determine the cause of febrile thrombocytopenia.

Material & Methods

This was a hospital-based prospective observational study conducted in the JLN Medical College and Hospital, Bhagalpur, Bihar, India. The study included 100 consecutive patients who were admitted during the period of one year.

The inclusion criteria were patients admitted with acute febrile illness defined by a duration of less than 2 weeks and having platelet count less than 150,000/micro litre. Fever is defined as an oral A.M. temperature of >37.2 C (>98.2 F) or a P.M. temperature >37.7 C (99.9 F). Those patients who had immune thrombocytopenic purpura or thrombocytopenia secondary to haematological disorder/ malignancy/chemotherapy/immunosuppressive agents, were excluded from the study even when the diagnosis was established during the course of study.

Patients who fulfilled the above criteria were subjected to a detailed history and clinical examination related to pyrexia and investigations were done to find out the etiology. Laboratory analysis included complete hemogram with peripheral smear, renal function test, serum electrolytes, liver function test, blood glucose, chest X-ray, malarial parasite, widal, IgM dengue, IgM leptospira, IgM scrub typhus, HIV, HbsAg, HCV, ultrasound abdomen and brain imaging if further warrant.

Statistical analysis was done by applying appropriate statistical methods to data collected through this study.

Results

Table 1: Distribution of patients according to age, gender and etiology

| Age (years) | N | % |
|-------------------|-------------|-----|
| 18-40 years | 65 | 65% |
| 41-60 years | 25 | 25% |
| >60 years | 10 | 10% |
| Mean±SD | 38.22±10.20 | |
| Gender | | |
| Male | 60 | 60% |
| Female | 40 | 40% |
| Etiology | | |
| Dengue | 62 | 62% |
| Septicaemia | 15 | 15% |
| Malaria | 9 | 9% |
| Kala Azar | 3 | 3% |
| Scrub typhus | 2 | 2% |
| Enteric Fever | 4 | 4% |
| Other Viral Fever | 5 | 5% |

Majority of the patients (65%) were from the age group of 18-40 years followed by 25% from the age group of 41-60 years, 10% from the age groups >60 years. The mean age of the patients was 38.22±10.20 years. In this study 60 (60%) patients were male

while female patients constituted 40% of the study group. The causes of febrile thrombocytopenia were dengue (62%), Septicemia (15%), Malaria (9%), Enteric fever (4%), Kala azar (3%), Scrub typhus (2%), other viral fever (5%).

Table 2: Distribution of patients according to clinical presentation

| Clinical presentation | N | % |
|-----------------------|----|----|
| Fever | 90 | 90 |
| Organomegaly | 74 | 74 |
| Jaundice | 64 | 64 |
| Lymphadenopathy | 51 | 51 |
| Abdominal pain | 42 | 42 |
| Rash | 30 | 30 |
| Vomiting | 20 | 20 |
| Bleeding tendency | 12 | 12 |

The most common clinical presentation was fever (90%) followed by Organomegaly (74%), Jaundice (64%), Lymphadenopathy (51%), abdominal pain (42%), Rash (30%), vomiting (20%) and bleeding tendency (12%).

Table 3: Distribution of patients according to site of bleeding manifestations

| Site of bleeding manifestations | N | % |
|---------------------------------|---|----|
| Petechiae/purpura | 8 | 40 |
| Epistaxis | 4 | 20 |
| Malena | 3 | 15 |
| Haematuria | 3 | 15 |
| Haematemesis | 1 | 5 |
| Gum bleed | 1 | 5 |

Among 20 (20%) patients had bleeding manifestations. Petechiae was the most common site of bleeding manifestation (40%) followed by Epistaxis (20%), Malena (15%), Haematuria (15%), Haematemesis (5%) and Gum bleed (5%).

Table 4: Distribution of patients according to platelet count

| Platelet count | N | % |
|--------------------------------|-----|------|
| $\leq 10,000/\mu\text{L}$ | 5 | 5 |
| 11,000 – 20,000/ μL | 8 | 8 |
| 21,000 – 50,000/ μL | 20 | 20 |
| $>50,000/\mu\text{L}$ | 67 | 67 |
| Total | 100 | 100% |

In this study 67 (67%) patients had platelet count of $>50,000/\mu$ followed by 20 (20%) patients with platelet count of 21,000-50,000/ μL , 8 (8%) patients with platelet count of 11,000-20,000/ μL and 5 (5%) patients with platelet count of $\leq 10,000/\mu\text{L}$.

Table 5: Association of bleeding manifestations and platelet count

| Platelet count (μL) | Total | Bleeding manifestations (n=20) | | p Value |
|----------------------------------|-------|--------------------------------|------|---------|
| | | N | % | |
| 10,000 | 5 | 5 | 25 | |
| 11,000-20,000 | 8 | 4 | 20 | |
| 21,000-50,000 | 20 | 7 | 35 | <0.05 |
| 50,000 | 67 | 4 | 20 | |
| Total | 100 | 20 | 100% | |

In the present study, out of the 20 patients who had bleeding manifestations, 5 (25%) patients each had platelet count $\leq 10000/\mu\text{L}$ and 11000-20000/ μL , 7 (35%) patients had platelet count 21000-50000/ μL and 4 (20%) patients had platelet count $>50000/\mu\text{L}$. There was no significant association between bleeding manifestations and platelet count as per Chi-Square test ($p < 0.05$).

Discussion

Diseases like dengue fever, malaria, chikungunya fever, leptospirosis, etc. are responsible for the clustering of febrile thrombocytopenia cases during this period. [14] Some of these diseases can cause severe thrombocytopenia, which can be life-threatening. The presence of thrombocytopenia in acute febrile illness should alert the clinician to

identify the etiology and prompt treatment of the patient. [15] The diagnosis of fever with thrombocytopenia cases can be challenging and physicians should be aware of the regional and endemic seasonal cause of this syndrome. Despite the number and diversity of disorders that may be associated etiologically, thrombocytopenia results from only four processes: Artifactual thrombocytopenia, deficient platelet production, accelerated platelet destruction and abnormal distribution or pooling of the platelets within the body. [16] It is the most common cause of abnormal bleeding. Thrombocytopenia develops when there is profound disequilibrium in the balance between platelet production, distribution and destruction. More than one component may be affected in some disorder. [17]

Thrombocytopenia in Dengue fever is caused by bone marrow suppression (i.e., decreased platelet synthesis and increased immune mediated destruction of platelets). [18] Autoimmune thrombocytopenia occurs during or immediately after acute viral infections. HIV associated thrombocytopenia arise through multiple mechanisms, including decreased platelet production, increased platelet destruction due to HIV-mimetic antiplatelet antibodies and increased use of activated platelets. [19] Majority of the patients (65%) were from the age group of 18-40 years followed by 25% from the age group of 41-60 years, 10% from the age groups >60 years. The mean age of the patients was 38.22±10.20 years. In this study 60 (60%) patients were male while female patients constituted 40% of the study group. This was similar to the study done by Nair et al [20], wherein out of 109 total cases studied, 69.7 % of the patients were male. This can be due to more outdoor activities of male counterparts, and thus increased risk of infections.

The causes of febrile thrombocytopenia were dengue (62%), Septicemia (15%), Malaria (9%), Enteric fever (4%), Kala azar (3%), Scrub typhus (2%), other viral fever (5%). The most common clinical presentation was fever (90%) followed by Organomegaly (74%), Jaundice (64%), Lymphadenopathy (51%), abdominal pain (42%), Rash (30%), vomiting (20%) and bleeding tendency (12%). Among 20 (20%) patients had bleeding manifestations. Petechiae was the most common site of bleeding manifestation (40%) followed by Epistaxis (20%), Malena (15%), Haematuria (15%), Haematemesis (5%) and Gum bleed (5%) and similar result was found in Nair et al²⁰ and Lohitashwa et al [21] study.

In this study 67 (67%) patients had platelet count of >50,000/ μ followed by 20 (20%) patients with platelet count of 21,000-50,000/ μ L, 8 (8%) patients with platelet count of 11,000-20,000/ μ L and 5 (5%) patients with platelet count of \leq 10,000/ μ L. A

platelet count of approximately 5000-10000/ μ L is required to maintain vascular integrity in the microcirculation. When the count is markedly decreased, petechiae first appear in areas of increased venous pressure, the ankle and feet in an ambulatory patient. Petechiae are pinpoint, non-blanching hemorrhages and are usually a sign of decreased platelet number and not platelet dysfunction. [22] In the present study, out of the 20 patients who had bleeding manifestations, 5 (25%) patients each had platelet count \leq 10000/ μ L and 11000-20000/ μ L, 7 (35%) patients had platelet count 21000-50000/ μ L and 4 (20%) patients had platelet count >50000/ μ L. There was no significant association between bleeding manifestations and platelet count as per Chi-Square test ($p < 0.05$).

Conclusion

The study showed that acute febrile thrombocytopenia is an important seasonal syndrome. The common causes are dengue fever and malaria. Early identification of these diseases and prompt treatment decreases complications and reduces mortality. Special consideration should be given to patients having bleeding manifestations, hepatic and renal dysfunction to reduce mortality.

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