



CLINICOPATHOLOGICAL SPECTRUM OF THROMBOCYTOPENIA – A PROSPECTIVE STUDY IN RAMA MEDICAL COLLEGE AND RESEARCH CENTRE

Pathology

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ABSTRACT

Background: Thrombocytopenia, or a low blood platelet count, is a common haematological finding with a variety of aetiologies. The clinical manifestation of thrombocytopenia can range from being symptomless to having bleeding episodes. Different mechanisms, including decreased production, increased destruction, and peripheral platelet pooling, underlie thrombocytopenia. Now a days thrombocytopenia is an emergency problem in the field of medicine. Dengue followed by malaria and then sepsis being the commonest cause of thrombocytopenia manifesting with seasonal variations commonly seen in monsoon season. The current study sought to investigate the clinicopathological profile of thrombocytopenia in patients at a tertiary care hospital. The current study also emphasizes that the emergence of the Covid 19 pandemic during the current study added a new dimension to the existing causes of thrombocytopenia. **Result:** Total of 100 patients were selected in 2 years. Maximum number of patients were in age group 31-40 year and were male. Dengue (51%) was the most common cause of thrombocytopenia followed by malaria (10%) and sepsis (7%). On distribution of cases based on clinical presentation 59.0% patients have found with bleeding manifestation followed by Splenomegaly in 10.0%. In cases of bleeding manifestations 47.4 % patients had petechia, 27.1% had epistaxis, 11.8% had purpura, 5.0 % had haematuria and 3.3% had Gum bleed. **Conclusion:** Now a days thrombocytopenia is an emergency problem in the field of medicine. Dengue followed by malaria and then sepsis being the commonest cause of thrombocytopenia manifesting with seasonal variations commonly seen in monsoon season. Not every case of thrombocytopenia is dengue. One should also search for non-infectious causes like liver disease, kidney disease and ITP. Thrombocytopenia with or without bleeding manifestations is a common problem in general clinical practice. To treat or not to treat and how to treat would depend a lot on etiopathogenesis.

KEYWORDS

Thrombocytopenia, dengue, malaria, covid19

INTRODUCTION

Thrombocytopenia, or a low blood platelet count, is a common hematological finding with a variety of etiologies. It is difficult to treat thrombocytopenia because of its complicated etiology, which includes multiple factors. Blood clotting depends on platelets, which are formed in the bone marrow from megakaryocytes and have a lifespan of 7-10 days [1].

True thrombocytopenia can be hereditary or acquired. The more frequent acquired causes of thrombocytopenia are infections, sepsis, bone marrow depression (aplastic anemia), hematological malignancies, myelosuppressive medications, irradiation, immune thrombocytopenia (ITP), thrombotic thrombocytopenic purpura (TTP), diffuse intravascular coagulation (DIC), and massive transfusion. With Wiskott-Aldrich syndrome being the exception and having micro platelets, hereditary causes are frequently syndromic and related to thrombocytopenia with giant platelets [2].

The etiology and severity of thrombocytopenia should be taken into consideration when managing it [3]. Different mechanisms, including decreased production, increased destruction, and peripheral platelet pooling, underlie thrombocytopenia [4,5]

The current study sought to investigate the clinicopathological profile of thrombocytopenia in patients at a tertiary care hospital.

Vaccination was promising approach for ending COVID-19 pandemic, but mass vaccination of many millions of individuals has resulted in several hundred patients developing VITT (vaccine-induced immune thrombotic thrombocytopenia). [6]

The current study also emphasises that the emergence of the COVID 19 added a new dimension to the existing causes of thrombocytopenia.

AIMS & OBJECTIVES

PRIMARY OBJECTIVE: To evaluate patients with thrombocytopenia presenting to the clinical pathology and medical OPD departments of Rama medical college and hospital.

SECONDARY OBJECTIVE:

To correlate clinical features laboratory studies & infective etiology. To evaluate seasonal trends if any

MATERIALS AND METHODS

The study was carried out in patients having Thrombocytopenia at RAMA Medical College Hospital, Kanpur (U.P.) a tertiary care teaching hospital.

Study Design: Prospective survey of patients with Thrombocytopenia.

Sample size -100

OBSERVATIONS DISCUSSION AND RESULTS

Total of 100 patients were selected in 2 years and were categorized according to age, sex, clinical history and other positive laboratory findings.

TABLES

In the current study, on basis of gender ratio Males was affected in more number 62.0% than females 38.0% (**Table 1**). Out of which maximum number of patients were in the age group of 31-40 Years and least in the age group of 51-60 Years.

In a study done by Lakshmikummar et al showed similar result male (60.5%) predominance to female (39.5%). In another study conducted by Gondhal et al showed similar results with male preponderance with males (56.0%) and females (44.0%).

Table 1. Gender Distribution Of Patient

Gender	Number of patients (%)
Female	38
Male	62
Total	100

Patients had low platelet count in which 25.0% patients had platelet count below 20000 cumm, 35.0% had between 20000 cumm to 50000 cumm, 30% had platelet count above 50000 cumm. Patient with low platelet count below 20000 cumm had prolonged Bleeding time and clotting time and prolonged Prothrombin time, APTT and INR (**Table 2**).

The findings were consistent with the study of Nair ps et al where (17.5%) patients had platelet count less than 20,000 and 25% had platelet count between 20,000-40,000 [7]

Table 2: Platelet Count Of Patients Presenting With Thrombocytopenia

Platelet's count (cumm)	No. of Patients	Percentage
<20000	25	25%
20,000-50,000	35	35%
50,000- 100000	30	30%
100000-150000	10	10%

Among all the cases in our study, most common infectious cause for thrombocytopenia was dengue fever which was present in 51% followed by malaria (10%). In viral fever other than dengue Thrombocytopenia was also observed in different proportions among patients with coronavirus disease (COVID-19) Moreover, a case of COVID-19-related ITP has been reported.

Chronic liver disease was 6%, Immune Thrombocytopenic purpura and Megaloblastic anemia 5.0%, Leukemia 4.0%, HIV 2.0%, Gestational thrombocytopenia, DIC 1.0% & and the rarest cases like Aplastic anemia, Multiple Myeloma, Drug Induced thrombocytopenia was found in 1.0% cases only (Table 3).

Findings of Laxmikumar et al were similar with our research that dengue (68.9%) was the most common cause of fever associated with thrombocytopenia followed by malaria which was the second most common cause. Purnima mitra et al also reported Dengue were most common cause of thrombocytopenia (23.7%). Malaria was the second common cause of thrombocytopenia (14.81%).

Two positive cases of COVID-19 were reported in the present study. In viral fever other than dengue Thrombocytopenia was also observed in different proportions among patients with coronavirus disease (COVID- 19) Moreover, a case of COVID-19-related ITP has been reported. 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.[8]

Alcoholic liver disease was found in 6.0% patients, which causes persistent thrombocytopenia and manifests as cirrhosis, fibrosis, and portal hypertension. According to a study done by Qamar A et al thrombocytopenia is the most common and first abnormal hematologic indices to occur in patients with cirrhosis [9]

Table 3. Distribution Of Cases Based On Aetiology

Diagnosis	Number of patients (percentage)
Dengue fever	51
Malaria	10
Sepsis	07
Viral fever other than Dengue	06
Chronic liver disease (ALD)	06
Immune Thrombocytopenic purpura	05
Megaloblastic anaemia	05
Leukaemia	04
HIV	02
Gestational thrombocytopenia, DIC	01
Aplastic anaemia	01
Multiple Myeloma	01
Drug Induced thrombocytopenia	01
Total	100

On basis of the distribution of cases based on clinical presentation, 59.0% patients were found to have bleeding manifestation followed by Splenomegaly in 10.0%, Arthralgia 8.0%. (Table 4).

Table 4. Distribution Of Cases Based On Clinical Presentation

Symptoms	No. of patients	Percentage
Bleeding manifestations	59	59%
Splenomegaly	10	10%
Hepatomegaly	5	5%
Arthralgia	8	8%
Restlessness	8	8%
Lethargy	7	7%
Retro orbital pain	3	3 %

In cases of bleeding manifestations 47.4 % patients had petechia, 27.1% had epistaxis, 11.8% had purpura, 5.0 % had haematuria and 5.0 % had venepuncture and 3.3% had Gum bleed (Table 5).

This was In contrast to study by Dr. Srinivas et al, purpura (63%) was the commonest bleeding manifestation[10] Nair et al.[11], 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.

Table 5. Distribution Of Cases Based On Mode Of Bleeding Manifestations (N=59)

BLEEDING MANIFESTATION	TOTAL	PERCENTAGE
PETECHIAE	28	47.4%
EPISTAXIS	16	27.1%
PURPURA	7	11.8%
HAEMATURIA	3	5.0%
VENEPUNCTURE	3	5.0%
GUM BLEED	2	3.3%

CONCLUSION

Thrombocytopenia is not a disease but is a diagnosis. Dengue followed by malaria and then sepsis being the commonest cause of thrombocytopenia manifesting with seasonal variations commonly seen in monsoon season with cumulative effect of endemicities in that particular region. Common complications of dengue being varied bleeding manifestations secondary to thrombocytopenia showing no direct correlation between platelet count and severity of bleeding as well as to mortality and morbidity. Prompt diagnosis and appropriate treatment of underlying etiology of febrile thrombocytopenia with maintenance of platelet count, adequate hydration and symptomatic management gives good recovery and better outcome.

The spectrum of hematological manifestation of COVID-19 is wide and frequently unpredictable. We presented two different extremes of severe thrombocytopenia (ITP and DIC), both precipitated by COVID-19 inflammation, without pulmonary manifestations and with good response to systemic corticosteroid therapy. The accumulation of more cases is warranted for a more comprehensive knowledge of similar diseases. In the future, the detailed mechanism of COVID-19-induced ITP and the best treatment strategy needs further investigation.

Thrombocytopenia with or without bleeding manifestations is a common problem in general clinical practice. To treat or not to treat and how to treat would depend a lot on etiopathogenesis of this problem. As pathologists, it is for us to highlight this point in order to help the clinician manage the patient in a scientific and beneficial manner. As we have seen, supportive parameters like a good peripheral smear examination, coagulation profile, comprehensive marrow evaluation and certain biochemical parameters with the clinical profile go a long way in narrowing the etiology and maximizing treatment benefits. It should be remembered that all thrombocytopenia are not immune mediated. Also, in cases of confirmed immune thrombocytopenia one should have an open mind about other non-immune processes creeping into pathogenesis during progression of disease.

REFERENCES

- Hine LK, Gerstman BB, Wise RP, T song Y. Mortality resulting from blood dyscrasias in the United States, 1984. *Ann J Med* 1990;88(2):151-153.
- Rodgers GM, Lehman CM. Diagnostic approach to the bleeding disorders. In: Greer JP, Arber DA, Glader B, List AF, Means RT, Paraskevas F, et al., editors. *Wintrobe's Clinical Hematology*. 13th ed. China: Lippincott Williams & Wilkins; 2014. 1043-57.
- Rutherford CJ, Frenkel EP: Common bleeding and clotting disorders. *The Medical Clin N Am*, May 1994, 78:3,555-575.
- George M. Rodgers. Thrombocytopenia Pathophysiology and Classification. [2]In: John P. Greer, John Foerester, George M. Rodgers; *Wintrobe's Clinical Hematology*, 12th ed. Lippincott Williams & Wilkins; 2009. Vol 2.
- Thrombocytopenia: Overview. In: Marshall A. Lichtman, Ernest Beutler, Thomas J. Kipps; *Williams Hematology*, 7th ed. Mc Graw-Hill Medical; Copyright©2007 ;P. 468-481.
- Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S *N Engl J Med*. 2021;384(22):2092. Epub 2021 Apr 9.
- Nair PS, Jain A, Khanduri U, Kumar V. "A study of fever with thrombocytopenia". *JAPI*, dec 51: 1173
- Neunert C, Lim W, Crowther M, Cohen A, Solberg L, Jr, Crowther MA, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood* 2011;117(16):4190-207.
- Qamar, A.A.; Grace, N.D. Abnormal hematological indices in cirrhosis. *Can. J. Gastroenterol*. **2009**, 23, 441-445.
- Srikanth J, Srinivas S, Krishna CR, Ramulu PR. Prevalence of thrombocytopenia in a diagnosed case of malaria in rural population of South India. *J NTR Univ Health Sci* 2012;1: 152-5.
- Nair PS, Jain A, Khanduri U, Kumar V. A study of fever associated thrombocytopenia. *JAPI* 2003;51:1173.