



## A STUDY ON ETIOLOGY AND CLINICAL PROFILE OF PATIENTS WITH THROMBOCYTOPENIA

**Dr. D. Sridhar**

M.D., Associate Professor of General Medicine; Osmania Medical College / General Hospital, Hyderabad, Telangana State.

**Dr. Anil Kumar Kotte\***

Postgraduate, General Medicine, Osmania Medical College / Osmania General Hospital, Hyderabad, Telangana State. \*Corresponding Author

### ABSTRACT

**BACKGROUND:** Thrombocytopenia refers to a reduction in platelet count below 1.5 lakh/microliter. The presence of thrombocytopenia in a hemogram should alert the physician to identify the underlying etiology for the prompt management of the patient. Timely identification and treatment prevent bleeding manifestations, requirement of platelet transfusions/steroids and overall impact on mortality of the patients.

**AIM OF STUDY:** Analysis to study the etiology, bleeding manifestation, percentage of patients requiring platelet transfusion, length of hospital stay in patients with thrombocytopenia.

**METHODOLOGY:** 100 cases thrombocytopenia both male and female were included in the study. The diagnosis was made on peripheral smear and Hemogram.

**RESULTS:** Dengue fever was the most common cause of thrombocytopenia with 43 cases. Sepsis with 23 cases was the second commonest. Bleeding manifestations were seen in 23% of the study population. 100% of the patients with platelet count less than 10,000/microlitre had bleeding manifestations. 26 patients (26%) received platelet transfusion out of which 23 were therapeutic and 3 were prophylactic transfusions. Steroid therapy was given in 11% of patients. Mortality was highest in patients with sepsis induced thrombocytopenia.

**CONCLUSION:** This study shows that Dengue fever is the commonest diagnosis made in patients who are detected to have thrombocytopenia. One fifth of patients with platelet count less than 1,00,000/microlitre tend to have bleeding manifestation, commonest being GI bleed, petechial rash and epistaxis. Majority of the bleeding occurs with platelet count less than 10,000. The proportion of patients receiving therapeutic platelet transfusion was higher compared to prophylactic transfusion.

**KEYWORDS :** ITP → Idiopathic thrombocytopenic purpura, CLD → Chronic Liver disease, DIC → Disseminated intravascular coagulation, AML/CML → Acute/Chronic myeloid leukemia, HELLP → Hemolysis elevated liver enzymes low platelet count.

### INTRODUCTION

Thrombocytopenia refers to a reduction in platelet count below 1.5 lakh/microliter. It is the commonest abnormality encountered in clinical practice with variable clinical expression. In a tropical country like India, infectious causes predominate and are usually associated with fever, also drugs, autoimmunity, Hypersplenism, DIC, malignancy are among the leading causes of thrombocytopenia. Pseudothrombocytopenia should always be ruled out first by peripheral smear examination. Because platelet counts are prone to error, a single platelet count that is lower than normal should be confirmed by a second count. It should also be confirmed by inspecting the blood film. The life span of platelets once they enter the circulation is about 8-10 days. Thrombocytopenia may result from impaired platelet production, accelerated platelet destruction, or dilution/splenic sequestration<sup>1</sup>. Of these infections being the commonest cause of thrombocytopenia. Diseases which commonly present with fever and thrombocytopenia are malaria, leptospirosis, rickettsial infections, septicemia, typhoid, borreliosis, arbovirus such as dengue or yellow fever, rodent-borne viruses, human immunodeficiency virus (HIV), leishmaniasis and Thrombotic thrombocytopenic purpura, Hemolytic uremic syndrome (TTP-HUS)<sup>1</sup>. The presence of thrombocytopenia in a hemogram should alert the physician to identify the underlying etiology for the prompt management of the patient. This study attempts to determine the common etiologies responsible for thrombocytopenia among patients admitted in Osmania general hospital and their clinical profile with relevance to bleeding manifestations, requirement of platelet transfusions/steroids and overall impact on mortality of the patients.

### AIMS AND OBJECTIVES

- To study the etiology of Thrombocytopenia in various patients.
- To study the proportion of patients with bleeding manifestations.
- To study the percentage of patients requiring platelet transfusion and steroids.
- To study the length of hospital stay in patients with thrombocytopenia.

### MATERIALS AND METHODS

**Type of study:** Observational study

**Place of study:** Osmania general hospital, Hyderabad

**Study population:** 100 Patients admitted in Osmania General Hospital.

### Inclusion criteria:

Patients admitted in Medical ward between November 2016 to October 2018, satisfying the following inclusion criteria were included in the study.

- Age > 18 years
- Patients with a platelet count of less than 1.5 lakhs/mm<sup>3</sup>

### Exclusion criteria

- Age < 18 years.
- Patients who have already received platelet transfusions prior to admission.
- Patients who were earlier diagnosed to have conditions that are known to cause thrombocytopenia.

### METHODOLOGY:

Patients with platelet count less than 1.5 lakhs/microliter on peripheral smear and Hemogram were included in the study. Patients were investigated for the cause of thrombocytopenia. Patients were followed daily and analyzed based on the need for platelet transfusion/steroids, severity of thrombocytopenia, development of bleeding manifestations, duration of hospital stay and the final outcome of hospital admission.

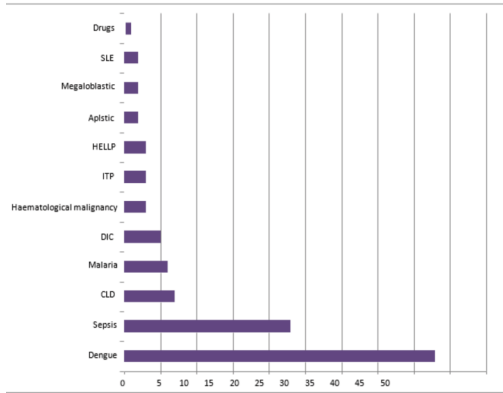
### RESULTS

During the study period of 24 months, 100 patients satisfied the inclusion criteria and were included in the study. There were 70 males and 30 females in the study population.

The commonest etiology for thrombocytopenia in patients admitted in to medical ward was Dengue. 43 patients were diagnosed to be Dengue making up 43% of the study population. 23 patients were diagnosed to be in sepsis making upto 23% of the study population. CLD was responsible for thrombocytopenia in 7 cases making in third in the list. Malaria was diagnosed in 6 cases. Out of 6 cases, falciparum malaria was diagnosed in 4 cases, vivax malaria in 1, mixed infection in 1 case. DIC was next in the list with 5 cases. Hematological malignancies were responsible in 3 cases. Out of 3 cases of malignancy AML, CML and Multiple Myeloma were responsible for 1 case each. ITP was the diagnosis in 3 cases. HELLP and Aplastic anemia accounted in 3 and 2 cases respectively. Megaloblastic anemia and connective tissue disorders were responsible for 2 cases each. Drug related thrombocytopenia seen in 1 case. It was suspected in patients where no

other etiology except the medication was attributable to thrombocytopenia. Heparin was responsible in that patient

**Chart 1. Etiology of Thrombocytopenia**



Most of the patients with sepsis as the cause of thrombocytopenia were diagnosed to have Pneumonia. Out of 23 patients with sepsis, 11 (48%) were diagnosed to have pneumonia as the focus of sepsis. UTI was diagnosed in 3 cases and all the 3 were females. The source of sepsis was unidentified in 6 cases.

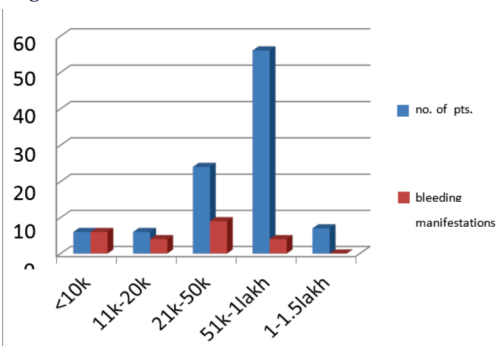
In 100 patients of thrombocytopenia Malaria was diagnosed in 6 cases. Out of 6 cases, falciparum malaria was diagnosed in 4 cases, vivax malaria in 1, mixed infection in 1 case.

**Bleeding manifestations**

Of the total 100 patients with Thrombocytopenia, bleeding manifestations occur in 23 patients (23%). 6 out of 6 patients (100%) with platelet count less than 10000/microlitre showed bleeding manifestations. Among 7 patients with platelet count between 11000-20000/microlitre, 4 patients (66%) showed bleeding manifestations. 8 patients (33%) out of 24 patients with platelet count between 21000-50000/microlitre showed bleeding manifestations.

Among 7 patients with platelet count of more than 1 lakh/microlitre, none of them had any bleeding manifestations.

**Chart 2. Number of patients in each Platelet range group and bleeding manifestations**



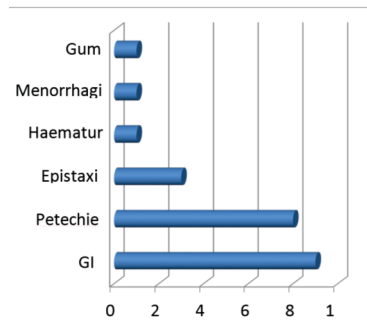
The commonest bleeding manifestation in patients secondary to thrombocytopenia was gastrointestinal bleed which was seen in 9 patients. Petechial rash was seen in 8 patients, epistaxis in 3 patients. Menorrhagia, gum bleed and hematuria was seen in one patient each.

Out of 43 patients with Dengue/Dengue like fever, 14 patients (32.5%) developed bleeding manifestations among which 6 developed petechiae, 5 developed GI bleed, 1 patient developed epistaxis, and 1 patient developed Menorrhagia.

Out of 23 patients with sepsis, 3 patients (13.2%) had bleeding manifestations out of which 1 patient had GI bleed, 2 patients developed petechiae.

One patient with CLD developed petechiae. One patient with aplastic anemia developed GI bleed. One patient with HELLP developed hematuria. One patient with DIC developed gum bleed. One patient each with CML, ITP developed epistaxis.

**Chart 3- Bleeding manifestations in various cases of thrombocytopenia**



**Interventions**

Out of 100 patients with thrombocytopenia, 26 (26%) patients were given platelet transfusions. All 6 patients with platelet count less than 10000/microlitre received therapeutic platelet transfusion and all 7 patients with platelet count between 11000/microlitre and 20000/microlitre received platelet transfusion, out of which 3 were prophylactic transfusions and 4 were therapeutic transfusions. Out of the remaining patients who received platelet transfusion 9 patients had platelet count between 21000/microlitre and 50000/microlitre, out of which 9 were therapeutic.

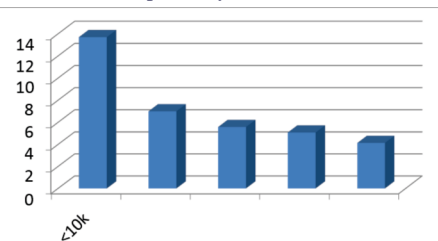
Coming to disease wise platelet transfusion, 3 patients (13.04%) with sepsis received platelet transfusion. 17 patients with dengue (39.5%) received platelet transfusion. 1 patient with ITP (33.3%) received transfusion. 2 out of 3 patients (66%) with HELLP received platelet transfusion. One patient each Aplastic anemia, Malaria, CLD received platelet transfusion.

**Steroid therapy**

Out of 100 patients with thrombocytopenia, 11 patients were given steroid therapy. All the patients with ITP, Connective tissue disorder, Aplastic anemia received steroid therapy. 4 patients out of 23 patients with sepsis were given steroid therapy.

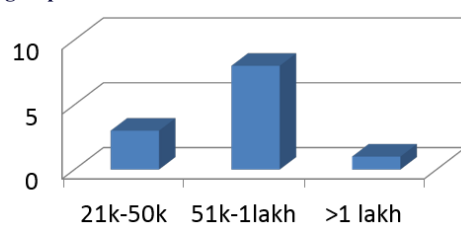
Duration of hospital stay: Apart from the primary disease platelet count also influenced the duration of hospital stay. Patients with platelet count of less than 10000/microlitre had an average hospital stay of 13.7 days. Patients with platelet count from 11000-20000/microlitre had an average stay of 7 days and similarly it was 5.58 days for patients with platelet count between 21000 to 50000. Patients with platelet range from 51000- 100000/microlitre stayed for an average of 5.08 days in Hospital.

**Chart 4 : Duration of hospital stay**



**Mortality:** Out of 100 cases with thrombocytopenia admitted in to hospital the mortality rate was 13%. Mortality was highest in patients with sepsis induced thrombocytopenia 9 (39.5%). Two patients of DIC one patient of hematological malignancy and one patient of CLD expired.

**Chart 5: Number of patients who expired in different platelet range groups**



**DISCUSSION**

Dengue was the most common etiology of Thrombocytopenia admitted into hospital. A total of 43 patients (43%) were diagnosed to be having dengue with thrombocytopenia. There were 70 males and 30 females in the study population. The mean age of the study population was 42.92 years.

A similar type of study conducted at the Mayo Clinic<sup>2</sup> Medical Center, St. Marys Hospital, Rochester, and MN. Study conducted by Chakradhar Venkata Rahul Kashyap, J Christopher Farmer and Bekele Afessa<sup>3</sup>. It concluded that 16% of patients with severe thrombocytopenia (that is platelet count <50,000) required platelet transfusion. In the present study the platelet transfusion was done in 26% of patients with severe thrombocytopenia. Major bleeding, seen in 14.4% patients in Mayo clinic study in this study it seen in 23% of patients.

**Table 1 : Comparison of percentage of patients who received platelet transfusion and percentage of mortality**

Parameter	Mayo clinic study <sup>2</sup>	Present study
% of Platelet transfusion	16%	26%
Mortality in thrombocytopenia	21.2%	12%
Bleeding manifestations	14.4%	23%

Vanderschueren, Steven MD, PhD, De Weerd, Annick MD; Malbrain, Manu MD et al<sup>4</sup> did a study on the prognosis of patients with thrombocytopenia in July 2000 and concluded that patients with thrombocytopenia had greater risk of bleeding manifestations, prolonged hospital stay and increased rate of Mortality.

Bleeding manifestations were seen in 52.6% of patients in that study where as in the present study it was only 23% in patients with a platelet count of less than 1,50,000/mm<sup>3</sup>. The mortality rate was 19.5% in that study and it was 12% in present study.

**Table 2 : Comparison of bleeding manifestations, mortality and duration of hospital stay**

Parameter	Vanderschueren study <sup>4</sup>	Present study
Bleeding manifestations	52.6%	23%
Mortality	19.5%	12%
Hospital stay	8 days	5.58 days

Most of the patients who presented as sepsis with thrombocytopenia were diagnosed with Pneumonia as the cause of Sepsis. A study done by Chakradhar Venkata et al<sup>3</sup> found Pneumonia to be the cause of sepsis with thrombocytopenia in 38.8% and in present study pneumonia was responsible for 46.5% of the cases of sepsis with thrombocytopenia.

**Table 3: Comparison of proportion of patients with thrombocytopenia in sepsis due to pneumonia**

	Chakradhar Venkata, et al <sup>3</sup>	Present study
Thrombocytopenia in sepsis due to pneumonia	38.8	47.8

**Comparison of clinical profile of patients with Dengue fever**

A Study of Clinical Profile of Dengue Fever in Kollam, Kerala, India Rachel Daniel, Rajamohan and Aby Zachariah<sup>5</sup> Philip Bishop Benziger Hospital, Kollam, Kerala, India showed The disease incidence was equally distributed among both sexes of 250 cases 130 males and 120 females in our study dengue fever is seen in 43 patients of which 24 are males and 19 are females.

The patients mean age was 42.6 (SD 20) years in dengue fever kollam Study<sup>5</sup>. In our study 32.6 years.

**Table 4: Comparison of mean age and sex distribution**

	Kollam study <sup>5</sup>	Present study
%males	52%	55.8%
%females	48%	44.2%
Mean age	42.6yrs	32.6yrs

In Kollam study bleeding manifestations seen in 58 patients. In our study bleeding manifestations seen in 14 of 43 patients

**Table 5: Comparison of bleeding manifestations in both studies:**

	Kollam study <sup>5</sup>	Present study
%patients developed bleeding manifestations	23.2%	32.5%
GIT bleed	32%	35.7%
Petechiae	25%	42.8%
Menorrhagia	18%	7.1%

In Kollam study platelet count less than ten thousand seen in 8.6%, platelet count of eleven thousand to fifty thousand seen in 47.4% and platelet count more than fifty thousand seen in 44% of patients.

**Table 6: comparison of platelet count in dengue patients**

Platelet count/(microlitre)	Kollam study <sup>5</sup>	Present study
<10k	8.6%	13.95%
11k-50k	47.4%	60.46%
>50k	44%	25.58%

Bleeding manifestations in Dengue fever in a study done in Hawaii, USA by Paul v Effler et al<sup>6</sup> in 2001-02 found petechiae to be the common bleeding manifestation followed by menorrhagia and epistaxis.

**Table 7 : Comparison of bleeding manifestations in patients with Dengue fever in 2 studies**

	Paul v Effler et al <sup>6</sup>	Present study
Petechaie	8%	13.9%
Menorrhagia	5.5%	7.1%
Epistaxis	4.4%	7.1%
GIT bleed	3.1%	35.7%
Haematuria	3.1%	7.1%

**CONCLUSION:**

This study shows that Dengue fever is the commonest diagnosis in thrombocytopenia. Patients with febrile illness with thrombocytopenia are likely to be suffering from dengue/dengue like fever. Sepsis is the second commonest diagnosis. Malaria and chronic liver diseases are also high in the list of diseases presenting as thrombocytopenia.

One fifth of patients with platelet count less than 1, 00,000/microlitre tend to have bleeding manifestation, commonest being GI bleed, petechial rash and epistaxis. Majority of the bleeding occurs with platelet count less than 10,000. In patients with sepsis bleeding is not related solely to platelet count but coagulopathy also contribute to it.

The proportion of patients receiving therapeutic platelet transfusion was higher compared to prophylactic transfusion. Majority of the patients received prophylactic platelet transfusion if the platelet count was less than 20000.

Patients with severe thrombocytopenia required a prolonged hospital stay and mortality rate was also higher in that patient group.

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