



## Clinicopathological Analysis of Thrombocytopenia: Cross-sectional Insights into Variability

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### KEYWORDS

Thrombocytopenia, platelet count, dengue, acute febrile illness, malaria

### ABSTRACT:

**Introduction:** Thrombocytopenia, characterized by low platelet levels, is common in hospitalized patients and can lead to excessive bleeding or bruising due to insufficient clotting. Causes include abnormal sequestration, increased peripheral destruction, or decreased bone marrow production. Symptoms range from asymptomatic presentation to easy bruising and prolonged bleeding, to even severe cases of internal bleeding.

**Objectives:** This study aimed to analyse adult thrombocytopenia cases through clinicopathological correlation, examining etiological factors, severity, and clinical presentations.

**Methods:** A three-month cross-sectional study was conducted, extracting data from patients with platelet counts below 100,000/ $\mu$ L.

**Results:** The study involved 100 patients (66% males, 34% females) aged 40-60 years. Platelet counts were <50,000 in 31% and 50,000-100,000 in 69% of patients. Causes included Dengue fever (26%), Malaria (8%), scrub typhus (8%), sepsis (9%), chronic liver disease (12%), acute kidney injury (3%), chronic kidney disease (13%), obstetric/gynaecological diseases (5%), malignancy (2%), acute decompensated heart failure (2%), acute gastroenteritis (5%), and haematological disorders (3%).

**Conclusions:** Dengue was the primary cause of thrombocytopenia, with chronic kidney and liver diseases as common non-infectious causes in our study. Fever and bleeding were the most prevalent symptoms. Early detection and ongoing care can prevent severe bleeding complications.

### 1. Introduction

Thrombocytopenia is a common occurrence in hospitalized cases, often going unnoticed if platelet counts are not regularly checked. A platelet count below 150,000 platelet / $\mu$ L is considered thrombocytopenia [1], but it does not provide insight into the underlying cause. Thrombocytopenia is classified into three stages based on platelet count – In the mild stage, platelet count ranges from 100,000 to 150,000/ $\mu$ L, the moderate stage is characterized by platelet counts between 50,000 and 100,000/ $\mu$ L and platelet counts lower than 50,000/ $\mu$ L indicate the severe stage of thrombocytopenia. This condition can stem from decreased production in the bone marrow, increased destruction in the periphery, abnormal sequestration, and pooling [2]. Timely identification and constant monitoring of patients with thrombocytopenia can prevent bleeding issues, including potentially deadly intracranial haemorrhage [3]. Numerous research studies have explored febrile thrombocytopenia in hospitalized

patients, with a strong focus on dengue fever. In addition to infectious causes, there are various other factors that can lead to thrombocytopenia in patients. Therefore, this study aimed to identify the different causes of thrombocytopenia in hospitalized patients, correlating their clinical and pathological features.

It is important for individuals experiencing symptoms of thrombocytopenia to seek medical attention promptly for proper evaluation and thrombocytopenia and to prevent potentially life-threatening complications from thrombocytopenia. One of the most significant complications is an increased risk of excessive bleeding and bruising, as platelets play a crucial role in clotting and stopping bleeding [4]. Additionally, individuals with thrombocytopenia may be at higher risk for internal bleeding, particularly in vital organs such as the brain causing stroke or gastrointestinal tract causing hematemesis or melena.



The primary focus of this research is to conduct a thorough clinicopathological analysis of different instances of thrombocytopenia in adult patients seeking treatment at the hospital. The goal of this study is to determine the distribution of age and sex among the cases, identify various causes of the condition, assess the severity of thrombocytopenia and examine different clinical presentations [5, 6].

## 2. Objectives

With an emphasis on etiological variables, severity, and clinical manifestations, this study attempted to analyze cases of adult thrombocytopenia using clinicopathological correlation.

## 3. Methods

The study was conducted over a period of three months at Vinayaka Mission's Medical College and Hospital (VMMC), Karaikal, a tertiary care hospital in South India. Ethical clearance was obtained from the Institutional Ethical Committee at VMMC. 2 ml of EDTA blood samples from patients were analysed in Mindray BC-6000 Auto Haematology Analyzer (Mindray, Shenzhen, China) – a six-part automated analyser at the Clinical Pathology Lab of VMMC. Those with a machine baseline platelet count below 100,000 platelet / $\mu\text{L}$  were confirmed by a peripheral smear and then included in the research. The smears with clumping i.e. EDTA induced thrombocytopenia were considered as pseudo-thrombocytopenia and excluded from the study.

*Inclusion criteria:* All cases of both sexes with a platelet count of less than 100,000 platelet / $\mu\text{L}$  i.e. cases of moderate and severe thrombocytopenia.

*Exclusion criteria:* Patients on antiplatelet drugs [7] and other medications known to cause thrombocytopenia. Patients with pseudo-thrombocytopenia (EDTA-induced thrombocytopenia) [8]. Patients whose incomplete clinical records.

The data regarding the age and sex distributions of the cases, clinical findings such as how the patients presented, any accompanying bleeding issues, and other relevant test results necessary for determining the exact cause of the illness were gathered. Diagnosing thrombocytopenia typically involves a physical examination, a review of medical history, and blood tests examining peripheral blood smears to confirm platelet counts and diagnose Malaria, acute febrile illness, dengue [9], chronic kidney

disease (CKD), Scrub typhus [10]. Additional tests such as analysing bone marrow samples and conducting serological tests for HIV [11], WIDAL [12], and other infectious diseases based on information from the patients' medical records was performed to determine the underlying cause of low platelet levels.

## Statistical analysis

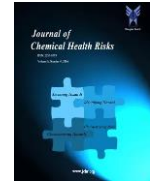
Analysis of the data entailed organizing it into tables using Microsoft Excel 2019 (Microsoft Corporation, USA), looking at the frequency of each diagnosis, its percentage representation, how it impacted different age groups and sexes, grading the severity of thrombocytopenia cases, and noting the occurrence of symptoms and signs within each classification. Analysis was done using SPSS (IBM, USA) v23.

## 4. Results

The results of this study on thrombocytopenia with relevant clinicopathology are discussed henceforth. Figure 1 shows the male to female breakdown of the study subjects – out of the total study population, 34% were females and 66% were males.

The platelet counts of the study subjects were categorized into moderate thrombocytopenia with 69 cases (69%) and severe thrombocytopenia with 31 cases (31%), as shown in Table 1, showing a higher prevalence of moderate in comparison to severe thrombocytopenia. The distribution of study subjects based on their age is shown in Table 2. The highest number of cases belonged to the age range of 40-60 years, accounting for 41 cases (41%), 31 cases (31%) in the 20-40 years range, followed by individuals over 60 years old with 17 cases (17%), and the smallest group being those under 20 years of age, with 11 cases (11%), as also seen in a graphical representation in Figure 2. Moderate thrombocytopenia was found to be more prevalent compared to severe thrombocytopenia in all age groups in our study population.

The etiological diagnosis of the subjects and the relative frequency of thrombocytopenia (severe and moderate) among the subjects is represented in Table 3. Figure 3 shows the etiological distribution of the data. Dengue fever was found to be the most common cause followed by CKD, chronic liver disease (CLD), sepsis, scrub typhus, malaria, acute gastroenteritis, obstetric and gynaecological causes, diabetes, acute kidney injury (AKI), haematological causes and acute decompensated heart failure (ADHF) as seen in Figure 4 which has the



frequency of moderate and severe thrombocytopenia of the major etiological causes. Moderate thrombocytopenia was more common compared to severe thrombocytopenia with all causes barring the obstetric and gynaecological aetiology, and an equal number of moderate and severe thrombocytopenia cases were seen in CLD and malignancy.

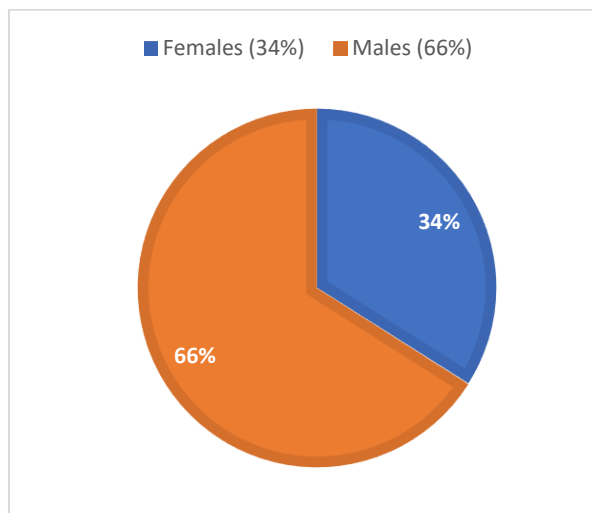


Figure 1: sex distribution of study subjects (Total n=100, female n=34)

Table 1: Platelet counts of study subjects for cases of moderate and severe thrombocytopenia

Platelet counts (in platelets/microliter)	Frequency
Severe thrombocytopenia (<50,000)	31 (31%)
Moderate thrombocytopenia (50,000 – 1,00,000)	69 (69%)
TOTAL	100 (100%)

Table 2: Age-wise distribution of study subjects

Age group (years)	Platelet count <50,000	Platelet count 50,000-100,000
<20	4%	7%
20-40	12%	19%
40-60	8%	33%
>60	7%	10%
TOTAL	31%	69%

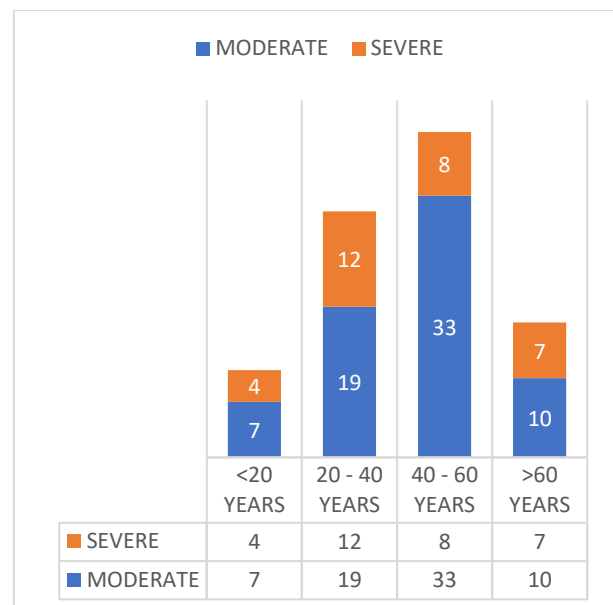


Figure 2: Age distribution of moderate and severe thrombocytopenia among the study participants

Table 3: Distribution of thrombocytopenia according to the underlying diagnosis

Etiological Diagnosis	Number of cases	Platelet count <50,000	Platelet count 50,000-100,000
Acute Decompensated Heart Failure (ADHF)	2	0	2
Acute Gastroenteritis (AGE)	5	2	3
Acute Kidney Injury (AKI)	3	0	3
Chronic Kidney Disease (CKD)	13	4	9
Chronic Liver Disease (CLD)	12	6	6



Haematological Disorders	3	1	2
Obstetric And Gynaecological (OBS & GYN)	5	3	2
Malignancy	2	1	1
Dengue Fever	26	7	19
Diabetes	4	1	3
Malaria	8	3	5
Scrub Typhus	8	1	7
Sepsis	9	2	7
TOTAL	100	31	69

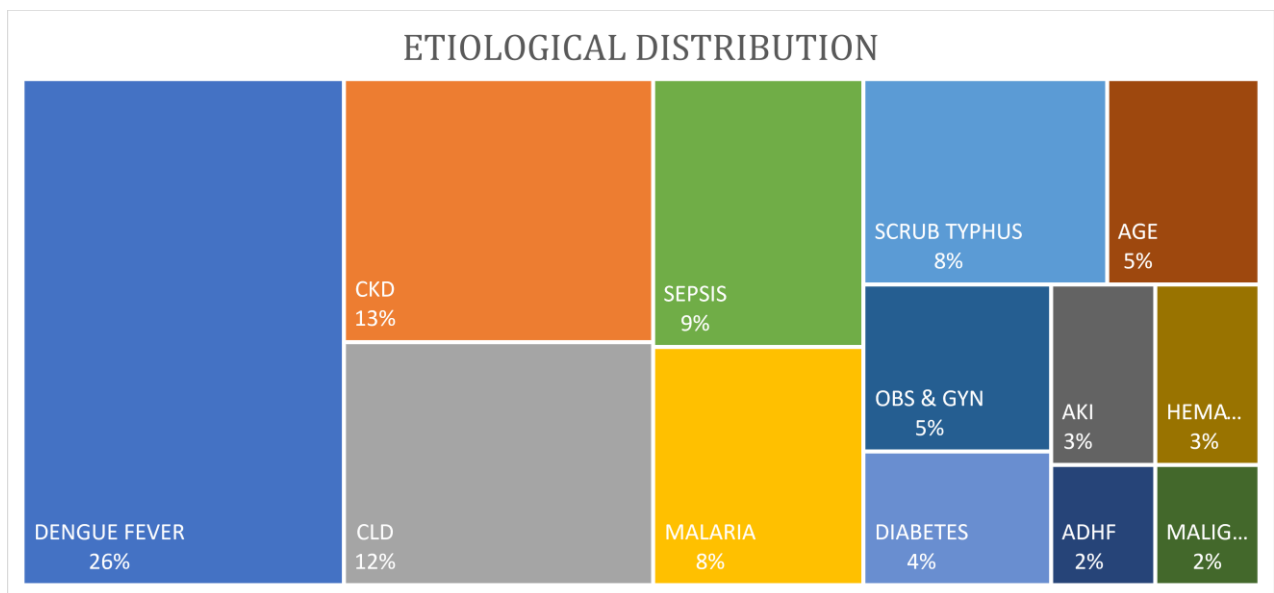


Figure 3: Etiological distribution of thrombocytopenia cases in the study shown in a treemap-style chart

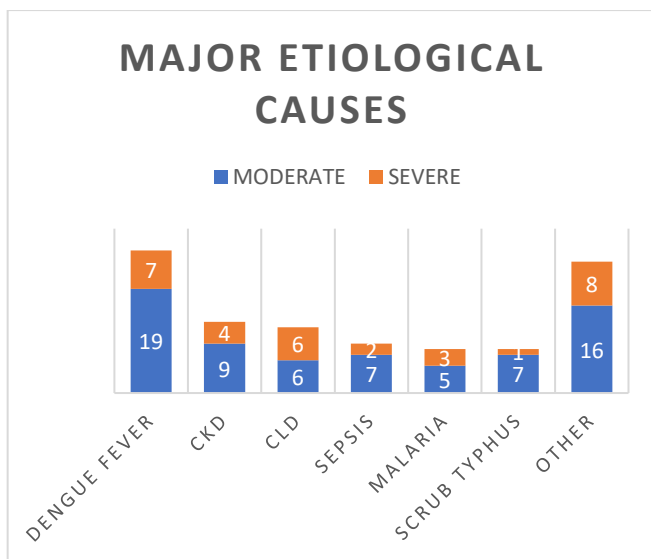


Figure 4: Major etiological causes with relative frequency of moderate and severe thrombocytopenia

### 5. Discussion

In our study, the age and severity of thrombocytopenia, along with the associated findings, are consistent with what has been observed in prior research. The leading cause of newly diagnosed thrombocytopenia of infective aetiology in this study is linked to acute febrile illnesses [13], with Dengue being the most common culprit, followed by scrub typhus and malaria [14]. Various theories have been suggested to explain the development of thrombocytopenia during Dengue infections. It is believed that during the early stages of the illness, bone marrow suppression may occur due to the impact on progenitor cells, infected stromal cells, and disrupted bone marrow [15]. In addition to platelet sequestration, the activation of the complement system and consumptive coagulopathy can also lead to thrombocytopenia. Autoantibodies targeting blood-coagulation-related



molecules and endothelial cells, as well as antiplatelet antibodies, have been linked to platelet lysis.

Thrombocytopenia is an early indicator of septicaemia [16] and can offer valuable insights to clinicians in suspected cases. It may result from platelet activation leading to binding and sequestration on the endothelium. Immunologically mediated platelet destruction can occur through non-specific antibodies and haemophagocytosis. Thrombocytopenia in liver disease arises from portal hypertension and splenic sequestration. Reduced thrombopoiesis in chronic liver disease [17], possibly due to a decline in functional liver cell mass, leads to peripheral thrombocytopenia.

Acute renal failure [20] is characterized by a sudden deterioration in the kidney's ability to remove waste, maintain pH balance, and regulate water levels. If this condition persists and becomes chronic, the kidney's production of erythropoietin decreases, leading to the accumulation of harmful metabolites that can result in changes in blood composition such as reduced levels of haematocrit, mean corpuscular volume, red blood cells, and platelets. Chronic kidney disease [18] often presents with mild thrombocytopenia, likely due to decreased thrombopoietic activity. Platelet dysfunction and impaired platelet-vessel wall interaction can contribute to complex haemostatic disorders in patients with end-stage renal disease. Diverse factors such as systemic chemotherapy, bone marrow involvement by tumours, and secondary immune thrombocytopenia contribute to thrombocytopenia in malignancies [19].

Thrombocytopenia occurring in the third trimester of pregnancy is a common condition that often resolves after childbirth. Abnormal uterine bleeding can also be seen in some cases. However, during pregnancy, life-threatening complications can arise from conditions such as preeclampsia, HELLP syndrome (Haemolysis, Elevated Liver enzymes, Low Platelets) and Immune thrombocytopenic purpura. Thrombocytopenia can also be a symptom of various haematological disorders such as megaloblastic anaemia, aplastic anaemia, and hypersplenism. [21] Reactive thrombocytosis is frequently associated with iron deficiency anaemia, although severe cases may result in thrombocytopenia. Infections like HIV, connective tissue disorders, and drug-induced reactions are some of the other potential causes of thrombocytopenia.

In conclusion, our study revealed that the majority of the subjects were aged 20 and older and had varying levels of thrombocytopenia, with some having severe thrombocytopenia (<50,000 cells/ $\mu$ L) while most had moderate levels (50,000 - 100,000/ $\mu$ L). The primary reason behind thrombocytopenia was found to be infectious diseases, particularly dengue. In addition, chronic liver disease and kidney disease were identified as the most common non-infectious causes of thrombocytopenia, with obstetric and gynaecological disorders also being prevalent. Symptoms such as fever and bleeding were commonly reported among patients with thrombocytopenia. Timely identification and regular monitoring of these patients can help prevent bleeding episodes, including potentially fatal intracranial haemorrhage, reduce hospital stays, alleviate the burden on both patients and doctors and ultimately save lives.

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