



ISSN (P): 2617-7226  
ISSN (E): 2617-7234  
www.patholjournal.com  
2019; 2(1): 357-360  
Received: 01-11-2018  
Accepted: 05-12-2018

**Dr. Sampat Kumar**  
Assistant Professor,  
Department of Pathology,  
Gadag Institute of Medical  
Sciences, Gadag, Karnataka,  
India

**Dr. Anushree CN**  
Associate Professor,  
Department of Pathology, Dr.  
BR Ambedkar Medical College,  
Bangalore, Karnataka, India

**Dr. Divya Nagaram**  
Assistant Professor,  
Department of Pathology,  
Vydehi Institute of Medical  
Sciences, Bangalore,  
Karnataka, India

#### Correspondence

**Dr. Divya Nagaram**  
Assistant Professor,  
Department of Pathology,  
Vydehi Institute of Medical  
Sciences, Bangalore,  
Karnataka, India

## Clinicopathological correlation of thrombocytopenia

**Dr. Sampat Kumar, Dr. Anushree CN and Dr. Divya Nagaram**

DOI: <https://doi.org/10.33545/pathol.2019.v2.i1f.93>

#### Abstract

Platelets are the prime movers in the clotting system. They are consumed in large numbers at every episode of clotting. Quantitative assessment is an important parameter in the study of coagulation. Platelets have proved more difficult to count than either red cells or white cells. It is well known that platelet count is a critical parameter in management of thrombocytopenia. Several factors are known to cause bleeding in association with infections, of which thrombocytopenia is the most common. Assessment of platelet count in routine haematology is essential, as numerical deficiency (usually below 150,000/ $\mu$ l) or defect in their function may lead to bleeding. Thrombocytopenia should also be confirmed by inspection of the stained blood film. Accurate and precise enumeration of platelets assists not only in diagnosis and treatment of various clinical disorders but also for standardizing counts with whole blood, platelet rich plasma or purified platelet preparations, used in therapy. Data will comprise of geriatric cases of age above 60 years from Outpatient Department (OPD) & In Patient Department (IPD) with low platelet count (less than  $150 \times 10^9/L$ ) on fully automated 5 part differential haematology analyser, Simens Advia 120. The EDTA blood sample from each case is processed in automated. Thrombocytopenia is a commonly observed haematological entity in geriatric age group. The causes for thrombocytopenia are varied and range from idiopathic infections to malignancies. Infections like Dengue, Malaria, are some of the common causes of fever with thrombocytopenia.

**Keywords:** Thrombocytopenia, febrile illness, clinicopathological, platelet count

#### Introduction

Thrombocytopenia can be classified as severe (platelet count less than  $20 \times 10^9/L$ ), moderate (platelet count  $20$  to  $70 \times 10^9/L$ ), or mild (above  $70 \times 10^9/L$ ). Although easy bruising occurs in patients with platelet counts less than  $50 \times 10^9/L$  and spontaneous life-threatening bleeding can be expected in patients with platelet counts less than  $15 \times 10^9/L$ , bleeding symptomatology is largely determined by comorbid conditions affecting platelets or the coagulation system, including liver cirrhosis, uremia, disseminated intravascular coagulation (DIC), or antiplatelet drug usage. In clinical practice, platelet counting is automated, and includes several different technologies: impedance, optical, two-dimensional laser, and optical fluorescence methods<sup>[1]</sup>.

The International Council for Standardization in Hematology (ICSH) recommends use of ethylenediaminetetraacetic acid (EDTA) as the anticoagulant. Adequate mixing of the blood sample with EDTA (the final EDTA concentration should be 1.5 to 2.2 mg/mL) is crucial to prevent clumping of the platelets. Blood samples should be kept at room temperature and analyzed within 6 hours of phlebotomy. If a sample is to be analyzed more than 6 hours after it is drawn, it can be kept at 4 °C for 24 hours. The blood count analyzer should be cleaned according to laboratory standards<sup>[2,3]</sup>.

On a Romanowsky-stained peripheral blood smear, platelets appear as small, lavender-blue or colorless bodies with reddish-purple (azurophilic) granules. They are generally 2–3  $\mu$ m (mm) in diameter, 0.5  $\mu$ m thick, and round to oval in shape. Ultra structurally, mature platelets lack nuclear material and contain only remnants of a Golgi complex, a relatively small number of ribosomes, and a small amount of mRNA. Newly released platelets, however, contain measurable RNA as do newly released erythrocytes (reticulocytes). These immature platelets containing RNA are called reticulated platelets<sup>[4]</sup>.

Occasionally, a platelet overlies an erythrocyte on a peripheral blood smear and can be mistaken for an erythrocyte inclusion. Differentiation is usually relatively easy because the superimposed platelet has a halo surrounding it and displays the classic morphologic characteristics of a normal platelet (e.g., azurophilic granules).

In improperly prepared smears, platelets can appear in aggregates in some areas and appear decreased or absent in others. These aggregates of platelets are typically seen in the-feathered edge of the blood smear. Aggregated platelets can be seen when the blood is not mixed well with the anticoagulant after collecting the sample, and platelet activation is initiated in vitro. Platelets can also appear decreased due to platelet satellitosis (platelet satellitism) when they adhere to neutrophils. Unusually large platelets-megathrombocytes or giant platelets (75 mcM diameter) are sometimes seen, particularly in myeloproliferative disorders or during recovery from severe thrombocytopenia [5, 6].

**Methodology**

Data comprised of geriatric cases from OPD & IPD with low platelet count on fully automated 5 part differential hematology analyzer, SIMENS ADVIA 2 120. The EDTA blood sample from each case is processed in automated hematology analyzer. At the same time blood smear is prepared and stained by Leishman stain. Peripheral smear examination of the stained smear is done using light microscope and details of the findings will be noted. Where ever possible bone marrow findings was correlated with thrombocytopenia.

This study was conducted in the department of pathology, Medical College Hospital. Data for analysis was obtained from patient medical files, in addition to detailed information gathered from patient. Details of history for each case will comprise of age, gender, clinical findings, medical history, history of medications, general physical examination and laboratory investigation. 100 geriatric patients diagnosed to have thrombocytopenia were included.

**Results**

**Table 1:** Chief complaints of patients diagnosed as viral fever

Chief complaints	Number of patients	Percentage
	(N= 15)	
Fever	15	100%
Headache	5	33.3%
Arthralgia	4	26.6%
Myalgia	4	26.6%
Vomiting	2	13.3%
Weakness	9	60%
Rash	5	33.3%
Bleeding	5	33.3%
Jaundice	2	13.3%
Rigors	9	60%
Bodyache	9	60%
Pain Abdomen	3	20%
Diarrhoea	1	6.6%

- The most common clinical feature after fever (100%)
- 5 patients (33.3%) presented with Headache.
- 4 patients (26.6%) presented with arthralgia.
- 4 patients (26.6%) presented myalgia
- 2 patients (13.3%) presented vomiting
- 9 patients (60%) presented with weakness.
- 5 patients (33.3%) presented with bleeding and rash each.
- 2 patients (13.3%) presented with jaundice.

- 9 patients (60%) presented with rigors and bodyache each.
- 3 patients (20%) presented with pain abdomen.
- 1 patients (6.6%) presented with diarrhea.

**Table 2:** Correlation of thrombocytopenia with chemotherapeutic drugs

Chemotherapeutic drugs	Number of Cases (N=7)	Percentage
Carboplatin	3	42.8%
Gemcitabine	2	28.57%
Cyclophosphamide	2	28.57%

- Out of 7 patients Carboplatin was the most common chemotherapeutic drug caused thrombocytopenia (42.8%)
- Gemcitabine in 2 patients (28.6%).
- Cyclophosphamide in 2 patients (28.6%).

**Table 3:** Correlation of drugs causing thrombocytopenia.

Drugs	Number of Cases (n=6)	Percentage
Heparin	3	50%
Aabciximab	2	33.4%
Isoniazid	1	16.6%

- Out of 6 patients Heparin was the most common drug caused thrombocytopenia 3 patients (50%)
- Abciximab in 2 patients (33.6%).
- Isoniazid in 1 patient (16.6%)

**Table 4:** Correlation of leukaemia with thrombocytopenia

Type of leukaemia	Number of cases N=12	Percentage
CML	7	58.2%
CLL	3	25%
AML	2	16.8%

- Out of 12 Leukaemic patients CML was most common and seen in 7 patients (58.2%)
- CLL in 3 patients (25%).
- AML in 2 patients (16.2%).

**Discussion**

**Table 5:** Comparative analysis of bleeding manifestation of dengue

Bleeding sign	Ing kit lew et al. [7]	Shivbalan et al. [8]	Present study
Petechiae	53%	46.6%	66%
Hematemesis	-	26%	3.3%
Malena	32%	21%	-
Sub conjunctival hemorrhage	4.5%	6.6%	-
Epistaxis	1.5%	-	3.3%
Skin bleeds	-	-	-
Bruising	-	-	9%
Bleeding gums	17%	-	18.5%

In our study the most common bleeding manifestation was Petechiae (66%), similar to a study done by Ing Kit Lew et al. and Shivbalan et al. other manifestation like Epistaxis (3.3%) and Bleeding gums (18.5%) were also similar to study done by Ing kit lew et al.

**Table 6:** Comparative analysis of clinical presentation of dengue patient

Clinical features	Dc Lye <i>et al.</i> [9]	Ing Kit Lew <i>et al.</i> [7]	Present study
Fever	92%	90.9%	100%
Headache	24%	45.5%	68%
Body pain	-	36.4%	55.2%
Vomiting	36%	16.7%	36%
Rash	38%	15.2%	44.7%
Pain abdomen	15%	33.3%	42.1%
Arthralgia	61%	10.6%	80.1%
Myalgia	61%	18.2%	80.1%
Retrobulbar pain	1%	12.1%	5.3%

As shown in the above table the most common presentation in our study was fever which accounted 100%, followed by arthralgia and myalgia both accounted for 80.1%. A study done by Dc Lye *et al.* and Ing Kit Lew *et al.* had similar results.

**Table 7:** comparative analysis of clinical features of viral fever

Clinicalfeatures	Kumar P <i>et al.</i> [10]	Nakhale BD <i>et al.</i> [11]	Present Study
Fever	100%	100%	100%
Chills and rigors	-	58.2%	-
Jaundice	-	27.9%	13.3%
Headache	82%	52%	33.3%
Vomiting	18.9%	46%	13.3%
Myalgia	-	68%	26.6%
Rash	3.6%	11.5%	33.3%
Bleeding	-	27%	33.3%
Body ache	4.2%	-	60%
Arthralgia	2.6%	-	26.6%
Abdomen pain	16%	-	20%
Diarrhoea	5%	-	6.6%

In our study most common clinical feature was fever 100%, followed by body ache 60%, head ache, rash, bleeding 33% each, myalgia and arthralgia 26.6%, abdomen pain 20%, jaundice and vomiting 13.3% each, diarrhoea 6.6%. A similar study done by Kumar P *et al.* and Nakhale BD *et al.* showed similar results.

Each chemotherapeutic agent differs in how it causes thrombocytopenia. Alkylating agents affects stem cells, cyclophosphamide affects megakaryocyte progenitors, bortezomib prevents platelet release from megakaryocytes and some chemotherapeutic promotes platelet apoptosis.

In our study out of 7 cases 3 cases reported due to carboplatin and 2 cases each due to Gemcitabine and cyclophosphamide. A study conducted by Kuter DJ *et al.* [12] also mentions that most common chemotherapeutic drugs causing thrombocytopenia are Gemcitabine and Platinum based regimen.

As many as 100 drugs are listed those cause thrombocytopenia, among them Heparin is most common drug to cause thrombocytopenia and next is Abciximab depending upon the age group where these drugs are often prescribed.

In our study among 6 patients 3 patients were probably diagnosed to have thrombocytopenia due to Heparin, 2 patients with Abciximab and 1 patient with Isoniazid drug. About 50% of cases showed Heparin induced thrombocytopenia as a most common cause which is similar

to study conducted by Jyoti Kotwal *et al.* [13], which showed heparin induced thrombocytopenia in patients aged more than 60 years.

In our study out of 100 cases 12 (12%) cases were thrombocytopenia associated with haematological malignancy. Among 12 cases 7 cases were CML, 3 cases CLL and 2 cases AML. A study conducted by Tejas N *et al.* [87] had similar results were out 53 cases 6 (11.3%) cases were thrombocytopenia associated with haematological malignancies.

**Conclusion**

Mortality is not directly associated with degree of thrombocytopenia but with concomitant involvement of other organs leading to multiorgan dysfunction. Treatment of the underlying condition leads to rapid improvement in platelet count.

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