OPEN ACCESS
Saudi Journal of Pathology and Microbiology
Abbreviated Key Title: Saudi J Pathol Microbiol
ISSN 2518-3362 (Print) |ISSN 2518-3370 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Platelet Indices in Differentiating Reactive Versus Clonal Thrombocytosis

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DOI: 10.36348/sjpm.2023.v08i03.002 | **Received:** 22.01.2023 | **Accepted:** 01.03.2023 | **Published:** 04.03.2023

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Abstract

Aim*:** To evaluate the platelet indices in differentiating reactive and clonal thrombocytosis. ***Study Design: Observational study Place and Duration of Study: Department of Pathology, Saveetha Medical College, Chennai, and the duration of study is one year. ***Methods*:** This is an observational study conducted at our college for a one-year duration. A total of 100 patients with thrombocytosis of platelet count over 4.5 lakhs/mm3 will be included in the study. The study sample consists of cases with thrombocytosis of over 4.5 lakhs. The utility of platelet indices Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) for the differential diagnosis of thrombocytosis were analysed and assessed. ***Results*:** Out of the total 100 cases, 94 were reactive thrombocytosis, and 6 were confirmed to be clonal in origin. Infectious and reactive aetiology was significantly more compared to clonal thrombocytosis. Patients with reactive thrombocytosis showed a lower mean platelet volume and platelet distribution width compared to primary thrombocytosis. In reactive thrombocytosis, MPV ranged from 8.0 - 9.0 fl with mean MPV of 10.6 fl and PDW ranged from 8.4 – 10.1 % with mean PDW of 10.26 %. In clonal thrombocytosis, MPV ranged from 8.2 –1 1.1 fl with mean MPV of 9.5 fl and PDW range was 8.9 – 11.2 % with mean PDW of 10·1%. ***Conclusions*:** The findings of our study favour a reactive cause in thrombocytosis when MPV and PDW are in the lower range and clonal causes had a high MPV and PDW in comparison to reactive causes.

Keywords: Thrombocytosis, Mean Platelet Volume, Platelet Distribution Width, platelet indices, plateletcrit.

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INTRODUCTION

Thrombocytes are essential components of blood utilized for various functions. They are cytoplasmic derivatives of megakaryocytes, small fragments of megakaryocyte cytoplasm and have characteristic discoid shape. To assemble and release platelets, megakaryocytes become polypoidal by endomitosis and follow the maturation that results in the conversion of the bulk of their cytoplasm into multiple long processes known as proplatelets. Megakaryocytes protrude as 10 to 20 proplatelets, to produce 1000 to 2000 platelets [19]. The platelets are formed at the end of the proplatelet, which begins as a process of thinning and branches of blunt protrusion. They are devoid of nucleus and bound by a lipid bilayer. As platelets develop, their content of granules and organelles is delivered to them in a stream of individual particles moving from the megakaryocytes cell body to the nascent platelet buds at the ends of proplatelets. The platelet formation can be divided into two phases. The first phase takes days to complete, in which nuclear proliferation, cytoplasmic enlargement and filling with platelet-specific granules, this phase megakaryocyte specific growth factor dependent. The second phase is fast completed in hours, remodelling of cytoplasm first into proplatelet then into preplatelet and discoid platelet. The platelets contain mainly three types of granules: dense granule, alpha granule, and lysosomal granule. The main function is the maintenance of hemostasis by forming a platelet plug formation that arrests blood loss [20]. Normally, platelets circulate in the blood without activation and are adherent to the vessel wall. The platelet adherence to the vessel will initiate with exposure of subendothelial collagen and Von Willebrand factor. ADP, TxA2 and thrombin convert integrin IIb to a high-affinity state [3]. Divalent fibrinogen and bridge between IIb on adjacent platelets result in aggregation and plug formation. The phosphatidylserine on the platelet surface creates a procoagulant-activated platelet surface for assembling the coagulation factor complex

that increases thrombin formation. Normal thrombocyte count ranges from 150,000 to 400,000 cells/µL. An increase in platelet counts above 4.5 lakhs is thrombocytosis. A decrease in platelet counts below 1.5 lakhs is called thrombocytopenia [1, 2]. The causes of thrombocytosis can be segregated as primary or reactive (secondary). Primary thrombocytosis is known as thrombocytosis because of myeloproliferative disorder. The aetiology under primary is Essential thrombocythemia, polycythaemia vera, chronic myeloid leukaemia and myelofibrosis. When there is leucocytosis, nucleated RBC's immature forms of white blood cells defect in platelet function and splenomegaly. Chronic inflammatory disease, trauma, haemorrhage, infection, iron deficiency and malignancy are the cause of reactive or secondary thrombocytosis. Thrombocytosis causes can be analysed using platelet indices and the present study aimed to differentiate the aetiology of thrombocytosis with the aid of platelet indices [21].

Inclusion Criteria: Age ranged from 18 to 75 years; All PLT indices and in-hospital information were fully available.

Exclusion Criteria: Patients Includes aged above 18 years with length of ICU stay >24 hours were included whereas pregnant and lactating women; patients with active haemorrhage; haematological and rheumatological diseases, diagnosed chronic liver disease.

MATERIALS AND METHODS

The aims and objectives of the present study are:

- To differentiate the aetiology of thrombocytosis using platelet indices.
- The indices like Mean platelet volume (MPV), Platelet distribution width (PDW) and Plateletcrit (Pct) were used in the present study to analyse the aetiology of thrombocytosis.
- To evaluate the platelet indices in differentiating reactive and clonal thrombocytosis.

The present study is an observational study conducted after obtaining permission from the Institutional review board. Patients belong to various departments of Saveetha medical college and Hospital, which referred to the pathology laboratory for investigation as a convenient sampling method. Patients who were excluded from the study are bleeding disorders or recent blood transfusion patients. The sample size comprises 100 patients. Their diagnosis was confirmed by our lab. 2 ml of fresh blood was drawn under aseptic conditions into EDTA vacutainers and processed immediately in one hour using a 5-part haematology analyser. Patients with platelet counts of 4.5 lakhs and above were selected. For the confirmation of high platelet counts by repeating the tests and peripheral smear examination and platelet indices were analysed. These are classified into five groups based on their age. Group 1: 1 - 20 years, Group 2: 21 - 40years, Group 3:41 to 60 years, Group 4:61 to 80, Group 5:81 to 100.

Clinical correlation along with physical examination and laboratory studies were done to eliminate other causes. The Cytogenetics reports were obtained for 2 cases and JAK2 mutational analysis was available for 4 cases.

Statistical Analysis:

All statistical analysis was done by Microsoft Excel, and the data were expressed as a percentage and difference between two groups (reactive & clonal thrombocytosis).

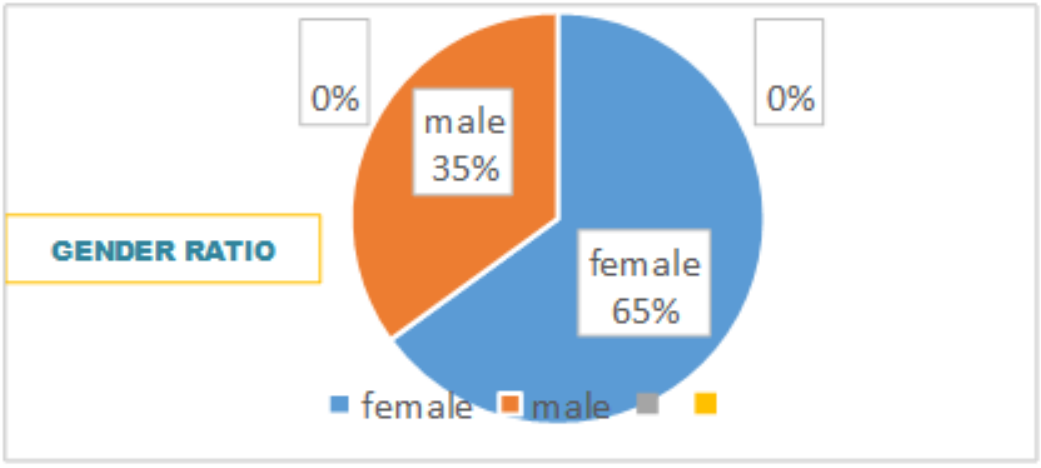

Fig 1: Thrombocytosis shows a female predominance

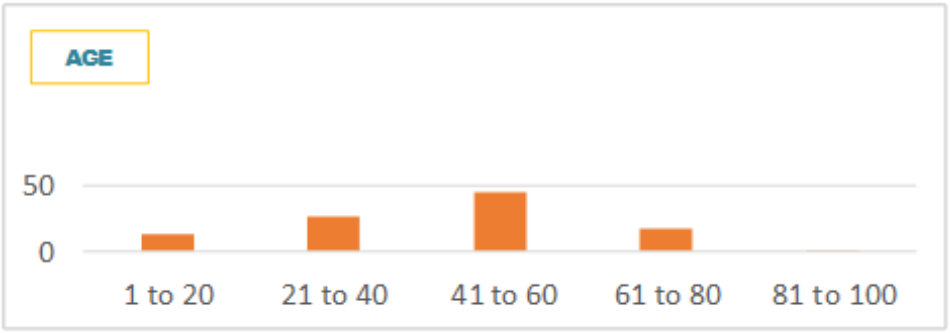

Fig 2: Thrombocytosis was more common in the age group of 41 to 60 years

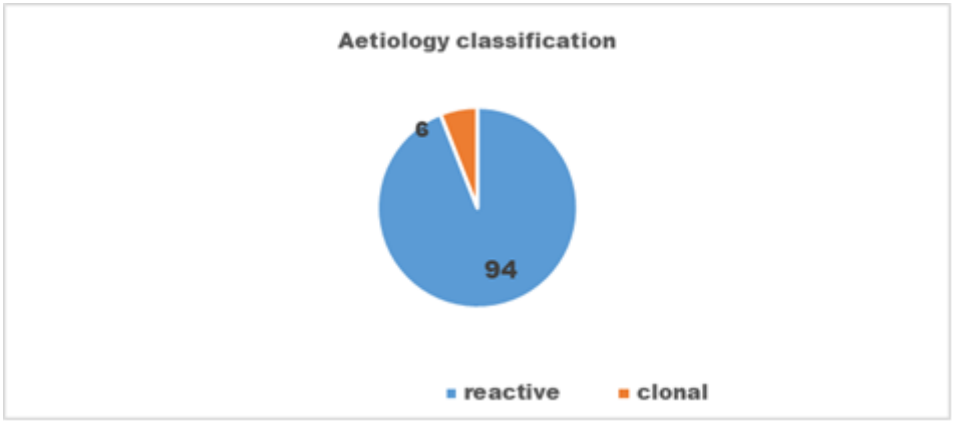

Fig 3: Reactive aetiology is more common compared to clonal causes

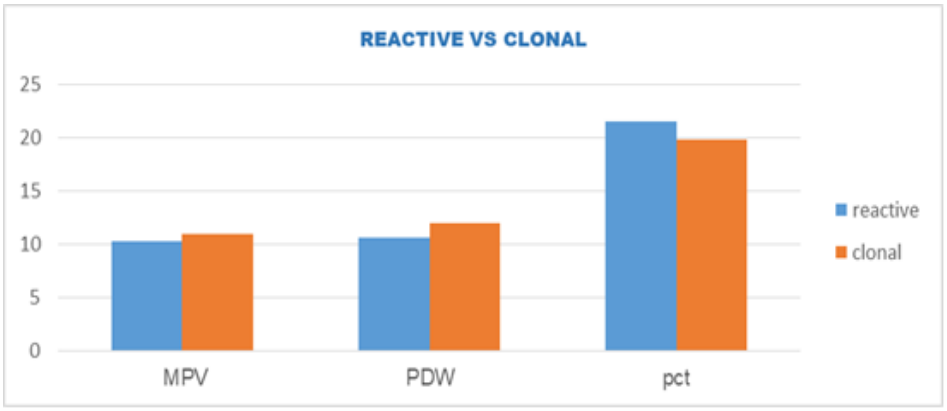

Fig 4: PDW and MPV values of clonal aetiology higher compared to reactive causes

The study population consisted of 100 subjects of which 94 were reactive aetiology and clonal causes [4]. There is a linear increase in the percentage of viewers according to the level of age. The y-axis shows the population age-wise distribution with 5 groups separated and 41 to 60 shows a predominance of thrombocytosis population (Fig 2). The pie chart depicts the proportion of two genders compared distribution. The pie chart depicts the thrombocytosis showing female predominance in blue colour (Fig 1).

Most causes for reactive aetiology are iron deficiency anaemia and infections, as for clonal it is myeloproliferative diseases and polycythaemia vera and essential thrombocythemia. The pie chart (Fig 3) depicts that reactive aetiology was more predominant than clonal aetiology proving that reactive causes are more common compared to clonal causes. Reactive aetiology in red colour more compared to clonal in blue colour. Y-axis shows platelet indices like mean platelet volume, platelet distribution width and platelet crit separated for reactive and clonal aetiology then plotted a bar diagram (Fig 4) for its which shows high statistics for MPV and PDW in clonal aetiology compared to reactive ones.

In reactive thrombocytosis, MPV ranged from 8.0 - 9.0 fl with mean MPV of 10.6 fl and PDW ranged from 8.4 – 10.1% with mean PDW of 10.26 %. In clonal thrombocytosis MPV ranged from 8.2 –11.1/fl

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with mean MPV of 11 fl and the PDW range was 8.9 – 15.2% with mean PDW of 12%.

DISCUSSION

Out of total 100 cases, 94 were reactive thrombocytosis, and 6 were confirmed to be clonal in origin. Infectious and reactive aetiology were significantly more compared to clonal thrombocytosis [8]. MPV is a measure of the average size of platelet in peripheral blood and its size is a potential determinant of production in the bone marrow. PDW compares the uniformity and heterogenicity of the platelet size thereby assessing the megakaryocyte development [18]. PDW can therefore be considered a useful tool in differentiating essential thrombocythemia from reactive thrombocytosis [16].

Platelet heterogeneity is higher in patients with original thrombocytosis, whereas in secondary (reactive) thrombocytosis this heterogeneity in platelets only occurs occasionally [17]. The examination of platelet indices by coulter counters and large platelets on peripheral smears both support this [12]. Naveen Naz Syed and Ravuri S study Patients with reactive thrombocytosis showed a lower mean platelet volume and platelet distribution width compared to primary thrombocytosis [5, 6]. Bashar Saeed et al and Naveen Nazy *et al*., shows infections and iron deficiency anaemias contributed significantly to the causes of reactive thrombocytosis [5, 15]. Usually, these indices are useful in analysing causes of thrombocytopenia and differentiating immune and non-immune causes. The present study analysed these indices for differentiating causes of thrombocytosis [14].

Morphological platelet differentiation was noted in the groups, many studies found that platelets in reactive thrombocytosis show normal in the peripheral smear, activation of these in the marrow results from inflammation-induced stimulators [7, 8]. In clonal thrombocytosis, patients show an increased percentage of micro-platelets and mega platelets, which leads to improved heterogenicity and results in an increase in PDW, probably maybe the reflection of megakaryocyte abnormality in the marrow of clonal thrombocytosis [11-13].

According to the MPV study by Priyanka Meena *et al*., and Ravuri S study, there is a statistically significant difference between cases and controls, which are 11 (8.0 to 9.0) and 10.6 (8.2 to 11.1). MPV programmes relevance when compared to the major clonal risk factor [9, 10]. Hence differentiating causes of thrombocytosis according to indices can be cost-effective and time-sparing and requires only the creation of a laboratory database for proper utilization.

CONCLUSION

As an acute phase response to infections, anaemias, and other rebound causes, thrombocytosis is commonly linked to reactive aetiology. The clonal expansion that is to blame. The present study highlights the significance of platelet indices as a sensitive method in predicting the clonal thrombocytosis prior to any invasive procedure. Thrombocytosis is typically validated with bone marrow tests. Even though there aren't many cases of clonal thrombocytosis, this case demonstrates that platelet indices are a more relevant non-invasive indicator for discriminating thrombocytosis than reactive thrombocytosis. The findings of our study favour a reactive cause in thrombocytosis when MPV and PDW are in the lower range and clonal causes had a high MPV and PDW in comparison to reactive causes. These are non-invasive parameters useful in differentiating thrombocytosis. Hence platelet indices help to predict whether thrombocytosis is of reactive or clonal aetiology. This may reduce using invasive ancillary tests and their cost.

ACKNOWLEDGEMENT

I sincerely thank Saveetha Medical College and Hospital, Chennai, for their continued support in the procurement of the data.

Statement of Ethics

This study was approved by Ethics Committee of Saveetha Medical and Hospital. As this study was a retrospective study, there was no patient's privacy data such as patient name, ID number, telephone and address were involved. Only demographic information and laboratory testing data of patients were collected and analyzed in this study.

Disclosure Statement: All authors declared no conflicts of interest.

Funding Sources: No funding sources supported this work.

REFERENCES

1. Platelet distribution curves: interpretation, potentials, and limitations; Sysmex Xtra Online June 2011.
2. Skoda, R. C. (2009). Thrombocytosis. *ASH Education Program Book*, *2009*(1), 159-167.
3. Ruggeri, Z. M. (2003). Von Willebrand factor, platelets and endothelial cell interactions. *Journal of thrombosis and haemostasis*, *1*(7), 1335-1342.
4. Ravuri, S., Bolineni, C., & Jeshtadi, A. (2020). Role of platelet indices in determining the type of thrombocytosis. *J Evid Based Med Healthc*, 7(44), 2539-2543.
5. Syed, N. N., Usman, M., & Khurshid, M. (2007). Thrombocytosis: age dependent aetiology and analysis of platelet indices for differential

diagnosis. *Indian Journal of Pathology & Microbiology*, *50*(3), 628-633.
6. Chandrashekar, V. (2013). Plateletcrit as a screening tool for detection of platelet quantitative disorders. *Journal of Hematology*, *2*(1), 22-26.
7. Tafazzoli, M., Keramati, M. R., & Vakili, R. (2006). Etiology of thrombocytosis and the use of platelet parameters to distinguish between clonal and reactive thrombocytosis. *International Journal of Hematology and Oncology*, *32*(3), 71-76.
8. Saeed, B. A., Taib, S. M., & Nafih, K. (2009). Platelet indices in the differential diagnosis of thrombocytosis. *Annals of the College of Medicine*, *35*(1), 33-36.
9. Karpatkin, S., & Charmatz, A. (1969). Heterogeneity of human platelets: I. Metabolic and kinetic evidence suggestive of young and old platelets. *The Journal of clinical investigation*, *48*(6), 1073-1082.
10. Karpatkin, S. (1969). Heterogeneity of human platelets: II. Functional evidence suggestive of young and old platelets. *The Journal of clinical investigation*, *48*(6), 1083-1087.
11. Cortelazzo, S., Barbui, T., Bassan, R., & Dim, E. (1980). Abnormal aggregation and increased size of platelets in myeloproliferative disorders. *Thrombosis and Haemostasis*, *43*(02), 127-130.
12. Zeigler, Z., Murphy, S., & Gardner, F. H. (1978). Microscopic platelet size and morphology in various hematologic disorders. *Blood*, *51*(3), 479-486.
13. Holme, S., Simmonds, M., Ballek, R., & Murphy, S. (1981). Comparative measurements of platelet size by Coulter Counter, microscopy of blood smears, and light-transmission studies. Relationship between platelet size and shape. *The Journal of laboratory and clinical medicine*, *97*(5), 610-622.
14. Van der Lelie, J., & Von dem Borne, A. K. (1986). Platelet volume analysis for differential diagnosis of thrombocytosis. *Journal of clinical pathology*, *39*(2), 129-133.
15. Meena, P., Khare, M., & Airun, A. (2017). A study of platelet indices in patients of acute ischemic stroke: a prospective study. *IOSR Journal of Dental and Medical Sciences*, 16(8), 26-29.
16. Sachdev, R., Tiwari, A. K., Goel, S., Raina, V., & Sethi, M. (2014). Establishing biological reference intervals for novel platelet parameters (immature platelet fraction, high immature platelet fraction, platelet distribution width, platelet large cell ratio, platelet-X, plateletcrit, and platelet distribution width) and their correlations among each other. *Indian Journal of Pathology and Microbiology*, *57*(2), 231-235.
17. Tafazzoli, M., Keramati, M. R., & Vakili, R. (2006). Etiology of thrombocytosis and the use of platelet parameters to distinguish between clonal and reactive thrombocytosis. *International Journal of Hematology and Oncology*, *32*(3), 71-76.
18. Toprak, S. K., Erismis, B., Karakus, S., Kursun, N., Haberal, A., & Ulusoy, M. G. (2012). Does thrombocyte size give us an idea about thrombocytosis etiology?. *The Scientific World Journal*, *2012*, 1-5.
19. Italiano, J. E. (2017). Megakaryocyte development and platelet production. *Platelets in Thrombotic and Non-Thrombotic Disorders: Pathophysiology, Pharmacology and Therapeutics: an Update*, 39-53.
20. Sharda, A., & Flaumenhaft, R. (2018). The life cycle of platelet granules. *F1000 Research*, 7.
21. Rokkam, V. R., & Kotagiri, R. (2020). Secondary thrombocytosis.