Published by
Saidu Medical College

OPEN ACCESS

Original Article

Diagnostic Utility of Platelet Indices in Differentiating Clonal and Reactive Thrombocytosis: A Comparative Cross-Sectional Study

Javeria Rauf Saeed[1], Maryam Gul[2], Syed Rohail Shah[3], Kashif Shehzad[4] Asim Khan[5] & Tajdar Ali[4]

[1] Saidu Medical College, Swat, Pakistan
[2] Lady Reading Hospital, Peshawar, Pakistan
[3] DHQ Hospital, Ghallanai, Mohmand, Pakistan
[4] Northwest Teaching Hospital, Peshawar, Pakistan
[5] Queen Elizabeth Hospital, Birmingham, United Kingdom

https://doi.org/10.52206/jsmc.2026.16.2.1309

Abstract

Background: Thrombocytosis, defined as an elevated platelet count, can be broadly categorized into clonal and reactive types. Clonal thrombocytosis is associated with myeloproliferative neoplasms, whereas reactive thrombocytosis occurs secondary to inflammatory, infectious, or neoplastic conditions. Differentiating between these entities is clinically important, as management strategies and prognostic implications differ significantly. Platelet indices have emerged as accessible and cost-effective markers that may aid in this distinction.

Objective: To compare platelet indices—platelet count, mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW)—between clonal and reactive thrombocytosis.

Methodology: This comparative cross-sectional study was conducted at Saidu Medical College, Swat, and included 70 patients diagnosed with thrombocytosis (35 clonal and 35 reactive). Platelet indices were measured using an automated hematology analyzer. Statistical analysis was performed using R software version 4.3.1, and group comparisons were made using independent samples t-test. A p-value of <0.05 was considered statistically significant.

Results: The mean age and gender distribution were comparable between the two groups ($p > 0.05$). Platelet count was significantly higher in the clonal thrombocytosis group (771.54 ± 217.90 $\times 10^9$/L) compared to the reactive group (665.23 ± 162.48 $\times 10^9$/L) ($p = 0.024$). MPV and PCT were also significantly elevated in clonal thrombocytosis ($p < 0.001$). In contrast, PDW was significantly higher in reactive thrombocytosis ($p < 0.001$). Stratified analysis by gender demonstrated consistent findings across both subgroups.

Conclusion: Platelet indices, particularly MPV, PCT, and PDW, demonstrate significant differences between clonal and reactive thrombocytosis and may serve as practical, cost-effective tools for preliminary differentiation. However, confirmation with molecular and histopathological investigations remains essential.

Keywords: Clonal thrombocytosis, MPV, Platelet indices, PCT, PDW, Platelet count, Reactive thrombocytosis.

ISSN (P): 1819-4583
ISSN (E): 3007-9470

Copyright © Copyright (c) 2026 The authors retain the copyrights. Authors are permitted and encouraged to post their work online (e.g. in institutional repositories or on their website), as it can lead to productive exchanges, as well as greater citation of published work.

Citation:
Saeed JR, Gul M, Shah SR, Shehzad K, Khan A, Ali T. Diagnostic utility of platelet indices in differentiating clonal and reactive thrombocytosis: a comparative cross-sectional study. *J Saidu Med Coll.* 2026;16(2):281–287.

Corresponding Author:
Dr. Javeria Rauf Saeed
Assistant Professor Haematology,
Department of Pathology,
Saidu Medical College, Swat, Pakistan
javeriarauf9@yahoo.com

Funding:
The authors received no external funding for this study.

Conflicts of Interests:
The authors have declared that no competing interests exist.

Data Sharing Statement:
The data that support the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Received: April 28, 2025
1st Revision: October 08, 2025
2nd Revision: December 11, 2025
3rd Revision: December 24, 2025
Accepted: February 22, 2026

Introduction

Platelets play a fundamental role in hemostasis and thrombosis, contributing to vascular integrity and clot formation. The normal platelet count ranges from 150,000 to 400,000 platelets/μL of blood.[1] Thrombocytosis is defined as a platelet count exceeding 400×10^9/L and is often identified incidentally during routine laboratory investigations.[2] While frequently asymptomatic, thrombocytosis may indicate an underlying pathological process and therefore requires careful clinical evaluation.[3]

Thrombocytosis is broadly classified into two categories: clonal (primary) and reactive (secondary).[4-6] Clonal thrombocytosis arises from myeloproliferative neoplasms such as chronic myeloid leukemia, essential thrombocythemia, polycythemia vera, and primary myelofibrosis. These disorders are commonly associated with somatic mutations, including JAK2, MPL, and CALR, which lead to uncontrolled proliferation of megakaryocytes and increased platelet production.[7,8] In contrast, reactive thrombocytosis occurs as a physiological response to external stimuli such as infection, inflammation, malignancy, or iron deficiency anemia.[9] This form is typically driven by elevated levels of cytokines and thrombopoietin, resulting in increased platelet production without intrinsic bone marrow pathology.

Differentiating between clonal and reactive thrombocytosis is clinically critical, as clonal forms are associated with a higher risk of thrombotic and hemorrhagic complications and often require cytoreductive therapy, whereas reactive thrombocytosis is usually managed by addressing the underlying cause.[5] Despite the importance of accurate diagnosis, the gold standard investigations, including bone marrow biopsy and molecular testing, are expensive, time-consuming, and not readily available in many resource-limited settings.

Platelet indices, including mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), and platelet large cell ratio (P-LCR), provide insight into platelet size, morphology, and heterogeneity [10]. These indices are routinely generated by automated hematology analyzers and are therefore inexpensive and widely accessible. In clonal thrombocytosis, abnormal megakaryopoiesis results in the production of larger and more heterogeneous platelets, reflected by increased MPV and PDW.[11] Conversely, reactive thrombocytosis typically exhibits relatively normal platelet morphology, with less variation in platelet size.[11]

Given the diagnostic challenges and limitations of advanced testing, platelet indices offer a promising alternative for initial differentiation between clonal and reactive thrombocytosis. However, there is limited data available from the local population regarding their diagnostic utility. Therefore, this study aims to compare platelet indices between clonal and reactive thrombocytosis and evaluate their potential role as practical diagnostic markers in routine clinical practice.

Methodology

Participants

This study was designed as a comparative cross-sectional analysis aimed at evaluating differences in platelet indices between patients diagnosed with clonal and reactive thrombocytosis. The design enabled simultaneous assessment of exposure (type of thrombocytosis) and outcome variables (platelet indices), facilitating direct comparison between the two groups.

Ethics

Ethical approval was obtained from the Institutional Ethical Review Committee of Saidu Medical College, Swat. All procedures were conducted in accordance with established ethical standards for human research. Written informed consent was obtained from all participants prior to inclusion, ensuring confidentiality, voluntary participation, and the right to withdraw at any stage.

Setting

The study was conducted in the Department of Pathology at Saidu Medical College, Swat, Pakistan. Data collection was carried out over a period from June 2022 to October 2024. Laboratory analyses were performed within institutional diagnostic facilities under standardized conditions.

Participants

A total of 70 patients with thrombocytosis were included through non-probability consecutive sampling. Participants were equally divided into two groups: clonal thrombocytosis (n = 35) and reactive thrombocytosis (n = 35). Inclusion criteria comprised patients aged 20–80 years, of both genders, and confirmed thrombocytosis based on platelet count. Exclusion criteria included pregnant or lactating women, patients with active hemorrhage, hematological or rheumatological disorders, chronic liver disease, and cases with incomplete or missing data. A total of 130 patient records were initially reviewed, with 70 meeting eligibility criteria for final analysis (Figure 1).

Variables

The primary independent variable was the type of thrombocytosis (clonal vs reactive). Dependent variables included platelet indices: platelet count ($\times 10^9$/L), mean platelet volume (MPV, fL), plateletcrit (PCT), and platelet distribution width (PDW, %). Demographic variables included age and gender.

Data Sources/Measurement

Blood samples (3 mL) were collected using standard aseptic venipuncture techniques and transferred into EDTA tubes. Samples were gently mixed and analyzed within one hour using a Sysmex KX-21N automated hematology analyzer (Sysmex Corporation, Kobe, Japan). The analyzer was calibrated daily, and internal quality control was maintained using standard reference materials. Platelet indices were recorded automatically. Classification of thrombocytosis into clonal and reactive types was based on clinical assessment, including patient history, physical examination, and laboratory findings. Due to limited availability, bone marrow examination and molecular testing were not performed, and classification relied on exclusion of reactive causes.

Bias

Selection bias was minimized through predefined inclusion and exclusion criteria, while measurement bias was reduced by using standardized laboratory procedures and calibrated equipment. However, the absence of molecular confirmation may have introduced misclassification bias. Additionally, the use of consecutive sampling may limit external generalizability.

Study Size

The sample size of 70 (35 per group) was calculated using OpenEpi at a 95% confidence level and 80% study power, based on previously reported platelet count values for reactive and clonal thrombocytosis [12].

Quantitative Variables

Continuous variables, including age and platelet indices, were expressed as mean ± standard deviation (SD). Categorical variables such as gender were presented as frequencies and percentages.

Statistical Method

Data analysis was performed using R software version 4.3.1. Normality of distribution was assessed prior to analysis. Independent samples t-test (Welch two-sample t-test where appropriate) was used to compare mean platelet indices between groups. Chi-square test was applied for categorical variables. Stratified analysis by gender was also performed. A p-value of <0.05 was considered statistically significant.

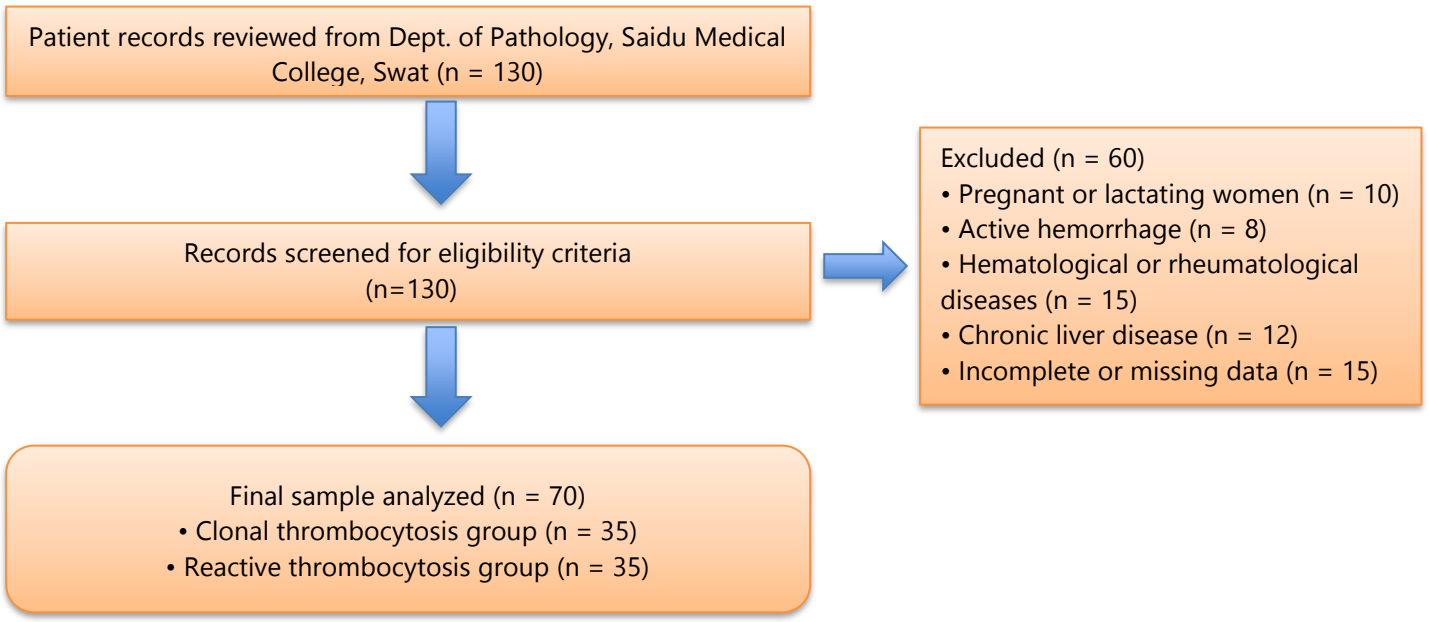


Figure 1: STROBE Flow Diagram: Participant Selection and Analysis Process

Results

Participants

A total of 130 patient records were initially reviewed for eligibility, out of which 60 were excluded based on predefined criteria, including pregnancy or lactation, active hemorrhage, hematological or rheumatological disorders, chronic liver disease, and incomplete data. The final sample comprised 70 patients, equally divided into clonal thrombocytosis (n = 35) and reactive thrombocytosis (n = 35). The participant selection process is illustrated in the STROBE flow diagram (Figure 1).

Descriptive Data

The age distribution of participants was assessed and found to be normally distributed, as indicated by the bell-shaped histogram and a non-significant p-value (p = 0.25) (Figure 2). The mean age was comparable between the clonal thrombocytosis group (54.40 ± 7.63 years) and the reactive thrombocytosis group (53.49 ± 11.09 years), with no statistically significant difference (p = 0.69). Gender distribution was also similar across groups, with females comprising 54.29% in the clonal group and 57.14% in the reactive group (p = 0.81). Furthermore, the distribution of participants across age categories (35–55 years and 56–80 years) was identical between the groups (p = 1.00). These findings indicate that the two groups were demographically comparable (Table 1).

Outcome Data

Comparison of platelet indices revealed significant differences between clonal and reactive thrombocytosis groups. The mean platelet count was significantly higher in the clonal thrombocytosis group (771.54 ± 217.90 $\times 10^9$/L) compared to the reactive thrombocytosis group (665.23 ± 162.48 $\times 10^9$/L) (p = 0.024). Similarly, mean platelet volume (MPV) was significantly elevated in the clonal group (9.20 ± 1.04 fL) compared to the reactive group (6.14 ± 1.83 fL) (p < 0.001). Plateletcrit (PCT) also showed significantly higher values in clonal thrombocytosis (0.71 ± 0.21) versus reactive thrombocytosis (0.43 ± 0.11) (p < 0.001). In contrast, platelet distribution width (PDW) was significantly lower in the clonal group (11.47 ± 0.92%) compared to the reactive group (13.38 ± 0.65%) (p < 0.001). These findings are summarized in Table 2.

Main Results

Stratified analysis based on gender demonstrated consistent trends across both male and female subgroups. In females, platelet count, MPV, and PCT were significantly higher in the clonal thrombocytosis group compared to the reactive group (all p < 0.001), while PDW remained significantly lower (p < 0.001). Similarly, in males, the clonal group exhibited significantly higher platelet count (824.25 ± 162.53 $\times 10^9$/L vs 578.93 ± 93.45 $\times 10^9$/L), MPV (9.01 ± 1.11 fL vs 6.67 ± 2.26 fL), and PCT (0.75 ± 0.19 vs 0.43 ± 0.07), with all comparisons reaching statistical significance (p ≤ 0.002). PDW was again significantly lower in the clonal group compared to the reactive group (p < 0.001). These subgroup findings reinforce the overall results and are detailed in Table 3.

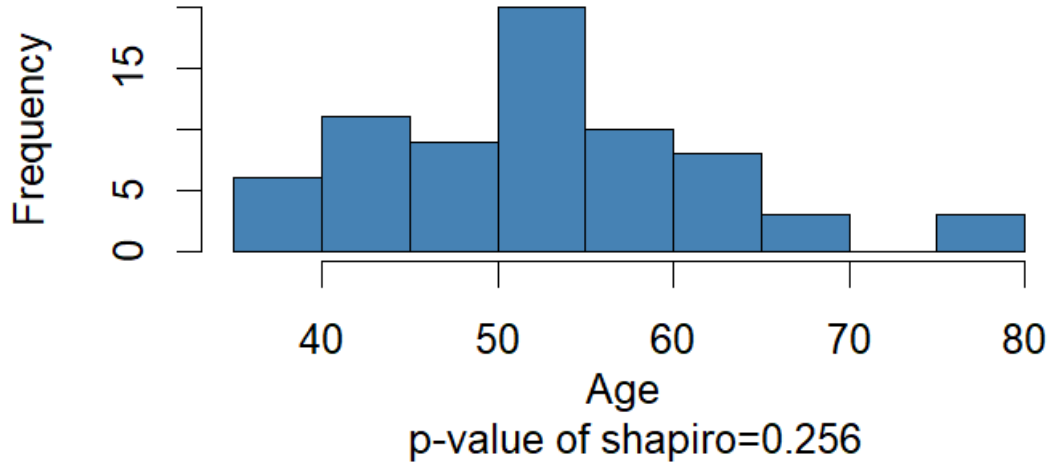


Figure 2. Histogram of the age

Table 1. Demographic distribution of the participants in both groups

Characteristic	Clonal thrombocytosis, N = 35	Reactive thrombocytosis, N = 35	p-value
Age (years)	54.40 ± 7.63	53.49 ± 11.09	0.69*
Gender, n (%)			0.81**
female	19 (54.29)	20 (57.14)	
male	16 (45.71)	15 (42.86)	
Age group(years)			1.00**
35-55	23 (65.71)	23 (65.71)	
56-80	12 (34.29)	12 (34.29)	

*Welch Two Sample t-test; **Pearson's Chi-squared test

Table 2. Comparison of platelet indices between clonal and reactive thrombocytosis

Characteristic	Clonal thrombocytoiss, N = 35	Reactive thrombocytosis, N = 35	p-value*
Platelet count(x10^9/L),	771.54±217.90	665.23 ± 162.48	0.024
Mean platelet volume(fL)	9.20 ± 1.04	6.14 ± 1.83	<0.001
Platelet crit (PCT)	0.71±0.21	0.43 ± 0.11	<0.001
Platelet distribution width (%)	11.47±0.92	13.38 ± 0.65	<0.001

*Independent two Sample t-test

Table 3. Comparison of platelet indices between clonal and reactive thrombocytosis stratified by gender

Characteristic	N	Clonal thrombocytosis	Reactive thrombocytosis	p-value*
Female, N = 39				
Platelet count(x10^9/L),	39	727.16 ± 251.25	629.95 ± 174.69	<0.001
Mean platelet volume(fL)	39	9.36 ± 0.97	5.75 ± 1.37	<0.001
Platelet crit (PCT)	39	0.68 ± 0.23	0.43 ± 0.13	<0.001
Platelet distribution width (%)	39	11.54 ± 0.86	13.35 ± 0.64	<0.001
Male, N = 31				
platelet count(x10^9/L)	31	824.25 ± 162.53	578.93 ± 93.45	<0.001
mean platelet volume(fL)	31	9.01 ± 1.11	6.67 ± 2.26	0.002
platelet crit (PCT)	31	0.75 ± 0.19	0.43 ± 0.07	<0.001
Platelet distribution width (%)	31	11.39 ± 1.01	13.42 ± 0.69	<0.001

*Independent two Sample t-test

Discussion

The present study demonstrated significant differences in platelet indices between clonal and reactive thrombocytosis, highlighting their potential diagnostic utility. Patients with clonal thrombocytosis exhibited significantly higher platelet count, mean platelet volume (MPV), and plateletcrit (PCT), while platelet distribution width (PDW) was significantly lower compared to those with reactive thrombocytosis. These findings suggest that platelet morphology and production dynamics differ substantially between the two conditions and can be reflected through routinely available hematological parameters [12].

The observed elevation in MPV and PCT in clonal thrombocytosis can be attributed to dysregulated megakaryopoiesis and the production of larger, functionally abnormal platelets, which is characteristic of myeloproliferative neoplasms.[13] In contrast, reactive thrombocytosis is primarily driven by external stimuli such as inflammation or infection, resulting in increased platelet production without significant alteration in platelet size or

morphology [14]. This biological distinction likely explains the comparatively lower MPV and PCT values observed in the reactive group.

Interestingly, PDW was found to be significantly lower in clonal thrombocytosis in this study, which contrasts with some previous reports suggesting increased variability in platelet size in clonal disorders. However, similar findings have been reported in certain populations, indicating that PDW may behave inconsistently depending on disease heterogeneity, stage, and underlying etiological factors [11]. This variability underscores the importance of interpreting PDW in conjunction with other platelet indices rather than as an isolated marker.

Our findings are consistent with those reported by Selvaraju et al. [11], who demonstrated that MPV and PCT were significantly higher in clonal thrombocytosis, supporting their role in differentiating between primary and secondary causes. Similarly, Hafeez et al. [12] reported significantly elevated MPV, PCT, and platelet large cell ratio in clonal thrombocytosis, reinforcing the diagnostic value of platelet indices. These studies, along with the present findings, emphasize the utility of automated hematological parameters as cost-effective screening tools, particularly in settings where advanced molecular diagnostics are not readily accessible[16].

Furthermore, stratified analysis by gender in the present study revealed consistent trends across both male and female subgroups, strengthening the robustness of the findings[15]. The persistence of significant differences across subgroups suggests that the observed variations in platelet indices are independent of gender and are primarily driven by underlying pathophysiological mechanisms.

Despite these strengths, it is important to interpret the findings within the broader clinical context. Platelet indices alone cannot replace definitive diagnostic modalities such as bone marrow examination and molecular testing, but they may serve as valuable adjuncts in initial clinical assessment and triage.

Conclusion

This study demonstrates that platelet indices, particularly mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW), differ significantly between clonal and reactive thrombocytosis. Clonal thrombocytosis is characterized by higher platelet count, MPV, and PCT, along with comparatively lower PDW, reflecting underlying abnormalities in megakaryopoiesis and platelet production.

Authors' Contributions:

All authors meet the ICMJE criteria for authorship.

Author 1: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 2: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 3: Analysis and interpretation of data, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 4: Analysis and interpretation of data, critical revision, final approval, agreed to be accountable for all the work.
Author 5: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 6: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.

References

1. Chaudhary PK, Kim S. An insight into recent advances on platelet function in health and disease. *Int J Mol Sci.* 2022;23(11):6022. https://doi.org/10.3390/ijms23116022
2. Ghafoor MB, Sarwar F, Durrani TA, Azher ZQ, Jabeen S, Khan MHA. Pattern of thrombocytopenia in pregnancy at a teaching hospital of Rahim Yar Khan, Pakistan. *J Rawalpindi Med Coll.* 2022;26(4):688–692. https://doi.org/10.37939/jrmc.v26i4.2053
3. Gauer RL, Whitaker DJ. Thrombocytopenia: evaluation and management. *Am Fam Physician.* 2022;106(3):288–298. PMID: 36126009
4. Tremblay D, Yacoub A, Hoffman R. Overview of myeloproliferative neoplasms: history, pathogenesis, diagnostic criteria, and complications. *Hematol Oncol Clin North Am.* 2021;35(2):159–176. https://doi.org/10.1016/j.hoc.2020.12.001
5. Iurlo A, Bucelli C, Cattaneo D. Essential thrombocythemia in adolescents and young adults: clinical aspects, treatment options, and unmet medical needs. *Curr Treat Options Oncol.* 2023;24(7):802–820. https://doi.org/10.1007/s11864-023-01099-8
6. Stockklausner C, Duffert C, Cario H, Knöfler R, Streif W, Kulozik A, et al. Thrombocytosis in children and adolescents—classification, diagnostic approach, and clinical management. *Ann Hematol.* 2021;100:1647–1656. https://doi.org/10.1007/s00277-021-04500-0

7. Edahiro Y, Kurokawa Y, Morishita S, Yamamoto T, Araki M, Komatsu N. Causes of thrombocytosis: a single-center retrospective study of 1,202 patients. *Intern Med.* 2022;61(22):3323–3328. https://doi.org/10.2169/internalmedicine.9282-21
8. Han EY, Catherwood M, McMullin MF. Hereditary thrombocytosis: the genetic landscape. *Br J Haematol.* 2021;194(6):1098–1105. https://doi.org/10.1111/bjh.17741
9. Chiba N, Sugita A, Mizuochi M, Sato J, Saito T, Sakurai A, et al. Clinical significance of reactive thrombocytosis in the course of acute pancreatitis. *BMC Gastroenterol.* 2023;23(1):206. https://doi.org/10.1186/s12876-023-03047-5
10. Al-Tameemi WF, Noori AK. The impact of platelet indices in the evaluation of different causes of platelet count disorders. *Iraqi J Hematol.* 2022;11(1):32–37. https://doi.org/10.4103/ijh.ijh_47_21
11. Selvaraju V, Jayaganesh N. Platelet indices in differentiating reactive versus clonal thrombocytosis. *Saudi J Pathol Microbiol.* 2023;8(3):50–54. https://doi.org/10.36348/sjpm.2023.v08i03.002
12. Hafeez A, Naeem S, Robert HM, Mohsin S, Mahmood A. Platelet indices as a tool for differentiation between clonal thrombocytosis and reactive thrombocytosis. *Pak Armed Forces Med J.* 2023;73(Suppl-1):S79–S83. https://doi.org/10.51253/pafmj.v73iSUPPL-1.6350
13. Mohtashami M, Razavi A, Abolhassani H, Aghamohammadi A, Yazdani R. Primary immunodeficiency and thrombocytopenia. *Int Rev Immunol.* 2022;41(2):135–159. https://doi.org/10.1080/08830185.2021.1980160
14. Jaffer M, Shahid O, Aslam R, Saeed F, Arshad A, Hanif MT. Frequency of different causes of thrombocytosis among patients presenting to a tertiary care hospital. *Prof Med J.* 2024;31(4):581–587. https://doi.org/10.29309/TPMJ/2024.31.04.8129
15. Syed NN, Usman M, Khurshid M. Thrombocytosis: age-dependent aetiology and analysis of platelet indices for differential diagnosis. *Indian J Pathol Microbiol.* 2007;50(3):628–633.
16. Saeed BA, Taib SM, Nafih K. Platelet indices in the differential diagnosis of thrombocytosis. *Ann Coll Med Mosul.* 2009;35(1):31–33. https://doi.org/10.33899/mmed.2009.8895