

Study of Platelet Indices and Their Interpretation in Thrombocytopenia in a Tertiary Care Hospital

¹Dr. Sanjay R. Telwelkar, Associate Professor, Department of Pathology, P.D.U. Government Medical College, Rajkot.

²Dr. Manisha k. Chaudhary, Resident Doctor, Department of Pathology, P.D.U. Government Medical College, Rajkot.

³Dr. Rushang Dave, Senior Resident, Department of Pathology, P.D.U. Government Medical College, Rajkot.

⁴Dr. Gauravi A. Dhruva, Professor & Head, Department of Pathology, P.D.U. Government Medical College, Rajkot.

Corresponding Author: Dr. Rushang Dave, Senior Resident, Department of Pathology, P.D.U. Government Medical College, Rajkot.

Citation this Article: Dr. Sanjay R. Telwelkar, Dr. Manisha k. Chaudhary, Dr. Rushang Dave, Dr. Gauravi A. Dhruva, “Study of Platelet Indices and Their Interpretation in Thrombocytopenia in a Tertiary Care Hospital”, IJMSIR- February - 2022, Vol – 7, Issue - 1, P. No. 109 – 116.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Thrombocytopenia may either be due to increased destruction or impaired production of platelets. Platelet count alone is not enough to determine the mechanism of low platelets. Platelet indices like mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR) and platelet crit (PCT) can help determine the cause and we aimed at finding their role and function in cases of thrombocytopenia.

Methods: An observational cross-sectional study of 605 patients with thrombocytopenia and 200 controls was done for a period of one year in civil hospital Rajkot to determine the mechanism behind the low platelet count with the help of these indices.

Results: The mean values of the platelet indices (PDW, P-LCR and PCT) were found to be higher in accelerated destruction group ($P < 0.05$) in comparison to hypo productive group, whereas, mean MPV values were higher in the former, but were not statistically significant. On comparison with the controls, both the groups of

thrombocytopenia showed a statistically significant difference with $P < 0.005$ in all the four indices. Mean PCT values showed a highly significant difference between the two groups as well as with controls ($P < 0.001$) and also the relationship of PCT with severity of thrombocytopenia showed a direct relationship which was also significant ($P < 0.001$).

Conclusions: In distinguishing between the cause of thrombocytopenia i.e., hypo productive or hyper destruction, platelet parameters play an important role. These platelet indices are easily available with the help of automated haematology analysers and can reduce the need for costly and invasive tests for evaluation of thrombocytopenia.

Keywords: Mean Platelet Volume, Platelet crit, Platelet Distribution Width, Platelet Large Cell Ratio, Thrombocytopenia.

Introduction

Thrombocytopenia is one of the common findings among patients in a clinical setting. It is defined by platelet count below the normal values and has a significant role in both

hospitalised and non-hospitalised patients. The counts below 1,50,000 / μL are considered as thrombocytopenia. The clinical manifestation varies from mild symptoms such as easy bruising / mild bleeding to massive bleeding /haemorrhage that may result in death.

Platelets play a vital role in homeostasis and also have non-homeostatic role in angiogenesis, repairing of tissue and inflammation. In order to evaluate the cause of low platelet count, it is necessary to relate whether it is due to hyper destruction or impaired production. Hyper destructive thrombocytopenia is a result of extramedullary destruction of platelets with a normal or an increased bone marrow production; causes comprise of malaria, dengue, idiopathic thrombocytopenic purpura (ITP), disseminated intravascular coagulation (DIC), haemolytic uremic syndrome (HUS). The category of impaired production is a result of primary or secondary bone marrow diseases with a decreased bone marrow production. It includes causes such as bone marrow aplasia, haematological malignancies, post chemotherapy, post radiation, hypersplenism etc. After evaluating the mechanism behind the low platelet count, which can be helpful to the clinician in providing proper treatment to the patient. Bone marrow aspiration study is the gold standard for finding the cause for thrombocytopenia, but its use is restricted since it is an invasive procedure. There is also a high risk of bleeding complication associated with the procedure.

Automated cell counters are used widely these days which furnish us the valuable information of various blood cell parameters including red blood cells, white blood cells and platelets with platelet parameters. Recently platelet parameters like mean platelet volume (MPV), platelet distribution width (PDW), platelet crit (PCT) and Platelet large cell ratio (P-LCR) have been

investigated as important platelet activation markers. All these parameters are provided by automated blood cells analysers and these indices can be correlated with platelet counts. Quantification of platelet indices in automated analysers has superiority over the manual estimation because it is quick, effortless and cost-effective method which also eliminates the observer bias and artifactual problems of manual method.

The study of these platelet indices can help establish the mechanism behind thrombocytopenia. MPV and PDW are both derived from platelet distribution curve and related to change in platelet size and shape. P-LCR can be used as an effective tool in distinguishing between hyper destruction and impaired production. P-LCR is directly related to PDW and MPV, whereas it is inversely related to platelet count. PCT is the volume occupied by the platelets in the blood and is expressed in terms of percentage and plays an important role in diagnosing platelet quantitative abnormalities.

Platelet indices can have a significant prognostic role as early evaluation of thrombocytopenia can help reduce morbidity and mortality of patients with low platelet count. This study aims to find the usefulness of these platelet indices in initial evaluation, as their role is still not clear in patients with thrombocytopenia.

Methods

An observational cross-sectional study was undertaken for a period from august 2020 to September 2021 in the pathology laboratory at civil hospital Rajkot. All the blood samples of patients which were received in K3-EDTA anti-coagulated vacutainers in the laboratory were processed within one hour of collection using the 5-part automated haematology analyser. From the analyser generated reports, platelet count and platelet parameters i.e., mean platelet volume (MPV), platelet distribution

width (PDW), platelet large cell ratio (P-LCR) and platelet crit (PCT) were recorded and platelet count was reassessed by peripheral blood smear examination on Leishman-stained slides in all the cases. We included 605 patients of age more than 1 year with thrombocytopenia (platelet count $< 150 \times 10^9 / L$). Control group included 200 persons who had all the haemogram parameters within normal limits.

Approval for patient consent and patient information sheet (PIS) was obtained from institutional ethical committee since the study involved the data available in the records that was anonymised and coded so as to delink any data related to identification of the patient.

Exclusion Criteria

- Patients of age < 1 year (infants) – to avoid age related changes in platelet indices.
- Patients with myelodysplastic syndrome. (MDS)
- Patients with autoimmune disorders such as systemic lupus erythematosus (SLE), Type 1 diabetes mellitus (DM), vitiligo, juvenile rheumatoid arthritis.
- Patients on anti-platelet drugs and drugs causing thrombocytopenia.

Table 1: Age and Sex Distribution of Cases of Thrombocytopenia.

Sn.	Age Group (In Years)	Male	Female	Total No	%
1	01-10	45	21	66	11.2
2	11-20	80	35	115	19.0
3	21-30	117	52	169	28.1
4	31-40	118	46	164	27.9
5	41-50	36	12	48	7.8
6	51-60	13	5	18	3.0
7	61-70	14	4	18	2.7
8	71-80	5	2	7	1.3
Total		428 (70.25%)	177 (29.75%)	605	100

- Platelet parameters were then assessed in both the groups and compared with those of the control group.

Results

A total of 605 patients with thrombocytopenia after informed consent were included in the study. There were 70 % males and 30 % were females in this study. Table I shows the age sex wise distribution of the cases with thrombocytopenia. Our age group ranged from 1 - 80 years, with more than 54 % of the cases falling in the age group of 21 - 40 years. Comparison of the platelet indices with the severity of thrombocytopenia was also assessed. (Table II) They were categorised into 3 categories: mild thrombocytopenia with platelet count ≥ 100 to $< 150 \times 10^9 / L$, moderate thrombocytopenia with platelet count $> 50 \times 10^9 / L$ and $< 100 \times 10^9 / L$ and severe thrombocytopenia with platelet count $\leq 50 \times 10^9 / L$. Our study showed a significant difference only in one of the platelet parameters i.e., platelet crit ($P < 0.001$), while the rest of the parameters showed no significant difference.

Table 2: Relationship of Platelet Indices with Severity of Thrombocytopenia.

Platelet Count	Cases	PDW (fL) (Mean ± SD)	MPV (fL) (Mean ± SD)	P-LCR (%) (Mean ± SD)	PCT (%) (Mean ± SD)
≤ 50 x 10 ⁹ / L	90	18.06 ± 3.29	13.21 ± 1.07	49.36 ± 7.03	0.03 ± 0.01
> 50 - < 100 x 10 ⁹ / L	193	18.71 ± 3.10	13.48 ± 1.18	52.37 ± 9.32	0.06 ± 0.02
≥ 100 - < 150 x 10 ⁹ / L	322	19.02 ± 3.32	13.55 ± 1.18	52.60 ± 9.18	0.08 ± 0.03
P-value (between groups)		0.428	0.460	0.269	< 0.001*

PDW – Platelet Distribution Width, MPV – Mean Platelet Value.

P - LCR – Platelet Large Cell Ratio, PCT – Platelet crit

* The mean difference is significant at the level 0.05 level.

Table 3: Platelet Count and Platelet Parameters According to Each Group.

Group	Cases	Platelet (x10 ⁹ / L) (Mean ±SD)	DW (fL) (Mean ±SD)	MPV (fL) (Mean ±SD)	-LCR (%) (Mean ± SD)	PCT (%) (Mean ±SD)
A -Accelerated destruction	381	103.7 ± 23.6	19.37 ±3.04	13.66 ±1.15	53.64 ±8.98	0.08 ±0.02
B - Impaired production	224	71.5 ± 32.3	17.60 ±3.34	13.11 ±1.10	48.85 ±8.03	0.03 ±0.01
Control	200	249.7 ± 77.5	16.01 ±4.40	12.21 ±1.75	41.85 ±13.63	0.25 ±0.09

PDW – Platelet Distribution Width, MPV – Mean Platelet Value,

P - LCR – Platelet Large Cell Ratio, PCT – Platelet crit.

* The mean difference is significant at the level 0.05 level.

Table 4: Statistical Comparison of Platelet Parameters within Groups.

Platelet Parameters	Group A vs. Control			Group B vs. Control			Group A vs. Group B		
	Mean	SD	P-Value	Mean	SD	P-Value	Mean	SD	P-Value
PDW	3.3623	0.5550	P <0.001*	1.5925	0.6519	P =0.046*	1.7698	0.6081	P =0.012*
MPV	1.4485	0.2109	P <0.001*	0.9057	0.2477	P =0.001*	0.5428	0.2310	P =0.05 9
P-LCR	11.786	1.6206	P <0.001*	7.0007	1.9033	P =0.001*	4.7856	1.7754	P =0.023*
PCT	0.1643	0.00868	P <0.001*	0.22041	0.0101	P <0.001*	0.05602	0.0095	P <0.001*

PDW – Platelet Distribution Width, MPV – Mean Platelet Value, P-LCR –

Platelet Large Cell Ratio, PCT – Platelet crit

* The mean difference is significant at the level 0.05 level.

Patients with thrombocytopenia were grouped into 2 groups according to the mechanism causing low platelet

count i.e. group A included those with hyper destructive causes of low platelet count and group B included causes leading to impaired production of platelets. Group A included 381 patients who were diagnosed as either of the following: dengue, burns, pregnancy, malaria, typhoid, disseminated intravascular coagulation, sepsis, viral infections, idiopathic thrombocytopenic purpura, or

renal diseases. Group B included 224 patients who were diagnosed as either of the following: tuberculosis, chicken pox, deep vein thrombosis, chikungunya, megaloblastic anaemia, iron deficiency anaemia, pancytopenia, leukemia, or cirrhosis. Group A cases 62.7 % as compared to 37.3 % cases in Group B.

Table III and IV comparison and statistical analyses between the mean platelet parameters within the two groups of PCT and also the controls. It shows a significant difference i.e., P value < 0.05 in PDW, P-LCR and highly significant difference i.e., P < 0.001 in mean PCT values of the three categories. Mean MPV shows slight difference when thrombocytopenia is compared with control but, there is no difference between the 2 mechanisms of low platelet count (P = 0.05).

Discussion

Thrombocytopenia is one of the common findings in many disease conditions. The major pathogenesis behind this is basically either due to decreased or impaired bone marrow production, peripheral accelerated destruction or due to increased splenic sequestration. Clinically, it is difficult to ascertain the reason behind the decrease in platelet count. Bone marrow studies, reticulated platelets and platelet associated IgG have been done in the past to evaluate the reason causing thrombocytopenia, but these are costly, invasive and not easily available procedures. Recently, many studies have taken the help of various platelet indices to assess the cause of thrombocytopenia. Platelet indices are easily available as most of the automated haematology analysers calculate these values. We studied four platelet parameters i.e., MPV, PDW, P-LCR and PCT in cases of thrombocytopenia in order to interpret their importance, if any, behind the mechanism of low platelet count and also compared these values with those of the controls.

Our study included 605 patients of thrombocytopenia, who were predominantly males, which was similar in many studies. Correlation of severity of thrombocytopenia was studied with the changes in the platelet count and the platelet parameters. It was found that although as the platelet count decreases there was reduction in the mean values of all the platelet indices, only PCT showed a direct relationship with the platelet count with P-value < 0.05. The mean PCT in cases of mild, moderate and severe thrombocytopenia was 0.08 %, 0.06 % and 0.03 % respectively.

Cases of thrombocytopenia were classified according to the mechanism behind thrombocytopenia, and the relationship between values of the platelet indices with the cause was examined. The mean platelet count in group A and group B was $103.7 (\pm 23.6) \times 10^9 / L$ and $71.5 (\pm 32.3) \times 10^9 / L$ respectively, showing significant difference between the two and with the control group (mean = $249.7 \pm 77.5 \times 10^9 / L$), which was also the case in other studies. In this study, all the four parameters showed a noteworthy difference when group A i.e., cases of hyper destruction of platelets were compared with the control group, with a high significance of P < 0.001. Group B i.e., hypo production cases on comparison with control group also showed a significant difference in mean PCT (P < 0.001), mean PDW (P = 0.046), mean MPV (P = 0.001) and mean P-LCR (P = 0.001), all indices displayed a P-value of less than 0.05. Mala K.G et al. in their study on platelet count, MPV and PDW also found significant difference when the groups were compared with the control. Studies by Elsewefy DA et al. and Borkatky S et al. also showed significant difference P = 0.035, P = 0.017 in mean P-LCR values of patients with hypo productive thrombocytopenia with those of the control group. Significance in PCT was

similar to few other studies where the mean PCT in hypoproduction group was 0.45 (\pm 0.44) % and in hyper destruction group was 1.16 (\pm 0.48) % with a P value of 0.0001.

On comparison between the two groups of thrombocytopenia, mean PDW (P = 0.012), mean P-LCR (P = 0.023) and mean PCT (P < 0.001) showed a difference, whereas P value for mean MPV was 0.59. PDW which was associated with variability in platelet size was higher in the cases of group A with the mean of 19.37 (\pm 3.04) fL as compared to 17.60 (\pm 3.34) fL in group B. Other studies also showed high PDW in hyper destruction thrombocytopenia attributing to the release of heterogenous population of platelets with anisocytosis, the reason behind it.^{15,17-20} While one of the study stated that due to dysplasia in mega karyopoiesis, there was high PDW in impaired production group.²¹ MPV is a known marker of megakaryocytic activity.²² A high value is seen when there is excessive platelet lysis as it leads to increased bone marrow production of immature platelets.²³ Mean MPV was 13.66 fL in group A as compared to 13.11 fL in group B, which was in accordance with studies like Vinholt PJ et al., Borkataky S et al. and Reddy RS et al.,^{2,15,17} but the difference was not significant, which was the same in studies by Nakadate H et al. and Baynesti RD et al.^{24,25} Mean P-LCR was 53.64 % and 48.85 % in group A and group B respectively, which was consistent with other studies.^{14,26,27} The study by Babu E et al. showed no statistically significant difference in P-LCR value but it was also higher in hyper destructive cases as compared to impaired production.⁵ PCT value measures the total platelet mass, and is dependent on MPV.²² Its value varies with platelet count and we found significantly higher values in group A and lower in group B. In group

B cases, megakaryocytes also decrease in the bone marrow leading to increased tendency of bleeding manifestation, so PCT along with platelet count can prove to be a useful marker in patients with bleeding diathesis

On reviewing the literature, many studies have shown higher values of these parameters in hyper destructive group as compared to hypo productive group, but their significance has not been verified.²⁹⁻³¹ As a result the cut off value has not been set by which one can place a case in one of the two categories. So further studies on platelet indices and with other markers like immature platelet fraction should be done so as to have a criterion for classifying thrombocytopenia with the help of these easily available markers.

Conclusions

Platelet crit can help assess both quantitative as well as qualitative platelet disorders and there is direct relation between PCT and platelet count. Other parameters like PDW, PLCR and MPV along with PCT can be used to interpret the mechanism behind the low platelet count, where high values of indices indicate increased breakdown of platelets in the bloodstream and low values are possibly due to impaired production due to primary or secondary bone marrow disease. These parameters need to be studied more, as their significance if recorded, can prove to be very useful in establishing causes of thrombocytopenia and will also reduce the need for the costly and invasive procedures at least in routine cases.

References

1. Rodgers GM. Thrombocytopenia: pathophysiology and classification. In: Win Trobe's Clinical Hematology. 13th edn. Philadelphia: Lippincott Williams and Wilkins 2014:1058-60.

2. Sekhon SS, Roy V. Thrombocytopenia in adults: a practical approach to evaluation and management. *South Med J* 2006;99(5):491-533.
3. Khaleel KJ, Ahmed AA, Anwar MAA. Platelet indices and their relations to platelet count in hypo productive and hyper-destructive thrombocytopenia. *Karbala Journal of Medicine* 2014;7(2):1952-8.
4. Borkatakya S, Jain R, Gupta R, et al. Role of platelet volume indices in the differential diagnosis of thrombocytopenia: a simple and inexpensive method. *Hematology* 2009;14(3):182-6.
5. Katti TV, Mhatre SC, Anni Geri C. How far are the platelet indices mirror image of mechanism of thrombocytopenia-mystery still remains? *Int J of Adv in Med* 2014;1(3):200-5.
6. Parveen S, Vimal M. Role of platelet indices in differentiating hypo productive and hyper destructive thrombocytopenia. *Annals of Pathology and Laboratory Medicine* 2017;4(3):288-91.
7. Greer P, Arber DA, Glader B, et al. *Rodgers in Williams's hematology*. Chap. 49. Thrombocytopenia. 8th edn. Mac Graw-Hill 2010:1101-02.
8. Mala KG, Bhandari BJ, Kittur SK. Paramountcy of platelet parameters in thrombocytopenia-our hospital experience. *Indian J Pathol Oncol* 2018;5(4):558-62.
9. Vinholt PJ, Hvas AM, Nybo M. An overview of platelet indices and methods for evaluating platelet function in thrombocytopenic patients. *Eur J Haematol* 2014;92(5):367-76.
10. Vidyadhar S. Diagnostic implication and utility of platelet indices in differentiating hypo productive and hyper destructive thrombocytopenia. *IOSR Journal of Dental and Medical Sciences* 2019;18(8):07-11.
11. Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. *Platelets* 2002;13(5-6):301-6.
12. Baig MA. Platelet indices-evaluation of their diagnostic role in pediatric thrombocytopenia's (One year study). *Int J Res Med Sci* 2015;3(9):2284-9.
13. Babu E, Basu D. Platelet large cell ratio in the differential diagnosis of abnormal platelet counts. *Indian J Pathol Microbiol* 2004;47(2):202-5.
14. Giacomini A, Legovini P, Gessoni G, et al. Platelet count and parameters determined by the Bayer ADVIA 120 in reference subjects and patients. *Clin Lab Haematol* 2001;23(3):181-6.
15. ICMR. Informed consent process. Conditions for granting waiver of consent. National ethical guidelines for biomedical and health research involving human participants. Indian Council of Medical Research 2017.
16. Vani C. Plateletcrit as a screening tool for detection of platelet quantitative disorders. *J Hematol* 2013;2(1):22-6.
17. Negash M, Tsegaye A, G/Medhin A. Diagnostic predictive value of platelet indices for discriminating hypo productive versus immune thrombocytopenia purpura in patients attending a tertiary care teaching hospital in Addis Ababa, Ethiopia. *BMC Hematol* 2016; 16:18.
18. Kim MJ, Park PW, Seo YH, et al. Comparison of platelet parameters in thrombocytopenic patients associated with acute myeloid leukemia and primary immune thrombocytopenia. *Blood Coagul Fibrinolysis* 2014;25(3):221-5.
19. Elsewefy DA, Farweez BA, Ibrahim RR. Platelet indices: consideration in thrombocytopenia. *Egypt J Haematol* 2014;39(3):134-8.

20. Reddy RS, Phansalkar MD, Ramalakshmi PVB. Mean Platelet Volume (MPV) in thrombocytopenia. *J Cont Med A Dent* 2014;2(2):45-50.
21. Farias MG, Schunck EG, Bó SD, et al. Definition of reference ranges for the platelet distribution width (PDW): a local need. *Clin Chem Lab Med* 2010;48(2):255-7.
22. Khaikar SP, More S, Pandey A, et al. Role of mean platelet volume (MPV) in diagnosing categories of thrombocytopenia. *Indian Journal of Pathology and Oncology* 2016;3(4):606-10.
23. Reddy RS, Khan MI, Phansalkar MD. Platelet distribution width (PDW) in thrombocytopenia. *Indian Medical Gazette* 2015;149(5):169-73.
24. Xu RL, Zheng ZJ, Ma YJ, et al. Platelet volume indices have low diagnostic efficiency for predicting bone marrow failure in thrombocytopenic patients. *Exp Ther Med* 2013;5(1):209-14.
25. Nehara HR, Meena SL, Parmar S, et al. Evaluation of platelet indices in patients with dengue infections. *International Journal of Scientific Research* 2016;5(7):78-81.
26. Nelson RB, Kehl D. Electronically determined platelet indices in thrombopenic patients. *Cancer* 1981;48(4):954-6.
27. Nakadate H, Kaida M, Furukawa S, et al. Use of the platelet indices for differential diagnosis of pediatric immune thrombocytopenic purpura (ITP). *Blood* 2008;112(11):4557.
28. Baynes RD, Lamparelli RD, Bezwoda WR, et al. Platelet parameters. Part II. Platelet volume-number relationships in various normal and disease states. *S Afr Med J* 1988;73(1):39-43.
29. Rajashekar RB, Mahadevappa A, Patel S. Evaluation of thrombocytopenia in megaloblastic anemia by platelet indices and megakaryocytes-comparison with hypoproduction and hyper destruction. *National Journal of Laboratory Medicine* 2017;6(1):18-22.
30. Aponte-Barrios NH, Linares-Ballesteros A, Sarmiento-Urbina IC, et al. Evaluation of the diagnostic performance of platelet-derived indices for the differential diagnosis of thrombocytopenia in pediatrics. *Rev Fac Med* 2014;62(4):547-5.
31. Mohr R, Martinowitz U, Golan M, et al. Platelet size and mass as an indicator for platelet transfusion after cardiopulmonary bypass. *Circulation* 1986;74(5 Pt 2):III153-8.