

Evaluation of platelet parameters (PDW and MPV) for differentiation between clonal thrombocytosis and reactive thrombocytosis

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Objective: To establish the diagnostic effectiveness of platelets parameters i.e. platelets distribution width (PDW) and mean platelet volume (MPV) in differential diagnosis of thrombocytosis (clonal thrombocytosis /reactive thrombocytosis).

Methodology: This cross-sectional study was carried out at Hematology department at Fauji Foundation Hospital, Rawalpindi, Pakistan from Feb 2012 to March 2013. A total of 148 patients were studied. Out of these, equal number had myeloproliferative disorders (MPD) and reactive thrombocytosis (RT). The complete blood picture was done on auto-analyzer Sysmex XT (2000i) and platelet count, PDW and MPV were determined.

Results: Out of 148 patients with thrombocytosis, the range of PDW was 10-20% for clonal thrombocytosis (CT) with a mean value of

14.3±2.2% and for RT the range of PDW was 7-13% and the mean value was 9±1.3%. The mean MPV for CT was 11.7±1.6fl and for RT was 8.50±0.6fl with a range of 8.7-18.5fl for CT and 7.2-10.4fl for RT. The t test was applied on the mean of MPV and PDW of clonal and reactive thrombocytosis ($p < 0.0001$), which was statistically significant.

Conclusion: Interpretation of platelet parameters i.e. PDW and MPV with platelet counts are useful for the differentiating CT from RT. By increasing awareness of our clinicians in utilizing these simple parameters will aid in diagnosis of CT when platelets counts are markedly elevated. (Rawal Med J 201;42:302-305)

Keywords: Clonal thrombocytosis, Reactive thrombocytosis, platelets distribution width PDW, Mean platelet volume MPV.

INTRODUCTION

Platelets are part of cellular component of blood platelet count ranges between $150450 \times 10^9/L$ and their normal life span is 710 days. Thrombocytosis is an increase in the number of circulating platelets and defined as a platelet count $>450 \times 10^9/L$.¹ Once the thrombocytosis has been reported, repeat testing and examination of the peripheral blood smear needs to be done to confirm the findings and differentiate between the two types of thrombocytosis, i.e reactive and clonal.^{2,3} CT also called myeloproliferative disorder is a primary hematologic disease.³⁻⁵ According to revised WHO classification, the term myeloproliferative disorders (MPD) includes the clonal hemopoietic diseases like chronic myeloid leukemia (CML), polycythemia Vera (PV), idiopathic myelofibrosis (IMF), essential thrombocythemia (ET) and rarer

conditions like chronic neutrophilic leukemia and hypereosinophilic syndrome.⁵ Among the chronic myeloproliferative disorders thrombocytosis is more common in patients with CML and essential ET.⁶

The MPV is the measure of platelet size. When there is an increase in turnover as in MPD like CML, PV, ET etc the MPV also increases.⁷⁻⁹ The PDW is the width of the curve of distribution of platelets according to the different sizes. The sensitivity of platelets parameter (MPV and PDW) is 74.2% and the and specificity of platelets parameters (MPV and PDW) is 84.4% for MPD, when platelet count is >450 . Zhang et al explored the clinical application of MPV, PDW, platelet-large cell ratio (P-LCR), lactate dehydrogenase (LDH) level in the differential diagnosis of thrombocytosis. They proposed that the characteristics of these parameters may be useful

for differential diagnosis of CT and RT.¹² Another study reported 82% thrombocytosis in reactive disorders while 14% thrombocytosis in clonal disorders and 4% thrombocytosis of unknown etiology.¹⁰

RT is quite commonly seen in routine practice. MPV and PDW as well as other non invasive tests like peripheral blood smear, ESR, C-reactive protein and LDH may be used to distinguish between reactive and clonal thrombocytosis.^{4,9} In our study, we wanted to establish the role of MPV and PDW as receptive and precise markers for differentiating between clonal and reactive thrombocytosis. With the help of these parameters the differentiation can be done readily as they are available in all automated hematology analyzers and they are economical as well.^{8,9,11}

METHODOLOGY

This was a cross sectional study in which a total of 148 patients with platelets count >450 x 10⁹/L from both genders were included while infants and patients taking growth factors like thrombopoietin stimulatory factors were excluded. In the study, 74 patients were diagnosed cases of MPD according to WHO criteria³ and 74 patients were diagnosed RT according to criteria¹³ registered at Fauji Foundation Hospital Rawalpindi.

Patients complete history, clinical examination and relevant test i.e bone marrow /trephine biopsy, reticulin staining, molecular testing (JACK 2 mutation, BCR ABL transcript) and CRP etc were recorded on proforma especially designed for the study. The complete blood count was done on automated hematological analyzer Sysmex XT (2000i) and platelet count, PDW and MPV were determined.

RESULTS

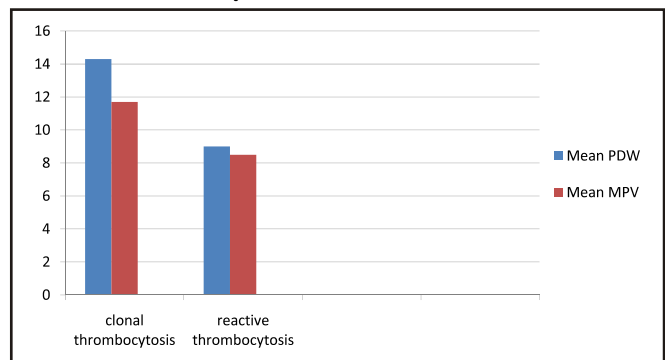
A total number of 148 patients diagnosed with thrombocytosis on CBC were included in the study. The comparison of platelets count, PDW and MPV in reactive and clonal group is in Table 1. Causes of CT included CML in 70.27%, essential thrombocytosis (ET) in 13.51%, Primary myelofibrosis (PMF) in 4.05% and Polycythemia rubra vera (PRV) in 12.16%

Table 1. Comparison of platelets count, PDW And MPV In Clonal and Reactive Thrombocytosis.

Disease	Mean Platelet Count	Range	Mean PDW	Range	Mean MPV	Range
Clonal Thrombocytosis	759 x 10 ⁹ /L	489-2370	14.3±2.2fl	10-20fl	11.7±1.6fl	8.7-18.5
Reactive Thrombocytosis	642 x 10 ⁹ /L	479-1401	9±1.3fl	7-13fl	8.50±.6fl	7.2-10.4fl

While in RT group, out of 74 patients, infection was seen in 57%, post operation in 13.5%, iron deficiency anemia in 20% and thalassemia in 9.45%. The PDW and MPV of clonal and reactive thrombocytosis is as shown in Fig. 1.

Fig. 1. Comparison of PDW And MPV in Clonal and Reactive Thrombocytosis.



The t test was applied on the mean of MPV and PDW of CT and RT (p value <0.0001) which was considered statistically significant similar to the previous studies. The ROC curve showing sensitivity and specificity of PDW and MPV in clonal and reactive thrombocytosis: The area under the curve was significantly higher i.e. 0.989 for MPV and 0.981 for PDW which is statistically significant (P<0.008) (Fig. 2).

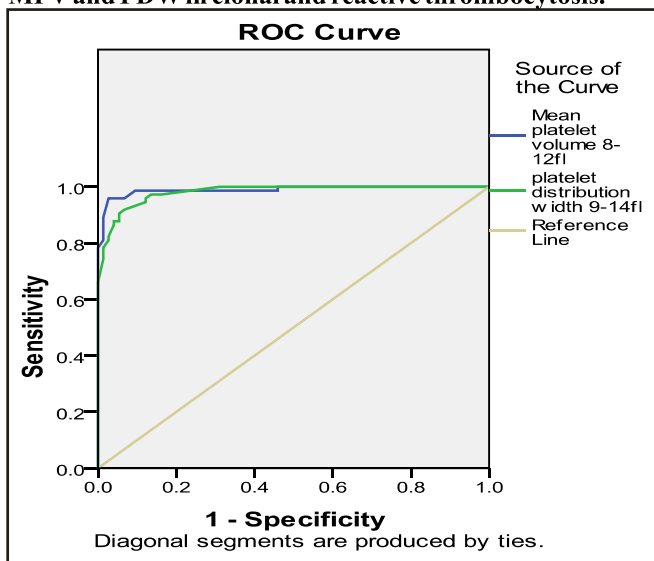
DISCUSSION

Platelet count and other platelet parameters like PDW and MPV have become available for quite some time by modern automated hematology analyzers as a part of routine CBC. Therefore, many studies have been conducted to explore the usefulness of platelet parameters PDW and MPV in diagnosis of thrombocytosis and they have gained importance over the last few years as well.^{6,9} Thrombocytosis is classified according to its origin

into clonal and reactive types. It has been observed that platelets heterogeneity is more marked in CT than in RT.^{1,4}

The mean platelets count in our study of clonal group was $759 \times 10^9/l$ and it was $642 \times 10^9/l$ for reactive group. Syed et al study the mean platelets count of CT was $799 \times 10^9/l$ and the mean platelet count of RT was $721 \times 10^9/l$, which was higher than our study as they have analyzed large number of patients with thrombocytosis.⁸ Similarly, the mean PDW in the clonal group in our study was 14.3 ± 2.2 and for reactive was 9 ± 1.3 which was also low than Syed et al in which the mean PDW in the clonal group was 17.8 ± 0.82 and in reactive was 16.6 ± 0.72 . On the other hand, MPV of clonal group was 11.7 ± 1.6 and of reactive group was 8.5 ± 0.6 in our study while in Syed et al MPV in the clonal group was 8.8 ± 1.4 and in reactive thrombocytosis MPV was 7.2 ± 0.98 . Our this findings of raised MPV were in opposition to Syed et al results, as it was higher in both clonal and reactive thrombocytosis in our study.⁸

Fig 2. ROC curve indicating sensitivity and specificity of MPV and PDW in clonal and reactive thrombocytosis.



Similarly, in CT raised platelet count, PDW and MPV as compared to reactive thrombocytosis were observed by Saeed et al. The mean platelet count, PDW and MPV were $625 \times 10^9/l$, 8.7% and 7.45 fl in clonal thrombocytosis patients while in RT

$537 \times 10^9/l$, 7.4 and 6.7 were observed, which was lower as compared to our findings perhaps of their small study population. The cut off value is 14fl for PDW in CT in our study. In 89% patients the PDW of more than 14 fl was observed while in 10.8% patients PDW was below 14%, while none case out of 74 patients of RT had PDW more than 14% was observed.

The cut off value for MPV is 12 fl in CT and 89% patients with MPV of more than 12 fl were observed while in 10.8% patients the MPV was found below 12fl. In comparison, no patient out of 74 with RT had MPV greater than 12 fl was observed. In comparison to our study the study done by Syed et al the cut off value for PDW >17% was taken 85.2% with CT had PDW >17% while it was noted only in 24.8% of RT. Similarly in their study cut for MPV was taken > 7.0 fl and was found in 95.4% of CT while 56.6% of RT had value greater than 7 were observed.⁸

Among the CT, CML was the most common entity in our study. CML represented 70% of population of our study, 75% cases in Saeed et al⁸ and 36.6% cases in Syed et al study.⁹ While this was in opposition to the Tafazzoli et al in which E.T was the most frequent finding followed by CML.¹⁰ In our study, infection was the most common cause of reactive thrombocytosis comprising 57% patients in all ages in this group this was in accordance with Syed et al study and international studies.⁸

In Tafazzoli study, among RT group after infections, second cause was post operative cases 13.5%. This was followed by iron deficiency anemia 20% and thalassemia 9.45% as the main causes of RT in our research. Tissue trauma was the second most common 19.8% etiological factor in Tafazzoli et al's study.¹⁰

CONCLUSION

We conclude in our study that by interpreting the results of platelet parameters MPV and PDW combined with platelet count can be helpful to the clinicians in differentiating clonal from reactive thrombocytosis as raised PDW and MPV strongly suggest CT.

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Conception and design: Tanzeel Imran
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 Critical revision of the article for important intellectual content: Lubna Zafar, Tariq Butt
 Statistical expertise: Humera Naz Altaf, Saif Orakzai
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