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International Journal of Current Research
Vol. 10, Issue, 03, pp.67160-67163, March, 2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

UTILITY OF PLATELET VOLUME INDICES IN THROMBOCYTOPENIA

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ARTICLE INFO

Article History:
Received 17th December, 2017
Received in revised form
22nd January, 2018
Accepted 04th February, 2018
Published online 30th March, 2018

Key words:
Platelet volume indices,
Mean platelet volume,
Platelet distribution width,
Platelet large cell ratio,
Immune thrombocytopenia.

ABSTRACT

Background: Thrombocytopenia is one of the most frequent causes for hematologic consultation in the practice of medicine. It results from a wide variety of conditions and can produce severe morbidity and mortality. Two main mechanisms involved in the pathogenesis of thrombocytopenia are increased destruction and decreased production of platelets. Recent advances in automated blood cell analyzers have made it possible to measure the various platelet indices and to differentiate the causes of thrombocytopenia as hyper destructive or hypo productive.
Methodology: The blood samples were analyzed for platelet count and platelet volume indices using the automated haematology analyzer.
Results: The platelet volume indices - mean platelet volume, platelet distribution width and platelet large cell ratio showed significantly higher values in the immune thrombocytopenia cases.
Conclusion: The platelet volume indices can be considered as an effective non invasive tool in discriminating immune thrombocytopenia from hypo productive thrombocytopenia.

Citation: Dr. Meghana P. and Dr. Bharathi Muniyappa, 2018. "Utility of platelet volume indices in thrombocytopenia", *International Journal of Current Research*, 10, (03), 67160-67163.

INTRODUCTION

Platelets are cytoplasmic fragments of bone marrow megakaryocytes and are dynamic blood particles whose primary function, along with the coagulation factors, is haemostasis. Thrombocytopenia is a reduction in the peripheral blood platelet count below 150 x 10^9/L and is one of the most frequent causes for hematologic consultation in the practice of medicine. Thrombocytopenia results from a wide variety of conditions and can produce severe morbidity and mortality (Junmei Chen *et al*., 2010) due to intensive bleeding to major organ or intra cerebral bleeding. (Lynne *et al*., 2010).

Two main mechanisms involved in the pathogenesis of thrombocytopenia are increased destruction or peripheral consumption i.e. hyper destructive thrombocytopenia [e.g. immune thrombocytopenic purpura (ITP), disseminated intravascular coagulation (DIC), and thrombotic thrombocytopenic purpura (TTP)] and decreased platelet production i.e. hypo productive thrombocytopenia which is associated with a number of bone marrow diseases. (Sekhon and Roy, 2006).

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Incidence of ITP is 58-66 new cases per million population per year in the US (McMillan, 1997) with similar incidence in the UK. There is no diagnostic test to absolutely say a patient has ITP. Platelet-associated immunoglobulin G (PAIgG) is often elevated in ITP, but it is not specific to ITP and an increased PAIgG level is often found in many other diseases. (Mueller *et al*., 1980) In fact, the necessity for both bone marrow aspiration and PAIgG in ITP is not accepted in the recent guidelines (British Committee for Standards in Haematology, 2003). Thus ITP has remained as a diagnosis of exclusion.

Recent advances in automated blood cell analyzers have made it possible to measure various blood cell parameters automatically. Among these parameters, platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR) provide some important information but are not accepted for routine clinical use. (Threatte, 1993; Niethammer and Forman, 1999) If these indices were to shed more light on platelet kinetics, they might become very useful laboratory measures for thrombocytopenia.

This study tries to highlight the importance of non invasive, inexpensive and easily accessible test, measure its consistency and importance in thrombocytopenic state, thereby devising shortcuts to diagnosis and maximizing the clinical outcomes.

MATERIALS AND METHODS

Study population

The study included 70 consecutive cases with thrombocytopenia i.e. platelet count less than 150 x 10^9/L. Key patient data consisting of name, age, gender, platelet counts along with any special tests performed for determining the etiology of thrombocytopenia were recorded.

The patients were divided into two groups

- **Group I:** 35 cases of thrombocytopenia due to ITP (hyper destructive etiology).
- **Group II:** 35 cases of thrombocytopenia due to hypo productive etiology

As a Control group, 35 healthy individuals undergoing a routine medical check up or minor elective surgery were included.

Laboratory analysis

Blood samples collected in a 5 ml EDTA anti-coagulated tubes were analyzed using automated haematology analyzer. All blood samples were processed soon after the collection to avoid false high MPV value due to EDTA induced platelet swelling. The platelet volume indices - MPV, PDW and P-LCR - were recorded from the cell counter report. The data thus obtained was analyzed to correlate with the patient diagnosis.

RESULTS

Study population consisted of 105 cases including the control group. The total number of male and female patients in the Group I diagnosed with ITP were 15 and 20 respectively, whereas the Group II consisted of 18 male and 17 female patients. Therefore the females were the predominant study participants among ITP patients, while males were predominant in the hypo productive group. The age ranged from 5 – 42 years in the Group I, while the Group II consisted of patients with age ranging from 22 to 65 years. Group II consisted of thrombocytopenia patients diagnosed with acute leukemia, aplastic anemia, myelodysplasia, megaloblastic anemia and chemotherapy patients.

Table 1. Mean platelet count and indices in the Group I patients

Parameter	Group I
Platelet count (x 10^9/L)	42.6
MPV (fL)	12.2
PDW (fL)	15.6
P – LCR (%)	41.6

The platelet count and the platelet indices were compared between ITP, hypo productive patients and healthy controls. Mean platelet count of Group I and Group II patients were 42.6 x 10^9/L and 40.6 x 10^9/L respectively, whereas the Control group had the mean platelet count of 290 x 10^9/L. The mean MPV values were 12.2 fL and 8.8 fL respectively in Group I and Group II patients, while the Control group showed the mean MPV of 9.8 fL.

The mean PDW in Group I and II were 15.6 fL and 11.2 fL respectively. The Control group had the mean PDW of 12.2 fL. The mean P – LCR values of patients in Group I, II and Controls were 41.6%, 25.4% and 28.2% respectively (Table 1-3).

Table 2. Mean platelet count and indices in the Group II patients

Parameter	Group II
Platelet count (x 10^9/L)	40.6
MPV (fL)	8.8
PDW (fL)	11.2
P – LCR (%)	25.4

Table 3. Mean platelet count and indices in the Control group

Parameter	Control
Platelet count (x 10^9/L)	290
MPV (fL)	9.8
PDW (fL)	12.2
P – LCR (%)	28.2

The platelet count was not significantly different in hypo productive and ITP patients. However, all the platelet indices - MPV, PDW and P-LCR were significantly higher in patients with ITP than in patients with hypo productive thrombocytopenia and control group. The hypo productive group though showed the mean platelet indices values lesser than the control group, the difference in the values were not significant (Figure 1-3).

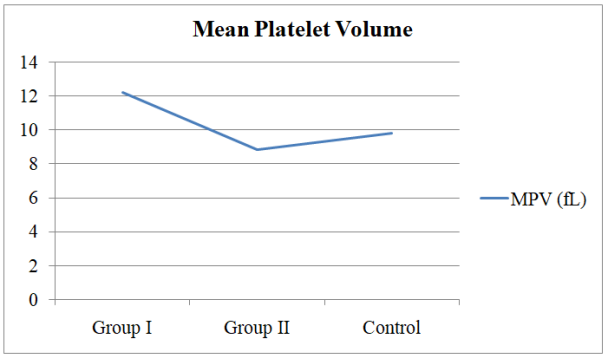

Figure 1. Comparison of mean MPV between Group I, Group II and the Control group

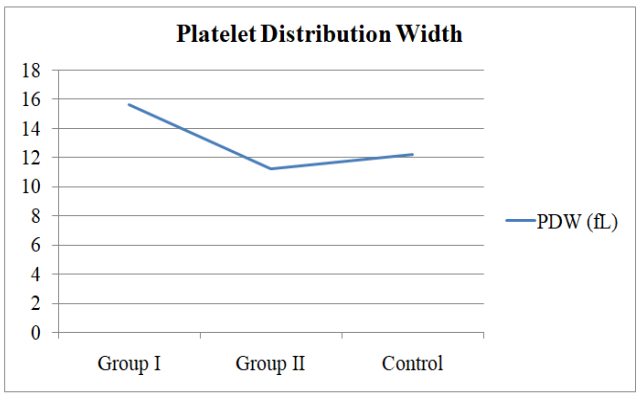

Figure 2. Comparison of mean PDW between Group I, Group II and the Control group

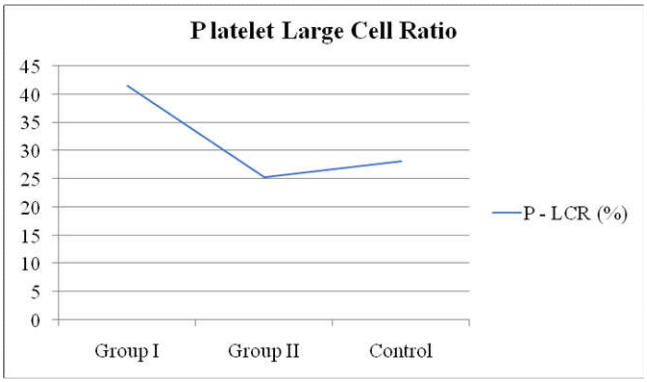

Figure 3. Comparison of mean P - LCR between Group I, Group II and the Control group

DISCUSSION

The most common cause of thrombocytopenia is peripheral platelet destruction where even the compensatory increase in the platelet production is at times not ample to maintain the counts within the normal range. The differential diagnosis for thrombocytopenia in both adults and children is quite broad. Though bone marrow examination is a valuable test, it is invasive and with repeated examination the patient acceptability of the procedure is poor. It provides information about platelet production such as the number and morphology of the megakaryocytes. It is important to know the etiology of thrombocytopenia and to differentiate between the hyper destructive and hypo productive causes for correct patient management and to avoid needless procedures, transfusions and potentially harmful medications. Thus, new non invasive, simple and rapid diagnostic approaches for thrombocytopenia are needed. Recent advances in technology have made it possible to record various platelet indices such as MPV, PDW and P-LCR, with an automated haematology analyser.

There have been some reports about these platelet indices and platelet disorders. (Endler *et al*., 2002; Henning *et al*., 2002) However they are not clinically accepted as conventional checkpoints for thrombocytopenia. We evaluated the efficacy of these indices by comparing their values between hypo productive thrombocytopenia and hyper destructive thrombocytopenia (ITP) (Gardner and Bessman, 1983).

The in vitro studies have showed that plasma auto antibodies from ITP patients not only are involved in platelet destruction, but may also contribute to the inhibition of platelet production by affecting megakaryocyte production and maturation (McMillan *et al*., 2004; Chang *et al*., 2003). Despite hyper destructive thrombocytopenia which is characterized by higher MPV, these chronic patients may have normal or even suppressed platelet production rate. This show the platelet indices, particularly, MPV and P-LCR could have a better discriminating or prediction capacity for ITP where they are needed the most, during the early investigation and diagnosis of thrombocytopenic patients. Size of the thrombocytes has been studied by Garg et al., 1971, who demonstrated that the megathrombocyte percentage in peripheral blood smear correlates with the number of megakaryocytes in the bone marrow smears and thus with a state of platelet hyper production.

Vukelja *et al*., 1993 found MPV to be a good indicator of bone marrow production state. Consistent with their findings the present study showed significantly higher MPV in ITP patients i.e hyper destructive etiology group when compared with the values obtained for the hypo productive group. And thus could clearly differentiate the two important groups causing thrombocytopenia. However, little is known about other platelet indices i.e PDW and P-LCR and thrombocytopenia, and whether these indices are satisfactory laboratory tests for thrombocytopenia has not fully been discussed. In our evaluation, not only MPV, but also PDW and P-LCR were significantly higher in ITP than in the hypo productive group. Therefore, these indices were effective in distinguishing these two types of thrombocytopenia.

The platelet indices, if reported, provide a lot of clinical information about the underlying conditions of thrombocytopenia. Whether platelet indices are useful in other conditions that cause thrombocytopenia except ITP and hypo productive patients remains unknown. More attention should be paid to these indices for the diagnosis of thrombocytopenia.

CONCLUSION

Platelet volume indices, if reported, provide a lot of clinical information about the underlying conditions of thrombocytopenia and have potential for clinical utility as supported by compelling evidence in certain clinical scenarios, especially in haematology and vascular medicine. The platelet indices can discriminate ITP from hypo productive thrombocytopenia and they may help in avoiding or delaying the ITP patients from undergoing unnecessary, invasive bone marrow aspiration or prevent undesirable platelet transfusion. Further studies in broader patient groups could enable us to use these cost effective newer parameters to offer better patient management.

Conflicts of interest: There are no conflicts of interest.

Source of funding: Nil.

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