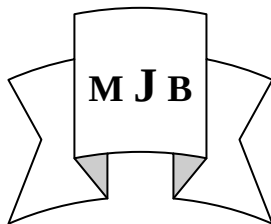


## Mean Platelet Volume, Platelet Distribution Width and Plateletcrit Values in Differentiating Clonal from Secondary Thrombocytosis

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### Abstract

**Objective:** To assess whether platelet indices [platelet count, mean platelet volume (MPV), platelet distribution width (PDW)) and plateletcrit (PCT) could serve as diagnostic tools to differentiate between primary and secondary thrombocytosis.

### Subjects and Methods:

A total of 83 Iraqi patients with thrombocytosis attending the Iraqi centre for cancer research & medical genetics and the National Iraqi Centre for Blood Diseases were included in this prospective case series study. A group of 20 healthy persons were included as a control. Complete blood count was done using Mindwayhaematologicautoanalyser.

**Results:** Mean platelet volume, platelet distribution width & plateletcrit in primary thrombocytosis were significantly higher than in secondary thrombocytosis. In primary thrombocytosis group platelet count inversely correlate with both Hb & MCV, while in secondary thrombocytosis platelet count inversely correlates with MCV only but less significantly than the correlation found in primary thrombocytosis.

**Conclusions:** MPV, PDW and PCT can be used as helpful parameters in the differential diagnosis of thrombocytosis.

### الخلاصة

**أهداف البحث:** تم إجراء هذه الدراسة لمعرفة فيما إذا كانت مؤشرات تقييم الصفائح الدموية: الطيف التوزيعي للاقراص، معدل حجم الاقراص والبليتكريت يمكن أن تكون بمثابة أدوات التشخيص للتمييز بين زيادة (فرط) الاقراص الأولية نتيجة اعتلال نخاع أولي وزيادة الاقراص نتيجة اسباب ثانوية.

**طريقة البحث:** شملت هذه الدراسة المستقبلية ٨٣ مريضاً مصابين بفرط (زيادة) الاقراص الدموية من مراجعي المركز الوطني لأمراض الدم والمركز العراقي لبحوث السرطان والوراثة الطبية، وتم إجراء الفحوصات المتعلقة بالاقراص الدموية باستخدام الجهاز الالكتروني نوع (مندوي). شملت الدراسة ٢٠ شخصاً طبيعياً لديهم عدد طبيعي من الاقراص الدموية للمقارنة.

**النتائج:** وجد أن هناك اختلاف واضح ذو أهمية في المؤشرات المتعلقة بالاقراص الدموية بين المرضى المصابين بزيادة الاقراص نتيجة اعتلال نخاعي أولي وزيادة الاقراص نتيجة اسباب ثانوية. ان الطيف التوزيعي للاقراص الدموية، معدل حجم الاقراص والبليتكريت تكون لدى المرضى المصابين بزيادة الاقراص الدموية نتيجة اعتلال أولي نخاعي أكبر من أقرانهم ذوي زيادة الاقراص الموية لاسباب ثانوية.

**الاستنتاج:** ان المؤشرات المتعلقة بالاقراص الدموية يمكن ان تعتبر مؤشراً ذو أهمية للتشخيص التفريقي في حالات زيادة الاقراص الدموية بنوعيه.

## **Introduction**

**T**hrombocytosis is an increased platelets count[1] which is usually discovered as an incidental laboratory abnormality when the complete blood count is obtained for some unrelated reason. When found, however, it creates an important diagnostic challenge [2].

Generally thrombocytosis is either a reactive process (secondary thrombocytosis), which occurs secondary to a variety of acute and chronic clinical conditions including: acute infection or inflammation, response to exercise, acute blood loss, iron deficiency, postsplenectomy, malignancy, chronic inflammatory and infectious diseases ,response to drugs like vincristine and epinephrine and haemolyticanaemia or it is autonomous caused by a clonal bone marrow disorders including essential thrombocythemia and other myeloproliferative disorders.[2,3]

Differentiating clonal from secondary causes of thrombocytosis can be extremely difficult, yet the distinction has important therapeutic implications. Secondary thrombocytosis per se does not result in vascular or hemostatic problems, but its underlying cause must be identified and treated, if possible. In contrast, clonal thrombocytosis (essential thrombocythemia and the other, related chronic myeloproliferative disorders) is associated with thrombotic and bleeding complications.[2]

Automated hematological analyzers have contributed to precise and fast results. They also make it possible to measure several blood cell parameters automatically. Among the parameters provided, platelet indices are probably the most ignored by clinical laboratories due to the difficulty of standardization, as well as being affected by a range of methodological problems.[4]

The platelet parameters that have been investigated in our study include:

Mean platelet volume (MPV):mean platelet volume (MPV) is a measurement that describes the average size of platelet cells in the blood.[5]

The platelet distribution width (PDW): is a measure of platelet anisocytosis.[6]

The plateletcrit : is the product of the MPV and platelet count and, by analogy with the haematocrit, maybe seen as indicative of the volume of circulating platelets in a unit volume of blood.[6]

## **Aim of the Study**

is to investigate whether platelet indices [platelet count, mean platelet volume (MPV), platelet distribution width (PDW)) and plateletcrit(PCT)] could serve as diagnostic tools to differentiate between primary and secondary thrombocytosis.

## **Subjects and Methods**

A total of 83Iraqi patients (38 males and 45 females) with thrombocytosis, platelets count more than  $400 \times 10^9/l$  attending the Iraqi centre for cancer research & medical genetics and the National Iraqi Centre for Blood Diseases were included in this prospective case series study,their age range was(20-63 yr) .A group of 20 healthy person (age & sex matched) were included as a control .

These patients were subjected to the followings:

1. Complete blood count using mind way haematologic auto analyser.
2. Peripheral blood film .
3. Bone marrow aspirate  $\pm$ bone marrow trephine biopsy when indicated.

Computerized statistical analysis was performed using SPSS (statistical package of social sciences), version 17. The statistical significance of difference was assessed using

independent t test & correlation study. P value less than 0.05 was considered indicative of statistically significant difference.

### **Results**

According to aetiology ,Patients were divided into two main groups:

Group (1) : 12 patients with primary thrombocytosis representing 14.5% of total patients.

Group (2): 71 patients with secondary thrombocytosis representing 85.5% of total patients.

**Table 1** classification of patients according to the cause of thrombocytosis.

| Group ( 1 )                    | No. of cases | Group ( 2 )                                | No. of cases |
|--------------------------------|--------------|--------------------------------------------|--------------|
| <b>Primary thrombocytosis:</b> | 12           | <b>Secondary(reactive) thrombocytosis:</b> | 71           |
| 1-Essential thrombocythemia.   | 2            | 1-iron deficiency anaemia.                 | 24           |
| 2-polycythemia vera.           | 4            | 2-infection .                              | 19           |
| 3-chronic myeloid leukemia.    | 6            | 3-non hematological neoplasm.              | 16           |
|                                |              | 4-haemolysis                               | 7            |
|                                |              | 5-postoperative                            | 4            |
|                                |              | 6- collagen diseases                       | 1            |

Patients with reactive thrombocytosis (85.5%) represent the higher percentage of patients with thrombocytosis, while cases with primary thrombocytosis contribute to 14.5% of total patients.

Mean platelet volume, platelet distribution width & plateletcrit in primary thrombocytosis were significantly higher than in secondary thrombocytosis , p value less than 0.05, as summarized in table (2)

**Table 2** Mean values of different platelet indices & P-value in primary & secondary thrombocytosis.

| Parameters                                  | Primary thrombocytosis                | Secondary thrombocytosis             | P value |
|---------------------------------------------|---------------------------------------|--------------------------------------|---------|
| Platelet count $\times 10^9/L$              | 691.92 $\pm$ 270.53<br>(409.0-1260.0) | 526.97 $\pm$ 108.28<br>(402.0-953.0) | 0.001   |
| Mean platelet volume (femtoliter) MPV       | 11.05 $\pm$ 2.74<br>(8.2-15.5)        | 9.28 $\pm$ 1.14<br>(7.6-15.4)        | 0.001   |
| Platelet distribution width PDW(femtoliter) | 14.81 $\pm$ 0.37<br>(14.2-15.6)       | 13.73 $\pm$ 1.14<br>(11.1-15.3)      | 0.002   |
| Plateletcrit% PCT                           | 1.29 $\pm$ 2.66<br>(0.02-9.7)         | 0.47 $\pm$ 0.09<br>(0.28-0.68)       | 0.009   |

Data were presented as Mean  $\pm$  SD (Range).

MPV correlates significantly with both platelet count & PCT (P-value < 0.05,  $r = 0.848$  and  $0.415$  respectively) in primary thrombocytosis. The same correlations are also found in secondary thrombocytosis, (P-value < 0.05,  $r = 0.298$ ,  $0.415$  respectively). In primary thrombocytosis group platelet count inversely correlate with

both Hb and MCV, while in secondary thrombocytosis although no correlation was found between platelet count & Hb, platelet count inversely correlates with MCV but less significantly than the correlation found in primary thrombocytosis, as summarized in table 3 and 4.

**Table 3** The correlation of platelets count with Hb & MCV in primary thrombocytosis.

| Platelet count | Hb     | MCV    |
|----------------|--------|--------|
| r              | 0.629- | 0.873- |
| p              | 0.092  | 0.000  |

**Table 4** The correlation of platelets count with Hb & MCV in secondary thrombocytosis.

| Platelet count | Hb     | MCV    |
|----------------|--------|--------|
| r              | 0.195- | 0.262- |
| p              | 0.104  | 0.027  |

### Discussion

As multiple causes may be involved in thrombocytosis, differential diagnosis is not always obvious.. Moreover, the available means to differentiate primary from secondary causes are not

specific enough. Some authors tried to distinguish thrombocytosis in primary thrombocytosis from reactive thrombocytosis by using platelet parameters provided by blood analyzers[7]. The present study was

designed in an attempt to characterize the different thrombocytosis states by platelet parameters (MPV, PDW, PCT). The finding of thrombocytosis in the majority (85.5%) of cases studied was in the context of secondary (reactive) thrombocytosis with iron deficiency anaemia & infection representing the most common causes. Similar results were obtained by Mata et al [8]. By far the most common cause of thrombocytosis in general medical populations is a reactive, or secondary, process. The degree of elevation in the platelet count does not clearly differentiate clonal from reactive thrombocytosis [2].

Mean platelet count was significantly higher in primary than in secondary thrombocytosis, similar results were obtained by Selami Kocak et al. [9]

We observed that MPV was significantly higher in primary thrombocytosis than in reactive thrombocytosis. Similar results were reported by Osselaer et al [7]. This significant increase in MPV may contribute at least partly to the increase in thrombotic complication seen in primary thrombocytosis as larger platelets are enzymatically and metabolically more active and have a higher potential thrombotic ability as compared with smaller platelets. [10]

Primary thrombocytosis group show significantly higher level of PDW than secondary thrombocytosis; In primary thrombocytosis, the blood film shows a thrombocytosis with varying degrees of platelet anisocytosis. Platelet morphology can vary from those of normal size and granulation to larger atypical forms. [11]

As MPV correlates significantly with both platelet count and PCT in primary as well as secondary thrombocytosis groups, we cannot depend on this relation to differentiate between primary and secondary thrombocytosis. The MPV is generally

increased in the myeloproliferative disease [12]. However, there is a nonlinear inverse relationship between the MPV and the PLT count within normal individual [13].

In primary thrombocytosis group, platelets count also shows an inverse correlation with Hb and MCV. In a study by Abdulkarim et al. from Sweden, it was found that the only independent parameter affecting survival was lower Hb, also a higher transformation risk into acute myeloid leukemia was associated with a lower Hb level [14].

### **Conclusions**

MPV, PDW and PCT can be used as helpful parameters in the differential diagnosis of thrombocytosis, so more attention should be directed towards these parameters and their role in the differential diagnosis of thrombocytosis.

### **References**

1. Bain JB, Gupta R, editors. A-Z Hematology. Oxford: Blackwell; 2003.
2. Schafer AI, Thrombocytosis. N Engl J Med. 2004 March 18; 350:1211-1219
3. Griesshammer M, Bangerter M, Sauer T, et al: Aetiology and clinical significance of thrombocytosis: analysis of 732 patients with an elevated platelet count. J Intern Med 245:295, 1999.
4. Farias MG, Schunck EG, et al. Definition of reference ranges for the platelet distribution width (PDW): a local need. Clin Chem Lab Med. 2010 Feb; 48 (2):255-7.
5. Martin C. What is mean platelet volume?. Conjecture corporation; 2003-2012. Available from: <https://twitter.com/wiseGEEK>.
6. Briggs C, Bain BJ. Basic haematological techniques. In: Bain BJ, Bates I, Laffan MA, Lewis SM, editors. Dacie and Lewis Practica

- Haematology. 11<sup>th</sup> ed. Churchill Livingstone 2011.p.30-51.
- 7.. Osselaer JC, Jamart J, ScheiffJM. Platelet distribution width for differential diagnosis of thrombocytosis. Clinical Chemistry. 1997; 43(6): 1072–1076
  8. Mata Fernández C, Pérez-Miranda Castillo J, GalarónGarcía P, Cela de Julián E, Beléndez Bieler C. Thrombocytosis in the oncology-haematologyclinic: description, aetioloical diagnosisand progression thrombocytosis. AnPediatr (Barc). 2008 Jul;69(1):10-4.
  - 9.Toprak KS, Erismis B, Karakus S, Kursun N Haberal A, Ulusoy MG. DoesThrombocyte Size Give Us an Idea about Thrombocytosis Etiology. The ScientificWorld Journal .2012 Sep 10.
  - 10.Ranjith MP, Divya R, Mehta VK, Krishnan MG, KamalRaj R, Kavishwar A. Significance of platelet volume indices and platelet count in ischaemic heart disease. J Clin Pathol.2009 Sep;62(9):830-3.
  11. Harrison CN, Bareford D, Butt N, Campbell P, Conneally E, Drummond M,et al . Guideline for investigation and management of adults and children presenting with a thrombocytosis.Br J Haematol.2010 Mar 15; 149(3):352-75.
  12. Miller JL. Blood platelets.In: JB Henry, editors. Clinical Diagnosis and Management by Laboratory Methods. 20th ed. Philadelphia, USA: Saunders, 2001. p 632–641,
  13. Graham SS, Traub B, Mink IB.Automatedplateletsizing parameters on a normalpopulation. American Journal of Clinical Pathology.1987 ; 87( 3) 365–369.
  14. Abdulkarim K, Ridell B ,Johansson P, Kutti J, Safai-Kutti S, Andr´easson B. The impact of peripheral blood values and bone marrow findings on prognosis for patients with essential thrombocythemia and polycythemia vera. European Journal of Haematology. 2011 ; 86 (2 ): 148–155.