Original paper

Platelet indices and their relations to platelet count in hypo-productive and hyper-destructive Thrombocytopenia

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Abstract

Background: Thrombocytopenia is low platelets count which is either due to defective platelet production (hypo-productive thrombocytopenia) or due to increased platelet breakdown (hyper-destructive thrombocytopenia). Measurement of platelet counts alone do not explain the underlying patho-mechanism of thrombocytopenia.. Recent advances in automated blood cell analyzers facilitate the measurement of several blood cell parameters automatically such as, platelet indices including mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) and these parameters could provide some important clinical information.

Aim of the study: to investigate whether platelet indices(MPV,PDW,PCT) could serve as diagnostic tools in the differential diagnosis of thrombocytopenia and, if there is any correlation between platelet count and platelets indices .

Subjects and Methods: A total of 77 Iraqi patients (28 males and 49 females) with thrombocytopenia were subjected to the following tests:
1. Complete blood count using Mindway haematologic autoanalyser.
2. Peripheral blood film .
3. Bone marrow aspirate with bone marrow trephine biopsy when indicated.

A group of 50 healthy person (age & sex matched) were included as a control

Results: hyper-destructive thrombocytopenia (immune thrombocytopenia) representing 12.9% of total patients, while hypo-productive thrombocytopenia due to various causes representing 87.1% of total patients. The MPV, PDW are significantly higher in immune thrombocytopenia group as compared with thrombocytopenia of hypo-productive patho-mechanism and there were no correlations between platelets count and both MPV and PDW in hyper-destructive and hypo-productive thrombocytopenia but there was a direct correlation between platelet count and PCT .

Conclusion: Platelet indices provide plenty of clinical information about the causes and patho-mechanism of thrombocytopenia and could be helpful tests to distinguish hyper-destructive thrombocytopenia from hypo-productive thrombocytopenia easily, so more interest for the use of these indices in differential diagnosis of thrombocytopenia is required.

Key words: platelet indices, platelet count, thrombocytopenia.

Introduction

Thrombocytopenia is one of the most frequent causes for hematologic consultation in the practice of medicine, and potentially one of the most life-threatening conditions. The normal platelet count in humans (150–400 x 10^9/L) is higher than the minimal level required to avoid hemorrhage

which is less than 50 x 10^9/L[1] , and as long as platelet counts are above 20 x 10^9/L, clinical manifestations are mild and often limited to easy bruising. Below 10 x 10^9/L, the risk of spontaneous mucocutaneous bleeding and life threatening, spontaneous intracranial hemorrhage or gastrointestinal bleeding increases rapidly. [2]

Thrombocytopenia can arise as a result of multiple conditions. These can be divided into four mechanism-related categories that are: a reduction in platelet production (hypo-productive thrombocytopenia), increased platelet consumption/destruction (hyperdestructive), abnormal platelet distribution and dilutional loss.

hypo-productive thrombocytopenia is either specific megakaryocyte suppression as in congenital mutation of c-MPL thrombopoetin receptor, may–Hegglin syndrome, Wiscott–Aldrich syndrome and drugs, chemicals and viral infections, or generalized bone marrow failures in haematological malignancy(leukaemia, aplastic anaemia, myeloma, myelodysplasia, myelofibrosis), secondary to cytotoxic drugs and radiotherapy, infections (human immunodeficiency virus (HIV), cytomegalovirus (CMV), hepatitis B and C), alcohol excess. and megaloblastic anemia.

Hyper-destructive Thrombocytopenia is either Immune as in idiopathic/primary autoimmune (ITP), Secondary (systemic lupus erythematosus, chronic lymphocytic leukaemia, lymphoma), Infections (HIV, hepatitis B and C, malaria), Drug induced (rifampicin, penicillins, sulphonamides, Heparin, quinine), Post-transfusion pupura and Disseminated intravaccular haemolysis (DIC)

Abnormal distribution of platelets occur in Splenomegaly and Dilutional thrombocytopenia in Massive blood transfusion [1,3, 4.]

Identification of the underlying cause of thrombocytopenia is necessary to decide appropriate treatment so it is important to differentiate between hypo-productive and hyper-destructive thrombocytopenia. [4]

For the diagnosis of thrombocytopenia, platelet counts alone do not explain the underlying patho-mechanism, and which is more dominant, hypo-productive ytopenia or hyper-destructive thrombocytopenia. For this purpose bone marrow study provides information about platelet production and the number of megakaryocytes, this invasive test, is necessary for some conditions like aplastic anemia (AA), but there is no agreement regarding its necessity for immune thrombo-cytopenia (ITP) as the first-line diagnostic procedure. [5]

platelet associated immunoglobulin PAIgG is another test that identifies the presence of anti-platelet antibodies that cause platelet destruction which is often increased in ITP, but it is not specific to ITP because high PAIgG level is also found in many other diseases [6], so it is not recommended as a diagnostic test in recent guidelines. [7] Recent advances in automated blood cell analyzers facilitate the measurement of several blood cell parameters automatically and provide more knowledge on platelet size and volume, and could enable the distinction of hypo-productive thrombocytopenia from hyper-destructive thrombocytopenia.[8], among these parameters, the platelet indices, which are mean platelet volume (MPV), platelet size deviation width (PDW) and plateletcrit (PCT) ,so far these indices are not used routinely for clinical diagnosis, but if these indices are informative regarding platelet kinetics, they could be useful laboratory tests for the diagnosis of thrombocytopenia. [9]

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

Mean platelet volume (MPV) which is a machine calculated measurement that describes the average size of platelet cells in the blood, it provides an indicator whether the bone marrow is manufacturing platelets normally. A high MPV is associated with increased platelets production , and a low MPV indicates decreased production.[10,11]

Normal MPV ranges are approximately 6.8 - 10.4 fL .MPV is calculated by dividing plateletcrit by the platelet count multiplied by 10 (MPV= plateletcrit/ platelet count ×10) [12]

The platelet distribution width (PDW): is a measure of platelet anisocytosis.[13] and can indicate if thrombocytes are normally distributed or if there is technical error and if the measured cells are thrombocytes [12] Standard PDW ranges from 9 to 14 fL [14] The plateletcrit : is the product of the MPV and platelet count and, by analogy with the haematocrit, may be seen as indicative of the volume of circulating platelets in a unit volume of blood.[13] normal range of PCT is 0.15 - 0.32 % and can be calculated by multiplying PDW by platelet count (Thrombocytocrit (Tct) = PDW x platelet count) [12]

Aim of the study

To evaluate platelet indices [platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT)] in hypo-productive and hyper-destructive Thrombocyto-penia, and investigate whether these could serve as diagnostic tools in the differential diagnosis of thrombocytopenia and if there is any correlation between platelet count and platelets indices.

Subjects and Methods

Patients: During the year 2012, a total of 77 Iraqi patients (28 males & 49 females) with thrombocytopenia (platelets count less than $100_{×}10^{9}$/L) attending the Iraqi centre for cancer research and medical genetics and the Iraqi National Centre of hematology (NCH) were included in this study, their ages were ranged from 15 to 60 years .

Control group: fifty healthy medication free volunteers matched for age & sex .
The patients were subjected to the following tests:

1. Complete blood count using Mindway haematologic autoanalyser.
2. Peripheral blood film.
3. Bone marrow aspirate and 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 etiology & patho-mechanism of thrombocytopenia, the Patients were divided into two main groups:

Group (I) : Ten patients (representing 12.9% of total patients) with immune thrombocytopenia (hyper destructive).

Group (II): sixty seven patients (representing 87.1% of total patients) with thrombocytopenia caused by decreased production of platelets due to various causes as described in table (1) .

The Mean platelet volume (MPV) in control group was ranged from 8.20 to 10.70 (9.25 ± 0.62) fl, platelet distribution width (PDW) was 11.10 to 14.30 (12.69 ±1.09) fl and Plateletcrit

was ranged from 0.16 to 0.37 (0.24± 0.05) all these values were comparable to the normal values mentioned in other series. [12.13,14] One research revealed that the size of platelets may differ in healthy people from different parts of the world and individuals of Mediterranean descent have a higher than average platelet size. [11]

Table 1. Classification of patients according to the patho-mechanism of thrombocytopenia

Group (I)	No. of cases	Group (II)	No. of cases
Hyper-destruction of platelets	10	Hypo-production of platelets	67
Immune thrombocytopenia purpura	10	1-chemotherapy for haematological malignancy	24
		2.Acute leukaemia	21
		3.Chemotherapy for non-haematological malignancy	12
		4. Aplastic anaemia .	3
		5-non hematological neoplasm	3
		6.Myelodysplastic syndrome	2
		7.lymphoma	2

The values of Mean platelet volume (MPV), platelet distribution width (PDW) were significantly higher in immune thrombocytopenia group as compared with thrombocytopenia of hypo-productive patho-mechanism as described in table (2).

Table 2. Mean values of different platelet indices and P-value in Hyper- destruction Immune thrombocytopenia and hypo- production thrombocytopenia.

Parameters	Hyper-destruction Immune thrombocytopenia (Group I)	Hypo- production (Group II)	P value
Platelet count ×10 ^{9}/L	39.30 ± 15.34	64.23 ±34.68	0.053
Mean platelet volume (fimtoliter)	12.33 ± 0.46	10.08 ± 1.81	0.000
Platelet distribution width (fimtoliter)	15.61 ± 0.73	13.83 ± 1.75	0.002
Plateletcrit%	0.06 ± 0.03	0.06± 0.03	0. 97
Hb (gm/dl)	11.3 ± 2.23	9.23± 2.13	0.006
PCV (Htc) %	35.84± 6.77	29.43±7.20	0.010
RBCs (cell/dl)	4.42 ± 0.75	3.35 ± 0.87	0.000
MCV (fimtoliter)	82.19 ± 6.30	88.71 ±10.13	0.052
MCH(pictogram)	26.13 ± 3.17	28.02 ±4.44	0.199
MCHC %	316.80 ±19.71	319.30 ± 49.17	0.874
RDW (SD)	39.877± 4.20	50.98 ±16.01	0.43

Data were presented as Mean ± SD (Range).

there were no correlations between platelets count and both MPV and PDW in hyper-destructive and hypo-productive thrombocytopenia but there was a direct correlation between platelet count and PCT as shown in table 3.

Discussion

It is important to differentiate between thrombocytopenia caused by

hypo-production of platelets from that caused by hyper-destruction or to know which is more dominant. [15]
measurement of the platelet indices by using automated hematological analyzer is simple , inexpensive ,quick test and obviate examiner bias[16,17],also avoid changes in

platelets diameter that occur due to enhanced adhesiveness with flattening and increasing size of the platelets on the glass slide during blood smears and the changes that result from delayed time between venipuncture and preparation of smears.[18]

Table 3. Correlation of platelets count with platelets indices (MPV,PDW and PCT) in hyper-destructive (ITP) , hypo-productive thrombocytopenia and all thrombocytopenia cases

Correlation of platelets count with platelets indices	MPV		PDW		PCT	
	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)	Pearson Correlation	Sig. (2-tailed)
In hyper-destructive (ITP)	.164	.651	.297	.405	.817[**]	.004
In hypo-productive	-.101-	.416	.218	.076	.787[**]	.000
In all	-.196-	.088	.106	.357	.742[**]	.000

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

However it is not always possible to measure platelet indices such as in severe thrombocytopenia, and in red cell fragmentation because a platelet histogram cannot be appropriately drawn, and the platelets indices cannot be measured. In this study such obstacles did not occurred and the results of platelet indices revealed that the MPV was significantly higher in hyper-destruction (ITP) than hypo-productive thrombocytopenia (p–value = 0.000), a higher MPV in hyper-destructive thrombocytopenia was reported in different series [18,19 ,20]

Many workers have reported that platelet volume is increased in ITP who have very strikingly elevated MPVs. The finding of some subjects with acute ITP who have low MPVs are reported in one study by Tomita E et al . [21]and there were no significant differences in MPV   and   PDW between ITP patients and non-ITP according to Nakadate H et al and Baynes RD et al study [22,23]

The high MPV in ITP could be explained by the fact that newly produced platelets are larger than circulating platelets, which tend to decrease in size with age in the circulation over the 7-10 day platelet

lifespan. As a result, in patients with thrombocytopenia secondary to peripheral destruction the MPV is increased, reflecting active bone marrow compensation with release of young platelets "left shifted"[24 ,25,26]

Also a significantly higher PDW in hyper-destructive thrombocytopenia was reported in this study (P value =0.002). again the increased bone marrow production of platelets is associated with heterogenic population of platelet (platelet anisocytosis) A similar results were reported in other studies [27,28]

Both MPV and PDW are reliable tests for a positive diagnosis of ITP and considered as tests of 100% sensitivity and specificity for the diagnosis of ITP [9,27,28,29]

PCT was not significantly different in both groups similarly no study consider it as a valuable indices to differentiate between hypo-productive and hyper-destructive thrombocyte-penia , PCT represent a volume percent of platelets and its value is a result of PDW multiplied by platelet count so it is affected by the severity of thrombocytopenia of any cause. [11]

There were no correlations between platelets count and both MPV and

PDW in hyper-destructive and hypo-productive thrombocytopenia but a direct correlation between platelet count and PCT was reported .while according to Baynes RD et al study there was an inverse relationship between MPV and platelet count in subjects with ITP and preserved volume-number relationship in non ITP cases. [23]

In conclusion platelet indices is useful method to distinguish hyper-destructive thrombocytopenia from hypo-productive thrombocytopenia and provide clinical data about the causes and patho- mechanism of thrombocytopenia. More attention and interest to use these indices for the differential diagnosis of thrombocytopenia.

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