ORIGINAL ARTICLE

COMPARISON OF PLATELET INDICES IN HYPOPRODUCTIVE AND HYPERDESTRUCTIVE THROMBOCYTOPENIA

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Background: Thrombocytopenia is one of the most common haematological disorders and is also a life-threatening condition. The two types of thrombocytopenia, hypoproductive and hyperdestructive can best be distinguished by bone marrow examination; but it is an invasive, time-consuming and expensive process. The aim of this study was to determine the role of platelets indices in distinguishing between the two types which is a cost-effective and non-invasive modality of investigations. **Methods:** It was a cross-sectional study, conducted in the Pathology Laboratory, Rehman Medical Institute, Peshawar, conducted from 1st July 2019 to 30th June 2020. Non-probability convenience sampling technique was used. Sample size was calculated using WHO formula, and a total of 74 thrombocytopenic patients referred for bone marrow aspirate and trephine biopsy were included in the study. Clinical record, complete blood count (CBC) and bone marrow trephine biopsy were obtained and computed. **Results:** Mean Platelet Volume was 10.57±1.33 fl in hypoproductive group and 11.637±1.98 fl in hyperdestructive group. The difference between the groups was statistically significant (p=0.017). Platelet Distribution Width was 12.68±3.16 fl in hypoproductive group and 14.811±3.61 fl in hyperdestructive group (p=0.014). Platelet Large Cell Ratio was 30.81±9.23% in hypoproductive group and 36.993±10.25% in hyperdestructive group (p=0.010). **Conclusion:** Platelet indices can be used as a reliable tool for distinguishing between hypoproductive and hyperdestructive thrombocytopenia.

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

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INTRODUCTION

Platelets, also called thrombocytes are derived from megakaryocytes in the bone marrow. In circulation, their main function is to stop bleeding by forming primary platelet plug at the site of vessel injury.[1] The normal platelet count is 150,000 to 450,000 per µL of blood. In a healthy person, platelets live for about 10 days in circulation.[2] Platelet count of less than 150,000 is considered as thrombocytopenia.[2,3] The MPV ranges from 6.8–10.4 fL, PDW ranges from 9–14 fL and PLCR ranges between 15 and 35% in normal individuals.[4]

Thrombocytopenia is one of the most common haematological disorders and can become life-threatening in case of severe disease. The various mechanisms involved in thrombocytopenia are decreased platelet production (hypoproductive thrombocytopenia) or increased platelet breakdown (hyperdestructive thrombocytopenia).[4] The causes of hypoproductive thrombocytopenia are drugs, chemicals, radiotherapy, leukaemia, lymphoma, chemotherapeutic agents, aplastic anaemia, infections like HIV and megaloblastic anaemia. The causes for hyperdestructive thrombocytopenia are either idiopathic also known as immune thrombocytopenic purpura, secondary to systemic lupus erythematous, infections (HIV, hepatitis, malaria), drug induced, e.g., heparin, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura and enlarged spleen.[5] For proper management of patients, it is important to know whether thrombocytopenia is due to decreased production or increased breakdown of platelets. For differentiating between them, bone marrow examination is gold standard but it is an invasive, expensive and time consuming procedure.[4]

Due to recent advances in automated blood cell analysers, it is possible to measure various parameters. These include platelet indices like platelet distribution width (PDW), mean platelet volume (MPV) and platelet large cell ratio (PLCR).[6]

A study conducted in India showed that Platelet distribution width (PDW) is higher in hyperdestructive thrombocytopenia with a mean value of 16.07±0.17, while in hypoproductive thrombocytopenia its value was low with a mean PDW 12.15±0.25.[4] Another study in Iraq also showed that platelet distribution width and mean platelet volume were higher in hyperdestructive thrombocytopenia and vice versa in hypoproductive cases. Mean value of PDW in patients with hyperdestruction was 15.61±0.73 while in hypoproduction it was 13.83±1.75 and mean value of MPV was 12.33±0.46 and 10.08±1.81 respectively.[7] These platelet indices provide some

important information but are not accepted for routine clinical use. If these indices are really informative regarding platelet kinetics, they might become very useful laboratory measures for thrombocytopenia.[8] Thus, by using a cost-effective, non-invasive, non-ionizing modality of investigation, thrombocytopenic purpura can be detected at earlier stage.

The objective of this study was to compare the platelet indices (PDW, MPV, PLCR) in hypoproductive and hyperdestructive thrombo-cytopenia and to determine the role of platelet indices for differentiating hypoproductive from hyperdestructive thrombocytopenia.

MATERIAL AND METHODS

It was a cross-sectional, analytical study, conducted in the Pathology Laboratory, Rehman Medical Institute (RMI), Peshawar, from 1st July 2019 to 30th June 2020. The study was approved from RMI Ethical and Research Board. A total of 74 thrombocytopenic patients were included. The sample size was calculated using WHO formula with prevalence of thrombocytopenia taken as 2.3% in Pakistan[9] and margin of error kept at 3.5%. Non-probability convenience sampling technique was used. Patients of all age groups and both genders visiting the RMI Laboratory for bone marrow biopsy for haematological diseases, and with platelet counts less than 100×10^9/L, confirmed after peripheral blood film review were included in the study. Patients having artefacttual thrombocytopenia, pregnant women or those taking drugs like heparin, quinine, quinidine etc. were excluded from the study.

After informed consent, a detailed personal and medical history was taken and recorded on hospital notes. Bone marrow aspirate and trephine biopsy were done from posterior iliac crest. Bone marrow aspirate slides were stained with Giemsa stain. Bone marrow trephine biopsy was performed in standardized manner according to the protocol[3] and stained with Hematoxylin and Eosin.

A sample of 3 ml venous blood was drawn in EDTA vacutainer from all patients and complete blood count was performed by Haematology Analyser (Sysmex, XN-1000) to determine platelet count and platelet indices. Total leukocyte count (TLC) and haemoglobin (Hb) estimation was also done. A peripheral blood film was examined to estimate platelet count and to rule out pseudo-thrombocytopenia. Data were collected on a structured proforma which elicited information regarding patients' demographics, platelet indices and bone marrow findings.

The data was entered and analysed using SPSS-22. Mean and standard deviation were calculated for numerical variables and statistical comparison was performed using Student's *t*-test keeping $p\leq0.05$.

RESULTS

Out of 74 thrombocytopenic patients recruited in the study, 47 (63.51%) were grouped as hypoproductive and 27 (36.49%) were grouped as hyperdestructive thrombocytopenia patients on the basis of bone marrow examination. The mean age was 33.81±22.1 years. MPV was 10.57±1.33 fL in hypoproductive group and 11.637±1.98 fL in hyperdestructive group. The difference between the groups was statistically significant (p=0.017). PDW was 12.68±3.16 fL in hypoproductive group and 14.811±3.61 fL in hyperdestructive group (p=0.014). PLCR was 30.81±9.23% in hypoproductive group and 36.993±10.25% in hyperdestructive group (p=0.01) (Table-1).

Other compared blood parameters included TLC, Hb and Platelet count. Mean TLC was $47.94\pm100.35\times10^3$/µL in hypoproductive group and $7.38\pm4.73\times10^3$/µL in hyperdestructive group (p=0.040). Mean Hb was 8.52±2.35 gm/dL in hypoproductive group and 11.6±2.74 gm/dL in hyperdestructive group (p<0.001). The mean platelet count was $60.74\pm37.3\times10^3$/µL in hypoproductive group and $58.88\pm36.6\times10^3$/µL in hyperdestructive group, with insignificant statistical difference (Table-2). In hypoproductive thrombocytopenia patients the major cause was leukaemia followed by aplastic anaemia. All hyperdestructive thrombocytopenia patients showed normo-cellular bone marrow with increased megakaryopoiesis (Table-3).

Table-1: Platelet indices in hypoproductive and hyperdestructive thrombocytopenia

Parameter	Hypoproductive thrombocytopenia (n=47)	Hyperdestructive thrombocytopenia (n=27)	*p*
MPV (fL)	10.57±1.33	11.637±1.98	0.017
PDW (fL)	12.68±3.16	14.811±3.61	0.014
PLCR (%)	30.81±9.23	36.993±10.25	0.010

Table-2: Blood parameters in hypoproductive and hyperdestructive thrombocytopenia

Parameter	Hypoproductive thrombocytopenia (n=47)	Hyperdestructive thrombocytopenia (n=27)	*p*
TLC ($\times10^3$/µL)	47.94±100.35	7.38±4.73	0.040
Hb(gm/dL)	8.52±2.35	11.6±2.74	<0.001
Platelets ($\times10^3$/µL)	60.74±37.3	58.88±36.6	0.835

Table-3: Bone marrow findings of thrombocytopenia patients [n=74, n (%)]

Thrombocytopenia	Bone marrow findings	Frequency
Hypoproductive thrombocytopenia	ALL	17 (23)
	AML	15 (20)
	Multiple myeloma	4 (5.5)
	Aplastic anaemia	4 (5.5)
	CLL	4 (5.5)
	Megaloblastic anaemia	3 (4.5)
Hyperdestructive thrombocytopenia	Normo-cellular bone marrow with increased megakaryopoiesis	27 (36)

DISCUSSION

In the present study MPV was significantly higher in hyperdestructive thrombocytopenic patients than hypoproductive group. A study conducted by Khairkar *et al*[10] compared similar groups and concluded that MPV was significantly higher in hyperdestructive as compared to hypoproductive thrombocytopenia patients. Similar studies comparing MPV in these two groups also reported MPV to be significantly higher in hyperdestructive than hypoproductive thrombocytopenic patients.[4,11–17] The cause of this is that newly formed platelets are larger in size than the circulating platelets and with increase in age of the platelets, their size decreases. As there is an active production of platelets by the bone marrow in case of hyperdestructive thrombocytopenia, this leads to a higher MPV in these patients.[5,18] In spite of this fact certain researchers like Khanna *et al*, and Xu *et al*, found MPV to have low sensitivity and specificity to predict the bone marrow involvement in thrombocytopenia.[19,20] Vinholt *et al* reported that MPV along with other platelet indices can be helpful in distinguishing the type of thrombocytopenia.[21]

In the present study PDW was significantly higher in hyperdestructive thrombocytopenic patients compared to hypoproductive thrombocytopenic patients. The findings of the present study were consistent with other studies[11,13,17,22] but Elsewefy *et al*[2] reported this increase to be insignificant, the reason might be the use of different analyzer (Beckman Clouter) than ours.

In the present study, PLCR was significantly higher in hyperdestructive group as compared to hypoproductive thrombocytopenic patients. This is in accordance with similar studies reporting significant increase in PLCR in hyperdestructive thrombocytopenic patients.[2,11,12] Some researchers like Babu and Basu[23] and Borkataky *et al*[22] reported this increase to be insignificant between the two groups but still concluded that PLCR can be a good tool in differential diagnosis of patients with abnormal platelet count.

Another study in which platelet indices were studied along with platelet antibodies in thrombocytopenic patients, the platelet indices were reported to be significantly higher in hyperdestructive thrombocytopenic patients as compared to hypoproductive thrombocytopenic patients and it was endorsed that these indices may be considered as a reliable diagnostic tool for determining the type of thrombocytopenia.[24]

CONCLUSION

Platelet indices can be used as a reliable tool to distinguish between hypoproductive and hyperdestructive thrombocytopenia. This diagnostic tool can be beneficial for thrombocytopenia patients in terms of cost, time, and invasion. Further studies with larger sample size are recommended to validate the findings of this study.

LIMITATIONS OF THE STUDY

Sample technique was non-random convenience sampling so there can be a potential bias.

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