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ROLE OF MEAN PLATELET VOLUME (MPV), PLATLET DISTRIBUTION WIDTH (PDW) AND PLATELET LARGE CELL RATIO (PLCR) IN DIAGNOSIS OF HYPERDESTRUCTIVE THROMBOCYTOPENIA.

Hamzullah Khan[1], Adnan Masood[2], Fazle Bari[3], Naila Tabassum[4], Ameezullah[5]

1. MBBS, M.Phil Hematology
Associate Professor
Department of Hematology
Nowshera Medical College, Nowshera.
2. MBBS, MS
Assistant Professor
Department of Microbiology
Nowshera Medical College, Nowshera.
3. MBBS, M.Phil Microbiology
Professor
Department of Microbiology
Nowshera Medical College, Nowshera.
4. MBBS
Medical Officer
Department of Pathology
Nowshera Medical College, Nowshera.
5. Lab Technician
Department of Pathology
Nowshera Medical College, Nowshera.

Correspondence Address:
Dr. Hamzullah Khan
Department of Hematology
Nowshera Medical College, Nowshera.
hamzakmc@gmail.com

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ABSTRACT… Thrombocytopenia has been shown to have significant mortality if ignored. Platelet indices have been reported to be useful prognostic indicators. The objectives of this study was to determine the diagnostic importance of the platelet indices in diagnosis of hyperdestructive thrombocytopenia i.e ITP. **Study Design:** Cross sectional observational study. **Setting:** Department of Pathology (MTI) Qazi Hussain Ahmed Medical Comeplex Nowshera Medical College. **Period:** Aug 2017 to Jan 2018. **Materials and Methods:** These blood samples were analyzed in clinical Pathology laboratory of QHAMC. Required information's were recorded on predesigned proforrma as per objectives of the study. **Results:** The peripheral smears of 139 cases were reported in the study. Detailed history and Thorough clinical examination was conducted. Mean age of the study population of the patients with standard deviation was 30.90(±6.4) years. Mean platelet count was 27. 37(±12.8) x109/. Mean platelet volume MPV was 11.4(±1.4) fl. Mean platelet distribution width (PDW) was 15.4(±3.3) fl. Mean platelet large cell ratio (PLCR) was 39.6(±8.9) %. Eight cases with MPV lower than 11fl and cases with PDW more than 15fl that were also having pancytopenia or bycytopenic picture were advised bone marrow aspiration for further diagnosis if clinically indicated. Six cases out of eight to whom bone marrow was advised were sent for bone marrow examination by the clinicians and we found that three of them were idiopathic thrombocytopenia and one Megaloblastic anemia, one case with pancytopenia due to hyperspleenism and one with acute leukemia with eosinophilia. **Conclusion:** From the above we concluded that all cases with MPV>11fl and PDW>14fl are sensitive and specific indicators for ITP and These indices help to distinguish hyper-destructive thrombocytopenia and hypo-productive thrombocytopenia very easily and it is also cost effective on a very simple test that is special smear. We must look for platelet indices very keenly while reporting a case with bi-cytopenia and pancytopenia.

Key words: Immune Thrombocytopenic Purpura (ITP), Pancytopenia, Periphral Smear, Platelet Indices, Smear

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INTRODUCTION

Immune thrombocytopenic purpura (ITP) is an immune mediated disorder characterized by low platelet count (peripheral platelet count <100000/ cmm3) due to autoantibody binding to platelet antigen(s) causing their peripheral destruction predominantly in the spleen.[1] ITP has two distinct clinical syndromes, manifesting as an acute condition in children and a chronic condition in adults.[2] With advancements in the technologies, automated cell counters like hematology analyzers measurements for different blood cells are widely used for diagnosis of different hematological disorders. Among the Platelet counts, mean platelet volume (MPV) and platelet distribution width (PDW) are important parameters that helps to diagnose disorders related to platelet production and abnormal platelet peripheral destruction.[3,4] Platelet activation due to any cause leads to changes in platelet shape and size that results in platelet swelling leading to an increase in MPV and PDW.[5]

Mean Platelet Volume (MPV) can be used to make inferences about platelet production in the marrow or peripheral platelet destruction

problems including ITP. The PDW represents the heterogeneity/anisocytosis of thrombocyte volume like RDW for RBCs.[6] Mean platelet volume (MPV) is as mean corpuscular volume (MCV) in case of red blood cells. Determinations of platelet size by MPV nad its anisocytosis by PDW is clinically important in variety of clinical conditions most importantly ITP (increased MPV and PDW) and Aplastic anemia (decreased MPV and PDW).[7,8] Various studies have been reported to show that platelet indices like Mean Platelet Volume (MPV) and Platelet Large Cell ratio (PLCR) are sensitive, specific in diagnosis of ITP (hyper-destructive thrombocytopenia) from hypoproductive.[9,10]

Present study was therefore designed to evaluate the platelet indices for their diagnostic values in immune mediated thrombocytopenic purpura.

MATERIAL AND METHODS

Setting of Study
Department of Haematology, QHAMC Nowshera.

Duration of Study
From Aug 2017 to Jan 2018.

Design of Study
Prospective Observational study.

Study Sampling
Sampling was collected via convenient purposive type Non-Probability sampling. A total of 139 patient's blood smears done and enrolled as part of study. Inclusion criteria were all patients irrespective of age, or cause for attending the hematology lab, were included. Patients with platelet count below 100000/cu mm and with MPV>11fl and PDW>14fl were further suggested bone marrow examination to know the cause of thrombocytopenia. Exclusion criteria were all those patients with other causes of thrombocytopenia (like Systemic lupus erythmatosis, Rheumatoid arthritis, lymphoproliferative disorder and use of anti-platelet medications etc) were excluded. Similarly patients who were transfused with platelet within 7 days were also excluded.

Data Collection Procedures
Data collection procedure was determined by using pre-formed questionnaires.

Blood samples taken from all patients. 3ml of venous blood was collected by veine-puncture under aseptic techniques using disposable syringes. The blood was added to EDTA tubes and mixed gently. Then using Automated hematology analyzer (Sysmex 2000i, Japan) and peripheral smear reporting for low platelets on slide were recorded. Then platelet indices (platelet distribution width PDW, mean platelet volume MPV, and platelet large cell ratio) was recorded.

Bone marrow aspiration was done of six patients during this trial under aseptic condition. Site was properly covered only working area (PSIS) was visible and dressed with pyodine. Majority of the aspirated sampling collected from the posterior superior iliac spine. In pediatric cases specially in age less than ten years the bone marrow aspiration was done from anterior superior aspect of shin bone.

Initially local anesthesia was given at the site and skin and periosteum anesthetized. Then proper aspiration needles for specific age was used to aspirate the bone marrow. 10-12 slides were prepared and stained with Giemsa and iron (Persian blue) stain for proper study. Where any suspicion in cell morphology expected then peroxide (POX) stain was used to differentiate myeloid series pathology from lymphoid one. After collecting sampling the dressing pad applied to the site and thanked to patient.

All the slides were reported by the consultant Haematologist.

Data was entered in software SPSS (Statistical Package for Social Sciences) version 16 for further analysis.

RESULTS
The peripheral smears of 139 cases were reported in the study. Detailed history and thorough clinical examination was conducted. Mean age of the

study population of the patients with standard deviation was 30.90(±6.4) year. Median of the age was 30 years, Mode 30 years. The age range of the patients was from 8 to 75 years of age (Table-I).

Mean platelet count was 27. 37(±12.8) x109/. Mean platelet volume MPV was 11.4(±1.4) fl. Mean platelet distribution width (PDW) was 15.4(±3.3) fl. Mean platelet large cell ratio (PLCR) was 39.6(±8.9) %. (Table-II)

Eight cases with MPV lower than 11fl and cases with PDW more than 15fl that were also having pancytopenia or bycytopenic picture were advised bone marrow aspiration for further diagnosis if clinically indicated. (Table-III)

Six cases out of eight to whom bone marrow was advised were sent for bone marrow examination by the clinicians and we found that three of them were idiopathic thrombocytopenia and one Megaloblastic anemia, one case with pancytopenia due to hyperspleenism and one case with bicytopenia in age 8 years was acute leukemia with eosinophilia.

Total No of Patients= 139	Age
Mean	30.90
Median	30.00
Mode	30.00
Std. Deviation	6.34
Range	68.00
Minimum	8.00
Maximum	75.00

Table-I. Age and platelet statistics

Parameters	No. of Patients	Mean	Std. Deviation
Age	139	30.90	6.3
Weight	139	48.51	11.62
HB	139	11.20	1.8
TLC	139	9527.84	4.09
Platelet	139	273791.36	12.8
PLCR	139	39.60	8.95
PDW	139	15.41	3.3
MPV	139	11.40	1.4

Table-II. Different demographic and Research Variables statistics.

MPV	Count
10-11	8
12-13	45
14-15	23
16-17	20
18-19	25
20-21	12
22-23	6
Grand Total	139

Table-IIIa. MPV & PDW Statistics: MPV range

PDW	Count
8-12	10
12-16	115
16-18	14
Grand Total	139

Table-IIIb. PDW range

Bone Marrow Finding	Count
Immune Thrombocytopenic purpora	3
Megaloblastic Anemia	1
Pancytopenia due to hyperspleenism	1
Acute Leukemia with eosinophilia	1
Grand Total	6

Table-IV. Bone Marrow findings of the five cases.

DISCUSSION

Thrombocytopenia is diagnosed by bone marrow examination that is invasive and expensive one but Simple, inexpensive and non invasive tests like MPV on CBC have been noted to identify causes of thrombocytopenia as hyperdestructive (ITP) or hypoproductive (Aplastic) with remarkable sensitivity and specificity. In present study we studied two main platelet indices MPV, PDW and looked into for their diagnostic predictive capacity in different patients with thrombocytopenia. Many studies have been conducted to show that The MPV and PDW provide information about the underlying conditions of thrombocytopenia. These indices should be considered in the diagnosis of thrombocytopenia.[11-12] Thrombocytopenia is a VER common clinical disorder that has many causes, like decreased bone marrow production of megakaryocytes, increased spleen destruction, and peripheral platelets destruction due to antibodies.[13] One of the major causes of thrombocytopenia is increased platelet peripheral destruction as occur in immune thrombocytopenia, where auto-antibodies take

their places on platelet antigens, and results in premature destruction of platelets in particularly in spleen.[14] Other causes of thrombocytopenia that causes decreased platelet on CBC includes Decreased bone marrow production due to malignant hematological conditions, aplastic anemia, and drugs like chemotherapy. These are diagnosed by bone marrow and by visualization of abnormal malignant cells called blast in the bone marrow that are further confirmed on immunophenotyping, and karyotyping studies. That are too expensive and needs presences of hematologists.[15,16] But simple tests by hematology analyzer can differentiates these disorders and causes of thrombocytopenia (into decreased production like in malignancies and aplastic anemia) and increased destruction of platelet by auto antibodies like in ITP just by simple decease or increase in MPV and PDW respectively.[17,18]

In present study Mean platelet count was 27. 37(±12.8) x109/cmm^3. Mean platelet volume MPV was 11.4(±1.4) fl. Mean platelet distribution width (PDW) was 15.4(±3.3) fl. Mean platelet large cell ratio (PLCR) was 39.6(±8.9) %. Another study from India reported that MPV in hyperdestructive thrombocytopenia was more than (10.46 fl) when compared with hypoproductive thrombocytopenia due to many causes were equal or less than (8.7 fl) that showed statistically significant difference in comparison to control.[19]

Eight cases with MPV lower than 11fl and cases with PDW more than 15fl that were also having pancytopenia or bycytopenic picture underwent bone marrow aspiration and we noted that three of them were idiopathic thrombocytopenia and one Megaloblastic anemia, one case with pancytopenia due to hyperspleenism and one case with bicytopenia in age 8 years was acute leukemia with eosinophilia.

Studies have shown that Platelet counts below normal can give you a click that there is thrombocytopenia but it does not reveal the patho-mechanism for it.[20] With recent advances in hematology the Platelet indices, such like (MPV), (PDW), (P-LCR) on simple CBC may provide some important Valuable information about the pathogenesis of ITP.[21]

P-LCR is also a best determinant to differentiate between ITP and hypoproductive thrombocytopenia patients. A Cut off value for P-LCR >33.6% has been reported to be diagnostic marker for ITP with 99.6% accuracy.[22] The major etiological causes of accelerated peripheral platelet destruction is immune thrombocytopenia, in which autoantibodies bind to platelet surface antigens, resulting in premature destruction of platelets in reticularendothelial of more than 9.7 fl was enough to suspect ITP with accuracy of 70%. Similarly, previous work by researchers such as Ntaios et al and Shah et al reported that MPV was higher in ITP whichshows an increase in the production rate, and these researchers established cutoff values rang for MPV ranging 9 fl to 11 fl.[23-24]

Regarding PDW, there was no significant significant raise in our study groups that is ITP, Acute Leukemia and Megaloblastic Anemia. In comparison, Shah et aland Borkataky et al reported PDW was higher in ITP patients compared with acute myeloid leukemia patients and megaloblastic anemia patients, respectively.[24,25] Kaito et al Reported a cutoff value of greater than 17 fl for PDW helps to distinguish ITP from hypoproductive thrombocytopenia, and the its is 71.8% sensitive and 95% specific in this value.[26]

Hence we conclude that as bone marrow aspiration and examination studies are the gold standard for diagnosis of thrombocytopenia, MPV, PDW and PLCR are useful and reliable parameters that can easily be reported on simple CBC test helps the clinicians to differentiate between hyperdestructive thrombocytopenia and multiple causes of hypo-productive thrombocytopenia.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Hamzullah Khan	Data collection, analysis, interpretation, article writing.	
2	Adnan Masood	Data collection, analysis, Interpretation.	
3	Fazle Bari	Article revision, analysis, proof reading.	
4	Naila Tabassum	Data collection.	
5	Ameezullah	Data collection.	