Role of Platelet Large Cell Ratio (P-LCR) for Diagnosis of Immune Thrombocytopenia (ITP)

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Abstract

Objective: To determine the diagnostic accuracy of platelet large cell ratio (P-LCR) in diagnosis of immune thrombocytopenia taking bone marrow examination as gold standard.

Material and Methods: A total number of 194 patients of confirmed hematological patients with platelet counts below 50 × 109/L were included from Department of hematology, AIMC/Jinnah Hospital Lahore from 01-Oct-2020 to 30-April-2021. In all patients, venous blood samples were taken and CBC along with P-LCR analysis was done. Final values of P-LCR were noted. Patients having P-LCR ≥33.15% was labelled as having ITP. After that patients bone marrow samples were taken for confirmation of bone marrow suppression.

Results: Mean age of patients was 40.39±8.58 years. Mean P-LCR was 32.58±4.11%. There were 126 (64.95%) male and 68 (35.05%) female patients. ITP on P-LCR was found in 84 (43.30%) patients and ITP on bone marrow was found in 100 (51.55%) patients. P-LCR was 85.10% sensitive, 72.70% specific, had 70.00% PPV and 83.30% NPV for diagnosis of ITP.

Conclusion: P-LCR at cut off - ≥33.15% found to be highly sensitive for diagnosis of ITP in patients with thrombocytopenia.

Keywords: Platelet large cell ratio (P-LCR), immune thrombocytopenia, bone marrow.

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Introduction

When it comes to halting blood loss, platelets act as first line of defence. They stick together and aggregate to preserve the integrity of endothelium.[1] "Thrombocytopenia" refers to platelet count that is lower than 150 × 10^9/L. Common autoimmune condition, immune thrombocytopenia (ITP) is characterised by low platelet count, which can cause bleeding and petechiae.[2] ITP affects about 6 out of every 100,000 people in US each year; comparable prevalence has been documented in other states too. Occurrence is roughly 2.68 per 100,000 people in Europe.[3] Because of circulating autoantibodies that attach to surface of platelets and cause the spleen to destroy them, platelet count falls in ITP. This illness frequently follows upper respiratory tract virus infections. Clinically, ITP usually shows up as minor mucosal surface petechiae, but it can also show up as severe bleeding in the gastrointestinal tract or epistaxis.[4]

In order to rule out thrombocytopenia causes other than ITP, bone marrow aspiration is carried out. ITP patients can have antiplatelet antibodies found in their blood, although these tests do not identify the illness specifically. This is due to the fact that these antibodies may not be discovered in certain ITP patients, but they may be found in other illnesses. Haematology analyzers may now provide specific parameters that provide information about platelets thanks to technological advancements.

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In the literature, these measurements are known as platelet indices.[5]

Screening tests are prioritized initially due to potential cost, invasiveness, or time constraints associated with gold standard diagnostic tests. The platelet large cell ratio (PLCR) and platelet distribution width (PDW) are examples of platelet indicators.[6] The MPV typically falls between 7.2 and 11.7 fL. Increased MPV is the result of freshly generated platelets in the bone marrow being larger than normal in immune thrombocytopenia, a condition where plate-lets are destroyed in the spleen. PDW shows the variation in platelet size and ranges from 8.3% to 56.6% in healthy people. PDW and MPV changes usually follow the same pattern: when MPV rises, PDW rises as well, and vice versa. The fraction of bigger platelets in circulation, or PLCR, ranges normally from 15% to 35% in healthy people. The values of these indices are comparable in both genders.[6,7]

Platelet activity is tracked using the platelet-large cell ratio (P-LCR), which is a measure of number of bigger platelets in circulation. It also has inverse relationship with platelet count. Because of this, platelet indices such as P-LCR, MPV, and PDW are important in differentiating between hyper-destructive and hypo-productive thrombocytopenia.[8]

Red cell indices, including mean cell volume and red cell distribution width, are widely recognized as useful tools for analyzing different kinds of anaemias.[9] Researchers are still unclear about the function of platelet indices in thrombocytopenia, nevertheless. The main focus of current research is on how well platelet indices differentiate between hyper destructive and hypo productive types of thrombocytopenia.[10,11] Thus, the purpose of this study was to investigate the potential diagnostic use of P-LCR as a means of screening for immune thrombocytopenia in particular.

Materials and Methods

This Cross sectional study was conducted at Department of hematology, AIMC/Jinnah Hospital Lahore from 01-Oct-2020 to 30-April-2021. After approval of research proposal from CPSP (REU 43450; Dated October 2020), After approval of research proposal, 194 patients with clinical diagnosis of thrombocytopenia were included in this study. A written infor-med consent was taken from all patients before their inclusion in the study. 194 patients sample size was estimated by taking prevalence of ITP 44.00%, and expected sensitivity of P-LCR at cut-off value of ≥ 33.15%, 67% and specificity 88% with desired precision level 10%. Confirmed hematological patients with platelet counts below 50 × 109/L of age 15-50 years, both male and female patients were included. Patients who had received platelet transfusion in last 48 hours at the time of inclusion, confirmed cases of dengue fever and known cases of chronic liver disease or renal disease were excluded. In all patients, 3ml venous blood samples was taken and stored in vacuum tube containing K2EDTA and were sent to the laboratory. CBC along with P-LCR analysis using automated analyzer was done within 7 hours after taking the blood sample. Final values of P-LCR were noted on the basis of criteria; P-LCR ≥33.15% was labelled as Immune thrombocytopenia while P-LCR <33.15% was labelled as thrombocytopenia due to hypo-production of platelets. Diagnosis of thrombocytopenia in positive cases was further confirmed by histological examination of bone marrow only if there is no response to treatment with steroids. Consultant Hematologist confirmed the diagnosis of thrombocytopenia either it is hypo-productive thrombocytopenia or hyper-destructive thrombocytopenia. Data analysis was performed by using SPSS v26. Mean and SD were calculated for age and mean P-LCR. Frequency and percentage were calculated for qualitative variables. 2×2 contingency table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of P-LCR taking bone marrow examination as gold standard. Effect modifiers such as age and gender were controlled through stratification post-stratification sensitivity, specificity, positive predictive value, and negative predictive value, diagnostic accuracy of P-LCR were calculated again.

Results

Mean age of patients included in this study was 40.39± 8.58 years. Mean P-LCR of patients was 32.58±4.11%. There were more male patients as compared to females. There were 126 (64.95%) males and 68 (35.05%) female patients. ITP on P-LCR was found in 84 (43.30%) and it was not found in 110 (56.70%) patients. ITP on bone marrow was found in 100 (51.55%) and it was not found in 94 (48.45%) patients. (as shown in figure 1) As shown

Table 3: *Patient characteristics and study variables*

Sr.	Statistical Analysis		n=194
1	**Age (Mean±SD) years**		40.39±8.58
2	**Gender**	Male n(%)	126 (64.95%)
		Female n(%)	68 (35.05%)
3	**P-LCR (Mean±SD) %**		32.58±4.11
4	**P-LCR≥33.15%**	Yes n(%)	84 (43.30%)
		No n(%)	110 (56.70%)

in table 2, Regarding diagnostic accuracy, P-LCR found

Table 2: *Diagnostic Accuracy of P-LCR for ITP*

ITP on P-LCR	ITP on Bone Marrow Biopsy		Total
	Yes	No	
Yes	70	14	84
No	30	80	110
Total	**100**	**94**	**194**

to be 85.10% sensitive, 72.70% specific, had 70.00% PPV and 83.30% NPV. Data stratification is shown in

Table 3: *Data Stratification*

ITP on P-LCR		ITP on Bone Marrow Biopsy		Total
		Yes	No	
Male	**Yes**	42	9	51
	No	23	52	55
	Total	**55**	**61**	**116**
Female	**Yes**	28	5	33
	No	7	28	35
	Total	**35**	**33**	**68**
15-40 years	**Yes**	27	13	40
	No	10	42	52
	Total	**37**	**55**	**92**
41-50 years	**Yes**	43	1	44
	No	20	38	58
	Total	**63**	**39**	**102**

table 3 below, in patients having age 15-40 years, P-LCR was 76.40% sensitive, 80.80% specific, having 73.00% PPV and 67.50% NPV for diagnosis of ITP. In patients having age 41-50 years, P-LCR was 97.40% sensitive, 65.50% specific having 68.30% PPV and 97.70% NPV. In male patients, P-LCR was 85.20% sensitive, 69.30% specific, had 64.60% PPV and 82.40% NPV. In female patients, P-LCR was 84.80% sensitive, 80.00% specific, had 80% PPV and 84.80% NPV.

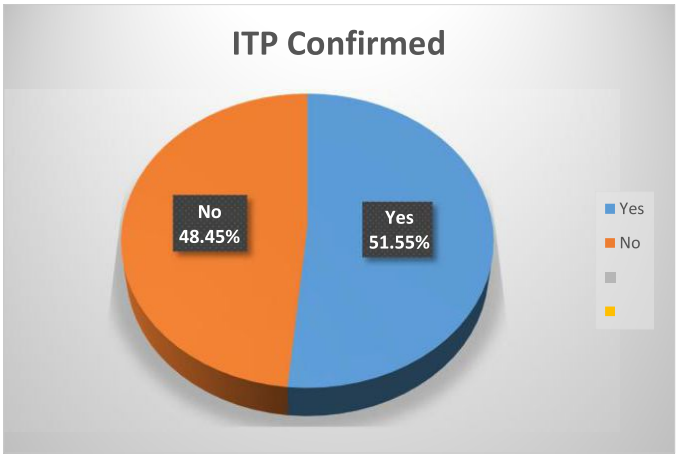

Figure 1: *Frequency of confirmed ITP on bone marrow biopsy.*

Discussion

P-LCR, has become an important metric for diagnosing ITP, disease marked by a low platelet count as result of immune-mediated destruction. P-LCR is measure of platelet turnover and activity that indicates the percentage of bigger platelets in circulation. In clinical practice, P-LCR is essential for differentiating between thrombocytopenia, especially ITP, in conjunction with other platelet indices.[12] This lays the groundwork for understanding the role that P-LCR plays in ITP diagnostic method and emphasizes its applicability in clinical settings where prompt and accurate diagnosis is critical to good patient outcomes and management.

In our study, mean age of patients was 40.39±8.58 years. Mean of P-LCR was 32.58±4.11%. There were 126 (64.95%) male and 68 (35.05%) female patients. ITP on P-LCR was found in 84 (43.30%) patients and ITP on bone marrow was found in 100 (51.55%) patients. P-LCR was 85.10% sensitive, 72.70% specific, had 70.00% PPV and 83.30% NPV for diagnosis of ITP. A study conducted by Nagesh et al. reported that P-LCR is a valuable test to differentiate ITP from hypo-productive thrombocytopenia and found that P-LCR at cut-off ≥33.15% is 88% specific and 67% sensitive in diagnosing ITP.[13] In one study, patients with thrombocytopenia of mean age 23.4±12.1 years were involved, having 38 (45.2%) males and 46 (54.8%) females and occurrence of ITP found in 40 patients. Sensitivity and specificity for P-LCR found to be 50% and 52.9%, respectively. In contrast to our findings, found to be low.[14] In contrast one study, 53.75% more male than females 46.25% found to have thrombocytopenia, however, it was drug induced.[15]

Although expensive, intrusive, and risky, bone marrow biopsy is important diagnostic technique for determining the underlying reasons of thrombocytopenia. As result, measuring platelet indices may be used as substitute for time-consuming and highly skilled bone marrow biopsies in order to distinguish between different causes of thrombocytopenia. Due to insufficient bone marrow production, platelet indices were shown to be considerably higher in patients with ITP when compared to those with thrombocytopenia in recent prospective research.[16] According to study, Platelet indices proved to be reliable indicators of difference between hypo productive and hyper destructive thrombocytopenia. They also serve as prognostic markers for determining the severity of the disease in dengue patients. Low MPV less than 9 fL and high PDW of more than 13 fL are specifically associated with higher risk of developing severe thrombocytopenia in dengue patients.[17] One study discovered that while the levels of platelet indices were within normal range among controls (healthy), they were higher among patients with cardiac disease, showing significance in cardiovascular disease too.[18] Additionally, results from another imply that platelet indices may be useful indicators of therapy effectiveness, which may help with treatment selection and lessen the need for 2nd-line therapies.[19]

In order to diagnose ITP, one study has evaluated extended platelet indices and their relationship to the severity and duration of the illness. Significant variations were seen in measures such as platelet count, and immature platelet fraction and between ITP patients and controls. Patients with recently diagnosed ITP had highest mean IPF and very low platelet counts. In ITP patients, there were additional changes in other platelet indices, including MPV, P-LCR, and PDW. [20]

In our study, we concluded that increased P-LCR provide reliable positive diagnosis of ITP, especially high P-LCR. In future, improved research designs and standardized measurements for platelet indices may significantly increase the diagnostic predictive power of platelet indices in the differential diagnosis of thrombocytopenia.

Conclusion

P-LCR at cut off -≥ 33.15% found to be highly sensitive for diagnosis of ITP in patients with thrombocytopenia.

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Authors Contribution

SZ: Conceptualization of Project
AM, ZI: Data Collection
AG: Literature Search
SI: Statistical Analysis
MG: Drafting, Revision
SK: Writing of Manuscript