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Role of Platelet Indices in the Evaluation of Thrombocytopenia

Ms. Nafeesath Suzna[1], Dr. Lovely George [2], Dr. Aravind Pallipady[3]

[1]Msc Mlt Student, A.J. Institute of Medical Sciences & Research Centre, Mangalore, India.

[2]Associate Professor, Department of Pathology, A.J. Institute of Medical Sciences & Research Centre, Mangalore, India.

[3]Professor & Blood Centre Officer, Department of Pathology, A.J. Institute of Medical Sciences & Research Centre, Mangalore, India.

Corresponding Author: Dr Lovely George,Associate Professor, Department of Pathology, A.J. Institute of Medical Sciences & Research Centre, Kuntikana, Mangalore, Karnataka, India.

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KEYWORDS

Platelet indices, Thrombocyt openia

ABSTRACT:

Background: Thrombocytopenia (TCP) is a condition characterized by a reduced platelet count, typically below 150,000/cumm. It can result from decreased platelet production, increased destruction, or abnormal pooling, with accurate diagnosis crucial for targeted treatment. While bone marrow examination is the gold standard for diagnosing the underlying cause, it is invasive and not always readily available. Recent advancements in automated hematological analyzers allow for the assessment of platelet indices (PIs) such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Platelet-Large Cell Ratio (P-LCR), Plateletcrit (PCT), and Platelet-Large Cell Coefficient (P-LCC). These PIs can provide valuable diagnostic and prognostic information, helping to distinguish between causes of thrombocytopenia and potentially reducing the need for invasive procedures like bone marrow aspiration and unnecessary platelet transfusions. Early detection using platelet indices could also help decrease morbidity and mortality associated with thrombocytopenia. This study aims to explore the role of platelet indices in identifying the causes of thrombocytopenia.

Materials and Methods: This was a prospective study carried out for a duration of 1 year from June 2022 to June 2023. All cases of thrombocytopenia received in the central laboratory of tertiary care hospital were included in the study. Assessment of CBC, MPV, PDW, PLCR AND PCT were done on Sysmex XN-1000 haematology analyser. A manual microscopic examination of peripheral blood film stained with Leishman stain was done to look for platelet clumps. Cases of thrombocytopenia were further divided into hypo proliferative and hyper destructive thrombocytopenia depending on clinical and laboratory parameters and bone marrow (BM) studies whenever available. Z test was used to test the significance difference in the outcomes such as MPV, PDW, PCT and PLCR between the groups.

Results: The study comprised of 93 study participants of which 66.7% (n=62) had thrombocytopenia and 33.3% (n=31) were healthy controls. The mean age of the study participants was 42.27 ± 15.27 years, with male predominance. Mean PDW was significantly higher in hyper destructive group compared to hypo proliferative and control groups. The mean PCT was lower in both hypo proliferative and hyper destructive groups compared to controls.

Conclusion: The study included 63 thrombocytopenic samples of which 31 were of hypo-proliferative group and 31 were of hyper-destructive group. Thrombocytopenia is one of the most common hematological disorders and can become life-threatening in case of severe disease. Platelet indices such as MPV, P-LCR, PCT can be used as an useful indicator in discriminating hypo-productive thrombocytopenia from hyper-destructive thrombocytopenia. Among those PDW provides much more reliable results in distinguishing both groups. These indices may be beneficial for patients by preventing invasive procedures and unnecessary platelet transfusion and is time saving and cost effective

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INTRODUCTION

Thrombocytopenia(TCP), is a common medical condition associated with a wide variety of diseases. It can be defined as subnormal number of platelets in the circulating blood. Platelet count below 1,50,000/cumm is considered as thrombocytopenia, but they do not reveal underlying pathophysiology. During the assessment of thrombocytopenic patients, it is important to know whether it is due to decreased production (hypo-proliferative), increased destruction (hyper-destructive) or abnormal platelet pooling as this will help in targeted treatment of the patient, thus avoiding unnecessary investigations and narrowing the differentials.

There is no simple diagnostic test available for diagnosis of pathogenesis of thrombocytopenia. Bone marrow examination is the gold standard test to differentiate the causes of thrombocytopenia, but the procedure is invasive and time consuming and not routinely available[(1)].

With advanced technology, the complete automated haematological analysers now give us few parameters that can give information about platelets. These parameters are referred as platelet indices. Platelet indices (PI) are the biomarkers of platelet activation. These includes mean platelet volume (MPV), platelet distribution width (PDW), Platelet – Large cell ratio (P-LCR), Plateletcrit (PCT), Platelet- Large cell coefficient (P-LCC). Recent evidences suggest that PIs may have diagnostic and prognostic values in certain diseases. The combined interpretation of these parameters are useful in discriminating diagnosis of platelet related disorders.[(2)]

Role of platelet indices in differentiating thrombocytopenia may postpone patients from performing bone marrow aspiration and also unnecessary platelet transfusion[(3)].

Platelet indices have important prognostic role as early detection of thrombocytopenia may help to reduce morbidity and mortality of the patients with thrombocytopenia[(4)].

This study intends to determine the significance of platelet indices in establishing the causes of thrombocytopenia.

OBJECTIVE OF THE STUDY

The objective of this study is,

1. To evaluate the variation in platelet indices in patients presenting with thrombocytopenia.
2. To study the relationship of platelet indices with respect to underlying mechanism of thrombocytopenia.

MATERIALS AND METHODS

SOURCE OF DATA

Blood samples of the patients received in the central laboratory of tertiary care hospital, Mangalore.

INCLUSION CRITERIA

All cases of thrombocytopenia received in the laboratory during the study period.

EXCLUSION CRITERIA

1. Patients below 1 year of age to avoid age related changes in platelet indices.
2. Patients with autoimmune disorders like Systemic Lupus Erythematosus(SLE) , Rheumatoid arthritis.
3. Patients on anti-platelet drugs.

STUDY DESIGN

Observational comparative study.

SAMPLE SIZE

On the basis of study conducted by Elsewefy DA et al[5], in order to detect the difference of 0.89 (L) in the mean MPV between the group assuming 95% confidence interval, 80% power, pool Standard Deviation of 1.25, the sample size estimated for the study was 30.9 approximately equal to 31 in each group and 31 in control. Hence, a total of 93 samples were considered.

$$n = \frac{(Z_{1-\alpha} + Z_{1-\beta})^2 (2SD)^2}{L^2}$$

DURATION OF STUDY

1 year

METHODOLOGY

2mL of venous blood will be collected in EDTA anticoagulant tube.

- Samples with platelet count less than 1,50,000 cells/cu.mm were selected for the study.
- Assessment of CBC, MPV, PDW, PLCR AND PCT will be done on Sysmex XN-1000 haematology analyser.
- A manual microscopic examination of peripheral blood film stained with Leishman stain will be done to look for platelet clumps.
- Cases of thrombocytopenia will be further divided into hypo proliferative and hyper destructive thrombocytopenia depending on

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clinical and laboratory parameters and bone marrow(BM) studies wherever available.

STATISTICAL ANALYSIS

Z test will be used to test the significance difference in the outcomes such as MPV, PDW, PCT and PLCR between the groups.

RESULTS

The study comprised of 93 study participants of which 66.7% (n=62) had thrombocytopenia and 33.3% (n=31) were healthy controls. The thrombocytopenia cases were further divided into hypo proliferative and hyper-destructive thrombocytopenia, comprising of 31 study participants in each sub-group.

- The study participants comprised of 55.1% (n=54) males and 39.8% (n=39) females. (Fig 1)
- The mean age of the study participants was 42.27 ± 15.27 years, ranging from 7 to 84 years.
- The severity of thrombocytopenia was categorized into mild, moderate and severe based on the platelet count. There was significant association between gender and severity of thrombocytopenia ($\chi 2(2) = 11.262$, p=0.004).
- The percentages of males were higher in mild and moderate thrombocytopenia (51.1% and 94.4% respectively). The percentage of females was higher in study participants with severe thrombocytopenia (53.3%).

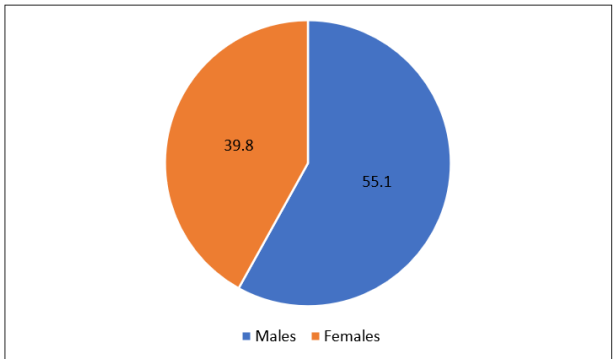

FIGURE 1: Gender distribution of the study participants

The platelet count and indices were compared between cases and controls as shown in Table 1.

TABLE 1: COMPARISON OF HEMATOLOGICAL PARAMETERS BETWEEN CASES AND CONTROLS

Parameter	Cases (n=62)	Controls (n=31)	p value
	Mean ± SD (Min- Max)		
Platelet count	59.80 ± 35.91 (6.00 – 135.00)	276.74 ± 49.87 (166.00 – 363.00)	<0.001
PDW	14.39 ± 4.59 (7.70 – 25.00)	10.66 ± 1.94 (7.10 – 17.90)	<0.001
MPV	10.37 ± 1.23 (8.00 - 17.10)	9.86 ± 0.84 (7.80 – 11.70)	0.041
PLCR	27.98 ± 7.00 (9.20 – 44.00)	23.36 ± 6.73 (8.80 – 39.80)	0.003
PCT	0.08 ± 0.05 (0.01 – 0.21)	0.25± 0.03 (0.20 – 0.33)	<0.001

- The mean platelet count, MPV and PCT were significantly lower in cases compared to controls.
- The mean PDW and PLCR were significantly higher in cases compared to controls.
- The platelet count and indices were further compared between hypo proliferative, hyper destructive and control groups. (Table 2)

TABLE 2: COMPARISON OF HEMATOLOGICAL PARAMETERS IN HYPO PROLIFERATIVE, HYPER DESTRUCTIVE AND CONTROLS

Parameter	Hypoproliferative (n=31)	Hyperdestructive (n=31)	Controls (n=31)	p value
	Mean ± SD (Min- Max)			

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Platelet count	44.22 ± 31.33 (6.00 – 135.00)	75.38 ± 33.75 a* (13.00 – 125.00)	276.74 ± 49.87 b**c** (166.00 – 363.00)	<0.001
PDW	10.96 ± 2.22 (7.70 – 16.00)	17.82 ± 3.69 a** (12.70 – 25.00)	10.66 ± 1.94 b** (7.10 – 17.90)	<0.001
MPV	10.34 ± 0.92 (8.30 – 12.40)	10.39 ± 1.48 (8.00 – 17.10)	9.86 ± 0.85 (7.80 – 11.70)	0.123
PLCR	29.02 ± 7.67 (12.00 – 44.00)	26.94 ± 6.22 (9.20 – 37.90)	23.36 ± 6.74 c* (8.80 – 39.80)	0.006
PCT	0.04 ± 0.02 (0.01-0.10)	0.11 ± 0.04 a** (0.02 – 0.21)	0.25 ± 0.03 b**c** (0.20 – 0.33)	<0.001

a, comparison between hypo proliferative and hyper destructive groups;
b, comparison between hyper destructive and control groups;
c, comparison between hypo proliferative and control groups;
*, p<0.05; **, p<0.001

- The mean platelet count was significantly lower in both hypo proliferative and hyper destructive groups compared to controls. Mean platelet count was found to be significantly higher in the hyper destructive group compared to the hypo proliferative group.

Distribution of study participants based on diagnosis is shown in Table 3.

TABLE 3: DISTRIBUTION OF STUDY PARTICIPANTS BASED ON DIAGNOSIS

Type	Diagnosis	Frequency	Percentage
Hypo proliferative	Leukemia	12	38.7
	Myelodysplastic syndrome	3	9.7
	Aplastic anemia	3	9.7
	Pancytopenia	10	32.3
	Megaloblastic anemia	3	9.7
	Total	31	100.0
Hyper destructive	Viral fever	7	22.6
	ITP	5	16.1
	Sepsis	5	16.1
	Dengue	7	22.6
	Malaria	4	12.9
	Chronic Liver Disease	3	9.7
	Total	31	100.0

- A large percentage of individuals with hypo proliferative thrombocytopenia has leukemia (38.7%) followed by pancytopenia (32.3%)
- Among those with hyper destructive thrombocytopenia, majority had viral fever (22.6%) and dengue (22.6%).
- Mean PDW was significantly higher in hyper destructive group compared to hypo proliferative and control groups. However, there was no significant difference in the means between hypo proliferative and control groups.
- There was significant difference in the mean levels of PLCR between hypo proliferative and control groups. (p<0.001)
- The mean PCT was lower in both hypo proliferative and hyper destructive groups compared to controls. Mean PCT was higher in

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hyper destructive group compared to hypo proliferative group.

- No significant difference in mean MPV was observed across the groups.
- Overall, platelet count and PCT showed significant variations between the three groups.
- Platelet count, PDW, PLCR and PCT showed no significant differences in means across the groups.
- However, mean MPV was found to be higher among those with sepsis compared to those with viral fever and dengue. ($p<0.05$)

DISCUSSION

Thrombocytopenia is a common medical condition associated with wide variety of diseases. Though automated hematological analysers now give us platelet indices, the significance of using platelet indices as a diagnostic parameter has not been established fully.

Our study included 93 samples, of which 62 were of thrombocytopenic patients and 31 were control. Thrombocytopenic samples were further divided in hypo-proliferative(31) and hyper-destructive(31) groups.

Hypo-proliferarive group in our study included leukemia, myelodysplastic syndrome, aplastic anemia, pancytopenia and megaloblastic anemia.

Hyper-destructive group included viral fever, ITP, sepsis, dengue, malaria and chronic liver disease.

TABLE 4: COMPARISON OF GENDER DISTRIBUTION WITH OTHER GROUPS:

S.I NO	Author	Male	Female
1	Khairkar PS *et. Al*[3]	318	192
2	Shubha H *et.al*[1]	295	210
3	Present study	39	23

In the study conducted by Khairkar PS *et al,* thrombocytopenia was found higher in males compared to females[3]. In the another study conducted by Shubha H *et,al,* thrombocytopenia was found higher in males compared to females[1] which was similar to our present study.

Platelet count less than 1,50,000 cells/cu.mm is thrombocytopenia. The platelet counts and platelet indices were compared in both groups.

TABLE 5: COMPARISON OF MEAN PLATELET COUNT(*10^3/cu.mm) IN BOTH GROUPS IN VARIOUS STUDY.

Study	Hypo proliferative group (Mean ± SD)	Hyper destructive group (Mean ± SD)	p-value
Kaito *et al*[6]	6.0±0.4	5.9±0.4	ns
Elsewefy *et al*[5]	45.3±29.7	35.8±32.3	0.387
Al Tameemi *et al*[7]	34.4±20.92	39.27±19.89	0.289
Mittal V *et al*[4]	71.5±32.3	10.37±23.6	
Zulfania *et al*[8]	60.74±37.3	58.88±36.6	0.835
Present study	44.22±31.33	75.38±33.75	<0.001

In the study conducted by Kaito *et al*[6], platelet count were similar in both the groups with no statistical significance. In the study by Elsewefy *et al*[5], platelet counts did not show significant difference between two patient groups. In the present study, mean platelet count was found to be significantly higher in hyper-destructive group compared to hypo-proliferative group which is similar to the study conducted by Al Tameemi *et al*[7].

TABLE 6: COMPARISON OF PDW(fL) IN BOTH GROUPS IN VARIOUS STUDY.

Study	Hypo proliferative group (Mean ± SD)	Hyper destructive group. (Mean ± SD)	p-value
Kaito *et al*[6]	11.6±0.3	16.8±0.5	<0.0001
Elsewefy *et al*[5]	16.90±1.88	17.11±1.87	0.008

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Al Tameemi *et al*[7]	14..47±2.88	16.48±1.79	0.000
Mittal V *et al*[4]	71.5±32.3	103.7±23.6	0.428
Zulfania *et al*[8]	12.68±3.16	14.811±3.61	0.014
Present study	10.96±2.22	17.82±3.69	<0.001

Platelet distribution width is a measure of platelet anisocytosis.

In a study conducted by Elsewefy *et al*[5], PDW did not show significance difference between the two patient groups and the statistically insignificant. But in our present study, PDW was significantly higher in hyper-destructive compared to the hypo-proliferative group which were consistent with other studies.

TABLE 7: COMPARISON OF MPV(fL) IN BOTH GROUPS IN VARIOUS STUDY.

Study	Hypo proliferative group (Mean ± SD)	Hyper destructive group (Mean ± SD)	p-value
Kaito *et al*[6]	10.2±0.2	12.2±0.2	<0.0001
Elsewefy *et al*[5]	9.08±1.25	9.97±1.35	0.008
Al Tameemi *et al*[7]	7.84±0.88	12.05±1.07	0.000
Mittal V *et al*[4]	13.11±1.10	13.66±1.15	0.460
Zulfania *et al*[8]	10.57±1.33	11.637±1.98	0.017
Present study	10.34±0.92	10.39±1.48	0.123

In a study, Kaito *et al*[6], MPV was significantly higher in ITP (hyper-destructive) group than aplastic anemia (hypo-proliferative) group which were similar to the studies conducted by Al Tameemi *et al*[7] and Zulfania *et al*[8]. In other studies by Elsewefy *et al*[5] and Mittal *et al*[4], there was no significant difference in mean MPV across the group which was corresponding to our study.

TABLE 8: COMPARISON OF P-LCR(%) IN BOTH GROUPS IN VARIOUS STUDY.

Study	Hypo proliferative group (Mean ± SD)	Hyper destructive group (Mean ± SD)	p-value
Kaito *et al*[6]	25.7±1.1	42.2±1.5	<0.0001
Elsewefy *et al*[5]	27.57±4.57	41.68±4.33	<0.001
Al Tameemi *et al*[7]	16.12±4.82	38.41±8.14	0.000
Mittal V *et al*[4]	48.85±8.03	53.64±8.98	0.269
Zulfania *et al*[8]	30.81±9.23	36.993±10.25	0.010
Present study	29.02±7.67	26.94±6.22	0.006

P-LCR is the measure of platelet mass which is occupied by large platelets.

The study conducted by Kaito *et al*[6], Elsewefy *et al*[5], Al Tameemi *et al*[7], Mittal V *et al*[4], Zulfania *et al*[8] compared similar groups and concluded that PLCR was significantly higher in hyper destructive group as compared to hypo proliferative group. In contrast to these studies, in our present study mean P-LCR was significantly higher in hypo-productive group compared to hyper-destructive group.

TABLE 9: COMPARISON OF PCT(%) IN BOTH GROUPS IN VARIOUS STUDY.

Study	Hypo proliferative group (Mean ± SD)	Hyper destructive group (Mean ± SD)	p-value
Al Tameemi *et al*[7]	0.02±0.01	0.04±0.001	0.000
Mittal V *et al*[4]	0.03±0.01	0.08±0.02	<0.001
Present study	0.04±0.02	0.11±0.04	<0.000.1

Plateletcrit is the total mass occupied by the platelets.

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The study conducted by Al Tameemi, *et al*[7] and Mittal V, *et al*[4] correlated with our present study in which mean PCT was higher in hyper destructive group when compared with hypo proliferative group.

CONCLUSION

The study included 63 thrombocytopenic samples of which 31 were of hypo-proliferative group and 31 were of hyper-destructive group. Thrombocytopenia is one of the most common hematological disorders and can become life-threatening in case of severe disease. Platelet indices such as MPV, PDW, P-LCR, PCT can be used as an useful indicator in discriminating hypo-productive thrombocytopenia from hyper-destructive thrombocytopenia. Among those PDW provides much more reliable results in distinguishing both groups. These indices may be beneficial for patients by preventing invasive procedures and unnecessary platelet transfusion and is time saving and cost effective

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