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Original Article

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Evaluation of platelet parameters and their prognostic significance in anemia and leukemia

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Abstract

***Background & Aims*:** Most commonly assessed Platelet indices include the mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR), and the plateletcrit (PCT). The platelet behavior is often unpredictable and complicated in Iron Deficiency Anemia. High MPV and low PDW were reported in patients with leukemia. The present study aimed to evaluate the significance of platelet parameters in anemia and leukemia cases.

***Materials & Methods*:** A cross-sectional and observational case-control study was carried out at a teaching hospital of Andhra Pradesh. We measured the platelet indices using an automated counter. Laboratory data from 200 patients of anemia and leukemias were analysed.

***Results*:** Hematological disorders such as anemia in 168 cases and leukemia in 32 cases were recorded. Platelet parameters specifically platelet count (PC), MPV, PDW, and P-LCR were significantly lowered in acute leukemia patients than them of the control group. In chronic leukemia (both CML & CLL) patients, all the platelet parameters such as mean platelet component (MPC), MPV, PDW, and P-LCR were found to be higher than them of the control group. In the majority of chronic leukemia cases, platelets on PBS were discrete (81%) and hypogranular (55%). Inverse relationship noted between MPV and PC among anemic patients. PC in acute leukemia (both AML & ALL) patients was lower than that of the control group. PDW was significantly lower in acute leukemia patients compared to that in the control group. P-LCR was also found to be significantly lower in the acute leukemia group compared to the control group. The PC was higher and the MPV was lower in the anemic group compared to the control group.

***Conclusion*:** In chronic leukemia patients, all the platelet parameters such asPC, MPV, PDW, and P-LCR were found to be significantly higher than them of the control group. PC was higher and the MPV was lower in the anemic group compared to the control group. All the platelet parameters such as MPV, PC, PDW, and P-LCR were significantly lower in acute leukemia patients compared to them in the control group, in contrast with chronic leukemia patients where the parameters were significantly higher compared to them in the control group.

***Keywords*:** Anemia, Leukemia, Platelet Indices, Peripheral Blood Smear

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Introduction

Iron deficiency is one of the world's most common and potentially treatable health problems. Several changes in platelet behavior have been reported in iron deficiency anaemia (IDA) (1). Moderate IDA usually shows reactive thrombocytosis (RT) while thrombocytopenia is usually found in severe IDA suggesting a biphasic mechanism. Platelets are small discoid structures lacking a nucleus. Their size is 1-3 µm in diameter and they have a thickness of 1 µm. Their volume is approximately 7 fL, though varying substantially. In health, platelet counts normally vary between 150 and 400 x 10^9/L. Platelets are produced by cytoplasmic fragmentation of large cells in bone marrow called as megakaryocytes. A mature megakaryocyte extends cytoplasmic processes through the sinusoidal wall in bone marrow and platelets are released directly into the blood stream by fragmentation of cytoplasm. Each megakaryocyte produces about 4000 platelets during its lifespan (2). The main physiologic function of platelets is hemostasis or the formation of a hemostatic plug to prevent microvascular hemorrhage. Platelet activation leads to changes in platelet shape with an increase in platelet swelling leading to an increase in MPV (3, 4).

The MPV is an indicator of the average size and activity of platelets. Younger platelets are larger and exhibit more activity. The PDW is a measure of degree of variation in size of platelets and P-LCR indicates the percentage of large platelets with a volume of >12fL (5). Automated hematology analyzers generate various platelet parameters like platelet count, mean platelet volume, platelet distribution width, plateletcrit, platelet large cell ratio, mean platelet component, and reticulated platelets. Correlation of various platelet parameters with one another in both health and disease conditions yield a great deal of information about the behavior of platelet production and their later alterations. High MPV and low PDW were reported in patients with leukemia (6). Previous studies have shown lower mean platelet volume (MPV) and higher platelet distribution width (PDW) levels in cases of complications in IDA (1). The relationship between different platelet parameters such as MPV, PDW, and risk of complications of thrombosis in anemia gained attention to the researchers (7). However, there are no reports in the literature on the significance of platelet profile in anemia and leukemia. This study aims to analyse the platelet parameters in patients presenting with hematological disorders anemia and leukemias.

Materials & Methods

This prospective case-control study collected the data for the duration of 25 months at Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Vijayawada, India. The study was conducted among patients presenting with hematological disorders attending outpatient department or admitted in the hospital. A hundred age and sex matched controls were alsochosen. The institutional ethical committee approved the study protocol.

Patients with hemoglobin <10 gm/dL were included. Patients with acute hemorrhage and infections, neoplastic, and chronic inflammatory disorders such as rheumatoid arthritis, ankylosing spondylitis, and systemic lupus erythematosus were excluded.

Patients diagnosed of acute and chronic leukemias with typical clinical manifestations (such as generalized lymphadenopathy, hepatomegaly), peripheral smear findings showing abnormalities in number, appearance, and maturity of WBCs and/or bone marrow examination (with >30% blast cells are considered acute leukemia) were included. Patients using medications that can reduce platelet count including hydroxyurea, antineoplastic agents, and inhibitors of the platelet integrin αIIbβ3 as well as known cases of hereditary disorders of large platelets were excluded. Controls were primarily hospital-based or who came for routine check-up. Individuals with normal hemogram (Hb >12 gm%), normal normocytic normochromic peripheral blood smear, and random blood glucose < 80 mg/dL were included.

Individuals with neoplastic and chronic inflammatory disorders such as rheumatoid arthritis and systemic lupus erythematosus as well as on anti-inflammatory, anti-coagulants or anti-platelet therapy

were excluded. Venous blood samples were collected from the antecubital vein using a 5 cc syringe and transferred to vacutainers containing dipotassium EDTA. We measured the blood platelet indices using Sysmex KX-21 automated hematology analyzer. The hemograms were studied with special emphasis on platelet parameters specifically, PC, MPV, PDW, and P-LCR. Aperipheral smear was done. Platelet count was done on peripheral blood smear for all the hemograms showing platelet counts out of the normal range to rule out spurious causes of either thrombocytopenia or thrombocytosis by Fonio method. With a 1,000-fold magnification (eyepiece 10, lens 100), one platelet per field is equivalent to twenty thousand platelets/μL in circulating blood. The platelet morphology was studied considering the arrangement, granularity, and size of platelets.

Statistical analysis**:** The mean and standard deviation were calculated for different parameters in both the patient and control groups. The comparison of the means was done using students unpaired 't' test. Test of proportion was applied wherever necessary. In all above tests 'p' < 0.05 was taken to be statistically significant. Hematological disorders were further categorized into anemia (sub-categorized into microcytic hypochromic, normocytic normochromic, and macrocytic anemias) and leukemias (sub-categorized into acute and chronic leukemias). We studied the age, sex, hematological parameters, and platelet morphology in both the groups.

Results

On Peripheral Blood Smear (PBS), the platelet morphology of control group appeared as 93% discrete, 95% granular and there was no increase in the percentage of large platelets. Hematological disorders, such as anemia in 168 cases, and leukemia in 32 cases were recorded. Comparison of platelet parameters between the anemia group and control group showed statistically significant higher PC and lower MPV, irrespective of the morphological type of anemia (Figure 1,2).

Table 1. Characteristics of the control group

Characteristic	Control group
Number	100
Age (years)	39.86 + 11.98
Male (%)	51 (51%)
Female (%)	49 (49%)
Hemoglobin (gm%)	14.2 + 0.69
MCV (fL)	87.4 + 4.6
MCHC (gm/dL)	32.5 + 1.7
TLC (x μL)	6911.2 + 1313.98
PC (x 109/L)	249.94 + 56.38
MPV (fL)	9.5 + 0.89
PDW (fL)	11.0 + 1.14
P-LCR (%)	20.5 + 2.99

Table 2. Comparison of various parameters between the patients of anemia and the control group

CharacteristicS	Anemia			Control group	P-value
	Microcytic hypochromic	Normocytic normochromic	Macrocytic		
Number (n)	74	57	37	100	-
Age (years)	43 + 8.6	43 + 9.0	46 + 9.1	39.86 + 11.98	-
Male (%)	31 (42%)	18 (32%)	16 (43%)	51 (51%)	-

CharacteristicS	Anemia			Control group	P-value
	Microcytic hypochromic	Normocytic normochromic	Macrocytic		
Female (%)	43 (58%)	39 (68%)	21 (57%)	49 (49%)	-
Hb (gm%)	6.4 + 1.6	6.7 + 1.8	6.6 + 1.8	14.2 + 0.69	-
MCV (fL)	58 + 8	87.2 + 4.6	110.5 + 5.9	87.4 + 4.6	-
MCHC (gm/dL)	21 + 2	32.6 + 1.7	32.6 + 1.8	32.5 + 1.7	-
PC (x 109/L)	348.7 + 134.7	339.9 + 136.3	321.9 + 140.2	249.94 + 56.38	0.03
MPV (fL)	9.2 + 0.9	9.1 + 1.0	9.0 + 1.1	9.5 + 0.89	0.02
PDW (fL)	11.5 + 2.3	11.7 + 2.2	11.3 + 2.4	11.0 + 1.14	0.06
P-LCR (%)	20.6 + 6.8	20.8 + 7.2	20.7 + 7.5	20.5 + 2.99	0.08

Comparison of platelet parameters between the acute leukemia (AML & ALL) group and control group showed statistically significant decrease in PC, MPV, PDW and P-LCR (Table 3).

Table 3. Comparison of various parameters between the patients of acute leukemia and the control group

Characteristic	Acute Leukemia		Control group	P-value
	AML	ALL		
Number (n)	9	12	100	-
Age (years)	52.6 + 8.5	7.3 + 2.2	39.86 + 11.98	-
Male (%)	5 (56%)	6 (50%)	51 (51%)	-
Female (%)	4 (44%)	6 (50%)	49 (49%)	-
Hb (gm%)	6.7 + 0.9	6.2 + 0.8	14.2 + 0.69	-
TLC (x 109/L)	108 + 29	86 + 17	6911.2 + 1313.98	-
PC (x 109/L)	60.8 + 6.8	60.8 + 5.2	249.94 + 56.38	0.01
MPV (fL)	6.7 + 0.7	6.6 + 0.9	9.5 + 0.89	0.03
PDW (fL)	8.0 + 1.2	8.2 + 0.9	11.0 + 1.14	0.02
P-LCR (%)	12.4 + 1.3	12.0 + 1.4	20.5 + 2.99	0.04

Comparison of platelet parameters between the chronic leukemia (CML & CLL) group and control group showed a statistically significant increase in PC, MPV, PDW and P-LCR (Table 4).

Table 4. Comparison of various parameters between the patients of chronic leukemia and the control group

Characteristic	Chronic Leukemia		Control group	P-value
	CML	CLL		
Number (n)	5	6	100	-
Age (years)	29.6 + 4.8	54.7 + 8.4	39.86 + 11.98	-
Male (%)	3 (60%)	3 (50%)	51 (51%)	-
Female (%)	2 (40%)	3 (50%)	49 (49%)	-
Hb (gm%)	6.2 + 0.56	5.9 + 0.8	14.2 + 0.69	-
TLC (x 109/L)	87 + 24.3	120 + 12	6911.2 + 1313.98	-
PC (x 109/L)	287.6 + 154.8	376.3 + 74.5	249.94 + 56.38	0.03
MPV (fL)	11.0 + 1.2	10.7 + 1.1	9.5 + 0.89	0.02
PDW (fL)	11.6 + 1.0	11.8 + 0.6	11.0 + 1.14	0.01
P-LCR (%)	28.1 + 2.4	24.1 + 2.5	20.5 + 2.99	0.04

Study showed discrete arrangement of platelets in 95% of Anemia, 86% of acute leukemia, and 81% of chronic leukemia (Table 5).

Table 5. Arrangement of platelets on PBS in hematological disorders

Hematological disorders	Discrete	Clump
Anemia (n=168)	159 (95%)	9 (5%)
Microcytic hypochromic (n=74)	70 (95%)	4 (5%)
Normocytic normochromic (n=57)	54 (95%)	3 (5%)
Macrocytic (n=37)	35 (95%)	2 (5%)
Leukemia		
Acute leukemia (n=21)	18 (86%)	3 (14%)
AML (n=9)	7 (78%)	2 (22%)
ALL (n=12)	11 (92%)	1 (8%)
Chronic leukemia (n=11)	9 (81%)	2 (18%)
CML (n=5)	4 (80%)	1 (20%)
CLL (n=6)	5 (83%)	1 (17%)

In our study, the following observations were made regarding the granularity of platelets on PBS in various clinical conditions showing granularity of platelets in 97% of anemia, 86% of acute leukemia, and 45% of chronic leukemia (Table 6).

Table 6. Granularity of platelets on PBS in hematological disorders

Hematological disorders	Granular	Hypogranular
Anemia (n=168)	163 (97%)	5 (3%)
Microcytic hypochromic (n=74)	72 (97%)	2 (3%)
Normocytic normochromic (n=57)	55 (96%)	2 (4%)
Macrocytic (n=37)	36 (97%)	1 (3%)
Leukemia		
Acute leukemia (n=21)	18 (86%)	3 (14%)
AML (n=9)	7 (78%)	2 (22%)
ALL (n=12)	11 (92%)	1 (8%)
Chronic leukemia (n=11)	5 (45%)	6 (55%)
CML (n=5)	0 (0%)	5 (100%)
CLL (n=6)	5 (83%)	1 (17%)

In our study, the following observations were made regarding the percentage of large platelets on PBS in various clinical conditions showing increased percentage of macrothrombocytes as 64% of chronic leukemia. No increase in the percentage of megathrombocytes is noted in anemia, irrespective of the morphological type and acute leukemia patients (Table 7).

Table 7. Percentage of large platelets on PBS in hematological disorders

Hematological disorders	Absent	Normal (<5%)	Increased (>5%)
Anemia (n=168)	140 (83%)	28 (17%)	-
Microcytic hypochromic (n=74)	61 (82%)	13 (18%)	-
Normocytic normochromic (n=57)	48 (84%)	9 (16%)	-
Macrocytic (n=37)	31 (84%)	6 (16%)	-
Leukemia			
Acute leukemia (n=21)	18 (86%)	3 (14%)	-
AML (n=9)	8 (89%)	1 (11%)	-
ALL (n=12)	10 (83%)	2 (16%)	-
Chronic leukemia (n=11)	1 (9%)	3 (27%)	7 (64%)
CML (n=5)	-	1 (20%)	4 (80%)
CLL (n=6)	1 (17%)	2 (33%)	3 (50%)

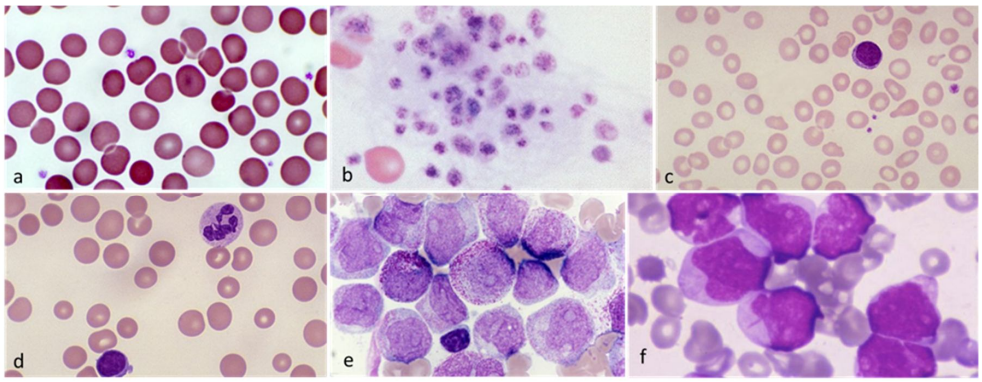

Fig1. a. PBS showing discrete and granular platelets.b. platelet clump with a mixture of granular and hypogranular platelets.c. microcytic hypochromic anemia.d. macrocytic anemia.e. BMA smear showing acute promyelocytic leukemia (AML M3).f. BMA smear of acute myeloblastic leukemia with maturation (AML M2).

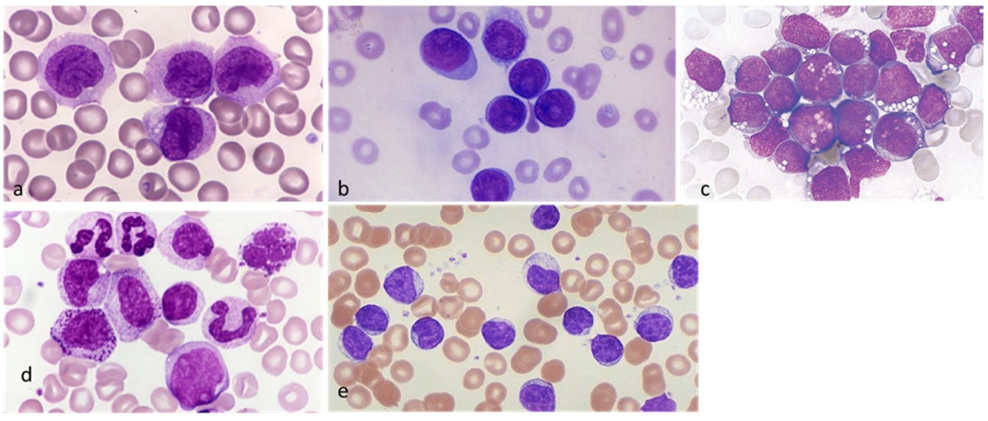

Fig 2. a.PBS showing acute monocytic leukemia (AML M5).b. PBS showing ALL L1.c. BMA smear of ALL L3.d. PBS of CML.e. PBS of CLL

Discussion

Anemia is usually diagnosed based on a reduction in the hematocrit and the hemoglobin levels that are below the normal range (8). It was reported that megakaryopoiesis (the process by which megakaryocytes, and ultimately platelets, develop) was stimulated in anemia. In moderate anemia (Hb: 8.0 - 9.5 g/dL), the causes of thrombocytosis may be: 1) increased rate of influx of precursor cells into the megakaryocyte compartment with an increased rate of efflux; 2) shortening of megakaryocyte maturation; 3) stem-cell shunt due to inhibition of erythropoiesis, resulting in increased production of other pluripotent cells (hemostatic compensatory mechanism) (8, 9). In our study, the platelet count in the anemic group was higher than that of the control group, and mean platelet volume was lower in the anemic group than that of the control group. These findings were similar to the study done by Shah et al. (10). There was no statistically significant difference in PDW and P-LCR between anemic group and control group in our study.

Even though the PC in anemic group was higher, the percentage of large platelets on PBS in these patients was not increased beyond normal limits, indicating that there is no increase in the size of the platelets. In the majority of the cases, platelets on PBS were discrete (95%) and granular (97%). Hypogranularity was observed in few cases which could be an artifactual change due to the formation of clumps.

In our study, inverse correlation between platelet counts and mean platelet volume might be due to shortened maturation time and increased polyploidy of megakaryocytes with normal lifespan, as it is well known that the youngest platelets have the largest size (11, 12).

Leukemias may be acute (myeloid or lymphocytic) or chronic (myeloid or lymphoid). Thrombocytopenia is one of the common manifestations of acute leukemias (AML & ALL). In chronic leukemias (CML & CLL), platelet count can be variable depending on the course of disease (13).

In our study, the PC in acute leukemia (AML & ALL) patients was lower than that of the control group. This finding was similar to the study done by Shah et al. (10), although MPV was found to be lower in contrast to the studies done by Shah et al. (10) and Alsweedan SA .et al. (6) which showed higher MPV. In our study, PDW was significantly lower in acute leukemia patients compared to the control group similar to the study done by Alsweedan SA et al. (6). P-LCR was found to be significantly lower too in the acute leukemia group compared to the control group.

In the majority of the acute leukemias, platelets on PBS were discrete (86%) and granular (86%). Hypogranularity was observed in few cases which could be an artifactual change due to formation of clumps and the percentage of large platelets in these patients was not increased beyond normal limits, indicating that there is no increase in the size of the platelets.

In chronic leukemia (CML & CLL) patients, all the platelet parameters such as MPC, MPV, PDW, and P-LCR were found to be higher than them of the control group. In the majority of chronic leukemia cases, platelets on PBS were discrete (81%) and hypogranular (55%). The percentage of large platelets in these patients was increased beyond normal limits in 64% of cases, indicating that there is an increase in size of the platelets supporting an increase in MPV. With improvement in the technologies, advancement occurs in all fields including medicine.

In our study, the PC was higher and the MPV was lower in the anemic group compared to the control group. There was an inverse relationship noted between MPV and PC among anemic patients. The percentage of large platelets on PBS in these patients was not increased beyond normal limits, indicating that there is no increase in the size of platelets. A reduction of the total circulating red cell mass below normal limits may affect thrombopoiesis leading to several changes in platelets indicating the importance of evaluation of platelet parameters.

In our study, platelet parameters specifically PC, MPV, PDW, and P-LCR were significantly lowered in acute leukemia patients than them of the control group. The percentage of large platelets on PBS in these patients was not increased beyond normal limits,

indicating that there is no increase in the size of the platelets.

The percentage of large platelets in these patients was increased beyond normal limits in 64% of cases, indicating that there is an increase in size of the platelets, supporting an increase in MPV. Considering these values of the platelet parameters, a distinction can be made between acute and chronic leukemias.

Conclusion

In our study, the PC was higher and the MPV was lower in the anemic group compared to the control group. All the platelet parameters such as MPV, PC, PDW, and P-LCR were significantly lower in acute leukemia patients in contrast to chronic leukemia patients where the parameters were significantly higher compared to the control group. Platelet parameters are readily available, relatively inexpensive and useful markers, which may vary in different clinical conditions. So, they should be used as routine investigatory measures to aid in diagnosis of the conditions.

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Not declared.

Conflict of interest

The authors have no conflict of interest in this study.

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Nil

Ethical Statement

This study was conducted in accordance with the Declaration of Helsinki and the guidelines of the Indian Council of Medical Research. The study protocol was approved by the institutional ethical committee of Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Vijayawada, India.

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