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STUDY OF PLATELET INDICES IN DIFFERENTIAL DIAGNOSIS OF THROMBOCYTOPENIA CASES IN TERTIARY CARE HOSPITAL, MAHARASHTRA, INDIA

Haematology

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ABSTRACT

Background: Quantification of platelet indices in automated analyzers' has superiority over the manual estimation because it is quick, effortless and cost-effective method which also eliminates the observer bias and artefactual problems of manual method. We studied four platelet parameters i.e., MPV, PDW, LCR and PCT in cases of thrombocytopenia in order to interpret their importance, if any, behind the mechanism of low platelet count **Methods:** An observational study was undertaken for a period of six months from September 2023 to February 2024 in the pathology laboratory at Shrimati Kashibai Navale Medical College And General Hospital, Pune , Maharashtra using 6 part (SYSMEX 350) automated hematology analyzer . **Result:** A total of 200 patients with thrombocytopenia (<1,50,000 / µL) were included in the study. There were 64% males and 36% females in this study. In our study MPV & LCR increased as platelet count decreased . Thrombocytopenia cases were divided into two groups , namely group A which included thrombocytopenia due to Hyper destructive cause while group B included thrombocytopenia due to Impaired production of platelets. MPV, LCR, PCT and PDW platelet indices were higher Group A than Group B **Conclusion** : Platelet parameters like PDW, LCR,MPV and PCT can be used to interpret the mechanism behind the low platelet count. In our conclusion, any alterations in platelet volume indices can give an initial hint about the possible mechanism of thrombocytopenia like hypo proliferative category and increased peripheral destruction categories

KEYWORDS

Thrombocytopenia, PDW, LCR,MPV and PCT

BACKGROUND:

Thrombocytopenia is the presence of subnormal number of platelets in circulating blood. It may be the result of inadequate production of platelets or their peripheral destruction. The former are known as hypo proliferative thrombocytopenia's, while the latter are categorized as destructive thrombocytopenia's. [1]Thrombocytopenia is one of the common findings among patients in a clinical setting. It is defined by platelet count below the normal values and has a significant role in both hospitalized and non-hospitalized patients. [2]The counts below 1,50,000 / µL are considered as thrombocytopenia. [3]The clinical manifestation varies from mild symptoms such as easy bruising / mild bleeding to massive bleeding / hemorrhage that may result in death. [4] Platelets play a vital role in homeostasis and also have non-homeostatic role in angiogenesis, repairing of tissue and inflammation. [2] In order to evaluate the cause of low platelet count, it is necessary to relate whether it is due to hyper destruction or impaired production. Hyper destructive thrombocytopenia is a result of extramedullary destruction of platelets with a normal or an increased bone marrow production; causes comprise of malaria, dengue, idiopathic thrombocytopenic purpura (ITP), disseminated intravascular coagulation (DIC), hemolytic uremic syndrome (HUS). The category of impaired production is a result of primary or secondary bone marrow diseases with a decreased bone marrow production. It includes causes such as bone marrow aplasia, hematological malignancies, post chemotherapy, post radiation, hypersplenism etc. [5,6]After evaluating the mechanism behind the low platelet count, which can be helpful to the clinician in providing proper treatment to the patient. [7]Bone marrow aspiration study is the gold standard for finding the cause for thrombocytopenia, but its use is restricted since it is an invasive procedure. There is also a high risk of bleeding complication associated with the procedure. [8]Automated cell counters are used widely these days which furnish us the valuable information of various blood cell parameters including red blood cells, white blood cells and platelets with platelet parameters. [9]Recently platelet parameters like mean platelet volume (MPV), platelet distribution width (PDW), platelet crit (PCT) and large cell ratio (LCR) have been investigated as important platelet activation markers. All these parameters are provided by automated blood cells analyzer's and these indices can be correlated with platelet counts. [10] Quantification of platelet indices in automated analyzers' has superiority over the manual estimation because it is quick, effortless and cost-effective method which also eliminates the observer bias and artefactual problems of manual method. [11]The study of these platelet indices can help establish the mechanism behind thrombocytopenia. MPV and PDW are both derived from platelet distribution curve and related to change in platelet size and shape. [12]P-LCR can be used as an effective tool in distinguishing between hyper destruction and impaired production. [13] P-LCR is directly related to PDW and MPV, whereas it is inversely related to platelet count. [14]PCT is the volume occupied by the platelets in the blood and is expressed in terms of percentage and plays an important role in diagnosing platelet quantitative abnormalities. [2,15]Platelet indices can have a significant prognostic role as early evaluation of thrombocytopenia can help reduce morbidity and mortality of patients with low platelet count. This study aims to find the usefulness of these platelet indices in initial evaluation of possible pathogenesis of thrombocytopenia.

METHODS:

An observational study was undertaken for a period of six months from September 2023 to February 2024 in the pathology laboratory at SKNMC, Pune. All the blood samples of patients which were received in K3 EDTA anti-coagulated vacutainer in the laboratory were processed within one hour of collection using 6 part (SYSMEX 350) automated hematologyanalyzer. From the analyzer generated reports, platelets count, and platelet parameters that is mean platelets reports (MPV), platelet distribution width (PDW), platelet large cell ratio(P-LCR) and platelet crit (PCT) were recorded and platelet count was reassessed by peripheral blood smear examination on Leishman stained slides in all the cases. We studied 200 patients with thrombocytopenia (platelet count <1,50,000 / µL) from new born to old age.Control group included 50 persons who had all the hemogram parameters within normal limits.

Inclusion Criteria:

We have included patients of thrombocytopenia (below 1,50,000 / µL) of all age groups including new born.

Exclusion Criteria:

Patients on anti-platelet drugs and drugs causing thrombocytopenia were not included in present study.

Data is collected and analyzed. Platelets parameters (LCR, PCT, MPV

PDW) were then assessed in both the groups and compared with those of the control group.

Data Analysis And Statistical Interpretation:

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Association between Variables was analyzed by using Chi-Square test for categorical Variables. Normality of data was checked by using Shapiro-wilk test. Unpaired t test was used to compare mean of quantitative variables between 2 groups. Bar charts and Pie charts were used for visual representation of the analyzed data. Level of significance was set at 0.05.

RESULTS:

A total of 200 patients with thrombocytopenia (<1,50,000 / µL) were included in the study. There were 64% males and 36% females in this study. Also control (50 cases) group with all age group were studied for comparison of platelet indices with normal platelet count according to the age.

TABLE 1: shows the distribution of the case study with thrombocytopenia according to age (years) and gender(sex). Our age group ranged from new born (0 day) to old age (>60years). Maximum number of cases in females were seen in 11-20 years of age group (21%) and in males >60 years (34%).

Table 1: Distribution Of Study Subjects According To The Age (years) And Sex (male And Female) (n=200)

Age (Years)	Female n (%)	Male n (%)	Total n (%)
≤ 10	11 (15.3)	14 (10.9)	25 (12.5)
11-20	21 (29.2)	5 (3.9)	26 (13.0)
21-30	7 (9.7)	11 (8.6)	18 (9.0)
31-40	6 (8.3)	25 (19.5)	31 (15.5)
41-50	3 (4.2)	32 (25.0)	35 (17.5)
51-60	5 (6.9)	26 (20.3)	31 (15.5)
>60	19 (26.4)	15 (11.7)	34 (17.0)
Mean (SD)	34.23 (24.76)	42.14 (19.47)	39.29 (21.79)

Table 2: Comparison Of Platelet Indices With Severity Of Thrombocytopenia Among Cases (n=200)

Parameter	PLT <50000/ µL Mean (SD)	50000/ µL - 100000/ µL Mean (SD)	100000 / µL - 150000/ µL Mean (SD)	P Value
MPV	11.40 (0.67)	10.54 (0.73)	9.43 (0.85)	<0.001*
LCR	38.70 (11.40)	32.10 (9.39)	29.42 (10.71)	<0.001*
PDW	18.97 (2.09)	19.03 (2.07)	19.15 (2.27)	0.930
PCT	0.073 (0.095)	0.060 (0.029)	0.060 (0.030)	0.479

PDW – Platelet Distribution Width, MPV – Mean Platelet Value,LCR – Large Cell Ratio, PCT– Platelet crit,* The mean difference is significant at the level 0.05 level.

In TABLE 2 Comparison of the platelet indices with the severity of thrombocytopenia was also assessed. They were categorized into 3 categories: mild thrombocytopenia with platelet count ≥ 100000 / µL to <1,50,000 / µL, moderate thrombocytopenia with platelet countbetween > 50,000/ µL and ≤ 100000 / µL and severe thrombocytopenia with platelet count ≤ 50000/ µL. Our study showed a significant difference in MPV & LCR platelet parameters i.e.in our study MPV & LCR increased as platelet count decreased which appeared statistically significant (P < 0.001) while the rest of the parameters i.e. PDW &PCT didn't showed significant difference with platelet count In Table 3, Thrombocytopenia cases were divided into two groups , namely group A which included thrombocytopenia due to Hyper destructive cause while group B included thrombocytopenia due to Impaired production of platelets

Table 3- Classification of thrombocytopenia cases in Groups A and B

GROUPA (126 CASES) 63.0% (Hyper destructive causes)	GROUP B (74CASES) 37% (Impaired production of platelets)
Dengue (62 cases)	**Pancytopenia (23 cases)**
Sepsis (14 cases)	**Liver disease (22 cases)**
Renal diseases (12 cases)	**Iron deficiency anemia (9 cases)**
Viral infection (12 cases)	**Megaloblastic anemia (7 cases)**
DIC (11 cases)	**DVT (4 cases)**
ITP (3 cases)	**ALL (4 cases)**
Malaria (4 cases)	**TB (3 cases)**
Burns (4 cases)	**Chikungunya (2 cases)**
Pregnancy (3 cases)	
Respiratory distress (3 cases)	
Hemolytic anemia (1 case)	
Inborn errors (1 case)	

Table 4: Comparison of Lab parameters with Study Groups (N=200)

Parameter	Group A Mean (SD)	Group B Mean (SD)	Controls Mean (SD)	P Value
PCT	0.0879 (0.0673)	0.0303 (0.0126)	0.229 (0.007)	<0.001*
MPV	10.76 (1.13)	10.68 (0.92)	10.94 (0.60)	0.347
LCR	39.63 (12.28)	36.06 (10.88)	34.58 (2.76)	0.257
PDW	19.87(1.74)	17.62(1.85)	12.92 (0.54)	<0.001*

(PDW – Platelet Distribution Width, MPV – Mean Platelet Value, LCR – Large Cell Ratio, PCT– Platelet crit,* The mean difference is significant at the level 0.05 level.)

Table 5: Comparison Of Lab Parameters With Study Groups (n=200) Group A Vs Group B

Parameter	Group A Mean (SD)	Group B Mean (SD)	P Value
LCR	39.63 (12.28)	36.06 (10.88)	0.400
MPV	10.76 (1.13)	10.68 (0.92)	0.647
PDW	19.87 (1.74)	17.62 (1.85)	<0.001*
PCT	0.0879 (0.0673)	0.0303 (0.0126)	<0.001*

(PDW – Platelet Distribution Width, MPV – Mean Platelet Value, LCR – Large Cell Ratio, PCT– Platelet crit,* The mean difference is significant at the level 0.05 level.)

Table 4 and 5 showed decreased in mean PCT, MPV in group A and group B as compared to control group and increase in PDW as compared to control group**.** Mean MPV was 10.76 fL in group A which was higher as compared to 10.68 fL in group B. Mean LCR in our study was higher in group A (39.63)as compared to group B (36.06) . Mean PDW was higher in the cases of group A with the mean of 19.87 fL as compared to 17.62 fL in group B. Mean PCT was noted higher in group A (0.0879)as compared to Group B (0.0303) . So, MPV, LCR, PCT and PDW platelet indices were higher Group A than Group B. PDW (which was associated with variability in platelet size) and PCT both were higher in the cases of group A than group B which was statistically significant (P < 0.001)

DISCUSSION:

Thrombocytopenia is one of the common findings in many disease conditions. The major pathogenesis behind this is basically either due to decreased or impaired bone marrow production, peripheral accelerated destruction or due to increased splenic sequestration. Clinically, it is difficult to ascertain the reason behind the decrease in platelet count. Bone marrow studies, reticulated platelets and platelet associated IgG have been done in the past to evaluate the reason causing thrombocytopenia, but these are costly, invasive and not easily available procedures. Recently, many studies have taken the help of various platelet indices to assess the cause of thrombocytopenia. Platelet indices are easily available as most of the automated hematologyanalyzers' calculate these values. We studied four platelet parameters i.e., MPV, PDW, LCR and PCT in cases of thrombocytopenia in order to interpret their importance, if any, behind the mechanism of low platelet count and also compared these values with those of the controls.

Our study included 200 patients of thrombocytopenia, who were predominantly females. Correlation of severity of thrombocytopenia was studied with the changes in the platelet count and the platelet parameters. It was found that as the platelet count decreases there was increase in the mean values of MPV and LCR which was noted statistically significant in our study. Studies by Elsewefy DA et al.[20] and Borkataky S et al. [5]showed significant difference in mean LCR

values of patients with hypo productive thrombocytopenia with those of the control group. Our Study also showed similar findings.

MPV is a known marker of megakaryocytic activity. A high value is seen when there is excessive platelet lysis as it leads to increased bone marrow production of immature platelets. On reviewing the literature, many studies have shown higher values of these parameters in hyper destructive group as compared to hypo productive group,similar finding was noted in our study. Mean MPV was 10.76 fL in group A was high as compared to 10.68 fL in group B, which was in accordance with studies like Vinholt PJ et al.[10], Borkataky S et al. [5] and Reddy RS et al.[21] Nakadate H et al.[22] and Baynes RD et al.[23] .

Mean LCR in our study was higher in group A as compared to group B, which was consistent with other studies.[15, 24,22]

In this study, PCT and PDW showed a noteworthy difference when group A and B i.e. cases of hyper destruction and hypoproduction of platelets when compared with the control group, with a high significance of $P < 0.001$. PCT was noted higher in group A as compared to Group B.Mala K.G et al.[9] showed similar findings. PCT value measures the total platelet mass, and is dependent on MPV. Its value varies with platelet count and we found significantly higher values in group A and lower in group B which was statistically significant(P value<0.001)

PDW which was associated with variability in platelet size was higher in the cases of group A with the mean of 19.87 fL as compared to 17.62 fL in group B which was statistically significant ($P < 0.001$). Other studies also similarly showed high PDW in hyper destruction thrombocytopenia attributing to the release of heterogenous population of platelets with anisocytosis, the reason behind it.

CONCLUSION:

Platelet parameters like PDW, LCR,MPV and PCT can be used to interpret the mechanism behind the low platelet count, where high values of indices indicate increased breakdown of platelets in the bloodstream and low values are possibly due to impaired production due to primary or secondary bone marrow disease. In our conclusion, any alterations in platelet volume indices can give an initial hint about the possible mechanism of thrombocytopenia like hypo proliferative category and increased peripheral destruction categories, which can possibly reduce the need for the costly and invasive procedures at least in routine cases to know possible pathogenesis of thrombocytopenia cases.

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