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Role of Platelet Indices for Evaluation of Thrombocytopenia among Paediatric Age Group in A Tertiary Care Centre

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ABSTRACT
BACKGROUND: *Thrombocytopenia is common finding in pediatric age group. Though the platelet count below 150000 define thrombocytopenia do not reveal the underlying pathology can be assessed with platelet indices by avoiding the use of an invasive procedures like bone marrow aspiration or biopsy. The aim of our study is to evaluate the efficacy of platelet indices in differentiating hypoproductive from hyperdestructive thrombocytopenias and to assess sensitivity, specificity, positive predictive value, negative predictive value.*
METHODOLOGY: *Study done from October 2018 to September 2020, in a tertiary care center, during which 250 cases and controls were studied. Peripheral smear was done and stained withLeishman's stain. Rest of the sample was subjected to SYSMEX 6-PART- HEMATOLOGY- ANALYZER to determine the platelet indices. Bone marrow aspiration was done wherever indicated.*
RESULTS: *Out of total 250 cases 154 were included under the hyperdestructive type and 96 under the hypoproductive type. The platelet indices of hyperdestructive thrombocytopenias (Group I) was platelet count = (72.5 ± 37.4) x10^3 /mm, MPV = (10.9 ± 2.6) fl, PDW = (16.6 ± 2.05) fl, P-LCR = (42.3 ± 14.7) %. The platelet indices of hypoproductive thrombocytopenias (group II) was platelet count = (50.7 ± 32.9) x10^3 /mm, MPV = (7.9 ± 2.06) fl, PDW = (15.5 ± 3.5) fl, P-LCR = (19.90 ± 11.2) %. Comparative analysis of MPV, PDW & P-LCR of groupI and group II showed p value <0.05 proving it to be statistically significant.*
CONCLUSION: *Platelet indices provide useful information regarding the mechanism of thrombocytopenia and form a great diagnostic tool to differentiate hyperdestructive thrombocytopenias from hypoproductive thrombocytopenias as these are simple, cost effective,noninvasive & reliable. Among the platelet indices, mean platelet volume (MPV) provides muchmore reliable results in distinguishing both groups Interpretation of these platelet indices can help the patients to avoid unnecessary invasive investigations like bone marrow aspiration and unnecessary platelet transfusion.*
KEY WORDS: *Hyperdestructive thrombocytopenia, Hypoproductive thrombocytopenia, Mean platelet volume, Platelet distribution width, Platelet large cell ratio, Plateletcrit.*

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I. INTRODUCTION:

Platelets are produced by megakaryocytes within the bone marrow, count range from 1,50,000/mm^3 to 4,50,000/mm^3. Thrombocytopenia is defined as platelet count below 1,50,000/mm^3 [(1)] . Bone marrow aspiration remains the gold standard method for evaluating the causeof thrombocytopenia, but it is an invasive procedure and consumes a lot of time. There is a risk of bleeding in patients with severe thrombocytopenia. [(2)] The usage of Serology (for infectious diseases), Platelet associated Immunoglobulin G (PAIgG) and Molecular markers for Disseminated Intravascularcoagulation (DIC) in evaluating thrombocytopenia are relatively costly. [(3)]

Etio-pathologically thrombocytopenias can be categorized into hypoproductive & hyperdestructive types which can be differentiated by the combined interpretation of platelet indices with automation . These platelet indices include Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Plateletcrit (PCT), and Platelet large cell ratio (PLCR) which are obtained with a simple complete blood count and these parameters may provide some valuableinformation [(4)] and these are simple, cost-effective, noninvasive & reliable. The aim is to study clinicopathological spectrum in various thrombocytopenias, and evaluate the efficacy of plateletindices in differentiating hypoproductive type from hyperdestructive thrombocytopenias, and assess the sensitivity, specificity, positive predictive value, negative predictive value. To study bone marrow findings in various thrombocytopenias whenever needed and to correlate with platelet indices.

II. MATERIALS & METHODS:

It is an observational study for a period of 2 years with a sample size of 250 cases & 250 controls. All paediatric patients aged less than 18 years of both sexes with a platelet count of less than 1.5 lakh/$mm^3$are included and cases aged more than 18 years, patients on medications causing thrombocytopenias, those cases with unavailable platelet indices and who received multiple platelet transfusions were excluded from the study.

Clinical data recorded as per proforma. 2ml Blood was collected in EDTA vacutainer. Peripheral smear was done and stained with Leishman 's stain**.** Rest of the sample was subjected to SYSMEX 6-PART-HEMATOLOGY- ANALYZER to determine the platelet indices. Stastical analysis was done using Microsoft Excel 2010 and Statistical Package for the Social Sciences (SPSS) for Windows version 21.0 .

Mean platelet volume (MPV): It signifies the average size of platelets in the blood. Normal range- 7.5 to 11.5 fl[(5)].Increases in hyperdestruction and decreases in hypoproduction.
Platelet distribution width (PDW): PDW is a marker of platelet anisocytosis, which increases upon platelet activation. [(6)] PDW range between 10 and 18%. Increases in hyperdestruction anddecreases in hypoproduction.

Platelet large cell ratio (P-LCR): It is a percentage of all platelets with a volume measuring over 12 fl circulating in the bloodstream. It normally ranges between 15 and 35%. [(7)] Increases in hyperdestruction and decreases in hypoproduction.

Plateletcrit (PCT) : Plateletcrit (PCT) measures total platelet mass as a percentage of volume occupied in the blood. The normal range for PCT is 0.12–0.24%[(8)] .Its value is not altered by severity of thrombocytopenia of either hypoproductive or hyperdestructive etiology.

III. OBSERVATIONS & RESULTS:

A total of 250 patients and 250 controls were included in the study. Out of total number of cases(n=250), 102 patients were under the severe category with platelet count less than 50000/cu mm. (Table Fig.1). Majority of the cases were in the age group of < 6 years (50%). Among 250 cases, 133 were males (53.2%) and 117 were females (46.8%) M: F ratio was 1.13:1. Males are more commonly affected. Fever was the most common chief complaint of presentation (48.4%). Dengue was the most common cause of hyperdestructive thrombocytopenia amounting to 23.3 %. Out of 96 cases of thrombocytopenia due to hypoproduction 16 cases (16.6%) were leukemia, 25 cases (26.0%) pancytopenia (Table.2)(Fig.2)**.**Bone marrow aspiration was done in a total number of 34 cases (n=34) Out of these 34 cases, 4 cases (11.76%) were hyperdestructivetype and 30 cases (88.23%) were thrombocytopenia of hypoproductive type (Table.5). MPV, PDW, P-LCR increased in hyperdestructive thrombocytopenia (Group I) cases with a P value of <0.0001 (p- value < 0.05 significant (Table.5). MPV, P-LCR decreased in hypoproductive thrombocytopenia (Group II) cases with a P value of 0.0017, 0.0013 respectively (p- value < 0.05 significant) (Table.5). MPV, PDW, P-LCR increased in hyperdestructive cases and decreased in hypoproductive cases. PLT- crit decreased in both groups. (Table.5). The sensitivity, specificity, positive predictive value and negative predictive value of MPV were representative. PDW increased in hyperdestructive cases and the statistical analysis was representative (Table.6). P-LCR increased in hyperdestructive cases and decreased in hypoproductive cases. The sensitivity, specificity, positive predictive value, negative predictive value was representative. (Table.6)

Table 1. Distribution of cases based on severity of thrombocytopenia

Platelet count per cu mm	Number of cases (n=250)	%
Mild (100000- 150000)	52	20.8
Moderate(50000- 100000)	96	38.4

Severe (<50000)	102	40.8
Total	250	100

Table 2: Etiological distribution of cases with thrombocytopenia in whom bone marrowaspiration was done (n=34)

Etiological distribution		**Number ofcases (n=34)**	**Percentage**
Hyperdestructive	ITP	2	5.8
	Dengue	2	5.8
Hypoproductive	Leukemia	5	14.7
	Megaloblastic anemia	4	11.7
	Aplastic anemia	1	2.9
	Myeloproliferative disorder	1	2.9
	Storage disorder	1	2.9
	Hypoplastic marrow	10	29.4
	Pancytopenia	5	14.7
	Anemia	3	8.8

Table 3: Comparison of PLT indices between group I and control

Parameter	**Cases**	**Controls**	**P Value**
PLT count (mean ± SD)	72.51 ± 37.47 x10^3/mm	276.7 ± 92.6 x10^3/mm	P<0.0001
MPV (mean ± SD) fl	10.98± 2.60 fl	8.77 ± 1.29 fl	P<0.0001
PDW (mean ± SD) fl	16.69 ± 2.05 fl	14.12 ± 2.60 fl	P<0.0001
P-LCR (mean ± SD) %	42.31 ± 14.75 %	24.64 ± 8.31 %	P<0.0001
PLT-crit (mean ± SD) %	0.075 ± 0.039 %	0.236 ± 0.734 %	

Table 4: Comparison of PLT indices between group II and control

Parameter	**Cases**	**Controls**	**P Value**
PLT count (mean ± SD)	50.79 ± 32.99 x10^3/mm	274.4 ± 91.63 x10^3/mm	P<0.0001
MPV (mean ± SD) fl	7.96 ± 2.06 fl	8.59 ± 1.21 fl	P= 0.0017
PDW (mean ± SD) fl	15.54 ± 3.50 fl	14.27 ± 2.55 fl	P= 0.0044
P-LCR (mean ± SD) %	19.91 ± 11.23 %	24.60 ± 8.47 %	P= 0.0013

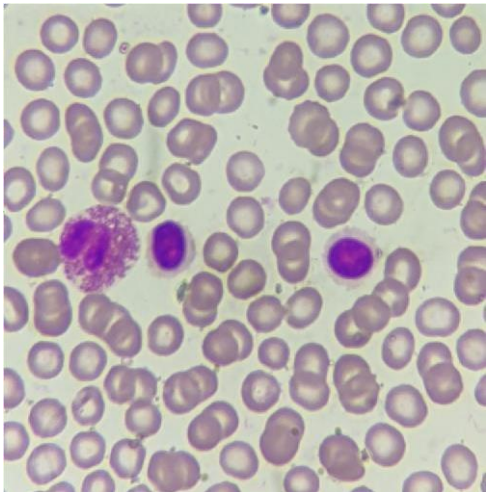
Table 5: Comparison of PLT indices in cases where bone marrow aspiration was indicated.

Parameter	**Hyperdestructive**	**Hypoproductive**
PLT count (mean ± SD)	25.000 ± 0.99 x10^3/mm	39.6 ± 24.0 x10^3/mm
MPV (mean ± SD) fl	13.65 ± 2.20 fl	6.95 ± 0.47 fl
PDW (mean ± SD) fl	18.12 ± 2.45 fl	15.06 ± 4.25 fl
PLT-crit (mean ± SD) %	0.03 ± 0.01 %	0.03 ± 0.02 %
P-LCR (mean ± SD) %	69.6 ± 7.67 %	15.84 ± 9.29 %

Table6: Statistical analysis of MPV, PDW, P-LCR in Group I and Group II

	MPV		**PDW**		**P-LCR**	
	GROUP 1	**GROUP 2**	**GROUP 1**	**GROUP2**	**GROUP 1**	**GROUP 2**
SENSITIVITY	**92.2%**	**95.8%**	**96.1%**	**98%**	**97.4%**	**99%**
SPECIFICITY	**96.1%**	**94.7%**	**97.4%**	**93.7%**	**98%**	**96.8%**
+VE PREDICTIVEVALUE	**95.9%**	**94.8%**	**97.3%**	**94%**	**98%**	**96.9%**
-VE PREDICTIVEVALUE	**92.5%**	**95,7%**	**96.1%**	**97.8%**	**97.4%**	**99%**

PHOTOMICROGRAPHS



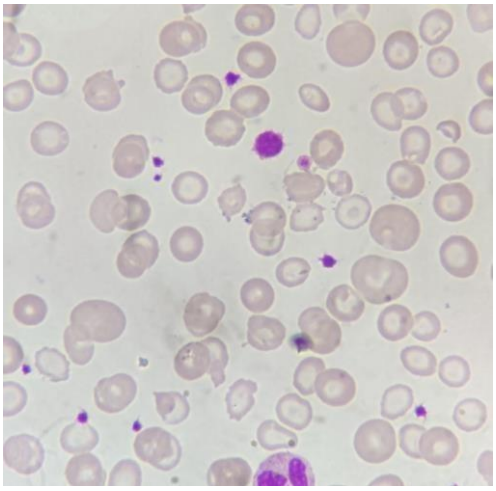
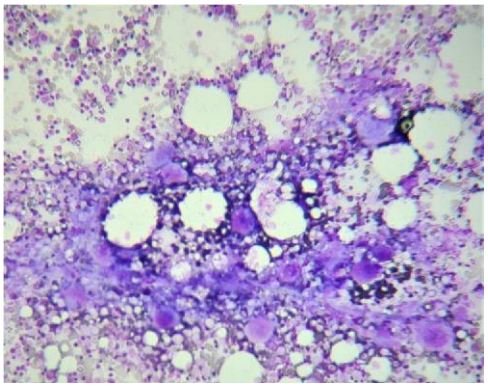


Fig1: Peripheral smear showing eosinophil and lymphocytes. Platelets are absent. (Leishman stain 1000x)
Fig 2: Peripheral smear showing giant platelet with adjacent normal platelets (Leishman's stain 1000x)



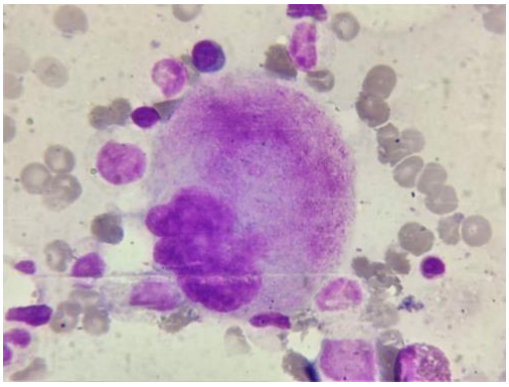


Fig 3a- BMA smear shows increased in number of megakaryocytes (Leishman) 40x
Fig 3b- BMA smear shows hypolobated megakaryocyte (Leishman) 100x

IV. Discussion :

Platelets play a significant role in normal hemostasis.Quantitative alterations in platelets (thrombocytopenia) cause great morbidity. Automated hemogram is a test that is quick , easily available , very simple, inexpensive. Platelet indices (MPV, PDW, PCT ,PLCR) offer an additional diagnostic, as well as, prognostic value. In this study platelet indices of 250 cases with thrombocytopenia among pediatric age group were assessed (Table .1) The controls were age matched. Cases were categorized into two groups based on the mechanism of thrombocytopenia. Group I were cases of thrombocytopenia due to hyperdestruction. Group II were cases of thrombocytopenia due to hypoproduction.

Age distribution: The most frequently encountered age group in this study was 0- 6 yrs (50%) which is comparable to the study conducted by Muhury M. et.al, ([9]) Pokharel S et.al. [(10)] in which the most common age group was <10 years.

Sex Distribution: Male population was predominant in this study (53.2%) which was also a finding in studies of Choudhary et.al. [(11)] (61.9%), Gupta et.al. [(12)] (58%) and Muhury et.al (65.9%)
[(9)], Reddy et al, [(13)] Afsar et al. [(14)]

Chief complaints: most common chief complaint was fever (48.4%) similar complaint was noted in >50% of patients in study done by Shigeki H. et al. [(15)] Out of total 250 thrombocytopenia cases in this study 154 were of hyperdestructive type and 96 hypoproductive type which correlate with the study done by Shaheena et al [(16)] in which out of 120 cases hyperdestructive cases were 94 and hypoproductive cases were 26.

Etiological distribution: Dengue was the most common in hyperdestructive group similar to Katti et al [(17)] and Shaheena et al [(16)] ,Leukemia was the most common in hypoproductive group similar to Numbenjapon et al. [(18)]

Platelet count: In the present study mean platelet count in hyperdestructive and hypoproductive cases were 72.51x 10^3 / cumm and 50.79x 10^3 / cumm respectively. Counts decreased in both groups with no statistical significance this correlated with the studies of Kaitoet al and Parveen et al [(16)]. (Table.3 &4)(Fig.1)

Mean Platelet Volume (MPV): Mean platelet count of Group I cases was 72.51x10^3 /cu mm ,Mean MPV of Group I cases was 10.98 fl. Mean platelet count of Group II cases was 50.791x10^3 / cu mm ,Mean MPV of Group II cases was 7.96 fl . This study showed linear correlation between platelet count and MPV in hypoproduction group (group II) and inverse relation in hyperdestruction group (Group I). Thrombocytopenia secondary to increased destruction have larger platelets, reflecting active bone marrow compensation with release of young platelets. MPV was higher than normal in hyperdestructive cases (ITP) with a P value of <0.001 (P <0.05 - significant) and was low in hypoproductive cases (acute leukemias & aplastic anemias) with a P value of 0.0017 (P <0.05 - significant). (Table3&4). The mean MPV increased in hyperdestructive thrombocytopenias and decreased in hypoproductive thrombocytopenias which correlated with Baig MA [(19)] Numbenjapon et al [(18)] and Ntaios et al [(20)] . The sensitivity (92.2%), Specificity (96.1%), Positive predictive value (95.9%), Negative predictive value (92.5%) of MPV in differentiating hyperdestructive thrombocytopenias from hypoproductive thrombocytopenias in this study correlated with Ntaios et al [(20)], Baig MA.[(19)]

Platelet distribution with (PDW) : In cases of hyperdestructive thrombocytopenia PDW increased which coincided with the study Baig MA [(19)], Borkataky et al. [(21)]

Mean PDW for Group II cases and controls in our study is 15.54 fl and 14.2 fl respectively. PDW increased in hypodestructive cases which did not correlate with the study of Baig MA[(19)] but coincided with the study of Negash et al [(22)].This contrasting result was attributed to significant dysplasia of hematopoiesis in the bone marrow in the hypoproductive group.(Table.3&4)

In the present study the sensitivity (96.1%), Specificity (97.4%), Positive predictive value (97.3%), Negative predictive value (96.1%) of PDW in diagnosing hyperdestructive thrombocytopenia correlated with Ntaios et al [(20)], Baig MA [(19)].

Platelet Large Cell Ratio (PLCR) :In the present study Mean PLCR in hyperdestructive cases was increased(42.3%) and and decreased (19.9%) in hypoproductive cases. This correlated with the studies of Negash et al [(22)] and Baig MA [(19)].

The sensitivity (97.4%), Specificity (98%), Positive predictive value (98%), Negative predictive value (97.4%) of PLCR in diagnosing hyperdestructive thrombocytopenia correlated with Baig MA. (19)

Plateletcrit (PCT) :PCT was not significantly different in both groups similar to the studies of Parveen et al and khaleel et al. No study considers it as a valuable indices to differentiate between hypo-productive and hyper-destructive thrombocytopenia , PCT represent a volume percent of platelets and its value is a result of PDW multiplied by platelet count so it is affected by the severity of thrombocytopenia of any cause. [(23)]

V. Conclusion:

To conclude, platelet indices especially MPV, PDW, P-LCR can be used as a diagnostic tool to differentiate hyperdestructive thrombocytopenia from hypoproductive type. Among these indices MPV being most reliable. Though bone marrow aspiration being gold standard platelet indices can avoid unnecessary invasive procedures and unwanted platelet transfusions.

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