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Research Article

Platelet indices- evaluation of their diagnostic role in pediatric thrombocytopenias (one year study)

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ABSTRACT

Background: Thrombocytopenias can be categorised into hypoproliferative (group I) & hyperdestructive types (group II) based on their etiology. Platelet indices (MPV, PDW, P-LCR, platelet-crit) can be used to differentiate this type of thrombocytopenias & these are simple, cost-effective, noninvasive & reliable. The main objective of this study was to evaluate the efficiency of platelet indices to differentiate hypoproductive type from hyperdestructive thrombocytopenias.
Methods: Automated Hematology Analyzer Sysmex XT-2000i used to assess platelet indices. 100 Cases of thrombocytopenia & age adjusted (similar age group) controls with normal CBC & peripheral blood smears were included in the study. The gender was not taken into account as the ranges of platelet indices are almost the same for boys & girls of similar age groups.
Results: The platelet indices of group I was platelet count = (51.8 ± 31.6) $x10^3$/mm, MPV = (8.5 ± 1.27) fl, PDW = (14.10 ± 1.15) fl, P-LCR = (31.90 ± 3.46)%. The platelet indices of group II was platelet count = (39.6 ± 32.7) $x10^3$/mm, MPV = (11.6 ± 2.25) fl, PDW = (15.16 ± 1.36) fl, P-LCR = (34.30 ± 2.2)%. Comparative analysis of MPV, PDW & P-LCR of group I and group II showed p value <0.05 proving it to be statistically significant.
Conclusions: The combined interpretation of MPV, PDW & P-LCR by automated cell counters can be very useful parameters in differentiating thrombocytopenias due to various etiologies. Platelet indices showed inverse relationship with platelet count as they are increased in hyperdestructive type & shows linear relationship in hypoproliferative type. MPV, PDW & P-LCR can be precisely used to differentiate hyperdestructive type (ITP) from hypoproliferative type (acute leukemias, aplastic anemias). Platelet-crit & platelet large cell ratio are less sensitive parameters to differentiate these thrombocytopenias.

Keywords: Hyperdestructive thrombocytopenia, Hypoproductive thrombocytopenia, Platelet large cell ratio, ITP, MPV, PDW, Sensitivity, Specificity, Positive predictive value

INTRODUCTION

Platelets (PLT) are membrane bound discoid structures that play a central role in hemostasis.

Normal platelet count range from 1,50000/mm^3 to 4,50000/mm^3. Thrombocytopenias is defined as platelet count below 1,50000/mm^3 after control of pre-analytical and analytical variables.[1]

Thrombocytopenias can be divided into Mild (<100000/mm^3), Moderate (20000-50000/mm^3) & Severe (<20000/mm^3). Aetio-pathologically thrombocytopenias can be categorised into hypoproliferative & hyperdestructive types (Levine, 1999).

Thrombocytopenia (hypoproduction)[2]

- Impairment of platelet production
  - Drug-induced:
  - Infections: measles, HIV
- Nutritional deficiencies
  - B_{12}, folate deficiency
- Bone marrow failure
  - Aplastic anemia, Fanconi anemia
- Bone marrow replacement
  - Leukemias, granulomatous diseases
  - MDS

Thrombocytopenia (hyperdestruction)[2]

- Immune Thrombocytopenic Purpura (ITP)
- Primary
- Secondary
  - Non Immunological
  - DIC

Platelet size is a useful indicator to differentiate between hypoproliferative & hyperdestructive thrombocytopenias. The combined interpretation of platelet (PLT) count, platelet-crit (PCT), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) & Platelet Large Cell Ratio (P-LCR) by automated cell counters can be very useful parameters in differentiating thrombocytopenias due to various etiologies.

PLT indices forms a great diagnostic tool to differentiate ITP from acute leukemias as these are simple, cost-effective, noninvasive & reliable.

Mean Platelet Volume (MPV) is average size of the platelets in Blood. Normal range of MPV = (7.5-11.5 fl). Usually MPV >13 occurs in hyperdestruction & MPV <8 in hypoproduction of platelet.

Best cut off value for MPV for ITP was greater than 9.7 fl.[3] Platelet Distribution Width (PDW) is an indication of variation in platelet size which can be a s ign of active platelet release. The PDW median was 13.3%, with a reference range of 10.0%-17.9% for the 5^{th}-95^{th} percentiles, with a confidence interval of 95%.[3]

Platelet-crit is a measure of total platelet mass. The cut off value in thrombocytopenias[3] is 0.2-0.36%. Platelet-crit is an effective screening tool for detecting platelet quantitative abnormalities.

Platelet Large Cell Ratio (P-LCR) is increased in destructive thrombocytopenia than those with hypoproliferative thrombocytopenia. P-LCR was inversely related to platelet count and directly related to PDW and MPV. Platelet large cell ratio if properly utilised can be a good aid in the differential diagnosis of conditions associated with abnormal platelet counts.

P-LCR was greater than 33.6%, with a diagnostic accuracy of 70.1 and 99.6%, respectively.[4]

Need for study

Studies done to evaluate the usefulness of platelet indices for the differential diagnosis of the causes of thrombocytopenia showed a good diagnostic correlation with the bone marrow aspirate findings. These studies have been performed on the adult population, but very few on the pediatric population.

PLT indices forms a great diagnostic tool to differentiate ITP from acute leukemias as these are simple, cost-effective, noninvasive & reliable.

This has prompted me to do this study.

Aims and objectives

- To evaluate the efficiency of platelet indices to differentiate hypoproductive type from hyperdestructive thrombocytopenias
- To assess the sensitivity, specificity, positive and negative predictive values of platelet indices
- To study the platelet morphology in few rare hematological disorders

METHODS

This was an one year study (April 2012 - March 2013) conducted in a Pediatric tertiary Referral Hospital. This study comprises a total of 100 pediatric cases referred to the hospital during 1 year period.

For convenience in tabulation, the results of the patients were categorised into hypoproductive & hyperdestructive types based on the etiology of thrombocytopenias.

Sysmex Automated Hematology Analyzer XT-2000i advanced instrument was used for CBC & platelet indices. The specific parameters included in the study were PLT count, MPV, PDW, P-LCR, PLT-crit. The controls for PLT indices were taken from 100 children of similar age groups with normal CBC & PBS. The cases & controls were age adjusted (similar age groups). The

gender was not taken into account as the range of PLT indices are almost the same for male & female children of similar age groups.

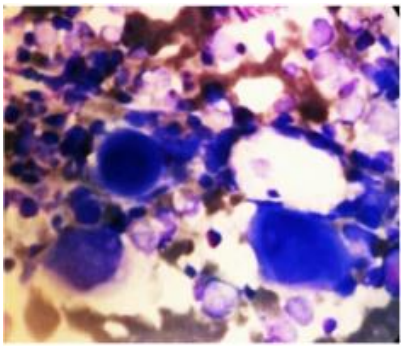

Figure 1: Megakaryocytic hyperplasia (ITP).

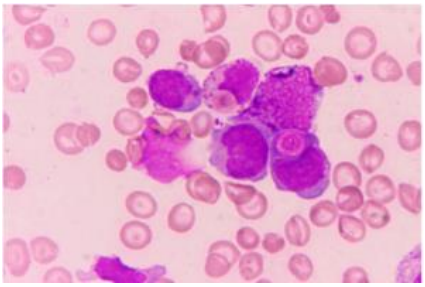

Figure 2: Single large and multiple small giant purple granules (Chediak Higashi syndrome).

The various defining criteria are as follows

Platelet count for control group = (mean ± SD) x 10^9/l; PLT = (210 ± 40) x 10^9/l

MPV is Average size of the platelets in Blood. MPV = (mean ± SD) (fl), MPV = (9.7 ± 1.48) fl

PDW: an indication of variation in platelet size which can be a sign of active platelet release. PDW = (mean ± SD)%, PDW = (14.46 ± 1.68)%

Platelet-crit is a measure of total platelet mass. Normal range of PCT for controls is 0.1-0.31%.

P-LCR is increased in destructive thrombocytopenia than those with hypoproliferative thrombocytopenia. P-LCR was inversely related to platelet count and directly related to PDW and MPV. P-LCR = (mean ± SD) (%); P-LCR = (33.40 ± 2.96)%

The diagnosis of various hematological disorders like ITP, aplastic anemias, ALL & its subtyping, AML & its subtyping, MDS, were made on PBS examination, bone marrow aspiration slides examination, flow cytometry, molecular & cytogenetic studies.

Inclusion criteria: All patients with confirmed diagnosis by peripheral blood smear, bone marrow aspiration & flow cytometry were included in the study.

Exclusion criteria: Patients receiving drugs like aspirin were not included in the study because aspirin interferes with platelet production.

RESULTS

Total number of cases in the present study = 100
Total number of age matched controls = 100

Sex wise distribution of cases was not done because age matched controls of different gender have almost same PLT indices.

For mathematical convenience,

Thrombocytopenia (Hypoproduction) = Group I
Thrombocytopenia (Hyperdestruction) = Group II

Table 1: Etiological distribution of cases.

Hypoproduction (65 Cases)			**Hyperdestruction (35 cases)**		
Thrombocytopenia causes	**Total number of cases**	**% of hypoproduction cases**	**Thrombocytopena causes**	**Total number cases**	**% of hyperdestrction cases**
ALL	38	58%	ITP	30	85%
AML	09	13%			
AA	10	15%	DIC	05	15%
MA	02	03%			
MDS	02	03%			
Rare cases					
AML (M6B)	01	1.5%			
CHS	01	1.5%			
MH	01	1.5%			
FA	01	1.5%			

AA - Aplastic anemia; MA- Megaloblastic anemia; CHS - Chediak Higashi syndrome; MH - May Hegglin; FA - Fanconi anemia

Table 2: PLT indices in group I, group II and control.

PLT indices[5]	Group I	Control	Group II
PLT count (mean ± SD)	(51.8 ± 31.6) x 10^3/mm	(210 ± 40) x 10^3/mm	(39.6 ± 32.7) x 10^3/mm
MPV = (mean ± SD) fl	(8.5 ± 1.27) fl	(9.7 ± 1.48) fl	(11.6 ± 2.25) fl
PDW = (mean ± SD) fl	(14.10 ± 1.15) fl	(14.46 ± 1.68) fl	(15.16 ± 1.36) fl
P-LCR = (mean ± SD)%	(31.90 ± 3.46)%	(33.40 ± 2.96)%	(34.30 ± 2.20)%
PLT-crit = %	(0.08-0.12)%	(0.1-0.31)%	(0.09-0.14)%

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

PLT indices	Group I	Control	P value
PLT count	(51.8 ± 31.6) x 10^3/mm	(210 ± 40) x 10^3/mm	0.068
MPV = (mean ± SD) fl	(8.5 ± 1.27) fl	(9.7 ± 1.48) fl	0.02*
PDW = (mean ± SD) fl	(14.10 ± 1.15) fl	(14.46 ± 1.68) fl	0.02*
P-LCR = (mean ± SD)%	(31.90 ± 3.46)%	(33.40 ± 2.96)%	0.03*
PLT-crit	(0.08-0.12)%	(0.1-0.31)%	0.1

*P value <0.05: Statistically significant

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

PLT indices	Group II	Control	P value
PLT count	(39.6 ± 32.7) x 10^3/mm	(210 ± 40) x 10^3/mm	0.080
MPV = (mean ± SD) fl	(11.6 ± 2.25) fl	(9.7 ± 1.48) fl	0.022*
PDW = (mean ± SD) fl	(15.16 ± 1.36) fl	(14.46 ± 1.68) fl	0.02*
P-LCR = (mean ± SD)%	(34.30 ± 2.20)%	(33.40 ± 2.96)%	0.01*
PLT-crit	(0.09-0.14)%	(0.1-0.31)%	0.15

*P value <0.05: Statistically significant

Table 5: Statistical analysis of MPV in Group I and Group II.

MPV	Group I	Group II
Sensitivity	98%	97.8%
Specificity	98%	97.8%
+Ve predictive value	98%	97.8%
-Ve predictive value	98%	97.8%

Table 6: Statistical analysis of PDW in Group I and Group II.

PDW	Group I	Group II
Sensitivity	98%	98%
Specificity	98%	98%
+Ve predictive value	98%	98%
-Ve predictive value	98%	98%

Table 7: Statistical analysis of P-LCR in Group I and Group II.

P-LCR	Group I	Group II
Sensitivity	97%	99%
Specificity	97%	99%
+Ve predictive value	97%	99%
-Ve predictive value	97%	99%

DISCUSSION

Thrombocytopenia is defined as platelet count below 150000/mm^3 after control of pre-analytical and analytical variables. It is frequently found in patients that access emergency care, and for that reason it is important to have a diagnostic tool that helps distinguish between its two main causes: the reduction of platelet production and the destruction of platelets. Availability of an automated hemogram, a test that is quick and easily available in a clinic, makes this test a very useful element.[6]

In this study thrombocytopenia is divided into hypoproductive (Group I) and hyperdestructive (Group II) type based on the etiology.

In this study PLT indices (MPV, PDW, P-LCR) measured by SYSMEX XE 2100 very well correlated with other published studies Pekelharing, J Botma, Kaito (Table 8).

The most common cause of thrombocytopenia in this study ALL comprised 38% of the total cases. This can be explained by the fact that: ALL is the commonest type of Leukemia in children comprising 80 % of all leukemias.[2] As this is tertiary terminal referral centre all the cases of leukemias are transferred here.

Table 8: Comparison of PLT indices with other published studies.

Author	Auto-analyzer	MPV fl	PDW fl	P-LCR %
Pekelharing [7]	SYSMEX XE - 2100	9.1-12.1	9.9-16.1	29.6-35.8
J. Botma [8]	SYSMEX XE - 2000	8.8-12.5	0.19-0.40	34-43
Kaito [9]	SYSMEX XE - 2001	8.7-13.1	10.1-17.9	31-37
Present study	SYSMEX XE – 2000i	9.3-13.8	12.4-16.1	30.4-36.3

In this study, it was found that the platelet-derived indices of mean platelet volume, platelet distribution width, and platelet-large cell ratio show significantly high values for cases of ITP compared with hypoproductive type. The sensitivity, specificity, positive p-value, and the negative p value of the platelet-derived indices were appropriate for differentiating between thrombocytopenias due to platelet destruction (ITP) and low platelet production as was observed in studies carried out by Bowles et al.;[10] Lee WS;[11] Briggs C;[12] Farias;[13] Brummitt;[14] Lanzkowsky P.[15]

In the present study average MPV for Controls was 9.7 fl & for Group I is 8.5 fl & for Group II is 11.6. The MPV was clearly higher than normal in ITP & was low in case of acute leukemias & aplastic anemias. P value = 0.002 (P <0.05 - significant).

Mean PDW for control = 14.46 fl & was 14.1 fl in hypoproductive & 15.16 fl in hyperdestructive types. P value = 0.002 (P <0.05 - significant).

In the present study, the P-LCR was significantly higher in ITP patients compared with the control group and significantly lower in hypoproductive thrombocytopenia patients compared with the control group. These results are in comparison with Borkataky et al. P value = 0.002 (P <0.05 - significant).

CONCLUSION

The combined Interpretation of MPV, PDW & P-LCR by automated cell counters can be very useful parameters in differentiating thrombocytopenias due to various etiologies.

Platelet indices forms a great diagnostic tool to differentiate ITP from acute leukemias as these are simple, cost effective, noninvasive & reliable.

The results of present study conclude that:

PLT indices showed inverse relationship with platelet count as they are increased in hyperdestructive type & linear relationship in hypoproliferative type

Platelet counts are less sensitive parameters to differentiate ITP from ALL & AA.

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Ethical approval: Not required

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