Platelet Distribution Width (PDW) - A Rarely Studied Platelet Indice for Determining the Causes of Thrombocytopenia.

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ABSTRACT

Background: Thrombocytopenia (TCP) is low platelets count, which is either due to defective platelet production or due to increased platelet breakdown. The platelet number alone does not give a complete picture of platelet maturity and function, therefore, the platelet indices have been the subject of intensive study in recent years, but they have not been firmly established. Mean platelet volume (MPV) and platelet distribution width (PDW) are useful parameters in evaluating disorders of platelets. This study was undertaken to evaluate the effectiveness of PDW in diagnosing causes of thrombocytopenia. Methods: 510 cases of thrombocytopenia and 500 cases of Control group with normal platelet count were included in the study. TCP was defined as platelet counts below 1.5 lacs/cumm. Hematological analysis was done on Mindray BC-3000 plus automated hematology analyzer. All cases were reevaluated by peripheral smear examination. Only those cases were included in the study, which showed platelet count and platelet volume parameters with graph both in cases and in control group. Results: Hyper-destructive group constituted majority of the cases 352 (69%), while hypo-production group and abnormal pooling constituted 30% and 1.42% cases respectively. The mean PDW was significantly higher in hyper-destructive group when compared with hypo-productive group, Abnormal pooling and control group. The difference was statistically significant. Conclusion: PDW provides plenty of clinical information about the causes and patho-mechanisms of thrombocytopenia and could be helpful to distinguish hyper-destructive thrombocytopenia from hypo-productive thrombocytopenia. More attention should be paid to PDW along with other platelet indices to differentiate between hyper-destructive TCP from hypo-productive and abnormal pooling TCP. Keywords: Platelet distribution width (PDW), Platelet indices, Platelet volume parameters & Thrombocytopenia (TCP).

INTRODUCTION

Thrombocytopenia (TCP) may be defined as a subnormal number of platelets in the circulating blood. It is the most common cause of abnormal bleeding. Despite the number and diversity of disorders that may be associated etiologically, TCP results mainly from three processes: Hyper-destruction of platelets, hypo-production of platelets and abnormal pooling of the platelets within the body.¹ It is important to know whether TCP is due to one of the above three causes.

In many cases of TCP, larger platelets are seen in peripheral smear, this size of platelets was suggested to help in deciding the category of TCP long back. Initially size was noted by microscopic studies only.² The diagnosis of TCP requires bone marrow examination, platelet-associated immunoglobulin G (PAIgG) and reticulated platelets. These methods are either invasive &/or costly and not available routinely. With the advancements in automated hematology analyzers new platelet parameters are available resulting in greater precision and faster processing of specimens. Some of these parameters include platelet indices, such as mean platelet volume (MPV) and platelet distribution width (PDW). However, despite being routinely available, these indices are generally considered as not interpretable and are rarely used by laboratories and physicians.³¹ MPV and PDW are increased in TCP.³² Several studies on these parameters have shown that they can be used to determine the cause of TCP and they have sufficient sensitivity and specificity in the diagnosis of TCP.¹⁴–⁶ The platelet distribution width (PDW) is a measure of platelet anisocytosis and can indicate if thrombocytes are normally distributed or if there is technical error and if the measured cells are thrombocytes.¹⁷ PDW
expresses the distribution of the size of platelets produced by the megakaryocyte. Most of the clinicians are interested in patients platelet (PLT) count, some give attention to MPV, however PDW is the least looked upon platelet indice. Osselacr JC in his study observed that PDW is certainly an important but forgotten platelet parameter. Thus we have undertaken this study to ascertain the value of this forgotten parameter, PDW in distinguishing various categories of thrombocytopenia.

**MATERIALS AND METHODS**

The present study was carried out from January to December 2015 in the department of pathology at Chirayu medical college and hospital, Bhopal, India. During this period, 510 cases of thrombocytopenia were studied. Control group included 500 cases with normal platelet count, RBC count and WBC count. Detailed history was obtained regarding age, sex, clinical diagnosis and other hematological parameters from the case records of the patients. Hematological analysis was done on Mindray BC-3000 plus automated hematology analyzer with blood collected in K-EDTA blub within 30 minutes to 5 hours of collection. Only those cases were included in the study, which showed platelet count and platelet volume parameters with graph both in cases and in control group. Peripheral smear examination was done in each case of TCP and those cases with different results by these methods were excluded from the study. Proportion, mean and standard deviation was calculated. TCP was defined as platelet counts below 1.5 lakhs/ul. Clearance was obtained from institutional ethical committee. Data was analyzed and ANOVA test was applied as a test of significance. P value <0.05 was considered as significant.

**RESULTS**

Total 510 cases of TCP were studied for the present study. Out of these 318 (62.35%) were males and 192(37.65%) were females with a male to female ratio of 1.6:1. A slight male preponderance was seen for the whole study and also in all age groups. Age ranged from 4 months to 87 years. Most of the cases of TCP was seen between 11-20 years age group accounting for 92(18.03%) cases. 75 cases (14.70%) were seen in age group of 31-40 years while 13 % cases belonged to age group of 21-30, 41-50, 51-60 & 61-70 years each. [Table 1].

| Table 1: Age and sex distribution. |
|-----------------------------------|
| Age    | No of cases | Male | Female | %   |
| < 1 year | 1           | 1    | 0      | 0.19 |
| 1-10 year | 48          | 35   | 13     | 9.41 |
| 11-20 year | 92          | 63   | 29     | 18.03|
| 21-30 year | 70          | 48   | 22     | 13.72|
| 31-40 year | 75          | 39   | 36     | 14.70|
| 41-50 year | 70          | 51   | 19     | 13.72|
| 51-60 year | 68          | 37   | 31     | 13.33|
| 61-70 year | 69          | 31   | 38     | 13.52|
| 71-80 year | 11          | 9    | 2      | 2.15 |
| 81-90 year | 6           | 4    | 2      | 1.17 |
| 91-100 year | 0           | 0    | 0      | 0    |
| TOTAL | 510 | 318(62.35%) | 192(37.65%) | 100 |

All cases were grouped into three groups based on the predominant underlying mechanism of thrombocytopenia. Group A – Hyper-destructive TCP, Group B – Hypo-productive TCP and Group C–Abnormal platelet pooling. Group A constituted majority of the cases 352 (69%). This group was further subdivided into various categories based on the clinical diagnosis [Table 2]. In Group A, bacterial infections accounted for the maximum number of cases i. e. 100 (28.40%). Cardiac cases, Dengue, malaria and renal diseases constituted 25%, 13.06%, 6.8% & 5.3 % respectively. All the categories in Group A had variable mean PDW with highest mean PDW in pregnancy (17.1±1.1) while PDW was lowest in cardiac diseases. (15.05±0.55) [Table 2]. Group B constituted 30% of cases which included anemia 23(6.53%), aplastic anemia 3(0.85%), leukemia 42 (11.93%) and solid malignancy 85 cases (24.14%).In this group also PDW was variable with highest in aplastic anemia (13.5±0.3) followed by anemia (12.95±0.05) and solid malignancies (12.45±0.05). [Table 3].
Group C included 5 cases (1.42%) with splenomegaly suggesting abnormal pooling. The mean PDW was 12.15±0.25 [Table 4].

Control group included 500 cases of normal platelet counts with 280 (56%) males & 220 (44%) females. The mean platelet count in control group was 1.72±0.12 lacs/cumm, in Group A it was 0.755±0.05 lacs/cumm , in Group B- 0.585±0.09 lacs/cumm while in Group C it was 0.55±0.1 lacs/cumm [Table 3 & 4].

Table 2: GROUP A= Hyper-destruction of platelets (n=352) (69%)

| Categories                  | Cases | %     | Mean plt count lacs/cumm | Mean MPV (fl, mean±SD) | Mean PDW (Mean±SD) |
|-----------------------------|-------|-------|--------------------------|------------------------|-------------------|
| Bacterial infections        | 100   | 28.40909 | 0.705                   | 10.35±2.15             | 15.3±1.5          |
| Cardiac diseases            | 88    | 23    | 0.895                    | 10.45±0.1              | 15.05±0.35        |
| Dengue                      | 46    | 13.06818 | 0.25                    | 10.90±0.4              | 17.6±0.11         |
| Malaria                     | 24    | 6.818182 | 0.77                    | 10.15±0.65             | 15.55±0.05        |
| Renal diseases              | 19    | 5.397727 | 1.15                    | 10.75±0.55             | 15.7±0.33         |
| Burns                       | 14    | 3.977273 | 0.615                   | 10.16±0.2              | 16.5±0.6          |
| Liver diseases              | 8     | 2.272727 | 0.555                   | 10.35±0.55             | 16.65±0.05        |
| Sepsis                      | 7     | 1.988636 | 0.68                    | 10.35±0.85             | 16.05±0.25        |
| Viral infections            | 1     | 0.288462 | 0.87                    | 10.05±0.15             | 16.15±0.15        |
| Pregnancy                   | 5     | 1.420455 | 0.725                   | 9.7±0.4                | 17.1±1.1          |
| Snake bite                  | 3     | 0.852273 | 0.66                    | 10.55±0.44             | 16.5±0.2          |
| ITP                         | 2     | 0.568182 | 0.26                    | 11.9±0.4               | 15.9±0.1          |
| Blood transfusion           | 2     | 0.568182 | 0.81                    | 10.25±0.05             | 16.4±0.0          |
| Miscellaneous               | 27    | 7.670455 | 0.805                   | 10.55±0.75             | 15.65±0.25        |
| Mean±SD                     |       |       | 0.755±0.05              | 10.46±0.15             | 16.07±0.17        |

Table 3: GROUP B = Hypo-production of platelets (n=153) (30%)

| Categories   | Cases | %     | Mean plt count lacs/cumm | Mean MPV (fl, mean±SD) | Mean PDW (Mean±SD) |
|--------------|-------|-------|--------------------------|------------------------|-------------------|
| Anemia       | 23    | 6.53  | 0.495                    | 7.9±0.2                | 12.95±0.05        |
| Aplastic anemia | 3 | 0.85  | 0.135                    | 10.45±0.95             | 13.5±0.3          |
| Leukemia     | 42    | 11.93 | 0.57                     | 12±0.8                 | 11.5±0.8          |
| Solid malignancy | 85 | 24.14 | 0.675                     | 9.5±1.1                | 12.45±0.05       |
| TOTAL        | 153   |       |                          |                        |                   |
| Mean±SD      |       |       | 0.585±0.09               | 8.7±0.8                | 12.6±0.73         |

Table 4: GROUP C = Abnormal pooling (n=5) (1%)

| Category          | Cases | %     | Mean plt count lacs/cumm | Mean MPV (fl, mean±SD) | Mean PDW (Mean±SD) |
|-------------------|-------|-------|--------------------------|------------------------|-------------------|
| Spleenic pooling  | 5     | 1.42  | 0.55                     | 8.15±0.35              | 12.15±0.25        |

To know the statistical significance, Z Test was applied among three groups and with control group. In all groups the values were highly significant (P<0.0001) when compared with control group and also among the three groups [Table 5]. There was no significant variation among the mean platelet counts of all the three groups.

Table 5: Statistical significance (PDW)

| Group A Vs Control | Z      | p-value | Group B Vs Control | Z      | p-value | Group C Vs Group A | Z      | p-value | Group B Vs group C | Z      | p-value |
|--------------------|--------|---------|--------------------|--------|---------|--------------------|--------|---------|--------------------|--------|---------|
| Group A Vs Control | Z = 277.60 | <0.0001 | Group B Vs Control | Z = 44.31 | <0.0001 | Group C Vs Group A | Z = 177.04 | <0.0001 | Group B Vs group C | Z = 99.00 | <0.0001 |

(P<0.0001 is extremely significant)

DISCUSSION

Thrombocytopenia (TCP) can be due to hyper-destruction of platelets, hypo-production of platelets or abnormal splenic pooling. Platelet destruction may result from both intracorpuscular defects and extracorpuscular abnormalities. One of the major causes of increased destruction is by immunological mechanism in which antibodies against platelets cause their premature destruction. 1, 9 The platelet number alone does not give a complete picture of platelet maturity and function, therefore, the platelet indices have been the subject of intensive study in recent years, but they have not been firmly established. Of all the platelet indices, MPV has been extensively studied but PDW has been neglected. PDW represents the

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heterogeneity of platelets. Increased PDW is an indication of anisocytosis of platelets. Recently PDW has been receiving attention due to its usefulness for distinguishing hyper-destructive and hypo-productive groups of TCP.\[5,7,9,10\] In our study bacterial infections constituted the majority of cases for TCP (28.40%) followed by cardiac diseases (25%) and solid malignancies (24.14%). While Alam M et al found malaria and other infections as major causes of TCP, Ross C et al found anemia (38.2%) as the major cause of TCP followed by ITP (10.9%).\[12\] Solid malignancy and leukemia constituted a higher percentage of cases in our study when compared with other studies.\[4,13\] This difference is due to the fact that this hospital caters more to oncology patients. The present study revealed that mean PDW was significantly higher in hyper-destructive group (Group A) as compared to Hypo-productive group (Group B), abnormal pooling (Group C) and control group. Various other authors like Kaito et al, Ntaios et al, Khaleel et al and shah et al also reported that PDW was higher in ITP patients when compared with Hypo-productive thrombocytopenic patients, which reflected an increase in the production rate of platelets. The high PDW in platelet destruction could be explained by the fact that newly produced platelets are larger than circulating platelets, which tend to decrease in size with age in the circulation similar to reticulocytes with increased mean volume. As a result, in patients with thrombocytopenia secondary to peripheral destruction the PDW is increased, reflecting active bone marrow compensation with release of young platelets.\[7\] Some studies suggest that it is not always possible to record platelet indices in severe TCP and in the presence of red cell fragmentation, a platelet histogram cannot be adequately drawn, and the indices cannot be recorded. Babu E and Basu D also mentioned the difficulties in getting these parameters and discarded those cases lacking these parameters.\[16\] We avoided this problem by discarding cases without indices and histogram and selected only those cases which had platelet indices and provided a histogram. In control group all cases had showed values and histogram. Nelson et al in their study mentioned that patients with thrombocytopenia due to loss or destruction of platelets have larger platelets, whether the loss is due to infection, hemorrhage, or immune destruction. When thrombocytopenia was due to lack of production, the platelet volume was similar to that seen in patients with normal blood cell counts.\[17\] In our study the mean PDW in hyper-destructive group was significantly higher than in hypo-productive group and abnormal pooling group. The differences between these values were highly significant statistically. [Table 5] Borkataky et al also noticed high mean PDW values except for non-megaloblastic subgroup of impaired production.\[18\] Similar results were obtained by Islam S et al and Aponte-Barrios NH et al.\[20\] Though the present study included all age groups, study by Aponte-Barrios NH et al in pediatric age group found that PDW can distinguish between thrombocytopenia due to an increase in the destruction of platelet and thrombocytopenia due to a reduction in platelet production.\[20\] 

**CONCLUSION**

Although platelet parameters such as MPV and PDW have been available now for quite a time, their clinical usefulness hitherto was not obvious, especially as they may be influenced by the delay between blood collection and analysis. Furthermore, PDW is calculated differently on various instruments. Although bone marrow examination remains the gold standard for TCP, MPV and PDW are definitely useful and reliable tests to differentiate between hyper-destructive TCP from hypo-productive and abnormal pooling TCP. The results of our study for differentiating cause of TCP are statically significant. More attention should be paid to these indices for causes of TCP. PDW should be combined with other platelet indices for more accurate results and further studies with combining these indices will definitely provide promising results.

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