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Role of Platelet Indices in Various Causes of Thrombocytopenia: A Tertiary Care Hospital Study

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Abstract

Introduction:- Platelet indices (PI) — plateletcrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW) — are a group of derived platelet parameters obtained as a part of the automatic complete blood count. Emerging evidence suggests that PI may have diagnostic and prognostic value in certain diseases. This study aimed to summarize the current scientific knowledge on the potential role of PI as a diagnostic tool in patients having thrombocytopenia.

Objectives: To study variations in platelet parameters in relation to the cause of thrombocytopenia

Materials and methods: This cross sectional study was carried out in the Pathology department of a teaching tertiary care hospital, after obtaining Institute Ethics committee clearance. Patients admitted with thrombocytopenia were enrolled in the study. This study spanned over 2 years. A total of 319 cases were studied.

Conclusion: Thrombocytopenia remains one of the commonly encountered abnormalities in clinical situations. Identification of cause of thrombocytopenia is crucial in patient management. Platelet parameters (MPV, PCT, PDW) assessed according to patho-physiological mechanisms were not significantly different. Of the three parameters, alteration in PCT was found to have statistical significance, in patients of thrombocytopenia.

Keywords: Platelet indices, thrombocytopenia.

Introduction

Haemostasis is one of the most important functions of the human body and involves a myriad of physiological processes. Normal haemostasis involves blood and its components, the blood vessel and blood flow. Platelets are the multifunctional anucleate cells formed by fragmentation of megakaryocytes in blood.[1,2] Dysfunction of platelets can result from either congenital or acquired causes. Low platelet counts may result in clinical episodes of bleeding ranging from mild to lethal bleeding that may result in death. Thrombocytopenia is usually defined as a platelet count below the normal range for the population (±2 standard deviations). Counts less than 1,50,000 cells per µL are regarded as low counts and are further classified according to number of platelets present in circulation.[2] Cases are considered mild if counts are between 75to 150 × 10^3 per µL, moderate if between 20 to 75 x 10^3 per µL and severe if less than 20 × 10^3 per µL (20 × 10^9 per L).[2]

Amongst the causes of thrombocytopenia, decreased production may be due to many causes like haematologic malignancies, aplastic anemia, chemotherapy, radiation, vitamin D deficiency, hereditary thrombocytopenias, etc. Increased destruction may be due to variety of causes like immune thrombocytopenia, disseminated intravascular

coagulation (DIC), sepsis, thrombotic thrombocytopenic purpura (TTP), hypersplenism, etc.[2,3]Among these causes, sepsis is one of the important causes especially in developing countries. Almost all organs and systems may be affected by sepsis. Immune and non-immune mechanisms may be involved in causing thrombocytopenia in sepsis. Malarial infection is also an important cause of thrombocytopenia. Malaria is widely prevalent in countries like India. Anemia and thrombocytopenia has been the commonly reported hematologic abnormalities in malaria.[4,5] Dengue hemorrhagic fever (DHF) caused by flavivirus is another important public health concern infection that causes reduced platelet count.[6]

Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder may result in low platelet count because of decreased production and accelerated destruction.[7]

While evaluating thrombocytopenia in a patient, bone marrow examination has been one of the procedures that have been employed since long but it has limitations. Instead, platelet indices which are possible to measure automatically by automated blood cell analysers may be of value in such cases. Platelet indices include platelet count, mean platelet volume (MPV), platelet size deviation width (PDW), plateletocrit (PCT), large platelet (LP).[8] These indices may be helpful in evaluation of thrombocytopenias. MPV has been proposed to be a potentially useful screening test for platelet activation.[9]Furthermore; PDW may reflect change in morphology of platelet due to platelet activation. PCT is important measurement of platelet biomass which combines MPV with absolute platelet count. These indices are altered in different clinical conditions like cardiovascular (CV) disease, infectious diseases including tuberculosis, malarial infection, dengue fever and immune related conditions.[10]

Platelet indices may also be the marker of mechanisms of thrombocytopenia in a patient. MPV which measures average size of platelet in blood may reflect destructive thrombocytopenia with increased MPV and hypoproliferativethrombocytopenia with decreased MPV. PDW may vary by different mechanisms.[4] Increased MPV and PDW have been reported with immune thrombocytopenia compared to aplastic anemia. Plateletcrit may be another effective tool for detecting platelet quantitative abnormalities.[11]

With such higher prevalence, characterization of thrombocytopenia as per the etiology and pathophysiologic mechanism becomes important. Platelet indices further add diagnostic and prognostic value to the causes of thrombocytopenia. Hence we planned this study to assess platelet indices in cases of thrombocytopenia and to differentiate mechanisms as per etio-pathogenesis of thrombocytopenia.

Materials and methods

This cross sectional study was carried out in the Pathology department of a teaching tertiary care hospital, after obtaining Institute Ethics committee clearance. Patients admitted with thrombocytopenia were enrolled in to the study. This study spanned over 2 years. A total of 319 cases were studied.

Inclusion criteria

Indoor patients of all age groups with thrombocytopenia i.e. platelet count less than 150000/cumm (as per automatic 3 part cell counter) and confirmed by peripheral smear (PS) examination), where the cause of thrombocytopenia could be detected.

Patients with thrombocytopenia were divided in three groups of pathogenic mechanism as discussed below.

Based on the clinical diagnoses, patients were considered in the respective groups.

Group 1 : Increased destruction of platelets

Group 2 : Inadequate production of platelets

Group 3 : Increased pooling of platelets

Exclusion criteria

Cases of thrombocytopenia where cause could not be detected

Observations and results

Table 1: Age – wise distribution of total number of cases

Age group (Years)	Patients with thrombocytopenia Number (%)
≤ 10	19 (5.96)
11-20	38 (11.91)
21-40	151 (47.33)
41-60	88 (27.59)
≥ 61	23 (7.21)
Total	319 (100.00)

Table 1: describes age group wise distribution of patients. Of total 319 patients of thrombocytopenia enrolled in to the study, the maximum numbers of patients were in age group of 21 – 40 years (47.33%, 151/319) followed by 41 – 60 years age group (27.59%, 88/319). Numbers of patients in age group below 10 years were 5.96% (19/319), in 11 to 20 years group were 11.91% (38/319), and in patient aged above 60 years were 7.21% (23/319).

Table 2: Clinical diagnosis in patients with thrombocytopenia

Clinical Diagnosis	Gender		Total (%)
	Female (%)	Male (%)	
Increased destruction			
Dengue	21 (6.59)	24 (7.52)	45 (14.11)
Malaria-P. vivax (22)P. falciparum (9)	11 (3.45)	20 (6.27)	31 (9.72)
Pre-Eclampsia	7 (2.20)	0	7 (2.20)
Sepsis	6 (1.88)	5 (1.57)	11 (3.45)
Typhoid Fever	6 (1.88)	4 (1.25)	10 (3.13)
Postnatal Infection	4 (1.25)	8 (2.51)	12 (3.76)
Necrotising Enterocolitis	4 (1.25)	7 (2.20)	11 (3.45)
Obstructed Hernia	4 (1.25)	6 (1.88)	10 (3.13)
Perforation Peritonitis	4 (1.25)	6 (1.88)	10 (3.13)
Respiratory Distress Syndrome	4 (1.25)	6 (1.88)	10 (3.13)
Idiopathic Thrombocytopenia	1 (0.31)	0	1 (0.31)
Inadequate production			
MegaloblasticAnemia	15 (4.70)	12 (3.76)	27 (8.46)
Leukemia- Acute (19) Chronic (7)	9 (2.82)	17 (5.33)	26 (8.15)
Aplastic Anemia	0	2 (0.62)	2 (0.62)
Increased sequestration or pooling			
Chronic Liver Disorder (Cirrhosis)	50 (15.67)	45 (14.11)	95 (29.78)
Congestive Heart Failure	3 (0.94)	8 (2.51)	11 (3.45)
Total	149 (46.70)	170 (53.30)	319

Table 3: Severity of thrombocytopenia in patients

Severity of thrombocytopenia (cells/cumm)	Number	Percentage (%)
Mild (<1.5 – 0.750)	179	56.11
Moderate (<0.750 – 0.200)	134	42.00
Severe (<0.200)	6	01.89
Total	319	100.0

Table 3 describes severity of thrombocytopenia. Majority of cases had mild (56.11%, 179/319) with platelet counts < 1.5 to 0.75 cells/cumm and moderate (42.0%, 134/319)

with platelet counts < 0.75 to 0.20 cells/cumm thrombocytopenia. There were only six cases of severe thrombocytopenia with platelet counts < 0.20 cells/cumm.

Table 4: Severity of thrombocytopenia in different clinical diagnoses

Clinical Diagnosis	Severity of thrombocytopenia			Total (%)
	Mild (%)	Moderate (%)	Severe (%)	
Chronic Liver Diseases	57 (17.87)	37 (11.60)	1 (0.31)	95 (29.78)
Dengue	23 (7.21)	20 (6.27)	2 (0.62)	45 (14.11)
Malaria	20 (6.27)	09 (2.82)	2 (0.62)	31 (9.72)
Megaloblastic Anemia	10 (3.13)	7 (2.2)	0	27 (8.46)
Leukemia	7 (2.2)	19 (5.95)	0	26 (8.15)
Aplastic Anemia	7 (2.2)	5 (1.56)	0	2 (0.62)
Postnatal Infection	8 (2.51)	4 (1.25)	0	12 (3.76)
Congestive Heart Failure	6 (1.89)	5 (1.56)	0	11 (3.45)
Necrotising Enterocolitis	8 (2.51)	3 (0.94)	0	11 (3.45)
Sepsis	6 (1.89)	4 (1.25)	1 (0.31)	11 (3.45)
Typhoid Fever	4 (1.25)	6 (1.88)	0	10 (3.13)
Obstructed Hernia	4 (1.25)	6 (1.88)	0	10 (3.13)
Perforation Peritonitis	9 (2.82)	1 (0.31)	0	10 (3.13)
Respiratory Distress Syndrome	6 (1.88)	4 (1.25)	0	10 (3.13)
Pre-Eclampsia	4 (1.25)	3 (0.94)	0	7 (2.19)
Idiopathic Thrombocytopenia	0	1 (0.31)	0	1 (0.31)
Total	179	134	6	319

Table 5: Platelet parameters in patients with thrombocytopenia

Platelet parameter	Mean± SD (n=319)
PLT (cumm)	0.806±0.306
MPV (fl)	7.89±0.99
PDW %	9.86±3.24
PCT %	0.088±0.106

Table 6: Comparative platelet parameters by pathogenic mechanism

Platelet parameter	Increased destruction (n=157)	Decreased production (n=57)	Increased pooling (n=105)
PLT (cumm)	0.811±0.298	0.725±0.311	0.843±0.311
MPV (fl)	7.95±0.996	7.67±0.981	7.92±1.00
PDW %	10.06±3.14	8.99±3.69	10.03±3.08
PCT %	0.082±0.089	0.061±0.028*	0.112±0.146*

Table 6 describes platelet parameters as per pathogenic mechanism of thrombocytopenia. Platelet count did not differ significantly in the three mechanisms namely increased destruction (0.811±0.298, n=158), decreased production (0.725±0.311, n=55) and increased sequestration (0.843±0.311, n=106). Similarly there was no significant difference for MPV with mean values being 7.95±0.996, 7.67±0.981 and 7.92±1.00 respectively and for PDW with mean values being 10.06±3.14, 8.99±3.69 and 10.03±3.08 respectively in three groups described as earlier. PCT differed in three groups with mean of 0.082±0.089 in increased destruction mechanism and 0.061±0.028 in decreased production mechanism (p>0.05

fo intergroup comparison). But there was significant difference in PCT% between decreased production (0.061±0.028) and increased sequestration group (0.112±0.146) (p=0.011).

Discussion

Platelets are one of the main functional units in blood involved in the hemostatic process. The process of synthesis of platelets is highly regulated megakaryopoiesis in bone marrow. Thrombopoeitin regulates this process along with other factors. Assessment of platelet function is done by various methods. Platelet parameters comprise one of the important assessment tools for platelet function. Platelet count, mean platelet volume, platelet distribution width and plateletcrit are major parameters that are assessed clinically with the help of automatic cell counter.

In our study we had total 319 patients of thrombocytopenia.The age group ranged from neonates to elderly. Mean age of the patients was 35.83 years. Three-fourth number of patients (239/319, 74.92%) were in age group of 21 to 60 years. 19 (5.96%) were children below 10 years including neonates, 38 (11.91%) were adolescents (11 – 20 years) and 23 (7.21%) were elderly above 60 years. Males (170/319 53.3%) were more than females (149/319, 46.7%). Consistent with this finding, Gill MK, et al. (2013) observed that adult males have been frequently diagnosed with thrombocytopenia caused by malarial infection.[5]

Among various causes of thrombocytopenia chronic liver disorders (29.78%) was the most common cause observed in our study followed by dengue infection (14.11%), malarial infection (9.72%) and others (table 5). Based on pathogenic mechanisms, causes of thrombocytopenia with increased destruction of platelets were dengue fever (14.11%), malarial infection (9.72%), post-natal infection (3.76%), necrotising enterocolitis (3.45%), sepsis (3.45%), typhoid fever (3.13%), obstructed hernia (3.13%), perforation peritonitis (3.13%), respiratory distress syndrome (3.13%), pre-eclampsia (2.19%) and one case of idiopathic thrombocytopenia. Mean platelet count for causes with this mechanism was 0.811 cells/cumm.

Inadequate production of platelets may occur due to many etiologies such as megaloblasticanemia(8.46%) was most common etiology in this category followed by Leukemia(8.15%), and aplastic anemia (0.62%). Mean platelet count for causes with this mechanism was 0.725 cells/cumm.

Platelet parameters assessed in our study did not differ significantly in the three groups of patients as defined by pathogenic mechanism of thrombocytopenia except for significant difference in PCT% for mechanisms of decreased platelet production and increased platelet sequestration (0.061±0.028 vs 0.112±0.146, p=0.011 respectively).

Overall lower values of all parameters was observed with decreased production mechanism. Similar trend has been reported by Shah AR, et al. (2013) with mean values of platelet count, MPV and PDW in patients of infectious diseases being 0.258 cells/cumm, 9.6 fl and 11.2% whereas in cases of anaemia, values were 0.368 cells/cumm, 9.3 fl and 11.1 respectively.[8]Kaito K, et al. (2005) in aplastic anaemia and ITP patients reported overall non-significant but mean lower platelet count (0.590 vs 0.600 cells/cumm) whereas other parameters were significantly lower in aplastic anaemia patients [MPV (10.2 vs 12.2, p<0.0001, PDW (11.6 vs 16.8, p<0.0001)] respectively.[8]This suggests that with inadequate production of platelets, platelet parameters tend to be lower compared to normal. Thus in patient of thrombocytopenia where cause is uncertain, platelet

parameters may provide clue to the diagnosis and may help in early assessment of bone marrow for specific diagnosis.

MPV has been reported to be a useful marker to differentiate between thrombocytopenia of central and peripheral origin and to predict haemorrhagic diathesis in thrombocytopenic patients.

Age group wise analysis showed lower counts in children and adolescents with higher MPV and PDW compared to adult and elderly population.Majority of the patients in our study had mild-moderate (0.75 to 1.5 cell/cumm and 0.2 to 0.75 cell/cumm) thrombocytopenia and six cases had severe thrombocytopenia (<0.20 cell/cumm). In our study, we had two cases of denguewho had severe thrombocytopenia.The importance of studying severity of thrombocytopenia lies in the fact that the prognosis of patients may become worse with decreasing platelet count. The degree of thrombocytopenia has been shown to be useful as a prognostic

marker because the finding of thrombocytopenia $<50x10^9$/L in liver disease is associated with significant morbidity.

Conclusion

Thrombocytopenia remains one of the commonly encountered abnormalities in clinical situations. Identification of cause of thrombocytopenia is crucial in patient management to safe guard prognosis of the patients Platelet parameters (MPV,PCT,PDW) assessed according to patho-physiological mechanism were not different. Of the three parameters, alteration in PCT was found to have statistical significance, in patients of thrombocytopenia.

Assessing platelet count and severity of thrombocytopenia is essential to reduce morbidity and mortality. Thus diagnosis of thrombocytopenia is essential and platelet parameters may be valuable is assessing prognosis in a patient.

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