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Study of Platelet Indices in Patients with Febrile Thrombocytopenia

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Abstract

Background: Platelet indices viz. Mean platelet volume (MPV), Platelet distribution width (PDW) and Platelet large cell ratio (P-LCR) are measured in the automated cell counter. These indices are well utilized for certain conditions like idiopathic thrombocytopenic purpura, aplastic anemia and other hemotological disorders to assess the prognosis. Platelet count is decreased in various conditions including infectious and non-infectious disease processes. Infectious conditions like dengue fever, malaria, rickettsia, leptospirosis cause fever and variable degree of thrombocytopenia. Hence a detailed study of platelet indices is undertaken in patients having fever with thrombocytopenia. *Materials & Methods*: Present study was a prospective study. A total of 150 patients were included over a period of 1 year from Jan 2011 to Dec 2011. Detailed histories, physical and clinical examination of the patients were done to assess the etiology of febrile thrombocytopenia. Serological investigations for dengue fever, leptospirosis and rickettsia were done for confirmation. *Results*: Majority of the cases were of viral fever (72.6%), which includes dengue fever (10.6%), followed by malaria (15.3%), septicemia (4.6%), enteric fever (4%), leptospirosis (2%), rickettsia & brucellosis (0.6%). The platelet indices PDW (74.6%), MPV (86.6%), P-LCR (80.6%) showed less significant changes. *Conclusion*: Platelet indices are not changed significantlyin febrile thrombocytopenic patients. Whenever patient with thrombocytopenia presents with changes in platelet indices, non infectious conditions should also be considered in differential diagnosis to manage the patients effectively for better clinical outcomes.

Keywords: Febrile Thrombocytopenia; Platelet Indices.

Introduction

Complete blood count (CBC) test is one among the commonest investigation requested in the laboratory in day today clinical practice, which measures White blood cell count (WBC), Red blood cell count (RBC) and Platelet counts, also measures various indices of RBCs and Platelets. Automation in hematology is available since 1950's with the introduction of Technicon Auto Analyzer followed by automated electronic cell counting instruments in 1960's. Few important factors that serve to drive automation include turn around time demands, specimen integrity and reduced laboratory errors[1]. The principles applied in electronic cell counters are mainly electrical impedance and optical light scattering. The complete blood count is a primary and an important investigation that is frequently performed for screening, diagnosing and monitoring variety of conditions like anemias, leukemias and systemic illness etc. and with the availability of automated cell counters in smaller cities and towns, it is easier to get critical information, helping clinicians to intervene more effectively and improving patient outcomes.

Platelet indices viz –MPV. PDW and P-LCR are measured in the automated cell counter as a part of CBC tests. These parameters are well utilized for certain conditions like idiopathic thrombocytopenic

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purpura (ITP), aplastic anemia and other hemotological disorders to assess the prognosis[2].

Platelet count is decreased (thrombocytopenia) in various conditions including infectious and non-infectious disease processes. Infectious conditions like dengue fever, malaria, rickettsia, leptospirosis cause fever and variable degree of thrombocytopenia, sometimes even death of the patient[3]. Some of the non infectious conditions causing thrombocytopenia include ITP, megaloblastic anemia, acute leukemias, aplastic anemia etc.

Platelet indices like MPV, PDW, P-LCR are easily recorded by automated cell counter but are underutilized. The changes in these indices in patients with fever and thrombocytopenia are scarcely documented in the published literatures.Hence, a detailed study of changes in platelet indices is undertaken in patients presenting with febrile thrombocytopenia.

Materials and Methods

The present study was a prospective study done over a period of one year from 1st Jan. 2011 to 31st Dec. 2011. A total of 150 patients presenting with fever of less than 7 days in duration and decreased platelet count of less than 150,000 cells/µl admitted in BLDEU Shri.B.M.Patil Medical College, Hospital and Research Centre, Vijayapur were included in the study.

The complete blood count analysis of the samples were made using the 3 part differentiated automated hematology analyzer (Sysmex KX-21) including the platelet indices (MPV, PDW, P-LCR). The peripheral smear slides of the samples were made and stained using Leishmann's stain to counter check the red cell morphology, WBC total count, WBC differential count, platelet count and morphology obtained from the automated hematology analyzer and also to look for the presence of malarial parasite.

Detailed history, physical and clinical examination of the patients was done to assess the etiology of febrile thrombocytopenia. Relevant investigations like serological investigations for dengue fever, leptospirosis and rickettsia were done for confirmation.

Patients with thrombocytopenia other than associated with acute febrile illness like ITP, aplastic anemia, megaloblastic anemia, functional platelet disorders and other hematological disorders were excluded from the study.

Results

The distribution of study subjects according to their age is shown in table 1. It shows majority of the patients 16.6% (25 cases) belonged to 11-20, 21-30 and >60 years of age groups. Sex distribution showed males comprising 52%(78cases) and females 48% (72cases).

Present study showed viral fever 62% (93cases) was the leading cause of fever with thrombocytopenia, followed by malaria 15.3%(23 cases), dengue fever 10.6% (16 cases), septicemia 4.6% (7 cases), typhoid fever 4%(6cases), leptospirosis 2% (3cases), rickettsia 0.6% (1 case) & brucellosis 0.6% (1 case). (Figure 1)

In the present study, 4.6% (7 cases) had a platelet count between 0-20,000 cells/µl, 16% (24 cases) had count between 20,000 – 50,000 cells/µl & 79.3% (119 cases) had count between 50,000 – 150,000 cells/µl with viral fever being the major cause. (Table 2)

The platelet indices in majority of the cases, PDW

Table 1: Distribution of study subjects according to their age

Age (in years)	No. of patients	Percentage
0-10	17	11.3
11-20	25	16.6
21-30	25	16.6
31-40	24	16.0
41-50	21	14.0
51-60	13	8.6
>60	25	16.6
Total	150	100

Table 2: Distribution of cases according to platelet count & disease category

Platelet count in thousands/µl	Viral fever	Malaria	Septicemia	Dengue	Typhoid	Leptospirosis	Rickettsia	Brucellosis
<20,000 4.6% (7 cases)	4	-	-	2	-	-	-	1
20,000– 50,000 16% (24 cases)	11	3	3	6	-	1	-	-
50,000-150,000 79.3% (119 cases)	78	20	4	8	6	2	1	-

Table 3: Distribution of cases according to platelet indices

	PDW (9-18fl)	MPV (8-12 fl)	P-LCR (18.5 – 42.5 %)
Low	6 (4%)	3 (2%)	11 (7.3%)
Normal	112 (74.6%)	130 (86.6%)	121 (80.6%)
High	32 (21.3%)	17 (11.3%)	18 (12%)
Total	150 (100%)	150 (100%)	150 (100%)

Table 4: Incidence of diseases according to individual platelet indices:

Indices	Range	Viral fever	Malaria	Septicemia	Dengue	Leptospirosis	Typhoid	Rickettsia	Brucellosis	Total
PDW	Low (<9)	4	1	1	-	-	-	-	-	6
	Normal (9-18)	69	18	4	12	3	4	1	1	112
	High (>18)	20	4	2	4	-	2	-	-	32
MPV	Low (<8)	2	-	-	-	-	-	-	1	3
	Normal (8-12)	82	21	7	13	5	2	1	-	131
	High (>12)	9	2	-	3	1	1	-	-	16
P-LCR	Low (<18.5)	5	2	-	3	-	-	-	1	11
	Normal (18.5-42.5)	78	19	7	10	5	2	1	-	122
	High (>42.5)	10	2	-	3	1	1	-	-	17

Table 5: Comparison of causes of fever with thrombocytopenia

Diagnosis	Present study (%)	Patil P et al (%)
Viral fever	62.0	17
Malaria	15.3	54
Dengue	10.6	15
Septicemia	4.6	4
Typhoid	4.0	6
Leptospirosis	2.0	2
Rickettsia	0.6	-
Brucellosis	0.6	-

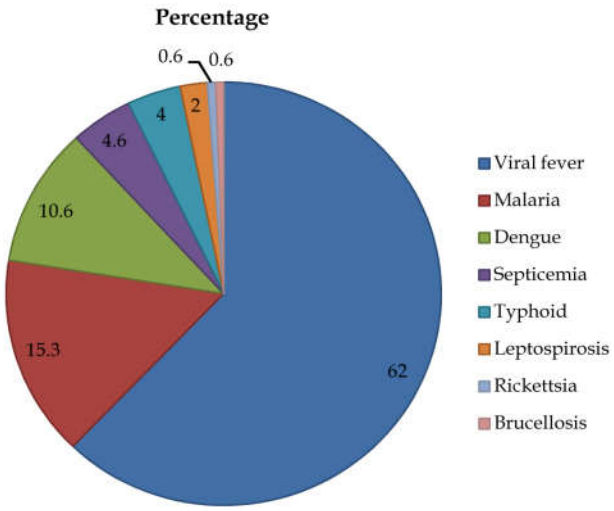

Fig. 1: Percentage of causes of febrile thrombocytopenia

74.6% (112 cases), MPV 86.6% (130 cases), P-LCR 80.6% (121 cases) are not changed significantlyin any of the febrile thrombocytopenia cases (Tables 3, 4).

Discussion

It is important to know whether thrombocytopenia is a result of hypo-production of platelets or hyper-destruction of platelets. The changes in platelet indices were studied in cases of ITP and aplastic anemia where MPV, PDW & P-LCR were elevated in ITP increasing the number of megakaryocytes indicating that ITP was associated with higher platelet index values. The increased values of platelet indices have also been observed in cases of pre-eclampsia and eclampsia that may be due to hyper destruction of platelets as a result of shorter platelet half-life & increased bone marrow activity.

Similar study was done by Patil P et al [4] with the same criteria as in the present study. In their study, Malaria 54% was the major cause of fever with thrombocytopenia, followed by viral fever 17%, Dengue 15%, typhoid fever 6%, septicemia 4% and leptospira 2 % of cases (Table 5).

In contrast to present study, malaria was the common cause in the other study, where as in the present study it is the second common cause, attributed probable by judicial use of insecticides in and around residential areas of malaria infested cases, Secondly, Dengue incidence in both the studies showed a small difference may be due to it is spread by day time indoor mosquito bites.

In the present study, 4.6% (7 cases) had a platelet count between 0-20,000 cells/µl, 16% (24cases) had count between 20,000 – 50,000 cells/µl & 79.3%(119 cases) had count between 50,000 – 150,000 cells/µl. The platelet indices in majority of the cases, PDW 74.6% (112 cases), MPV 86.6% (130 cases), P-LCR 80.6% (121 cases) showed no significant changes seen any of the febrile thrombocytopenia cases.

A study by Kaito et al found that platelet indices were significantly higher in ITP than in aplastic anemia and platelet indices showed an increased platelet indices in ITP than in aplastic anemia [2].

A study by Waseem FA & Mouayed BH found that increased platelet volume was associated with a higher risk of suffering an acute coronary event independent of the extent of a previous coronary artery disease (CAD) [5].

A study by Vamseedhar A et al found a relationship between platelet indices and severity of pre-eclampsia where the all platelet indices were increased [6].

The viral causes for fever with thrombocytopenia include CMV, Dengue, Parvo-B19, HSV, HIV, Hantana virus etc [7] and the mechanisms involved may beimpaired platelet production due to invasion of megakaryocytes by the virus, toxic effects of viral protein onprogenitor cells, virus induced haemo-phagocytosis, destruction of circulating platelets by viral antigen antibody complexes [8].

Thrombocytopenia resulting from septicemia may be caused by disseminated intravascular coagulation (DIC). Platelets adherence to damaged vascular surfaces also accounts for thrombocytopenia in certain bacterial infections, such as meningococcemia. Endotoxin, exotoxin, platelet activating factor may damage platelets, resulting inincreased clearance and phagocytosis of platelets, white cells in bone marrow may also occur in patients with sepsis syndrome [9].

Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have been described as possible causes forthrombocytopenia in 75% cases of malaria [10].

The release of high levels of platelet-activating factor by monocytes with heterologous secondary infection may explain the hemorrhage and platelet-activating factor may induce platelet consumption and increase adhesiveness of vascular endothelial cells may explain thrombocytopenia in dengue fever [11].

In leptospirosis & brucellosis, thrombocytopenia could possibly be attributed to disseminate dintravascular coagulation (DIC) or a toxin or cytotoxin mediated mechanism [12,13].

In typhoid fever, the mechanism is uncertain but may be attributed to bone marrow suppression during initial septicemic phase of the illness and it has also been suggested that DIC may account for thrombocytopenia [14].

The probable reasons forless significant changes in platelet indices might be due impaired production rather that defective platelets and impaired consumptions in the vessels or due to actions of chemical mediators rather than increased destruction or increased productionas in ITP cases due to autoantibodies.

Conclusion

To conclude, platelet indices in majority of cases PDW (74.6%), MPV (86.6%),P-LCR (80.6%) are not changed significantly in febrile thrombocytopenic patients, caused by infectious etiology. Whenever a patient with thrombocytopenia presents with changes in platelet indices, non infectious conditions should also be considered in differential diagnosis to manage the patients effectively for better clinical outcomes.

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