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Clinical profile of patients with thrombocytopenia at tertiary health care centre

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ABSTRACT

Background: In tropical countries like India thrombocytopenia is commonly encountered by clinicians in any speciality. Thrombocytopenia present as asymptomatic condition to sometimes becomes a life-threatening condition requiring blood transfusion in various etiological conditions. Infections like malaria and dengue are invariably associated to thrombocytopenia with changing trends in clinical features. Infection is the commonest cause of thrombocytopenia. The objective of study was to evaluate the different causes of thrombocytopenia along with study of clinical profile and laboratory parameters in patients with thrombocytopenia.

Methods: A cross-sectional hospital based study was conducted in Department of Medicine at Indian Institute of Medical Science and Research Medical College, Badnapur, Dist. Jalna, Maharashtra, India from November 2015 to August 2017. This study comprises cases of thrombocytopenia of age more than 12 years admitted with platelet count <1 lack/mm³ was included in study, whereas patients with malignancy and chemotherapy induced thrombocytopenia, idiopathic thrombocytopenic purpura, cirrhosis of liver were excluded.

Results: Study shows almost 55.83 % of total patients were below age of 30 years and 44.17% patients were above 30 years of age. The highest incidence of thrombocytopenia was seen in the age group of 21-30 years (32.50%) followed by 31-40 (25.83%) and 12-20 years (23.33%). The most common diseases that causes thrombocytopenia were infections (63.33%) [i.e. Dengue (30%), Malaria (20.83%), Enteric fever (5%), HIV (4.166%), Leptospirosis (1.66%) and DIC (1.66%)] and Megaloblastic anemia (21.66%) were common in younger population.

Conclusions: Study concluded that most common causes of thrombocytopenia were infections (63.33%) and megaloblastic anemia (21.66%). Bleeding manifestations were present in 37.50% of patients and the most common site of bleeding was skin and mucous membrane. The main etiological cause of bleeding in our study was dengue hemorrhagic fever followed by megaloblastic anaemia and malaria.

Keywords: Bleeding manifestation, Infection, Thrombocytopenia, Splenomegaly

INTRODUCTION

Thrombocytopenia is a common clinical condition and is caused by infectious and noninfectious etiology. Thrombocytopenia results from one or more of three processes: Decreased bone marrow production; Sequestration, usually in an enlarged spleen; and /or

Increased platelet destruction. Disorders of production may be either inherited or acquired. In evaluating patient with thrombocytopenia, a key step is to review the peripheral blood smear and to first rule out pseudothrombocytopenia, particularly in a patient without an apparent cause for the thrombocytopenia. Pseudothrombocytopenia is an in vitro artifact resulting

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from agglutination via antibodies (usually IgG but also IgM and IgA) when the calcium content is decreased by blood collection in ethylenediamine tetra acetic (EDTA). If a low platelet count is obtained in EDTA-anticoagulated blood, a blood smear should be evaluated, and a platelet count determined in blood collected into sodium citrate (blue top tube) or heparin (green top tube) or smear of freshly obtained unanticoagulated blood, such as from finger stick, can be examined.¹

Thrombocytopenia may be defined as a subnormal number of platelets in the circulating blood. A normal human platelet count ranges from 1,50,000 to 4,50,000 platelets/mm³ of blood. Often patients with thrombocytopenia are asymptomatic and are diagnosed by routine complete blood count. Occasionally, there may be bruising, purpura, petechiae, nose bleeding and gum bleeding. Rarely, platelet count may be as low as 5,000/mm³ predisposing the patients to life-threatening bleeding in the central nervous system (CNS) or from the gastrointestinal and genitourinary tracts.²

Common causes of thrombocytopenia are infections, drugs, autoimmunity, hypersplenism, DIC, etc. Pseudothrombocytopenia should always be ruled out first by peripheral smear examination. Thrombocytopenia results in abnormality of platelet plug formation which leads to defects in primary homeostasis and characterized by prolonged bleeding time, and the characteristic physical examination findings are petechia, purpura and bleeding from other sites. Studies have shown significant association between malaria and thrombocytopenia; the incidence of which ranges from 40.5-85%.³

Febrile thrombocytopenia is the thrombocytopenia associated with fever. Diseases which commonly present with fever and thrombocytopenia are malaria, leptospirosis, rickettsial infections, septicemia, typhoid, borreliosis, arbovirus such as dengue or yellow fever, rodent-borne viruses such as Hanta and Lassa fever, human immunodeficiency virus (HIV), visceral leishmaniasis and TTP-HUS.⁴

Hence the present study was aimed to evaluate the different causes of thrombocytopenia along with study of clinical profile and laboratory parameters in patients with thrombocytopenia.

METHODS

This cross-sectional hospital based study was conducted amongst 120 patients in Department of General Medicine of JIIU's Indian Institute of Medical Science and Research Medical College, Badnapur, Jalna, Maharashtra, India from November 2015 to August 2017.

Inclusion criteria

• All the patients more than 12 years of age,

- Patient with platelet count <1 lack/ mm3 (with or without clinical bleeding),
- If a low platelet count is obtained in EDTA-anticoagulated blood, a blood smear is evaluated, and a platelet count determined in blood collected into sodium citrate (blue top tube) or heparin (green top tube) to avoid pseudothrombocytopenia cases.

Exclusion criteria

- Patients less than 12 years of age,
- Patients having congenital thrombocytopenia,
- Patient having malignancy with thrombocytopenia or due to treatment with cancer chemotherapy is excluded,
- Drug induced thrombocytopenia,
- Diagnosed cases of Idiopathic thrombocytopenic purpura,
- Patients with cirrhosis of liver.

Sample size

Those patients fulfill the inclusion and exclusion criteria and randomly selected 120 patients were enrolled for the study.

Detailed clinical history was noted in each patient including site of bleeding, past history of drug and major medical illness in the past. Detailed physical examination was carried out in all patient. Routine Investigation in the form of peripheral smear, complete blood count, malaria antigen test, ultrasonography abdomen, chest x-ray, Renal function test, Liver function test, Coagulation profile etc. were carried out in all patients. The special investigations like Bone marrow examination, Serum widal, serology for leptospirosis, Dengue serology, Coomb's test, G6PD Test, LE Cells, Sucrose Lysis Test, RA Factor, ANA/Anti-Ds DNA, NCCT brain etc. were done as and when required. All the patients were treated with disease specific treatment and platelet transfusion was given as per indication.

If a low platelet count is obtained in EDTA-anticoagulated blood, a blood smear is evaluated, and a platelet count determined in blood collected into sodium citrate (blue top tube) or heparin (green top tube) to avoid pseudothrombocytopenia. The classification of platelet transfusion into either therapeutic, to treat bleeding or prophylactic, to prevent bleeding, was based on the modified world health (WHO) bleeding score. Recommendations for prophylactic transfusion relate to patients with bleeding scores 0 or 1 and therapeutic transfusion to patients with bleeding scores of 2 or higher.

All the data of each patient were recorded in separate proforma and analyzed. Data collection was started after institutional ethical committee approval. Statistical analysis was done by calculating percentages and proportions whenever necessary.

RESULTS

Table 1 shows that maximum number of cases were seen in 21-30 years of age group (32.5%) followed by 31-40 years (25.8%) and 72 (60.0%) were males and 48 (40.0%) were females.

Table 1: Age and sex wise distribution of study population.

Age group (in years)	No. of patients (n=120)	%
12-20	28	23.3
21-30	39	32.5
31-40	31	25.8
41-50	15	12.5
51-60	07	5.8
Sex		
Male	72	60.0
Female	48	40.0

It was seen from Table 2 that most common cause of thrombocytopenia was infection dengue (30%), megaloblastic anemia (21.66%) and followed by malaria (20.83%) and enteric fever (5%).

Table 2: Etiology of Thrombocytopenia (n=120).

Name of disease	No. of patients	%
Dengue	36	30.0
Megaloblastic anemia	26	21.6
P. Falciparum malaria	15	12.5
P. Vivax malaria	10	8.3
HELLP syndrome	02	1.6
Enteric fever	06	5.0
Thalassemia	04	3.3
Hypersplenism	04	3.3
Leptospirosis	02	1.6
Direct intravascular coagulopathy (DIC)	02	1.6
Human immunodeficiency virus (HIV)	05	4.2
Aplastic anemia	03	2.5
Snake bite	02	1.6
Systemic lupus erythematous (SLE)	02	1.6
Rheumatoid arthritis (RA)	01	0.8

HELLP- (HE)-hemolysis, (EL)-elevated liver enzymes, (LP)-low platelet count

It was observed from Table 3 that out of 120 patients, 45(37.5%) had bleeding menifestations, of which most common site of bleeding was skin and mucous membrane (40%) (i.e. Petechiae, ecchymosis, purpura) followed by gum bleeding (13.3%) and malena (4.5%).

As Table 4 shows that 25 patients (20.83%) received blood transfusion, out of that 14 patients had platelet

count less than 10000/mm³ and 11 patients had platelet count more than 10000/mm³.

Table 3: Hemorrhagic manifestations associated with thrombocytopenia.

Site of bleeding	No. of patients (n=45)	%
Skin and mucous membrane		
(patechiae, ecchymosis, purpura)	18	40.0
Gum bleeding	06	13.3
Bleeding per vagina	04	8.8
Hematemesis	03	6.6
Hematuria	02	4.5
Epistaxis	02	4.5
Bleeding per rectum	02	4.5
Malena	02	4.5
Bleeding into joints	01	2.3
Intracranial hemorrhage	02	4.5
Bleeding from IV-line site	01	2.3
Multisite bleeding	02	4.5

Table 4: Total number of patients with thrombocytopenia received platelet transfusion.

Name of disease	No. of patients with platelet count <10000	No. of patients with platelet count >10000	Total
Dengue	07	02	09
Falciparum malaria	02	01	03
Vivax malaria	00	01	01
Falciparum malaria with dengue	01	00	01
Enteric fever with dengue	00	01	01
Megaloblastic anemia with dengue	01	01	02
HELLP syndrome	00	02	02
Leptospirosis	01	01	02
DIC	01	01	02
HIV	01	00	01
Snake bite	00	01	01
Total	14	11	25

(Note: 1 patient had Falciparum Malaria with dengue; 2 patients had Megaloblastic anemia with dengue; 1 patient had Enteric fever with dengue)

It was seen from Table 5 that the lowest platelet count in male and female patient but there is no significant difference between sex and platelet count. It was evident from Table 6 that various signs with thrombocytopenia, most common sign was splenomegaly (16.66%) followed

by hepatomegaly (13.33%), hepatosplenomegaly (7.5%), jaundice (11.66%) and reactive lympadenopathy (6.66%).

Table 5: Sex-wise distribution of lowest platelet Count.

Disease	Lowest platelet Count in male	Lowest platelet Count in female
Dengue	9000	12000
P. Vivax malaria	26000	21000
P. Falciparum malaria	14000	27000
Enteric fever	90000	50000
Leptospirosis	78000	72000
Snake bite	70000	850000

Table 6: Various signs with thrombocytopenia.

Signs	No. of patients	%
Splenomegaly	20	16.66
Hepatomegaly	16	13.33
Hepatosplenomegaly	09	7.5
Jaundice	14	11.66
Reactive lymphadenopathy	12	6.66

It was seen from Table 7 that maximum number of patient had platelet count less than 20,000/mm³ and we had categorized patients (with low platelet) with etiology into mild (50,000/mm³-1,00,000/mm³), moderate (20,000/mm³-50,0000/mm³) and severe (< 20,000 mm)³ as shown in Table.

Table 7: Correlation of etiology with platelet count.

Name of disease	No. of patients	Platelet count <10,000/mm ³	Platelet count >10,000/mm ³	Platelet count in 20,000/mm ^{3 to} 50,000/mm ³	Platelet count >50,000/mm³ but <1,00,000/mm³
Dengue	36	14	09	07	06
Megaloblastic anemia	26	04	06	12	04
P. falciparum malaria	15	03	02	04	06
P. vivax malaria	10	02	01	02	05
HELLP syndrome	02	00	01	01	00
Enteric fever	06	01	01	01	03
Thalassemia	04	00	01	01	02
Hypersplenism	04	01	02	00	01
Leptospirosis	02	01	01	00	00
DIC	02	01	01	00	00
HIV	05	01	01	01	02
Aplastic anemia	03	01	02	00	00
Snake bite	02	00	01	01	00
SLE	02	00	01	01	00
RA	01	00	00	01	00
Total	120	29	30	32	29

Table 8: Blood count suppression in peripheral smear.

Peripheral smear	No. of patients	%
Anemia	52	42.0
Selective thromocytopenia	34	28.0
Pancytopenia	26	21.0
Lecopenia	08	09.0
Total	120	100.0

As seen in Table 8 that blood count suppression in peripheral smear was seen anemia in (42%), selective thrombocytopenia in (28%), pancytopenia in (21%) and Leucopenia in (9%).

DISCUSSION

Thrombocytopenia is raising problem in tropical countries. Thrombocytopenia may be defined as a subnormal number of platelets in the circulating blood. A normal human platelet count ranges from 1,50,000 /mm³ to 4,50,000 platelets/mm³ of blood. Both infectious and non-infectious diseases cause thrombocytopenia. The diseases that cause thrombocytopenia in younger population commonly are infections (i.e. dengue, malaria, enteric fever, HIV, DIC) and megaloblastic anemia. Our study shows that almost 55.83% of total patients were below the age of 30 years. Similarly, a study has shown significant association between malaria thrombocytopenia; the incidence of which ranges from 40.5-85%.5

In our study, megaloblastic anemia was a major cause for pancytopenia which was described in the literature both function and number of platelet is important for bleeding tendancies. In our study, bleeding time was also normal in patients with mean platelet count <15,000/mm³, but function of platelets is also responsible for raised bleeding time. In our study, maximum number of cases were seen in 21-30 years of age group (32.50%) followed by 31-40 years (25.83%) and 12-20 age group (20.33%). As India is endemic for malaria, dengue and enteric fever, majority of patients with these diseases showed splenomegaly, iaundice associated thrombocytopenia. Similar findings were also observed in study done by Bizzaro N.6

In our study, maximum cases were seen in age less than 30 years (55.83%) and 72 (60%) were males and 48(40%) were females. Most common cause of thrombocytopenia was infection (i.e. dengue (30%), malaria (20.83%), enteric fever (5%) HIV (4.16%) followed by megaloblastic anemia (21.66%). Similar findings were also noted in systematic review by Liu Shelan et al.⁷

In our study, 25 patients (20.83%) received blood transfusion out of that 14 patients had platelet count less than 10000/mm³ and 11 patients had platelet count more than 10000/mm³. In our study we had noted highest and lowest platelet count in male and female patient but there was no significant difference between sex and platelet count. Similar findings were also observed in study done by Godhani UR et al.⁸

In our study, we tried to see certain signs and organomegaly with thrombocytopenia and most common sign was splenomegaly (16.66%) followed by hepatomegaly (13.33%), hepatosplenomegaly (7.5%), jaundice (11.66%) and reactive lympadenopathy (6.66%). Similar findings were aslo observed in study done by Raikar SR et al.⁹

In our study, we categorized platelet count with etiology into mild, moderate and severe thrombocytopenia and peripheral blood smear study in our patient had anemia in (43.33%), selective thrombocytopenia in (28.33%), pancytopnia in (21.66%) and leucopenia in (6.66%) of patients. Similar findings were also observed in various studies. ¹⁰⁻¹⁴

In our study, two patients had snake bite in those cases thrombocytopenia could be because of toxin causing platelet destruction. In SLE and RA thrombocytopenia is because of immune mediated reaction. In enteric fever transient bone marrow suppression causes thrombocytopenia. In HIV immunosuppression and bone marrow suppression is cause for thrombocytopenia but we had not taken drug induced thrombocytopenia cases. In DIC cases main cause of thrombocytopenia is consumption coagulopathy and toxin mediated platelet destruction. ¹⁵⁻¹⁷

CONCLUSION

In our study thrombocytopenia was more common in age group below 30 years of age, where men were more affected than women. The commonest etiology was dengue in 30% of patients followed by megaloblastic anemia in (21.66%) and malaria in (20.83%), enteric fever in (5%) and HIV in (4.16%). Bleeding manifestations were present in 37.50% of patients and the commonest site of bleeding was skin and mucous membrane. In our study, 25 patients (20.83%) received blood transfusion out of that 14 patients had platelet count less than 10000/mm³ and 11 patients had platelet 10000/mm³. We had count more than splenomegaly in (16.66%), hepatomegaly in (13.33%), hepatosplenomegaly in (7.5%), jaundice in (11.66%) and reactive lymphadenopathy in (6.66%) of patients. Peripheral blood smear in our patient had anemia in (43.33%), selective thrombocytopenia in (28.33%), pancytopenia in (21.66%) and leucopenia in (6.66%) of patients.

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