ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 10, Issue, 11, pp.75610-75613, November, 2018

DOI: https://doi.org/10.24941/ijcr.33195.11.2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

CLINICAL STUDY OF THROMBOCYTOPENIA IN PATIENTS WITH ACUTE FEBRILE ILLNESS AT C.U.SHAH MEDICAL COLLEGE AND HOSPITAL, SURENDRANAGAR

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ARTICLE INFO

Article History:
Received 03rd August, 2018
Received in revised form
16th September, 2018
Accepted 04th October, 2018
Published online 30th November, 2018

Key Words:

Thrombocytopenia,
Febrile illness,
Anemia, Hematuria.

ABSTRACT

Background: Thrombocytopenia is not a disease but a symptom. For investigating causes of thrombocytopenia in patients, the aetiology can be achieved by taking a good clinical history, physical examination and basic laboratory tests. Thrombocytopenia has an inverse relation to mortality and morbidity is various febrile illnesses, serial monitoring of platelet counts has prognostic value. This highlights the importance of thrombocytopenia in various febrile disorders. **Objective:** To assess etiological factors of thrombocytopenia in acute febrile illness in indoor patients in our hospital. To assess the prognosis of acute febrile illness in relation with severity of thrombocytopenia. To correlate platelet count with bleeding and effectiveness of platelet replacement therapy. To assess the complications and mortality in relation to thrombocytopenia. **Materials and Methods:** The study is a observational randomised case study carried out from January 2016 to September 2017 at C.U. Shah Medical College and Hospital, Surendranagar (Gujarat). Hundred patients of acute febrile illness admitted to the medicine Department with platelet count less than 1,50,000 per microliter of blood with evidence of infection. The study protocol was approved by the institutional research review board and ethical committee. **Result:** Maximum number of patients were in age group 31 to 40 years (27%) and Male predominance was observed in all the age groups. Out of 100 patients, Maximum number of 81 (81%) patients presented within 7 days with complain of fever.21 patients had some kind of bleeding manifestation. Hematuria was the most common bleeding manifestation. 14 (14%) number of patients had very severe thrombocytopenia, 55 (55%) number of patients had severe thrombocytopenia, 29(29%) number of patients had moderate thrombocytopenia and 2(2%) patients had platelet count between 1,00,000-1,50,000/ml on presentation. Out of 100 patients 2 were expired and 98 patients were discharged. Anemia was the most common complication other than bleeding. **Conclusion:** Febrile illness accounts for large number of cases with thrombocytopenia. Most common cause of thrombocytopenia in patients presented with acute febrile illness was Malaria in 55 patiens, among them 40 patients had P. vivax and 15 patients had P. falciparum followed by dengue fever (22%). Anemia (36%) was the most common sequelae other than bleeding manifestation and Hematuria (9%) was the most common bleeding manifestation. Thrombocytopenia has an inverse relation to mortality and morbidity is various febrile illnesses, serial monitoring of platelet counts has prognostic value. This highlights the importance of thrombocytopenia in various febrile disorders.

Citation: Dr. Palak Patel and Dr. Nitesh Patel. 2018. "Clinical study of thrombocytopenia in patients with acute febrile illness at c.u.shah medical college and hospital, surendranagar", *International Journal of Current Research*, 10, (11), 75610-75613.

INTRODUCTION

Thrombocytopenia is not a disease but a symptom. For investigating causes of thrombocytopenia in patients, the aetiology can be achieved by taking a good clinical history, physical examination and basic laboratory tests. The normal blood platelet count is 1,50,000-4,50,000/microlitre (Kasper, 2015). Thrombocytopenia is described as the platelet count below 1,50,000 per microlitre.

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Thrombocytopenia results from one or more of three processes (Kasper, 2015):

Decreased bone marrow production; Sequestration, usually in an enlarged spleen; and/or Increased platelet destruction. Fever is the most ancient hallmark of disease. Thrombocytopenia with fever most commonly caused by various infections named Dengue, Chikungunya, Plasmodium Vivax and Plasmodium falciparum Malaria, Scrub typhus, Viral Hepatitis, HIV, etc. Thrombocytopenia is characterized by bleeding most often from small vessel. This bleeding can manifest as petechiae over skin, heamorrhages from mucosa of gastrointestinal and

genitourinary tract. Intra cranial bleed is a dangerous consequence in thrombocytopenia patient. In mild trauma, bleeding may be observed at counts 20.000-50.000 / µL, platelet counts below 20.000/µL, spontaneous bleeding is observed, and there is a risk of serious bleeding at values lower than 10.000/µL (Jensen, 2003 and Veneri, 2009).

Thrombocytopenia has an inverse relation to mortality and morbidity is various febrile illnesses, serial monitoring of platelet counts has prognostic value. This highlights the importance of thrombocytopenia in various febriledisorders (Frank firkin).

Objectives

To assess etiological factors of thrombocytopenia in acute febrile illness in indoor patients in ourhospital. To assess the prognosis of acute febrile illness in relation with severity of thrombocytopenia. To correlate platelet count with bleeding and effectiveness of platelet replacement therapy. To assess the complications and mortality in relation to thrombocytopenia.

MATERIALS AND METHODS

The study is a observational randomised case study carried out from January 2016 to September 2017 at C.U. Shah Medical College and Hospital, Surendranagar (Gujarat), which is a tertiary care centre. Hundred patients of acute febrile illness admitted to the medicine Department with platelet count less than 1,50,000 per microliter of blood with evidence of infection. The study protocol was approved by the institutional research review board and ethical committee.

Cases were recruited till at least 100 subjects in each study group were enrolled. Blood samples were taken and sent for routine investigations including complete blood count, peripheral blood smear, liver function test, renal function test, Erythrocyte Sedimentation Rate, C- Reactive Protein, Urine routine Micro, MP by card method, Dengue NS1 antigen, Dengue IgM and IgG antibody, Blood culture and sensitivity, serum HIV, Widal test and imaging test including chest X-ray and USG abdomen. Assessment of severity of thrombocytopenia: (Jensen, 2003).

Mild: 1,00,000 - 1,50,000
Moderate: 50,000 - <1,00,000
Severe: 20,000 - <50,000
Very severe: <20,000

Data thus collected will be entered in MS Excel 2007 worksheet in the form of master chart. These data will be classified and analysed as per aims and objectives of the study. Inferences will be drawn with use of appropriate test of significance.

RESULTS

100 admitted patients of Thrombocytopenia with evidence of infection according to inclusion and exclusion criteria were taken in this study from C.U.SHAH. MEDICAL COLLEGE, SURENDRANAGAR.

Table 1. Age distribution in study population

		No.		
		Female	Male	Total
Age Group (years)	<20	6	16	22
	21-30	3	18	21
	31-40	7	20	27
	41-50	3	8	11
	>50	8	11	19
Total		27	73	100

Table 1 shows that male predominance was observed in all the age groups. Maximum number of patients were in age group of 31 to 40 years (27%). Youngest patient in the study is 14 years old. Oldest patient is 75 years.

Table 2. Distribution of patients according to duration of fever

Duration of Fever (days)	No. of patients	(%)
<7	81	81
7~13	9	9
14-20	9	9
≥21	1	1
Total	100	100%

Maximum number 81(81%) patients were having fever for less than 7 days. Patients with duration of fever for 21 days or more were only 1 (1%).

Table 3. Clinical signs in study population

Signs	No.	%
Hypotension	7	7%
Pallor	20	20%
Icterus	7	7%
Splenomegaly	7	7%
Hepatomegaly	4	4%
Hepatosplenomegaly	5	5%

Above described table and graph shows clinical signs on general physical examination of patients, in which Hypotension was found in 7(7%) patients, pallor was found in 20 (20%) patients, icterus in 7 (7%) patients, Splenomegaly was present in 7 (7%) patients, Hepatomegaly was present in 4 (4%) patients, and hepatosplenomegaly was detected in 5 (5%) patients.

Table 4. Distribution of patients of different ranges of platelet count on Day of admission, Day 3 and day of discharge

Platelate count	No. of Patients		
	On Admission	On Day 3	On Discharge
<20,000	14	2	0
20,000-50,000	55	10	0
51,000-1,00,000	29	70	11
1,00,000-1,50,000	2	17	55
>1,50,000	0	0	32
Total	100	99	98

According to the table and, 14 patients had very severe thrombocytopenia (<20,000/ml), 55 patients had severe thrombocytopenia (20,000-50,000/ml), 29 had moderate thrombocytopenia (51,000-1,00,000) and 2patients had platelet count between 1,00,000-1,50,000 on admission. At the time of discharge out of 100 patients 2 were expired and 98 patients were discharged, out of that 11(11.22%) patient's platelet count between 51,000-1,00,000; 55 (56.13%) patient's platelet count between 1,00,000-1,50,000; 32(32.65%) patient's platelet count more than 1,50,000 on discharge.

Table 5. Result of Urine R/M examination, X-ray chest findings and USG Abdomen in Study Population

Urine R/M	No.	USG Abdomen	No
BS/BP+	4		
RBC+	8	Hepatomegaly	4
Pus cells+	3		
RBC+ Pus cells	1	Hepatosplenomegaly	5
Total	16	Splenomegaly	7
X-Ray Chest	No.	Kidney Stone	1
Consolidation	5	Perichole--cystic edema	10
Pleural effusion	10		
Normal	85	Normal	73
Total	100	Total	100

Above table shows that out of 100 patients total 16 patients shows specific finding in urine routine micro examination; out of 16, 8 (50 %) patients showing hematuria (RBC +) in their urine, 3(18.75%) patients showing Pus cells in their urine, and 4 (25 %) patients showing bile salt and bile pigment in their urine and 1 (6.25%) showing both RBC+ and Pus cells. Out of 100 patients, 5 (5%)patient's X-ray shows Consolidation, 10(10%) patient's X-ray shows Pleural effusion and another 85 patient's X-ray was normal. And USG abdomen shows Hepatomegaly in 4% of patients; Hepatosplenomegaly in 5% patients; Splenomegaly in 7% of patients; Kidney stone present in 1%; Pericholecystic edema in 10% of patient and Normal USG in 73% of patients.

Table 6. Etiology of pyrexia with thrombocytopenia in patients

Diagnosis	No.
Dengue fever	22
Mixed(Malaria plus Dengue)	10
Malaria	55
P.vivax	40
P.falciparum	15
Sepsis	9
UTI	4
Pneumonia	5
HbsAg	4
Total	100

Amongst all of them 22 (22%) patients were diagnosed as dengue fever; 55(55%) were diagnosed as malaria; 10(10%) patients were diagnosed as mixed infection dengue plus malaria; Sepsis due to UTI and pneumonia was the cause for thrombocytopenia in 9 (9%) patients;4(4%) patients were diagnosed as HBSAg positive.

Table 7. Complications other than bleeding manifestations

Complications	No.
Leukocytopenia	20
Anemia	36
Hyperbilirubinemia	27
AKI	15
Hypotension	7

Table 7 suggests that complications other than bleeding occurs in our cases. In this, Anemia was the most common complication, occurs in 36 patients, followed by hyperbilirubinemia found in 27 patients, Leukocytopenia in 20 patients, AKI found in 15 patients, and hypotension found in 7 patients. Patients who presented with bleeding manifestation were correlated with their platelet counts. Out of 14 patients whose platelet counts were <20,000/ml at presentation, 10 patients had one or other bleeding manifestation. Out of 55 patients whose platelet counts were between 20,000 and 50,000/ml, 9 patients had bleeding manifestations. Out of 29 patients whose platelet counts were between 51,000 and 1,00,000/ml ,only 1 patient had bleeding manifestation in the form of bleeding gums. Out of 2 patients whose platelet counts were more than 1,00,000/ml, only 1 patient had bleeding manifestation in the form of hematuria.

Table 8. Distribution of patients according to platelet transfusion

Platelet transfusion	No.	%
No transfusion	93	93%
RDP transfused	7	7%
Total	100	100%

Table and graph shows that out of 100 cases of thrombocytopenia, 93 patients did not require platelet transfusion while those who required platelet transfusion, random donor platelet was transfused in 7 number of patients. Patients who required platelet transfusion were correlated with their plaletet counts on presentation. Out of 14 patients, whose platelet counts were less than 20,000/ml on presentation only 5 patients required platelet transfusion in the form of RDP. Out of 55 patients whose platelet counts were between 20,000-50,000/ml on presentation only 2 patients required platelet transfusion in the form of RDP.

Table 9. Outcome of patients in the study

Outcome	No.	%
Improved	98	98%
Expired	2	2%
Total	100	100%

Out of 100 cases, 98 (98%) patients were improved with treatment as per their diagnosis but 2 (2%) patients were died unfortunately.

DISCUSSION

We studied clinical features, haematological and biochemical profile and etiological analysis of 100 patients presented with thrombocytopenia with specific reference to various infection as well as correlation of bleeding manifestation and platelet transfusion with thrombocytopenia and outcome in these patients. A total of 100 patients (73 males, 27 females) diagnosed as febrile thrombocytopenia were evaluated. All patients were between 14 years and 75 years of age. Nearly, half of the patients were between 20-40 years of age. There was a male preponderance of 2.7:1, which was nearly similar to the study done by Nair PS *et al*, by Dash HS *et al* in Nov.2013 (Nair, 2003 and Dash, 2013). Patients who presented with bleeding manifestation were correlated with their platelet counts at presentation in this study. Out of 14 patients whose platelet counts were <20,000/ml at presentation, 10 patients had one or other bleeding manifestation. Out of 55 patients whose platelet counts were between 20,000 and 50,000/ml,9 patients had bleeding manifestations. Out of 29 patients whose platelet counts were between 51,000 and 1,00,000/ml ,only 1 patient had bleeding manifestation. Out of 2 patients whose platelet counts were more than 1,00,000/ml, only 1 patient had bleeding manifestation. Study done by Gandhi AA *et al* found that, out of 15 patients with platelet counts <20,000/ml, 12.5% had some bleeding manifestation, out of 33 patients with counts between 20,000-50,000/ml, 24.11% were having bleeding manifestation and 2% of patients out of 64 patients with counts >50,000 had some bleeding manifestation

(Gandhi, 2015). In our study Out of 100 cases of thrombocytopenia, 93% of patients did not require platelet transfusion while 7% of patients who required platelet transfusion in the form of random donor platelet. While Subrata Das *et al* in her study discussed that 58 (31%) out of 187 patients needed platelet transfusion (Subrata Das, 2006). 23% of patients needed platelet transfusion in study done by Nazeer Ahmed *et al* (Dash, 2013 and Gandhi, 2015). Naveen Kulkarni *et al* study discussed that out of 200 patients 18.5% of patients required platelet transfusion (Naveen Kulkarni, 2017). Complications other than bleeding were also discussed here. In this, Anemia was the most common sequelae, found in 36% of patients followed by hyperbilirubinemia was found in 27% of patients, Leukocytopenia in 20% of patients, AKI was seen in 15% of patients and Hypotension was detected in 7% of patients. Nazeerahmed *et al* studied various complications and he also observed that leucocytopenia was the most common complication, seen in 28% of patients followed by anemia in 26%, AKI in 13% and altered sensorium in 4% of patients. All cases of thrombocytopenia with evidence of infection were analysed for aetiology. Amongst them 55 patients were diagnosed as malaria, similar findings were seen in a study done by Gandhi AA *et al* 68. While Bhalara SK, shah S, *et al* study found dengue fever as most common (28.6%) aetiology of thrombocytopenia with fever followed by malaria in 22.8%, septicemia in 6.3% (Bhalara, 2015). USG findings in study done by Nair P S *et al* in June 2003 was comparable (Nair, 2003). He also discussed peri GB odema as most common USG finding. While Nazir Ahmed *et al* found ascitesas a most common USG finding in his study (Ahmed, 2011). Out of 100 patients, 14 numbers of patients had very severe thrombocytopenia, severe thrombocytopenia were detected in 55 number of patients. 29 patients were having moderate thrombocytopenia and mild thrombocytopenia was seen in 2 number of patients at the time of presentation. This results were comparable with study conducted by Gandhi AA *et al*. in which out of total 112 patients 15(13.39%) patients had platelet counts <20,000/ml, 33(29.47%) patients had counts between 20,000-50,000/ml, 64(57.14%) patients had platelet counts more than 50,000/ml.[68] In study, done by M.P Gondhali *et al*, out of 100 cases 7% of patients had platelet counts < 20,000/ml, 15% had counts between 20,000-50,000/ml and 78% of patients had platelet counts more than 50,000/ml (Gondhali, 2016). Mortality (2%) in our study was comparable with that of mortality (5%) in studydone by PrithvirajPatil*et al* (PrithvirajPatil, 2014), whereasmortality (6%) in study conducted by M.P. Gondhali *et al.* (Gondhali, 2016), Mortality (22%) in study conducted by Dash HS *et al* was higher (Veneri, 2009).

Conclusion

Febrile illness accounts for large number of cases with thrombocytopenia. Maximum prevalence is seen in up to 40 years of age group, less prevalence (30%) is seen in more than 40 years of age group. Most common cause of thrombocytopenia in patients presented with acute febrile illness was Malaria. Anemia is the most common sequelae other than bleeding manifestation and Hematuria is the most common bleeding manifestation. Person with platelet count less than 20,000/microliter has increased bleeding risk. Also person with this much less platelet count are more likely to need platelet transfusion.

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