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Study of thrombocytopenia in patients of acute febrile illness

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***Abstract*---**Introduction: Many viral and bacterial infections result in thrombocytopenia and are most common non-iatrogenic cause of thrombocytopenia. Infections can affect both platelet production and platelet survival. In addition, immune mechanisms can also be a cause, as in immune-mediated thrombocytopenia (ITP) in children following viral infection. In our setup, tropical infections like malaria, dengue and leptospirosis formed the most common and important causes of thrombocytopenia. Objectives: To correlate the bleeding manifestations of thrombocytopenia with platelet count in patients with acute febrile illness and to document the incidence of thrombocytopenia and most common cause of thrombocytopenia among patients with acute febrile illnesses. Methodology: A minimum of 200 patients admitted to tertiary care center with documented fever of >37.50C and platelet count <1,50,000/µL were selected using purposive sampling techniques. They were followed from admission till recovery, discharge or death. Correlation of bleeding manifestations like petechiae, gum bleeding, hematuria, menorrhagia, epistaxis in relation with lowest platelet count was done along with categorization of patients according to different platelet count ranges. Results: Out of total 200 patients 65% were male and 35% were female. Most common tropical infection was P. Vivax Malaria than P. Falciparum Malaria followed by Dengue Fever followed by leptospirosis and least common is Enteric Fever but P. Falciparum was associated with severe

thrombocytopenia than P. Vivax Malaria. Maximum number of patients with thrombocytopenia was having platelet counts in the range of 20,000-50,000. As per WHO anemia is severe if Hb< 8 gm/dl and moderate if Hb<11 gm/dl in both sexes greater than 15years of age. Moderate anaemia in 55 cases (27.5%), and severe anaemia in 15 cases (7.5%). Highest mortlity is due to leptospirosis 42.8%, though P. Vivax was the most common infection but carried least mortality and in dengue 2.7% mortality in the presence of severe thrombocytopenia. But the mortality is higher with P. Falciparum 6.8%. The lowest platelet counts were seen in dengue patients, majority of them had Platelet counts < 50,000/cm. Out of 200 patients 45 pateints showed bleeding manifestations. Petechiae were seen in 33 Patients as major bleeding manifestation, followed by gum bleeding, hematuria, epistaxis &menorrhagia. Conclusion: P. vivax malaria is the most common cause of fever with thrombocytopenia. In majority of patients, thrombocytopenia was transient and asymptomatic; however commonest bleeding manifestations were petechiae and purpura. Leptospirosis is common in south Gujarat and mortality was maximum due to renal, liver and pulmonary involvement in these patients.

***Keywords*---**malaria, leptospirosis, thrombocytopenia.

Introduction

“Fever is an elevation of body temperature that exceeds the daily variation and occurs in conjunction with an increase in the hypothalamic set point”.[1] Fever is the most common symptom of presentation in a hospital with a spectrum of causes including infections and non-infectious disease that range from benign to life threatening epidemiologically common tropical infections like malaria, dengue, enteric fever and leptospirosis are common in our setup and alteration of various haematological parameters have been observed in all these patients.[2] Multiple studies have been done prognosticating the role of various haematological and biochemical parameters, however each tends to stress on a specific clinical entity like malaria, dengue, enteric fever and leptospirosis. The diagnostic dilemma in clinical practice is that we don’t have the diagnosis of cause of fever but most of common disease have non-specific clinical picture.[3] We aim to preview the role of thrombocytopenia, one of the commonest haematological abnormalities in acute tropical fevers (of less than 14 days duration). We have found many haematological abnormalities in case of fever but thrombocytopenia is commonest haematological abnormality. Therefore, the present study “Study of thrombocytopenia in patients of acute febrile illness.” We aim to investigate the cause of fever in these patients and try to establish their relationship with thrombocytopenia and also to correlate the bleeding menifestations of thrombocytopenia in acute febrile illness.

Materials and Methods

This study entitled "study of thrombocytopenia in patients of acute febrile illness." Was carried out on minimum of 200 patients admitted to tertiary care center with documented fever of >37.5ºC and platelet count <1,50,000/µL.

Inclusion Criteria

- Those admitted in tertiary care centre having temperature of >37.5ºC and duration of fever <14 days
- Platelet count <1,50,000/µL
- Age ≥18 years

Exclusion Criteria

- Platelet count >1,50,000/µL
- Age < 18 years
- Pregnant women
- On long term medications which causes thrombocytopenia. (Heparin, rifampicin, carbamazepine, acetaminophen etc.)
- Patients with known chronic illnesses like Systemic lupus erythemetosus, Idiopathic thrombocytopenic purpura, chronic liver diseases, malignancies and autoimmune diseases.

Methodology

A minimum of 200 patients admitted to tertiary care center with documented fever of >37.5ºC and platelet count <1,50,000/µL were selected using purposive sampling techniques. They were followed from admission till recovery, discharge or death. If patient was diagnosed of having any chronic illness we had excluded it from our study. The following investigations had been done in all patients with acute fever: Hemoglobin, total leucocyte count, differential count, packed cell volume and platelet count. If platelet count was <1,50,000/µL, the following investigations were done to find out the cause of thrombocytopenia: Peripheral smear for Malaria parasite test, Dengue ELISA (NS1 and IgM), IgM Leptospirosis in particular season, Blood culture, Chest Xray, USG abdomen and pelvis, Liver function test, viral markers, urine routine and microscopy and stool routine and microscopic examination had done whenever required. If diagnosed with a specific disease, subsequent investigations were not done. Platelet count was repeated on alternate day during the course of admission of the patient. Based on the outcome and complications, other tests were also repeated.

Statistical analysis

The data from patients who had laboratory confirmatory diagnosis was analysed by frequency distribution and central tendancy.

Results

Table 1: In our study out of total 200 patients 65% were male and 35% were female. Among this 45% were in age group between 18 to 25 years and 25% in age group between 26 to 35 years with an average age of 25 years, so 70% were belongs to age group between 18-35 years. Table 2: In our study 46% patients were positive for P. Vivax Malaria on peripheral smear (Thick and Thin smear), which is a gold standard test for diagnosis and identification of malaria. 22% were positive for P. Falciparum Malaria on peripheral smear. 18% were positive for dengue; both antibody and antigen test were applied for the diagnosis of dengue fever. 7% were positive for Enteric Fever diagnosed using the rapid antigen test, Enterocheck. Only 7% were diagnosed with leptospirosis and the diagnosis was made by IgM ELISA as well as by MAT for leptospirosis. Table 3: Maximum number of patients with thrombocytopenia was having platelet counts in the range of 20,000-50,000. Lowest platelet count in both male and female patients were found in dengue fever and highest platelet counts were found in enteric fever Table 4: As per WHO anemia is severe if Hb< 8gm/dl and moderate if Hb<11 gm/dl in both sexes greater than 15years of age. Moderate anaemia in 55 cases (27.5%), and severe anaemia in 15 cases (7.5%). Patients with severe anaemia were transfused with red cell concentrate. Platelet concentrate were given to patients with counts <10,000/cumm.

Table 5: In our study highest mortlity is due to leptospirosis 42.8%. Through P. Vivax was the most common infection but carried least Mortality and in dengue 2.7% mortality in the presence of severe thrombocytopenia. But the mortality is higher with P. Falciparum 6.8%. In P. Falciparum infection higher mortality is due to more severe thrombocytopenia which is associated with bleeding, liver dysfunction, renal dysfunction because of high parasitic index which has direct lytic effect on RBC resulting in multi organ dysfunction, whereas in P. Vivax malaria even with severe thrombocytopenia there is no multi organ dysfunction so carries better prognosis. Table 6: Out of 200 patients, 45 patients showed bleeding manifestations. Petechiae were seen in 33 patients as a major bleeding manifestation followed by 5 patients having gum bleeding, 3 patients had hematuria, 2 patients had epistxis, 1 patient had hematuria and 1 patient had menorrhagia

Tables

Table 1
Age and sex incidence of fever with thrombocytopenia

Age Groups In Years	Number of Cases Male N=130 (%)	Number of Cases Female N=70 (%)
18-25 Years	60 (30%)	30 (15%)
26-35 Years	30 (15%)	20 (10)
36-45 Years	13 (6.5%)	10 (5%)
46-55 Years	12 (6%)	5 (2.5%)
56-65 Years	12 (6%)	3 (1.5%)
>65 Years	3 (1.5%)	2 (1%)

Total	130	70

Table 2
Various causes of the fever with thrombocytopenia

Causes	No. of Patients
P. Vivax	92
P. Falciparum	44
Dengue	36
Enteric Fever	14
Leptospirosis	14

Table 3
Gender-wise platelet counts of cases

Disease	Lowest Platelet Count In Males	Lowest Platelet Count In Females
Dengue Fever	10,000	13,000
P.Vivax Malaria	14,000	17,000
P.Falciparum Malaria	12,000	18,000
Enteric Fever	94,000	52,000
Leptospirosis	45,000	43,000

Table 4
Anemia and blood transfusion amongst the cases

Haemoglobin (gm/dl)	No. Of Cases
< 8	15
8- 10.9	40
≥11	145
Transfusion Medium	No. Of Units Of Blood Product Used
Whole Blood	00
Red Cell Concentrate	12
Platelet Concentrate	24
Apheresis Platelet	00

Table 5
Prognosis in various causes of the fever

Etiology	No. Of Patients	No. Of Deaths	Percentage
P. Vivax	92	0	0%
P. Falciparum	44	3	6.8%
Dengue	36	1	2.7%
Enteric Fever	14	0	0%
Leptospirosis	14	6	42.8%

Table 6
Various bleeding manifestation at different platelet count

Site of bleeding	Platelet count <20,000	Platelet count 20,000-50,000	Platelet count 50,000-1,00,000	Platelet count 1,00,000-1,50,000	total
Petechiae/ecchymosis	11	12	8	2	33
Gum bleeding	4	1	0	0	5
Hematuria	1	1	1	0	3
Menorrhagia	1	0	0	0	1
Melena	0	1	0	0	1
Epistaxis	1	1	0	0	2
No bleeding	2	46	49	58	155

Discussion

In our study maximum incidence of tropical infection was found in age group of 18 to 35 years (70%). Because this age group belongs to working age group and frequent visitor to endemic area and slum area because of low socio economic status they are more prone to get affected by tropical infection and males are engaged with outdoor activities, thus highlighting the socio-economic burden of the disease. In the present investigation the lowest platelet counts were seen in the dengue patients, majority of them had platelet counts <50,000/cumm which is comparable to the study done at Brazil Coelho HC et al.[4]. In our study most common tropical infection was P. Vivax Malaria than P. Falciparum Malaria followed by Dengue Fever followed by leptospirosis and least common is Enteric Fever but P. Falciparum was associated with severe thrombocytopenia than P. Vivax Malaria. This was found in agreement with the study conducted by Krishna S et al.[5], where only 2% of the patients with thrombocytopenia had Leptospirosis. In another study by AramburuGuarda J et al.[6] shows P. Vivax infection in 51% and P. Falciparum infection in 38% cases. Faseela TS et al.[7] shows P. Vivax infection in 53% and P. Falciparum in 42% which was comparable to our study.

Moderate anaemia in 55 cases (27.5%), and severe anaemia in 15 cases (7.5%). The pathogenesis of anaemia is multifactorial. A complex chain of pathogenesis involving mechanical destruction of RBC's, marrow suppression, ineffective erythropoiesis and accelerated immune destruction of parasitized RBC's have been implicated. Majority of moderate to severe anaemia patients in our study were found to be normocytic normochromic, microcytic hypochromic picture was seen in 13 cases and macrocytes seen in few cases. Saini T et al.[8] has also found severe anaemia in 8.82% cases which is comparable to my results. In study done at Kolkata Sarkar D et al found moderate to severe anaemia in 46% cases.[9] In our study patients with severe anaemia were transfused with red cell concentrate. Platelet concentrate were given to patients with counts <10,000/cumm, which is in accordance to the WHO guidelines for the transfusion of platelet in patients with thrombocytopenia.

In our study highest mortlity is due to leptospirosis 42.8%. Through P. Vivax was the most common infection but carried least Mortality and in dengue 2.7% mortality in the presence of severe thrombocytopenia. But the mortality is higher with P. Falciparum 6.8%. In a study done by Faseela TS et al. [7] in her study found 38.3% mortality seen in severe P. Falciparum infection with severe thrombocytopenia. A study done by Gerardin P et al. [10] shows mortality of 8% for P. Vivax malaria with severe thrombocytopenia. Out of 200 patients, 45 patients showed bleeding manifestations. Petechiae were seen in 33 patients as a major bleeding manifestation followed by 5 patients having gum bleeding, 3 patients had hematuria, 2 patients had epistxis, 1 patient had hematuria and 1 patient had menorrhagia compared to study by Nair PS et al.[11] spontaneous bleeding in 77.78% was a major manifestation followed by petechiae/purpura accounting for 22.22%. In another study done by Patil P petechiae was the major manifestation 73.9% followed by spontaneous bleeding (26.9%).[12]

Conclusion

Fever with thrombocytopenia is commonly seen in Malaria and Dengue patients with overall no correlation to mortality and morbidity. In present study, mild bleeding manifestations with insignificant mortality due to thrombocytopenia per se were found only in ten patients having severe thrombocytopenia. In present study P.vivax malaria is the most common cause of fever with thrombocytopenia. In majority of patients, thrombocytopenia was transient and asymptomatic; however commonest bleeding manifestations were petechiae and purpura. On treating the specific cause, improvement in platelet count was noted in majority of patients at the time of discharge and during further follow up. Leptospirosis is common in south Gujarat and mortality was maximum due to renal, liver and pulmonary involvement in these patients. In nutshell, any patient coming with fever must be investigated for Malaria and Dengue Fever, as haematological abnormality in form of thrombocytopenia is very common in these fever cases and it may contribute in morbidity and mortality. Also during rainy season, patients must also be investigated for leptospirosis, particularly in endemic area like South Gujarat

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