

Spectrum and Their Correlation with Severity of Thrombocytopenia in Patients of Acute Febrile Illness: A Tertiary Care Hospital Experience Bikaner Rajasthan

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Abstract

Background: Acute febrile illness with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infection is a common cause of thrombocytopenia. Infections like Malaria, Dengue, Typhoid and septicemia are some of them.

Methods: Total 394 patients of age more than 18 years with acute febrile illness with thrombocytopenia attending medicine department were enrolled and studied for demographic details along with severity of thrombocytopenia among different infections.

Results: In present study, 54.06% patients were diagnosed with severe thrombocytopenia among the infections while 30.20% patients were moderate and 15.74% patients were mild. Patients with mix infection were more severe than single infection.

Conclusion: Early diagnosis and appropriate treatment is rewarding and prevents morbidity and mortality in patients with febrile thrombocytopenia. Febrile thrombocytopenia is an important clinical condition commonly caused by infections, particularly viruses and malaria.

Keywords: Infection, Acute febrile illness (AFI), Thrombocytopenia, Severity, Dengue, Malaria.

Introduction

Thrombocytopenia is defined as platelet count less than 150,000 / μ l. This is due to decreased production, increased destruction (immunogenic and non-immunogenic) and increased sequestration in spleen. Thrombocytopenia cases are considered mild if counts are between 1,00,000 and 1.5 lakh, moderate if between 50,000 and 1,00,000, and severe if less than 50,000 per μ l. Patients with platelet count less than 10,000/ μ l have increased risk of spontaneous bleeding, petechiae and

bruising.¹ Febrile thrombocytopenia is the thrombocytopenia associated with fever. Diseases which commonly present with fever and thrombocytopenia are malaria, leptospirosis, rickettsial infections, septicemia, typhoid, arbovirus disease such as dengue fever, rodent-borne viruses such as Hanta and Lassa fever, human immunodeficiency virus, visceral leishmaniasis and TTPHUS. Viruses produce thrombocytopenia by various mechanisms like impaired platelet production as a result of direct viral invasion, toxic effect of viral proteins on thrombopoiesis, virus induced hemophagocytosis and increased platelet destruction caused by binding of virus induced autoantibodies or viral antigen antibody complexes. Autoimmune thrombocytopenia occurs during or immediately after acute viral infections. Thrombocytopenia in Dengue fever is caused by bone marrow suppression (i.e., decreased platelet synthesis and increased immune mediated destruction of platelets).² Bleeding may occur at higher platelet counts when qualitative platelet defects, such as those caused by medication that impair platelet function, have been superimposed or when underlying anatomic defects that predispose to bleeding are present. Febrile thrombocytopenia accounts for the majority of outpatient visits and inpatient admissions in India. The causes for the same are variable and need a systematic approach to identify the cause of appropriate therapy.³ Present study was done to assess spectrum of infections in febrile thrombocytopenia patients at a tertiary care hospital.

Materials and Method

Place of Study: This study was carried out in Department of Microbiology, Sardar Patel Medical College and associated group of Hospitals, Bikaner (Raj.).

Study Design: Cross Sectional Observational study.

Inclusion Criteria

1. All Adult patients (Age \geq 18 years).
2. All Adult patients (Age \geq 18 years) who were diagnosed with fever (temperature \geq 38°C) within last 24 hours, duration of fever ranging from 5-14 days.
3. All Adult patients (Age \geq 18 years) who were diagnosed with thrombocytopenia, i.e., platelet count $<$ 1.5 lakhs.

Exclusion Criteria

1. Neonates, Children and Patients (Age \leq 18 years).
2. Patients of fever with thrombocytopenia other than infective etiology like immune thrombocytopenia, drug-induced thrombocytopenia, hemolysis, and low platelets, myeloproliferative diseases, disseminated intravascular coagulation of non-infective etiology (abruptio placentae, snake bite).
3. Patients on antimicrobials, antipyretics, and anti-platelets drugs.
4. Patients with chronic liver disease.
5. Patients with autoimmune diseases.

Sample Collection: In total, 10 ml blood was collected from each adult patient. 5ml of blood sample were inoculated in blood culture bottles and transported to the laboratory within 2 hours. The remaining 5 ml of blood were collected in plain and ethylene diamine tetra acetic acid (EDTA) bulb. Blood collected in the plain bulb were centrifuged at 3000 g for 10 min, and serum was stored at 20°C for serological testing.

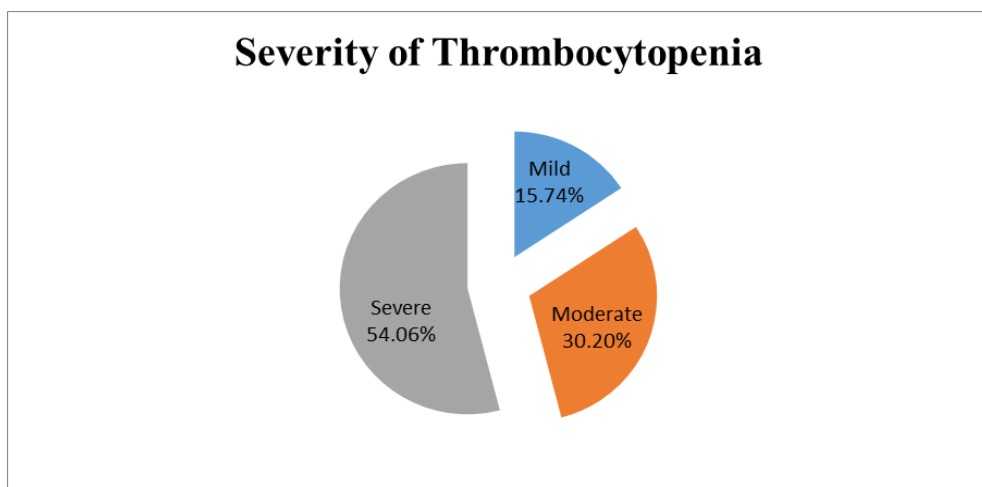
Statistical Analysis: Categorical variables were expressed as a frequency and percentage. Continuous variables were expressed as mean and standard deviation. Ethical Clearness was taken from institutional ethical committee.

Results

Table 1. Demographic profile

S. No.	Age Group (In Years)	Male		Female		Total	
		Number	%	Number	%	Number	%
1	18 - 25	74	66.07	38	33.93	112	28.43
2	25 - 40	75	58.59	53	41.41	128	32.49
3	40 - 60	60	56.60	46	43.40	106	26.90
4	> 60	22	45.83	26	54.17	48	12.18
Total		231	58.63	163	41.37	394	100

In our study, maximum number of patients (32.49%) were between the age group of 25 to 40 years followed by 28.43% patients were belong to 18 to 25 years age group. Male female ratio was 1.42:1.



In present study, 54.06% patients had severe thrombocytopenia followed by 30.20% patients with moderate and 15.74% patients with mild thrombocytopenia.

Etiology	Severity of Thrombocytopenia						Total	
	Mild		Moderate		Severe		No.	%
	No.	%	No.	%	No.	%		
Dengue	13	9.77	35	26.32	85	63.91	133	33.76
Dengue with COVID-19	2	50.00	1	25.00	1	25.00	4	1.02
Dengue with HBV	0	0.00	1	100.00	0	0.00	1	0.25
Dengue with Malaria	0	0.00	3	27.27	8	72.73	11	2.79
Chikungunya	1	100.00	0	0.00	0	0.00	1	0.25
HAV	8	80.00	2	20.00	0	0.00	10	2.54

HAV with HEV	1	50.00	1	50.00	0	0.00	2	0.51
HEV	7	100.00	0	0.00	0	0.00	7	1.78
Malaria	3	6.00	16	32.00	31	62.00	50	12.69
Malaria with Typhoid	0	0.00	0	0.00	1	100.00	1	0.25
Brucella	7	77.78	2	22.22	0	0.00	9	2.28
Scrub Typhus	0	0.00	3	42.86	4	57.14	7	1.78
Leptospirosis	0	0.00	9	100.00	0	0.00	9	2.28
Typhoid	1	50.00	1	50.00	0	0.00	2	0.51
Staphylococcus aureus	2	22.22	6	66.67	1	11.11	9	2.28
Enterococcus faecalis	1	25.00	2	50.00	1	25.00	4	1.02
Escherichia coli	2	40.00	2	40.00	1	20.00	5	1.27
Klebsiella spp	0	0.00	2	100.00	0	0.00	2	0.51
Pseudomonas aeruginosa	1	50.00	1	50.00	0	0.00	2	0.51
Unidentified	13	10.40	32	25.60	80	64.00	125	31.73
Total	62	15.74	119	30.20	213	54.06	394	100

Patients with mix infection were more severe than single infection.

Discussion

Fever with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infections like malaria, dengue, typhoid and septicemia are some of the common causes of fever with thrombocytopenia. Demographic Profile

In our study, maximum number of patients (32.49%) were between the age group of 25 to 40 years followed by 28.43% patients were belong to 18 to 25 years age group. Male female ratio was 1.42:1.

These findings are consistent with the result of study done by Gondhali et al. (2016),⁴ in which maximum prevalence was in this age group only i.e. 26%. Similarly, in study done by Nakhle et al. (2016),⁵ prevalence of febrile thrombocytopenia in the age group of 21-30 years was even higher. Younger age group are the most active working group of population and hence are at increased risk of exposure to vector borne diseases like dengue, malaria and scrub typhus.

In our study, there was male preponderance with 231 males and 163 females which is in concordance with studies conducted by Nair et al. (2003),⁶ Gondhali et al. (2016) and Modi et al. (2016),^{4,7} which had 76%, 56% and 70% males respectively. Male preponderance can be attributed to increased outdoor activities among men.

In present study, 54.06% patients had severe thrombocytopenia followed by 30.20% patients with moderate and 15.74% patients with mild thrombocytopenia. Patients with mix infection were more prone to severe thrombocytopenia than single infection.

Many undifferentiated febrile illnesses are very common in tropical countries like India which may mimic like dengue, salmonella typhi, malaria, Leptospirosis, influenza etc.⁸ Reduced platelet count might also be due to pseudo thrombocytopenia, which may be caused by EDTA is a common laboratory phenomenon.⁹ 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 prick, can be examined.¹⁰ Dengue fever, plasmodium falciparum malaria fever, plasmodium vivax malaria fever, septicemia and viral fever other than dengue were most common etiology for febrile thrombocytopenia in present study.

A related study noted the most common cause for febrile thrombocytopenia is Malaria in 54% followed by other infections in 21%, dengue in 15%, and enteric fever in 6% and sepsis in 4%.⁹ The study by Gandhi AA et al.¹¹ found malaria being the commonest etiology in febrile thrombocytopenia patients with P. Falciparum malaria (20.54%) as predominant type of malaria followed by P. vivax malaria (16.07%) and mixed malaria (4.46%). Compared to study done by PS Nair et al.⁶ septicemia (26.6%) was the major cause of febrile thrombocytopenia, whereas studies done by Gandhi et al.¹¹ and Lakum et al.¹² showed Malaria (41.07%) and (46.8%) respectively as the major cause, this difference was noted due to seasonal and regional variation. Dengue was the most common cause of febrile thrombocytopenia in our study, early diagnosis of dengue infection remains a challenge to all clinicians. Ho et al.¹³, in his study noted that a combination of several lab parameters such as leukopenia, elevated aminotransferase, TLC and low CRP gave a positive predictive value of about 89.5% The value of positive predictive value (PPV) of this given combination was increased to 93.1% by just adding prolonged aPTT and this combination served as a very good predictor marker for acute dengue infections.

Conclusion

Early diagnosis and appropriate treatment is rewarding and prevents morbidity and mortality in patients with febrile thrombocytopenia. Febrile thrombocytopenia is an

important clinical condition commonly caused by infections, particularly viruses and malaria. Prompt diagnosis and immediate specific treatment of underlying etiology of febrile thrombocytopenia with maintenance of platelet count and hemostatic function gives good recovery.

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