ORIGINAL ARTICLE

CLINICAL AND LABORATORY EVALUATION OF PATIENTS WITH FEBRILE THROMBOCYTOPENIA

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ABSTRACT

Background: Infection is a common cause of thrombocytopenia. Fever with thrombocytopenia is a common condition that is associated with an increased risk of morbidity and mortality. Infections like Malaria, Dengue, Typhoid and septicaemia are some of the common causes of fever with thrombocytopenia.

Methods: 112 patients aged > 18 years with fever and thrombocytopenias were observed for bleeding manifestations.

Aims and objectives: To determine the relative frequency of different diseases in fever with thrombocytopenia and to observe the different bleeding manifestations in order of their incidence in fever with thrombocytopenia and their relation with platelet count.

Results: Dengue was the commonest cause of fever with thrombocytopenia (26.79%) followed by P.falciparum malaria (20.54%) and P. Vivax malaria (16.07%). Bleeding manifestations were seen in 38.40% of patients. 76.74% of patients had patechie/purpura as the commonest bleeding manifestation followed by gum bleeding in 16.28 %.

Conclusions: Dengue was the commonest cause of fever with thrombocytopenia. Common Bleeding manifestations were patechie /purpura and gum bleeding.

Keywords: Fever, Thrombocytopenia, Malaria, Dengue

INTRODUCTION

F ever is the most ancient hallmark of disease. Fever is known as pyrexia from Greek "pyretus" meaning fire; Febrile is from the Latin word Febris, meaning fever.[1]

It is a frequent medical sign that describes increase in internal body temperature to the level above normal. It is considered as one of the body's immune mechanisms to attain neutralization of perceived threat inside the body.[2] Fever is a response to cytokines and acute phase proteins and occurs in infections and in non infectious conditions.[3] The normal platelet count is 150000-450000/mm³. Thrombocytopenia is defined as platelet count less than 150000/mm³. It results from one of three mechanisms i.e. reduced production, excessive peripheral destruction and increased platelet sequestration in spleen.[4] The causes for thrombocytopenia are varied and range from idiopathic, in-

fectious to malignancies. Patients with acute febrile illnesses in a tropical country like India usually have an infectious aetiology and may have associated thrombocytopenia. Infections like malaria, dengue and typhoid are some of the common causes of fever with thrombocytopenia.

Patients having thrombocytopenia with fever many times do not have bleeding manifestations. Hence study of correlation between platelet counts and hemorrhagic manifestations will help us to know the correct time for infusion of platelets, thus avoiding unnecessary platelet transfusion Pseudo thrombocytopenia is false low platelet count and is suspected when there is no bleeding despite very low platelet count.[4]

This study aims to determine the relative frequency of different diseases presenting as newly found thrombocytopenia in adult patients, to determine the proportions of patients who had bleeding

manifestations and the different bleeding manifestations in order of their incidence of occurrence.

Table 1: Severity of thrombocytopenia and clinical manifestations[4]

Platelet count/mm³	Clinical Manifestations
>100000	Asymptomatic
50000-100000	Haemorrhage after injury
20000-50000	Skin purpura
<20000	Spontaneous bleed from mucus membrane

MATERIALS AND METHODS

This study was carried out in 112 adult patients (age above 18 years) presenting with fever having thrombocytopenia (platelet count <1,50,000/mm³). Detailed history was taken. Presenting complaints and haemorrhagic manifestation were noted. The bleeding manifestations that the patients presented with or developed during their course in hospital were recorded. All the patients were subjected to routine haematological investigation like haemoglobin, total leukocyte count, platelet count, peripheral smear study, peripheral smear for malarial parasites, MCV (mean corpuscular volume), Dengue NS1antigen, Dengue IgM and IgG, Prothrombin time with INR, Activated partial thromboplastin time, renal function test and liver function test. Baseline platelet counts were done on the day of presentation. Repeat platelet counts were done in subjects with marked thrombocytopenia until normal or near-normal values were reached. Other investigations as necessary were done to achieve diagnosis such as bone marrow trephine biopsy, serological study for HIV infection, TSH, S. Widal, D-Dimer, Serum vitamin B12 level, Anti Nuclear Antibody (ANA).

Inclusion criteria: Patients with fever and thrombocytopenia above 18 years of age.

Exclusion criteria: Patients with fever and no thrombocytopenia were excluded. Patients with thrombocytopenia and no fever were also excluded from study. Previously diagnosed conditions which can lead to thrombocytopenia such as ITP, cirrhosis, chronic liver disease, patients on drugs (aminosalicylic acid, Linezolid, Amiodarone Carbamazepine, Captopril, Methyldopa) causing thrombocytopenia were excluded.

RESULTS

The commonest causes of thrombocytopenia in our study were Malaria 41.07%(46) followed by Dengue 26.7%(30), viral fever 17%(18), megaloblastic anaemia 5.36%(6),enteric fever 4.46%(5) and septicaemia 4.46%(5).

Table 2: Cause of Disease

Disease	Male	Female	Total (%)
Dengue fever	17	13	30 (26.79)
P.falciparum Malaria	14	9	23 (20.54)
P..Vivax Malaria	8	10	18 (16.07)
P.falciparum + P.Vivax Malaria	3	2	5 (4.46)
Enteric fever	3	2	5 (4.46)
Septicemia	2	3	5 (4.46)
Megaloblastic Anemia	2	4	6 (5.36)
Viral fever other than dengue	10	8	18 (16.07)
Hematologic Malignancy	0	2	2 (1.67)
Total	**59**	**53**	**112 (100)**

The causes of febrile thrombocytopenia in our study was Malaria 41.6% followed by dengue 26.7%, viral fever 16.07%, enteric 4.46% and septicaemia 4.46%.(table 3) Similar results were obtained in Patil study and Dash study, while Nair study had septicaemia as the major cause of thrombocytopenia.

In our study, among 30 patients with dengue fever 15 (50%) had moderate thrombocytopenia. Out of 23 patients with P.Falciparum malaria 13 (56%) had mild thrombocytopenia and 9 (39%) had severe thrombocytopenia. Out of 18 patients with

Table 3: Comparison of causes of thrombocytopenia

Disease	Present study	Nair et al[5]	Patil et al[6]	Dash et al[7]
Dengue	26.79%(n=30)	13.8%	15%	20%
Malaria(P.falci and P.vivax)	41.07%(n=46)	9.2%	54%	45%
Enteric fever	4.46%(n=5)	14.7%	6%	10%
Septicaemia	4.46%(n=5)	26.6%	4%	21%
Megaloblastic anaemia	5.36%(n=6)	11.9%	-	1%
Hematologic malignancy	1.79%(n=2)	3.7%	-	1%
Other viral fever	16.07%(n=18)	18.3%	21%	2%

Table 4: Fever-associated thrombocytopenia in different platelet count ranges

Disease	Platelet Count>50000	20000-50000	10000-20000	5000-10000	<5000	Total
Dengue	11	15	3	1	0	30
P.Falciparum	13	7	2	1	0	23
P.Vivax	13	3	2	0	0	18
Enteric fever	4	1	0	0	0	5
Septicemia	4	0	0	1	0	5
P.Falciparum+P.Vivax	0	2	1	1	1	5
Viral Fever other then dengue	14	3	1	0	0	18
Megaloblastic anemia	4	2	0	0	0	6
Hematologic Malignancy	1	0	0	0	1	2
Total	64	33	9	4	2	112

P.vivax malaria 13(72.2%) had mild thrombocytopenia. In study done by Bhalra et al.[8] moderate thrombocytopenia was more common among all types of malaria, whereas severe thrombocytopenia was more common in P.falciparum infection.

Table 5: Fever-associated thrombocytopenia in different platelet count ranges: Comparison between different studies

Platelet count range	Present study	Nair et al(3)	Bhalara et al(6)
>50000	64(57.14)	62(56.8)	196(59.8)
20000-50000	33(29.47)	28(25.7)	77(23.5)
<20000	15(13.39)	19(17.4)	54(16.3)
Total	112	109	327

Figure in parenthesis indicate percentage

Table 6: Correlation of site of bleeding with different platelet count

Site of bleeding	<20000/µL	20000-50000/µL	>50000/µL	Total
Petechiae/ ecchymosis	10	22	1	33
Gum bleeding	6	1	0	7
Hematuria	0	1	1	2
Menorrhagia	1	1	0	2
Melena	1	2	0	3
Epistaxis	1	0	0	1
No bleeding	1	6	62	69

Out of 112 patients, 69 patients showed bleeding manifestations. Petechiae were seen in 33 patients as a major bleeding manifestation followed by 7 patients having gum bleeding3 patients had melena and then 2 patients each had hematuria and menorrhagia. The platelet count at which each of these manifestations was seen is summarized in the table below.

In our study platelet count range of >50000/mm³ was found in 64(57.14%) patients, while 33 (29.47%) had platelet count in range of 20000-50000/ mm³.15 patients had count <20000/ mm³. These findings correlate with Nair and Bhalara study were they found 56.8%and 59.8% incidence of platelet count >50000/mm³ respectively.

DISCUSSION

Compared to study by P.S. Nair et al[5] spontaneous bleeding in 77.78% was a major manifestation followed by petechiae/purpura accounting for 22.22%.While in a similar study by Dr. Srinivas et al[9] purpura (63%) was the commonest bleeding manifestations followed by spontaneous bleeding (37%). In study done by Patil[4] petechiae was the major manifestation73.9% followed by spontaneous bleeding (26.9%).

In this study, the most common aetiology responsible for newly diagnosed thrombocytopenia in adult patients was found to be Dengue fever (26.79%). The two mechanisms probably involved in dengue-induced thrombocytopenia are impaired thrombopoiesis and peripheral platelet destruction.[10] P. falciparum infection was present in 20.54% followed by P. vivax in16.07%. Mixed infection was present in 4.46% patients. Both non-immunological destruction and immune mechanism involving specific platelet-associated IgG antibodies that bind directly to malarial antigen in the platelets have been reported to play a role in the lysis of platelets.[11] Dengue and malaria were the common causes due to the higher prevalence of these infections during the rainy season, which may be the reason for variation between different studies. Megaloblastic anemia was found in 5.36% patients due to vitamin B12 and folic acid deficiency as a result of ineffective thrombocytopoiesis. In Patients with leukemia 1.79% particularly in acute leukemia, patients have petechiae, ecchymosis and nose bleeding associated with thrombocytopenia because of bone marrow infiltration.[12]

In our study distribution of platelet count in the range of > 50000-150000/mm³ was seen in 57.14 %. Platelet count in the range of 20-50000/mm³ was seen in 29.47% and Platelet count in the range of 0-20000/mm³ was seen in 13.39%. Severe thrombocytopenia was seen more with P.falciparum malaria compare to P. Vivax malaria.

CONCLUSION

Thrombocytopenia is a commonly observed hematological entity. Our study of fever with thrombocytopenia reveals among infections dengue and malaria are common causes because of seasonal and regional variations. Common Bleeding manifestations are petechiae /purpura and gum bleeding.

REFERENCES

1. Lee-Chiong, TL Jr, Stitt, JT. Disorders of temperature regulation. Comprther 1995; 21:697

2. Mackowiak, PA, Wasserman, SS, Levine, MM.A critical appraisal of 98.6 degrees F, the upper limit of the normal body temperature, and other legacies of Carl Reinhold August Wunderlich. JAMA 1992; 268; 1578.

3. Dockrel D.H, Sundar I.S, Angus B.J, Hobson R.P, Chapter13 Infectious disease In: Walker R.B,Colledge R.N,Ralston S.H,Penman I.D,Editors Davidson's principles& practice of medicine 22nd edition Churchill Livingston Elsevier limited 2014 Page 296

4. S.K.Bichile: Chapter 16 Platelet Disorders In: MunjalYP, SharmaSK, AgrawalAK, GuptaP, KamathSA, NadkarSA, SingalRK, SundarS, VarmaS, PangteyGS, PrakashA, ShahSN editors API textbook of medicine 9th edition Jaypee Brothers 2012 table2 Page.987

5. Nair PS, Jain A, Khanduri U, Kumar V. A Study of fever associated with thrombocytopenia. JAPI . Dec 2003; 1151-73.

6. Patil P, Solanke P, HarsheG International Journal of Scientific and Research Publications, Volume 4, Issue 10, October 2014 1 ISSN 2250-3153 www.ijsrp.org To Study Clinical Evaluation and Outcome of Patients with Febrile Thrombocytopenia

7. Dash H S ,Ravikiran P,Swarnlatha Astudy of clinical and laboratory profile of fever with thrombocytopenia and its outcome during hospital stay IJSR Vol. Issue:11/November2013.ISSN no2277-8179 Page 445-447

8. Bhalara SK, Shah S, Goswami H, Gonsai RN. Clinical and etiological profile of thrombocytopenia in adults:A tertiary-care hospital-based cross-sectional study: Int J Med SciPublic Health 2015;4(Online First). DOI: 10.5455/ijmsph.2015.

9. Lohitashwa SB, Vishwanath BM, Srinivas G A Study of Clinical and Lab Profile of Fever with Thrombocytopenia JAPI volume 57 March 2009.

10. ME Yeolekar In Munjal YP, SharmaSK, AgrawalAK, GuptaP, KamathSA, NadkarSA, SingalRK, SundarS, VarmaS, PangteyGS, PrakashA, ShahSN editors API Textbook of Medicine 9th edition Jaypee brothers 2012 Chapter42 DenguePage 1158

11. Makkar RP, Mukhopadhyay S, Monga A, Monga A, Gupta AK.Plasmodium vivax malaria presenting with severe thrombocytopenia.Braz J Infect Dis 2002;6:263–5.

12. Levine SP. Thrombocytopenia: Pathophysiology and classification.In: Greer JP, Foerster J, Rodgers GM, Paraskevas F, Glader B,Arber DA, Means RT, editors. Wintrobe's clinical hematology Table3 Correlation.12th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.p.1289–334