CLINICAL PROFILE, LABORATORY PARAMETERS AND SEVERITY PREDICTORS IN PATIENTS WITH FEVER AND THROMBOCYTOPENIA- EXPERIENCE OF A TERTIARY CARE CENTRE

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ABSTRACT

Fever with thrombocytopenia is a distinct clinical entity that refers to a reduction in platelet count <1,50,000/µL. This is due to decreased production, increased destruction (immunogenic and non-immunogenic) and increased sequestration in the spleen. There were 100 patients presenting with fever with thrombocytopenia taken up for study. Out of these 100 cases, 59 cases were male and 41 were female with a male-female ratio is 1.44:1. The patients' age ranged from 18 years to 67 years with a mean age of 33.3.8±14.19 years. Out of the 100 thrombocytopenic patients, only 29 (29 %) were symptomatic and suffered from bleeding manifestations, whereas the majority of the patients (71%) had no bleeding manifestation. Fever with thrombocytopenia consists of the occult presentation of a common disease rather than a rare disease. Febrile thrombocytopenia, a commonly observed problem is most frequently caused by infections: viral diseases (dengue, chikungunya, and other viruses), malaria, enteric fever etc. Febrile illness patients should be investigated irrespective of the bleeding manifestations. Bleeding occurs usually but not always with more severe thrombocytopenia. Late presentation to the hospital, prolonged fever, and signs of end organ damage influence outcomes in these patients.

KeyWords: Thrombocytopenia, Fever, Viral diseases, Febrile thrombocytopenia.

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Introduction:

Fever has been recognized as a cardinal manifestation of disease since ancient times, as recorded by ancient scholars like Hippocrates. [1] Seen first as a disease but later recognized as an accompaniment to a variety of disease entities, fever is an easily noted and reliable marker of illness. [2] Fever is a pervasive and ubiquitous theme in human myth, art and science.

A growing body of research in immunology and neuro-physiology has led to the recent understanding that fever is generally an adaptive physiology response to some threat. This notion goes against the thinking of the last two centuries that fever was a sinister sign and required intervention to lower or control it. An AM temperature of >37.2°C (98.9°F) or a PM temperature of >37.7°C (99.9°F) would define fever. [3]

Fever with thrombocytopenia is a distinct clinical entity that refers to reduction in platelet count <1,50,000/µL. This is due to decreased production, increased destruction (immunogenic and non-immunogenic) and increased sequestration in spleen. Of these infections being the commonest cause of thrombocytopenia. [3,4] Infections like Dengue, Scrub Typhus, Malaria, Typhoid, Miliary TB, HIV, Septicaemia are some of the common causes of fever with thrombo-cytopenia.[5]

Clinical features are quite variable. However, early recognition, risk stratification and prompt initiation of treatment , disease related morbidity and mortality can be limited.[6] Therefore a well-organized systematic approach was carried out with an awareness of causes of fever with thrombocytopenia which narrows the differential diagnosis of the clinical entity and brings out diagnosis.

Based on this background we intended to study the clinical profile, laboratory parameters, short term outcome and prognostic factors in adult patients with fever and thrombocytopenia at our tertiary care center.

Aims and Objectives:

1. To study the common causes of febrile thrombo-cytopenia .
2. To study the clinical and laboratory parameters in these patients.
3. To study the severity of thrombocytopenia and factors predicting bleeding in these patients.

Materials and Methods:

This study was carried out on 100 patients presenting with fever with thrombocytopenia for a period of 9 months at a tertiary care center.

Inclusion Criteria:

1. Both sexes (Male & Female).
2. Age ≥ 18 years.
3. Patients presenting with fever i.e AM temperature of >37.2^{o} C and PM temperature of >37.7^{o} C.
4. Platelet count at the time of admission of <1.5 lakhs
5. 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:

1. Age < 18 years
2. Patients with fever without thrombocytopenia
3. Patients with thrombocytopenia without fever
4. Inherited causes for thrombocytopenia
5. Patients on drugs causing thrombocytopenia
6. Autoimmune causes for thrombocytopenia
   - HIV infection
   - Cirrhosis of liver & Hypersplenism
   - Leukaemia's & Myelodysplastic Syndromes

After obtaining informed consent from patient, we enrolled participants in the present study and were subjected to focused history taking and thorough clinical examination. Investigations sent included CBC, peripheral blood smear in all patients. Rapid diagnostic test for malarial parasites, blood culture, Widal test, ELISA tests for dengue virus, etc were done as per clinical suspicion of the primary disease. Coagulation studies, L.F.T, R.F.T, C.S.F analysis, bone marrow aspiration, serum B12 level and radiological investigations were done as needed in selected cases. During the hospital stay, all the patients were subjected repeat CBC once in 2 days.

Observation and Results:

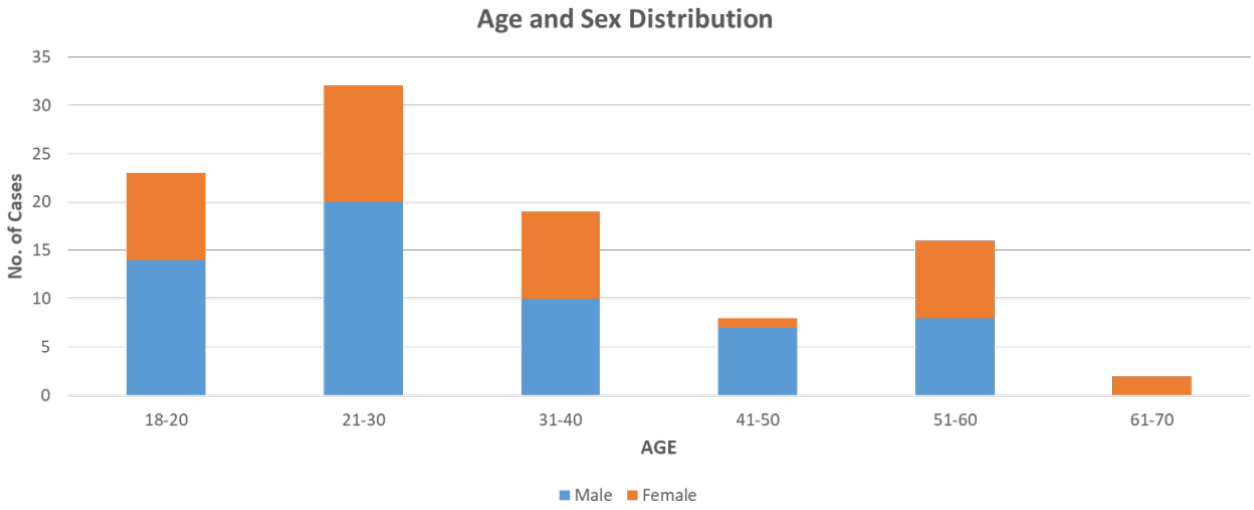
This study was conducted in the Department of Internal Medicine with aim of studying clinical profile, lab parameters and severity of fever with thrombocytopenia. Further it was aimed to establish probable etiology and diagnosis in these patients where ever possible.

There were 100 patients presenting with fever with thrombocytopenia were taken up for study. Out of this 100 cases, 59 cases were male and 41 cases were female with male female ratio is 1.44:1. The patients age ranged from 18 years to 67 years with mean age of 33.3.8±14.19 years. (Table 1, Figure 1)

Table 1: Age and sex distribution

Age (years)	Male (n=59)	Female (n=41)
18-20	14	9
21-30	20	12
31-40	10	9
41-50	7	1
51-60	8	8
61-70	0	2

Figure 1: Age and sex distribution



We also studied the clinical features of these 100 patients in our study. The most common presenting feature after fever was headache (32%), myalgia(31%) and vomiting(27%). Table 2 and table 3 along with fig 2 and fig 3 depicts the clinical features of these patients.

Table 2: Symptoms distribution

Symptoms	No.	%
Fever	100	100
Chills and Rigors	11	11
Head ache	32	32
Vomiting	27	27
Pain abdomen	6	6
Joint pain	10	10
Myalgia	31	31
Altered sensorium	1	1

Figure 2: Distribution of Symptoms

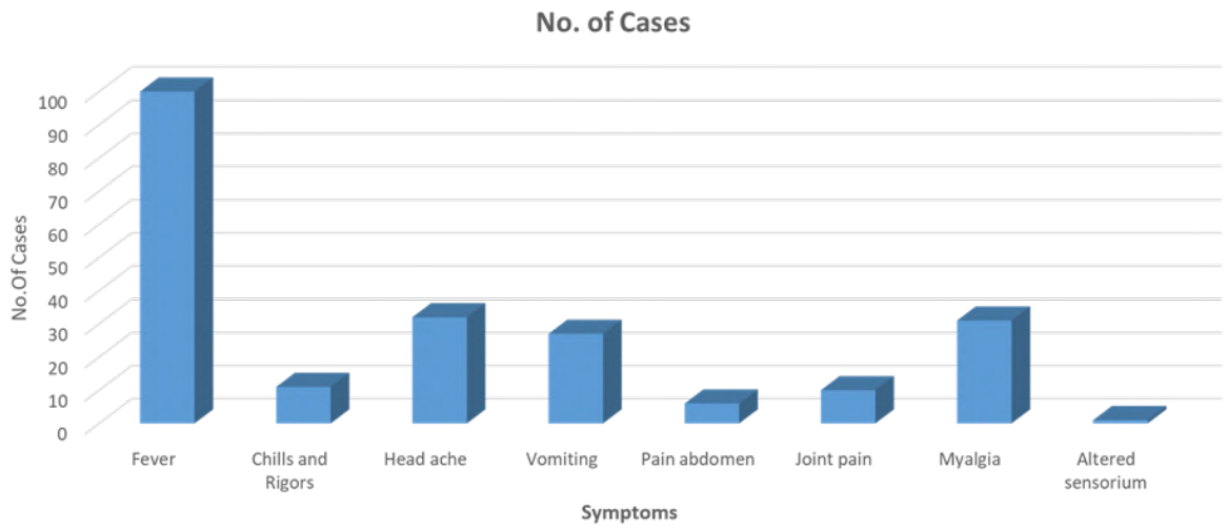
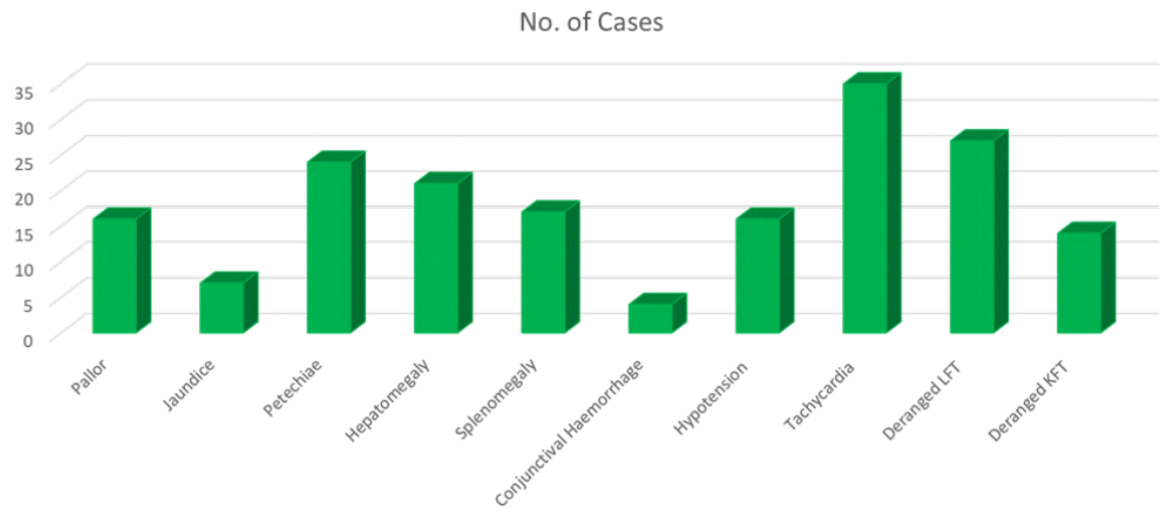


Table 3: Sings in present study

Signs	No. (n=100)	%
Pallor	16	16
Jaundice	7	7
Petechiae	24	24
Hepatomegaly	21	21
Splenomegaly	17	17
Conjunctival Haemorrhage	4	4
Hypotension	16	16
Tachycardia	35	35
Deranged LFT	27	27
Deranged KFT	14	14

Figure 3: Distribution of Signs

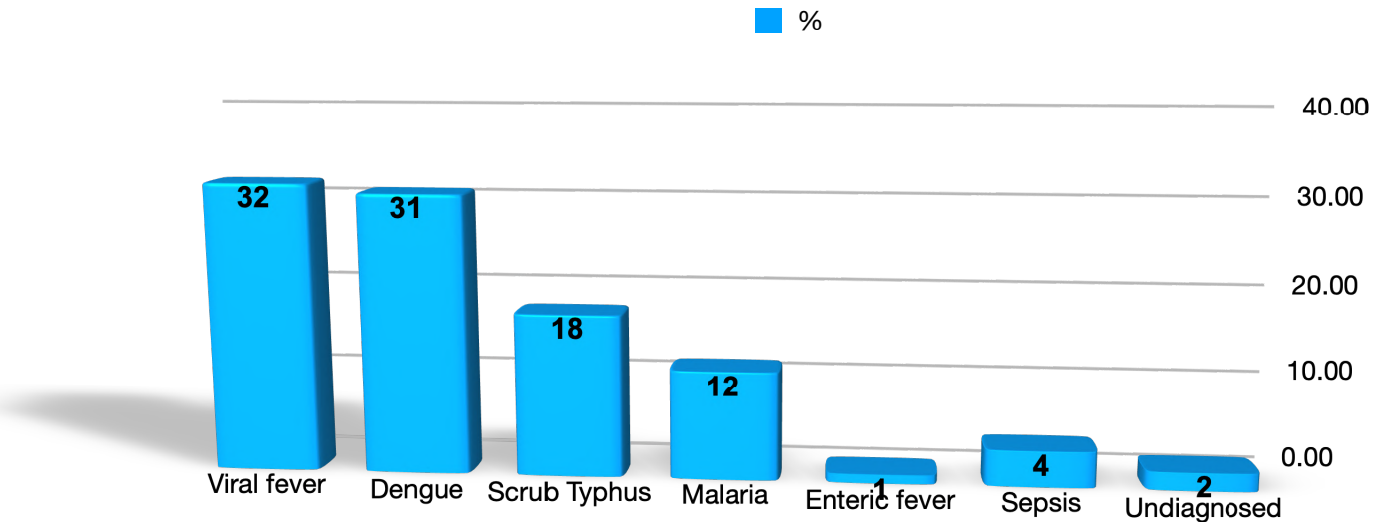


Common causes of thrombocytopenia in our study were viral fever (32%), followed by dengue fever (31%), Scrub Typhus (18%), malaria (12%) etc in the present study. (Table 4, Fig 4).

Table 4: Etiology

Diagnosis	No. (n=100)	%
Viral fever	32	32
Dengue	31	31
Scrub Typhus	18	18
Malaria	12	12
Enteric fever	1	1
Sepsis	4	4
Undiagnosed	2	2

Figure 4: Etiology



The duration of fever and platelet count in these patients are depicted in Table 5 and 6.

Table 5: Duration of fever on presentation in the present study

Days	No.	%
1-5	55	55
6-10	37	37
11-15	6	6
>15	2	2

Table 6: Platelet count in present study

Platelet count/cumm	%
<10,000/cu mm	6
10,000-50,000/cu mm	38
50,000-1,00,000/cu mm	29
1,00,000-1,50,000/cu mm	27

Bleeding Manifestations

Out of the 100 thrombocytopenic patients, only 29 (29 %) were symptomatic and suffered from bleeding manifestations, whereas majority of the patients (71%) had no bleeding manifestation. Petechiae were the commonest bleeding manifestation as seen in 17 patients followed by gum bleeding (5%) etc. Table 7. Only five patients (5%) with platelet count <10,000/ mm3 suffered hemorrhagic manifestations required platelet transfusions and this was independent of their platelet count.

Table 7: Bleeding manifestations in the present study

Site of bleeding	No. of patients	%
Petechiae	17	17
Gum bleeding	1	1
Conjunctival hemorrhage	3	3
Petechiae + Gum bleeding	5	5
Petechiae + Epistaxis	1	1
Malaena	1	1
Petechiae + Conjunctival hemorrhage	1	1

We also studied influence of various parameters on occurrence of bleeding in these patients as shown in table 8. We observed that in univariate analysis, following parameters were associated with a significant higher risk of bleeding: duration of fever >5 days, hemodynamic instability, hepatomegaly, platelets count <10,000/cu mm, abnormal KFT and elevated liver enzymes.

Table 8: Factors associated with a higher risk of bleeding

Parameters	No bleeding(n=71)	Bleeding(n=29)	P Value
Duration of fever>5 days	39	6	0.01
Hemodynamic instability	6	10	<0.001
Warning signs	9	6	0.07
Hepatomegaly	8	13	<0.001
Splenomegaly	8	9	0.7
Platelets count <10,000/cu mm	1	5	<0.001
Abnormal KFT	6	8	<0.001
Elevated liver enzymes	10	17	<0.001

Discussion:

In the present study we intended to study the pattern and profile of thrombocytopenia in febrile adult patients. Thrombocytopenia is said to occur when platelet count falls below 1,50,000/cu mm. Such low platelet counts are suspected when there is a history of easy bruising or bleeding, or it may be detected as an incidental finding during investigations done for other reasons. In the present study, we enrolled 100 patients with febrile thrombocytopenia. Most of the affected patients were in mean age of 33.3.8±14.19 years with male female ratio is 1.44:1. In a study of fever with thrombocytopenia conducted by Dash et al [7] male to female ratio was 1.5:1 and in Raiker et al study this ratio was 2.7:1 [8] The most common causes of thrombocytopenia in our (31%), Scrub Typhus (18%), Malaria (12%), Sepsis (4%), Undiagnosed (2%), Enteric fever(1%).

Septicemia (26.61%) was the leading cause of fever with thrombocytopenia in Nair et al. study, followed by typhoid fever 14.68%, dengue 13.8% megaloblastic anemia 11.9%, malaria 9.2%, haematological malignancy 3.7%[9]. Similarly a study conducted by Lakshmi et al viral fever was the most common cause (34%) followed by Dengue 29%. [10]This may be due to seasonal and regional variations. But infection was the commonest cause of fever with thrombocytopenia.

In the present study, common symptomatology apart from fever were headache (32%), myalgia(31%) and vomiting(27%). Such high incidence of these constitutional symptoms can be attributed to the fact that the most common etiology in our study was related to viral illness. In the study by Lakum N et al fever was the presenting complaint in all cases, weakness in 40% of cases, weight loss in 10% of cases and bleeding was the presenting complaint in 10% of cases. [11] In our study we found deranged renal function tests in 14% and deranged LFT in 27% of patients with fever and thrombocytopenia. In the present study, most commonly detected signs: deranged LFT (27%), petechiae (24%). In the study by Lakum N et al most common finding was pallor (70%), followed by splenomegaly(45%), hepatomegaly (35%) and lymphadenopathy (10%).[11] Out of the 100 thrombocytopenic patients, only 29% of patients suffered from bleeding manifestations. In the study by Dash et al bleeding manifestations in the form of petechiae and purpura were seen in 35% of cases and spontaneous bleeding was seen in 18% of the cases.[7]

We also studied the factors associated with a higher risk of bleeding. We observed that in univariate analysis, following parameters were associated with a significant higher risk of bleeding: duration of fever >5 days, hemodynamic instability, hepatomegaly, platelets count <10,000/cu mm, abnormal KFT and elevated liver enzymes.These probably represent the sub group of patients with a more severe disease as well as end organ damage.

Conclusion:

Fever with thrombocytopenia is one of the most challenging problems in the field of medicine. Fever with thrombocytopenia consists of the occult presentation of a common disease rather than rare disease. Febrile thrombocytopenia, a commonly observed problem is most frequently caused by infections: viral diseases (dengue, chikungunya, and other viruses), malaria, enteric fever etc. Febrile illness patients should be investigated irrespective of the bleeding manifestations. Bleeding occurs usually but not always with more severe thrombocytopenia. Late presentation to the hospital, prolonged fever, and signs of end organ damage influence outcomes in these patients.

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