

# Study of patients with acute fever and thrombocytopenia

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## Abstract

**Background:** Fever is an elevation of body temperature that exceeds the normal daily variation and occurs in conjunction with an increase in hypothalamic set point. This study comprised of all hospitalized patients with fever of less than seven days in duration *and* thrombocytopenia which is divided into Mild (<150,000 to >100,000/mcl), moderate (<100,000 to >50,000/mcl) and severe (<50,000/mcl) categories. **Aims and Objectives:** To study the common causes of acute fever *and* thrombocytopenia like Dengue fever, Chikungunya fever, Malaria, and Leptospirosis in relevance to Indian subcontinent by relevant laboratory and immunological tests. **Materials and Methods:** A single centric, prospective study of 50 indoor patients with fever < 7 days was carried out at B J Medical college and civil hospital and relevant biochemical and laboratory tests were done. **Conclusion:** Fever with thrombocytopenia occurs more commonly in younger age group (12-30 years) with dengue as most common cause and males preponderance. The cases showed seasonal variability with most cases occurring between June to September.

**Key Word:** acute fever, thrombocytopenia.

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## INTRODUCTION

The healthcare fraternity working in tropical conditions is faced with challenge of managing wide spectrum of infectious diseases, which are unique in their country. Acute febrile illness with thrombocytopenia is one such condition. The vector borne viral infections, parasitic infections and bacterial infections often present with non specific symptoms making job of clinician very difficult. The clinical manifestations include permutations and combinations of various symptoms such as rash, arthralgia, backache, retro orbital pain, fever, headache etc. The clinical diagnosis, indicating most probable cause of this condition is must be fore patient is subjected to various lab investigations which will help clinician to confirm the diagnosis

and manage the case. In some clinical conditions these investigations also have prognostic significance and indicators of complications. A study of these diseases will help an insight view in the understanding and clinching of diagnosis of some of the important treatable infectious diseases. This study comprised of all consecutive hospitalized patients with fever of less than seven days in duration *and* thrombocytopenia which is divided into three categories.

1. Mild thrombocytopenia <150,000 to >100,000/mcl.
2. Moderate thrombocytopenia <100,000 to >50,000/mcl.
3. Severe thrombocytopenia <50,000/mcl.

A vast majority of diseases present with fever of acute onset with thrombocytopenia as a haematological finding in the hemogram. The list includes: 1) Viral fevers like: Dengue fever, Chikungunya, West Nile fever, Sindbis fever, Ebola fever, Hantavirus infection, Mumps, Hepatitis B infection, Parvovirus B19, Lassa fever, Kayasanur forest disease. 2) Parasitic infections: Falciparum malaria. 3) Bacterial infections: Leptospirosis.

Disease entities included in our study included following diseases

1. Dengue fever

2. Malaria fever
3. Chikungunya
4. Leptospirosis

Being a tropical country, the prevalence of tropical disease poses a great threat to the country's Social and Economical progress. Hence forth, a study of the prevalent tropical diseases would provide a better prospective for the benefit of the individual and the country as a whole and would further help to improve the management guidelines used in treating these diseases<sup>1</sup>.

### AIMS AND OBJECTIVES

1. To Study the clinical presentations of Acute Febrile illnesses with Thrombocytopenia assessed by relevant laboratory and immunological investigations.
2. To study the common causes of acute fever and thrombocytopenia like Dengue fever, Chikungunya fever, Malaria, and Leptospirosis in relevance to Indian subcontinent.
3. To study the comparison of WBC count, platelet count and platelet distribution width (PDW) in between patients of malaria and dengue.
4. To evaluate warning signs and hence to correlate their significance for early recognition of complications.
5. To study the relation of platelet distribution width with bleeding manifestation and it's correlation with dengue fever.
6. To study the degree of thrombocytopenia in patient with fever.
7. To study the USG findings in patients presented with fever and thrombocytopenia.

### MATERIALS AND METHODS

It was an analytical study of **prospective type**.  
 Sample Size: The no. of patients included in the study were **50**.  
 Statistics: Diagnostic accuracy is measured by computing sensitivity, specificity,

### OBSERVATION AND RESULTS

**Table 1:** Case distribution and study

Case Distribution	Total (n=50)
Dengue IgM	20
Dengue IgG	9
P.Vivax	12
P.Falciparum	4
Chikungunya	1
Leptospira	0
Other fever with thrombocytopenia*	4

\*Acute viral fever, acute viral hepatitis

predictive values and likelihood ratios. The precision of these estimates is evaluated using 95% confidence intervals.

#### Methods: Biochemically:

1. Seropositive for dengue Ig G and IgM [IgG 4 times rise titre]
2. Seropositive for Leptospirosis Ig G and Ig M
3. Seropositive for Chikungunya Ig G and IgM
4. Rapid Malaria Antigen test Positive
5. Radiology: USG, CXR (PA view)

#### Inclusion Criteria:

- All hospitalized patients with complaints of fever <7 days and without any signs diagnosing specific illness.
- Hematological parameters derived from automated analyzer.
- Patients with thrombocytopenia were divided in three different category.
  1. Mild thrombocytopenia <150,000 to >50,000/mcl
  2. Moderate thrombocytopenia <500,00 to >20,000/mcl
  3. Severe thrombocytopenia <20,000/mcl

#### Exclusion Criteria:

- Patient with fever with localized cause can be determined.
- Patient with chronic liver disease.
- Diagnosed patient with DIC, deep venous thrombosis or any bleeding disorder.
- Patient with history of any drug exposure like septran, thaizides, anti- cancerdrug.
- Age < 12 years.

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**Table 2: Sex Distribution**

Age	Male	Female	Total	Percentage (n=50)
12-20	10	3	13	26%
21-30	20	4	24	48%
31-40	4	3	7	14%
41-50	1	1	2	4%
51-60	2	1	3	6%
61-70	1	-	1	2%

**Table 3: Admissions in months**

Month	Number of patients admitted
June	9
July	12
August	14
September	15
Total	50

**Table 4: Bleeding wise distribution**

Bleeding manifestations	No. of patients
Malena	2
Subconjunctival hemorrhages	1
Hemoptysis	1
Total	4

**Table 5: Patient having ascites**

USG finding of ascites	No of patients
Yes	21
No	29
Pleural effusion on chest x ray	7

**Table 6: Patient having splenomegaly on USG**

Splenomegaly	No. of patients
Yes	8
No	42

**Table 7: Platelet wise distribution**

Platelet count	No. of patients
<50,000/mcl (severe thrombocytopenia)	15
50,000 to 1,00,000/mcl (moderate thrombocytopenia)	20
1,00,000 to 1,50,000/mcl (mild thrombocytopenia)	15

**Table 8: Hematocrit wise distribution of patients**

Hematocrit (%)	No. of patients
<30	12
31-35	8
36-40	6
41-45	4
>45	20

**Table 9: Signs of plasma leak associated with dengue IgM**

Plasma leak	No. of patients
No Plasma leak	24
Plasma leak with dengue IgM positive	15
Plasma leak with dengue IgG positive	6
Plasma leak with dengue negative	5
Patient with sign of plasma leak	26

**Table 10:** Association of increase in platelet count with days of illness in dengue IgM positive patients.

No. of Dengue IgM positive	Platelet count on 8th day (/mcl)	Platelet count on 9th day (/mcl)
1	142000	158000
2	135000	152000
3	125000	142000
4	148000	175000
5	155000	190000
6	128000	152000
7	132000	151000
8	167000	192000
9	178000	210000
10	156000	167000
11	157000	190000
12	190000	210000
13	123000	138000
14	154000	157000
15	123000	154000
16	134000	157000
17	110000	134000
18	145000	210000
19	178000	230000
20	167000	182000

**Table 11:** Association of platelet distribution width (PDW) in Dengue IgM and Malaria positive patients

No. of patients	Malaria positive (PDW)v	Dengue IgM positive(PDW)
1	14	18
2	9.7	17
3	18	16
4	8.8	20
5	10	23
6	16	22.2
7	10	18
8	9.8	21
9	20	8.5
10	11.2	18
11	9	16
12	10.2	23
13	9	22
14	21	19.7
15	10	9
16	9.8	16
17	10	14
18	22	13
19	15	19
20	18	17

## DISCUSSION

A total of 50 patients were studied and found to have acute fever and thrombocytopenia. Table 1 shows that 58% cases were dengue, 32% were malaria, 8% were other fever associated with thrombocytopenia and 2% were chikungunya. Study from Uttar Pradesh by Praveen Kumar and Kalpna Chandra (172) shows 32.33% cases of malaria, 15.78% cases of dengue, unlike ours. And 6.31% cases of other fever with thrombocytopenia which is closely correlating with this

study<sup>2,3</sup>. Table 2 shows that most of the patients were younger. 74% of patients were of age group of 12 to 30 years. Least affected population was the geriatric, only 2% of patients were in geriatric population. Median age of the patients was 25 years, which is similar to the study from AIIMS by Sharma *et al*<sup>4</sup> i.e. 26.3 years. This study was carried out in a period from September 2017 to September 2018. Most of the patients were admitted in the months of June to September. In the month of August there were 28%

of admission while in the month of September 30% admissions of patients. It also indicates that dengue fever has seasonal pattern and its frequency increases during rainy seasons. (Table 3) The study from Indonesia<sup>5</sup> also indicated that dengue infection has seasonal variation and frequency increases during the month of June to September. The study from mangalore by V.S. Padabidri<sup>6</sup> also indicated the same. Table 4 shows that total of 4 patients had bleeding among them 50% of patients had complain of malena 25% of patients had subconjunctival haemorrhage and 25% of patients had hemoptysis. As study done at AIIMS by Sharma *et al.*<sup>4</sup>, 70% of patients had complain of bleeding, as opposed to this study where only 8% had complain of bleeding. The AIIMS study showed that 36.5% patients had skin rashes which is closely correlating with this study of 28%. In the mangalore study by V.S.Padabidri,<sup>6</sup> retroorbital pain was in 46% of patients, closely correlating with this study of 48%. Table 5 shows that 42% of patients had USG finding of ascites and 58% of patients had no finding of ascites. As shown in table 6 only 16% of patients had USG finding of splenomegaly and 84% of patients had no finding of splenomegaly. Splenomegaly was found in 16% cases in this study which closely correlates with other Indian studies. AIIMS study by S. Sharma showed splenomegaly in 8.2% patients and other one in Delhi by B.K.Tripathi<sup>7</sup> showed it in 6% patients while the Chennai study by Manjit Narayan<sup>8</sup> showed it in 11% of cases. Thrombocytopenia was present in 100% of patients as it was an inclusion criteria. 30% of cases were having severe, 40% of cases having moderate and 30% of cases having mild thrombocytopenia. (Table7) As shown in Table8  $<30$  haematocrit was in 24% of cases and  $>40$  was in 48% of cases. 48% of patients had no signs of plasma leak. 52% of patients had signs of plasma leak. 30% of cases of dengue IgM positive were showing signs of plasma leak and only 12% of cases were dengue IgG positive with signs of plasma leak. Signs of plasma leak is suggestive of third space loss<sup>9,10</sup>. (Table9). As shown in table 10 only 15% of dengue IgM positive patient had mild thrombocytopenia on 9<sup>th</sup> day and their platelet count were normal on 10<sup>th</sup> day. 45% of dengue IgM positive patient had normal platelet count on 8<sup>th</sup> day and rest 40% of patient had normal platelet count on 9<sup>th</sup> day. (normal platelet count 150000 to 450000/mcl).

## SUMMARY AND CONCLUSIONS

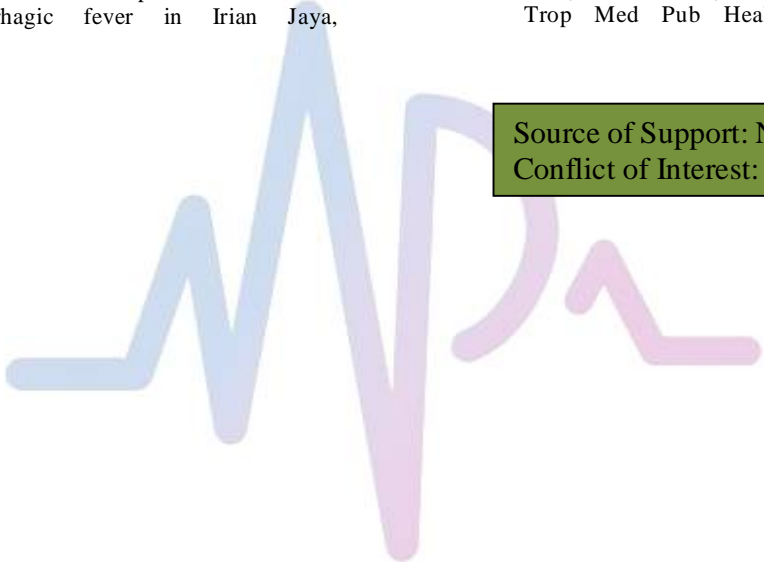
A total number of 50 randomly selected patients were studied, who presented with fever and thrombocytopenia. Dengue, malaria and chikungunya are the major diseases presenting as

fever with thrombocytopenia. CBC, clinical and Biochemical parameters, USG findings and CXR findings were studied for all 50 patients. Fevers with thrombocytopenia have a seasonal variability and cases increase during rainy season. Most of the cases presented between June to September out of which maximum number of cases occurred in the month of August and September, which indicates the association of these illness with rainy season due to breeding habits of vector for the arbo virus, parasites etc. Fever with thrombocytopenia occurs more commonly in younger age group and males are more commonly affected than females. 74% of patients were age group of 12-30 years, as they are the active group who are not confined in the single controlled environment. So, measures to curb the disease rate should be on large public scale. Bleeding is not due to thrombocytopenia alone but it is multifactorial. Leucopenia and moderate to severe thrombocytopenia with PDW  $>12$ fl is suggestive of dengue fever while normal or raised WBC count and mild thrombocytopenia with PDW  $<12$ fl is suggestive of malaria. Warning signs in dengue patients: Thrombocytopenia with a platelet count of  $<50,000$ /mcl Hemoconcentration with a hematocrit of  $>45$  Raised PDW levels These signs are associated with bleeding in all 4 patients in this study, among which Malena was the commonest manifestation. Low platelet counts and high hematocrit is suggestive of warning sign and must be treated aggressively. Spontaneous bleeding occurs below 20,000/mcl platelet count. So, all patients with  $<20,000$ /mcl platelet count in background of fever should be treated aggressively with blood component therapy. PDW is increased in cases of Dengue fever with thrombocytopenia. Signs of plasma leak in the form of third space loss like ascites, and pleural effusion is associated more with dengue fever. Dengue is the most common disease presenting with fever and thrombocytopenia. Ascites was the commonest USG finding followed by GB wall thickening. Other findings like splenomegaly and hepatomegaly are less common. 30% had mild, 40% had moderate and 30% had severe Thrombocytopenia. In this study no case of leptospira is found. Leptospira is the least common cause of fever with thrombocytopenia in my study populations, which suggests that it has an endemic preponderance requiring specific environment. PDW (Platelet Distribution Width) was raised in patients with bleeding suggestive of hyperdestructive Thrombocytopenia, which denotes disturbance in platelet activity. Thrombocytopenia in dengue IgM positive patient, recovers by 8<sup>th</sup> to 10<sup>th</sup> days of illness, which go hand-in-hand with clinical improvement.

So, all patients with dengue IgM positive should be monitored for atleast 7days.

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