



## A STUDY OF PATIENTS OF FEVER WITH THROMBOCYTOPENIA ADMITTED IN GOVT. GENERAL HOSPITAL, KURNOOL.

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### ABSTRACT

**BACKGROUND:** Fever is a common manifestation of illness that is not surprising to find accurate description of the febrile patients in early recorded history. Through thrombocytopenia is encountered in various diseases, it is fortunate that potentially fatal bleeding due to thrombocytopenia is rare. Platelets play an important role in normal haemostasis and also in thrombosis. The common causes of fever with thrombocytopenia are infections like dengue, leptospirosis, malaria, typhoid, military TB, HIV, septicaemia. Early diagnosis and treatment of the underlying condition and platelet transfusions are required to prevent fatal outcomes. Hence there is a need for the study to know the clinical profile and complications of fever with thrombocytopenia in the local regions. The objective of the study was to evaluate the clinical profile of patients with fever and thrombocytopenia, attending the Govt. General Hospital, Kurnool.

**METHODS:** 100 patients presenting with fever and thrombocytopenia were taken up for study.

**INCLUSION CRITERIA:** Patients presenting with fever of  $>38^{\circ}\text{C}$  and thrombocytopenia that is a platelet count of  $<1$  lakh.

**EXCLUSION CRITERIA:** Patients aged  $<18$  years without fever and thrombocytopenia; Inherited causes for thrombocytopenia; HIV infection; Cirrhosis of liver; Leukemias and myelodysplastic syndromes. The diagnostic work up of patients with fever and thrombocytopenia should include a battery of investigations including biochemical tests; haemograms; peripheral smear etc.

**RESULTS:** Male to female ratio in the present study was 3:1. The patients age ranged from 18-80 yrs. The maximum occurrence of fever with thrombocytopenia was in the 3<sup>rd</sup> decade (32%) followed by 4<sup>th</sup> decade (28%) and 5<sup>th</sup> 17% respectively in the present study.

Dengue fever was the commonest aetiology (47%), followed by viral fever (29), Malaria (13%), Typhoid (6%), Sepsis (4%), Leptospirosis (1%) in the present study. The duration of fever in 92% of cases was  $\leq 10$  days in the present study.

Petechiae and conjunctival haemorrhage was found in 20% of patients, 50% had abnormal bilirubin levels, 5.88% had abnormal SGOT and 6.25% had abnormal SGPT in patients with dengue fever in present study.

In patients with viral fever 61.54% had abnormal bilirubin levels, 15.38% had abnormal SGOT levels and 40% had abnormal SGPT levels. In patients with malaria 75% had abnormal bilirubin levels, 66.67% had abnormal SGOT and SGPT levels, In patient with typhoid 50% had abnormal bilirubin levels, 66.67% had elevation of both SGOT and SGPT levels.

**CONCLUSION:** All febrile illness patients should be investigated for platelet count irrespective of bleeding manifestation or not. Strong probability of dengue fever or other common causes like viral fever, malaria and leptospirosis should be kept in mind in any case of fever and manifestation and could be of bad prognosis if not treated with platelet transfusion early.

**KEYWORDS:** Acute phase proteins; C-reactive protein; Interferons; Tumour necrosis factor; Interleukin-2; Interleukin-6; Prostaglandin E2.

### INTRODUCTION:

Fever is a pervasive and ubiquitous theme in human myth, art and science. Fever is a common manifestation of illness and it is not surprising to find accurate descriptions of the febrile patients in early-recorded history<sup>1</sup>.

Normal body temperature ranges are between  $35.8^{\circ}\text{C}$  ( $96.5^{\circ}\text{F}$ ) and  $37.2^{\circ}\text{C}$  ( $99^{\circ}\text{F}$ ). But normal body temperature varies diurnally with lower values in the early morning and higher values in the afternoon. Fever is superimposed on this pattern and thus temperatures are usually greatest in the afternoon and evening.

Fever is defined as an elevation of the body temperature above the normal circadian range as the result of a change in the thermoregulatory centre located in the anterior hypothalamus.

Morning temperature of  $>37.2^{\circ}\text{C}$  ( $98.9^{\circ}\text{F}$ ) or evening temperature of  $>37.7^{\circ}\text{C}$  ( $99.9^{\circ}\text{F}$ ) would define fever.

The causes of thrombocytopenia are impaired platelet production, accelerated platelet destruction or dilution and/or splenic sequestration<sup>2</sup>. Even though there is no absolute relation between platelet counts and bleeding, certain broad generalizations can be made, with counts less than  $10,000/\mu\text{l}$ , bleeding is usual and may be severe<sup>3</sup>.

Thrombocytopenia is defined as platelet count  $<1,50,000/\mu\text{L}$ . This is due to decreased production, increased destruction (immunogenic and non-immunogenic), and increased sequestration in spleen. The commonest cause of thrombocytopenia is infection<sup>4,5</sup>.

The common causes of fever with thrombocytopenia are infections like dengue, leptospirosis, malaria, typhoid, military TB, HIV, septicaemia. Therefore through systematic approach is carried out

with an awareness of causes of fever with thrombocytopenia narrows the differential diagnosis of the clinical entity and brings our diagnosis.

Fever with thrombocytopenia is inversely proportion with mortality and morbidity. So, serial monitoring of platelet counts has more prognostic value. This highlights the importance of thrombocytopenia in various febrile disorders<sup>6</sup>.

Early diagnosis and treatment of the underlying condition, platelet transfusions are required to prevent fatal outcomes. Hence a need for study to know the clinical profile and complications of fever with thrombocytopenia.

### OBJECTIVES

To determine the etiology, clinical manifestations, treatment efficacy and outcome of fever with thrombocytopenia seen among patients admitted in Govt. General Hospital, Kurnool.

### REVIEW OF LITERATURE

Thrombocytopenia associated with infection Purpura was recognized as a manifestation of peltisutial fever 2000 years ago. Several factors are known to cause bleeding in association with infections of which thrombocytopenia is the common cause<sup>7</sup>.

### Viral cause

CMV, Dengue, Parvo-B19, HIV, Hantana virus, etc.

### Mechanism

Virus produced thrombocytopenia by impaired platelet production as a result of invasion of megakaryocytes by the virus, toxic effects of viral protein on progenitor cells, virus induced haemophagocytosis, destruction of circulation platelets by viruses –by viral antigen antibody complexes<sup>7</sup>.

**Diagnosis of Thrombocytopenia**

Thrombocytopenia is said to be present when the platelet count is <1.5 lakhs/ microlitre. A single platelet count that is lower than normal should always be confirmed by a second count<sup>8</sup>

**MATERIALS AND METHODS**

**Source of data**

Patients with fever and thrombocytopenia attending Govt. General Hospital, Kurnool during the period from

**Method of collection data**

**Sample Size:** 100 Patients presenting with fever and thrombocytopenia are taken up for study.

**Sampling Method:** Simple random sampling

**Inclusion Criteria**

Patients aged more than 18 years presenting with fever of >38°C and thrombocytopenia admitted in Govt. General Hospital, Kurnool.

**Exclusion criteria**

1. All patients <18 years without fever and thrombocytopenia
2. Patients with inherited causes for thrombocytopenia
3. Patients on drugs causing thrombocytopenia
4. Patients with Autoimmune causes for thrombocytopenia
5. Patients with HIV infection
6. Patients with Cirrhosis of liver
7. Patients with Leukemias and myelodysplastic syndrome

**INVESTIGATIONS**

The diagnosis work up of patients with fever and thrombocytopenia included a battery of investigations like biochemical tests; haemograms; peripheral smear etc.

**a) Complete haemogram**

1. ESR- It is a non specific test, it is raised in most conditions
2. Leucopenia – seen in viral fever
3. Leucocytosis – predominantly neutrophils indicates septicaemia
4. Blood smear – Dohle bodies; toxic granules suggests septicaemia, also should be examined for malarial parasites in both thick and then smears.

**b) Rapid spot test**

For plasmodium vivax and plasmodium falciparum species. It is very sensitive for detection of malaria.

**c) WIDAL** – Test tube agglutination method for identification of enteric fever

**d) IgM ELISA dengue**- will be positive after 5<sup>th</sup> day of feve and rising titres are indicative of dengue

**e) IgM ELISA leptospiral** antibodies – In very acute, toxic presentation with conjunctival suffusion with renal and liver parameters being abnormal.

**f) Blood culture** – at least 3 blood culture samples should be taken, special technique are required, for fastidious organisms to grow and incubation has to be continued for at least 2 weeks.

- g) Test for Chickungunya fever.
- h) Test for Scrub typhus
- 1) Indirect fluorescent antibody,
- 2) Indirect immunoperoxidase
- 3) Enzyme immunoassays
- i) Test for Hanta virus wherever feasible
- j) Viral isolation

**Routine Tests**

1. X-ray chest.
2. Urine analysis.
3. Liver Function Tests.
4. Renal Function Tests.

**RESULTS**

Among different age groups, males were affected more than females in all age groups in the present study. The male: female ratio was 3:1

**Table-1- Age distribution:**

Age	No (n=100)	%
8-20	13	13
21-30	32	32
31-40	28	28
41-50	17	17
51-60	6	6
61-70	2	2
71-80	2	2

The patients age ranged from 18 yrs to 80 yrs. The febrile illness with thrombocytopenia had maximum occurrence in the age group of 3rd decade (32%) followed by 4th decade (28%) and 5th decade 17% respectively.

**Table-2 – Age distribution in different etiologies:**

Age	Dengue	Viral fever	Leptospirosis	Malaria	Sepsis	Typhoid
8-20	6	4	0	0	0	2
21-30	17	7	1	5	2	1
31-40	13	7	0	5	0	2
41-50	8	6	0	2	0	1
51-60	2	4	0	0	1	0
61-70	0	1	0	1	0	0
71-80	1	0	0	0	1	0

The six diseases which contributed mainly to febrile thrombocytopenia in the present study were Dengue (47%), viral fever (29%), Malaria (13%), Typhoid (6%), sepsis (4%) and Leptospirosis (1%). Acute febrile illness with thrombocytopenia due to the above cases occurred maximum in 3<sup>rd</sup> & 4<sup>th</sup> decade.

**Table-3- Duration of fever on presentation**

Days	No	%
1-5	64	64
6-10	28	28
11-15	4	4
>15	4	4

The duration of fever in the present study ranged from 1-20 days and 92% of them had duration of < 10 days.

Fever was the leading symptom (100%), Headache was the next common symptom (32%) in the present study. Other prominent symptoms in the descending order includes vomiting (27%), myalgia (22%), joint pain (10%) pain abdomen (6%) and altered sensorium (3%).

The hepatosplenomegaly contributed to major signs in the present study (21-24%). The petechiae and conjunctival haemorrhage contributed to 20% followed by jaundice (11%) in the present study.

In the present study, the platelet count varied from 10,000 to 1 lakdh/cumm. 28% of patients had platelet count <40000, 23% in the range of 40,0001-60,000/cumm, 11% had platelet count in the range of 60001-80000/cumm and 22% had platelet count in the range of 80001 to 100000/cumm. The platelet count for the patients with bleeding episodes ranged from 18000 to 40000/cumm in the present study.

**Table-4- Platelet count in the different etiologies**

Age	Dengue	Viral fever	Leptospirosis	Malaria	Sepsis	Typhoid
10000-20000	11	4	0	3	0	1
20001-40000	12	11	0	3	0	1
40001-60000	10	5	0	3	2	1
60001-80000	6	1	1	0	1	2
80001-100000	8	7	0	4	1	1

Total platelet count varied according to the etiology. Dengue fever caused severe thrombocytopenia. Out of 47 cases of Dengue fever, 23.4% had platelet count <20000, 25.53% had platelet count in the range of 20001-40000/cumm. Of 29 cases of viral fever 13.79% had severe thrombocytopenia <20000/cumm, 379.93% had counts in the range of 20000-40000, 48.28% had platelet count of >40000/cumm. In Malaria, 23.08% of the patients had platelets in the range of 60000-

100000.

In 92.31% of the patients, the platelet count was >40000/cumm. In typhoid the platelet count was >40,000/cumm. In the present study severe thrombocytopenia occurred in patients with dengue fever.

**Table-5- Etiology profile with present study**

Diagnosis	No (n=100)	%
Dengue	47	47
Viral fever	29	29
Malria	13	13
Typhoid	6	6
Sepsis	4	4
Leptospirosis	1	1

Out of 100 patients of fever with thrombocytopenia, Dengue fever (47%) was the commonest cause followed by viral fever (29%), Malaria (13%), Typhoid septicemia (4%) and leptospirosis (1%) in the present study.

Bleeding manifestation in the form of petechiae was common manifestation of thrombocytopenia. Petechiae with and without gum bleeding/epistaxis/conjunctival hemorrhage occurred in 16% of patients. The conjunctival hemorrhage alone occurred in 3% of patients, gum bleeding alone occurred in 1% of patients, and Malaria in 1% patients in the present study.

There was no correlation between platelet count and bleeding manifestation. However the maximum number of bleeding episodes occurred when the platelet count was in the range of 20000-40000/cumm.

The majority of the patients on our study had Dengue fever and total leukocyte count was in the range of 2000 to 4000/cumm (32%).

Half of the patients had abnormal total bilirubin levels. In dengue fever 5.88% had abnormal SGOT and 6.25% had abnormal SGPT levels.

Abnormal total bilirubin values were found in 61.54%, in viral fever, 15.38% had abnormal SGOT levels and 40% had abnormal SGPT levels.

## DISCUSSION

The present study included 100 patients of fever with thrombocytopenia in which males were affected more than females in a ratio 3:1.

In a similar study of fever associated thrombocytopenia by Nair et al., the male of female ratio was 2.3:1 at place New Delhi in the year 2003. The patients age ranged from 18 to 80 yrs.

In the present study the maximum prevalence of fever with thrombocytopenia was in the age group of 21-30 yrs (32%). The lowest number of patients were in >60 year age group (4%).

All the patients in the study presented with fever. The duration of fever in the present study was <5 days in 64% and <10 days in 92% of patients with a mean duration of 6 days.

Other than fever, the patients presented with multiple other symptoms of which headache was the most common (32%). Other prominent symptoms were vomiting (27%), myalgia (22%), joint pain (10%), pain abdomen (6%) and altered sensorium (3%).

Most commonly detected signs in the present study were splenomegaly (24%), hepatomegaly (21%), petechiae (16%), jaundice (11%), pallor (9%) and conjunctival hemorrhage (4%) in the present study.

The commonest cause was Dengue fever, 47% with present study. The other etiologies were viral fever (29%), Malaria (13%), Typhoid (6%), sepsis (4%) and Leptospirosis (1%).

Septicaemia was the leading cause of fever with thrombocytopenia in Nair et al. study (26.61%) followed by typhoid fever (14.68%), Dengue (13.8%), Megaloblastic anemia (11.9%), Malaria (9.2%) and Haematological malignancy (3.7%).

**Table-6- Comparison of etiology at present study with Nair study**

Disease Category	Nair study (%) New Delhi	Present study GGH, Kurnool
Sepsis	26.6	4
Enteric	14.6	6
Dengue	13.8	47
Malaria	92	13

In the present study, the platelet count varied from 15000 to 98000/cumm and the mean platelet count being 62,420+24104(SD)/cumm. A platelet count of <40000/cumm was seen in 28% of patients, 23% of patients had platelet count of 40000-60000/cumm, 11% patients had platelet count of 60000-80000/cumm, 22% of patients had platelet count in the range of 80000 to 100000/cumm, 28% of patients had platelet count between 20,000-40,000/cumm and 56% had platelet count above 40,000/cumm. In Nair et al study 56.8% had platelet count between 50,000 to 100000/cumm and 43.2% had platelet count of 50,000 and 25.7% of the total platelet count varied according to the etiology. Above mentioned diseases occur mostly in rainy season from June to October.

Out of 47 cases of dengue fever 23.4% had platelet count <20000/cumm, 25.53% had platelet count in the range of 21000-40000/cumm. Of all the etiologies, dengue fever caused severe thrombocytopenia in the present study. This showed that dengue should be suspected in any patient coming with fever and thrombocytopenia with bleeding symptoms.

In the viral fever cases, out of 29 cases, 13.79% had platelet count with range < 20,000/ cumm 37.93% had platelet count with range of 20000-40000/cumm and 48.28% of patients had platelet count >40000/cumm.

In patients with leptospirosis one case had platelet count with range of 60000-80000/ cumm and 56% of patients had platelet count >40000/cumm. This clearly shows that severe thrombocytopenia occurred in more number of dengue fever cases compare to viral fever or leptospirosis in the present study. The degree of thrombocytopenia has prognostic value because of fatal outcome if not properly recognized and treated with platelet transfusion. Platelet count in infectious disease is important since early and appropriate treatment of the condition results in better outcome. Thrombocytopenia has an inverse correlation to mortality and morbidity. The platelet count was in the range of 18000-40000/cumm in patients who had bleeding episodes.

The bleeding episodes with petechiae, conjunctival haemorrhage, gum bleeding and malena was found in 21% of patients in the with present study. The bleeding episodes were seen in 41.3% of patients in Nair et al study. In the present study the petechiae was the commonest bleeding manifestation followed by spontaneous mucosal bleeding. In Nair et al study spontaneous mucosal bleeding was the commonest bleeding manifestation followed by petechiae purpura.

The total bilirubin level was abnormal in 50% of dengue fever cases, 61.54% of viral fever cases and 75% of malaria cases in the present study. The abnormal SGOT was seen in 5.88% of Dengue fever cases, 15.3% of viral fever cases, 66.67% of malaria cases in the present study.

The abnormal SGPT was seen 6.25% of Dengue fever cases, 40% of viral fever cases, 66.67% of malaria and Typhoid fever cases, 100% of Leptospirosis and sepsis cases in the present study. This shows that abnormal liver function test was more prevalent in leptospirosis.

**There is no deaths in the present study.**

## CONCLUSION

All febrile illness patients should undergo serial platelet count irrespective of presence of absence of bleeding manifestation.

Strong probability of dengue fever or other common causes like viral fever, malaria and leptospirosis should be kept in mind in any case of fever and thrombocytopenia as decreased platelet count =< 4000/ cumm) could be severe even without external bleeding manifestation and contribute to bad prognosis if not treated with platelet transfusion early.

**REFERENCES**

1. Woodward TE, The fever pattern as a diagnostic aid In: Fever; basic mechanisms and management , Mackowlack PA, ed. New York: Lippincott-Raven Publishers; 1997.p.215-35
2. Levine SP, Wintrobe's Clinical Haematology, 10th ed. 1993: 1579-1632.
3. Colman RW, Hirsch J, Marder VJ, Salzman EW, Hemostasis and Thrombosis Basic Principles and clinical practice. 1982-p.246-7.
4. Firkin F. Degruchy's Clinical Haematology in Medical Practice. 5th ed. 1990.p.375.
5. George JN, Aizvi MA. Thrombocytopenia. 6th ed. Chapter 117. In: Williams Haematology, Beutler E. ed. New York: McGraw-Hill; 2001. P.1501.
6. William WJ, eaenst Beutler E, Erslev AH, Litchman MA, Haematology. 3rd ed. P.1290-342.
7. Aster R. Drug-induced thrombocytopenia. In: Platelets, Michelson AD, ed. New York: Academic Press; 2007-p.887-902.
8. Stephenson LA. Circadian time keeping. In: Fever; basic mechanisms and management, Mackowjack PA, ed. New York: Lippincott-Raven Publishers; 1997.p.59-77.