



A STUDY OF FEVER WITH THROMBOCYTOPENIA

Dr. Naveen S. Kulkarni

Associate Professor, General Medicine, SDMCMSH, SDM University, Dharwad, Karnataka

Dr. Aron V. Thomas*

Registrar In Internal Medicine, KIMS Trivandrum, Kerala. *Corresponding Author

Dr. Prashant Hubballi

Assistant Professor, A J Institute Of Medical Sciences, Mangaluru, Karnataka.

ABSTRACT

Background: Fever as a symptom provides important information about the presence of illness particularly infections and about changes in the clinical status of the patient. As fever is one of the most common presenting symptoms, there is a need to study clinical and laboratory profile of fever with thrombocytopenia.

Objective: To study clinical profile and laboratory evaluation of fever with thrombocytopenia. The study aims in evaluating the cause for fever with thrombocytopenia and also course of diseases.

Methods: This is a prospective study of 52 individuals aged more than 15 years presenting with fever and thrombocytopenia. The study was conducted at S. Nijalingappa Medical College and HSK Hospital and Research Centre, Bagalkot from December 2015 to December 2016.

Results: In this study, among 52 patients, 15 were males and 37 females. Platelet counts below 20,000 were seen in 11 cases, between 20,001-50,000 were seen in 16 cases and platelet counts between 50,001-1.5 lakhs were seen in 25 cases. In 52% cases a diagnosis was possible, most common being malaria next in order being Dengue, Sepsis and Enteric fever. One case was positive for both Malaria and Dengue. There was a single case each of Systemic lupus erythematosus, Myelodysplastic syndrome, Acute myeloid leukemia and Miliary tuberculosis. 48% cases remained undiagnosed. Megaloblastic anaemia was seen in 18 cases and these individuals had Urinary tract infections. A few cases were due to viral fever.

Conclusion: Infections are most common cause for fever with thrombocytopenia. The most common infection being malaria, other infections are dengue and enteric fever. Sepsis also is one of the important and common causes.

KEYWORDS : fever , thrombocytopenia, infections, anaemia .**INTRODUCTION**

Fever is one of the most common presenting complaints. Fever is defined as A.M. temperature more than 37.2 degree Celsius (98.9 degree F) or P.M. temperature more than 37.7 degree Celsius (99.9 degree F)². The fever pattern is of marginal value for most specific diagnosis except for Malaria, Borreliosis and occasional cases of Lymphomas¹. Fever may be due to infectious or non-infectious aetiologies. It is a challenging task to diagnose aetiologies of fever. Many a times fever presents with thrombocytopenia, this association of fever with thrombocytopenia may be helpful to narrow down the differential diagnosis. Thrombocytopenia is defined as platelet count less than 150000/ μ l in blood³. Fever with thrombocytopenia may be due to malaria, dengue, sepsis, leptospirosis etc. Following study was undertaken to evaluate the clinical profile and laboratory evaluation of fever with thrombocytopenia.

METHODS**Setting**

This study was undertaken at SNMC and HSK, Bagalkot in the department of General medicine.

Design

Prospective, Observational, non-comparative, non-randomised, analytical study

Participants

Individuals aged more than 15 years presenting with fever and thrombocytopenia were included for this study.

Individuals with fever without thrombocytopenia and those with thrombocytopenia without fever were excluded from the study. Individuals with positive retroviral status, Hepatitis B, Hepatitis C, chronic liver disease were excluded from the study.

Sample size

52 individuals admitted in the department of medicine were included based on above inclusion and exclusion criteria.

Protocol

Individuals were evaluated with thorough history and examination at

admission. All the relevant investigations based on history and examination was carried out. The cases were followed daily and relevant necessary investigations were repeated based on complaints. They received treatment based on the clinical diagnosis and investigations, blood and blood products were considered for few individuals.

RESULTS

In our study a total of 52 cases were evaluated, in this 15 males and 37 females. The duration of stay in the hospital was 3 to 15 days. Patients whose platelets were between 50000 to 1.5 lakhs were 25 in number, with 20001 to 50000 were 16 in number and less than 20000 of platelets counts were seen in 11 individuals.

Table Number-1: Platelet Counts And Cases

Platelet counts	Cases	Percentage
<20000	11	21.15
20001- 50000	16	30.76
>50001	25	48.00

In our study among 52 cases 6 reported significant bleeding tendencies. Below table states the bleeding manifestations

Table Number-2: Bleeding Manifestation In Cases

Bleeding Manifestations	Cases	Percentage
Melena	3	50
Hematemesis	1	16.9
Blood tinged sputum	1	16.9
Epistaxis	1	16.9

In our study involving 52 cases, on evaluation the following aetiologies of fever with thrombocytopenia were noted.

Table Number-3 Aetiologies Of Fever With Thrombocytopenia

Etiology	Cases	Percentage
Malaria	10	19.2
Dengue	7	13.4
Sepsis	3	5.76
Enteric fever	2	3.84
Falciparum malaria with Dengue	1	1.92

AML	1	1.92
Miliary Tuberculosis	1	1.92
SLE	1	1.92
MDS	1	1.92
Others	25	48.00

In our study definitive diagnosis was made in 27 cases. Other 25 cases could not be diagnosed with specific etiology with available investigations. In these 25 cases, anaemia was associated in 19 cases, Megaloblastic anaemia was noted 18 cases where as a single case was due to microcytic hypochromic anaemia. We observed 10 cases among these 25 cases to have urinary tract infections.

There were few cases that developed renal dysfunction, hepatic dysfunction and combination of two.

Table Number-4: Organ Dysfunction In Fever With Thrombocytopenia

Dysfunction	Cases	Percentage
Renal	3	5.76
Hepatic	10	19.2
Renal and Hepatic	4	7.68

DISCUSSION

In our study of fever with thrombocytopenia a definitive diagnosis was made in 27 cases (51.92%). The most common cause for fever with thrombocytopenia in our study was malaria (19.2%). Four cases among ten were due to falciparum, four due to vivax and two cases had mixed infection with falciparum and vivax. A study done at Sir T. Hospital and GMC¹, Bhavnagar, Gujarat associated 46% of the cases due to malaria. A related study at Dr D Y Patil Medical College, Kolhapur² associated 54% cases due to malaria. A study at Sri Ram Murti Smarak Institute of Medical sciences (SRMS-IMS) at Bhojipura, Barielly, UP⁶ associated malaria as a cause in 32.6% of cases. Other studies associated malaria as a cause in cases of fever with thrombocytopenia are – Nair et al⁷ study and Srinivas et al⁸ study in 9% and 41% respectively. Shaikh et al, JPMC, Karachi⁹ associated malaria and thrombocytopenia in majority of cases and Malik et al, Karachi¹⁰ noted 11.7% patients had malaria and among these 70% had thrombocytopenia. A study at Hayat Abad Medical Complex¹¹ between 2008-2010 noted malaria in 53% of cases.

A study done by Umang Patel et al at New York community hospital¹² any patient with fever and recent travel history and low platelets, malaria can be possible. Peripheral smear is a gold standard for malaria. To detect low levels of parasitemia multiple peripheral smears and more sensitive ELISA test will yield the diagnosis.

A similar study at KIMS, Hubli by N. Kulkarni associated malaria as an aetiology in 13% cases¹⁸.

Table Number-5: Studies Comparing Malaria

Studies	Malaria (in %)
GMC, Gujarat	46
D.Y.Patil Hospital	54
SRMS-IMS	32.6
Nair et al	9
N. Kulkarni et al	13
Srinivas et al	41
Our study	19.2

In our study Dengue was seen 13.4% cases. A study done at D.Y Patil Hospital found out 15% cases due to Dengue. Other related Indian studies showed dengue cases as a cause of fever with thrombocytopenia are SRMS-IMS study dengue was noted in 15% cases, Nair et al study in 14% cases and Srinivas et al study in 14% cases. A study at GMC and Sir T hospital showed 52% cases due to dengue. A study at KIMS,Hubli by Kulkarni noted 6.5% cases of dengue.

Table Number-6: Studies Comparing Dengue

Studies	Dengue
D.Y.Patil Hospital	15
SRMS-IMS	15
Nair et al	14
Srinivas et al	14
GMC	52
N. Kulkarni et al	6.5

Our study	13.4
-----------	------

Sepsis was noted in 5.76% cases. Other Indian studies which have shown sepsis to be a cause for fever with thrombocytopenia are- D.Y Patil Medical college hospital noted in 4% cases, Nair et al study in 26% cases, Srinivas et al study noted sepsis in 19% cases, SRMS-IMS study found out sepsis in 31.2% cases. Sepsis was noted in 8% cases of fever with thrombocytopenia at KIMS, Hubli by N.Kulkarni

Table Number 7: Studies Comparing Sepsis

Studies	Sepsis (%)
D.Y.Patil	4
Nair et al	26
Srinivas et al	19
Kulkarni et al	8
SRMS-IMS	31.2
Our study	5.76

Enteric fever was noted in 3.84% cases. Srinivas et al study showed a significant association of 24% cases as an etiological factor in fever with thrombocytopenia cases. A study at GMC Gujarat, SRMS-IMS, D.Y. Patil Hospital and Nair et al study found out enteric fever to be an aetiology in 3%,7%,6% and 15% respectively. Enteric fever was noted in 6.5% cases of fever with thrombocytopenia at KIMS, Hubli by Kulkarni et al

Table Number 8: Studies Comparing Enteric Fever

Studies	Enteric fever (%)
Srinivas et al	24
GMC	3
SRMS-IMS	7
D.Y.Patil	6
Nair et al	15
Kulkarni et al	6.5
Our study	3.84

One case in our study presented with falciparum malaria and dengue as a cause for fever with thrombocytopenia.

On evaluation we found out a single case of AML,SLE,MDS and miliary tuberculosis in evaluation of fever with thrombocytopenia.

In 48% of cases studied, a specific aetiology could not be established. However among these 25 patients, 19 cases had anaemia- majority were megaloblastic anaemia (18 cases) and a single case was of microcytic hypochromic (iron deficiency anaemia). 10 cases among 25 patients had investigation profile suggestive of urinary tract infection.

Megaloblastic anaemia can present with anorexia, weight loss, diarrhoea, constipation, glossitis, angular cheilosis, fever, jaundice, hyperpigmentation and thrombocytopenia. Fever may be due to respiratory tract infection or urinary tract infection¹³.

Among these 25 cases, 6 cases (11.52%) were classified as viral fever. A study at D.Y.Patil hospital found out viral fever in 21% cases, Nair et al study in 18% cases, Srinivas et al study in 2% cases and SRMS-IMS study in 6.31% cases.

A virus – SFTS (Severe fever with thrombocytopenia syndrome) – was discovered in east Asian region which was a Phlebovirus¹⁴.

Table Number 9: Aetiologies Of Fever With Thrombocytopenia In Others Category

Aetiologies	Number of cases
Megaloblastic anaemia	18 (34.56%)
Viral fever	6 (11.52%)

We noted renal dysfunction in 5.76% cases, hepatic dysfunction in 19.2% cases and renal with hepatic dysfunction in 7.68% cases presenting with fever with thrombocytopenia. A study at SRMS-IMS showed hepatitis in 24.76% cases and renal dysfunction 32.63% cases.

A high index of suspicion is needed in evaluating certain cases especially when laboratory diagnosis is not established. Megaloblastic anaemia predisposes to respiratory tract infection and urinary tract infection¹³. Malaria can be seen in individuals with anaemia and thrombocytopenia and intermittent fever¹⁵. Dengue is a possibility when patient has fever with thrombocytopenia, myalgia, back pain and improves only with symptomatic treatment¹⁶. Fever with thrombocytopenia and GI

disturbances- Enteric fever can be a possibility¹⁷.

In our study of fever with thrombocytopenia, aetiology has been established in 52% cases. The remaining 48% cases are due to secondary infection in anaemia patients and few among these may be due to some unknown virus in the community. On comparing our study with the related studies the following things need to be considered. (1) Diagnosis varies according to the severity of clinical manifestations as sub clinical cases are easily missed. (2) Diagnosis vary according to seasonal variation. (3) Before evaluation of a case there is a need for finding out drug treatment history- partially treated and referred cases may be missed or under diagnosed during evaluation. (4) Antigenic variations of etiological agents can alter the diagnosis. (5) Our diagnosis can be strengthened by getting repeated investigations and/or getting investigations in appropriate phases of the illness. (6) Laboratory variations – trained personnel, sensitivity of the available tests etc. will alter diagnosis. (7) The number of cases included in the study also makes difference in thorough evaluation.

CONCLUSION

We see many cases of fever with thrombocytopenia in our day to day practice. The diagnosis of this entity is challenging and difficult. On comparison of our study with available related Indian studies infections are the most common cause for fever with thrombocytopenia. In our study most common was malaria followed by dengue, sepsis and enteric fever. Megaloblastic anaemia predispose individuals to few infections in our study it was urinary tract infection. Some cases remain undiagnosed as viral fever. In evaluating fever with thrombocytopenia cases we need to consider drug history, seasonal trends, habits, microbial changing patterns, varied clinical manifestations. However there is a need to setup clinical criteria along with lab diagnosis in evaluation of these cases.

REFERENCES

- Ralph G, Paul L.N. 2 Common symptoms; Fever and Hyperthermia; CMDT 2015, page 34.
- Dinarello C.A., Porat R.; Harrison's principles of internal medicine 18 edition volume 1, section 2, chapter 16 – fever and hyperthermia, page 143.
- Konkle B.; Harrison's principles of internal medicine 18 edition volume 1, section 3, chapter 115- disorders of platelets and vessel wall, page 965-966.
- Raikar S. et al, Clinical and Laboratory Evaluation of Patients with Fever with Thrombocytopenia Indian Journal of Clinical Practice, 2013; 24 (4): 3060-363
- Prithviraj Patil et al, To Study Clinical Evaluation and Outcome of Patients with Febrile Thrombocytopenia International Journal of Scientific and Research Publications, 2014; 4 (10):01-03.
- Praveen et al, An Incidental Finding of Splenomegaly Syndrome in a Geriatric Patient: A Case Report. Indian Journal of Clinical Practice 2014; 24 (10): 657-659.
- Nair et al, A study of fever with thrombocytopenia, JAPI 2003, Dec 51 – 1513
- Lohitashwa, Vishwanath, Srinivas, a study of clinical and lab profile of fever with thrombocytopenia, JAPI; 2009: 57.
- Shaikh et al, Thrombocytopenia in malaria, J. College Physician Surg Pak 2009; 19(11); 708-10.
- Malik et al, haematological findings and endemicity of malaria in Gadap region, J. Coll Phys Surg Pak 2010; 20(2); 12-6.
- Khan et al, thrombocytopenia as an ind of malaria in adult population. Malar Res Treat – 2012, 2012; 405981.
- Umang P, Gaurang G, Sandor, Selvanayagam N. Thrombocytopenia in malaria. Journal of the national medical association. September 2004; Vol. 96, no. 9; 1212-14
- Hoffbrand A.V., Harrison's principles of internal medicine 19 edition, volume 2, part 7, section 1, chapter 128 – Megaloblastic Anemias, pages 641-42.
- Yan Liu, the pathogenesis of severe fever with thrombocytopenia syndrome virus infection in alpha/beta interferon knockout mice: insights into the pathologic mechanisms of a new viral hemorrhagic fever. Journal of Virology 2014; 88(3): 1781-86.
- White N.J., Breman J.G., Harrison's principles of internal medicine 19 edition, volume 2, part 8, section 18, chapter 248 – Malaria, pages 1374/1378.
- Peters C.J., Harrison's principles of internal medicine 19 edition, vol 2, part 8, section 15, chap 233, page 1322 and Yeolekar ME and Sukumaran S, API vol 2, 10 edition, part 17, Chapter 42 – Dengue, page 1583.
- Pegues D.A. and Miller S.I., Harrison's principles of internal medicine 19 edition, vol 2, part 8, section 6, chap 190- Salmonellosis pages 1050-1051.
- Naveen Kulkarni et al., International Journal of Biomedical Research 2017; 8(01):15-19