

A Study of Clinical Profile of Pyrexia with Thrombocytopenia

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Abstract

Background: Thrombocytopenia is defined as decrease in number of circulating platelets in the blood. Normal platelet counts range from 1,50,000 to 4,50,000 platelets/ μ l. Often patients with thrombocytopenia are asymptomatic, and are diagnosed incidentally by routine complete blood count (CBC).

Methods: The study was conducted in patients coming to Mahatma Gandhi Medical College And Hospital, Jaipur with fever in association with decreased platelets.

Results: 67.3% cases had complaint of pain abdomen, 62.7% had complaint of vomiting, 54% headache, 46% myalgia, 38% joint pain, 25.3% cough, 13.3% dyspnea, 0.7% had complaint of altered sensorium.

Conclusion- In our study we concluded that most common cause of pyrexia with thrombocytopenia was dengue fever.

Keywords: Platelet count, Fever, Thrombocytopenia

Introduction

In day to day life, fever is a common complaint for which patients consult a doctor. It is a manifestation of various infections as well as non-infective disease processes. “Fever is defined as A.M. temperature more than 98.9 degree F and P.M. temperature more than

99.9 degree F¹”. Any organ system of the body may be affected by fever. Fever is manifested as the final result of a series of events that take place- starting from infection or injury, involvement of blood cells, generation of pyrogens and release of cytokines ILs, IFNs, TNF, PGE₂; and the hypothalamic response to these changes. The diagnosis of the cause of fever is a challenging task and may include a wide spectrum of disorders. However the possible causes may be narrowed down when fever is associated with thrombocytopenia.

Thrombocytopenia is defined as decrease in number of circulating platelets in the blood. Normal platelet counts range from 1,50,000 to 4,50,000 platelets/ μ l. Often patients with thrombocytopenia are asymptomatic, and are diagnosed incidentally by routine complete blood count (CBC). Occasionally, there may be bruising, purpura, petechiae, black coloured stools, nasal bleeding and gum bleeds, hematuria and, rarely, life threatening bleeding in central nervous system, especially at platelet counts below 5000/ μ l².

There are many mechanisms and causes of thrombocytopenia. It may occur due to decreased platelet production in conditions such as folic acid and

vitamin B12 deficiency, sepsis (bacterial or viral), leukemia, hereditary diseases and some other disorders. Thrombocytopenia may also occur due to increased destruction of platelets such as in idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), paroxysmal nocturnal hemoglobinuria (PNH), systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APLA), post transfusion purpura and hypersplenism. There are many drugs which can cause thrombocytopenia. Drugs such as quinine, methotrexate, valproic acid, isotretinoin, heparin, carboplatin, interferon are commonly responsible for the same²⁻⁷.

Parasitic diseases such as malaria, arbovirus infections such as dengue fever and chikungunya, and many others like leptospirosis, rickettsial infections, septicemia, typhoid, brucellosis, borreliosis, rodent borne viruses such as hanta and lassa fever, human immunodeficiency virus (HIV), visceral leishmaniasis and TTP-HUS¹⁻¹⁰ may commonly present with fever and thrombocytopenia.

Nowadays there has been an increase in the incidence of febrile thrombocytopenia. During monsoon and post monsoon period a large number of patients present with fever and thrombocytopenia. Sometime they can go on to develop a stormy course with multi organ dysfunction requiring strict monitoring and treatment in intensive care unit. Such cases are associated with high morbidity and mortality^{8,9}.

Therefore, systematic approach to evaluate these patients is required to ascertain the underlying etiology on the basis of clinical presentation imaging techniques and other ancillary studies. This goes a long way in

deciding the appropriate treatment and positive clinical outcome, saving precious lives.

Materials and Methods

1. Source of Data

The study was conducted in patients coming to MAHATMA GANDHI MEDICAL COLLEGE AND HOSPITAL, JAIPUR with fever in association with decreased platelets.

2. Inclusion Criteria

- Patients presenting with fever, i.e. A.M temperature of $>37.2^{\circ}\text{C}$ ($>98.9^{\circ}\text{F}$) and P.M temperature $>37.7^{\circ}\text{C}$ ($>99.9^{\circ}\text{F}$), and thrombocytopenia i.e. platelet count of <1.5 lakhs/ μl .

3. Exclusion Criteria

- Patients presenting with thrombocytopenia without fever.
- A diagnosed case of immune thrombocytopenic purpura.
- Thrombocytopenia due to haematological or malignant disorders, patients on chemotherapy or immunosuppressant drugs and other known causes of thrombocytopenia.
- A diagnosed case of platelet disorder and dysfunction.

Investigations Required

Patients related to the above criteria will be subjected to detail clinical profile related to pyrexia and investigations will be done to find out the aetiological factors.

- Complete hemogram
- Bleeding time and Clotting time (if required)
- ESR
- RBS
- Blood Urea
- Serum creatinine

- Urine analysis
- MP card test
- Serological test to detect (if clinically required):
Dengue, Leptospira, Chikungunya, Scrub typhus, Widal
- Chest X- ray
- Ultrasound abdomen
- ELISA for HIV1 and 2
- Bone marrow study, if required
- Blood culture , if necessary
- PT and APTT (if required)

A detailed analysis of clinical presentation and laboratory profile of fever with thrombocytopenia will be done and with available investigations cause of febrile thrombocytopenia will be identified.

Statistical analysis will be done by applying appropriate statistical methods to data collected through this study.

Results

Table 1: Distribution of cases on the basis of age and sex

Age (years)	Male	Female	Total
11-20	42 (28.0%)	16 (10.7%)	58 (38.7%)
21-30	32 (21.3%)	13 (8.7%)	45 (30.0%)
31-40	15 (10.0%)	3 (2.0%)	18 (12.0%)
41-50	9 (6.0%)	5 (3.3%)	14 (9.3%)
51-60	8 (5.3%)	1 (0.7%)	9 (6.0%)
>60	4 (2.7%)	2 (1.3%)	6 (4.0%)
Total	110 (73.3%)	40 (26.7%)	150 (100%)

Above table shows total 150 cases were included in this study. There were 110 male from 150 and 40 were females. Above table shows most of the cases(38.7%) were <20 years age group.

Table 2: Distribution of cases on the basis of etiology

Etiology	No. of patients	Percentage
Dengue	97	64.7
PF	6	4.0
PV	19	12.7
Scrub typhus	17	11.4
Sepsis	3	2.0
Enteric fever	2	1.4
Chikungunya	1	0.7
Unknown	5	3.4

Above table shows maximum cases were of dengue (64.7%) followed by malaria(16.7%) and scrub typhus(11.4%), Sepsis(2.0%), Enteric fever(1.4%), Chikungunya(0.7%).

Table 3: Distribution of cases on the basis of clinical manifestations

Clinical features	No. of patients	Percentage
Fever	150	100.00
Headache	81	54.0
Vomiting	94	62.7
Pain abdomen	101	67.3
Myalgia	69	46.0
Joint pain	57	38.0
Cough	38	25.3
Altered sensorium	1	0.7
Dyspnea	20	13.3

Above table shows all cases had complaint of fever. In these cases 67.3% cases had complaint of pain abdomen, 62.7% had complaint of vomiting,54% headache, 46% myalgia, 38% joint pain, 25.3% cough, 13.3% dyspnea,0.7% had complaint of altered sensorium.

Table 4: Distribution of cases on the basis of bleeding manifestations

Bleeding manifestation	No. of patients	Percentage
None	71	47.3
Haematuria	9	6.0
Petechiae/Purpura	3	2.0
Epistaxis	12	8.0
Melena	61	40.7
Gum bleed	3	2.0
Sub Conjunctival Haemorrhage	1	0.7
Hematemesis/Hemoptysis	3	2.0
Menorrhagia	8	5.3

Above table shows out of 150 cases 71 patients did not have any bleeding manifestation, 61 patients had history of melena, 12 patients had history of epistaxis, 9 patients had history of, 8 patients had history of menorrhagia, remaining patients had other manifestation like gum bleeding, petechiae, sub conjunctival hemorrhage, hemoptysis etc.

Discussion

Fever 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 fever¹. 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 body². It is a symptom which is caused by different illnesses. Fever usually occurs in response to an infection or inflammation. However drugs, poisons, cancer, heat exposure, injuries or abnormalities in the brain, or disease of the endocrine (hormonal or

glandular) system may also cause fever. A fever rarely comes without other symptoms and sign. It is often accompanied by specific complaints or pattern. Many times it is associated with low platelet count. The normal platelet count is 150000-450000/cumm. Thrombocytopenia is defined as platelet count less than 150000/cumm. It results from either decreased production, increases sequestration or destruction of platelets³.

Thrombocytopenia occurs due to decreased platelet production, which occurs in conditions such as vitamin B12 and folate deficiency, leukemia, sepsis (bacterial or viral infection) and hereditary disease. Thrombocytopenia may also occur due to increased destruction such as idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), paroxysmal nocturnal hemoglobinuria (PNH), systemic lupus erythematosus (SLE), antiphospholipid syndrome (APLA), post-transfusion purpura and hypersplenism. Drugs, which can cause thrombocytopenia are quinine, valproic acid, methotrexate, carboplatin, interferon, isotretinoin and heparin⁴⁻⁹.

The causes for thrombocytopenia are varied and range from idiopathic, infectious to malignancies. Patients with an acute febrile illnesses in a tropical country like India usually have an infectious etiology and may have associated thrombocytopenia.

Febrile thrombocytopenia is the thrombocytopenia associated with fever. Diseases which commonly present with fever and thrombocytopenia are malaria, leptospirosis, rickettsial infections, septicemia, typhoid, borreliosis, rodent-borne viruses such as Hanta and Lassa fever, arbovirus such as dengue or yellow fever,

human immunodeficiency virus (HIV), visceral leishmaniasis and TTP-HUS^{4,10}.

In our study we included total 150 patients. In these patients 110 were male and 40 were females. so we found male are more prone to different febrile illnesses. Mohammed Fawas N et al¹¹ in 2017 studied 251 patients of which 127 were males and 124 were females. male to female ratio was almost equal in their study.

In our study we found most of the cases 68.7% were <30 years age group. In dengue fever maximum 79 patients out of 97 patients(81.4%) were from age group <30 years. In case of malaria out of 25 patients 11 patients (44%) were in age group <30 years. In case of other diseases also like scrub typhus, sepsis, enteric fever, chikungunya mostly patients were of age group <30 years.

Our study results correlates with study conducted by Mohammed Fawas N et al¹¹ in 2017 in this study observed that males were more affected in the second and third decades which might be due to their increased travel. The age of patients varied from 15 to 85 yrs which includes all sections of the society. There was maximum incidence of fever among the age group of 21-30 years which constituted 22.3% of the study population. Only few cases were reported in the older age group.

Sanjay V. Patne et al¹² 2017 shows similar results in their study they found maximum cases were seen in age less than 30 years (55.83%) and 72 (60%) were males and 48(40%) were females.

In our study we found maximum cases were of dengue(64.7%) followed by malaria(16.7%) and scrub typhus(11.4%), Sepsis(2.0%), Enteric fever(1.4%), Chikungunya(0.7%).

Mohammed Fawas N et al¹¹ This study has shown that commonest cause of fever with thrombocytopenia was Dengue (54.5%). They found Malaria was the third most common cause of fever with thrombocytopenia which constitutes around 8% of the patients .

A study conducted by Nair et al¹³, Septicemia was the leading cause of fever with thrombocytopenia (26.61%) followed by Typhoid fever (14.68%), Dengue (13.8%), Megaloblastic anemia (11.9%), Malaria (9.2%), Hematological malignancies (3.7%). This might be due to the seasonal and regional variability where the study was conducted. In our study more than 64.7 % cases had dengue but in the study by Nair et al¹³ showed only 13.8% had dengue fever. This may be due to the regional variation in the epidemics or due to seasonal variations. This may be due to the fact that most of the patients in our study admitted during the period have dengue.

Study conducted by Gandhi et al¹⁴ leading cause of fever with thrombocytopenia was Malaria (42%) followed by Dengue (26%), and other viral fever (17%), septicemia (4.5%), enteric fever (4.45%). Where as in our study dengue fever is the common cause followed by other viral fever. In Raikar et al¹⁵ study dengue (52%), malaria (42%) and enteric fever (3%)

In our study all cases who were included had complaint of fever. Out of these 150 cases 67.3% cases had complaint of pain abdomen, 62.7% had complaint of vomiting, 54% headache, 46% myalgia, 38% joint pain, 25.3% cough, 13.3% dyspnea, 0.7% had complaint of altered sensorium.

Mohammed Fawas N et al¹¹ found in their study that Headache was the second most common symptom which was reported in 52% of patients after fever. Other common symptoms were joint pain (42%),

myalgia (35%), abdominal pain (22%) and vomiting (17%). If a patient presented with these symptoms, we should actively search for diseases like Dengue fever, Leptospirosis, Malaria etc.

Praveen Kumar et al¹⁶ in 2014 Commonest symptom after fever was vomiting in 18.94%, abdominal pain in 16.31%, loose motion in 4.73% cases, GI bleed in 5.26% cases and respiratory symptom like cough and dyspnea in 7.89%. Abnormal renal function was detected in 32.63% and abnormal liver function test in 24.73%. So, GI symptoms were the most common symptoms associated with febrile thrombocytopenia.

Mohamed Murtuza Kauser et al¹⁷ in 2014 The commonest presenting clinical symptoms in patients are fever (in all patients, 100%), followed by headache followed by fatigue, myalgia and backache; whereas Mavilla anuradha et al, shows frequently affected symptoms in their study population are myalgia, followed by headache, vomiting etc¹⁹ which shows vise-a-versa result but M. Neeraja et al, reported similar frequency of all symptoms related to our study²⁰. Retroorbital pain was observed in 12.32% of patient; whereas Denys Eiti Fugimoto reported it in 16.1% of patients²¹. Bleeding manifestations were revealed in 9.58% of patients while Ashwini Kumar et al, reported in 26.6%¹⁸ and Tejashree .A et al, were reported in 3.84% of patients²².

Conclusion

In our study we concluded that most common cause of pyrexia with thrombocytopenia was dengue fever.

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