

# Acute Febrile illness with Thrombocytopenia, Common Etiologies in Khyber Pakhtunkhwa

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## ABSTRACT

**Objective:** To know the common causes of febrile illness with thrombocytopenia in Khyber Pakhtunkhwa province.

**Study Design:** Retrospective study.

**Place and Duration of Study:** This study was conducted at two Major Tertiary Care Hospitals of Khyber Pakhtunkhwa from January 2018 and October 2018.

**Materials and Methods:** Demographics, clinical features and laboratory findings were recorded on pre-designed performa.

**Results:** Common conditions causing febrile thrombocytopenia included Malaria (60.00%), Dengue fever (20.50%) and sepsis (9.80%). Enteric fever (3.50%) and Leptospirosis (2.60%) were found less commonly responsible.

**Conclusion:** Infection is the leading cause of fever with thrombocytopenia.

**Key Words:** Fever, Thrombocytopenia.

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## INTRODUCTION

Fever is a common manifestation of illness and is recognized as a cardinal feature of disease.<sup>1</sup> It is defined as an elevation of core body temperature above the normal circadian range. This is due to a change in the thermoregulatory center located within the anterior hypothalamus.

A morning temperature of >37.2 degree centigrade (98.4 degree F) or an evening temperature of >37.7 degree centigrade (99.9 deg F) would define fever.<sup>2</sup> A normal platelet count ranges from 150,000 to 450,000 per micro liter of blood. Thrombocytopenia is defined as platelet count less than 150,000 per micro liter. This is due to decreased production such as leukemia, sepsis, vitamin B12 and folate deficiency, increased destruction (immune thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), paroxysmal nocturnal hemoglobinuria (PNH) and systemic lupus erythematosus (SLE) and increased sequestration in spleen such as hypersplenism.<sup>3-8</sup> Acute fever with thrombocytopenia is called febrile thrombocytopenia.

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It is a common clinical problem faced by physician in medical units especially during the monsoon and perimonsoon period. Infection being the commonest cause of febrile thrombocytopenia such malaria, dengue, typhoid fever, leptospirosis and septicemia. Less common causes include rickettsial fever, borreliosis, rodent-borne viruses such as flanta and lassa fever, HIV.<sup>3,9</sup>

This study is intended to know the underlying etiology of febrile thrombocytopenia in our population.

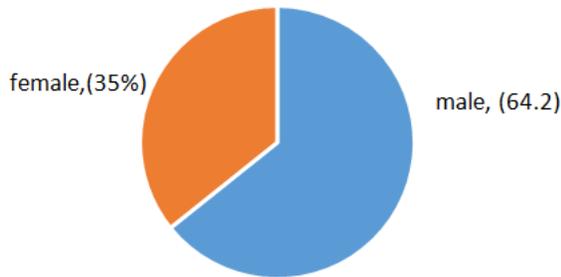
## METIRIALS AND MATHODS

This retrospective study was conducted in the department of Medicine, Lady reading hospital Peshawar and Mardan medical complex Mardan. Medical records of patients admitted between January 2018 and October 2018 with fever and thrombocytopenia (Platelet count <150,000 ×10<sup>9</sup>/L) were reviewed.

Patients less than 18 years of age and those having afebrile thrombocytopenia, congenital thrombocytopenia and chronic liver disease were excluded from the study. Demographic characteristics including age, gender, occupation, clinical and laboratory features were recorded on a pre- designed performa. Data entry and analysis was done through SPSS version 22. For numerical values age, mean ± SD was calculated while for categorical features like gender and clinical features, frequencies and percentages were calculated. Our research is according to declaration of Helsinki and was approved by Institutional ethical review board.

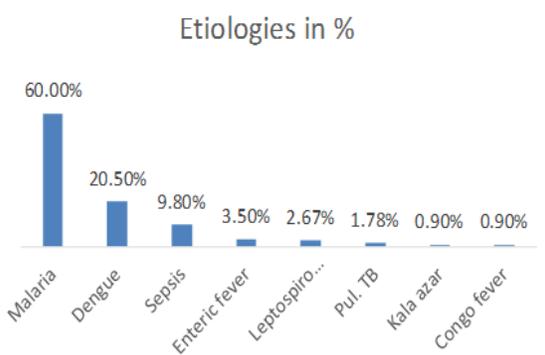
**RESULTS**

A total of 112 patients with febrile thrombocytopenia were included in the study. Out of these 112 patients, 72 patients (64.2%) were male and 40 (35.8%) were females as shown in figure 1.



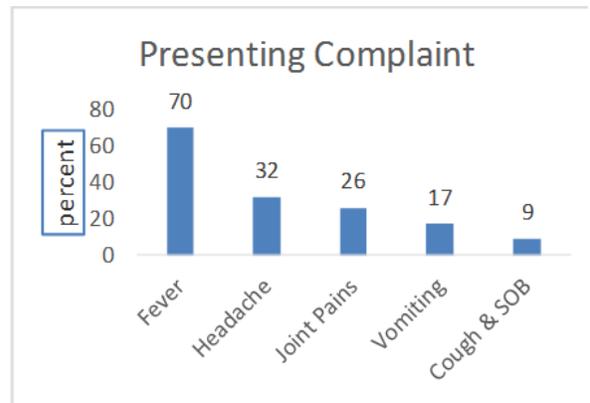
**Figure 1. Gender of Patients**

Male to female ratio was 1.8 : 1. The age of the studied patients ranged from 18-80 years with mean age of 37±6 years. The cases included in our study were divided into three age groups. Febrile thrombocytopenia was commonly seen in patients below 40 year age. The maximum cases were found to be in the age group of 21-40 years accounting 65 cases (58.0%). It was demonstrated in 26 patients (23.2%) in the age group of 41-60 years while 21 cases (18.75%) were above 60 years age. We observed that majority of the patients (52 patients, 46%) were affected between May to September followed by first quarter of the year affecting 32 patients (29%). Malaria was found in 67 patients (60%) and was the leading cause of febrile thrombocytopenia (P.vivax and falciparum were most common). Dengue fever formed the second most common group (23 cases, 20.5%), followed by sepsis (11 cases and 9.8%), typhoid fever ( 04 cases and 3.5%) and leptospirosis ( 03 cases and 2.67%). Pulmonary tuberculosis, kala azar and congo fever constituted 02 (1.78%), 01(0.9%), 01(0.9%) respectively as shown in figure 2.



**Figure No. 2. Etiologies of Febrile thrombocytopenia.**

Fever was the most common presenting complaint noted in 70% patients. Other clinical features observed were headache (32%), joint pains (26%), vomiting (17%), cough and dyspnea (9%) . (Figure 3)

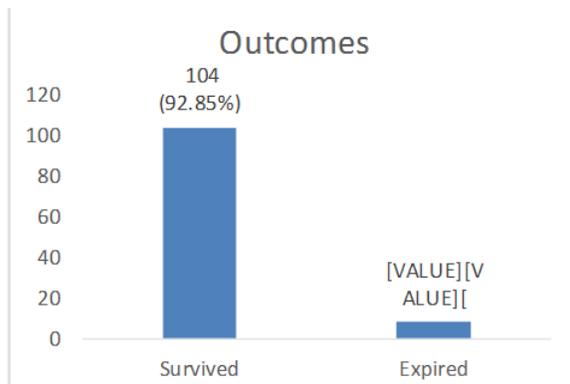


**Figure No.3. Presenting Complaints of Patients with Febrile thrombocytopenia.**

Our patients displayed different types of bleeding manifestations. Petechial hemorrhages were present in 42 patients (37.5%), hematuria in 13 patients (11.6%). Bleeding from the gums was seen in 9 patients (8.03%). Bleeding per rectum and menorrhagia was seen in one patient each (0.89%). Maximum number of patients had platelet count between 50,000 to 100,000 cells per micro liter.

**Table No.1: Platelet count of Patients.**

Platelet count	Patients	Percent
Less than 20,000 (severe thrombocytopenia)	20	17.85
20,000-50,000 (moderate thrombocytopenia)	17	15.17
More than 50,000 (mild thrombocytopenia)	75	66.96



**Figure No.4: Outcome of patients with Febrile thrombocytopenia.**

In our study, leucopenia was seen in 33 patients (29.46%). Out of these, 15 were dengue cases followed by CCHF in 10 cases. Leukocytosis was seen in 40 cases (35.71%) and was mostly seen in cases of septicemia (23 cases, 20.5%). Abnormal renal function tests were reported in 20 cases with most number in septicemia (12 cases, 10.71%) followed by typhoid

fever (5 cases, 4.46%). In general, 104 patients (92.85%) had good recovery and 08 cases (7.15%) expired. (Figure 4).

## DISCUSSION

Fever with thrombocytopenia is one the most challenging problem faced by all physicians of medical units. It is the paraneoplastic presentation of common disease rather than rare disease. A retrospective study of 112 patients who had fever and thrombocytopenia was conducted in two tertiary level hospitals of Khyber Pakhtunkhwa (KPK).

In the present study, majority of patients with febrile thrombocytopenia were in the age group of 21 to 40 years constituting about 58%. We observed large number of cases in the month of June to September. It is due to the fact that malaria and dengue fever are highly widespread during this particular time period.

In our study, malaria was the commonest cause of febrile thrombocytopenia establishing 60% cases. Vivax malaria was seen in 40%, while 15% were those of falciparum malaria. Similar results were observed by Nair in his study in which out of 41 cases of malaria, 20 cases were those of vivax malaria, falciparum 13 cases and mixed infection was (falciparum plus vivax) seen in 08 cases.<sup>10</sup> Khan SJ and his colleagues conducted study at HMC Peshawar. They enrolled 228 adult patients of fever with thrombocytopenia over a period of 02 years. They observed that malaria was the commonest cause of febrile thrombocytopenia constituting 53% cases.<sup>11</sup> In another study conducted by Srinivas at India, malaria was reported in 41 out of 100 cases being the leading cause of febrile thrombocytopenia and majority of these cases were reported from March to September.<sup>12</sup>

Pathophysiology of thrombocytopenia in malaria is multifactorial including immune mediated platelets destruction, splenic sequestration, decrease survival of platelets and depletion by DIC. We observed mild to moderate thrombocytopenia in malaria in 73% patients. This is comparable to Jadhav and Shaikh Study (85.5%).<sup>13,14</sup>

Shaikh and his co-workers in their research documented that 171 patients (85.5%) were having low platelet count, 141 patients (70.5%) had mild and 21 (10.5%) moderate and 09 (4.5%) had severe thrombocytopenia.<sup>14</sup> Jadhav et al from India in their study thrombocytopenia in malaria found that 78% of patients with vivax malaria had mild thrombocytopenia, a very similar finding to our study.<sup>13</sup>

Dengue fever was found to be the second most common cause of thrombocytopenia in our study, reportedly in 23 patients (20.5%). Dengue is the most important arthropod borne viral disease and a major health problem in tropics with increased mortality and morbidity. Thrombocytopenia is a constant feature and

one of the diagnostic criteria of dengue hemorrhagic fever.<sup>15</sup>

The etiology of thrombocytopenia in dengue is multifactorial. It is caused by decrease platelet production and immune mediated and splenic destruction of platelets. In addition, dengue infection also activate the intrinsic pathway of apoptosis, mitochondrial depletion and activation of caspase 3.<sup>16,17</sup>

In a study from Suneetha, 150 patients of acute febrile illness, were diagnosed with dengue(25%), enteric fever(14%), malaria(8%).<sup>18</sup> The study by Patil et al mentioned malaria in 54% cases followed by dengue(15%), enteric fever (6%) in total 100 studied patients.<sup>19</sup>

We observed thrombocytopenia in 9.8% of patients with sepsis. The mechanism of thrombocytopenia in sepsis has not been fully understood. However increased platelet destruction as a result of either overt or subclinical DIC has been postulated. Previously Lee et al reported 57% of thrombocytopenia in septicemia patients.<sup>20</sup> Crafter- Gvili et al reported an incidence of thrombocytopenia of 22.3% in patient with sepsis.<sup>21</sup>

Sepsis is a major risk for the development of thrombocytopenia. It is common in clinically ill patients admitted to the ICU with sepsis. These patients are more likely to develop acute kidney injury, major bleeding episodes and to receive more blood product transfusion.<sup>9</sup>

In general, patients having fever with thrombocytopenia had good recovery and mortality occurred in 08 patients (7.15%). 06 out of 08 expired patients were due to septicemia with multi-organ dysfunction including acute kidney injury and respiratory distress syndrome. Complicated malaria accounted for 02 cases of mortality. The study conducted by Lohitashwa et.al indicated sepsis as the most common cause of death (70%) followed by dengue.<sup>12</sup> The range of platelet count in the mortality cases was less than 10,000 /micro liter in one case followed by 30,000 to 50,000/micro liter in the remaining 07 cases.

## CONCLUSION

Fever with thrombocytopenia is an important clinical problem. Infection is the commonest cause. Among infections, malaria was the leading etiology in Khyber Pakhtunkhwa. Health authorities should focus on the primary prevention.

### Author's Contribution:

Concept & Design of Study:	Ziauddin
Drafting:	Inayat Ullah, Muhammad Kashif
Data Analysis:	Rehman ud Din, Shah Zeb
Revisiting Critically:	Inayat Ullah, Zainuddin
Final Approval of version:	Ziauddin

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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