Original Research Article

PYREXIA WITH THROMBOCYTOPENIA- A RETROSPECTIVE STUDY ON EPIDEMIOLOGY, DIAGNOSIS, AND OUTCOME

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Abstract

Background: Fever is one of the most common complaints for which the patient approaches to the clinician in the outpatient department (OPD). The etiology of the fever with thrombocytopenia substantially revolves around the viral etiology and treatment of which remains mainly conservative. Our objective was to study the demographic details, diagnosis, and outcomes of patients presenting to us with acute febrile illnesses causing thrombocytopenia. **Materials and Methods:** We did a retrospective study and enrolled all patients presenting to our tertiary care centre with a provisional diagnosis of pyrexia with thrombocytopenia. We stratified the patients further based on their respective demographic details, age, sex, final diagnosis, and outcomes of the patients. A standard case report form was used to gather clinical and demographic data. A variety of laboratory tests were carried out depending on clinical indications, including complete blood counts, liver and renal function assessments, and other pertinent testing. **Result:** Our study showed that a comparatively younger population was afflicted by acute febrile illness since the majority of patients (82%) in this study were under 40 years of age. 18% of the population was above 40. The gender distribution of the study population was fairly balanced, with 56% women and 44% men. This suggests that thrombocytopenia associated with acute febrile illness can affect both sexes equally. Viral etiology is the most common (50%), followed by bacterial etiology (20%), other/undiagnosed etiologies (1%), and parasitic etiology (29%). Among 200 participants, 75 (37.5%) had organ dysfunction with most of them having moderate thrombocytopenia and it was statistically significant (p<0.05). Most of the patients (92%) recovered from acute febrile illness. **Conclusion:** Laboratory investigations when used judiciously along with the appropriate clinical scenario act as a strainer through which the provisional diagnosis of the illness sieves. Thus a well-organized systematic approach that is carried out with an awareness of causes of fever with thrombocytopenia narrows the differential diagnosis of the clinical entity and brings out the diagnosis.

INTRODUCTION

Fever was earlier seen as a disease but was later recognized as an accompaniment to a variety of disease entities.[1] Fever itself is often enfeebling to mankind but is the sole protective response of our immune system. Wonderlich in 1868 exclaimed that abnormality of temperature is a cardinal sign of diseases while normality a sign of health.[2] The Pathogenic microbes try to invade the human body and sabotage the competent immune system, the thermoregulatory system comes in the main play

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and raises the temperature of the body eventually. Fever when persisting for weeks, warrants rapid workup to search for the etiology of the same at the earliest, to prevent the debilitating consequences. The clinical features associated with the fever often narrow down the differentials in the clinician's mind, thus helping in reaching the final diagnosis. Lab investigations often reveal leukocytosis, leucopenia, thrombocytopenia, deranged LFT, AKI etc. Depending on the aforementioned lab findings the etiology segregates into various lanes and thus the treatment of the same varies. Infections like dengue, leptospirosis, and malaria, are some of the common causes of pyrexia with thrombocytopenia.

Thrombocytopenia is encountered in various diseases, although fatal bleeding due to thrombocytopenia is rare.[3] The causes of thrombocytopenia vary which can be impaired platelet formation, accelerated platelet destruction or dilution, and/or splenic sequestration.[4] Even though it would be dilemmatic to predict the exact numeral attributing to the platelet counts that would cause bleeding, certainly by broad generalizations, platelet counts less than 10,000/μL, bleeding may be usual and severe.[5] Bleeding due to thrombocytopenia occurs most often from small vessels, often manifested on the human body as petechiae over the skin and hemorrhages from the mucosa of the gastrointestinal and genitourinary tract.

Ultimately, the study's objective is to assess each patient's overall result according to their level of thrombocytopenia and related factors. Thrombocytopenia may be linked to higher rates of morbidity and mortality as well as an effect on the prognosis of the patient.[6] We seek to find indicators of unfavorable outcomes and create prognostic markers for risk stratification by analyzing the association between the degree of thrombocytopenia, clinical parameters, and patient outcomes.

MATERIALS AND METHODS

The retrospective study was conducted in the Department of Medicine, King George's Medical University Lucknow from 3rd July 2023 to 22nd September 2023. Randomly 200 patients were selected for the study. During the study period, all the patients presenting with Fever and Thrombocytopenia were screened for eligibility. Informed Consent was obtained.

A standard case report form was used to gather clinical and demographic data. A variety of laboratory tests were carried out depending on clinical indications, including complete blood counts, liver and renal function assessment, and other pertinent testing. For diagnosing third space fluid loss abdomen ultrasonography and chest X-ray was done. Based on the platelet count, the degree of thrombocytopenia was classified as mild (50,000-100,000/μL), moderate (20,000-50,000/μL), or

severe (<20,000/μL). When diagnosing organ dysfunction, certain signs and symptoms, aberrant test results, and imaging data were taken into account.

For diagnosing bacterial, viral and parasitic infection following tests were done:
Serological tests such as IgM ELISA for leptospira and scrub typhus, NS1Ag and IgM ELISA for dengue, IgM ELISA for chikungunya, Thick and thin peripheral smear along with rapid diagnostic antigen kit test for malarial parasite was used.

Inclusion Criteria
- All the patients more than 12 years of age.
- All the patients who presented with complaints of fever (>99.9ºF) with thrombocytopenia (platelet count less than 1,50,000/μL)

Exclusion Criteria
- Patients less than 12 years of age.
- Patients having afebrile thrombocytopenia.
- Known patients of primary thrombocytopenia.
- Drug-induced thrombocytopenia.
- Diagnosed cases of thrombocytopenic purpura on treatment.
- Patients with thrombocytopenia already diagnosed to have haematological disorder/malignancy, on treatment with chemotherapy and other immunosuppressant.

Statistical Analysis: The study population's clinical and demographic features were compiled using descriptive statistics. The chi-square test and other suitable statistical tests were used in association analysis to investigate the associations between the variables. The statistical analysis was performed using SPSS for Windows version 22.0 software. The critical value of P indicating the probability of significant difference was taken as <0.05 for comparison.

RESULTS
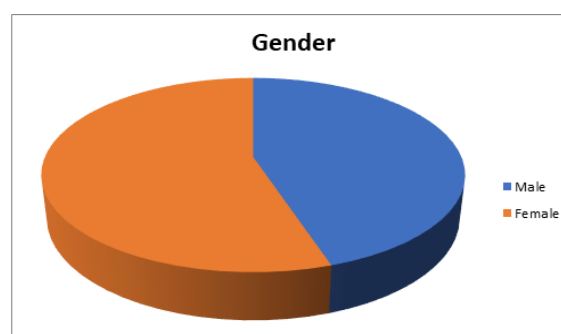
**Figure 1: Gender wise distribution**

In our study, most of the patients were females (n=112) 56%, males (n=88) 44%.

[Table 1] summarizes the demographic profile of the study population. It shows that a comparatively younger population was afflicted by acute undifferentiated fever since the majority of patients (82%) in this study were under 40 years of age. 18 percent of the population was above 40. The gender distribution of the study population was fairly balanced, with 56% women and 44% men. This

suggests that thrombocytopenia associated with acute undifferentiated fever can affect both sexes equally. 52 percent of the study participants did not have any recorded comorbidities. Nonetheless, with hypertension present in 32% of patients, it was the most prevalent comorbidity. These demographic details shed light on the age range and gender makeup of patients who present with thrombocytopenia and acute undifferentiated fever. Comprehending the study population's demographic profile is crucial in evaluating the findings' generalizability and recognizing any particular trends or patterns in the way this condition is presented.
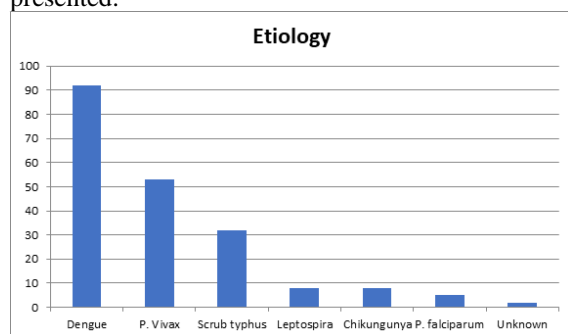
Figure 2: Etiology of fever with thrombocytopenia
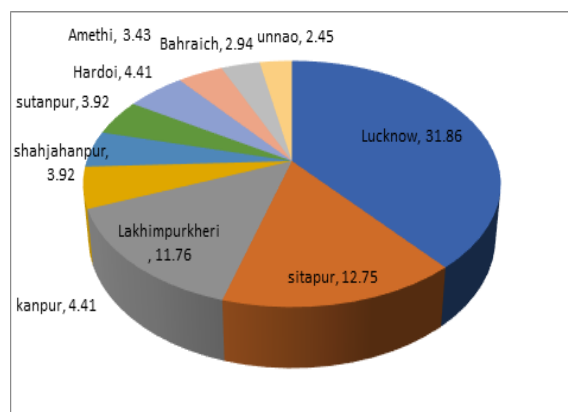
Figure 3: Distribution of Districts in Uttar Pradesh as per cases

As per [Figure 2] out of the total patients, most of the cases of pyrexia with thrombocytopenia were of dengue (n= 92) 46%, followed by malaria {Plasmodium vivax (n= 53) 26.5%, Plasmodium falciparum (n= 5) 2.5%}, Scrub typhus (n=32) 16%, Leptospirosis (n=8) 4%, Chikungunya (n=8) 4%, Unknown (n=2) 1%.

The study conducted in our hospital is a tertiary care center and is a refer hub, where patients from different parts of Uttar Pradesh are catered at our best available services. So, we did the slicing of our total inventory of records of patients according to the demographic profile. Most of the patients were of Lucknow itself (n=65) 31.86%, followed by Sitapur (n=26), 12.75%; Lakhimpur Kheri (n=24), 11.76%; Kanpur (n=9), 4.41%; Hardoi (n=9), 4.41%; Shahjahanpur (n=8), 3.92%; Sultanpur (n=8), 3.92%; Amethi (n=7), 3.43%; Bahraich (n=6), 2.94%; Unnao (n=5), 2.45%.

[Table 2] Suggests clinical characteristics along with the association of the degree of thrombocytopenia, among 200 participants, 75 (37.5%) had organ dysfunction with most of them having moderate thrombocytopenia and it was statistically significant (p<0.05). The shock was seen in 19.5% of study cases with a mild degree among the highest but it was not significant. Third space loss was seen in 49% of cases with a moderate degree of thrombocytopenia which is found to be statistically significant (p<0.05).

As per [Table 3] out of 100 (50%) of participants had moderate degree among them only 40% required platelet transfusion. Among Severe degree out of 25 cases, 84% required platelet transfusion.

As per [Table 4] most of the patients (92%) were recovered. 6 patients went LAMA and 10 patients expired.

Table 1: Demographic profile of the study population

Variables	Number (%)
Age	
>12-20 years	52 (26)
21-40 years	112 (56)
>40 years	36 (18)
Gender	
Males	88 (44)
Females	112 (56)
Comorbidities	
None	104 (52)
Diabetes	64 (32)
Hypertension	32 (16)

Table 2: Comparison of the degree of Thrombocytopenia with Complications

Parameters	Mild thrombocytopenia	Moderate thrombocytopenia	Severe thrombocytopenia	p-value
Organ dysfunction	31	42	2	0.01
Shock	4	22	12	0.11
Third space loss	30	36	7	0.01

Table 3: Requirement of Platelet transfusion in relation to degree of thrombocytopenia

Degree of thrombocytopenia	Platelet transfusion required (%)
Mild (50,000- 100,000/μL) (N=75)	10 (13)
Moderate (20,000-50,000/μL) (N=100)	40 (40)
Severe (<20,000/μL)v (N=25)	21 (84)

Table 4: Overall outcomes

Outcomes	Number (%)
Recovered	184(92)
LAMA	6 (3.0)
Expired	10(5.0)

DISCUSSION

The study in our tertiary care hospital led us to encounter some of the most prevalent differentials, including malaria, Dengue, Chikungunya, Leptospirosis, and Scrub typhus. We intended to collect the data and further stratify them according to their age, sex, demography, etc.

Thrombocytopenia is a prevalent characteristic of both infectious and non-infectious illnesses, and it can be linked to varying levels of organ dysfunction and sickness severity. The degree of thrombocytopenia was found to be significantly correlated with organ failure and loss of third space.[6]

Nair PS et al,[6] did a similar study in which they enrolled 109 patients, out of which 76 were male and 33 were female. In our study, we had 125 patients, out of which 58 were male and 67 were female.

Srinivas et al,[7] did a study in which malaria was the leading cause of pyrexia with thrombocytopenia followed by enteric fever, septicemia, dengue, and leptospirosis. This was congruent to our study also the most prevalent cause of the thrombocytopenia associated with fever was malaria.

Compared to patients with mild thrombocytopenia, individuals with moderate and severe thrombocytopenia had greater rates of organ malfunction, shock, and third-space loss. This association emphasizes the significance of keeping an eye on the platelet count to gauge the severity of the disease and the requirement for more stringent care.[8]

In order to avoid bleeding issues, platelet transfusion is frequently considered for patients with severe thrombocytopenia.[9] According to our research, there is a substantial correlation between the level of shock, organ failure, thrombocytopenia, and third space loss and platelet transfusion.[10] Platelet transfusion was more common in patients with severe thrombocytopenia, organ failure, shock, or third space loss. This finding highlights how crucial it is to handle each patient uniquely based on their clinical characteristics and platelet counts.[11]

In the present study shows that viral etiology is the most common (50%), followed by bacterial etiology (20%), other/undiagnosed etiologies (1%), and parasitic etiology (29%). These results are in line with earlier research that found that patients with acute undifferentiated fever had a comparable mix of infectious and non-infectious etiologies.[12]

There are a few noteworthy limitations to our study. First off, the fact that only one center was used for the study may restrict how broadly the results may be applied in different contexts. Furthermore, in the absence of particular laboratory testing, the diagnosis of viral etiology—aside from dengue—was mostly relied on clinical presentation and the exclusion of other aetiologies. This might have resulted in some viral aetiologies being misclassified or underestimated. To confirm these findings, more research with bigger multicenter cohorts and more thorough viral diagnosis techniques is needed.[13]

CONCLUSION

Laboratory investigations when used judiciously along with the appropriate clinical scenario act as a strainer through which the provisional diagnosis of the illness sieves. Thus a well-organized systematic approach that is carried out with an awareness of causes of fever with thrombocytopenia narrows the differential diagnosis of the clinical entity and brings out the diagnosis. Timely recognition and treatment of the underlying condition, and platelet transfusions are required to prevent fatal outcomes.

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