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Clinico-Etiological Profile and Outcome of Acute Febrile Illness with Thrombocytopenia in Children: A Hospital-Based Prospective Study.

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KEYWORDS

Acute febrile illness; Thrombocytopenia; Children; Dengue; Malaria; Scrub typhus; Etiological profile; Pediatric infections; Clinical outcome.

ABSTRACT:

Background: Acute febrile illness (AFI) with thrombocytopenia is a common clinical condition in children, particularly in tropical countries where infections such as dengue, malaria, and scrub typhus are prevalent. Early identification of the underlying cause and appropriate management are important to reduce complications and mortality.

Objectives: To study the clinico-etiological profile and outcomes of acute febrile illness with thrombocytopenia in children admitted to a tertiary care hospital.

Materials and Methods: This hospital-based prospective observational study was conducted at Sri Siddhartha Medical College and Hospital, Tumkur, over a period of 24 months after obtaining ethical approval. A total of 57 children aged 1 month to 18 years admitted with acute febrile illness and thrombocytopenia were included in the study. Detailed clinical history, examination findings, and laboratory investigations, including complete blood count and peripheral smear, were recorded using a predesigned proforma. Thrombocytopenia was classified as mild, moderate, and severe based on platelet count. Data were analysed using MS Excel and EPI INFO version 7.2.5, and statistical analysis was performed using descriptive statistics and the chi-square test.

Results: The mean age of the participants was 8.85 ± 5.19 years, with the majority belonging to the 1–5 year age group (33.33%). Male children constituted 61.40% of the study population. Dengue was the most common etiological cause (36.8%), followed by malaria (33.3%), scrub typhus (17.5%), typhoid fever (7%), and sepsis/others (5.3%). Mild thrombocytopenia was observed in 56.10% of cases, moderate in 38.60%, and severe in 5.30%. Hepatomegaly was present in 71.90% and splenomegaly in 22.80% of patients, while bleeding manifestations were seen in 17.50%. Most children recovered completely (68.43%), 28.07% recovered with complications, and mortality was 3.50%. No statistically significant association was found between the severity of thrombocytopenia and outcomes ($p = 0.451$).

Conclusion: Dengue, malaria, and scrub typhus are the leading causes of acute febrile illness with thrombocytopenia in children. Most patients recover with timely diagnosis and appropriate treatment. Early recognition and management are essential to reduce complications and improve outcomes.

INTRODUCTION

Acute febrile illness (AFI) is a common clinical presentation in pediatric practice and represents one of the leading causes of hospital admissions among children in developing countries. AFI is generally defined as a fever of short duration, usually less than two weeks, without an identifiable localised source of infection at the time of initial evaluation. In tropical and subtropical regions, a wide variety of infectious agents, such as viruses, bacteria, and parasites, contribute to AFI, making diagnosis and management challenging for clinicians (1).

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Thrombocytopenia, defined as a platelet count below 150 × 10^3/µL, is a frequently observed haematological abnormality in children presenting with acute febrile illness. It may result from decreased platelet production, increased peripheral destruction, splenic sequestration, or immune-mediated mechanisms. The occurrence of thrombocytopenia in febrile illnesses often indicates systemic infection and may be associated with increased disease severity and risk of complications (2).

In tropical countries like India, several infectious diseases such as dengue fever, malaria, scrub typhus, enteric fever, and septicemia are well-known causes of febrile illness associated with thrombocytopenia. Dengue infection, in particular, is a major public health concern and is characterized by bone marrow suppression, immune-mediated platelet destruction, and increased peripheral consumption of platelets. These mechanisms often result in significant thrombocytopenia and may lead to bleeding manifestations (3).

Malaria is another important cause of febrile thrombocytopenia in endemic regions. Thrombocytopenia in malaria occurs due to immune-mediated destruction of platelets, splenic sequestration, and platelet consumption. Studies have reported that thrombocytopenia is present in a significant proportion of malaria cases and may serve as an important diagnostic clue in endemic areas (4).

Scrub typhus, caused by *Orientia tsutsugamushi*, has emerged as an important cause of acute febrile illness with thrombocytopenia in many parts of India. The disease is transmitted through the bite of infected chigger mites and is characterized by fever, thrombocytopenia, hepatosplenomegaly, and sometimes multi-organ involvement. Early diagnosis and treatment are essential to prevent severe complications (5).

The severity of thrombocytopenia may vary from mild to severe, and the risk of bleeding complications generally increases with decreasing platelet counts. However, not all patients with thrombocytopenia develop bleeding manifestations. The occurrence of bleeding depends not only on platelet count but also on platelet function, vascular integrity, and the underlying disease process (6).

Clinical features such as hepatomegaly, splenomegaly, and bleeding manifestations are frequently observed in children with acute febrile illness and thrombocytopenia. These findings may provide important diagnostic clues to the underlying etiology. Laboratory investigations such as complete blood count, peripheral smear examination, and specific serological tests play a crucial role in identifying the cause of febrile thrombocytopenia (7).

Understanding the clinico-etiological profile of acute febrile illness with thrombocytopenia is essential for early diagnosis and appropriate management. Identifying the common etiological agents and their clinical patterns helps clinicians initiate prompt treatment and reduce complications. In addition, evaluating patient outcomes provides valuable information regarding disease severity, response to treatment, and mortality associated with different infections (8).

Despite the high burden of febrile illnesses associated with thrombocytopenia in children, limited data are available from many regions regarding their clinical profile and outcomes. Therefore, the present hospital-based prospective study was undertaken to evaluate the clinico-etiological profile and outcomes of acute febrile illness with thrombocytopenia in children admitted to Sri Siddhartha Medical College and Hospital, Tumkur.

MATERIALS AND METHODS

The present “hospital-based prospective observational study” was conducted in children admitted with AFI at Sri Siddhartha Medical College and Hospital, Tumkur, over 24 months, following institutional ethical committee approval. A total of 57 patents that met the inclusion and exclusion criteria were included in the study.

Inclusion criteria:

- Children for whom their parents gave written consent are included.
- Children aged 1 month to 18 years admitted with AFI in Sri Siddhartha Medical College and Hospital, Tumkur.

Exclusion criteria:

- Children with afebrile thrombocytopenia

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- Congenital heart diseases
- Platelet disorders
- Children on antiplatelet drugs

Sample size:

$n = (Z)^2(1-\alpha/2) \times p(1-p) \quad d^2$

Primary outcome variable: cases with fever

- Proportion=5.6%
- Absolute precision=13%
- Z-value for 99%CL=2.54

Minimum required sample is n=57

Methodology

Children who fulfilled the inclusion criteria were selected for the study. "Informed written consent was taken from their parents before inclusion". Data were collected using a predesigned pro forma, which included details such as age, sex, and socio-demographic profile. "A detailed history regarding presenting complaints, relevant history, family history, and significant birth history" was taken and noted in the proforma. Results from "general physical examination and systemic examination were also documented. Platelet count and white blood cell (WBC) count data were extracted from the complete blood count report". At the same time, peripheral smear findings were entered into the proforma accordingly.

Severity of Thrombocytopenia

Thrombocytopenia was classified based on platelet count as follows:

- Mild thrombocytopenia: Platelet count >70 × $10^3/\mu L$
- Moderate thrombocytopenia: Platelet count between 20–70 × $10^3/\mu L$
- Severe thrombocytopenia: Platelet count <20 × $10^3/\mu L$

Statistical analysis

"The collected data were entered and tabulated in MS Excel and analysed using EPI INFO software version 7.2.5". Descriptive statistics such as proportions, mean, and standard deviation were applied. Inferential statistics, including the chi-square test, were also employed for analysis.

RESULTS AND OBSERVATIONS;

Age

Fifty-seven patients were involved in the study. The mean age of the participants was 8.85 ± 5.19 years. The majority of subjects were in the 1–5 year age group, comprising 19 children (33.33%). This was followed by the 6–10 year age group with 15 patients (26.32%) and the 11–15 year group with 13 patients (22.81%). Infants below one year of age accounted for 2 patients (3.51%), while adolescents aged 16–18 years constituted 8 patients (14.04%) (Table 1).

Table 1. Distribution of age

Age (years)	Frequency (n)	Percentage (%)
<1	2	3.51
1-5	19	33.33
6-10	15	26.32
11-15	13	22.81
16-18	8	14.04
Total	57	100.00

Table 2. Distribution of sex

Sex	Frequency (n)	Percentage (%)
Male	35	61.40
Female	22	38.60
Total	57	100.00

Table 2 shows the distribution of study participants according to sex. Out of the total 57 children included in the study, 35 (61.40%) were males and 22 (38.60%) were females. This indicates a male predominance among children presenting with acute febrile illness with thrombocytopenia in the present study population.

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Table 3. Distribution of the etiological profile

Etiological Profile	Frequency (n)	Percentage (%)
Dengue	21	36.80
Malaria	19	33.30
Scrub typhus	10	17.50
Typhoid/enteric fever	4	7.00
Sepsis/others	3	5.30
Total	57	100.00

Table 3 shows the distribution of the etiological causes of acute febrile illness with thrombocytopenia among the study participants. Dengue was the most common cause, accounting for 21 cases (36.80%), followed by malaria with 19 cases (33.30%). Scrub typhus was observed in 10 patients (17.50%), while typhoid/enteric fever was seen in 4 cases (7.00%). Sepsis and other causes constituted 3 cases (5.30%). These findings indicate that dengue and malaria were the leading etiological factors responsible for febrile thrombocytopenia in children in this study.

Table 4. Distribution of the severity of thrombocytopenia

Severity of Thrombocytopenia	Frequency (n)	Percentage (%)
Mild	32	56.10
Moderate	22	38.60
Severe	3	5.30
Total	57	100.00

Table 4 shows the distribution of patients according to the severity of thrombocytopenia. The majority of children had **mild thrombocytopenia**, accounting for 32 cases (56.10%). This was followed by **moderate thrombocytopenia** in 22 patients (38.60%). Only a small proportion of children, 3 cases (5.30%), had **severe thrombocytopenia**. These findings indicate that most cases of thrombocytopenia associated with acute febrile illness were mild to moderate in severity.

Table 5. Distribution of hepatomegaly

Hepatomegaly	Frequency (n)	Percentage (%)
Yes	41	71.90
No	16	28.10
Total	57	100.00

Table 6. Distribution of splenomegaly

Splenomegaly	Frequency (n)	Percentage (%)
No	44	77.20
Yes	13	22.80
Total	57	100.00

Table 7. Distribution of bleeding

Bleeding	Frequency (n)	Percentage (%)
No	47	82.50
Yes	10	17.50
Total	57	100.00

Table 8. Distribution of outcomes

Outcomes	Frequency (n)	Percentage (%)
Recovered	39	68.43
Recovered with complications	16	28.07
Death	2	3.50
Total	57	100.00

Table 8 shows the distribution of clinical outcomes among the study participants. The majority of children, **39 cases (68.43%)**, recovered completely with treatment. **Sixteen patients (28.07%)** recovered but developed certain complications during the course of illness. **Two cases (3.50%)** resulted in death. These

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findings indicate that most children with acute febrile illness and thrombocytopenia had a favorable outcome with appropriate management.

Table 9. Association between the severity of thrombocytopenia and outcomes

Severity of thrombocytopenia	Outcomes n, (%)			P-value*
	Recovered	Recovered with complications	Death	
Mild	21 (53.80)	11 (68.75)	0 (0)	0.451
Moderate	16 (41.00)	5 (31.25)	1 (50.00)	
Severe	2 (5.10)	0 (0.0)	1 (50.00)	
Total	39 (100.00)	16 (100.00)	5 (100.00)	

*Chi-square test

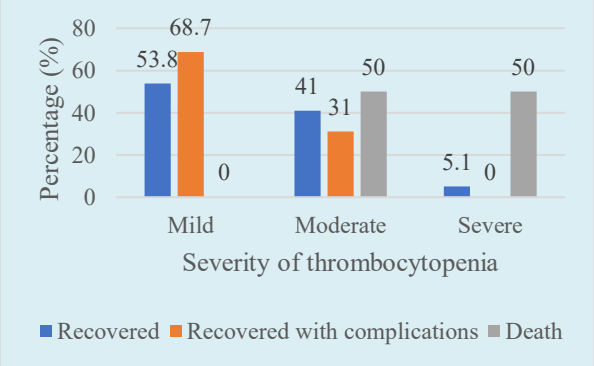

Figure 1. Association between the severity of thrombocytopenia and outcomes

DISCUSSION

Acute febrile illness with thrombocytopenia is a common clinical problem encountered in pediatric practice, particularly in tropical countries where infectious diseases are prevalent. Identifying the etiological factors and clinical profile of such cases is important for early diagnosis and appropriate management. The present study evaluated the clinico-etiological profile and outcomes of children admitted with acute febrile illness and thrombocytopenia.

In the present study, the mean age of the participants was 8.85 ± 5.19 years, with the majority of cases belonging to the 1–5 year age group. This finding indicates that younger children are more susceptible to febrile illnesses associated with thrombocytopenia. Similar observations were reported by Bhat et al., who found that most pediatric cases of febrile thrombocytopenia occurred in children below 10 years of age (9). Increased exposure to environmental pathogens and developing immunity may contribute to the higher incidence in this age group.

The present study also demonstrated a male predominance, with 61.40% of the cases being male. Similar findings have been reported in other studies evaluating febrile illnesses in children. Gupta et al. reported a higher incidence of dengue and other febrile infections among male children, which may be attributed to increased outdoor exposure and sociocultural factors affecting healthcare access (3).

Regarding the etiological profile, dengue fever was identified as the most common cause of acute febrile illness with thrombocytopenia in the present study, accounting for 36.8% of cases. This was followed by malaria (33.3%), scrub typhus (17.5%), typhoid fever (7%), and sepsis or other causes (5.3%). Similar findings have been reported in several studies conducted in India where dengue and malaria were the leading causes of febrile thrombocytopenia (10). The increasing recognition of scrub typhus as a cause of febrile illness in children has also been documented in recent literature.

In terms of severity of thrombocytopenia, most children in the present study had mild thrombocytopenia (56.10%), followed by moderate thrombocytopenia (38.60%) and severe thrombocytopenia (5.30%). These findings are consistent with previous reports which indicate that mild to moderate thrombocytopenia is commonly seen in infectious diseases, while severe thrombocytopenia occurs in a smaller proportion of patients (2).

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Clinical examination findings revealed hepatomegaly in 71.90% of children and splenomegaly in 22.80%. Hepatomegaly is commonly associated with infections such as dengue, malaria, and enteric fever due to hepatic involvement and systemic inflammatory response. Similar findings were reported by other studies evaluating the clinical profile of febrile thrombocytopenia in children (11). Splenomegaly, although less frequent in the present study, is typically associated with malaria and certain bacterial infections.

Bleeding manifestations were observed in 17.50% of cases in the present study. Although thrombocytopenia increases the risk of bleeding, most patients did not develop bleeding complications despite having low platelet counts. This observation is consistent with previous studies, which have shown that bleeding risk is influenced not only by platelet count but also by platelet function and vascular factors (6).

The outcome analysis in the present study showed that the majority of patients recovered completely (68.43%), while 28.07% recovered with complications and 3.50% resulted in death. These findings suggest that with early diagnosis and appropriate treatment, most children with acute febrile illness and thrombocytopenia have a favourable prognosis. Similar recovery rates with low mortality have been reported in other hospital-based studies (12).

The association between the severity of thrombocytopenia and outcomes in the present study did not show a statistically significant relationship ($p = 0.451$). This indicates that the severity of thrombocytopenia alone may not determine the outcome of the disease. Other factors, such as the underlying infection, severity of illness, and timely management, may play a more significant role in determining prognosis.

Overall, the findings of this study highlight that dengue, malaria, and scrub typhus are the most common causes of acute febrile illness with thrombocytopenia in children. Early clinical evaluation, appropriate laboratory investigations, and prompt treatment are essential to reduce complications and improve outcomes in affected children.

CONCLUSION

Acute febrile illness with thrombocytopenia is a common condition in children, mainly caused by infections such as dengue, malaria, and scrub typhus. In this study, most patients had mild to moderate thrombocytopenia, and the majority recovered with appropriate treatment. Severe thrombocytopenia and mortality were relatively uncommon. Early diagnosis and prompt management are essential to reduce complications and improve outcomes in affected children.

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