Clinical and Etiological Profile of Acute Febrile Illness Associated with Thrombocytopenia in Pediatric Patients

Hemachandran Jeldi Jesudoss[1], Kirtika Shrivastava[2], B Vamshi Krishna[3], Gouri Rajput[4]

[1]Professor, Department of Physiology, College of Medicine, Jazan University, Jazan, K.S.A.
[2]Assisstant Professor, Department of Physiology, Peoples College of Medical Sciences and Research Centre, Bhopal, Madhya Pradesh.
[3]Assistant Professor, Department of Paediatrics, RIMS, Adilabad, Telangana.
[4]Assistant Professor, Department of Paediatric, N. K. P. Salve Institute of Medical Sciences and Research Centre & Lata Mangeshkar Hospital, Nagpur, Maharashtra

Abstract

Background: Thrombocytopenia frequently presents as a common clinical condition in routine medical practice. Due to the multitude of potential causes, evaluating and treating patients with thrombocytopenia can be challenging. This study aimed to identify the diverse etiological factors and clinical characteristics of fever with thrombocytopenia in children aged 1 month to 12 years admitted to our hospital.

Methods: Acute febrile illness lasting for 5 days. Demographic data collection included age, gender, geographical location, and a detailed medical history. The investigations included Complete blood count, peripheral smear study, urine albumin, blood urea, serum creatinine, liver enzymes and serum bilirubin, xray chest depending upon detailed examination on suspicion of tropical infections MP smear, dengue IgM, scrub typhus 20 IgM ELISA, widal test, leptospirosis IgM were performed along with blood culture and urine culture.

Results: Distinct etiologies exhibit varying thrombocytopenia severities. Undiagnosed fever has the highest proportion of severe cases (53.12%). Dengue fever consistently presents with moderate or severe thrombocytopenia. Scrub typhus commonly has moderate (42.5%), mild (25.00%), and severe (9.37%) cases. Acute Lymphoblastic Leukemia (ALL) shows only moderate thrombocytopenia in 2 out of 8 cases. Malaria, enteric fever, viral encephalitis, and septicemia demonstrate low thrombocytopenia prevalence. Among 80 children, 77 improved with treatment, 2 were referred for hematological malignancy, and 1 for multiorgan dysfunction.

Conclusion: Febrile Thrombocytopenia, a benign illness in children, is characterized by common GI symptoms and is prevalent. Infants with thrombocytopenia often experience shock and an altered level of consciousness. Severe thrombocytopenia correlates with bleeding, primarily presenting as petechiae. Treating the primary condition led to a prompt improvement in platelet count, particularly in non-bleeding cases. Despite encountering platelet counts as low as five thousand cells/cumm, most of the cases improved.

Keywords: Bleeding Manifestations, Thrombocytopenia, Dengue Fever.

Introduction

Fever stands out as the most prevalent symptom prompting parents to seek early medical attention for their children. Recognized as a cardinal manifestation of disease since ancient times. [1] It results from a change in the thermoregulatory center in the anterior hypothalamus, coinciding with an increase in the hypothalamic set point (e.g., 37°C to 39°C). [2] Prolonged fever cases often represent known diseases with atypical manifestations. The variable pattern of fever graphic recording doesn't consistently lead to a specific diagnosis, justifying an aggressive diagnostic approach. Thrombocytopenia, defined as a platelet count <150,000/microliter, results from decreased production, increased destruction, and enhanced sequestration in the spleen. Notable febrile conditions, including dengue, viral fever, malaria, and enteric fever, are frequently associated with thrombocytopenia. [3, 4] The defined platelet count for thrombocytopenia is less than 150,000/μl, with severe thrombocytopenia falling below 50,000/μl. [3] Excessive EDTA use during sampling can lead to pseudo-thrombocytopenia. [5] Febrile thrombocytopenia, linked to fever, is prevalent in diseases such as malaria, leptospirosis, rickettsial infections, septicemia, typhoid, borreliosis,

arboviruses like dengue or yellow fever, HIV, and TTP-HUS. [6, 7] The tropical climate in countries like India facilitates the transmission of these infections. With the onset of monsoons, a surge in cases of febrile thrombocytopenia, characterized by varied clinical courses and unpredictable outcomes, has been observed annually. [8] The study aims to understand the underlying etiology, clinical profiles, and the correlation between platelet levels, disease severity, and prognosis in febrile thrombocytopenia within our study cohort. The specific objectives are to identify diverse causes and clinical profiles of fever with thrombocytopenia in children aged 1 month to 13 years admitted to this medical facility.

Material and Methods

This prospective observational study was conducted at the Department of Pediatrics. Institutional Ethical approval was obtained for the study. Written consent was obtained from the parents/guardians of the children while included in the study after explaining the nature of the study in the vernacular language.

Inclusion criteria

1. Acute febrile illness lasting for 5 days.
2. Aged aged 1 month to 12 years.
3. Males and females.
4. Admitted to pediatric wards.
5. Parents gave consent for the study.

Exclusion criteria

1. Afebrile thrombocytopenia.
2. ITP.
3. Hematological malignancies.
4. Cases of pseudothrombocytopenia.

Demographic data collection included age, gender, geographical location, and a detailed medical history. Clinical examinations recorded admission features such as fever, heart rate, respiratory rate, blood pressure, capillary refill time, hepatomegaly, eschar, splenomegaly, lymphadenopathy, petechiae, altered level of consciousness (ALOC), and the tourniquet test. The latter was considered positive when 10 or more petechiae per square inch were observed after inflating a blood pressure cuff to a point midway between systolic and diastolic pressure for 5 minutes.

In DHF the test usually gives a definite positive with 20 petechiae or more. The test may be negative during the phase of profound shock. It usually becomes positive, sometimes strongly positive after recovering from shock. Following clinical examination, all children were subjected to the investigations as per the unit protocol. The investigations included Complete blood count, peripheral smear study, urine albumin, blood urea, serum creatinine, liver enzymes and serum bilirubin, Xray chest depending upon detailed examination on suspicion of tropical infections MP smear, dengue IgM, scrub typhus 20 IgM ELISA, widal test, leptospirosis IgM were performed along with blood culture and urine culture. Children with suspected hematological malignancy underwent bone marrow examination. CSF study was not undertaken in any child with thrombocytopenia. However, if viral encephalitis was a suspicion CSF analysis was done after recovery from thrombocytopenia as per our unit policy. Children in the study group were followed up till the outcome for complications like shock, bleeding manifestations, hepatic failure, renal failure, respiratory distress, cardiac failure, pulmonary edema, and multi-organ failure. Platelet count and hematocrit were monitored frequently during complications like shock and bleeding in the pediatric intensive care unit (PICU). Platelet counts were repeated on alternate days in hemodynamically stable children until they reached 1,50,000 cells/cumm, for this study. The need for any blood product transfusion was documented. Platelet transfusion was not routinely undertaken among children in our unit. The presence of DIC or the need for surgical or invasive interventions was considered as the indication for transfusion of platelets in our unit. The outcome was determined by recovery to hospital discharge or death.

Statistical analysis: The statistical tests, including Chi-Square and T-test, were appropriately employed to compare parameters between children with and without bleeding. Data analysis sought statistical significance, with a P value < 0.05 considered significant.

Results

This study included 80 children with fever and thrombocytopenia. Out of the 80 cases 42(52.5%) were males and 38(47.5%) were females. The study group comprised children between 1 month to 12 years of age. They were categorized as infants, toddlers, preschool children, and school children.

Table 1: Age-wise distribution of cases with fever and thrombocytopenia included in the study

Age	Frequency	Percentage
< 1 year	6	7.5
1 -3 years	8	10
3-5 years	13	16.25
>5 years	53	66.25

Table 1 displays the age distribution of cases with fever and thrombocytopenia included in this study. It categorizes cases into four age groups and presents their frequencies and percentages: Significant

prevalence in older children: The majority of cases (66.25%) fall within the age group above 5 years. Relatively even distribution in younger groups: The remaining three age groups show a somewhat uniform distribution of cases, ranging from 7.5% to 16.25%. Fever and thrombocytopenia occur across all ages: While it suggests a higher prevalence in children over 5 years old, it is important to note that cases are present in all age groups, including infants and toddlers. While thrombocytopenia is a consistent occurrence in various common pediatric illnesses, an analysis of seasonal patterns in common infections indicated a higher prevalence of children with thrombocytopenia during specific months of the year. The distribution by month showed that more than 80% of the study group presented between August and November (figure 1).
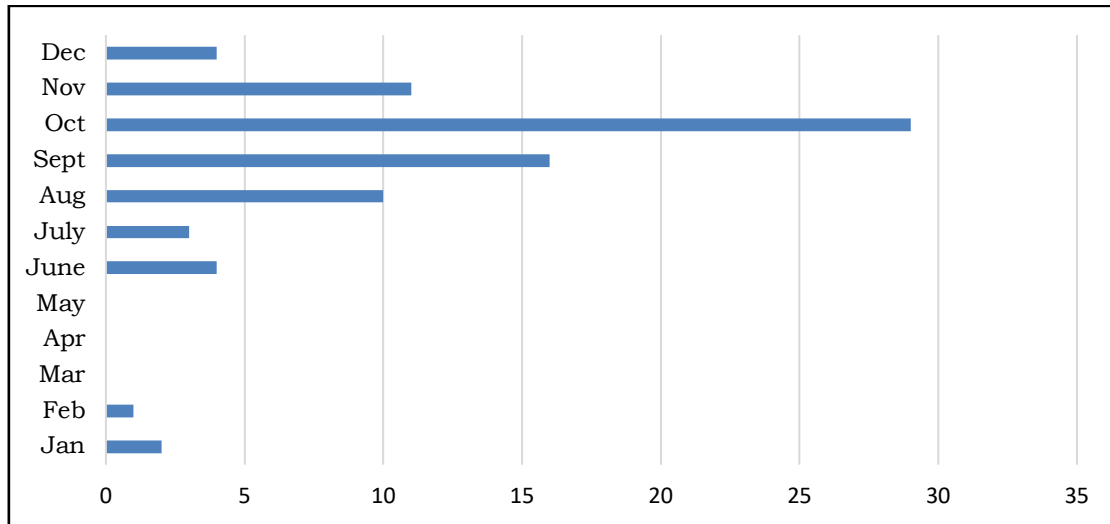

Figure 1: Presentation of cases of fever with thrombocytopenia in the study

Table 2 shows the frequency and percentage of various symptoms recorded in cases of fever and thrombocytopenia. High prevalence of gastrointestinal symptoms: GI symptoms, represented by a broad category, are the most common, affecting 45% of patients. Other frequent symptoms: Headache and myalgia (muscle aches) are present in 27.5% of cases, followed by gastrointestinal bleeding (10%), altered sensorium (8.75%), and cutaneous bleeds (10%). Less frequent symptoms: Seizures, rash (erythema), oliguria, and recurrent seizures occur less frequently, ranging from 3.75% to 6.25%.

Table 2: Symptom recorded in cases of fever and thrombocytopenia included in the study.

Symptom	Frequency	Percentage
GI symptoms	36	45.0
Headache, myalgia	22	27.5
GI bleeds	8	10.0
Altered sensorium	7	8.75
Cutaneous bleeds	8	10.0
Seizures	5	6.25
Rash(Erythema)	5	6.25
Oliguria	3	3.75
Seizures	3	3.75

Comparatively, most infants exhibited altered sensorium, as compared to the occurrence in children aged over 5 years. Infants also experienced a higher frequency of gastrointestinal bleeding, breathlessness, oliguria, and seizures.

Table 3: Examination findings in different age groups cases of fever and thrombocytopenia

Signs	< 1 years (n=6)	1 – 3 years (n=8)	3 – 5 years (n=13)	> 5 years (n=53)
Fever	6(100%)	8(100%)	11(84.62%)	50(94.34%)
Pallor	6(100%)	6(75%)	5(38.46%)	15(28.30%)
Lymphadenopathy	1(16.67%)	3(37.5%)	4(30.77%)	13(24.53%)

Petechiae	1(16.67%)	0(00.00%)	1(7.69%)	10(18.87%)
Hepatomegaly	3(50.0%)	7(87.5%)	10(76.92%)	35(66.04%)
Splenomegaly	2(33.33)	5(62.5%)	5(38.46%)	9(16.98%)
Eschar	0(0.00)	1(12.5%)	5(38.46%)	7(13.20%)

Table 3 displays the presence or absence of various physical examination findings in different age groups of patients with fever and thrombocytopenia included in the same study. Each column represents an age group with its sample size (n) in parentheses, while rows list specific clinical signs. Fever is present in almost all cases across all age groups, ranging from 84.62% in the 3-5 years group to 100% in the youngest and oldest groups. While pallor is observed in half of the cases in the youngest two groups, its prevalence significantly decreases to 28.30% in older children and even lower among teenagers and adults. Similar to pallor, the presence of lymphadenopathy is more frequent in younger children (up to 37.5% in 1-3 years) compared to older age groups (24.53% in the oldest group). Skin findings like petechiae (pinpoint bleeding) are more common in older children (18.87% in >5 years) compared to younger ones, while eschar (localized area of tissue death) is mostly absent in the youngest two groups and seen in a small percentage of older children and teenagers. Enlargement of the liver (hepatomegaly) and spleen (splenomegaly) is more frequent in the youngest groups, with prevalence decreasing with age. However, hepatomegaly remains relatively common in all age groups (66.04% in the oldest group).

Table 4: Parameters recorded in the cases of fever and thrombocytopenia

Parameter	< 1 years (n=6)	1 – 3 years (n=8)	3 – 5 years (n=13)	> 5 years (n=53)
Compensated shock	2(33.33%)	1(12.5%)	2(15.38%)	11(20.54%)
Hypotensive shock	1(16.67%)	0(0.00%)	1(7.69%)	2(3.77%)
Wide pulse pressure	1(16.67%)	2(25.0%)	1(7.69%)	5(9.43%)
Narrow pulse pressure	2(33.33%)	0(00.00%)	4(30.77%)	9(16.98%)
ALOC	4(66.67%)	1(12.5%)	1(7.69%)	6(11.32%)
Torniquet test positive	1(16.67%)	1(12.5%)	2(15.38%)	14(26.41%)

Table 4 presents various parameters recorded in cases of fever and thrombocytopenia, categorized by the patient's age group. Each column represents an age group with its sample size (n) in parentheses, while rows list specific parameters. Compensated shock: Occurs in 33.33% of the youngest group, decreasing with age to 20.54% in the oldest. Hypotensive shock: Less common than compensated shock, seen in only 1.67% of the youngest group and 3.77% of the oldest. Wide pulse pressure: Ranges from 7.69% to 25.0% across age groups. Narrow pulse pressure: More prevalent in the youngest group (33.33%) compared to older groups (0% to 30.77%). ALOC: Abnormal Liver Function Test (ALOC) is present in 66.67% of the youngest group, but significantly less frequent in older groups (12.5% to 7.69%). Tourniquet test: A positive test for capillary fragility, indicating potential bleeding issues, is seen in 16.67% of the youngest group and increases to 26.41% in the oldest.

Table 5 displays various laboratory parameters measured in cases of fever and thrombocytopenia, along with their range, mean, and standard deviation (SD). The mean total white blood cell count (WBC) falls within the lower end of the normal range (8600 cells/mm^3). The mean hemoglobin level (11.52 g/dl) indicates mild anemia across the study population. Mean hematocrit (34.5%) and PCV (packed cell volume) values fall within the normal range. As expected, platelet counts are significantly reduced, with both mean admission and lowest recorded platelet counts well below the normal range (76,000 and 51,500 cells/mm^3, respectively). Mean AST and ALT levels are slightly elevated, suggesting potential liver dysfunction. Mean serum bilirubin and creatinine levels fall within the normal range, indicating no significant evidence of liver or kidney impairment.

Table 5: Laboratory parameters recorded in cases of fever and thrombocytopenia

Parameters	Range	Mean	SD
Total count (cells/mm^3)	73000 - 1800	8600	107150.5
Hemoglobin(g/dl)	16.5 – 4.5	11.52	2.26
Hematocrit (%)	15 – 48	34.5	6.42
Highest PCV	16 – 48	35.0	5.68
Slowest PCV	15 – 45	30.22	4.58
Platelet count	5000 – 275000	76000	45620

(cells/mm³) at admission			
Lowest Platelet count (cells/mm³)	5000 – 135000	51500	30145
AST (IU/L)	12 – 51	25.59	5.32
ALT (IU/L)	14 – 45	26.54	6.35
Serum bilirubin (mg/dl)	0.7 – 2.0	0.92	0.17
Urea (mg/dl)	16 – 53	22.35	6.97
Creatinine (mg/dl)	0.55 – 2.0	0.66	0.22

Thrombocytopenia Grades: categorized by the severity of thrombocytopenia:

- Mild: Platelet count ≥ 50,000 cells/mm³, (n=8)
- Moderate: Platelet count 20,000 - 49,999 cells/mm³, (n=40)
- Severe: Platelet count < 20,000 cells/mm³, (n=32)

In this study, we found 40% of cases with severe thrombocytopenia and 50% of cases with mild thrombocytopenia as depicted in Figure 2.
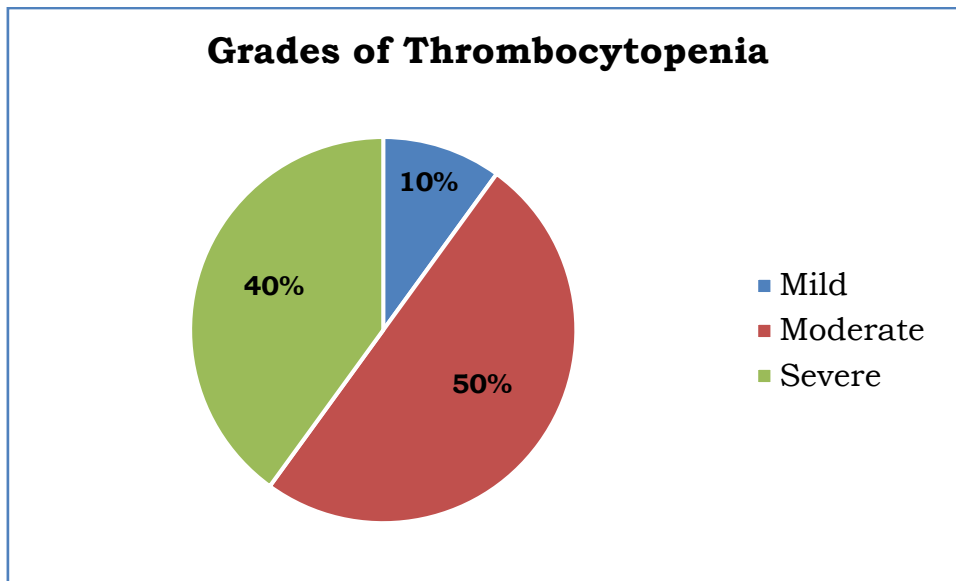

Figure 2: Grades of thrombocytopenia recorded in the cases of the study

Table 6: Comparison of physiological status with severity of thrombocytopenia

Parameters	Mild thrombocytopenia (n=8)	Moderate thrombocytopenia (n=40)	Severe thrombocytopenia (n=32)
Compensated shock	1(12.5%)	8(20%)	9(28.12%)
Hypotensive shock	0(00.0%)	0(0%)	3(9.37%)
Wide pulse pressure	2(25.0%)	6(15%)	3(6.25%)
Narrow pulse pressure	0(00.0%)	5(12.5%)	8(25%)
Tourniquet test positive	0(00.0%)	7(17.5%)	8(25%)

Table 6 compares the presence of various physiological findings across three groups of patients with fever and thrombocytopenia. Increased shock with greater thrombocytopenia: The prevalence of both compensated and hypotensive shock rises with increasing severity of thrombocytopenia. Compensated shock occurs in 12.5% of mild cases, 20% of moderate cases, and 28.12% of severe cases. Hypotensive shock is absent in mild and moderate groups but affects 9.37% of severe cases. The Wide pulse pressure is most common in the mild group (25%) and decreases with increasing severity, while narrow pulse pressure shows the opposite trend, being absent in the mild group and increasing to 25% in the severe group. This indicator of potential bleeding issues becomes more frequent with increasing thrombocytopenia severity, from 0% in the mild group to 17.5% in the moderate group and 25% in the severe group.

Table 7: Grades of thrombocytopenia in specific etiology

Etiology	Mild thrombocytopenia (n=8)	Moderate thrombocytopenia (n=40)	Severe thrombocytopenia (n=32)
Undiagnosed fever	4(50.00%)	9 (22.5%)	17(53.12%)
Dengue fever	0(0.00%)	10 (25.0%)	12(37.5%)
Scrub typhus	2(25.00%)	17 (42.5%)	3(9.37%)
ALL	0(0.00%)	2 (5.00%)	0(0.00%)
Malaria	1(12.5%)	0 (0.00%)	0(0.00%)
Enteric fever	0(0.00%)	1 (2.50%)	0(0.00%)
Viral encephalitis	0(0.00%)	1 (2.50%)	0(0.00%)
Septicemia	1(12.5%)	0(0.00%)	0(0.00%)

Table 7 shows the distribution of thrombocytopenia severity across different etiologies (underlying causes) in the study population with fever and thrombocytopenia. Different etiologies show distinct patterns in terms of thrombocytopenia severity. Undiagnosed fever: This group has the highest proportion of severe cases (53.12%) and the lowest proportion of mild cases (50.00%). Dengue fever: All cases present with moderate or severe thrombocytopenia, with no mild cases observed. Scrub typhus: Moderate thrombocytopenia is the most common (42.5%), followed by mild (25.00%) and severe (9.37%) cases. ALL (Acute Lymphoblastic Leukemia): Only moderate thrombocytopenia is present in 2 out of 8 cases. Malaria, enteric fever, viral encephalitis, and septicemia: These etiologies show a low prevalence of thrombocytopenia, with one or two cases falling into either moderate or severe categories. Out of 80 children, 77 showed improvement with suitable treatment, 2 were referred for evaluation and management of hematological malignancy, and 1 was referred because of multiorgan dysfunction.

Discussion

In this study we found the male-to-female ratio was nearly equally affected a finding consistent with the studies conducted by Rekha M.C et al. [9] P Kumar et al. [10] and S Ahmed et al. [11] all of which reported a male-to-female ratio of 1.2:1. The mean age of affected children in this study was 8.5 ± 2.95 years. Comparable mean ages of 8.3 ± 3.5 years were reported in the studies by S Ahmed et al. [11] and Shah G.S et al. [12] Additionally, there was a lower representation of infants and toddlers in comparison to preschool and school-going children in the present study. In this current study, 80% of the children exhibited symptoms during the months spanning from August to November. A study conducted by P Kumar et al. [10] demonstrated a significant concentration of cases from July to September, while M Ayub et al. [13] observed a heightened prevalence between June and August. These findings closely align with the temporal distribution observed in the present study. This pattern may represent a universal phenomenon, as certain infectious conditions such as dengue and scrub typhus are recognized for their seasonal presentation. In this current investigation, the majority of children exhibited gastrointestinal symptoms as the primary manifestation, followed by headache, myalgia, gastrointestinal bleeds, and altered sensorium. Similar trends were observed in studies conducted by P Kumar et al. [10] and S Ahmed et al. [12], where gastrointestinal symptoms were the most prevalent, followed by headache in P Kumar et al.'s [10] study and rashes in S Ahmed et al.'s [11] study. Yaramis et al. [14] A Sajid et al. [8] and Chitu CH et al. [15] also found gastrointestinal symptoms to be the most common in more than two-thirds of the cases, aligning with the findings of the present study.

In contrast, studies by Shah GS et al. [12] and Nikalje Anand et al. [16] reported that headache was the most common symptom, surpassing gastrointestinal symptoms. In the current study, most of the children presented with fever upon admission. 62.5% of the children exhibited hepatomegaly, 31.25% had pallor, 25% showed splenomegaly, and 15% displayed petechiae at the time of admission. Shah G.S et al.'s [12] study reported hepatomegaly in three-fourths of the children, splenomegaly in one-fourth, and petechiae in half of the study group. Similarly, A Yaramis et al. [14] found hepatomegaly in two-fifths of the children, splenomegaly in one-fifth, and altered sensorium in 6% of the cases, aligning with the results of the present study. In contrast, S Ahmed et al. [11] reported that pallor was the most common presentation in 67%, followed by hepatomegaly in 37%, and splenomegaly in 6% of children. A Sajid et al. [8] on the other hand, found that splenomegaly was the most common presentation in 94% of children, followed by pallor in 65%, and hepatomegaly in 64%. In our study with 80 children, 40% had severe thrombocytopenia, 50% had moderate, and 10% had mild thrombocytopenia. Comparable findings were observed in studies by M Ayub et al. [13] SK Bhalara et al. [17] and B Palange et al. [18] indicating the prevalence of severe, moderate, and mild thrombocytopenia. In contrast, K Mohan et al, [19] Shah G.S et al, [12] and A Sajid

et al. [8] reported varying proportions. Puttasuresh et al3 associated thrombocytopenia in malaria with sequestration and immune-mediated destruction, while M Ayub et al. [13] linked Dengue fever thrombocytopenia to marrow depression in the acute stage. In the present study petechiae was the commonest one accounting for 45 % followed by GI bleeds at 35% and other bleeds like epistaxis, subconjunctival hemorrhage, and gum bleeds collectively accounting for 18.75%. Among bleeding manifestations, GI bleeds were common in infants in contrast to school-going children where petechiae was the common one. In this study, bleeding manifestations were notably more frequent in children with severe thrombocytopenia, characterized by a platelet count of less than 50,000 cells/cumm. Similar findings were observed in studies by SK Bhalara et al. [17] and Prithvi Raj et al., [20] where the bleeding was more common when platelet count was below 50,000 cells/cumm. In contrast, studies by Pankaj K Palange et al. [18], Kriti Mohan et al. [19] Shah G.S et al. [12], and Shankar Raikar et al. [22] reported no significant correlation between platelet count and bleeding manifestations.

In our study, undiagnosed fever emerged as the most prevalent cause of fever with thrombocytopenia, followed by Dengue fever, Scrub typhus, leukemia, Malaria, Enteric fever, and Septicemia. Similar patterns were observed in studies by Prithvi Raj et al. [20] Rekha M.C et al. [5] and Nikhalje Anand et al.8, which indicated undiagnosed fever as the primary etiology, followed by Dengue fever and Enteric fever. Shankar Raikar et al. [21] and SK Bhalara et al. [17] identified Dengue fever as the most common etiology, followed by malaria and sepsis, aligning with our study. Conversely, Putta Suresh et al. [22] and Praveen Kumar et al. [3] reported malaria as the predominant cause, followed by dengue and undiagnosed fever. Regarding outcomes, 96% of participants in our study improved and were discharged, two cases were referred for hemato-oncological consultation, and one multiorgan dysfunction.

Conclusion

Febrile Thrombocytopenia, a benign illness in children, is characterized by common GI symptoms and is prevalent. Infants with thrombocytopenia often experience shock and an altered level of consciousness. Severe thrombocytopenia correlates with bleeding, primarily presenting as petechiae. Treating the primary condition led to a prompt improvement in platelet count, particularly in non-bleeding cases. Despite encountering platelet counts as low as five thousand cells/cumm, most of the cases improved. This underscores the overall benign nature of Febrile Thrombocytopenia in children, emphasizing its generally favorable prognosis.

References

1. Atkins E. Fever: its history, cause, and function. Yale J Biol Med. 1982; 55:283-89.
2. Gondhali MP, Vethekar M, Bhangale D, Choudhary K, Chaudhary M, Patrike G, Kundgir A: Clinical assessment of fever with thrombocytopenia - A prospective study. Int J Med Res Health Sci. 2016, 5:258-77.
3. Kumar P, Chandra K. A clinical study of febrile thrombocytopenia: a hospital-based retrospective study. Ind J Clini Pract. 2014 Mar;24(10):952-57.
4. World Health Organization. Comprehensive guideline for prevention and control of dengue and dengue hemorrhagic fever. PDF available from https://www.who.int/publications/i/item/97892 41547871 [Accessed on Jan 2021]
5. Rekha MC, Sumangala B, Ishwarya B. Clinical study of fever with Thrombocytopenia. J Evolut Medi Dent Sci. 2014 Oct 9;3(51):11983-91.
6. Yaramis A, Yildirim I, Katar S, Ozbek MN, Yalcin I, Tas MA, et al. Clinical and laboratory presentation of typhoid fever. Int Pediatr. 2001;16(4):227-31.
7. Rodríguez-Morales AJ, Sanchez E, Vargas M, Piccolo C, Colina R, Arria M. Anemia and thrombocytopenia in children with Plasmodium vivax malaria. J Trop Pediatr. 2006 Feb 1;52(1):49- 51.
8. Sajid A, Ikram A, Ahmed M. Dengue fever outbreak 2011: clinical profile of children presenting at Madina Teaching Hospital Faisalabad. J Univ Med Dent Coll. 2012 Jan;3(1):42-47.
9. Rekha M.C, Sumangala B, Ishwarya B. Clinical study of fever with thrombocytopenia. J of Evolution of Med and Dent Sci. Oct 2014;3(51):11983-90.
10. Praveen Kumar Kalpana Chandhra. A clinical study of febrile thrombocytopenia: A Hospital-based Retrospective Study. Indian Journal of Clinical Practice. March 2014;24(10):952-57.
11. Saba Ahmed, Fehmina Arif, Yousuf Yahya, Arshaloos Rehman, Kashif Abbas, Sohail Ashraf, Dure Samin Akram. Dengue fever outbreak in Karachi.A study of profile and outcome of children under 15 years of age. Jan 2008;58(1):4-7.
12. Shah GS, Islam S, Das BK. Clinical and laboratory profile of dengue infection in children. Clinical and laboratory profile of dengue infection in children. Kathmandu University Medical Journal. 2006;4(13):40-43.
13. Muhammed Ayub, Adel M Khazinder, Eman H Lubbad. Characteristics of dengue fever in a large public hospital, Jeddah, Saudi Arabia. J Ayub Med Coll Abottabad.2006;18(2): 9-13.
14. A Yaramis, I Yildirim, S Katar, M. Nuri Ozbek, I Yalcin, M. Ali Yalcin, M. Ali Tas, S Hosoglu,

Clinical and Laboratory presentation of Typhoid Fever. International Pediatrics. 2001;16(4): 227-231.

15. Chitu CH, Kalpana Chandhra. A clinical study of febrile thrombocytopenia: A Hospital-based Retrospective Study. Indian Journal of Clinical Practice. March 2014;24(12):45-49.

16. Nikalje Anand, Talib S.H, Pagar Bhushan, Patil Piyush, Kurhade Aniket. Clinical outcomes of patients presenting as fever with thrombocytopenia in Marathwada. Medicine, Environmental Science 2016; 5 (2):611-615.

17. Shruthi K Bhalara, Smitha Shah, Hansa Goswami. Clinical and etiological profile of thrombocytopenia in adults. International journal of medical science and public health.2015;4(1):7-10.

18. Pankaj B Palange, R B Kulkarni, R K Shrawasti. A study of Clinical profile of patients with dengue fever with thrombocytopenia. International journal of recent trends in science and technology. 2015;13(3):671-675.

19. Kriti Mohan, B J Omar, Rupa D Singh, Aaradhana, Ravi Sachan. Thrombocytopenia with bleeding manifestations in childhood malaria. Indian J Child Health. 2016;3(3):196-200.

20. Prithviraj Patil, Pranita Solanke, Gayathri Harshe. Clinical Evaluation and Outcome of Patients with Febrile Thrombocytopenia. International Journal of Scientific and Research Publications. October 2014;4(10):1-3.

21. Shankar R Raikar, Panna K Kamdar, Ajay S Dhabi. Clinical and laboratory evaluation of patients with fever with thrombocytopenia. Indian Journal of Clinical Practice. 2013;24(4):360-363.

22. Putta Suresh, Yamani Devi, Crams Kumar, Y. Jalapa. Evaluation of the cause of Fever with Thrombocytopenia cases. Journal of evidence-based Medicine and Healthcare. 2015; 2(15): 2134-37.