



Evaluation of Clinico-Etiological Profile in Children Having Febrile thrombocytopenia

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ABSTRACT

Background

An increase in body temperature that is more than the typical daily range because of a rise in the hypothalamic set point is referred to as a fever (e.g., Thirty seven to thirty nine degrees Celsius). It's a crucial sign that indicates a higher-than-normal internal body temperature. It is believed to be one of the body's immunological defence mechanisms against an inside threat. Febrile thrombocytopenia is thrombocytopenia associated with fever.

Aim

To analyse clinico-etiological profile in children having febrile thrombocytopenia.

Methods

The present retrospective study was conducted from 2nd March 2022 to 31st August 2023 in Sri Chamundeshwari medical College Hospital and Research Institute, Channapatna, Ramanagara, in the department of Pediatrics on 600 patients, age group between 2 months to 15 years of age presenting with fever. Date of onset of symptoms (fever, rash bleeding, joint swelling etc.), number of days for which symptoms continued, any history of blood disorder and any previous history of blood transfusion was asked. Details of specific diagnosis such as enteric fever, septicaemia and dengue were noted along with the treatment given. Entire clinical course till final outcome was studied and relevant details were noted.

Results

The vital cause for febrile thrombocytopenia were Dengue (32.83%) followed by malaria (18%). Bleeding manifestation was present in 123 (20.5%) subjects. Bleeding manifestations were recorded maximum



among subjects suffering from dengue (47.20%) while it was found least in subjects with Disseminated TB followed by typhoid. When bleeding manifestations was compared according to etiology, it was found to be statistically significant. Platelet transfusion was needed in 67 subjects, out of which 19 (7.64%) required SDP (Single Donor Platelet) and 48 (28.36%) needed RDM (Random Donor Platelet).

Conclusion

thrombocytopenia is a common problem encountered in clinical practice. Knowledge of common causes of thrombocytopenia and their clinical manifestations will help in deciphering the cause of thrombocytopenia and formulating diagnostic and therapeutic strategy. Rapid diagnostic tests for malaria and dengue are helpful in ruling out these diseases.

Keywords: thrombocytopenia, Febrile, Platelet, Dengue

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INTRODUCTION

Fever is described as an increase in body temperature above the normal daily range due to an increase in the hypothalamic set point (e.g., Thirty seven to thirty nine degrees Celsius)¹. It's a key symptom that describes an elevation in internal body temperature over normal. It is thought to be one of the body's immunological strategies for neutralizing a perceived threat within the body². The thrombocytopenia linked with fever is known as febrile thrombocytopenia³⁻⁵.

In children, thrombocytopenia was common symptom of both febrile and non-febrile illnesses⁵. thrombocytopenia described as decrease in the platelet count below 1.5 lakh/L⁶. thrombocytopenia is caused by a reduction in production, rapid breakdown of platelet or dilution, and splenic sequestration. Platelet counts and haemorrhage have no direct relationship⁷.

Thrombocytopenia is characterised by bleeding from tiny vessels, which is most common. This can show up as petechiae on the skin, as well as haemorrhages from the gastrointestinal and genitourinary tract mucosa. In thrombocytopenic patients, intracranial bleeding is a significant complication. Fever-related thrombocytopenia aids in narrowing the differential diagnosis and management of fever. Patients have lots of symptoms that range from asymptomatic or mild viral to severe cardiovascular shock. To avoid tragic results, early detection and treatment of the underlying disease, including platelet transfusions, are essential⁸.

Dengue fever, malaria, enteric fever, urinary tract infection, sepsis, leptospirosis, and scrub typhus frequent infectious causes of fever with thrombocytopenia in India⁹. It is usually caused by various infections in India, but it can also be caused by non-infectious illnesses such as malignancies or collagen vascular disorders⁸. In the Indian context, febrile patients with thrombocytopenia are encountered throughout the year in all age groups.

Due to the high prevalence of febrile thrombocytopenia in India, a well-organized systematic approach for fever with thrombocytopenia is required, which would aid in the early diagnosis and treatment of patients. This will lower the cost, as well as the morbidity and mortality rates.

MATERIALS AND METHODS

This retrospective observational study was performed in Sri Chamundeshwari medical College Hospital and Research Institute, Channapatna, Ramanagera, in the department of Pediatrics, among medical records of all Children between 2 months to 15 years of age who were admitted with fever and thrombocytopenia were collected for study purpose. 600 patients between age 2 months to 15 years of age admitted in paediatric ICU and respective paediatric wards were included in the study as per inclusion and exclusion criteria mentioned below.

Inclusion Criteria

All the patient between the age group 2 months to 15 years of age presenting with fever

(temperature >99.4 and thrombocytopenia (platelet count <1,500,00).

Exclusion Criteria

- 1) Patient presenting with thrombocytopenia without fever
- 2) Diagnosed case of immuno-thrombocytopenic purpura
- 3) Patient of thrombocytopenia already diagnosed with other haematological disorder and malignancy
- 4) Patient on chemotherapy or any other immune-suppressive agents
- 5) Diagnosed case of platelet disorder and dysfunction

Data Collection

Clinical picture and investigation were recorded as per the performa. Date of onset of symptoms (fever, rash bleeding, joint swelling etc.), number of days for which symptoms continued, any history of blood disorder and any previous history of blood transfusion was asked. Details of specific diagnosis such as enteric fever, septicaemia and dengue were noted along with the treatment given. Entire clinical course till final outcome was studied and relevant details were noted.

Statistical analysis

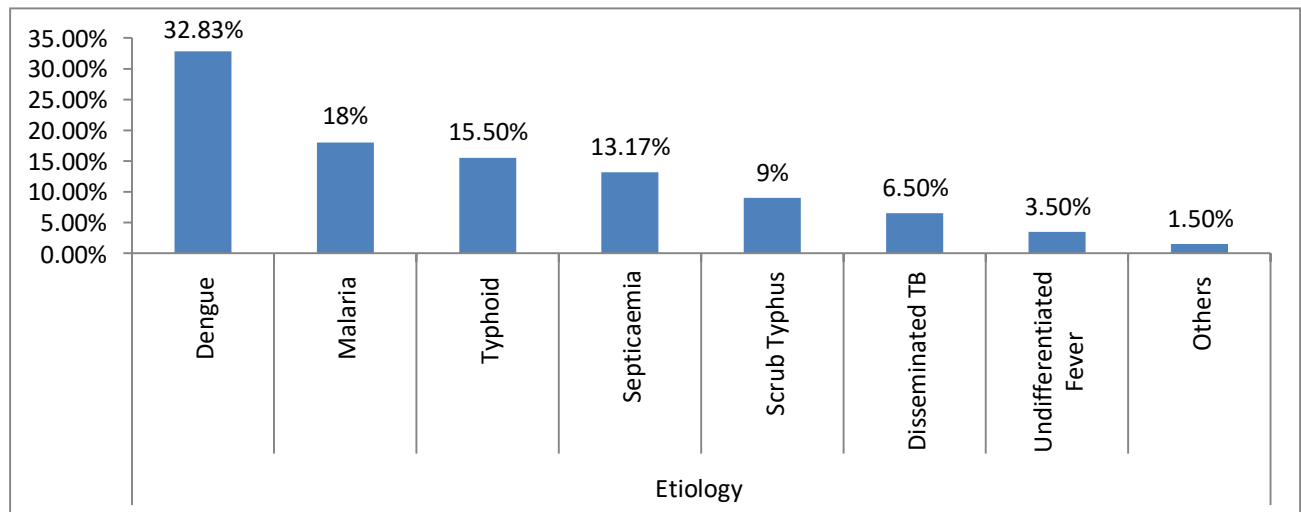
The data collected was entered in SPSS (statistical package social sciences) VERSION 20 and Microsoft excel sheet. Continuous numerical data was summarized using mean and standard deviation. T-Test and ANOVA test were used to find the significant difference of continuous variables as applicable. The P value<0.05 was considered significant.

RESULTS

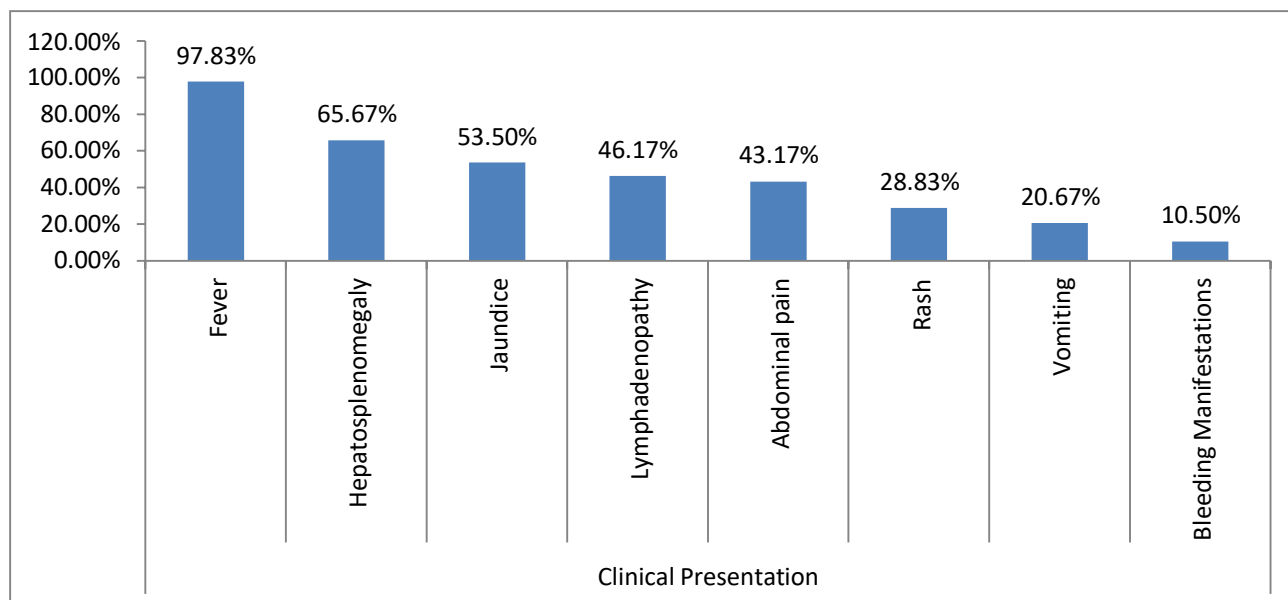
Maximum subjects were from the age group of >10 years followed by 5-10 years. The mean age among the study subjects was 7.34±3.71 years. Out of 600 subjects, 321 (53.50%) were females and 279 (46.50%) were males. 43.17% of the subjects live in urban area while 56.83% in rural area. The commonest cause of febrile thrombocytopenia was Dengue (32.83%) followed by malaria (18%), typhoid fever (15.5%) and septicaemia fever (13.17%) as shown in graph 1.

The most common clinical presentation was fever (97.83%) followed by hepatosplenomegaly (65.67%), Jaundice (53.50%), Lymphadenopathy (46.17%), abdominal pain (43/17%), Rash (28.83%), vomiting (20.67%) and bleeding tendency (10.50%) (graph 2).

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Graph 1: Distribution of study subjects according to etiology



Graph 2: Distribution of study subjects according to clinical presentation

Bleeding manifestation was found in 123 (20.5%) subjects. Petechiae was the most common type of bleeding manifestation (41.46%) followed by Epistaxis (19.51%), Malena (13.82%), Hematuria (13.01%), Hematemesis (8.94%) and Gum bleed (3.25%). 5.17%, 5.83%, 22.83%, 66.17% and 14% of the subjects had platelet count of $\leq 10,000/\mu\text{L}$, 11,000 – 20,000/ μL , 21,000 – 50,000/ μL , 50,000-1,00,000/ μL and 1,00,000/ μL -1,50,000/ μL respectively. In our study bleeding

manifestation was reported in 123(20.5 percent) subjects, 74.19% of the subjects with platelet count $\leq 10000/\mu\text{L}$ were having bleeding manifestation and only 2.38% of the children had platelet count 1,00,000/ μL -1,50,000/ μL were having bleeding manifestation. There was significant association between bleeding manifestations and platelet count and it was statistically significant as per Chi-Square test (Table 1).

Table 1: Association of bleeding manifestations and platelet count

Platelet Count	N	Bleeding Manifestations		p value
		N	%	
$\leq 10,000/\mu\text{L}$	31	23	74.19	<0.01*
11,000 – 20,000/ μL	35	19	54.29	
21,000 – 50,000/ μL	137	48	35.04	
50,000-1,00,000/ μL	313	31	9.90	
1,00,000/ μL -1,50,000/ μL	84	2	2.38	
Total	600	123	20.5	

*: statistically significant

Bleeding manifestations were recorded maximum among subjects suffering from dengue (47.20%) while it was found least in

subjects with Disseminated TB followed by typhoid. Bleeding manifestations were significantly more in dengue patients (table 2).



Table 2: Association of bleeding manifestations and etiology

Etiology	N	Bleeding Manifestations		P value
		N	%	
Dengue	197	93	47.20	0.002*
Malaria	108	8	7.41	
Typhoid	93	4	4.30	
Septicemia	79	5	6.33	
Scrub Typhus	54	4	7.41	
Disseminated TB	39	0	0.00	
Undifferentiated Fever	21	8	38.09	
Others	9	1	11.11	
Total	600	123	20.5	

*: statistically significant

The low platelet count were significantly seen more in dengue patients as compared to other etiology.74.19% of the children with dengue had platelet count

≤10,000/μL. 12.34% of the children with septicaemia had platelet count >50,000/ while 6.45% had platelet count ≤10000/μL. Dengue has highest mortality (table 3).

Table 3: Association of etiology and platelet count

Etiology	N	≤10,000		11-20,000		21-50,000		>50,000		1,00,000/μL-1,50,000/μL		p value
		N	%	N	%	N	%	N	%	N	%	
		Dengue	197	23	74.19	17	48.57	36	26.28	121	38.66	
Malaria	108	5	16.13	11	31.43	24	17.52	52	16.61	16	19.05	
Typhoid	93	1	3.23	3	8.57	22	16.06	53	16.93	14	16.67	
Septicemia	79	2	6.45	2	5.71	26	18.98	36	11.50	13	15.48	
Scrub Typhus	54	0	0.00	0	0.00	12	8.76	24	7.67	18	21.43	
Disseminated TB	39	0	0.00	1	2.86	8	5.84	16	5.11	14	16.67	
Undifferentiated Fever	21	0	0.00	1	2.86	6	4.38	8	2.56	6	7.14	
Others	9	0	0.00	0	0.00	3	2.19	3	0.96	3	3.57	
Total	600	31	5.17	35	5.83	137	22.83	313	52.17	84	14	

*: statistically significant

Among 600 patients recorded 46 patients died. The most number of mortality cases were observed in patients with dengue, malaria and septicemia as show in table 4.

Platelet transfusion was needed in 67 subjects, out of which 48 (71.64%) required RDP (Random Donor Platelet) and 19 (28.36%) needed SDP (Single Donor Platelet).

Table 4: Association of etiology and mortality in study subjects

Etiology	Died		Survived		p value
	N	%	N	%	
Dengue	16	34.78	181	32.67	0.001*
Malaria	7	15.22	101	18.23	
Typhoid	0	0.00	93	16.79	
Septicaemia	21	45.65	58	10.47	



Scrub Typhus	1	2.17	53	9.57	
Disseminated TB	1	2.17	38	6.86	
Undifferentiated Fever	0	0.00	21	3.79	
Others	0	0.00	9	1.62	
Total	46	7.67	554	92.33	

*: statistically significant

DISCUSSION

In our study most of the cases were above 5 year, suggesting greater exterior activities and, as a result, a higher risk of mosquito vector exposure when compared to pre-schoolers. The mean age among the study subjects was 7.34±3.71 years. Sujatha Ramabhatta et al¹⁰ in their study revealed similar age distribution too. Similarly Agarwal P et al¹¹ reported that 22% belong to 11-14 year & 19.5 % were from 6-9 years.

Out of 600 subjects, 321 (53.50%) were females and 279 (46.50%) were males. There was slightly more females as compared to males. Different authors have reported different gender predominance in their studies Male predominancy was also revealed by Saba Ahmed¹², and Shah GS¹³. According to Agarwal P et al¹¹ reported 58.5% male & 41.5 % female children. This might be due to difference in study area.

Fever was the most prevalent clinical manifestation (97.83%), followed by hepatosplenomegaly (65.67%), jaundice (53.50%), lymphadenopathy (46.17%), abdominal discomfort (43/17%), rash (28.83%), vomiting (20.67%), and bleeding propensity (20.67%). (10.50 percent). Fever (91 percent) was the most prevalent clinical manifestation in Agarwal P et al¹¹ research, followed by Organomegaly (72.5 percent) and Jaundice (66 percent).

Bleeding manifestation was found in 123 (20.5%) subjects. The site that causes maximum bleeding most was Petechiae (41.46%) after that Epistaxis (19.51%), Melena (13.82%), Hematuria (13.01%), Hematemesis (8.94%) and Gum bleed (3.25%). According to B D Nakhale¹⁴, bleeding manifestations were observed in 33 (27.04 percent) of the patients, with petechiae (13.39 percent) being the most

common. Nair PS et al¹⁵ found that the bleeding manifestation was 41.3 percent with petechiae/purpura (9.2%) being the most common bleeding symptom. In their study, Agarwal P et al¹¹ discovered that 19% of the children experienced bleeding symptoms, with petechiae being the most common site of bleeding manifestations (42.1 percent).

The platelet counts in 5.17%, 5.83%, 22.83%, 66.17% and 14% of the subjects were ≤10,000/μL, 11,000–20,000/μL, 21,000–50,000/μL, 50,000-1,00,000/μL and 1,00,000/μL-1,50,000/μL respectively in our study. Sujatha Ramabhatta et al¹⁰ in their study reported approximately similar distribution of platelet count i.e. 37% of the children had platelet count <50,000. Kumar P et al¹⁶ discovered moderate thrombocytopenia among 50% trial participants. Agarwal P et al¹¹ observed that 135 (67.5%) of the children had platelet counts more than 50,000/mm³ in their research. Children with platelet counts of 21,000-50,000/L, 14(7%) children with platelet counts of 11,000-20,000/L, and 12(6%) children with platelet counts of 10,000/L were followed by children with platelet counts of 21,000-50,000/L, 14(7%) children with platelet counts of 11,000-20,000/L, and 12(6%) children with platelet counts of 10,000/L.

The platelet count was 10,000/L in 74.19 percent of children with dengue fever and bleeding symptoms. Platelet counts of >50,000/L were found in 12.34 percent of children with septicemia, whereas platelet counts of >10000/L were found in 6.45 percent. 16.13 percent of the children with malaria had a platelet count of 100,000/L. No one with Scrub typhus had a platelet count between 11,000 and 20,000/L. There was significant relationship between aetiology and platelet count. Similar significant relationship between Platelet Count

and Etiology was found by Agarwal P et al¹¹ in their study.

The significant results showing 123 subjects with bleeding manifestations, 74.19% of the children had platelet count $\leq 10000/\mu\text{L}$ and only 2.38% of the children had platelet count $1,00,000/\mu\text{L}$ - $1,50,000/\mu\text{L}$ ($p < 0.05$). Agarwal P et al¹¹ in their study reported that 23.7 % have bleeding with platelet count $\leq 10000/\mu\text{L}$. However they didn't reveal any significant association.

Mortality was reported among 7.67% of the subjects. Mortality was reported in 45.65%, 34.78% and 15.22% of the subjects with septicaemia, dengue and malaria respectively. When mortality was compared according to etiology using chi square test, it was found to be statistically significant as $p < 0.05$. Muhammed Ayub et al¹⁷ discovered that marrow depression induces thrombocytopenia in the acute stage of Dengue infection, as well as in other viral etiologies. 183 (91.5%) of the children made a complete recovery, while 17 (8.5%) perished. 11 children had septicemia, four children had dengue fever and malaria, and one youngster had scrub.

According to Pankaj K Palange et al¹⁸, Kriti Mohan et al¹⁹, Shah G.S et al¹³ and Nikalje Anandh et al²⁰. There is no correlation between platelet count and mortality; everything is dependent on the severity of the disease and other co-morbid diseases. Agarwal P et al¹¹ in their study found mortality of 8.5% in the children. They too revealed mortality more among children with septicaemia followed by dengue and malaria.

LIMITATION OF THE STUDY

The retrospective nature of the current study can be drawback. Also, because this is a single-center research, it may not represent the entire population. The findings of this study cannot be applied to the entire population.

CONCLUSION

thrombocytopenia is a common problem encountered in clinical practice. Knowledge of common causes of thrombocytopenia and their

clinical manifestations will help in deciphering the cause of thrombocytopenia and formulating diagnostic and therapeutic strategy. Rapid diagnostic tests for malaria and dengue are helpful in ruling out these diseases. It is essential to work up all cases of thrombocytopenia so that curable disease can be segregated and treated. Present study will certainly help in identifying clinical and etiological profile of patients with thrombocytopenia in this part of country thus making prompt diagnosis and treating the cause.

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