

## Clinical profile and laboratory findings of patients with thrombocytopenia in hospital set up: A hospital based prospective study

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### Abstract

**Introduction:** Thrombocytopenia is commonly encountered in our routine clinical practice. Causes being numerous, it poses a challenge in evaluating and treating the patients.

**Objectives:** To determine the causes, clinical profile and outcome of thrombocytopenia in children aged 1 month to 14 years who were admitted in our set up.

**Method:** This was a prospective study done on 200 patients aged 1 month to 14 years with thrombocytopenia admitted to the Institute of Medical Sciences AND SUM Hospital, Bhubaneswar, Odisha, India with various complaints, from 01-08-2017 TO 01-08-2019.

**Results:** Fifty six (28%) children were in the 3-6 year age group. In 116 (58 %) children the thrombocytopenia was in the rainy season. Common causes of thrombocytopenia were dengue (18.5%), sepsis (16.5%) and scrub typhus (16%). Petechiae was the commonest bleeding manifestation (62%) followed by epistaxis (13.7%). Out of 32 cases of scrub typhus 23 (71.8%) had deranged liver function tests. Out of the 8 children that died, one had platelet count  $\leq 10,000/\mu\text{L}$ , one had platelet count 10,000-20,000/ $\mu\text{L}$  while 3 each had platelet counts in the range of 22,000 – 50,000/ $\mu\text{L}$  and  $>50,000/\mu\text{L}$  respectively

**Conclusions:** There was male predominance. The commonest age group was 3-6 years. Thrombocytopenia was more common during the rainy season. Common causes were dengue, septicaemia and scrub typhus. Common clinical

presentations were fever, organomegaly, generalised myalgia, lymphadenopathy and headache. Petechiae/Purpura was the most common bleeding manifestation. Mortality rate was 4%.

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(Key words: Thrombocytopenia, septicaemia, dengue fever, malaria, bleeding manifestations)

### Introduction

Thrombocytopenia is a common presentation of many febrile and a few non-febrile illnesses in children<sup>1</sup>. Thrombocytopenia denotes a platelet count lower than 150,000/cu mm whilst severe thrombocytopenia denotes a platelet count lower than 50,000/cu mm. Pseudo-thrombocytopenia can occur due to use of excessive ethylene diamine tetra-acetic acid (EDTA) while sampling<sup>2</sup>. Basic mechanisms of thrombocytopenia are impaired platelet production, consumption and sequestration of platelets and a combination of the above two factors<sup>2</sup>. Multiple mechanisms are involved in immune thrombocytopenia (ITP) and drug-induced thrombocytopenia<sup>3</sup>. Patients with acute febrile illness like dengue and malaria are often associated with thrombocytopenia<sup>4-8</sup>.

### Objectives

- To determine the causes and clinical manifestations of thrombocytopenia in children aged 1 month to 14 years who were admitted in our set up.
- To determine the incidence of various types of thrombocytopenia (i.e. febrile, immune, non-immune)


### Method

A hospital based observational study was conducted from 01-08-2017 to 01-08-2019 in the Department of Paediatrics, Institute of Medical Sciences (IMS) and SUM hospital Bhubaneswar, Odisha, India. Children in the age group of 1 month to 14 years whose haemogram revealed a total platelet count  $<150,000$  and who were admitted to the ward or intensive care unit were enrolled.

**Sample size:** 200 patients considering a confidence level of 98% and confidence interval of 4 the number of patients in our study to achieve

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statistical significance is 196. This was calculated by Survey System

(<http://www.surveysystem.com/sscalc.htm#one>).

The Survey System ignores the population size when it is "large" or unknown<sup>9</sup>. Hence a sample size of 200 was considered adequate for our study.

**Inclusion criteria:** Children aged 1 month to 14 years of age admitted in our hospital with a total platelet count less than 150,000/mm<sup>3</sup>.

**Clinical data:** Presenting symptoms were recorded as per Proforma. Date of onset of symptoms, duration of symptoms, history of drug intake, recent vaccination, family history of blood disorder, previous history of blood transfusion etc. were noted. A detailed examination of the child was done with special attention to the presence of any rash, mucosal bleed, hepatosplenomegaly, lymphadenopathy, sternal tenderness etc.

**Sample collection and laboratory analysis:** Two ml of blood was collected in EDTA vial through a clean venepuncture from children admitted in our hospital. Samples were sent immediately to the clinical laboratory. CBC was done using a 6 part auto-analyser XN-1000 series.

**Ethical issues:** Approval for the study was obtained from the IMS & SUM Hospital ethics committee (ERC No. DMR/IMS-SH/SOA/170065). Patients and/or parents were informed about the study in detail and written consent was taken for inclusion in study. Confidentiality was ensured and participants were informed about right to discontinue participation.

**Statistical analysis:** Quantitative data are presented using mean and standard deviation. Comparison among the study groups was done using unpaired t-test. Qualitative data are presented using frequency and percentages. Association among study groups is assessed using Fisher test, student t-test and Chi-Square test. 'p' value less than 0.05 is taken as significant. MS Excel, SPSS ver. 20 are used for statistical analysis. Graphical representation are done in MS Excel 2010<sup>9</sup>.

## Results

A total of 200 children were included in the study. There were 117 (58.5%) males and 83 (41.5%) females. The mean age of the children was 6.6 ± 4.5 years. The distribution of children according to age is shown in Table 1.

The distribution of children according to season is shown in Table 2. It was observed that the thrombocytopenia was more common (58%) during the rainy season.

**Table 1: Age distribution of children**

Age in years	n (%)
< 1	27 (13.5)
1 to <3	35 (17.5)
3 to <6	56 (28.0)
6 to <9	45 (22.5)
9 to 14	37 (18.5)
Total	200 (100.0)

**Table 2: Distribution according to season**

Season	n (%)
Winter	48 (24)
Summer	36 (18)
Rainy	116 (58)
Total	200 (100)

The distribution of children according to fever is shown in Table 3. It was observed that the thrombocytopenia was more common (83%) in patients with fever.

**Table 3: Distribution according to fever**

Type	n (%)
Febrile	166 (83)
Afebrile	34 (17)
Total	200 (100)

The distribution of children according to aetiology is shown in Table 4. It was observed that dengue was the most common (18.5%) cause of thrombocytopenia closely followed by septicaemia (16.5%) and scrub typhus (16.0%).

**Table 4: Distribution according to aetiology**

Aetiology	n (%)
Dengue	37 (18.5)
Septicaemia	33 (16.5)
Scrub typhus	32 (16.0)
Enteric fever	17 (08.5)
Leukaemia/Lymphoma	15 (07.5)
Immune thrombocytopenic purpura	11 (05.5)
Haemolytic uraemic syndrome	09 (04.5)
Hypersplenism	08 (04.0)
Meningitis	08 (04.0)
Encephalitis	06 (03.0)
SOJIA	06 (03.0)
Viral fever	03 (01.5)
Aplastic anaemia	03 (01.5)
Drug induced	03 (01.5)
Malaria	02 (01.0)
Megaloblastic anaemia	02 (01.0)
Storage disorder	02 (01.0)
Secondary HLH	02 (01.0)
Urinary tract infection	01 (0.5)
Total	200 (100)

SOJIA: Systemic onset Juvenile idiopathic arthritis, HLH: Haemophagocytic lymphohistiocytosis

The distribution of children according to clinical presentation is shown in Table 5. Common clinical presentations were fever (83%), organomegaly (72.5%), generalised myalgia/headache (66%) and lymphadenopathy (52.5%)

**Table 5: Distribution according to presentation**

Clinical presentation	n (%)
Fever	166 (83.0)
Organomegaly	145 (72.5)
Generalised myalgia/headache	132 (66.0)
Lymphadenopathy	105 (52.5)
Oedema	98 (49.0)
Vomiting	90 (45.0)
Abdominal pain	86 (43.0)
Jaundice	80 (40.0)
Bleeding tendency	58 (29.0)
Rash	55 (27.5)
Sore throat	12 (06.0)
Altered sensorium	11 (05.5)
Seizure	09 (04.5)
Joint pain	08 (04.0)

Fifty eight (29%) children had bleeding manifestations. Distribution of children according to the site of bleeding is shown in Table 6. Petechiae/Purpura was the most common bleeding manifestation (62%)

The distribution of children according to platelet count is shown in Table 7.

**Table 6: Distribution of children according to site of bleeding manifestation (n=58)**

Site of bleeding manifestation	n (%)
Petechiae/Purpura	36 (62.0)
Haematuria	10 (17.0)
Epistaxis	08 (13.7)
Gum bleed	08 (13.7)
Melaena	04 (06.0)
Haematemesis	02 (03.0)

**Table 7: Distribution according to platelet count**

Platelet count	n (%)
≤ 10,000/μL	12 (06.0)
10,000 to < 20,000/μL	14 (07.0)
20,000 to 50,000/μL	53 (26.5)
>50,000/μL	121 (60.5)
Total	200 (100)

The association of platelet count with socio-economic status is shown in Table 8. Out of the 200 children 89 (44.5%) belonged to the low socio-economic group.

The association of bleeding manifestations and platelet count is shown in Table 9.

The association of bleeding manifestations and aetiology is shown in Table 10.

The association of aetiology and platelet count is shown in Table 11.

**Table 8: Association of platelet count with socioeconomic status**

Socioeconomic status	<10,000/μL	10,000 to <20,000/μL	20,000 to 50,000/μL	>50,000/μL	Total	%
Low	5	6	18	60	89	44.5
Medium	4	5	11	33	53	36.5
High	3	3	24	28	58	29.0
Total	12	14	53	121	200	100

**Table 9: Association of bleeding manifestations and platelet count**

Platelet count (/μL)	Total	Bleeding manifestations (n=58)	
		n	%
<10,000	12	04	33.3
10,000 to < 20,000	14	04	28.5
20,000 to 50,000	53	07	13.2
>50,000	121	43	35.5
Total	200	58	29.0

**Table 10: Association of bleeding manifestations and aetiology**

Aetiology	Total	Bleeding manifestations (n=58)	
		n	%
Dengue	37	10	27.0
Septicaemia	33	13	39.3
Scrub typhus	32	04	12.5
Enteric fever	17	0	0
Leukaemia/Lymphoma	15	10	66.0
Immune thrombocytopenic purpura	11	11	100.0
Haemolytic uraemic syndrome	09	05	55.5
Hypersplenism	08	0	0
Meningitis	08	0	0
Encephalitis	06	0	0
SOJIA	06	01	16.6
Viral fever	03	0	0
Aplastic anaemia	03	0	0
Drug induced	03	03	100.0
Malaria	02	0	0
Megaloblastic anaemia	02	0	0
Storage disorder	02	0	0
Secondary HLH	02	01	50.0
Urinary tract infection	01	0	0
Total	200	58	29.0

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**Table 11: Association of aetiology and platelet count**

Aetiology	Platelet count ( $\mu\text{L}$ )				Total
	<10,000/ $\mu\text{L}$	10,000 to <20,000/ $\mu\text{L}$	20,000 to 50,000/ $\mu\text{L}$	>50,000/ $\mu\text{L}$	
Dengue	03	02	16	16	37
Septicaemia	05	03	10	15	33
Scrub typhus	0	02	10	20	32
Enteric fever	0	0	01	16	17
Leukaemia/Lymphoma	01	02	03	09	15
Immune thrombocytopenic purpura	02	03	03	03	11
Haemolytic uraemic syndrome	0	0	0	09	09
Hypersplenism	0	01	01	06	08
Meningitis	0	0	0	08	08
Encephalitis	0	0	0	06	06
SOJIA	0	0	05	01	06
Viral fever	0	0	0	03	03
Aplastic anaemia	0	0	0	03	03
Drug induced	0	0	03	0	03
Malaria	0	0	0	02	02
Megaloblastic anaemia	0	0	01	01	02
Storage disorder	0	0	0	02	02
Secondary HLH	01	01	0	0	02
Urinary tract infection	0	0	0	01	01
Total	12	14	53	121	200

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The association of thrombocytopenia with deranged liver function tests (LFTs) is shown in Table 12. All patients with total bilirubin level >2mg/dl and alanine transaminase level more than

2 fold rise of upper limit of normal for age were considered to have deranged liver function tests. In our study out of 32 cases of scrub typhus 23 (71.8%) had deranged LFTs.

**Table 12: Association of thrombocytopenia with deranged liver function tests**

Aetiology	AST/ALT	Serum bilirubin	Total
Dengue	06	02	06 (16.2%)
Septicaemia	14	14	14 (42.4%)
Scrub typhus	23	05	23 (71.8%)
Enteric fever	04	0	04 (23.5%)
Leukaemia/Lymphoma	03	04	04 (26.6%)
Immune thrombocytopenic purpura	0	0	0
Haemolytic uraemic syndrome	02	01	03 (22.3%)
Hypersplenism	01	0	01 (12.5%)
Meningitis	0	0	0
Encephalitis	0	01	01 (16.6%)
SOJIA	04	01	04 (66.6%)
Viral fever	0	0	0
Aplastic anaemia	03	01	03 (100%)
Drug induced	01	0	01 (33.3%)
Malaria	02	02	02 (100%)
Megaloblastic anaemia	0	0	0
Storage disorder	02	01	02 (100%)
Secondary HLH	02	02	02 (100%)
Urinary tract infection	0	0	0

SOJIA: Systemic onset Juvenile idiopathic arthritis, HLH: Haemophagocytic lymphohistiocytosis

The association of thrombocytopenia with deranged renal function tests (RFTs) is shown in Table 13. Patients with serum creatinine >0.5mg/dl, or more than twice the upper limit of normal for

age or 2 fold increase in baseline creatinine value were considered to have deranged renal function tests. In our study all the children suffering from HUS and secondary HLH had deranged RFTs

**Table 13: Association of thrombocytopenia with deranged renal function tests**

Aetiology	Creatinine	Total
Dengue	04	04 (10.8%)
Septicaemia	15	15 (45.5%)
Scrub typhus	02	02 (06.3%)
Enteric fever	0	0
Leukaemia/Lymphoma	03	03 (20.0%)
Immune thrombocytopenic purpura	0	0
Haemolytic uraemic syndrome	09	09 (100%)
Hypersplenism	01	01 (12.5%)
Meningitis	0	0
Encephalitis	01	01 (16.6%)
SOJIA	0	0
Viral fever	0	0
Aplastic anaemia	0	0
Drug induced	01	01 (33.3%)
Malaria	01	01 (50.0%)
Megaloblastic anaemia	0	0
Storage disorder	01	01 (50.0%)
Secondary HLH	02	02 (100%)
Urinary tract infection	01	01 (100%)

SOJIA: Systemic onset Juvenile idiopathic arthritis, HLH: Haemophagocytic lymphohistiocytosis

In our study, 192 (96%) children had complete recovery while 8 (4%) children died. The association between aetiology and mortality is shown in Table 14. It was observed that out of the 8

children that died, 3 had septicaemia, 1 had dengue, 2 had leukaemia and 2 had HLH.

The association between the platelet count and mortality is shown in Table 15.

**Table 14: Association between aetiology and mortality**

Aetiology	Mortality		Total
	Survived	Died	
Dengue	36	01	37
Septicaemia	30	03	33
Scrub typhus	32	0	32
Enteric fever	17	0	17
Leukaemia/Lymphoma	13	02	15
Immune thrombocytopenic purpura	11	0	11
Haemolytic uraemic syndrome	09	0	09
Hypersplenism	08	0	08
Meningitis	08	0	08
Encephalitis	06	0	06
SOJIA	06	0	06
Viral fever	03	0	03
Aplastic anaemia	03	0	03
Drug induced	03	0	03
Malaria	02	0	02
Megaloblastic anaemia	02	0	02
Storage disorder	02	0	02
Secondary HLH	0	02	02
Urinary tract infection	01	0	01
Total	192	08	200

SOJIA: Systemic onset Juvenile idiopathic arthritis, HLH: Haemophagocytic lymphohistiocytosis

**Table 15: Association between platelet count and mortality**

Platelet count	Total	Mortality (n=8)	
		n	%
<10,000	12	01	8.3
10,000 to < 20,000	14	01	7.1
20,000 to 50,000	53	03	5.6
>50,000	121	03	2.4
Total	200	08	4.0

## Discussion

Thrombocytopenia is defined as a platelet count less than 150,000/cu mm<sup>10</sup>. Xu Y, *et al*<sup>11</sup> observed that the commonest age group of children having thrombocytopenia (18.8 %) was 1 to 3 years but in our study the commonest age group of children having thrombocytopenia (28%) was 3 to 6 years. This difference in age groups may be due to more children in the 3-6 year age group being exposed to infections in our setup. Ahmed S, *et al*<sup>12</sup> and Shah GS. *et al*<sup>13</sup> observed male predominance. This was similar to our study where 58.5% were males. In the present study 58% cases were reported during the rainy season whereas Kumar P, *et al*<sup>14</sup> reported the majority of cases during the summer season. This may be because scrub typhus, a common aetiology in our study, is more prevalent during the rainy season due to increasing humidity which favours hatching of the mite egg into chigger which is responsible for disease transmission.

Isaac R, *et al*<sup>15</sup> found that 83% of cases with thrombocytopenia were infectious in aetiology and associated with fever. Patil P, *et al*<sup>16</sup>, Rekha MC, *et al*<sup>17</sup> and Anand N, *et al*<sup>18</sup> found that dengue fever

and enteric fever were the common aetiologies. Raikar SR, *et al*<sup>19</sup> and Bhalara SK, *et al*<sup>20</sup> found that dengue fever was the commonest aetiology. Suresh P, *et al*<sup>21</sup>, Kumar P, *et al*<sup>14</sup> and Gandhi AA, *et al*<sup>22</sup> found dengue and malaria to be common aetiologies. In the present study 18.5% were due to dengue, 16% to scrub typhus and 8.5% to enteric fever, malaria contributing to only 1% of cases. The low contribution of malaria in our study may be due to the Durgama Anchalare Malaria Nirakaram (DAMAN) programme in our state.

Shah GS. *et al*<sup>13</sup> found hepatomegaly in 75%, splenomegaly in 25% and bleeding tendency in 50% of children with thrombocytopenia. Yaramis A, *et al*<sup>23</sup> found hepatomegaly in 40%, splenomegaly in 20% and altered sensorium in 6% of thrombocytopenic children. Ahmed S, *et al*<sup>12</sup> found pallor in 67%, hepatomegaly in 37% and splenomegaly in 6% of children with thrombocytopenia whilst Sajid A, *et al*<sup>24</sup> found splenomegaly in 94%, pallor in 65% and hepatomegaly in 64% of children with thrombocytopenia. Kumar P, *et al*<sup>14</sup> and Ahmed S, *et al*<sup>12</sup> found that gastro-intestinal (GI) symptoms

were the commonest followed by headache and bleeding. Yaramis A, *et al*<sup>23</sup>, Sajid A, *et al*<sup>24</sup> and Chitu CH *et al*<sup>25</sup> also found GI symptoms in more than two third cases. Shah GS. *et al*<sup>13</sup> and Anand N, *et al*<sup>18</sup> found headache was more common than GI symptoms in children with thrombocytopenia. In the present study, on admission, 83% children were febrile, 72.5% had organomegaly (18% splenomegaly, 52% hepatomegaly and 30% hepatosplenomegaly), 52.5% had lymphadenopathy, 45% had vomiting, and 43% had abdominal pain.

In the present study 58 (29%) children had bleeding manifestations. Petechiae were found in 62%, gum bleeding in 13.7% and haematemesis in 3%. Similar findings were noted by Nair PS, *et al*<sup>26</sup> and Saini KC, *et al*<sup>27</sup>. Ayub M, *et al*<sup>28</sup> found severe thrombocytopenia (<10,000) in 60% children, moderate thrombocytopenia (10,000-50,000) in 20% and mild thrombocytopenia (>50,000) in 20%. Bhalara SK, *et al*<sup>20</sup> found severe thrombocytopenia in 50%, moderate thrombocytopenia in 29% and mild thrombocytopenia in 21% children. Palange PB, *et al*<sup>29</sup> found severe thrombocytopenia in 60%, moderate thrombocytopenia in 27% and mild thrombocytopenia in 13%. Mohan K, *et al*<sup>30</sup> found mild thrombocytopenia in 48%, moderate thrombocytopenia in 35% and severe thrombocytopenia in 17% of children. Shah GS. *et al*<sup>13</sup> found mild thrombocytopenia in 54%, moderate thrombocytopenia in 40% and severe thrombocytopenia in 16% of children. Sajid A, *et al*<sup>24</sup> found moderate thrombocytopenia in 68%, mild thrombocytopenia in 21% and severe thrombocytopenia in 11%. In the present study 121 (60.5%) children had platelet count of >50,000/ $\mu$ L whilst 12 (6%) children had platelet count of  $\leq$ 10,000/ $\mu$ L.

Studies by Bhalara SK, *et al*<sup>20</sup> and Patil P, *et al*<sup>16</sup> showed that bleeding manifestations were more common with platelet counts less than 50,000 cells/cu mm. In contrast, studies by Palange PB, *et al*<sup>29</sup>, Mohan K, *et al*<sup>30</sup>, Shah GS. *et al*<sup>13</sup>, Anand N, *et al*<sup>18</sup> and Raikar SR, *et al*<sup>19</sup> revealed that there was no relation between platelet count and bleeding manifestations and according to them it only depends upon the severity of the disease. In our study bleeding manifestations were seen in 35.5% children having total platelet count more than 50,000, particularly those suffering from infectious disease. Bleeding in these children (particularly in severe sepsis) was not directly associated with the degree of thrombocytopenia but with concomitant involvement of other organ leading to multi-organ dysfunction. Out of the 8 children that died, one had platelet count  $\leq$ 10,000/ $\mu$ L, one had platelet count 10,000-20,000/ $\mu$ L while 3 each had platelet

counts in the range of 22,000 – 50,000/ $\mu$ L and >50,000/ $\mu$ L respectively

In this study 89 (44.5%) belonged to low socioeconomic status group. There were no other studies relating platelet counts to socioeconomic status. In our study, out of 32 cases of scrub typhus 23 (71.8%) had deranged LFT. Similarly, 42.4% and 16.2% of patients with sepsis and dengue had deranged LFT. Similar findings were seen in a study by Gondhali MP, *et al*.<sup>7</sup> Of the 200 children included in the study 8 (4%) died. Of the eight 3 children had septicaemia, one child had dengue, 2 had leukaemia and 2 had haemophagocytic lymphohistiocytosis (HLH). Palange PB, *et al*<sup>29</sup>, Mohan K, *et al*<sup>30</sup>, Shah GS. *et al*<sup>13</sup>, Anand N, *et al*<sup>18</sup> and Raikar SR, *et al*<sup>19</sup> revealed that there was no relationship between platelet count and mortality and according to them the mortality depends only on the severity of the disease and the presence of other co-morbid conditions.

### Conclusions

There was male predominance. The commonest age group was 3-6 years. Thrombocytopenia was more common during the rainy season. Common causes were dengue, septicaemia and scrub typhus. Common clinical presentations were fever, organomegaly, generalised myalgia/headache and lymphadenopathy. Petechiae/Purpura was the most common bleeding manifestation. The mortality rate was 4%.

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