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Original Research Article

PREVALENCE, ETIOLOGICAL PROFILE AND CLINICAL OUTCOMES OF THROMBOCYTOPENIA IN HOSPITALIZED CHILDREN: A RETROSPECTIVE STUDY

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ABSTRACT

Background: Thrombocytopenia is commonly observed in hospitalized children and may occur due to infections, hematological disorders and other systemic illnesses. This study was conducted to determine its prevalence, etiology and association with clinical outcomes.

Materials and Methods: This retrospective observational study included 1176 children aged 1 month to 18 years admitted to a tertiary care teaching hospital from January 2018 to December 2019. Thrombocytopenia was defined as platelet count <150,000/µL and classified as mild, moderate and severe. Clinical characteristics, laboratory parameters, ICU admission, transfusion requirement, hospital stay and final outcome were analyzed.

Results: Thrombocytopenia was present in 175 (14.9%) children. Mild, moderate and severe thrombocytopenia were observed in 47.4%, 34.9% and 17.7%, respectively. Prevalence was significantly higher in children aged >6 years than in those aged ≤6 years (20.6% vs. 8.8%, p<0.001). Infections were the commonest etiology (73.7%), with dengue being the leading cause (34.9%). Severe anemia, leukopenia, elevated AST, ALT, bilirubin, BUN, prolonged PT and elevated INR were significantly more frequent in thrombocytopenic children. Bleeding (5.7% vs. 0.4%), ICU admission (22.3% vs. 11.1%) and transfusion requirement (21.1% vs. 6.7%) were significantly higher in thrombocytopenic children. Increasing severity was significantly associated with bleeding, ICU admission and transfusion requirement.

Conclusion: Thrombocytopenia affected nearly one in seven hospitalized children and was mainly associated with infections. Severe thrombocytopenia was associated with greater clinical severity and need for intensive monitoring.

Keywords: thrombocytopenia, children, dengue, infections, platelet count, ICU admission, bleeding, transfusion.

INTRODUCTION

Thrombocytopenia is a common hematological abnormality in hospitalized children and is defined as a platelet count below 150,000/µL. It may occur due to reduced platelet production, increased destruction, consumption or splenic sequestration. The severity varies from mild reduction in platelet count to severe thrombocytopenia associated with bleeding complications. Although thrombocytopenia may be transient, it can also indicate an underlying serious illness requiring immediate evaluation.[1,2]

The etiology of thrombocytopenia in children is diverse and includes infections, hematological disorders, malignancies, immune-mediated conditions and drug-induced causes. Infections are among the common causes in developing countries, particularly dengue, malaria, enteric fever and sepsis. Studies from India have reported infections as the predominant cause of thrombocytopenia in

hospitalized children. However, the etiological pattern varies according to geographical location, age and underlying disease.[3,4]

The clinical significance of thrombocytopenia depends on the underlying cause, severity of platelet reduction and associated complications. Children with thrombocytopenia may present with petechiae, purpura, mucosal bleeding or gastrointestinal hemorrhage, while many remain asymptomatic. Previous studies have reported an association between low platelet counts and bleeding manifestations, transfusion requirement and adverse clinical outcomes.[5,6] Thrombocytopenia has also been associated with increased severity of illness, prolonged hospitalization and mortality among critically ill children. Serial platelet count monitoring may therefore provide useful information regarding disease progression and clinical outcome.[7,8]

Most available studies have focused on children presenting with febrile thrombocytopenia or those admitted to intensive care units. Information regarding the overall prevalence and etiological distribution of thrombocytopenia among all hospitalized children remains important for clinical assessment and management. The present retrospective study was undertaken to determine the prevalence and etiology of thrombocytopenia among children aged 1 month to 18 years admitted to a tertiary care teaching hospital. The study also evaluated its association with clinical characteristics, duration of hospital stay, ICU requirement, transfusion requirement and mortality.

MATERIALS AND METHODS

This retrospective observational study was conducted in the Department of Pediatrics, Era's Lucknow Medical College & Hospital, and included all children aged 1 month to 18 years admitted between January 2018 and December 2019. Medical records of 1176 eligible children were reviewed after institutional permission, and waiver of informed consent was obtained from the Institutional Ethics Committee. Data regarding age, gender, diagnosis, bleeding manifestations, ICU admission, ventilatory support, transfusion requirement, duration of hospital stay, final outcome and relevant laboratory parameters were recorded in a predesigned proforma. Thrombocytopenia was defined as a platelet count <150,000/µL and classified as mild (100,000–149,999/µL), moderate (50,000–99,999/µL) and severe (<50,000/µL). Nutritional status was assessed using weight-for-height in children aged ≤5 years and BMI-for-age in older children. Data were analyzed using SPSS version 21.0. Categorical variables were expressed as number and percentage, and continuous variables as mean ± standard deviation. Chi-square test and Student's t-test were used as appropriate, and a p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Prevalence of thrombocytopenia according to age and gender

Characteristics	Total (n)	Thrombocytopenia n (%)	p-value
Overall	1176	175 (14.9)	—
Age ≤6 years	568	50 (8.8)	<0.001
Age >6 years	608	125 (20.6)	<0.001
Male	693	107 (15.4)	0.519
Female	483	68 (14.1)	0.519

Among 1176 hospitalized children, 175 (14.9%) had thrombocytopenia. Of these, 83 (47.4%) had mild, 61 (34.9%) had moderate and 31 (17.7%) had severe thrombocytopenia. The prevalence was significantly higher in children aged >6 years compared to those aged ≤6 years (20.6% vs. 8.8%, p<0.001). Thrombocytopenia was observed in 107 (15.4%) males and 68 (14.1%) females, with no significant difference between genders (p=0.519).

Table 2: Etiological distribution of thrombocytopenia

Etiology	n	%
Infectious causes	129	73.7
Dengue	61	34.9
Malaria	16	9.1
Enteric fever	14	8.0
Acute viral hepatitis	9	5.1
Lower respiratory tract infection	8	4.6
Acute encephalitis syndrome	7	4.0
Tuberculosis	6	3.4
Scrub typhus	5	2.9
Other infections	3	1.7
Hematological causes	41	23.4
Megaloblastic anemia	21	12.0
Iron deficiency anemia	9	5.1
Immune thrombocytopenia	8	4.6
Aplastic anemia	3	1.7

Malignancies	3	1.7
Drug-induced thrombocytopenia	2	1.1
Total	175	100.0

Infectious diseases were the most common cause of thrombocytopenia, accounting for 129 (73.7%) cases, followed by hematological disorders in 41 (23.4%) cases. Dengue was the predominant infectious cause, observed in 61 (34.9%) children, followed by malaria in 16 (9.1%) and enteric fever in 14 (8.0%). Among hematological disorders, megaloblastic anemia was reported in 21 (12.0%) children, iron deficiency anemia in 9 (5.1%) and immune thrombocytopenia in 8 (4.6%). Malignancies were observed in 3 (1.7%) children, while 2 (1.1%) had drug-induced thrombocytopenia.

Table 3: Comparison of laboratory parameters between children with and without thrombocytopenia

Laboratory parameter	Thrombocytopenia (n=175) n (%)	No thrombocytopenia (n=1001) n (%)	p-value
Severe anemia (Hb <8 g/dL)	52 (29.7)	137 (13.7)	<0.001
Leukopenia	43 (24.6)	38 (3.8)	<0.001
Lymphocytosis	85 (48.6)	351 (35.1)	0.001
Elevated AST	74 (42.3)	227 (22.7)	<0.001
Elevated ALT	68 (38.9)	146 (14.6)	<0.001
Elevated bilirubin	21 (12.0)	57 (5.7)	0.002
Elevated BUN	26 (14.9)	93 (9.3)	0.024
Prolonged PT	17 (9.7)	28 (2.8)	<0.001
Elevated INR	24 (13.7)	48 (4.8)	<0.001

Severe anemia was significantly more common in children with thrombocytopenia compared to those without thrombocytopenia (29.7% vs. 13.7%, p<0.001). Leukopenia was observed in 24.6% and 3.8% of children, respectively (p<0.001). Lymphocytosis was also more frequent in thrombocytopenic children (48.6% vs. 35.1%, p=0.001). Elevated AST (42.3% vs. 22.7%) and ALT (38.9% vs. 14.6%) were significantly associated with thrombocytopenia (both p<0.001). Elevated bilirubin (12.0% vs. 5.7%, p=0.002), BUN (14.9% vs. 9.3%, p=0.024), prolonged PT (9.7% vs. 2.8%, p<0.001) and elevated INR (13.7% vs. 4.8%, p<0.001) were also more common in thrombocytopenic children.

Table 4: Association of thrombocytopenia with clinical characteristics and hospital outcomes

Clinical characteristic	Thrombocytopenia (n=175) n (%)	No thrombocytopenia (n=1001) n (%)	p-value
Bleeding manifestations	10 (5.7)	4 (0.4)	<0.001
ICU admission	39 (22.3)	111 (11.1)	<0.001
Transfusion requirement	37 (21.1)	67 (6.7)	<0.001
Ventilatory support	5 (2.9)	18 (1.8)	0.351
Hospital stay >7 days	63 (36.0)	417 (41.7)	0.160
Discharged	131 (74.9)	808 (80.7)	0.288*
Referred	6 (3.4)	21 (2.1)	0.288*
Left against medical advice	38 (21.7)	171 (17.1)	0.288*
Mortality	0 (0.0)	1 (0.1)	0.288*

Bleeding manifestations were observed in 10 (5.7%) thrombocytopenic children compared to 4 (0.4%) children without thrombocytopenia (p<0.001). ICU admission was significantly higher in thrombocytopenic children (22.3% vs. 11.1%, p<0.001). Similarly, transfusion was required in 21.1% of thrombocytopenic children compared to 6.7% of non-thrombocytopenic children (p<0.001). No significant difference was observed in ventilatory support (2.9% vs. 1.8%, p=0.351) or hospital stay exceeding seven days (36.0% vs. 41.7%, p=0.160). The discharge rate was 74.9% in thrombocytopenic children and 80.7% in non-thrombocytopenic children. Final outcomes were comparable between the groups (p=0.288). Only one death was recorded in the study, which occurred in a child without thrombocytopenia.

Table 5: Association of severity of thrombocytopenia with clinical outcomes

Clinical characteristic	Mild (n=83) n (%)	Moderate (n=61) n (%)	Severe (n=31) n (%)	p-value
Bleeding manifestations	0 (0.0)	5 (8.2)	5 (16.1)	0.003
ICU admission	12 (14.5)	13 (21.3)	14 (45.2)	0.002
Transfusion requirement	9 (10.8)	11 (18.0)	17 (54.8)	<0.001
Ventilatory support	1 (1.2)	2 (3.3)	2 (6.5)	0.317
Hospital stay >7 days	32 (38.6)	21 (34.4)	10 (32.3)	0.783

Bleeding manifestations increased significantly with the severity of thrombocytopenia, being observed in 0%, 8.2% and 16.1% of children with mild, moderate and severe thrombocytopenia, respectively (p=0.003). ICU admission was required in 14.5% of mild, 21.3% of moderate and 45.2% of severe cases

(p=0.002). Similarly, transfusion requirement increased from 10.8% in mild to 18.0% in moderate and 54.8% in severe thrombocytopenia (p<0.001). Ventilatory support was required in 1.2%, 3.3% and 6.5% of children, respectively, but the difference was not statistically significant (p=0.317). Hospital stay exceeding seven days was also not significantly associated with the severity of thrombocytopenia (p=0.783).

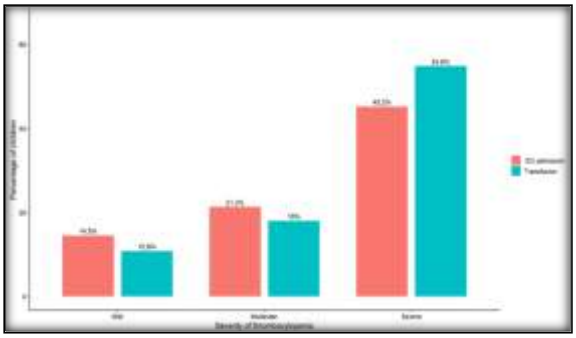

Figure 1: Clinical outcomes according to severity of thrombocytopenia.

DISCUSSION

The present study evaluated thrombocytopenia among 1176 hospitalized children aged 1 month to 18 years. The overall prevalence was 14.9%. Nearly half of the affected children had mild thrombocytopenia, while 17.7% had severe thrombocytopenia. The prevalence was significantly higher in children aged more than 6 years, while no significant difference was observed between males and females. Bhatia et al. also reported a greater burden of thrombocytopenia among older children, with nearly 45% of their cases being above 10 years of age.[3] This may partly reflect the increasing frequency of infections such as dengue and other febrile illnesses in school-going and adolescent children.

Infections were the predominant etiology in the present study and accounted for 73.7% of thrombocytopenic cases. Similar observations have been reported in other Indian studies. Deshpande et al. found infection to be the commonest cause of febrile thrombocytopenia in children, with dengue being the predominant infection.[4] Bhatia et al. reported septicemia as the most common etiology followed by megaloblastic anemia, local infections, hepatitis and scrub typhus.[3] In a multicentre study of tropical fever from Indian intensive care units, dengue was the most common identified infection, followed by scrub typhus and malaria.[9] These findings indicate that the etiological profile of pediatric thrombocytopenia is strongly influenced by the local burden and seasonal pattern of infectious diseases.

Dengue was the single most common cause in our study and accounted for 34.9% of all thrombocytopenic children. This is consistent with the recognized association between dengue infection and a fall in platelet count. Platelet reduction in dengue is multifactorial and may occur due to transient marrow suppression, immune-mediated destruction and peripheral consumption. Pathak et al. observed a significant negative correlation between dengue viral load and platelet count in pediatric patients.[12] The predominance of dengue in the present study also explains, at least partly, the relatively high frequency of thrombocytopenia among older children.

Malaria was the second major infectious cause of thrombocytopenia in our study. Thrombocytopenia is well documented in both Plasmodium vivax and P. falciparum infections. Tanwar et al. reported thrombocytopenia in 65.4% of hospitalized children with malaria and found it particularly frequent in P. vivax monoinfection.[10] Kumar et al. similarly observed thrombocytopenia in 22 of 39 children with vivax malaria, although platelet counts improved rapidly following treatment and significant bleeding was uncommon.[11] These observations support thrombocytopenia as a frequent hematological manifestation of childhood malaria, although its severity does not always correspond with clinically significant bleeding.

Other infections in the present study included enteric fever, acute viral hepatitis, lower respiratory tract infection, acute encephalitis syndrome, tuberculosis and scrub typhus. Thrombocytopenia is increasingly recognized as an important laboratory abnormality in pediatric scrub typhus. Ganesh et al. reported that thrombocytopenia along with elevated AST was associated with complications in children with scrub typhus.[13] In a recent Indian study, Murmu et al. reported thrombocytopenia in 40.3% of children with scrub typhus.[14] Although scrub typhus accounted for only a small proportion of cases in our study, its recognition remains important because it is a treatable cause of febrile thrombocytopenia.

Several laboratory abnormalities were significantly associated with thrombocytopenia in the present study. Severe anemia and leukopenia were more frequent among thrombocytopenic children. Elevated AST, ALT, bilirubin and BUN were also significantly more common in this group. Prolonged prothrombin time and elevated INR were observed more frequently in children with thrombocytopenia. These findings suggest that thrombocytopenia frequently occurs as part of a wider systemic illness rather than as an isolated hematological abnormality. Hepatic dysfunction, coagulation abnormalities, infection-related marrow suppression and increased peripheral consumption may contribute to these changes. Similar combinations of thrombocytopenia and elevated hepatic transaminases have been described in children with infectious illnesses including dengue and scrub typhus.[12-14]

Bleeding manifestations were significantly more frequent in thrombocytopenic children compared with children having normal platelet counts. More importantly, bleeding increased with the severity of thrombocytopenia, from no bleeding in mild cases to 8.2% in moderate and 16.1% in severe

thrombocytopenia. Deshpande et al. reported bleeding manifestations in 9.6% of children with febrile thrombocytopenia, with bleeding occurring more often at lower platelet counts.[4] Agrawal et al. also observed a significantly higher frequency of bleeding among thrombocytopenic children admitted to a pediatric intensive care unit.[7] These findings support the clinical importance of platelet severity, although platelet count alone should not be considered the only determinant of bleeding. Underlying disease, coagulation abnormalities and vascular involvement also influence bleeding risk.

The requirement for ICU care was significantly higher among thrombocytopenic children and increased progressively with severity. ICU admission was required in 14.5% of children with mild thrombocytopenia, 21.3% with moderate thrombocytopenia and 45.2% with severe thrombocytopenia. This suggests that severe thrombocytopenia may serve as a simple marker of greater clinical illness. Agrawal et al. reported that thrombocytopenia in PICU patients was associated with sepsis, coagulopathy and greater severity of illness.[7] Krishnan et al. also found thrombocytopenia and a progressive fall in platelet count to be associated with adverse PICU outcomes.[8] More recently, Lu et al. reported early severe thrombocytopenia as an independent risk factor for in-hospital mortality among critically ill children.[16]

Transfusion requirement was also significantly greater in thrombocytopenic children and showed a marked increase with increasing severity. More than half of the children with severe thrombocytopenia required transfusion compared with 10.8% of those with mild thrombocytopenia. This probably reflects both lower platelet counts and greater underlying disease severity. Platelet transfusion practices in critically ill children vary considerably and depend on active bleeding, platelet count, underlying disease and planned procedures. Du Pont-Thibodeau et al. reported thrombocytopenia and active bleeding as major determinants of platelet transfusion in critically ill children.[15] Current pediatric literature also supports a cautious approach to prophylactic platelet transfusion, as transfusion itself is not without risk and clinical context should be considered along with platelet count.[17] Recent large pediatric inpatient data have further demonstrated wide variation in platelet transfusion practices across age groups and clinical conditions.[18]

In contrast to ICU requirement and transfusion, thrombocytopenia was not significantly associated with ventilation requirement or hospital stay beyond seven days. Final outcome also did not differ significantly between children with and without thrombocytopenia. Only one death occurred in the entire cohort and this was in a child without thrombocytopenia. This differs from studies conducted exclusively in critically ill children, where thrombocytopenia has been associated with prolonged stay and increased mortality.[7,8,16] The difference is likely related to the study population. The present study included all hospitalized children rather than only PICU patients, and the very low number of deaths limited assessment of the relationship between thrombocytopenia and mortality.

The present study has some limitations. It was a retrospective single-centre study and depended on the completeness of medical records. Platelet counts were assessed primarily according to predefined severity groups, and serial changes during hospitalization were not evaluated. The etiological pattern may also vary according to geographical area and season. In addition the very low mortality rate limited evaluation of thrombocytopenia as a predictor of death. However, inclusion of all hospitalized children over a two-year period provides useful information regarding the prevalence, etiological spectrum and clinical significance of thrombocytopenia in a tertiary care setting.

Overall, thrombocytopenia was present in approximately one in seven hospitalized children and infections were the predominant cause, particularly dengue. Severe thrombocytopenia was associated with increased bleeding, ICU requirement and transfusion requirement. These findings indicate that platelet count is not only a hematological parameter but may also provide useful information regarding the severity of illness and need for closer clinical monitoring in hospitalized children.

CONCLUSION

Thrombocytopenia was present in 14.9% of hospitalized children and infections were the most common etiology, with dengue being the leading cause. Thrombocytopenia was more frequent in children aged above 6 years and was associated with severe anemia, leukopenia, deranged liver function, bleeding manifestations, ICU admission and transfusion requirement. Increasing severity of thrombocytopenia was significantly associated with higher bleeding, ICU requirement and transfusion requirement. However, duration of hospital stay, ventilatory support and final outcome were not significantly associated with thrombocytopenia. Platelet count may therefore serve as a useful indicator for identifying hospitalized children requiring closer clinical monitoring.

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