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Original Research Article

Clinicohematological Correlation of Thrombocytosis in Children at a Tertiary Care Centre of Barak Valley

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Abstract:

Background: Thrombocytosis is a common finding in the hemograms of children. While primary thrombocytosis is very rare in children, reactive thrombocytosis is frequently observed in children with infections, anemia, and other causes. This study aims to determine the etiology of thrombocytosis and analyze various platelet parameters (MPV, PDW) in children with thrombocytosis.

Methods: It was a prospective observational study carried out in the Department of Pathology, Silchar medical college and hospital, Cachar from June 2021 to May 2022. All children of age group 1 month to 18 years of age attending pediatrics outdoors and/or admitted to indoors, and whose complete blood counts (CBC) were done, were included in the study. The CBC parameters such as hemoglobin, red blood cell indices, and platelet indices like platelet distribution width [PDW], mean platelet volume [MPV] were noted.

Results: Of 370 patients, 99.72% had secondary thrombocytosis, and only one child had primary thrombocytosis (CML). The majority of the children belonged to the age group of 1year to 2 years (51.35%) and male to female ratio was approximately 2:1. Infection with anemia (56.76%) was the most common cause of secondary thrombocytosis followed by infection alone (21.62%) and iron deficiency alone (18.38%) . Respiratory tract infection (40%) was the predominant infectious cause observed. With increasing platelet count, there was a decrease in MPV.

Conclusions: Secondary thrombocytosis is more common in children than primary thrombocytosis. Infections in association with anemia is found to be the common cause associated with reactive thrombocytosis.

Keywords: Thrombocytosis, primary thrombocytosis, secondary thrombocytosis, platelet indices

Introduction

Thrombocytosis is defined as platelet count >4,00,000/mcL in the peripheral blood.[1] It can be classified into primary (essential) and secondary (reactive) forms based on its origin. Primary (essential) thrombocytosis is rare in the pediatric age group, mostly found in the second decade of life. It is a myeloproliferative disorder caused by monoclonal or polyclonal abnormalities of megakaryopoietic progenitors or abnormalities in the biology of Tpo.[2] The risk of thromboembolic complications seems to be higher in the case of primary thrombocytosis.[3]Secondary thrombocytosis is common in children having a variety of clinical conditions, occurring mainly in the first decade of life. It is caused by the stimulation of megakaryopoiesis due to various haematological or non-haematologic disorders. In children, secondary thrombocytosis occurs due to acute bacterial infections, viral infections, tissue damage, hemolysis and autoimmune disease.[4]

Once thrombocytosis is identified and confirmed by peripheral smear, the diagnostic evaluation turns to determine whether the process is reactive or clonal in nature.This study aims to chartthe etiological causes of thrombocytosis, and its correlation with the platelet parameters like mean platelet volume (MPV) and platelet distribution width (PDW).

Material and Methods

This is a prospective observational study that was carried out in the Department of Pathology, Silchar Medical College and Hospital (SMCH), Cachar from June 2021 to May 2022. The patients who were admitted in the Pediatrics department in SMCH, were selected for this study. Furthermore, those patients whose routine blood investigations exhibited signs/symptoms/traces of thrombocytosis (platelet >400000/mcL) were considered for this study. The age of these patients ranged from 1 month to 18 years.

Inclusion Criteria

Children in whom thrombocytosis was identified were included in the study.

Exclusion Criteria

Repeat samples with thrombocytosis were excluded from the study.

Two mL of EDTA blood was collected through a clean venipuncture from children admitted in the Department of Paediatrics, for whom blood investigations were planned and samples were sent immediately to clinical laboratory for testing. The duration from the time of venipuncture to time of using the autoanalyzer was observed to be less than 1 hour. Any history of blood transfusion in the previous two months, or history of receiving drugs that can cause thrombocytosis (steroid and vincristine), or splenectomy in the past was noted. Hemoglobin(Hb), WBC counts, red cell indices, platelet distribution width (PDW), mean platelet volume(MPV) and plateletcrit(PCT) as given by the automated blood cell analyzer (XN-550) were noted in all cases of thrombocytosis along with peripheral smear. Other relevant investigations done to establish the diagnosis were also noted. Severity of thrombocytosis was graded as follows:

- mild (400000/mcL–700000/mcL),
- moderate (700000/mcL–900000/mcL),
- severe (more than 900000/mcL).

Normal values of mean platelet volume (MPV)5, platelet distribution width (PDW) [6], and plateletcrit (PCT) [7] were 7.4 to 10.4 fL, 10 to 17.9%, and 0.17 to 0.34%, respectively. Based on hemoglobin levels (as per WHO classification)[8] cases were classified into mild, moderate and severe anemia in children <5 yrs and 5–18 yrs of age group.

The etiology of thrombocytosis was identified from clinical details and evaluating laboratory parameters. The data was analyzed using the software Statistical Package for the Social Sciences (SPSS v16.0). Mean, standard deviation and P value were calculated and $p< 0.05$ was considered statistically significant.

Results

In the present study of three seventy cases of thrombocytosis, the age ranged from 1 month to 18 years, the youngest was aged 1year and the oldest was aged 18 years. Majority were in the age group of 1 to 2 years (51.35%). The age distribution is shown in (Table 1).

Table 1: Age distribution of patients with thrombocytosis

Age Group in Years	No of Cases	Percentage(%)
1-2	190	51.35
2-5	120	32.43
>5	60	16.22
Total	370	100

Among all the age groups, it was observed that thrombocytosis was more common in male (64.68%) than females (35.14%) with an overall male to female ratio of 2:1. Figure 1 shows gender distribution of the cases in a simplified way.

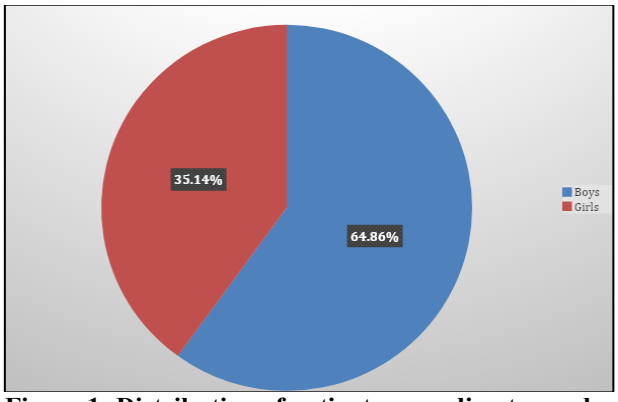

Figure 1: Distribution of patients according to gender

Majority of children in the study group had mild thrombocytosis (89.19%). Moderate thrombocytosis was seen in (8.65%) and severe in (2.16%) of all children. Table 2 shows distribution of cases depending on the severity of thrombocytosis.

Table 2: Table showing distribution of severity of thrombocytosis

Severity of Thrombocytosis	No Of Cases	Percentage
Mild	330	89.19
Moderate	32	8.65
Severe	8	2.16
Total	370	100

Among 370 children, primary thrombocytosis was found in only one case (one CML); the remaining children had secondary thrombocytosis. In secondary thrombocytosis, it was observed that infection with anemia (56.76%) was the most common, followed by 21.62% children with intercurrent infection alone, and anemia (without infection) was the etiological cause in 18.38% patients. Respiratory tract infections were the most common infection than urinary tract, gastrointestinal, hepatobiliary and central nervous system infections. Iron deficiency (18.38%) was most commonly associated with thrombocytosis among nutritional deficiency.

It was observed that thrombocytosis was found in 0.54% children with hemolytic anemia. Within the study population, 1.62% patients were given medication (mainly steroids) that could cause thrombocytosis, in the preceding one week. Table 3 shows the etiology of thrombocytosis in children.

Table 3: Etiology of thrombocytosis

Etiology of Thrombocytosis	No of Cases(N)	Percent
(I) Primary thrombocytosis (n=1)		
CML	1	0.27%
(II) Secondary (reactive) thrombocytosis (n=369)		
Infection and anemia	210	56.76%
Infection Alone	80	21.62%
Iron deficiency alone	68	18.38%
Hematological causes	2	0.54%
Medications	6	1.62%
Idiopathic	3	0.81%

Mean MPV of children with mild thrombocytosis was 7.40fL, moderate thrombocytosis was 7.10 fL, and of severe thrombocytosis was 7.05fL. With increasing platelet count, though there was a decrease in mean platelet volume, there was no significant negative correlation ($p < 0.09$). Mean PDW of children with mild thrombocytosis was 16.43% and those with moderate and severe thrombocytosis were 16.65% and 16.50%, respectively. There was no statistical correlation between severity of thrombocytosis and PDW. Table 4 shows correlation of platelet indices(MPV, PDW) with severity of thrombocytosis.

None of the children were observed to have thromboembolic manifestations during the study period.

Table 4: Correlation of platelet indices (MPV, PDW) with severity of thrombocytosis

Severity of Thrombocytosis	MPV (FL)		PDW (%)	
	Mean	SD	Mean	SD
Mild (n=330)	7.40	0.87	16.43	0.70
Moderate (n=32)	7.10	0.80	16.65	0.65
Severe (n=8)	7.05	0.69	16.50	0.56
P value	0.09		0.22	

Discussion

Thrombocytosis is common in childhood and is rarely a cause of symptoms as it is mainly secondary to other underlying conditions. Primary thrombocytosis is extremely rare in children, the incidence of newly diagnosed primary thrombocytosis in children is about 1 per 10 million, which is 60 times lower than adults.[9]

In our study one case of primary thrombocytosis was diagnosed. Reactive thrombocytosis has an estimated incidence of 6–15% among hospitalised children10 and in our study 99.72% of the children had reactive thrombocytosis. In the study by D. Yadav et all,[11] among 250 cases, 3 had primary thrombocytosis and in another study by M.D. Yohannan et al,[12] among 663 patients, no case of primary thrombocytosis was observed. Reactive thrombocytosis in children shows an age-dependent pattern, with the highest incidence up to 2 years of age. A similar observation was noted in our study where the incidence of reactive thrombocytosis was highest in the 1–2 years age group. After the age of 2 years, the incidence gradually decreases.13 In a study by D. Yadav et al thrombocytosis was found to be more common in infants and children aged less than 2 yrs of age (60%).[11] The increased susceptibility for thrombocytosis during the neonatal period may be due to various physiological phenomena such as a high Tpo gene expression in the bone marrow during the ontogeny of medullary haematopoiesis, high circulating Tpo concentrations in fetuses and neonates than in children and adults, and an increased sensitivity of megakaryocytic progenitor cells to Tpo.[14,15]

Thrombocytosis was observed to be more common among boys (64.86%) than among girls (35.14%) in all age groups. Similar results were observed in two other studies with male preponderance of 64% and 61.1% of cases, respectively.[11,12] Platelet count and function are mediated by sex hormones specifically androgens as suggested by various evidence.[16]

In the present study, mild thrombocytosis was seen in 89.19% cases, and moderate and severe thrombocytosis was seen in 8.65% and 2.16% cases respectively. Similar results were seen in studies by Mantadakis E et al and Matsubara K et al.[1,13] It was observed that with increasing age, degree of thrombocytosis was less severe, with mild cases comprising of 85% among the >10 years age group, and 65.3% among the 1–2 years age group, much in accordance to the literature review.[17]

It was observed that infection with anemia was the most common cause for secondary thrombocytosis (56.76%), intercurrent infections alone was seen in 21.62% children, and anemia alone (without infection) was seenin 18.3% children. Among infections, respiratory tract infections (40%) were most commonly associated with secondary thrombocytosis. A study by Dame et al concluded that the most common cause for reactive thrombocytosis during childhood is (acute or chronic) bacterial or viral infections,[17] among which respiratory tract infection is most common followed by gastrointestinal and urinary tract infection.[18,19].

Corticosteroids can lead to transient thrombocytosis, by releasing stored platelets from the spleen into the blood circulation.[20] Among study population, 6 children were found to be on corticosteroid medication that could cause thrombocytosis.

Among the non-infectious causes of secondary thrombocytosis, iron deficiency is the most common cause among the nutritional deficiency worldwide.[21] The fact that secondary thrombocytosis is more frequent in children up to 2 years of age is partly due to the higher incidence of iron deficiency in this age group. It was noticed that the severity of anemia had linear relationship with the severity of thrombocytosis. According to C. Sandoval, iron deficiency anemia remains the most common non-infectious cause of reactive thrombocytosis.[21]

The platelet indices were compared with the degree of severity of thrombocytosis. With the increase in the degree of thrombocytosis though there was decrease in MPVwas observed but no significant negative correlation was found. In contrast, Subramaniamet al. also compared the platelet indices with degree of thrombocytosis and found a weak significant negative correlation of mean MPV with degree of thrombocytosis.[22] In reactive thrombocytosis platelet counts normalize rapidly with treatment of underlying etiology without causing any thromboembolic manifestations.

However, there were few limitations in the study. The response of thrombocytosis to the treatment of underlying diseases could not be monitored in all cases. The platelet indices in cases of reactive thrombocytosis could not be compared with the indices in primary thrombocytosis (since we had only one case).

Conclusion

In the paediatric population under most circumstances, thrombocytosis is reactive(secondary) in nature, most commonly observed among boys under 2 years of age, while primary thrombocytosis is rare. No such thromboembolic complications were observed even in cases with severe thrombocytosis. Infections associated with anemia was the most common cause of reactive(secondary) thrombocytosis. Among platelet indices, no significant negative correlation could be found with MPV with increasing thrombocytosis. Raised MPV and PDW in a child with persistent thrombocytosis may suggest clonal proliferation and may need further evaluation.

Declarations

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Ethical approval: The study was approved by the Institutional Ethics Committee

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