e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(12); 793-797

Original Research Article

A Study Determining the Etiology of Thrombocytosis and Analyze Various Platelet Parameters in Children

Arvind Kumar Yadav[1], Manish Ranjan[2], Kripa Nath Mishra[3]

[1]Senior Resident, Department of Pediatrics, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India

[2]Senior Resident, Department of Pediatrics, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India

[3]Professor, Department of Pediatrics, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India

Received: 10-09-2023 Revised: 13-11-2023 Accepted: 24-12-2023
Corresponding author: Dr. Manish Ranjan
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was aims to determine the etiology of thrombocytosis and analyze various platelet parameters in children.

Methods: This was a prospective observational study carried out in the Department of Pediatrics, Darbhanga medical College and Hospital.All children of age group 1–14 years of age attending pediatrics outdoors and indoors of DMCH were included in the study. A total of 272 children presented with thrombocytosis.

Results: Age group ranged from 1 to 14 years out of which majority were in 1–2 years age group (45%). 70% children had mild thrombocytosis whereas moderate and severe thrombocytosis was seen in 24% and 3%, respectively. Etiology was secondary or reactive in 99.5% cases whereas only one case of primary thrombocytosis was encountered. Primary or clonal thrombocytosis was seen in one case of Philadelphia positive pediatric CML. No cases of ET were encountered. Etiological spectrum of secondary thrombocytosis was extremely varied. Infection was the most common cause for secondary thrombocytosis, with the highest number attributed to respiratory tract infections alone. For analyzing the association of platelet indices with the severity of thrombocytosis, the cases were grouped into three categories (mild, moderate, severe + extreme) and mean value, standard deviation and P value was calculated. On analysis, an inverse relationship between the platelet indices and the degree of thrombocytosis was observed. With increasing platelet counts, there was a decrease in MPV which had a significant negative correlation ($P < 0.05$). Mean PDW of children with mild and moderate thrombocytosis was 10.96 fl and 10.26 fl, respectively.

Conclusion: Thrombocytosis in children is predominantly secondary and primary (clonal) thrombocytosis is extremely rare. The most common etiology of secondary thrombocytosis in children is infections and is a transient phenomenon with no major clinical implications. However, if no secondary cause is found for increased platelet count or if it persists even after treating the primary cause, a search for underlying primary thrombocytosis should be done.

Keywords: Platelet indices, primary, secondary, thrombocytosis

Introduction

Thrombocytosis refers to platelet count >4,00,000/μL in the peripheral blood. [1] With the widespread use of electronic cell counters and the subsequent availability of a platelet count as part of a routine blood count, thrombocytosis is more often observed as an unexpected finding. Thus, an elevated platelet count has become an important clinical problem for differential diagnosis of various pathological and physiological processes. [2,3]

Thrombocytosis is classified according to its origin into primary and secondary forms. Primary (clonal) thrombocytosis is a myeloproliferative disorder, caused by abnormal and uncontrolled expansion of haematopoietic cells, which is likely to be complicated by thromboembolism. [2] Secondary (or reactive) thrombocytosis is due to a variety of underlying conditions like infection, inflammation, iron deficiency, tissue damage, hemolysis, severe exercise, malignancy, hyposplenism, and other causes of an acute phase response. [4] It is sometimes difficult to differentiate between both categories on clinical ground alone. Once thrombocytosis is identified and confirmed by peripheral smear, the diagnostic evaluation turns to

determine whether the process is reactive or clonal in nature. An important initial step in this is familiarity with the underlying causes of thrombocytosis.

Thrombocytosis is classified according to its origin into primary and secondary forms. Primary (clonal) thrombocytosis is a myeloproliferative disorder, caused by abnormal and uncontrolled expansion of haematopoietic cells, which is likely to be complicated by thromboembolism. [5] Secondary (or reactive) thrombocytosis is due to a variety of underlying conditions like infection, inflammation, iron deficiency, tissue damage, hemolysis, severe exercise, malignancy, hyposplenism, and other causes of an acute phase response. [6] In older adults an elevated platelet count can signify an underlying hematological disease, in children in almost every case the elevated platelet count is due to another medical condition, such as acute infection, chronic inflammation, collagen vascular and renal diseases, Langerhan's cell histiocytosis, iron deficiency, hemolytic anemia, and Kawasaki disease (KD). [7,8] Drugs are another less frequent cause of secondary thrombocytosis in children. [9,10]

The aim of the present study was aims to determine the etiology of thrombocytosis and analyze various platelet parameters in children.

Materials and Methods

This was a prospective observational study carried out in the Department of Pediatrics, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India for 12 months. All children of age group 1–14 years of age attending pediatrics and pediatric super specialty outdoors and indoors were included in the study. A total of 272 children presented with thrombocytosis. All cases with incomplete workup and repeat hemograms of same patients were excluded from the study. Routine Complete hemogram was done using 2 ml of ethylenediaminetetraacetic acid blood in 6 part differential hematology Autoanalyzer (XN-1000) and cases which showed thrombocytosis were reviewed on peripheral smear. Once it was confirmed on smear, case history, presenting signs and symptoms, history and drug history were recorded. The complete blood counts parameters such as hemoglobin, red cell indices, and platelet indices (platelet distribution width [PDW], mean platelet volume [MPV], platelet large cell ratio [P-LCR], and plateletcrit) were noted. Other relevant biochemical parameters such as C-reactive protein, erythrocyte sedimentation rate, serum iron profile, blood culture, and urine culture were also recorded as per the clinical indications in each case. Thrombocytosis was graded into mild (>500 × 103/μl–7 × 103/μl), moderate (>7 × 103/μl–9 × 103/μl), severe (>900 × 103/μl), and extreme (>1000 × 103/μl) as per Dame and Sutor[7] Etiology was determined after analyzing clinical along with relevant laboratory parameters and cases were categorized into subgroups accordingly. All the repeat hemograms of same patients were excluded from the study. The study was approved by the institutional ethical committee. Informed consent was taken from the parents of all patients included in the study.

Statistical analysis was performed on SPSS version 20. Mean, standard deviation and P value were calculated. $P < 0.05$ was considered statistically significant.

Results

Table 1: Grades of thrombocytosis with age groups

Grades of thrombocytosis	1-2 years, *n*	2-6 years, *n*	6-10 years, *n*	10-14 years, *n*	Total, *n* (%)
Mild	59	30	21	30	140 (70)
Moderate	28	10	8	2	48 (24)
Severe	0	5	1	0	6 (3)
Extreme	3	2	0	1	6 (3)
Total	90	47	30	33	200

Age group ranged from 1 to 14 years out of which majority were in 1–2 years age group (45%). 70% children had mild thrombocytosis whereas moderate and severe thrombocytosis was seen in 24% and 3%, respectively.

Table 2: Etiology of thrombocytosis

	n (%)
Primary (*n*=1)	1 (100)
CML	
Reactive (*n*=199)	27
Iron deficiency	20
anemia Infection and	80
anemia Infection	14
alone	36

Urinary tract infection	18
Respiratory tract infection	43
Gastrointestinal infection	64
Bacteremia	16
CNS infection	30
Hemoglobinopathies	20
Drugs	3
Surgery	
Trauma/burn	

Etiology was secondary or reactive in 99.5% cases whereas only one case of primary thrombocytosis was encountered. Primary or clonal thrombocytosis was seen in one case of Philadelphia positive pediatric CML. No cases of ET were encountered. Etiological spectrum of secondary thrombocytosis was extremely varied. Infection was the most common cause for secondary thrombocytosis, with the highest number attributed to respiratory tract infections alone.

Table 3: Correlation of platelet indices (platelet distribution width, mean platelet volume, P-large acell ratio)

Grades of thrombocytosis	PDW Mean SD	MPV Mean SD	P-LCR Mean SD
Mild	10.96 ±1.4	9.92 ±0.8	22.88 ±6.4
Moderate	10.26 ±1.5	9.53 ±1.0	21.68 ±6.2
Severe+extreme	10.05 ±2.7	9.32 ±0.8	20.6 ±7.3
Total	10.78 ±1.4	9.82 ±0.8	22.92 ±6.4
P	0.007	0.012	0.003

with Severity of thrombocytosis

For analyzing the association of platelet indices with the severity of thrombocytosis, the cases were grouped into three categories (mild, moderate, severe + extreme) and mean value, standard deviation and P value was calculated. On analysis, an inverse relationship between the platelet indices and the degree of thrombocytosis was observed. With increasing platelet counts, there was a decrease in MPV which had a significant negative correlation ($P < 0.05$). Mean PDW of children with mild and moderate thrombocytosis was 10.96 fl and 10.26 fl, respectively.

Discussion

Extreme thrombocytosis (platelets >1,000,000/μL) is uncommon, occurring in less than 2% of children [11], but may be more common in critically ill children. [12] Thrombocytosis is classified according to its origin into primary and secondary forms. Primary (clonal) thrombocytosis is a myeloproliferative disorder, caused by abnormal and uncontrolled expansion of haematopoietic cells, which is likely to be complicated by thromboembolism. [5] Once thrombocytosis is identified and confirmed by peripheral smear, the diagnostic evaluation turns to determine whether the process is reactive or clonal in nature. An important initial step in this is familiarity with the underlying causes of thrombocytosis. There have been few prospective studies on the clinical circumstances surrounding paediatric thrombocytosis and evaluation of platelet indices (mean platelet volume, platelet distribution width, and plateletcrit) in presence of thrombocytosis.

Age group ranged from 1 to 14 years out of which majority were in 1–2 years age group (45%). 70% children had mild thrombocytosis whereas moderate and severe thrombocytosis was seen in 24% and 3%, respectively. The frequency of reactive thrombocytosis in childhood is age-dependent with the highest incidence up to 2 years of age. [12] Literature review shows mild increase in platelet counts up to 7,00,000/μL in 72%–86% cases, moderate and severe thrombocytosis in 6%–8% and 2%–3% of children, respectively. [7] The incidence of newly diagnosed primary thrombocytosis in children is about 1 per 10 million, about 60 times lower than adults. [6]

Etiology was secondary or reactive in 99.5% cases whereas only one case of primary thrombocytosis was encountered. Primary or clonal thrombocytosis was seen in one case of Philadelphia positive pediatric CML. No cases of ET were encountered. Etiological spectrum of secondary thrombocytosis was extremely varied. Infection was the most common cause for secondary thrombocytosis, with the highest number attributed to respiratory tract infections alone. A study by Dame and Sutor concluded that the most common cause for reactive thrombocytosis during childhood is (acute or chronic) bacterial or viral infections. [7] In this group, respiratory tract infection is most common

followed by gastrointestinal and urinary tract infection. [13,14] For analyzing the association of platelet indices with the severity of thrombocytosis, the cases were grouped into three categories (mild, moderate, severe + extreme) and mean value, standard deviation and P value was calculated.

On analysis, an inverse relationship between the platelet indices and the degree of thrombocytosis was observed. With increasing platelet counts, there was a decrease in MPV which had a significant negative correlation ($P < 0.05$). Mean PDW of children with mild and moderate thrombocytosis was 10.96 fl and 10.26 fl, respectively. Drug-induced thrombocytosis following intake of corticosteroids and chemotherapeutic agents like vincristine was seen in a relatively higher number of cases in our center. Most of these cases were of Acute Lymphoblastic Leukemia on vincristine or steroid therapy who presented with reactive thrombocytosis on multiple occasions. It has been suggested that vincristine decreases platelet utilization resulting in increased platelet life span and also increases its marrow production. [15] This high number can be attributed to the fact that this hospital is a referral center for hemato-oncology cases. Two cases of ITP on steroids also presented with rebound thrombocytosis during treatment. Corticosteroids can lead to transient thrombocytosis, by releasing stored platelets from the spleen into the blood circulation. [16] In ITP, megakaryopoiesis is accelerated as a response to immune-mediated destruction of platelets. Sometimes, during therapy, compensatory platelet overproduction in the phase of decreased or normalized platelet destruction may lead to thrombocytosis. Three cases with ITP, who developed rebound thrombocytosis following steroid treatment was reported by Yohannan et al[11] IDA alone and with associated concurrent infections comprised 14.1% and 10.3% of secondary thrombocytosis, respectively.

Conclusion

Thrombocytosis in children is predominantly secondary and primary (clonal) thrombocytosis is extremely rare. The most common etiology of secondary thrombocytosis in children is infections and is a transient phenomenon with no major clinical implications. However, if no secondary cause is found for increased platelet count or if it persists even after treating the primary cause, a search for underlying primary thrombocytosis should be done.

References

1. Mantadakis E, Tsalkidis A, Chatzimichael A. Thrombocytosis in childhood. Indian pediatrics . 2008 Aug 1;45(8):669.
2. Syed NN, Usman M, Khurshid M. Thrombocytosis: age dependent aetiology and analysis of platelet indices for differential diagnosis. Indian Journal of Pathology & Microbiology. 2007 Jul 1;50(3):628-33.
3. Griesshammer M, Bangerter M, Sauer T, Wennauer R, Bergmann L, Heimpel H. Aetiology and clinical significance of thrombo cytosis: analysis of 732 patients with an elevated platelet count. Journal of internal medicine. 1999 Mar;245(3):295-300.
4. Harrison CN, Bareford D, Butt N, Campbell P, Conneally E, Drummond M, Erber W, Everington T, Green AR, Hall GW, Hunt BJ. Guideline for investigation and management of adults and children presenting with a thrombocytosis. British journal of haemat ology. 2010 May;149(3):352-75.
5. Syed NN, Usman M, Khurshid M. Thrombocytosis: age dependent aetiology and analysis of platelet indices for differential diagnosis. Indian Journal of Pathology & Microbiology. 2007 Jul 1;50(3):628-33.
6. Harrison CN, Bareford D, Butt N, Campbell P, Conneally E, Drummond M, Erber W, Everington T, Green AR, Hall GW, Hunt BJ. Guideline for investigation and management of adults and children presenting with a thrombocytosis. British journal of haematology. 2010 May;149(3):352-75.
7. Dame C, Sutor AH. Primary and secondary thrombocytosis in childhood. British journal of haematology. 2005 Apr;129(2):165-77.
8. Ishiguro A, Ishikita T, Shimbo T, Matsubara K, Baba K, Hayashi Y, Naritaka SI, Nakahata T. Elevation of serum thrombopoietin precedes thrombocytosis in Kawasaki disease. Thrombosis and haemostasis. 1998;79(06):10 96-100.
9. Frye JL, Thompson DF. Drug–induced thrombocytosis. Journal of clinical pharmacy and therapeutics. 1993 Feb;18(1):45-8.
10. Nako Y, Tachibana A, Fujiu T, Tomomasa T, Morikawa A. Neonatal thrombocytosis resulting from the maternal use of non-narcotic antischizophrenic drugs during pregnancy. Archives of disease in childhood. Fetal and neonatal edition. 2001 May;84(3):F198.
11. Yohannan MD, Higgy KE, Al-Mashhadani SA, Santhosh-Kumar CR. Thrombocytosis: etiologic analysis of 663 patients. Clinical ped iatrics. 1994 Jun;33(6):340-3.
12. Denton A, Davis P. Extreme thrombocytosis in admissions to paediatric intensive care: no requirement for treatment. Archives of disease in childhood. 2007 Jun;92(6):515.
13. Wolach B, Morag H, Drucker M, Sadan N. Thrombocytosis after pneumonia with empyema and other bacterial infections in children. The Pediatric infectious disease journal. 1990 Oct 1;9(10):718-21.
14. Garoufi A, Voutsioti K, Tsapra H, Karpathios T, Zeis PM. Reactive thrombocytosis in

children with upper urinary tract infections. Acta Paediatrica. 2001 Apr;90(4):448-9.
15. Robertson JH, Crozier EH, Woodend BE. Vincristine-induced thrombocytosis studied with 75Se selenomethionine. Acta Haemato logica. 1972 Mar 5;47(6):356-60.
16. Lin CY, Yang YH, Lee CC, Huang CL, Wang LC, Chiang BL. Thrombopoietin and interleukin-6 levels in Henoch-Schönlein purpura. Journal of Microbiology, Immu nology, and Infection= Wei Mian yu gan ran za zhi. 2006 Dec 1;39(6):476-82.