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Thrombocytosis in children

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SUMMARY

OBJECTIVE: We aimed to investigate the frequency and causes of thrombocytosis in patients admitted to the Department of Pediatric Hematology and Oncology of Elazig Fethi Sekin City Hospital, Elazig, Turkey.

METHODS: Between 2019 and 2021, the laboratory parameters of 2,500 patients admitted to the Hematology Department were studied. During this examination, 319 (12.76%) patients were found to have thrombocytosis. Demographic characteristics (age and gender), hematologic parameters (hemoglobin, white blood cells, and platelets), and ultimate diagnoses ot the cases were recorded from their files.

RESULTS: Of these 319 patients with thrombocytosis, 197 (1.8%) were male and 122 (38.2%) were female, and the mean age was 72.0±69.0 (1–216) months. The median platelet count of the patients was 590.43±280.12/μL (450,000–750,000). The most common cause of secondary thrombocytosis was infection, accounting for 37.9% of all patients. Other common causes were sickle cell anemia (21%), iron deficiency anemia (15.4%), colloid tissue disease (6.6%), hemolytic anemia (5.0%), splenectomy (4.5%), and other causes (9.7%).

CONCLUSION: In our study, infections were the most common cause of thrombocytosis. In addition to infections, sickle cell anemia and iron deficiency anemia should also be considered in the differential diagnosis of thrombocytosis.

KEYWORDS: Child. Etiology. Thrombocytosis.

INTRODUCTION

Thrombocytosis, also called thrombocythemia, is generally defined as a platelet count that is above the upper limit. The most commonly accepted cutoff value for normal is <450,000/μL. Platelet counts in the range of 450,000 to 700,000/μL are considered mild, between 700,000 and 900,000 /μL are considered moderate, between 900,000 and 1,000,000/μL are considered severe, and values above 1,000,000/μL are considered extreme thrombocytosis[1]. The main medical complications of thrombocytosis are hemorrhage and thrombotic events, but thrombocytosis often occurs without symptoms. Platelet counts greater than 1,500,000/μL carry an increased risk for bleeding. The most common cause of an increased platelet count is reactive (secondary) thrombocytosis. Secondary thrombocytosis is usually a normal physiological response to coexisting inflammation or surgery. In secondary thrombocytosis, the elevated platelet levels are the result of an extrinsic process (chronic or acute inflammation) that stimulates megakaryocytopoiesis. Bacterial infections, viral infections, iron deficiency, hemolytic anemia, tissue damage, asplenia, malignancies, autoimmune diseases, and drugs are triggers of secondary thrombocytosis[2]. Secondary thrombocytosis is commonly seen in children with a variety of clinical conditions. The most common cause of secondary thrombocytosis in children is respiratory infection[3].

Considerable differences were described in the epidemiology and the clinical presentation of thrombocytosis in children when compared to adults[4]. An elevated platelet count in pediatrics is usually a common incidental finding in hospitalized and outpatient children. Thrombocytosis in children is typically transient, occurring secondary to various underlying medical, and often inflammatory disorders as an increase in platelet count is part of the acute-phase response. Rarely, persistent thrombocytosis may be the result of inherited or acquired genetic mutations. The incidence of essential thrombocytosis is 0.6–2.5 per 100,000[5]. According to the World Health Organization guidelines, the persistent diagnosis of essential thrombocythemia requires a platelet count of ≥450,000/μL in patients with thrombocytosis, and it should be determined whether thrombocytosis is primary or secondary. The criteria of the World Health Organization are often used for diagnosis[6].

In our study, we aimed to determine the frequency of thrombocytosis in childhood and the causes of thrombocytosis among a large series of our patients who were admitted to our outpatient clinic. Thus, we aimed to review our findings

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and put forth our data to help create institutional, local, and international algorithms.

METHODS

The demographic characteristics and laboratory parameters of 2,500 patients aged 1–216 months who were admitted to our pediatric hematology outpatient clinic were retrospectively analyzed. In this analysis, patients with a platelet count >450,000 µL were examined. Patients' age, gender, thrombocyte counts, hemoglobin and white blood cell values, clinical findings, and ultimate diagnoses were recorded. In addition, patients were classified into three age groups, namely, 1–60 months, 61–120 months, and 121–216 months, to evaluate the frequency and factors of thrombocytosis according to age groups.

Statistical analysis

A statistical analysis of the data obtained from the study was performed using the Statistica Version 20.0 program. Descriptive statistics were used to summarize the data. Continuous variables such as age, mean, standard deviation, minimum and maximum values, platelets, white blood cells, and hemoglobin were summarized as median, 1st (Q1), and 3rd (Q3) quartile values. Categorical variables such as gender, age groups, and patient groups were summarized as numbers and percentages.

The conformity of the data to the normal distribution was determined by using the Shapiro-Wilk test. Due to the lack of conformity with the normal distribution, the medians of two independent groups were compared with the nonparametric Mann-Whitney U test and the medians of more than two independent groups with the nonparametric Kruskal-Wallis test. Dunn's test, one of the multiple comparison tests, was used to determine the groups that were found to be different as a result of the comparisons. The statistical significance level was taken as $p<0.05$ for all comparisons.

RESULTS

In the study, it was determined that 319 patients (12.76% of the total) met the inclusion criteria, of whom 197 (61.8%) were males and 122 (38.2%) were females, with a mean age of 72.0±69.0 months (min-max; 1 month–216 months) (Table 1).

The median platelet count of the patients was 510,000/µL (min-max; 450,000–750,000), the white blood cell count was 10,500/µL (min-max; 8,260–14,280), and the hemoglobin value was 11.5 g/dL (min-max; 9.0–12.0). While the median platelet value was 517,000/µL (min-max; 480,500–638,500) in female patients, this value was 516,000/µL (min-max; 478,000–634,000) in male patients, and no statistical difference was determined between these groups ($p>0.05$). All the patients had secondary thrombocytosis, and the most common cause was infection with a rate of 37.9%. Other common causes include sickle cell anemia (SCA, 21%), iron deficiency anemia (16.4%), colloid tissue diseases (6.6%), hemolytic anemias (5.0%), and patients undergoing splenectomy (4.4%) (Table 1). In addition, no clinical findings related to thrombocytosis were observed in any of the patients, and thrombocytosis treatment was not given except for hydration. When the thrombocyte values of the patients were examined according to age groups, median platelet values were detected as 506,000/µL for 1–60 months, 507,500/µL for 61–120 months, and 553,000/µL for 121–216 months. The difference between the median platelet values of the age groups 1–60 months and 121–216 months was statistically significant ($p<0.01$). The difference between the groups of 61–120 months and 121–216 months was also statistically

Table 1. Age groups, gender, and pathogenesis data of included patients.

Variables	n	Value
Age (months)	319	72.0±69.0 (average)
Age groups	n	%
1–60 months	139	43.6
61–121 months	75	23.5
121–216 months	105	32.9
Hematological parameters*	319	
Platelet count (/µL)		510,000 (450,000–750,000)
White blood cell count (/µL)		10,500 (8,260–14,280)
Hemoglobin value (g/dL)		11.5 (9–12)
Gender	n	%
Male	197	61.8
Female	122	38.2
Etiology	n	%
Infection	121	37.9
Sickle cell anemia	67	21.0
Iron deficiency anemia	49	15.4
Collagen tissue disease	21	6.6
Hemolytic anemia (OIHA, HV, etc.)	16	5.0
Splenectomy applied patients	14	4.4
Others	31	9.7

*Values are given as mean (min–max).

significant (p<0.01). Among the age groups, the highest platelet count was observed in pediatric patients aged between 121 and 216 months (Table 2).

Infections (55.4%) and iron deficiency anemia (18.7%) for children aged 1–60 months, and, similarly, infections (30.7%) and iron deficiency anemia (20.0%) for children aged 61–120 months were the most common causes of thrombocytosis. SCA (55.2%) and infections (20.0%) were the most common causes for the age group of 121–216 months (Table 3).

DISCUSSION

In our study, the frequency of thrombocytosis among patients admitted to the pediatric hematology outpatient clinic was investigated. In this study, we found that 12.76% of all patients had thrombocytosis, and we observed that all patients had secondary thrombocytosis, which is consistent with the literature. Thrombocytosis in children is often secondary and usually occurs when various underlying diseases stimulate the production of megakaryocytes. In previous studies conducted on children, the frequency of primary thrombocytosis was below 1/10,000,000 per year in children under 14 years of age, while the frequency of secondary thrombocytosis was estimated to be between 4.5 and 15.0% in hospitalized children[7,8]. Although the causes and formation mechanisms of primary thrombocytosis are not fully elucidated, infections were identified as the most common causes of secondary thrombocytosis in many studies. In a study, the most common causes of severe thrombocytosis were infections in 80 (56.8%) patients, anemia in 21 (14.9%) patients, and autoimmune diseases in 14 (9.9%) patients[9]. Clemens Stockklausner et al. reported that the most common causes were infections (49.5%), postsplenectomy (7.8%), Kawasaki disease (6.4%), tissue damage (4.5%), blood diseases (3.7%), malignancies (3.7%), renal diseases (3.2%), chronic inflammation (1.8%), essential thrombocythemia (0.5%), and other causes (3.7%)[10]. In some other studies, the frequencies of infections in secondary thrombocytosis were 39, 53, 30, and 63%, respectively[11-14]. In our study, infections (37.9%) were also the most common cause of secondary thrombocytosis in accordance with the previously published studies.

The incidence of thrombocytosis secondary to anemia was reported as 12.0, 3.7, and 8.5% in various studies[12-14]. Only iron deficiency anemia was found in 17.2 and 8.0% of the cases in two studies[8,13]. In our study, 16.4 and 5.0% of patients had iron deficiency anemia and hemolytic anemia, respectively, with a higher rate of secondary thrombocytosis when compared to previously published studies. Additionally, we observed that the frequency of iron deficiency anemia in secondary thrombocytosis was higher in younger ages. We estimate that high rates of secondary thrombocytosis due to iron deficiency may be associated with the high rates of iron deficiency anemia in childhood, which are as high as 70–80% in our study region in Turkey[7]. In addition, an important point we determined in our study is that 21% of our cases with thrombocytosis were SCA patients. SCA

Table 2. Platelet values of patients with thrombocytosis according to gender and age groups.

Variables	Median (Q1–Q3)	p-value
Gender		
Male	516,000 (478,000–634,000)	>0.05
Female	517,000 (480,500–638,500)	
Age groups (months)		
1–60	506,000 (477,000–579,000)	
61–120	507,500 (477,500–560,750)	<0.0001
121–216*	553,000 (485,000–700,000)	

*Difference making variable.

Table 3. Causes of thrombocytosis based on the age group of the patients.

Causes of thrombocytosis	Age groups						Total	
	0–60 months		61–120 months		121–216 months			
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Infection	77	55.4	23	30.7	21	20,0	121	37.9
SCA	2	1.4	7	9,3	58	55.2	67	21.0
Iron deficiency anemia	26	18.7	15	20.0	8	7.6	49	15.4
Collagen tissue disease	11	7.9	5	6.7	5	4.8	21	6.6
Hemolytic anemia	7	5.0	7	9.3	2	1.9	16	5.0
Splenectomy applied patients	3	2.2	7	9.3	4	3.8	14	4.4
Others	13	9.4	11	14.7	7	6.7	31	9.7

is a congenital hemolytic anemia with inflammation. In a study, 53% of patients with thrombocytosis had homozygous SCA, which is consistent with our study[15]. The occurrence of thrombocytosis in both acute and chronic inflammation in patients with SCA and autosplenectomy is an expected situation.

CONCLUSION

The most common cause of thrombocytosis in our study was infections, while SCA and IDA were the other most common respective causes of secondary thrombocytosis. In addition to the most common cause of thrombocytosis due to infections, SCA and IDA should also be considered in the differential diagnosis of thrombocytosis in children, especially in areas where iron deficiency is prevalent.

CONSENT TO PARTICIPATE

All patients involved in this study read and signed the "In-formed volunteer consent form."

AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this published article.

ETHICAL APPROVAL

Ethics approval and consent to participate: Ethics approval was obtained by the Ethics Committee of Elazig Firat University, Elazig, Turkey, with protocol number E-02.2022-6854.

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AUTHORS' CONTRIBUTIONS

AB: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Supervision. **FFŞ:** Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing.

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