Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

Study on Clinico Etiological Profile on Thrombocytosis in Children

Dr. Dhanush Balakumar [1], Dr. KV Pugalendhi Raja [2], Dr. MS Balaji Kumar [3]

(Received: 08 February 2024 Revised: 11 March 2024 Accepted: 08 April 2024)

KEYWORDS

ABSTRACT:

Background: With the increased use of electronic cell counters and routine inclusion of platelet counts in blood tests, thrombocytosis is more commonly detected incidentally. Elevated platelet counts have become an important clinical consideration in diagnosing various pathological and physiological conditions.

Aims and Objectives: Our aim is to research the fundamental causes of thrombocytosis and its clinical manifestations in our pediatric group. Objectives: study the clinico-etiological profile of thrombocytosis in children. Secondary objectives: evaluate platelet parameters in primary and secondary thrombocytosis, and study complications associated with thrombocytosis.

Results: Among 200 children studied, 84 (42%) were female and 116 (58%) were male, with a male-to-female ratio of 1.3:1. The mean age was 3.54 years (SD 3.79), primarily between 1-5 years. Fever was the most common symptom (73.5%), followed by cough (51.5%), fast breathing (31%), progressive pallor (23.5%), and gastrointestinal symptoms (16%). Other symptoms included joint swelling (13.5%), rash (3.5%), anasarca (3.5%), and abnormal body movements (4%). In this study, 73.5% had mild thrombocytosis, 15.5% had moderate, and 5.5% had severe/extreme thrombocytosis. Significant correlations were found between thrombocytosis severity, total leukocyte count, and CRP positivity ($p=0.01$). Mean platelet volume and platelet distribution width decreased with higher platelet counts ($p<0.01$). Anemia was common (66% had pallor), but hemoglobin levels did not correlate with thrombocytosis severity ($p=0.29$). All cases were reactive thrombocytosis, mostly due to infections (69.5%), with respiratory infections being most frequent. Other causes included iron deficiency anemia (14%) and autoimmune disorders (7.5%).

Conclusion: Thrombocytosis is common in children, often benign and reactive to conditions like trauma, surgery, infections, or iron deficiency. True myeloproliferative thrombocytosis is rare, affecting 1 in a million. Reactive thrombocytosis usually doesn't lead to complications. Platelet indices are useful biomarkers for diagnosing and prognosticating infections.

Introduction

Thrombocytosis refers to an elevated platelet count exceeding the normal range of 150-400 X 10^9/L and can be categorized into essential (primary) or secondary thrombocytosis. Essential thrombocytosis (ET), a subset of myeloproliferative neoplasms (MPN), includes classical ET, which involves autonomous platelet production due to genetic mutations such as JAK2V617F, MPL, or CALR. Another type of ET is familial and hereditary, caused by mutations in the THPO or MPL genes.

Secondary thrombocytosis, more common in children it results from increased cytokine release due to infections, inflammation, or other factors, stimulating platelet production. Serum cytokine levels may not correlate with thrombocytosis degree. Important immune mediators involved include thrombopoietin (THPO), interleukin-6 (IL-6), interleukin-1β (IL-1β), granulocyte-macrophage colony-stimulating factor (GM-CSF), and erythropoietin. Causes include infections (e.g., pneumonia), chronic conditions (e.g., anemia), or recovery phases (e.g., from chemotherapy). Thrombocytosis affects hospital stays and mortality rates. Asplenia can contribute, and genetic factors like MPL or THPO mutations can lead to familial or sporadic thrombocytosis. Understanding its complex aetiology is vital for management. It is usually transient and resolves when the primary cause is addressed. Unlike ET, secondary thrombocytosis rarely leads to thrombotic or hemorrhagic complications. Thrombocytosis can be graded on the basis of platelet counts as follows [2] thrombocytosis is classified as : 1.Mild - >500 to 699 × 10^9 2.Moderate - >700 to 899 × 10^9 /L 3.Severe - >900 to 999 × 10^9 /L 4.Extreme - >1000 x10^9 /L.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

When the total blood count is taken for some unrelated cause, thrombocytosis is often found as an accidental laboratory anomaly. However, once discovered, it poses a significant diagnostic problem. Most often, thrombocytosis is a reactive condition (clonal bone marrow) or is brought on by (secondary thrombocytosis) (myeloproliferative) condition; the essential thrombocythemia falls within this category. Clinical signs or laboratory test results are frequently not sufficient to distinguish between the reactive and clonal kinds of thrombocytosis. However, there are crucial distinctions between about their aetiology, pathophysiological characteristics, and clinical ramifications. On the basis of clinical signs or the results of laboratory tests, it is frequently extremely challenging to distinguish between the reactive and clonal kinds of thrombocytosis. However, there are significant disparities between in terms of their origin, pathophysiological characteristics, and practical significance. Due to different haematological or non-haematological problems, enhanced megakaryopoiesis results in secondary thrombocytosis. Multiple underlying diseases, including infection, inflammation, iron shortage, tissue damage, haemolysis, intense exercise, cancer, hyposplenism, and other causes of an acute phase response, can result in secondary (reactive) thrombocytosis. Thrombocytosis is now more frequently discovered as an unexpected discovery due to the widespread usage of electronic cell counters and the subsequent availability of a platelet count as part of a regular blood count. As a result, a high platelet count has emerged as a crucial clinical issue in the differential diagnosis of numerous pathological and physiological processes. Our aim is to research the fundamental causes of thrombocytosis and how it manifests clinically in our paediatric group. Our objectives are as follows : To study the clinico-etiological profile of thrombocytosis in children. Secondary objectives are : Evaluation of platelet parameters in primary and secondary thrombocytosis. Study of complications associated with thrombocytosis.

Methodology:

An informed consent was obtained from the patient or from the parents / guardian of the children accompanied.

All children aged less than 18 years admitted in Paediatrics Department of VMKV Medical College, Salem in whom thrombocytosis (platelet > 5.00 × 10^9/L) was identified during routine blood investigations were included in the study. 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], and platelet large cell ratio [P-LCR]) 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 on the basis of platelet count as[3]

a) Mild - >500 to 699 × 10^9/L

(b) Moderate - >700 to 899 × 10^9/L(c) Severe - >900 to 999 × 10^9/L

(d) Extreme - >1000x10^9/L

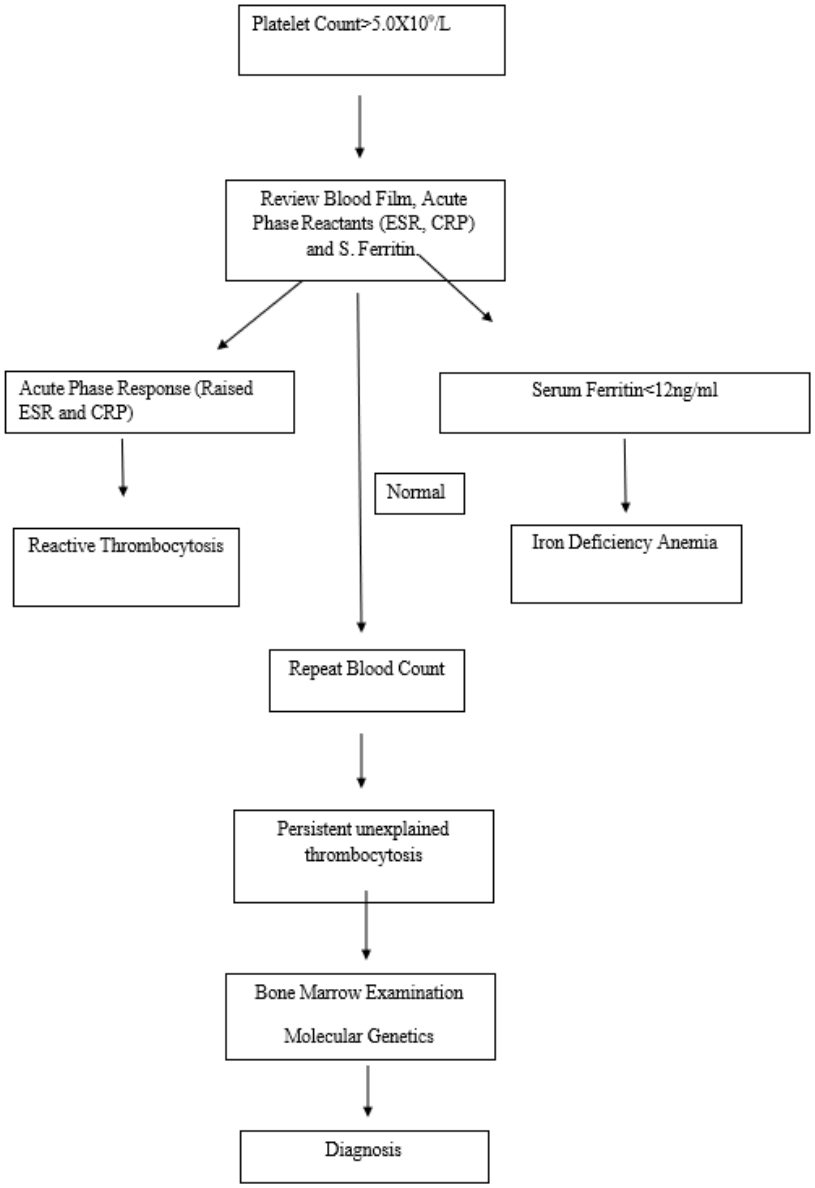
Iron Deficiency Anemia (IDA) was defined by microcytic hypochromic picture on peripheral smear with Serum ferritin <12 ng/ml13-14

Diagnostic algorithm for investigation of thrombocytosis

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727



STATISTICAL ANALYSIS

Collected data was entered in Excel Spreadsheet. Categorical data is presented in terms of frequency and percentage. Continuous data is presented in terms of mean/ median and standard deviation. For the comparison of means and proportions between different groups, unpaired Student's t-test and Chi-square test was used, respectively. For correlation studies, Pearson correlation coefficient (*r*) was used. Open source freely available statistical software was used.

ETHICAL JUSTIFICATION

Ethical clearance for the study was taken from the thesis review board and the Institutional Ethics Committee before commencement of the study.

Parents of the eligible children were approached for participation and subjects were enrolled only after obtaining written informed consent and assent (if needed), after explaining the nature of the study in detail, in their own language.

RESULTS

A total of 200 children aged less than 18 years who presented to Department of Pediatrics, VMKV Medical College, Salem (either as Out Patient or admitted in the wards) with platelet count of >500 X 10^9/L on routine blood investigations were evaluated for clinical features and etiological profile.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

Out of 200 children enrolled in the study, 84(42%) were females and 116(58%) were males, with a male to female ratio 1.3:1. Children aged less than 18 years were included in the study with a mean age of presentation of 3.54 years with a standard deviation of 3.79 most of the patients were between 1-5 years age group. 147 (73.5%) patients presented with fever, 103 (51.5%) patients presented with cough, 62 (31%) patients with fast breathing, 53(23.5%) patients with progressive pallor, and 32 patients had gastrointestinal symptoms like abdominal pain, vomiting and diarrhoea in isolation as well as in combination. Other presenting symptoms included joint swelling(13.5%), rash (3.5%), anasarca(3.5%) and abnormal body movements(4%).
Examination findings were depicted in figure 1(to see if all parameters are there in the table, if not to add)
Out of the study population, 147(73.5%) patients had mild thrombocytosis, 31(15.5%) patients had moderate thrombocytosis and 11(5.5%) patients had severe and extreme thrombocytosis respectively.

When haemoglobin values, total leucocyte count and ESR with severity of thrombocytosis were compared, mean and standard deviation values are calculated for each laboratory parameter. TLC values and CRP positivity showed a significant relation with severity of thrombocytosis (p value = 0.01).
For analyzing the association of platelet indices with the severity of thrombocytosis, the cases were grouped into four categories (mild, moderate, severe and extreme) and mean value, standard deviation and *P* value was calculated (Table 3.8). Mean MPV values in cases of mild, moderate, severe and extreme thrombcytosis were 9.29fL, 9.06fL, 8.94fL and 8.36fL respectively. 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 (*r =-0.19 and p value 0.01*). Mean PDW of children with mild and moderate thrombocytosis was 11.56fL and 11.84fL, respectively and 10.50fL and 9,52fL in cases with severe and extreme thrombocytosis. PDW and P-LCR also had significant association with platelet count (p value <0.01). Similar observation was seen with P-LCR where the mean P-LCR in mild and moderate thrombocytosis was 19.81% and 21.57%, respectively. In the group of severe and extreme thrombocytosis, mean P-LCR were 17.86% and 13.89% respectively.
125 patients with mild thrombocytosis, 25 patients with moderate thrombocytosis and 10 patients with severe and extreme thrombocytosis had anemia as was evident on the examination finding, 66% patients had pallor. However, no significant correlation was seen between haemoglobin levels and degree of severity of thrombocytosis(p value 0.29).
All 200 patients in our study had reactive thrombocytosis. 69.5% patients had underlying infectious etiology with anemia. Respiratory tract infections were the most commonly encountered infections. Iron deficiency anemia alone was seen in 14% patients. Other etiological causes included auto-immune (7.5%) and miscellaneous causes like Nephrotic Syndrome, Vasculitis, Thalassemia, Atypical Kawasaki Disease, Langerhans Cell Histiocytosis and Non-Hodgkin's Lymphoma.

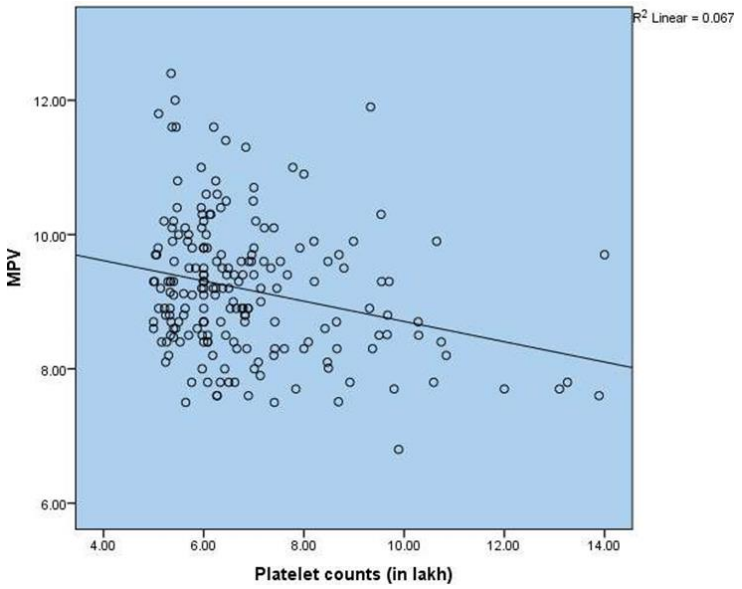
Investigations	**Mild**		**Moderate**		**Severe**		**Extreme**		**P value**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Hb(g/dl)	9.17	1.84	8.56	2.37	9.27	1.31	9.61	1.38	**0.51**
TLC (cells/mm^3)	15472	15455	17761	7832	22609	12077	21400	8988	**0.01**
ESR (mm/hour)	41.75	11.45	43.97	11.35	44.73	11.24	47.27	10.89	**0.32**

Comparison of Laboratory Findings in Patients with Thrombocytosis

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

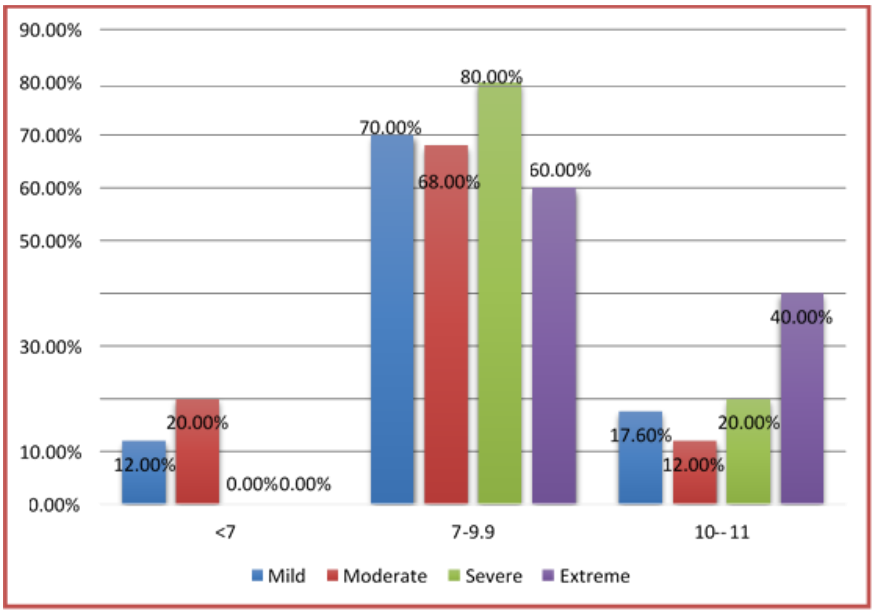


Association of CRP with severity of Thrombocytosis

CRP	Mild		Moderate		Severe		Extreme	
	No.	%	No.	%	No.	%	No.	%
Negative	49	33.3	10	32.3	0	0.0	0	0.0
Positive	98	66.7	21	67.7	11	100.0	11	100.0

P value=0.01

Scatterplot showing correlation between MPV and platelet counts

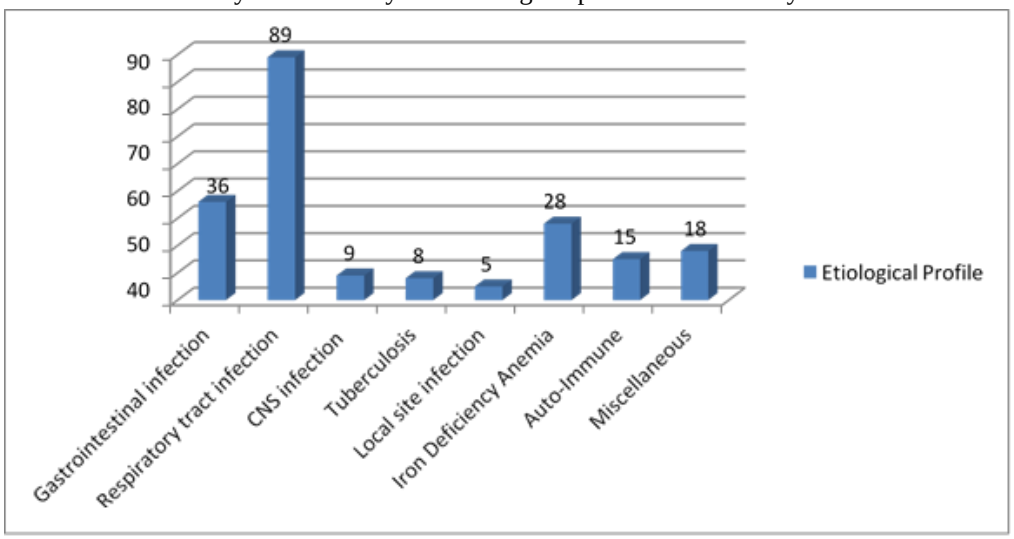


Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

Association of Anemia with severity of thrombocytosis Etiological profile of thrombocytosis



Aetiology	No. of patients(n)	Percentage (%)
Gastrointestinal infection (n=36)		
Acute gastroenteritis	4	11.1
Acute on chronic pancreatitis	1	2.7
Liver abscess	21	58.3
Appendicular perforation peritonitis	1	2.7
Enteric fever	6	16.7
Neonatal cholestasis	3	8.3
Respiratory tract infection (n = 89)		
Pneumonia	44	49.4
Empyema	21	23.6
Pyopneumothorax	5	5.6
Bronchiolitis	8	8.9
Foreign body aspiration	2	2.24
Tuberculosis	8	8.9
TEF	1	1.12
CNS infection (n=9)		
Epileptic encephalopathy	1	11.1
Meningitis	7	77.7
Acute necrotizing encephalitis	1	11.1
Iron Deficiency Anemia	**28**	14
Local site infection(n=5)		
Umbilical abscess	1	20.0
Thigh abscess	1	20.0
Right submandibular abscess	1	20.0
Right parotid abscess	1	20.0
Left lumbar abscess	1	20.0
Autoimmune	**15**	

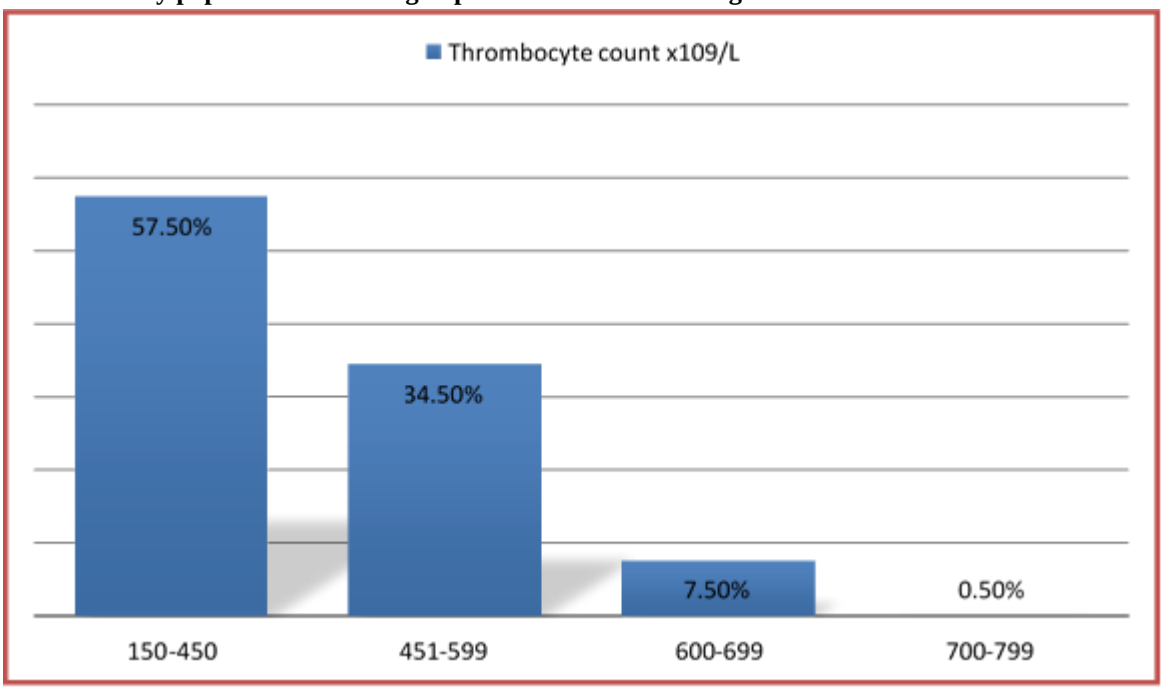
Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

Juvenile Idiopathic Arthritis (JIA)	3	20.0
Oligoarticular JIA	5	33.3
Polyarticular JIA	3	20.0
Systemic onset JIA	4	26.7
Miscellaneous	**18**	
Atypical Kawasaki disease	1	5.5
Non Hodgkin's Lymphoma	1	5.5
Nephrotic syndrome	7	38.9
Protein losing enteropathy	1	5.5
Langerhans Cell Histiocytosis	2	11.1
Thalassemia	4	22.2
Vasculitis	1	5.5
Transient erythroblastopenia of childhood	1	5.5

Distribution of study population according to platelet count at discharge



Discussion

Thrombocytosis in children is primarily reactive or secondary and occurs as an acute phase reaction. In hospitalized children, it has been reported to have an incidence of about 6%– 15%, though it is subject to variations in the definition of thrombocytosis, in study settings (hospitalized Vs outpatients), and most importantly the prevalence of causative factors suchas infections, anemia, and malignancies.[3]

This was a prospective observational study conducted on 200 children aged less than 18 years who had thrombocytosis defined as platelet count >500 X 10^9/L on routine blood investigations and were evaluated for clinical features, etiological profile and other laboratory parameters.

DEMOGRAPHY

In the present study, all 200 patients had reactive thrombocytosis suggesting the rarity of primary thrombocytosis. A study on 250 children by Yadav et al in 2010 showed 3 cases of primary thrombocytosis. Similarly another study by Subramaniam et al had 2 cases of primary thrombocytosis (CML and AML-M7).

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

Another recent study done in Orissa in 2018 comprising of 272 children reported secondary or reactive thrombocytosis in 99.6% cases whereas only one case of primary thrombocytosis was encountered. Primary or clonal thrombocytosis was seen in one case of Philadelphia positive pediatric CML.

The incidence of reactive thrombocytosis in childhood shows an age-dependent pattern. The highest incidence has been found in infants aged up to 24 months. After the age of 2 years, the incidence gradually decreases [28]. In our study, 46.5 % population was in the age group of1-5 years and 27% population in age group less than 1 year.

Out of 200 children enrolled in the study, 84(42%) were females and 116(58%) were males, with a male to female ratio 1.3:1. Similar results were observed in two other studies, [25, 31] with male preponderance of 64% and 61.1% of cases, respectively.

ETIOLOGICAL PROFILE

Our study showed an etiological spectrum with infections comprising 69.5% out of which respiratory tract infections (64%) was most common, followed by gastrointestinal infections (25.8%) and CNS (6.4%) infections. Pneumonia was the most common respiratory infection.

In our study, iron deficiency anemia was seen in 14% patients. 7.5% patients had underlying autoimmune etiology (Juvenile Idiopathic Arthritis). 7 patients had Nephrotic Syndrome, 2 patients were diagnosed cases of Langerhans Cell Histiocytosis, 1 case of atypical Kawasaki Disease, 1 case of Non Hodgkin's Lymphoma, 4 cases of Thalassemia (post splenectomy) and 1 case of protein losing enteropathy.

Dame and Sutor from Germany concluded in their study that the most common cause for reactive thrombocytosis during childhood is (acute or chronic) bacterial or viral infections.[3] In this group, respiratory tract infection was most common followed by gastrointestinal and urinary tract infections.

It was reported that anemia is a common cause of reactive thrombocytosis.

In a study by Yadav et al, investigators observed that 65% of children had thrombocytosis due to an infectious disease, of which 29% were also anemic. On the other hand, the authors reported the presence of anemia as the only likely cause of thrombocytosis in only 12.6% of patients.

Grade of Thrombocytosis

Our study had 73.5% cases of mild thrombocytosis, 15.5% moderate and 5.5% cases of severe and extreme thrombocytosis respectively. Similar observations were made in another study by Subramaniam et al, where mild thrombocytosis was most commonly observed. Mildthrombocytosis (88.9%) was seen more commonly than moderate (7.5%) and severe (3.6%) thrombocytosis. In another study by Sarangi et al, mild thrombocytosis was seen in 70.6%, moderate and severe thrombocytosis was seen in 25.7% and 1.5% cases, respectively and extreme thrombocytosis was seen in 2.2% cases.

Correlation between degree of thrombocytosis was seen with disease severity in our study. Severe and extreme thrombocytosis was identified in various infective conditions like liver abscess, pyopneumothorax, submandibular abscess and few cases of nephrotic syndrome.

Investigations

We observed CRP positivity in 66.7% of patients with mild thrombocytosis and 100% positivity in severe and extreme thrombocytosis. We also identified an increase in values of the acute phase reactants CRP and ESR in correlation with an increase in the extent of thrombocytosis. There was also a rise in TLC with increasing severity of thrombocytosis (p value=0.01). In a recently published study, the degree of reactive thrombocytosis was foundto be positively correlated with WBC count and negatively correlated with hemoglobin concentration, with no apparent correlation with CRP levels. In our study, however, both WBCs and CRP levels correlated positively with the degree of reactive thrombocytosis.

Platelet Indices

The platelet indices were compared with the degree of severity of thrombocytosis. Increase in the degree of thrombocytosis was associated with decrease in MPV, PDW, and P-LCR. In our study, all three platelet parameters had significant negative correlation with severity of thrombocytosis. Subramaniam et al also compared the platelet indices with degree of thrombocytosis and found a weak significant negative correlation of mean MPV with degree of thrombocytosis.

Sarangi et al also analysed the statistically significant relation between various platelet indices and the

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2114-2123 | ISSN:2251-6727

severity of thrombocytosis.

Complications

No thromboembolic complications were seen in our study. However, patients with severe/ extreme thrombocytosis had received thrombosis prophylaxis (low dose aspirin).

RT is usually a benign condition and platelet counts normalize rapidly with treatment of underlying etiology without causing any thromboembolic complications. No thromboembolic complications were observed in earlier pediatric series on thrombocytosis even in cases with severe and extreme thrombocytosis, suggesting that no active intervention is required for thrombocytosis in these children.

However, patients having underlying iron deficiency state or other prothrombotic factors (hyperhomocystinemia, nephrotic syndrome, anti phospholipids antibodies, inherited thrombophilia *etc.*) can have thromboembolic complications and these patients may require antithrombotic prophylaxis. There are reports of increased incidence of thrombotic

complications in association with IDA with or without thrombocytosis. Maguire et al [101] reviewed association between iron deficiency anemia and stroke in young children. They observed that IDA accounted for more than half of stroke cases in children without any other underlying illness, suggesting that iron deficiency anemia is itself a significant risk factor for stroke. Dame and Sutor had also suggested that individually tailored thrombosis prophylaxis should be considered in patients with RT, if additional thrombotic risk factors are present.

Hence, all RT patients may not have

benign course and antithrombotic prophylaxis should be considered in patients with severe/extreme thrombocytosis and patients with moderate thrombocytosis with associated prothrombotic factors.

Platelet count at discharge

In the present study, 115 patients (57.5%) had normal platelet counts at discharge soon after the recovery from illness indicating that reactive thrombocytosis is a transient process which resolves after treatment of underling etiology.

A total of 200 patients with thrombocytosis (defined as platelet count >500 $X10^9$/L) were enrolled in this study. Most of the patients were between 1-5 year age group (46.5%). Mean age of presentation of 3.54 years. Male to female ratio was 1.3:1. Most common presenting symptom in decreasing order were fever, cough, progressive pallor, gastrointestinal symptoms like abdominal pain, vomiting and diarrhoea in isolation as well as in combination. Other presenting symptoms included joint swelling, rash, anasarca and abnormal body movements. 73.5% patients had mild thrombocytosis 31(15.5%) patients had moderate thrombocytosis and 11(5.5%) patients had severe and extreme thrombocytosis respectively. TLC values and CRP positivity shows significant relation with severity of thrombocytosis (p value = 0.01). No significant association was seen with haemoglobin levels and degree of severity of thrombocytosis. All 200 patients in our study had reactive thrombocytosis. 69.5% patients had underlying infectious etiology and 62% had infections with anemia. Iron deficiency anemia alone was seen in 14% patients. Other etiological causes included auto- immune (7.5%) and miscellaneous causes like Nephrotic Syndrome, Vasculitis, Thalassemia, Atypical Kawasaki Disease, Langerhans Cell Histiocytosis and Non- Hodgkin's Lymphoma. The platelet indices were compared with the degree of severity of thrombocytosis. Increase in the degree of thrombocytosis was associated with decrease in MPV, PDW, and P-LCR. All the platelet indices were observed to have significant negativecorrelation with the degree of severity of thrombocytosis. No thromboembolic complications were observed in our study even in cases with severe and extreme thrombocytosis, suggesting that no active intervention is required for thrombocytosis in these children. Reactive thrombocytosis is a transient process which resolves on treatment of the underlying etiology.

CONCLUSION

Thrombocytosis is a frequent finding in children due to the widespread use of automated blood cell counters. The elevated platelet count in majority of children is a benign, reactive phenomenon due to another underlying medical condition. Reactive thrombocytosis is observed transiently in conditions like post trauma, major surgery, acute bleeding or more sustained in case of iron deficiency, chronic infection, chronic inflammatory disease, or neoplasia. Primary or essential thrombocytosis (thrombocythemia), which is a true myeloproliferative disorder, is extremely rare in

children with an incidence of 1 per million children, and is a diagnosis of exclusion. In childhood, RT usually does not result in thromboembolic or haemorrhagic complications. Platelet indices are biomarkers of platelet activation. It can be used a prognostic and diagnostic marker of infectious etiology.

References

1. Schafer AI. Thrombocytosis. N Engl J Med. 2004;350: 1211- 1219.
2. Sutor AH. Thrombocytosis in childhood. Semin Thromb Hemost. 1995; 21: 330-339.
3. Dame C, Sutor AH. Primary and secondary thrombocytosis in childhood. British journal of haematology. 2005 1;129:165-77.
4. Wang JL, Huang LT, Wu KH, Lin HW, Ho MY, Liu HE. Associations of reactive thrombocytosis with clinical characteristics in pediatric diseases. Pediatr Neonatol 2011; 52: 261-266
5. Yadav D, Chandra J, Sharma S, Singh V. Clinicohematological study of thrombocytosis. Indian Journal of Pediatrics. 2010; 77(6): 643-7.
6. Subramaniam N, Mundkur S, Kini P, Bhaskaranand N, Aroor S. Clinicohematological study of thrombocytosis in children. ISRN Hematology. 2014; 29: 2014.
7. Matsubara K, Fukaya T, Nigami H, Harigaya H, Hirata T, Nozaki H. Age-dependent changes in the incidence and etiology of childhood thrombocytosis. Acta haematologica. 2004;111(3) :132-7
8. Yohannan MD, Higgy KE, al-Mashhadani SA, Santhosh-Kumar CR. Thrombocytosis. Etiologic analysis of 663 patients. Clin Pediatr 1994; 33: 340-343
9. Wang JL, Huang LT, Wu KH, Lin HW, Ho MY, Liu HE. Associations of reactive thrombocytosis with clinical characteristics in pediatric diseases. Pediatr Neonatol 2011; 52: 261-266
10. Maguire JL, deVeber G, Parkin PC. Association between iron-deficiency anemia and stroke in young children. Pediatrics 2007; 120: 1053-1057.