

Original Research Article

Etiology of Reactive Thrombocytosis in Paediatrics and Adults and its Correlation with MPV

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Abstract

Context: The measurements of platelet count, mean platelet volume (MPV), are routinely available nowadays. So this study was designed to study the causes of reactive thrombocytosis. *Aims:* To study the association of reactive thrombocytosis in different underlying clinical conditions and its age dependent aetiology. Also to study the relation between reactive thrombocytosis and platelet volume. *Settings and Design:* Prospective study. *Methods and Material:* This descriptive study was done on 500 patients with platelet count > 450,000/ μ l and the cause being reactive. Platelet count and MPV were measured at the time of hospitalization. *Statistical analysis used:* Cross tabulations for categorical data & correlation for continuous data in the SPSS ver.19 programme. *Results:* Most common cause of reactive thrombocytosis was Infections (28.8%), Tissue damage (16.4%), Iron deficiency anemia (16.2%), Malignancy (9.6%) and Inflammation (9.4%). In infections, bacterial infections (88%) were found to be more common. In children, infections 24.7%, anemia 21.9 %, tissue damage 21.9, haemolytic anemia 5.7%, inflammation (non-tuberculosis) 5.7%, poisoning 5.7% and tuberculosis 4.8% were common causes studied. *Conclusion:* Thrombocytosis is not rare in children. Causes of reactive thrombocytosis were almost similar in both the paediatrics and adults. Secondary thrombocytosis is common and predominately attributed to infection. This study demonstrated a higher level of platelet count and lower MPV in all the patients having reactive thrombocytosis.

Keywords: Thrombocytosis; Mean platelet volume; Platelet count.

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Introduction

Thrombocytosis refers to a platelet count above the normal value with the use of electronic cell counters and availability of a platelet count as part of a 'routine' blood count, thrombocytosis

is observed as an unexpected finding. Thus, an elevated platelet count has become a clinical problem for differential diagnosis. Thrombocytosis is classified into primary and secondary forms.¹ Primary thrombocytosis occurs in chronic myeloproliferative and myelodysplastic disorders².

Secondary thrombocytosis is due to a variety of underlying conditions.^{3,4} It affects up to 15% of hospitalized children.^{10,11,14-18} The aim of this study was to determine the aetiology and correlation with MPV of an elevated platelet count.

Materials and Methods

The study area selected for the study was in a tertiary care hospital. The study was conducted between the period June 2010 and September 2011 over a period of 16 months. A total of 500 patients who had come to OPD or was admitted in the hospital having reactive thrombocytosis were taken up for the study. All the samples which were received by the Central Diagnostic Laboratory, at the hospital with requisition form for investigations from the respective OPD's or Wards and were found to have accidental thrombocytosis. The cause for thrombocytosis was found to be reactive after taking the clinical details from the consulting physician's or surgeons. The information thus collected was compiled in the master chart & also subjected to statistical analysis. Statistical analysis was done using the Cross tabulations for categorical data & correlation for continuous data in the SPSS ver.19 programme

Following parameters were included in my study

Histogram: The sample was run on the automated

blood cell counter (Sysmex KX-21, K-1000) to know the platelet count and MPV

Inclusion criteria: All patients who had come to OPD and was admitted in hospital (booked or emergency) having reactive thrombocytosis (platelet count $>450,000/\mu\text{l}$), where requisition for laboratory investigations was received by Central Diagnostic Laboratory in the hospital were included in the study.

Exclusion criteria: Patients having platelet count more than 4.5 lakh/ μl , but this was normal for their age as in paediatrics. Patient having thrombocytosis due to Myeloproliferative disorders (polycythemia vera, chronic myeloid leukaemia, chronic idiopathic myelofibrosis, essential thrombocytosis). Patient having thrombocytosis which is autonomous (primary) and not reactive (secondary).

Results

A total of 500 patients with the platelet count $>450,000/\mu\text{l}$ was observed during the study period. The various underlying conditions associated with reactive thrombocytosis are listed in (Table 1). Also showing comparison of causes of reactive thrombocytosis in paediatrics and adults in (Table 2). Causes of reactive thrombocytosis were almost similar in both the paediatrics and adults. But

Table 1: Table showing causes of Reactive Thrombocytosis

S. No	Causes	No. of cases	Percentage %
1.	Infections	144	28.8
2.	Tissue damage		
	a. Trauma	42	8.4
	b. Fracture	16	3.2
	c. Post operative	14	2.8
	d. Burns	10	2.0
3.	Anemia		
	a. Iron deficiency anemia	81	16.2
	b. Megaloblastic anemia	1	0.2
4.	Neoplastic		
	a. Malignant	48	9.6
	b. Benign	2	0.4
5.	Inflammation (non-tuberculosis)	47	9.4
6.	Diabetes mellitus	32	6.4
7.	Tuberculosis	30	6.0
8.	Poisoning	10	2.0
9.	Haemolytic anemia		
	a. Thalassemia major	7	1.4
	b. Sickle cell anemia	2	0.4

S. No	Causes	No. of cases	Percentage %
10.	Post splenectomy	5	1.0
11.	Hemorrhage	4	0.8
12.	Myocardial infarction	2	0.4
13.	CCF (ASO positive)	1	0.2
14.	Low birth weight	1	0.2
15.	Drug reaction	1	0.2
	Total	500	100.0

Table 2: Table showing comparison of causes of reactive thrombocytosis in paediatrics and adults

S. No	Causes	0-18 years		>18 years		Total	
		No.	%	No.	%	No.	%
1.	Infections	26	18.1	118	82.0	144	100
2.	Tissue damage						
	a. Trauma	13	31.0	29	69.0	42	100
	b. Fracture	2	12.5	14	87.5	16	100
	c. Post operative	5	35.8	9	64.3	14	100
	d. Burns	3	30.0	7	70.0	10	100
3.	Anemia						
	a. Iron deficiency anemia	23	28.4	58	71.6	81	100
	b. Megaloblastic anemia	0	0	1	100.0	1	100
4.	Neoplastic						
	a. Malignant	2	4.2	46	95.8	48	100
	b. Benign	2	100.0	0	0	2	100
5.	Inflammation(non-tuberculosis)	6	12.8	41	87.2	47	100
6.	Diabetes mellitus	3	9.4	29	90.6	32	100
7.	Tuberculosis	5	16.7	25	83.3	30	100
8.	Poisoning	6	60.0	4	40.0	10	100
9.	Haemolytic anemia						
	a. Thalassemia major	6	85.8	1	14.3	7	100
	b. Sickle cell anemia	1	50.0	1	50.0	2	100
10.	Post splenectomy	0	0	5	100.0	5	100
11.	Hemorrhage	0	0	4	100.0	4	100
12.	Myocardial infarction	0	0	2	100.0	2	100
13.	CCF (ASO positive)	1	100.0	1	0	1	100
14.	Low birth weight	1	100.0	0	0	1	100
15.	Drug reaction	0	0	1	100.0	1	100
	Total	105	21.0	395	79.0	500	100

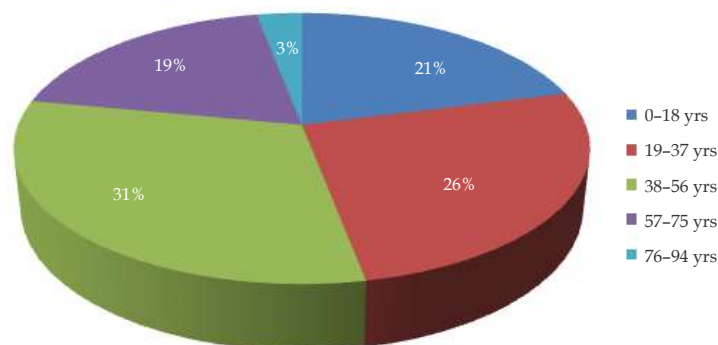


Fig. 1: No. of cases in relation to age group.

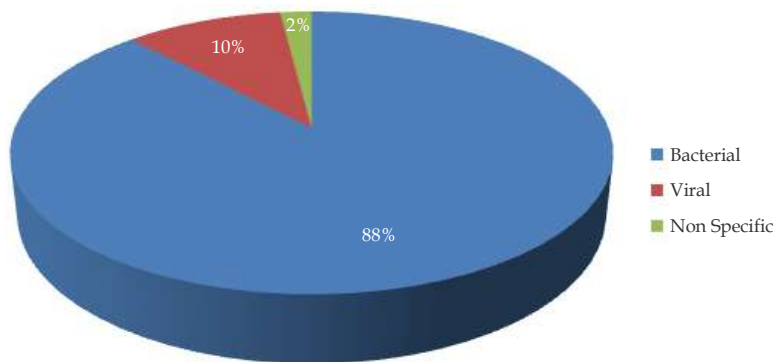


Fig. 2: No. of cases in relation to infection.

Table 3: Correlation of Platelet Count with MPV in all causes of reactive thrombocytosis (irrespective of the aetiology)

		Platelet count	MPV
Platelet count	Pearson Correlation	1	-0.128**
	Sig. (2-tailed)		0.004
	N	500	500
WBC	Pearson Correlation	-0.128**	1
	Sig. (2-tailed)	0.004	
	N	500	500

** Correlation is significant at the 0.01 level (2-tailed).

haemolytic anemia and poisoning were relatively more common with the paediatric age group. Majority of cases were in between 38–56 years (31%) and 19–37 years (26%) (Fig. 1). Almost equal number of cases was studied in both the genders, males (50.8%) and females (49.2%). The percentage of all causes of reactive thrombocytosis were more studied in males except Iron deficiency anemia and Burns which were more common in females. Most common cause of reactive thrombocytosis was Infections (28.8%), Tissue damage (16.4%), Iron deficiency anemia (16.2%), Malignancy (9.6%) and Inflammation (9.4%). In infections, bacterial infections (88%) were found to be more common (Fig. 2).

Discussion

In present study the most common cause of reactive thrombocytosis was found to be infection 28.8%, tissue damage 16.4%, iron deficiency anemia 16.2%, malignancy 9.6%, inflammation (non-tuberculosis) 9.4%, diabetes mellitus 6.4%, tuberculosis 6.0%, poisoning 2.0%, haemolytic anemia 1.8%, hemorrhage 0.8%, myocardial infarction 0.4%, Low birth weight and drug reaction 0.2% respectively.

The study also showed that among the infections most common was bacterial infection 87.5%, viral 10.4% and non-specific 2.1% respectively. Nagai T et al.⁵ reported a case of IDA with marked thrombocytosis (platelet > 100,000/cmm) that was complicated by central retinal vein occlusion. However in present study no case of IDA associated with complications were studied.

In the present study reactive thrombocytosis due to TB was found in 6.0% of the cases. However Bayness RD et al.⁶ have mentioned reactive thrombocytosis was common occurrence due to TB, while according to MC Donald⁷ and Omar et al.⁸ TB was an uncommon occurrence.

The aetiology of reactive thrombocytosis was studied in the paediatric age⁹ (0–18 years) comprising 105 cases (21%) out of total 500 cases. The causes of reactive thrombocytosis were found to be almost similar to adults.

In children, infections 24.7%, anemia 21.9%, tissue damage 21.9, haemolytic anemia 5.7%, inflammation (non-tuberculosis) 5.7%, poisoning 5.7% and tuberculosis 4.8% were common causes studied.

The similar study in paediatrics were done by the following authors Yohannan et al.,⁹ Heng et

al.,¹⁰ Vora et al.,¹¹ Chan et al.,¹² and Mantadakis et al.¹³ The causes of reactive thrombocytosis were found to be similar in all the studies.

However, the most common cause of reactive thrombocytosis in children, was infections, bacterial being more common. Presently, infections of the respiratory tract account for 60–80% cases of secondary thrombocytosis in children.^{10–12,15,17–19} followed by infections of the urinary²⁰ and gastrointestinal tracts, and of the bones.^{7,10–12,17}

From the non-infectious causes of secondary thrombocytosis, iron deficiency anemia was common, since it is the single most common nutritional deficiency worldwide (55.7% to 85.1% in different states in National Family Health Survey-III).²¹ In IDA, increased level of erythropoietin has been incriminated to have a possible role in stimulating megakaryopoiesis because of its structural homology with thrombopoietin.

Bilic and Bilic²¹ also reported that amino acid sequence homology of thrombopoietin and erythropoietin may explain the thrombocytosis in children in iron deficiency anemia.

In children with thalassemia 5.7% (none had undergone splenectomy) had thrombocytosis another frequent cause of thrombocytosis. Increased erythropoietin levels, stimulating megakaryopoiesis is possibly responsible for thrombocytosis in thalassemia. The findings were similar to the studied conducted by Dinesh yadav et al.²⁶

Tuberculosis was associated with reactive thrombocytosis in 4.8% cases. Tubercular infection has not been commonly reported to be a cause of reactive thrombocytosis in children, except in a study from Saudi Arabia and studied conducted by Dinesh yadav et al.²⁶

In this study single case of carcinoma testis associated with reactive thrombocytosis has been studied. Reactive thrombocytosis has also been described in children with other small, blue round cell tumors of childhood, such as neuroblastoma.²²

In our study no case of drug reaction causing reactive thrombocytosis in paediatrics age group has been studied. Miconazole, ciprofloxacin and tazobactam/piperacillin caused thrombocytosis in a single patient²³ since the platelet count started to increase immediately after initiation and dropped immediately after discontinuation of the drug.²³

Finally, reactive thrombocytosis may be due to multiple, simultaneous, causative factors. In

one paediatric series, 9% of cases of secondary thrombocytosis were multi-factorial.²⁴

Regarding the correlation of Platelet Count with MPV in all causes of reactive thrombocytosis (irrespective of the aetiology) showed significant inverse correlation. In normal subjects a non-linear relation between the platelet count and MPV has been found. The higher the platelet count, the lower the MPV. Correlation was also done between all the cases of reactive thrombocytosis and MPV. A significant negative correlation was found between them, $r = -0.128$, $p = 0.004$ (p -value significant at 0.01) (Table 3).

Similar study was done by Van der Lelie et al.²⁵ and Von dem Borne et al.²⁵ They found a mean platelet volume that is lower than that found in normal subjects. In normal subjects a non-linear inverse relation between platelet count and mean platelet volume has been found: the higher the platelet count, the lower the mean platelet volume. The low mean platelet volume in reactive thrombocytosis might be an extrapolation of this relation.

Conclusion

Among 500 cases the most common causes of reactive thrombocytosis were found to be Infections (28.8%), Tissue damage (16.4%), Iron deficiency anemia (16.2%), Malignancy (9.6%) and Inflammation (9.4%), Diabetes mellitus 6.4%, Tuberculosis 6.0%, Poisoning 2.0%, Haemolytic anemia 1.8%, Hemorrhage 0.8%, Myocardial infarction 0.4%, Low birth weight and Drug reaction 0.2% respectively. Among the infections, bacterial infection 87.5% was most common. The causes of reactive thrombocytosis in children were similar to adults. Most common cause being infections and iron deficiency anemia in children. Significant inverse correlation was seen between the platelet counts in the entire cases of reactive thrombocytosis studied and MPV ($r = -0.128^{**}$, $P = 0.004$).

Key Messages: Thrombocytosis is a frequent finding in hospitalized and ambulatory children and adults due to the widespread use of automated blood cell counters. Reactive thrombocytosis is very common and is due to a variety of conditions. The causes of reactive thrombocytosis were found to be almost similar in adults and children.

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