ORIGINAL ARTICLE

Thrombocytosis: Frequency and Etiologic Analysis

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ABSTRACT

Aim: To determine the frequency of thrombocytosis and to identify the underlying etiology.
Place and duration: This Cross sectional study was carried out at The Department of Pathology, Shalamar Hospital Lahore over a six months period from 1st January to 30th June 2014.
Methodology: All patients of both the sexes, ≥ 18 yrs of age having a platelet count > 450 x 10^3 / µL were identified during routine blood investigations. After confirming the platelet count by peripheral smear examination, detailed history, physical examination and relevant investigations were carried out to ascertain the underlying cause of elevated platelet count.
Results: A total of 23694 complete blood counts (CBCs) were performed during 6 months period from 1st January to 30th June 2014. Out of them 970 (4.09%) patients had thrombocytosis. Mean age in males was 41±14.6 (range 18-80) years while in females mean age was 52±17.3 (range 18-95) years. Mean platelet count in males was 558±106.7 (range 452-1319) x10^3/µL. In females, mean platelet count was 563±155.2(range 453-1580) x10^3/µL. Secondary thrombocytosis was seen in 99.4% cases. Infections were the most frequent cause of increased platelet count followed by iron deficiency, chronic inflammation and tissue damage.
Conclusion: Thrombocytosis is not an infrequent finding in routine hematology practice. Most commonly it is secondary to some underlying problem e.g. infections, inflammatory conditions, blood loss or malignancies.
Keywords: Thrombocytosis, Infections, Iron deficiency anemia, Essential thrombocythemia.

INTRODUCTION

Thrombocytosis is usually defined as a platelet count > 450x10^3/µL[1]. Thrombocytosis can occur due to a variety of causes and evaluation of a patient with thrombocytosis requires careful consideration of history, physical examination and other investigations. According to the pathogenic origin, thrombocytosis is classified into primary (essential) and secondary (reactive) forms–primary or clonal thrombocytosis is an unregulated abnormality of platelet production due to a clonal expansion of bone marrow progenitor cells. It is likely to be complicated by thromboembolism[2] or hemorrhage[3].

Secondary or reactive thrombocytosis is increased platelet count in response to various stimuli including systemic infections, inflammatory conditions, tissue damage, hemolysis and malignancies[4]. Although reactive thrombocytosis is generally not considered to be associated with clinical manifestations, recently several cases have been reported where thrombocytosis secondary to iron deficiency anemia led to the development of acute ischemic stroke[5,6]. This emphasizes the importance of prompt evaluation and treatment of the underlying cause of thrombocytosis to avoid serious consequences.

Many studies have been published regarding etiology of thrombocytosis in children but the local published data for adult patients are limited. We performed this study to determine the frequency and etiology of thrombocytosis in our adult population.

MATERIALS AND METHODS

This prospective, cross-sectional survey was carried out in the Department of Pathology Shalamar Hospital Lahore over a period of 6 months from 1st January to 30th June 2014. All patients of both the sexes, ≥18 yrs of age in whom thrombocytosis (platelet count >450x10^3/µL) was identified during routine blood investigations were included in the study. The approval of ethical committee was taken before the start of the study. Complete blood counts were performed on Sysmex XS 500i using EDTA anticoagulated blood. All the cases having a platelet count of >450x10^3/µL were included in the study. In case of patients having repeated thrombocytosis, only the initial value was taken. After confirming the platelet count by peripheral smear examination, detailed history, physical examination and relevant investigations were carried out to ascertain the cause. Data were recorded with the help of a

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proforma which included demographics of the patients, findings of history, physical examination and pertinent investigations. All the information was integrated to diagnose the underlying cause of thrombocytosis in every patient.

Thrombocytosis was divided into mild (>450 – 700 x 10^3 /µL), moderate (>700–900x10^3/µL), severe >900 and <1000x10^3/µL) and extreme thrombocytosis (>1000x10^3/µL).

Data were analyzed by using the software statistical package of social sciences (SPSS v 16). Nominal data e.g. sex and diagnoses were presented in frequency and percentages. Numerical data e.g. age and platelet counts were presented in the form of range, mean and standard deviation (SD).

RESULTS

A total of 23694 complete blood counts (CBCs) were performed during 6 months period from 1st January to 30th June 2014. Out of them 970 (4.09%) patients had thrombocytosis. Total CBCs and the frequency of thrombocytosis in males and females are shown in Table 1.

Mean age in males was 41±14.6 years (range 18-80 years) while in females mean age was 52±17.3 years (range 18-95 years). Mean platelet count in males was 558±106.7 (range 452-1319)x10^3/µL. In females, mean platelet count was 563±155.2 (range 453-1580) x10^3/µL.

Distribution of male patients according to severity of thrombocytosis is shown in Figure 1 which shows that most of the patients (87.8%) had mild thrombocytosis. Figure 2 shows distribution of female patients according to severity of thrombocytosis and again we see that majority of the patients had mild thrombocytosis (93%).

Extreme thrombocytosis was found in 1.7% males and 2% females and was associated with clonal thrombocytosis, splenectomy and autoimmune hemolytic anemia.

Etiology of thrombocytosis is shown in Table 2. Primary thrombocytosis was seen in 6 patients (0.6%), 4 of them had essential thrombocythemia, 1 had chronic myeloid leukemia and 1 patient had polycythemia rubra vera. Secondary thrombocytosis was the most common cause of thrombocytosis and was seen in 99.4% cases.

Table 1: Frequency of thrombocytosis

Gender	CBC	Thrombocytosis	%age
Male	9130	354	3.87
Female	14564	616	4.23
Total	23694	970	4.09

Fig: 1: Distribution of male patients according to severity of thrombocytosis.

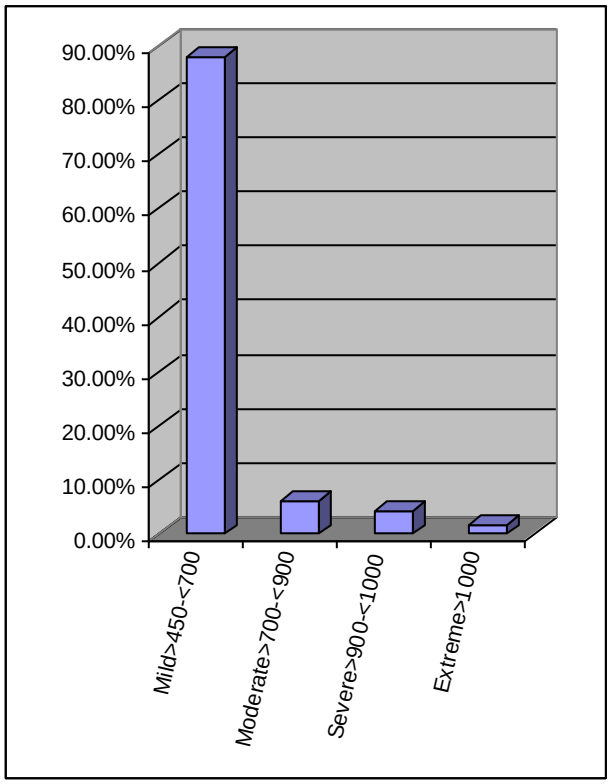

Fig. 2: Distribution of female patients according to severity of thrombocytosis.

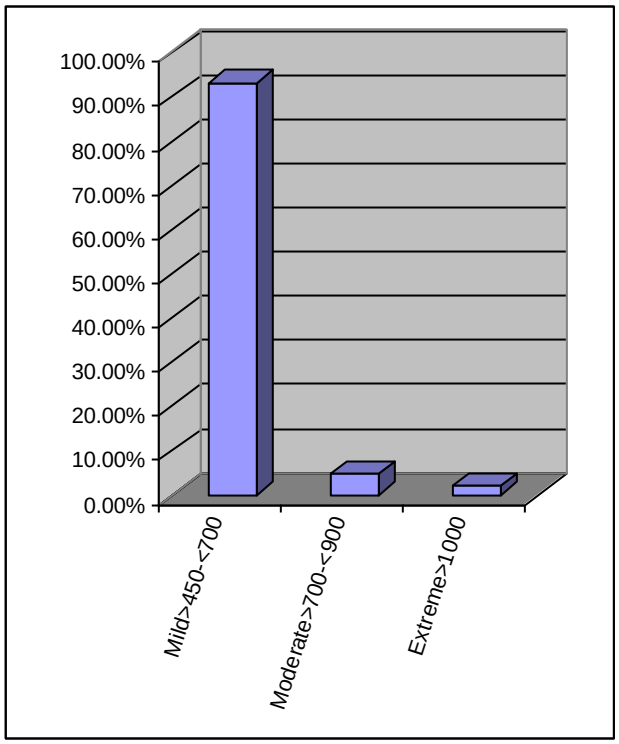

Table 2: Etiology of thrombocytosis

Etiology	Males *n*=354	Females *n* = 616	Total *n* = 970
Infection	176(49.7)	244 (39.6)	420 (43.3)
Iron deficiency anemia	56 (15.8)	120 (19.4)	176 (18.1)
Chronic inflammation	60 (16.9)	96 (15.5)	156 (16.1)
Tissue damage	30 (8.47)	88 (14.2)	118 (12.1)
Blood loss	6 (1.69)	32 (5.19)	38 (3.91)
Renal disorder	16 (4.51)	20 (3.24)	36 (3.71)
Malignancy	8 (2.25)	8 (1.29)	16 (1.64)
Clonal	2 (0.56)	4 (0.64)	6 (0.61)
Post splenectomy	0	2 (0.32)	2 (0.20)
AIHA	0	2 (0.32)	2 (0.20)

Abbreviation: AIHA, Autoimmune hemolytic anaemia.

DISCUSSION

Thrombocytosis is not an uncommon finding in routine haematology practice. Present study showed the incidence of thrombocytosis in our center to be 4.09%. Aydogan *et al*[7] reported thrombocytosis in 1.6% adult patients. The incidence of thrombocytosis depends upon the threshold for thrombocytosis. The cut off value of platelet count for thrombocytosis in their study was ≥ 500 x 10^3/µL which could be the reason of lower incidence in their population.

Previous studies showed male predominance in the incidence of thrombocytosis in adults as well as in children[7, 8]. Frequency analysis in our study showed slight female preponderance (4.23% v 3.87%). Multicentre studies with larger population size are required to validate these findings.

Current study showed that most of our patients had mild thrombocytosis (87.8% in males and 93% in females). This finding is in accordance with another study where mild thrombocytosis was reported in 85% of the patients[9].

Regarding etiology, clonal thrombocytosis was present in only 0.6% patients. Secondary thrombocytosis was the most frequent cause of increased platelet count and was found in 99.4% cases. This is in agreement with previous work where the incidence of primary thrombocytosis was reported as 3% and 3.3% respectively[10,7].

Among the secondary causes, infections were the most common cause of thrombocytosis in our study and were found in 43.3% cases. Aydogan *et al* [7] have reported infectious etiology in 50.1% of their patients. Rose *et al* [4] and Syed NN *et al*[11] have also reported infections as causative agents of thrombocytosis in 47.9% and 44.9% cases respectively. Interleukin 1(IL-1) and Thrombopoietin (TPO) levels increase during infections and lead to enhanced thrombopoiesis[12]. Thrombocytosis associated with infections is important because in addition to their role in hemostasis, platelets play an active part in antimicrobial host defense as they recognize bacteria, recruit phagocytic cells to the site of infection and secrete bactericidal mediators[13].

Iron deficiency anemia was found to be the cause of thrombocytosis in 18.1% cases. Another study reported iron deficiency anemia in 24.2% patients having thrombocytosis[7]. Iron deficiency is a known cause of reactive thrombocytosis even in the absence of inflammation or bleeding. Initially it was suggested that Erythropoietin (EPO) secretion is increased in response to anemia with resultant hypoxia and plays a synergistic role with TPO in platelet production[1] but recent studies suggest that iron deficiency causes enhanced thrombopoiesis independent of TPO levels and increases platelet aggregation which appears to be a physiological response to maintain or increase coagulation capacity in face of chronic bleeding[15].

Chronic inflammation was found to be associated with thrombocytosis in 16.1% cases. This is consistent with a previous study where chronic inflammation as a cause of thrombocytosis was reported in 13% patients[10]. The association of thrombocytosis with chronic inflammation is due to the release of cytokines such as IL-1, IL-4, IL-6, IL-11 and Tumor necrosis factor (TNF) which not only play a critical role in body's response to inflammatory conditions but also regulate thrombopoiesis. Many other markers of acute phase reaction, including C-reactive protein, ferritin and erythrocyte sedimentation rate are also significantly elevated in patients with reactive thrombocytosis and are in fact used to differentiate reactive from clonal thrombocytosis[1].

In current study, tissue damage (surgery or trauma) was found to be the cause of increased platelet count in 12.1% cases. This is supported by other studies where tissue damage was reported in 11.4% and 18% respectively[11,10]. Development of thrombocytosis is common after trauma and the possible causes are blood loss, adult respiratory distress syndrome or administration of steroids. Clinical evidence suggests that reactive thrombocytosis after severe trauma is associated with better survival than predicted by severity of illness score[16].

Blood loss was associated with thrombocytosis in 3.9% cases. It was seen more commonly in females than males (5.19% vs. 1.69%) and the most common site of bleeding in females was genital tract. Erythropoietin levels increase after blood loss and may play a synergistic role with Thrombopoietin in causing increased platelet count[17].

In the present study we found that renal disorders were associated with thrombocytosis in

3.71% patients. Santhosh-Kumar *et al*[10] reported renal disorders in 5% cases while analyzing 777 adult patients of thrombocytosis. Increased platelet count in chronic kidney disease is most likely mediated by EPO because studies have shown its ability to increase platelet production and activity in vivo and in vitro independent of its effects on erythropoiesis or iron metabolism[18].

Thrmbocytosis secondary to malignancy was present in 16(1.64%) patients. Previous studies have reported malignancy as a cause of thrombocytosis in 2.5% and 6% cases respectively[7,10]. Increased platelet count is associated with many solid tumors and often carries poor prognosis[19]. Recent studies suggest that tumors can stimulate platelet production and activation which in turn promote tumor growth and metastasis[20].

CONCLUSION

Thrombocytosis is not an infrequent finding in routine hematology practice. Most commonly it is secondary to some underlying problem e.g., infections, inflammatory conditions, blood loss or malignancies. Each patient who presents with an elevated platelet count should be carefully evaluated not only to differentiate primary from secondary thrombocytosis but also to identify the underlying cause in case of secondary thrombocytosis so that proper treatment can be instituted.

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