PREVALENCE OF THROMBOCYTOSIS IN ANEMIC PATIENTS OF AKHTAR SAEED TRUST HOSPITAL LAHORE, PAKISTAN

Alia Waheed,[1] Abdullah Farooq Khan,[2] Nosheen Salahuddin,[3] Raana Akhtar,[4] Zainab Yousaf,[5] Ahsan Farooq Khan[6]

Abstract

Background: Anemia is the one of the most widespread disorder all across the world characterized by low haemoglobin levels in blood causing reduced oxygenation of red blood cells and consequently producing symptoms such as lethargy, malaise and shortness of breath according to its severity. Thrombocytosis is a condition in which the number of platelets is increased and it can be identified by same methods which we use for the diagnosis of anemia. In previous studies, it has been found that thrombocytosis is associated with mild, moderate and severe forms of anemia.

Methods: In this cross-sectional study, the patients with anemia who were less than 18 years old were included. Samples were collected from the outdoor and indoor patients of Akhter Saeed Trust Hospital Lahore, who were not treated with any therapy to cure anaemia. About 2-3 ml of venous blood was drawn and sent to laboratory for CBC. Data regarding the MCV, MCH, and platelet count was collected on structured performa.

Result: From total 224 patients, 64.73% were males, and 35.27% were females. Statistically, the p-value showed a significant association between all age groups [first (p =0.001), second (p =0.001), third (p =0.001), and fourth (p =0.001)], and genders [males (p =0.001), and females (p =0.001)] with all (mild, moderate and severe) anemias. The prevalence of thrombocytosis in anemia patients was 23.57%.

Conclusion: The present study concluded that the patients having iron deficiency anemia can also be affected with thrombocytosis.

Keywords: Anemia, Thrombocytosis, Iron deficiency anemia

How to cite: *Waleed A, Khan AF, Salahuddin N, Akhtar R, Yousaf Z, Khan AF. Prevalence of Thrombocytosis in Anemic Patients of Akhtar Saeed Trust Hospital Lahore, Pakistan. JAIMC;20(4): 207-211*

Red blood cell counts below the normal range essentially determine the presence of anemia.[1] However, a heamoglobin concentration to the advised more inadequate criteria established by epidemiological population surveys or the local laboratory defines clinical anemia daily. It is convenient to utilize the World Health Organization's (WHO) heamoglobin criteria for making valid comparisons between various nations.[2] According to the WHO, anemia affects nearly two billion people worldwide or almost one-third of the roughly seven billion-person global population.[3]

Anemia is classified into three major categories. Microcytic, macrocytic and normocytic anemia. Microcytic cells are smaller than usual due to decreased heamoglobin synthesis, which is the main component of red blood cells. Lack of globin (thalassemia), restricted iron delivery to the heme group of heamoglobin (anemia of inflammation), insufficient iron delivery to the heme group (iron-deficiency anaemia), and errors

1. *Department of Pathology, Akhtar Saeed Medical & Dental College, Lahore, Pakistan*
2. *Department of Orthopaedic Surgery, Akhtar Saeed Medical & Dental College, Lahore, Pakistan.*
3. *Department of Obstetrics and Gynaecology, Akhtar Saeed Medical and Dental College, Lahore, Pakistan*
4. *Department of Histopathology, University College of Medicine and Dentistry, University of Lahore, Pakistan.*
5. *Department of Human Genetics & Molecular Biology, University of Health Sciences, Lahore, Pakistan*
6. *Department of Dermatology, Shalamar Hospital, Lahore, Pakistan*

Correspondence:
Zainab Yousaf, *Department of Human Genetics & Molecular Biology, University of Health Sciences, Lahore, Pakistan.*
Email: zainabyousaf00@gmail.com

Submission Date: 15-09-2022
1st Revision Date: 23-11-2022
Acceptance Date: 12-12-2022

in the synthesis of the heme group are the leading causes of microcytic anemia (sideroblastic anaemias). Patients with the trait thalassemias exhibit varied microcytosis, which is more apparent in those with the trait-2 type, and no or very little anemia. More pronounced anemia characterizes heamoglobin H disease, frequently with a heamolytic component, and is caused by deletion of or mutations in three α-chain genes. Lack of formation of the α-chain in heamoglobin Bart's causes hydrops fetalis because both fetal and adult hemoglobin is not produced.[4]

The biological processes of respiration, energy production, DNA synthesis, and cell division depend on iron. The human body has developed many mechanisms to conserve iron, including recycling iron after red blood cells break down and holding onto iron in the absence of an excretion mechanism. A decrease in iron reserves that occurs before overt iron deficiency anemia or that persists without worsening is referred to as an iron deficiency. Low iron levels are linked to anemia and the appearance of microcytic hypochromic red cells in iron-deficiency anaemia, a more severe illness. No matter how full the stores are, iron cannot be delivered to erythroid precursors, according to iron-restricted erythropoiesis. In situations of anemia of chronic inflammation, seen in individuals with autoimmune disorders, cancer, infections, and chronic kidney diseases, stores may be regular or even augmented due to iron sequestration. It is common for elderly patients and people with chronic kidney illness to have both iron deficiency and anemia of chronic diseases.[5]

Macrocytic anaemias have a wide range of causes. However, they can be separated into megaloblastic anaemias and non-megaloblastic anaemias. These characteristics include the presence of hypersegmented neutrophils and oval-shaped macrocytic erythrocytes (macroovalocytes) as opposed to spherical macrocytic erythrocytes. Megaloblastic anemia results from a flaw in DNA synthesis and repair, typically brought on by a shortage of or disruption of thymidine synthesis. As a result, uracil is mistakenly substituted for thymidine in developing hematopoietic progenitor cells. This disrupts normal nuclear development in the bone marrow, causing the nuclear stage to lag behind cytoplasmic maturity.[6] There are other causes of megaloblastic anemia than B12 and folate deficiency. A wide range of medications falls under this category, which can affect DNA synthesis and the absorption, metabolism, or processing of one or both vitamins. Other antifolates, such as methotrexate, can cause functional folate deficit, leading to megaloblastic alterations.[6]

Anemia is diagnosed based on heamoglobin concentration, mean corpuscular volume (MCV), mean corpuscular heamoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Iron binding capacity, serum iron, and ferritin are a few other chemical tests to confirm iron decrease. Platelet count can be performed manually on an automatic analyzer to identify thrombocytosis. An increase in platelet count of more than 450,000/ul shows the condition of thrombocytosis, and a decrease in platelet count below 150,000/ul indicates the state of thrombocytopenia. It is possible to develop thrombocytosis in anemic patients.[7,8]

The most common anemia in hospitalized and chronically ill individuals is anemia of inflammation, also known as anemia of chronic disease. Patients with chronic immune activating conditions, such as cancer, autoimmune disorders, and infections, are more likely to experience it. Obesity, chronic lung disorders, congestive heart failure, chronic renal disease, and others have recently been added to the list. Hepcidin, the master regulator of iron homeostasis, and inflammation-inducible cytokines prevent intestinal iron absorption and lead to iron retention in reticuloendothelial cells, which results in iron-restricted erythropoiesis. Additional factors contributing to anemia of inflammation in a disease-specific pattern include decreased erythrocyte half-life, inhibited erythropoietin response to anaemia, and suppression of erythroid cell differentiation by inflammatory mediators.[9]

When CBCs are taken for any unrelated cause, thrombocytosis, a rise in the number of circulating platelets, is typically detected as an incidental anomaly. Thrombocytosis is divided into primary (or essential)

and secondary (or reactive) types depending on where it originates.[10] In this study, we examined thrombocytosis in severe, moderate, and mild anemic patients. Statistical analysis showed the presence or absence of a correlation between anemia and thrombocytosis in different age groups and genders.

METHODS

This cross-sectional study was conducted in one year duration i.e. January 2022 to December 2022 at Akhter Saeed Trust Hospital Lahore. The research included less than 18 years old patients of both genders. Patients taking folic acid, iron therapy, or blood transfusion were excluded. All samples were collected from the outdoor and indoor patients of Akhter Saeed Trust Hospital Lahore. Sampling technique used was non-probability convenient sampling. After approval from the hospital ethical committee, 224 patients fulfilling inclusion criteria were included. About 2-3 ml of venous blood was drawn for complete blood count (CBC) in ethylenediamine tetraacetic acid (EDTA) vials. CBC was performed on all the samples on automated heamatology analyzer (Sysmex XP-100), and total erythrocyte count, heamoglobin, MCV, MCH, and MCHC were noted along with platelet count. Samples with heamoglobin less than 7 g/dl, 7-10 g/dl, and greater than 10-12 g/dl were denoted as severe, moderate, and mild anaemia, respectively. Platelet count of more than 450,000/ul was considered thrombocytosis. To verify the exact count and to rule out the platelet clumping blood smear was performed. Anemic stage and platelet count were noted from all the anemic samples. Results were recorded in a proforma and entered in SPSS 25.0. All the quantitative variable were presented as frequency and percenteage and the p-value was calculated using chi square test to find any association between anemia and thrombocytosis.

RESULTS

Of the 224 patients included in our study, 79 (35.3%) were females, and 145 (64.7%) were males. All patients were divided into four age groups depending on the data. The first age group consisted of patients less than one year old, and the second age group consisted of patients between one to six years, the third age group consisted of patients between seven to twelve years, and the fourt age group consisted of thirteen to eighteen years old patients (Table 1).

In first age group 48.76%, 40.48% and 11.21% developed mild, moderate and severe anemia respectively. The patient with age between seven to twelve years, 46.75% developed mild, 30.31% moderate and 22.94% severe anemia. The frequency of mild, moderate and severe anemia in pateints with age group between thirteen to eighteen years was 47.77%, 33.35% and 18.88% respectively (Table 2). Similarly, in patient with age between one to six years 47.36%, 26.31% and 26.31% developed mild, moderate and severe anemia respectively. Among females, 49.45% developed mild anemia, 40.5% moderate, and 10.1% severe anemia. In males, 47.6% presented with mild, 38.6% moderate, and 13.8% developed severe anemia. The chi-square test was performed to find any association.

Table 1: *Frequency and percentage of anemic patients in different age groups*

Age group	Age (years)	Frequency (n=)	Percentage (%)
First	< 01	47	20.98
Second	01 to 06	74	33.00
Third	07 to 12	84	37.51
Fourth	13 to 18	19	8.48

Table 2: *Association between anemia and thrombocytosis in both age groups*

Age Groups	Type of anemia	Prevalence of anemia (%)	P-value
First	Mild	48.76	0.001*
	Moderate	40.48	
	Severe	11.21	
Second	Mild	47.36	0.001*
	Moderate	26.31	
	Severe	26.31	
Third	Mild	46.75	0.001*
	Moderate	30.31	
	Severe	22.94	
Fourth	Mild	47.77	0.001*
	Moderate	33.35	
	Severe	18.88	

*P < 0.05 was considered significant.

The p-value of <0.05 was considered significant. The association between anemia and age groups were expressed (Table 2). The statistical significant association was also found in anemic males and females (Table 3). Thrombocytosis was common in mild, moderate, and severe anemic patients. The prevalence of thrombocytosis was 23.57% in anemic patients while 76.43% anemic patients had normal platelet count.

Table 3: *Association among both anemic genders and thrombocytosis*

Gender	Type of anemia	Prevalence of anemia (%)	P-value
Male	Mild	47.58	0.001*
	Moderate	38.62	
	Severe	13.79	
Female	Mild	49.36	0.001*
	Moderate	40.50	
	Severe	10.12	

*P < 0.05 was considered significant.

Table 4: *Prevelence of thrombocytosis in anemic patient*

Type of anemic patients	Thrombocytosis (%)	No Thrombocytosis (%)
Mild anemic	8.11	76.43
Moderate anemic	10.43	
Severe anemic	5.03	
Total	23.5	

DISCUSSION

The present study was done on 224 patients, and all patients were suffering from iron deficiency anemia. The prevalence of thrombocytosis in mild anemia, moderate anemia, and severe anemia were 8.11%, 10.43% and 5.03% respectively while 76.43% patients had no thrombocytosis. The overall prevelnce of thrombocytosis in all anemic patients were 23.57%. Moreover, it was independent of gender, age groups, and the state of anemia. Hemendra Mhadgut and Hadiza Galamdia did a study to check the association between anemia and thrombocytosis. They analyzed 4896 subjects, and 1225 were anemic among them. The mean hemoglobin concentration was 10.21 g/dl, and the mean platelet count was 319.24 ×10^9/l. 10.37% of anemic patients developed thrombocytosis, and the p-value compared with the control group showed the statistical significance between iron deficiency anemia and thrombocytosis.[11] A study was done on 45 years old chronically anemic female. She was not suffering from any other comorbidity except chronic anemia. Her heamoglobin level was 6.5 g/dl, and her platelet count was very high, around 880,000/ul. On different radiological scans, venous and arterial thrombosis was observed due to the severe anemia associated with thrombocytosis.[12]

Another study was done on 198 patients suffering from bowel disease. Platelet and RBC indices were measured in 13.6% of patients with thrombocytosis, and they analyzed ferritin level, iron level, and soluble transferrin receptor-ferritin index. The correlation was checked between thrombocytosis and all other parameters. It was concluded that the correlation between iron deficiency and thrombocytosis seems significant, as the p-value was less than p =0.05. It was reported that iron deficiency could lead to secondary thrombocytosis. An additional parameter highlighted in that study, the effects of iron therapy, was observed on heamoglobin count and platelet count. Inflammatory bowel diseased patients were treated with carboxymaltose, and all previously suffered secondary thrombocytosis. All patients were assessed for platelet count, megakaryopoiesis growth factors, and erythropoietin. It was observed that there was no increase in megakaryopoiesis growth factors, but heamoglobin levels were elevated. Platelet count becomes normal due to decreased platelet aggregation and P – selectin expression.[13] Among all the studies mentioned above, through different analysis and trials, it is clear that mild, moderate, and severe anemia can cause thrombocytosis, which is also expressed in the present study.

The generalizability of the results of this study should be done after considering the limitations of the study being single centered and limited sample size. Therefore, further studies on larger sample size is required to further explore this association.

CONCLUSION

The present study concluded that the mild, moderate and severe type of anemic patients can develop thrombocytosis. So, it is clear that if patients suffer from anemia, especially iron defeciency anemia, they are more prone to developing secondary thrombocytosis.

REFERENCES

1. Wintrobe MM. Wintrobe's clinical hematology: Lippincott Williams & Wilkins; 2008.
2. WHO C. Assessing the Iron Status of Populations. Geneva. World Health Organization. 2007.
3. Pasricha S. Iron deficiency can occur at any age and has a number of different causes Pasricha SS, et al. MJA. 2010; 193: 525-532.
4. DeLoughery TG. Microcytic Anaemia. New England Journal of Medicine. 2014;371(14):1324-31.
5. Camaschella C. Iron-deficiency anaemia. New England journal of medicine. 2015;372(19):1832-43.
6. Green R, Dwyre DM, editors. Evaluation of macrocytic anaemias. Seminars in hematology; 2015: Elsevier.
7. Tefferi A, Hanson CA, Inwards DJ, editors. How to interpret and pursue an abnormal complete blood cell count in adults. Mayo Clinic Proceedings; 2005: Elsevier.
8. George-Gay B, Parker K. Understanding the complete blood count with differential. Journal of PeriAnesthesia Nursing. 2003;18(2):96-117.
9. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood, The Journal of the American Society of Hematology. 2019;133(1):40-50.
10. Yadav D, Chandra J, Sharma S, Singh V. Clinicohematological study of thrombocytosis. The Indian Journal of Pediatrics. 2010;77(6):643-7.
11. Mhadgut H, Galadima H, Tahhan HR. Thrombocytosis in iron deficiency anaemia. Blood. 2018; 132: 4985.
12. Pathiyil DV, Henry RA, Joseph J, Oomen AT, Kakkra JJ. Severe iron deficiency anemialeading to thrombocytosis with arterial and venous thrombosis. Cureus. 2021;13(9).
13. Voudoukis E, Karmiris K, Oustamanolakis P, Theodoropoulou A, Sfiridaki A, Paspatis GA, et al. Association between Thrombocytosis and iron deficiency anemiain inflammatory bowel disease. European journal of gastroenterology & hepatology. 2013; 25(10): 1212-6.