Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Clinical Hematology

Platelet Count in Adults with Iron Deficiency Anemia and Its Correlation with Serum Iron Parameters: An Observational Study at a Tertiary Care Center in Northwestern India

Govind R. Patel[1*], Gopal R. Prajapati[2]

[1]Department of Clinical Hematology, Dr. SN Medical College, Jodhpur, Rajasthan, India
[2]Department of Emergency Medicine, Dr. SN Medical College, Jodhpur, Rajasthan, India

DOI: 10.36347/sjams.2022.v10i06.009 | **Received:** 03.05.2022 | **Accepted:** 11.06.2022 | **Published:** 16.06.2022

***Corresponding author:** Dr. Govind R. Patel
Department of Clinical Hematology, Dr. SN Medical College, Jodhpur, Rajasthan, India

Abstract **Original Research Article**

Background: Iron deficiency anemia (IDA) is the most common and potentially treatable nutritional anemia in the world. The platelet count is often unpredictable in IDA. It may lead to reactive thrombocytosis and rarely thrombocytopenia. In children with IDA, abnormal platelet counts were seen in several studies. However, studies evaluating abnormalities of platelet count in adults with IDA are scarce. ***Objectives:*** This study was aimed to evaluate platelet count abnormalities in adults with IDA and to correlate platelet count with serum iron parameters. ***Material and Methods:*** This was a prospective observational study conducted on 294 adults (age ranged from 18 to 85 years) with newly diagnosed IDA attending outdoor and indoor at a large tertiary care center in Northwestern India, from the April 2018 to March 2020. All patients were subjected to evaluation by meticulous history, thorough clinical examination, and hematological investigations including platelet count and serum iron parameters. ***Results:*** IDA was more common in females (63.9%). The initial platelet counts were normal in 176 (59.9%) patients. Thrombocytosis and thrombocytopenia were detected in 99 (33.7%) and 19 (6.4%) patients, respectively Majority of thrombocytosis cases (48.5%) were associated with moderate IDA. Mild thrombocytosis was the most common category (60.6%), followed by moderate (28.3%), severe (8.1%) and profound (3%) thrombocytosis. Majority of thrombocytopenia cases were mild (57.9%), and all cases of severe thrombocytopenia were observed in severe IDA. Platelet count had a significant negative correlation with serum iron and transferrin saturation ($p<0.01$) while a significant positive correlation was obtained with total iron-binding capacity ($p<0.05$). ***Conclusion:*** This study showed that thrombocytosis was a common platelet abnormality in adults with IDA. In addition, mild thrombocytopenia was not so rare in these patients. Furthermore, serum iron, transferrin saturation and total iron-binding capacity were the most important parameters affecting the platelet count.

Keywords: Iron deficiency anemia, platelet count, thrombocytosis, thrombocytopenia, serum iron parameters, serum iron, transferrin saturation, total iron-binding capacity, serum ferritin.

INTRODUCTION

Iron is an essential element for survival of almost all living organisms as it participates in a wide variety of metabolic processes, including oxygen transport, deoxyribonucleic acid synthesis, and electron transport [1]. Iron deficiency is incriminated in the causation of a wide variety of pathophysiological changes in the body resulting in diverse clinical manifestations. Iron deficiency is the potentially treatable global public health problem affecting both developing and developed countries at all ages. It results from the depletion of iron stores in the body. When the iron supply is insufficient to maintain normal levels of hemoglobin, iron deficiency anemia (IDA) develops. IDA is the most common type of anemia worldwide accounting for 50% of anemia cases [2]. It constitutes a major cause of morbidity, especially in developing countries like India.

Data have suggested that there exists a relationship between iron metabolism and thrombopoiesis [3]. Platelet parameters display several changes in IDA [4]. Moderate IDA is well known to cause reactive thrombocytosis [5-7] while severe IDA may lead to thrombocytopenia, suggesting a biphasic pattern of response [8-10]. Both thrombocytosis and thrombocytopenia may improve after iron therapy [6, 7,

9, 10]. Iron is postulated to play a key role in the synthesis of platelets and in the regulation of thrombopoiesis [11]. However, exact mechanism leading to these pathological changes is not well established [12]. Platelet parameters are usually altered in both reactive process as well as in neoplastic overproduction [13]. Infections, acute bleeding and IDA are the common causes of reactive thrombocytosis [14]. The amino acid sequence homology of thrombopoietin (TPO) and erythropoietin (EPO) may explain the phenomenon of thrombocytosis in patients with IDA [15]. There is an abundant evidence that megakaryocytic and erythroid cell lineages share a common progenitor cell. According to the hypothesis of stem cell competition, chronic EPO stimulation can lead to increased red cell production at the expense of platelet production resulting into thrombocytopenia [16].

As most of the studies on thrombocytosis in IDA are from developed countries where nutritional anemia is less prevalent, these studies do not truly reflect the proportion of cases of thrombocytosis due to underlying iron deficient state. Moreover, most of the previous studies reported platelet count abnormalities in children with IDA [7, 9, 15-19], whereas studies evaluating platelet counts in adults with IDA are scarce. Furthermore, there are very few reports in literature on correlation between platelet count and serum iron parameters, especially in India. We, therefore, conducted this study to evaluate the platelet count abnormalities in a large number of adults with IDA, and also to assess the correlation between serum iron parameters and platelet count. To the best of our knowledge, there was no such detailed previous study in this part of India.

MATERIAL AND METHODS

Study design and study population

The present study was a prospective observational study conducted in the Department of Clinical Hematology at Dr. SN Medical College and associated Mathura Das Mathur Hospital, Jodhpur, Rajasthan, India over the period of 24 months from April 2018 to March 2020. Our study included 294 patients of both sexes and ages 18-85 years with newly diagnosed IDA attending the inpatient or outpatient department Patients who had received recent blood transfusion or hematinics and those who had associated conditions known to cause thrombocytosis or thrombocytopenia were excluded from the study.

Study procedure

All included patients were subjected to meticulous history taking and thorough clinical examination. Analysis of complete blood count, peripheral blood smear, reticulocyte count, and serum iron parameters including serum iron, total iron-binding capacity (TIBC), transferrin saturation and serum ferritin was performed for all subjects. Bone marrow examination including iron stain was performed in selected patients of equivocal diagnosis of IDA, and also in selected cases of thrombocytosis to rule out suspected myeloproliferative neoplasm or of thrombocytopenia to rule out suspected immune thrombocytopenia. Furthermore, a complete work up to rule out other causes of thrombocytosis or thrombocytopenia was done in every case. IDA was diagnosed by presence of hemoglobin level <12 g/dL in women and <13 g/dL in men, and microcytic hypochromic red cell morphology on peripheral smear along with either serum ferritin level <15 µg/L or serum ferritin level >15 µg/L with serum iron <51 µg/dL or transferrin saturation <16% and TIBC >390 µg/dL; irrespective of age and sex (cut-offs were taken based on controls established in laboratory). Serum ferritin value of 15 µg/L was also considered as cut off point for iron-deficient state [20]. Anemia and thereby IDA was graded according to World Health Organization (WHO) classification as follows: mild IDA, hemoglobin 10.0 g/dL to lower limit of normal (Women: 11.9 g/dL; men: 12.9 g/dL); moderate IDA, hemoglobin 7.0 to 9.9 g/dL; and severe IDA, hemoglobin <7.0 g/dL. Thrombocytosis was defined as platelet count more than 450 x 10^9/L [21] while thrombocytopenia was defined by platelet count <150 x 10^9/L. The classification used to grade thrombocytosis was: mild (platelet count 450-700 x 10^9/L), moderate (platelet count 700-900 x 10^9/L), severe (platelet count 900-1000 x 10^9/L), and profound (platelet count >1000 x 10^9/L) [22]. Thrombocytopenia was categorized as mild (platelet count 101-150 x 10^9/L), moderate (platelet count 51-100 x 10^9/L) and severe (platelet count ≤50 x 10^9/L) [23].

Ethics

The study protocol was approved by the Institutional Ethics Committee before conducting the study. A written informed consent was obtained from each included patient after explaining the nature of the study and the benefit from it. Patient confidentiality was maintained during all research procedures.

STATISTICAL ANALYSIS

All analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 21.0 for Windows (Version 21.0 for Windows; SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as means ± standard deviation (SD). Categorical variables were expressed in terms of number (n) and percent (%). The correlation between platelet count and serum iron parameters was analyzed by Pearson's correlation test. A two-tailed P <0.05 was considered to be statistically significant.

RESULTS

Demographic data

The mean age was 47.3 (± 14) years with range of 18 to 85 years. Out of 294 patients enrolled in this study, 106 (36.1%) were males and 188 (63.9%) were females with male to female ratio of 0.56:1. Most common age group (32.7%) affected was 41-50 years. Both males (32.1%) as well as females (33%) were affected most commonly in this age group. Elderly people above 60 years were accounted for 12.9% of subjects (Table 1).

Table-1: Age and sex distribution of all cases of iron deficiency anemia (n=294).

Age groups (years)	All cases (n=294) n (%)	Male (n=106) n (%)	Females (n=188) n (%)
18-20	11 (3.7)	3 (2.8)	8 (4.3)
21-30	48 (16.3)	14 (13.2)	34 (18.1)
31-40	78 (26.5)	15 (14.2)	63 (33.5)
41-50	96 (32.7)	34 (32.1)	62 (33)
51-60	23 (7.8)	11(10.4)	12 (6.4)
61-70	20 (6.8)	16 (15.1)	4 (2.1)
71-80	13 (4.4)	9 (8.5)	4 (2.1)
>80	5 (1.7)	4 (3.8)	1 (0.5)
Total	294 (100)	106 (100)	188 (100)

Hematological data

Table 2 summarizes the hematological data of patients. The mean hemoglobin level was 8.5 (± 1.3) g/dl. Mild anemia was observed in 33.3% of patients, whereas 43.9% had moderate anemia and 22.8% had severe anemia. Mean platelet count of study subjects was 445.8 (± 132.6) x 10^9/L.

Table-2: Hematological parameters in patients with iron deficiency anemia

Hematological parameters	Mean±SD
CBC parameters	
Hemoglobin (g/dL)	8.5±1.3
RBC count (×10^{12}/L)	3.3±0.6
Hematocrit (%)	29.3±3.6
MCV (fL)	63.7±5.4
MCH (pg)	21.7±3.2
MCHC (g/dL)	28.4±1.7
RDW (%)	18.6±2.3
Reticulocyte count (%)	0.94±0.46
WBC count (×10^9/L)	7.41±2.5
Platelet count (×10^9/L)	445.8±132.6
Iron parameters	
Serum iron (µg/dL)	28.6±6.3
Serum ferritin (µg/L)	10.2±2.6
TIBC (µg/dL)	499.4±43.9
Transferrin saturation (%)	6.3±2.8

Abbreviations: CBC, Complete blood count; RBC, Red blood cell; MCV, Mean corpuscular volume; MCH, Mean corpuscular hemoglobin; MCHC, Mean corpuscular hemoglobin concentration; RDW, Red cell distribution width; WBC, White blood cells; TIBC, Total iron-binding capacity.

Platelet count was normal in 176 (59.9%) patients. Thrombocytosis and thrombocytopenia were detected in 99 (33.7%) and 19 (6.4%) patients, respectively. Thrombocytosis was consistently associated with all grades of IDA. Thrombocytosis cases were highest (48.5%) in moderate IDA, followed by mild IDA (27.3%) and severe IDA (24.2%). Most of these patients (60.6%) had mild thrombocytosis while moderate thrombocytosis was observed in 28.3%. Severe grade thrombocytosis was present in 8.1% patients, whereas only 3 (3%) patients had profound thrombocytosis. Severe IDA had no patients with severe and profound thrombocytosis. Thrombocytopenia was also consistently associated with all grades of IDA. The percentage of cases showing thrombocytopenia was 36.8% (7/19 cases) for mild IDA, and 31.6% (6/19 cases) each for moderate IDA and severe IDA. Most of cases had mild thrombocytopenia (57.9%) while moderate thrombocytopenia and severe thrombocytopenia were seen in 31.6% and 10.5% cases, respectively. All cases of severe thrombocytopenia were documented only in severe IDA (Table 3).

Table-3: Distribution of patients of different grades of IDA according to categories of platelet count abnormalities

Platelet count abnormalities	Grade	Mild IDA (n=98)	Moderate IDA (n=129)	Severe IDA (n=67)	Total (n=294)
Normal	All	64	75	37	176
Thrombocytosis	Mild	13	31	16	60
	Moderate	9	11	8	28
	Severe	4	4	0	8
	Profound	1	2	0	3
	All	27	48	24	99
Thrombocytopenia	Mild	5	3	3	11
	Moderate	2	3	1	6
	Severe	0	0	2	2
	All	7	6	6	19

Abbreviations: IDA, Iron deficiency anemia.

Correlation between platelet count and serum iron parameters

Pearson's correlation between platelet count and iron parameters are shown in Table 4. Platelet count showed a statistically significant negative correlation with serum iron ($r = -0.255$, $p<0.01$) and transferrin saturation ($r = -0.353$, $p<0.01$), while a statistically significant positive correlation was obtained between platelet count and TIBC ($r = 0.241$, $p<0.05$). Platelet count also had a negative correlation with serum ferritin, but this was not statistically significant ($r = -0.123$, $p>0.05$).

Table-4: Pearson's correlation between platelet count and serum iron parameters in patients with IDA.

Parameters	Correlation Coefficient (r)	p-value
Serum iron	-0.255	0.006
Transferrin saturation	-0.353	0.003
TIBC	0.241	0.025
Serum ferritin	-0.123	0.112

Abbreviations: IDA, Iron deficiency anemia; TIBC, Total iron-binding capacity

DISCUSSION

Our study showed that IDA was more common in females (63.9%), with female to male ratio being 1.77:1. Similar results were obtained by Kuku *et al.* [24] and Mishra *et al.* [25] in their studies. In general, IDA is more common in females worldwide. Inadequate intake of dietary iron, lack of awareness of iron deficiency, excessive menstrual loss and pregnancy are the possible causes of increased prevalence of IDA in females. On the other hand, iron deficiency was observed to be more prevalent in Indian males (55%-88% in different states) in National family health survey III, as quoted by Yadav *el al.* [26]. In fact, we also found that males were more commonly (76.3%) affected than females among elderly age group (>60 years). However, determining the overall prevalence of IDA among different population in the study area was not possible by the present study design, as we included only isolated IDA cases.

In the present study, thrombocytosis was seen in 99 (33.7%) patients. The contribution of IDA to thrombocytosis as well as the frequency of thrombocytosis in IDA is only scarcely reported. This is probably on account of the facts that most of these studies on thrombocytosis were from developed countries where IDA is not that much prevalent. There is a wide variation in the frequency of thrombocytosis associated with IDA reported in the medical literature. In pediatric patients with IDA, thrombocytosis was observed in 24.5% by Ray *et al.* [18], 39.2% by Duzgun *et al.* [17] and 69.5% by Fahim *et al.* [19]. Various studies in adults with IDA reported reactive thrombocytosis in 13.3%-65% cases [4, 11, 12, 24]. In the present study, we have taken adults patients of both sexes and our frequency of cases with thrombocytosis lies well within the reported range.

Although the relationship between IDA and thrombocytosis remains unclear, however, various studies suggested that megakaryopoiesis was stimulated in IDA. The duration and the degree of IDA may play a role in determining the mechanism of platelet production. In moderate IDA, the increase in platelet count may be secondary to increased rate of influx of precursor cells into the megakaryocyte compartment with an increased rate of efflux, shortening of megakaryocyte maturation, stem-cell shunt due to inhibition of erythropoiesis resulting in increased production of other pluripotent cells (hemostatic compensatory mechanism), stimulator effect of transferrin on megakaryopoiesis, inhibition of iron on megakaryocyte maturation or a combination of these

factors [27-29]. Although EPO is the primary growth factor for the red cell lineage which regulates the survival, proliferation, and differentiation of erythroid precursors, increased EPO production in IDA and its structural homology to TPO amino acid sequence have been incriminated as a possible mechanism for thrombocytosis in IDA [15]. A few studies showed that iron deficiency causes megakaryocytic expansion and stimulates megakaryocytic differentiation, independently from TPO, interleukin-6 and interleukin-11[30]. One study assayed serum levels of TPO, EPO, leukemia inhibiting factors, IL-6, IL-11 but none of these cytokines except for EPO showed any effect on reactive thrombocytosis in IDA [5]. Experimental studies demonstrated that iron replacement causes a decline in EPO and platelet counts simultaneously [5]. An animal study also reported the stimulatory effect of EPO on megakaryopoiesis [31].

Reactive thrombocytosis found in IDA is mostly of mild to moderate degree. Platelet count rarely exceeds 700 x 10^9/L [18]. In our study also, mild (60.6%) and moderate (28.3%) thrombocytosis was documented in majority of cases (88.9%), whereas severe thrombocytosis and profound thrombocytosis was observed in 8.1% and 3% cases, respectively. Similar findings were also seen in a previous study by Ray *et al*. [18].

In the current study, thrombocytopenia was seen in 19 (6.4%) patients. Both cases with severe thrombocytopenia were noticed in patients with severe IDA. This finding was in line with result of a study by Kadikoylu et al where two patients with thrombocytopenia had hemoglobin levels <6.5 g/dL [11]. Although we did not measure it in this study, thrombocytopenia might be related to high serum EPO levels. It was stated that thrombocytopenia in combination with IDA is not common, and the mechanism of such finding is not known, although theories exist about stem cell competition. Studies have shown that chronic EPO stimulation can lead to red cell production at the expense of platelet production, and thrombocytopenia is seen in severe IDA because of high EPO response [16, 32]. In other studies, it was reported that increased levels of endogenous EPO would stimulate megakaryopoiesis in moderate IDA, whereas high EPO response could cause thrombocytopenia in severe IDA [5, 6, 10]. While EPO therapy increases platelet counts initially, higher EPO doses cause thrombocytopenia in humans and rats with chronic renal failure [33].

Our study demonstrated a statistically significant negative correlation of platelet count with serum iron and transferrin saturation. The result coincides with the result of other previous studies [11, 24, 34-36]. There was a statistically significant positive correlation between platelet count and TIBC in our study. Fahim *et al*. also found a significant correlation between TIBC and platelet count [19]. On the contrary, Kadikoylu *et al*. [11] and Chalise *et al*. [36] found no significant correlation between TIBC and platelet count in their studies. Serum ferritin measurement is one of the most accurate diagnostic test for IDA [34]. In the current study, no significant correlation was exhibited between serum ferritin and platelet count. Our finding was consistent with those in studies by Kuku *et al.* [24] and Chalise *et al*. [36]. However, a significant negative correlation of platelet count with serum ferritin was observed in studies by Ray *et al*. [18] and Fahim *et al*. [19]. Hence, our study suggested that decreased serum iron and transferrin saturation, and thereby increased TIBC might stimulate megakaryopoiesis in IDA. Moreover, iron may have an inhibitor effect on platelet counts.

There are few limitations in our study. First, the comparison of platelet count and serum iron parameters of patients with non-anemic control subjects was not done. Second, there were no groups such as thalassemia and megaloblastic anemia to compare platelet count with iron parameters in this study. Finally, we didn't reevaluate statistically significant parameters in the end of treatment.

CONCLUSION

This study showed that thrombocytosis was a common platelet abnormality in adults with IDA. In addition, mild thrombocytopenia was not so rare in these patients. Furthermore, the most important parameters affecting platelet count in adults with IDA were serum iron, transferrin saturation and TIBC. Platelet count was negatively correlated to serum iron and transferrin saturation, whereas it was positively correlated to TIBC. A large and multicenter study of platelet count in adult patients with IDA is recommended to explore and generalize the results.

REFERENCES

1. Abbaspour, N., Hurrell, R., & Kelishadi, R. (2014). Review on iron and its importance for human health. Journal of research in medical sciences: the official *journal of Isfahan University of Medical Sciences*, *19*(2), 164–174.
2. Liu, K., & Kaffes, A. J. (2012). Iron deficiency anaemia: a review of diagnosis, investigation and management. *European journal of gastroenterology & hepatology*, *24*(2), 109–116.
3. Lamparelli, R. D., Baynes, R. D., Atkinson, P., Bezwoda, W. R., & Mendelow, B. V. (1988). Platelet parameters. Part I. Platelet counts and mean platelet volume in normal and pregnant subjects. *South African medical journal*, *73*(1), 36–39.
4. Chethan, S. S., & Veena, S. (2019). Red cell parameters and platelet parameters in women with iron deficiency anemia. *International Journal of Scientific Research*, *8*(10), 22-24.

5. Akan, H., Güven, N., Aydogdu, I., Arat, M., Beksaç, M., & Dalva, K. (2000). Thrombopoietic cytokines in patients with iron deficiency anemia with or without thrombocytosis. *Acta haematologica*, *103*(3), 152–156.
6. Beguin, Y. (1999). Erythropoietin and platelet production. Haematologica, 84(6), 541–547.
7. Hiçsönmez, G., Süzer, K., Süloglu, G., & Dönmez, S. (1978). Platelet counts in children with iron deficiency anemia. *Acta haematologica*, *60*(2), 85–89.
8. Sonneborn, D. (1974). Letter: Thrombocytopenia and iron deficiency. Annals of internal medicine, 80(1), 111.
9. Perlman, M. K., Schwab, J. G., Nachman, J. B., & Rubin, C. M. (2002). Thrombocytopenia in children with severe iron deficiency. *Journal of pediatric hematology/oncology*, *24*(5), 380–384.
10. Loo, M., & Beguin, Y. (1999). The effect of recombinant human erythropoietin on platelet counts is strongly modulated by the adequacy of iron supply. *Blood*, *93*(10), 3286–3293.
11. Kadikoylu, G., Yavasoglu, I., Bolaman, Z., & Senturk, T. (2006). Platelet parameters in women with iron deficiency anemia. Journal of the National Medical Association, 98(3), 398–402.
12. Chandna, A., Sharma, J., Sangwaiya, A., Samal, S., Sankala, M., & Garg, S. (2014). Iron deficiency anemia with thrombocytosis: A diagnostic challenge. International Journal of Healthcare and Biomedical Research, 03(1), 43-46.
13. Dan K. (2005). Thrombocytosis in iron deficiency anemia. *Internal medicine (Tokyo, Japan)*, *44*(10), 1025–1026.
14. Evstatiev, R., Bukaty, A., Jimenez, K., Kulnigg-Dabsch, S., Surman, L., Schmid, W., Eferl, R., Lippert, K., Scheiber-Mojdehkar, B., Kvasnicka, H. M., Khare, V., & Gasche, C. (2014). Iron deficiency alters megakaryopoiesis and platelet phenotype independent of thrombopoietin. American journal of hematology, 89(5), 524–529.
15. Bilic, E., & Bilic, E. (2003). Amino acid sequence homology of thrombopoietin and erythropoietin may explain thrombocytosis in children with iron deficiency anemia. Journal of pediatric hematology/oncology, 25(8), 675–676.
16. Akkermans, M. D., Uijterschout, L., Vloemans, J., Teunisse, P. P., Hudig, F., Bubbers, S., Verbruggen, S., Veldhorst, M., de Leeuw, T. G., van Goudoever, J. B., & Brus, F. (2015). Red Blood Cell Distribution Width and the Platelet Count in Iron-deficient Children Aged 0.5-3 Years. *Pediatric hematology and oncology*, *32*(8), 624–632.
17. Düzgün, S., Yildirmak, Y., & Cetinkaya, F. (2005). Neutrophil hypersegmentation and thrombocytosis in children with iron deficiency anemia. *The Turkish journal of pediatrics*, *47*(3), 251–254.
18. Ray, S., Chandra, J., & Sharma, S. (2019). Clinico-hematological study of abnormalities of platelet count in children with iron deficiency anemia. *International Journal of Contemporary Pediatrics*, *6*(4), 1519-1523.
19. Fahim, F. M., Helal, S. R., Fathalla, E., Saeed, A. N., & Galal, S. M. (2022). Platelets abnormalities in children with iron deficiency anemia. *Journal of Current Medical Research and Practice*, *7*, 22-28.
20. Goddard, A. F., James, M. W., McIntyre, A. S., Scott, B. B., & British Society of Gastroenterology (2011). Guidelines for the management of iron deficiency anaemia. *Gut*, *60*(10), 1309–1316.
21. Skoda, R. C. (2009). Thrombocytosis. Hematology. American Society of Hematology. Education Program, 159–167.
22. Dame, C., & Sutor, A. H. (2005). Primary and secondary thrombocytosis in childhood. *British journal of haematology*, *129*(2), 165–177.
23. Williamson, D. R., Albert, M., Heels-Ansdell, D., Arnold, D. M., Lauzier, F., Zarychanski, R., Crowther, M., Warkentin, T. E., Dodek, P., Cade, J., Lesur, O., Lim, W., Fowler, R., Lamontagne, F., Langevin, S., Freitag, A., Muscedere, J., Friedrich, J. O., Geerts, W., Burry, L., … PROTECT collaborators, the Canadian Critical Care Trials Group, and the Australian and New Zealand Intensive Care Society Clinical Trials Group. (2013). Thrombocytopenia in critically ill patients receiving thromboprophylaxis: frequency, risk factors, and outcomes. *Chest*, *144*(4), 1207–1215.
24. Kuku, I., Kaya, E., Yologlu, S., Gokdeniz, R., & Baydin, A. (2009). Platelet counts in adults with iron deficiency anemia. Platelets, 20(6), 401–405.
25. Mishra, S. K., Marasini, S., Gupta, B. K., Agrawal, K. K., & Gautam, N. (2018). Prevalence of Iron Deficiency Anemia in Anemic Patients: A Hospital Based Study. Journal of Universal College of Medical Sciences, 6(2), 41–45.
26. Yadav, D., Chandra, J., Sharma, S., & Singh, V. (2010). Clinicohematological study of thrombocytosis. *Indian journal of pediatrics*, *77*(6), 643–647.
27. Choi, S. I., & Simone, J. V. (1973). Platelet production in experimental iron deficiency anemia. *Blood*, *42*(2), 219–228.
28. Choi, S. I., Simone, J. V., & Jackson, C. W. (1974). Megakaryocytopoiesis in experimental iron deficiency anemia. Blood, 43(1), 111–120.
29. Stenberg, P. E., & Hill, R. J. (1999). Platelets and megakaryocytes. In: Lee, G. R, Foerster, J., Lukens, J., & et al (Eds.), Wintrobe's Clinical Hematology, 10th ed (pp. 615-660). Baltimore, Williams Wilkins.
30. Holbro, A., Volken, T., Buser, A., Sigle, J. P., Halter, J. P., Passweg, J. R., Tichelli, A., & Infanti, L. (2017). Iron deficiency and thrombocytosis. *Vox sanguinis*, *112*(1), 87–92.
31. Wolf, R. F., Gilmore, L. S., Friese, P., Downs, T., Burstein, S. A., & Dale, G. L. (1997). Erythropoietin potentiates thrombus development

in a canine arterio-venous shunt model. *Thrombosis and haemostasis*, *77*(5), 1020–1024.

32. Stohlawetz, P. J., Dzirlo, L., Hergovich, N., Lackner, E., Mensik, C., Eichler, H. G., Kabrna, E., Geissler, K., & Jilma, B. (2000). Effects of erythropoietin on platelet reactivity and thrombopoiesis in humans. Blood, 95(9), 2983–2989.
33. Eschbach, J. W., Abdulhadi, M. H., Browne, J. K., Delano, B. G., Downing, M. R., Egrie, J. C., Evans, R. W., Friedman, E. A., Graber, S. E., & Haley, N. R. (1989). Recombinant human erythropoietin in anemic patients with end-stage renal disease. Results of a phase III multicenter clinical trial. *Annals of internal medicine*, *111*(12), 992–1000.
34. Park, M. J., Park, P. W., Seo, Y. H., Kim, K. H., Park, S. H., Jeong, J. H., & Ahn, J. Y. (2013). The relationship between iron parameters and platelet parameters in women with iron deficiency anemia and thrombocytosis. *Platelets*, *24*(5), 348–351.
35. Han, D. D., Ma, C., Zhao, L., Gao, Y. J., & Su, Y. H. (2018). [Relationship between Iron Metabolism and Platelet Parameters in Patients with Iron Deficiency Anemia]. *Zhongguo shi yan xue ye xue za zhi*, *26*(6), 1738–1741.
36. Chalise, S., Acharya, N., & Pradhan, S. B. (2019). Correlation between Iron Parameters and Platelet Parameters in Iron Deficiency Anemia. *Journal of Institute of Medicine Nepal*, *41*(3), 35–38.