Original Article

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Study of Platelet Parameters in Women with Iron Deficiency Anaemia

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Abstract

Background: Several changes in platelet parameters have been reported in Iron deficiency anemia. But underlying mechanism between iron metabolism and megakaryopoiesis is not yet clear. Hence the aim of the study is to evaluate relation between iron and platelet parameters in women with IDA. *Materials and Methods:* Sixty women with mean age of 33 ± 11 (16 – 78) years with IDA were studied. The relationship between serum iron parameters such as iron, iron-binding capacity, iron saturation and ferritin and platelet parameters such as platelet counts, platelet crit, mean platelet volume (MPV), platelet distribution width (PDW) and large platelet (LPLT) were evaluated by using Pearson correlation and stepwise logistic regression tests. *Results:* Thrombocytosis and thrombocytopenia were noted about (77.46% and 22.54%) respectively. Platelet counts were inversely correlated with serum iron and transferrin saturation ($p<0.05$). Other iron parameter revealed no significant relationship with any platelet parameters. There was a linear relationship between platelet counts and platelet crit ($p<0.001$) but inverse relationships betweenplatelet counts and both mean platelet volume and ironsaturation ($p<0.001$, for both). Also there were a linear relationship between platelet distribution width and mean platelet volume ($p<0.001$) and an inverse correlationbetween platelet distribution width, Mean platelet volume, Platelet crit with both mean corpuscular volume and Mean corpuscular hemoglobin concentration p<O.O01). Platelet crit was linearly correlated with platelet count mean platelet volume, and LPLT ($p<0.05$). There is no significant correlation between platelet crit with any iron parameter. *Conclusion:* This study concludes important iron parameter affecting the platelet was serum iron and transferrin saturation. Patient with severe anemia had higher platelet count, PCT and MPV. Changes in platelet parameter are due to low levels of tissue iron. Decrease iron saturation also stimulates megakaryopoiesis and iron has inhibitory effect on platelet counts.

Keywords: Iron Deficiency Anemia; Platelets; Women; Thrombocytosis.

Introduction

Iron deficiency anemia (IDA) is the most common in our community [1]. Iron is the basic element for the production of new red blood cells (RBC). If it is not used in erythropoiesis it is stored as ferritin. Serum ferritin levels only estimates total body iron stores [2]. Iron deficiency anemia (IDA) occurs due to increased body requirements, insufficient iron supply (depending on dietary iron intake and duodenal absorption) and blood losses [3]. It has been estimated that 30% of the world population suffers from IDA and most of them live in the developing countries [3]. In IDA, several changes in platelets have been reported and a relationship between iron metabolism and thrombopoiesis are made out [4]. IDA may cause variable platelet dysfunction and this can be reversed by iron therapy [4,5]. A diphasic platelet response was identified in patients with IDA. Moderate IDA is usually associated with reactive thrombocytosis. Thrombocytopenia can be seen in patients with severe IDA, especially when hemoglobin level is <7 g/dL [5]. Several studies reported an inverse relationship between mean platelet volume and platelet counts in

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patients with IDA. This may be related to morphological features of platelets [6-8]. Iron not only induces erythropoiesis but also suppresses megakaryopoiesis [9]. Small thrombocytes lead to thrombocytosis that occurs in IDA due to not be suppressed megakaryopoiesis [10]. Platelet abnormality usually disappears after iron therapy [9,10]. In this study, a comparison is made between serum iron, total iron binding capacity, Transferrin saturation, serum ferritin with platelet count, platelet crit, mean platelet volume, platelet distribution width and large platelet (LPLT). The aim of this study is to evaluate the important determinant of iron parameter causing platelet abnormality in women with IDA. In addition, we compared iron parameters, red blood cell parameters, and platelet parameters in mild, moderate and severe IDA (Hb<7 g/dl).

Methodology

Overview of Study Design

The present cross sectional Analytical study was undertaken at Department of Pathology in our institution, a tertiary care center, conducted over the period of 3 months from March 2016 to May 2016, after obtaining approval from the Institutional Ethical Committee.

Study Population

A total of 60 female patients diagnosed as Iron deficiency anaemia (Hemoglobin Level < 11 g/dL, Serum ferritin level <15µg/L, Iron Saturation <16%)with altered platelet count (Thrombocytopenia and Thrombocytosis) were included in this study. Patients with acute hemorrhage and infections, pregnancy, neoplastic and chronic inflammatory disorders such as rheumatoid arthritis, ankylosing spondylitis and systemic lupus erythematosus were excluded.

Collection of Data

Hematological parameters such as Total count, Differential count, Hemoglobin, PCV, MCV, MCH, MCHC, RDW, Platelet count and PDWwere analyzed within 1-2 hours of collection by using Automated cell counter. (HoribaABX Pentra ES60, Japan). Serum iron parameters, other than ferritin, were measured bySpectrophotometric Method and ILAB-900 Instrument.Serum ferritin level were measured by Chemiluminescent Method and ImmuliteInstrument.

Statistical Analysis

Data were recorded in excel sheet and analyzed using SPSS software. Pearson's correlation test and Stepwise logistic regression test were performed for each significant correlation between platelet parameters and the studied iron variables. P values <0.05 were considered as statistically significant.

Observation and Results

Totally sixty women with mean age of 33 ± 11 (16 – 78) with IDA were enrolled in this study. The most common causes of IDA were dysfunctional uterine bleeding and chronic gastrointestinal bleeding which constituted 55.7%(33 patients)) followed by acute blood loss in trauma, perinatal blood loss and surgical blood loss together constituted about 36.1%. Remaining other minor causes such as increased demand in pregnancy, lactation etc constituted about 8.2%.

The mean hemoglobin level was 6.2 g/dl and out of 60 women with IDA, 13 patients had severe IDA (Hb< 7 g/dl). Table 1 summarizes complete blood count (CBC) data of the patient. Of the 60 women with IDA, Thrombocytosis and thrombocytopenia were detected in 77.46% and 22.54% respectively.

Pearson correlation shown in Table 2 and Table 3 showed inverse correlation between platelet count and hemoglobin, hematocrit, mean platelet volume, ferritin,iron saturation, mean corpuscular volume, mean corpuscularhemoglobin concentration; and linear correlationsbetween platelet counts and platelet crit, with red cell distribution width.

Logistic regression test, shown in Table 4, showed linear relationship between platelet counts andplatelet crit (p<0.00l) but inverse relationships between platelet counts and mean platelet volume, serum ferritin and iron saturation (p<0.001, for both) and there was no correlation between platelet counts and other iron parameters (p>0.05).

Platelet Crit

In Pearson's correlation test, inverse correlation between PCTand serum iron (p<0.001), Tfsat, Hb, HCT, MCH (p<0.05,for all), MCHC (p<0.001) and linear correlation between PCT and PLT, MPV(p<0.001, for both), and LPLT (p<0.05) was detected.

Mean Platelet Volume

In Pearson's correlation test, inverse correlation

between MPV with platelet count, platelet distribution width Hb, MCHC ($p<0.05$), HCT, and ($p<0.001$), whereas linear correlation between MPV and PCTand LPLT ($p<0.001$, for both) was detected. There was no correlation between other studied iron parameters and MPV.

Table 1: Hematological data in all enrolled patients

Hematologic Parameters	Mean ±SD	Reference Range
White blood cell counts ($\times 10^9$/ l)	4.5 ± 2.6	4.0–10.0
Hemoglobin (g/dl)	5.8 ± 1.7	12–16
HCT (%)	18.7 ± 6.7	36–48
MCV (fl)	63.9 ± 6.8	80–94
MCH (pg)	19.8 ± 2.6	26–33
MCHC (g/dl)	29.5 ± 1.8	33–37
RDW (%)	17.7 ± 2.3	11.5–14.5
PLT (_103/µl)	527.3 ± 93.4	150–450
PCT (%)	53.3 ± 9.1	N
MPV (fl)	9.1 ± 2.3	9–13
PDW (%)	43.7 ± 6.4	N
LPT ($\times 10^3$/ µl)	7.7 ± 4.1	N
Serum ferritin (µg/l)	3.2 ± 0.87	6–85
Serum iron (µg /dl)	21.3 ± 9.5	60–180
Iron-binding capacity (µg /dl)	468.5 ± 53.6	250–450
TF sat (%)	4.2 ± 1.8	N

Note: N: not determined reference range.

Table 2: Pearson's coefficients (r) between platelet parameters and iron parameters

	PLT	PCT	MPV	PDW
Serum iron	-0.453*	-0.449**	-0.279	-0.028
Serum ferritin	0.289	0.008	-0.056	-0.037
TIBC	0.093	-0.073	0.570	-0.067
Tfsat	0.427	0.276*	0.077	0.033

Notes: PLT - platelet count; Tfsat - transferrin saturation; PCT - platelet crit; MPV - mean platelet volume; PDW - platelet distribution width.; TIBC- total iron binding capacity, *$p<0.05$ and **$p<0.001$.

Table 3: Pearson's coefficients (r) between platelet parameters and red blood cell parameters

	PLT	PCT	MPV	PDW
Hb	-0.342	-0.436*	-0.357*	-0.175
Hct	-0.156	-0.229*	-0.539**	-0.022
MCV	-0.432	-0.125	0.193	-0.143
MCH	-0.298*	-0.478*	-0.037	-0.176
MCHC	-0.415*	-0.153**	-0.267*	-0.117
RDW	0.131	0.183	0.037	0.187

Note: RDW, red cell distribution width;MCV-Mean Corpuscular Volume, MCHC-Mean Corpuscular Hemoglobin Concentration; MCH-Mean Corpuscular Hemoglobin; Hct-Hematocrit; *$p<0.05$ and **$p<0.001$.

Table 5: Stepwise logistic regression test

	PLT	PCT	MPV	PDW	MCV	Iron Saturation
PLT						
β	-	0.717	-0.264	-	-	-0.196
p	-	<0.001	<0.001	-	-	<0.001
PCT						
β	0.893	-	-	-	-0.127	-
p	<0.001	-	-	-	<0.005	-
MPV						
β	-0.361	-	-	0.418	-	-
p	<0.001	-	-	<0.001	-	-
PDW						
β	-	-	0.687	-	-0.533	-
p	-	-	<0.001	-	<0.001	-

Âeta(â) – correlation index.

Platelet Distribution Width

In Pearson's correlation test, linear correlation between PDW and mean corpuscular Volume, mean corpuscular hemoglobin concentration,LPLT ($p<0.001$) and inverse correlation between platelet distribution width and mean platelet volume.There was no correlation between other studied iron parametersand PDW.

Discussion

Iron deficiency is the primary cause of anemia. IDA generally occurs in children due to inadequate intake and women primarily due to blood loss. Menstruating women losses 0.6–2.5% of iron per day.[11] Gastrointestinal tract blood loss is the most common cause of IDA (2-5%) adult males and post menopausal females [12]. In this study most common cause of IDA was dysfunctional uterine bleeding (30.25%), pregnancy, lactation and blood loss during delivery constitutes about (50.55%) similar to park et al and others [9,13]. The severity of IDA related thrombocytosis was moderate ($476 – 897 \times 10^9/l$) [13].

Among 60 patients with iron deficiency anemia, thrombocytosis and thrombocytopenia were about (77.46% and 22.54%) respectively.In the present study, Iron parameters such as serum iron, transferrin saturation and TIBC also had effects on platelets which was similar to the findings reported by Park et al [9]. In the present study, the platelet count was inversely correlated with serum iron, transferrin saturation and mean platelet volume ($p <0.05$) and linearly correlated with platelet crit ($p < 0.001$) and also platelet crit showed inverse correlation with serum iron and transferrin saturation ($p < 0.001$ and $p < 0.05$). From this it was found that, serum iron and transferrin saturation were the important determinants of platelet in IDA and it can be correlated with the studies of Park et al and Kadikoylu et al [9,14].

There was no correlation between serum ferritin and platelet parameters made out. Platelet crit was inversely correlated with serum iron ($r = - 0.348$ and $p < 0.001$) and no correlation between iron parameters with MPV and PDW(Statistically significant). This was similar to the findings of Kuku et al [15]. Similar to the findings of Park et al, Present study showed that there was no significant relation between platelet and Hb or HCT but the platelet crit and MPV was inversely correlated with Hb, HCT, Platelet count, PCT and MCHC [9]. In contrast, Kuku et al reported platelet count was inversely correlated with PCT, Hb, HCT, MCV, MCH, and MCHC. Thus patients with severe IDA showed higher platelet count, PCT and MPV which was due to low levels of tissue iron [15].

Similar to our finding, studies reported that MPV was significantly related to platelet morphologic features and its activation can lead to thromboembolic phenomenon [13,16,17]. There were few theories which could explainthromboembolic risks in IDA such as higher viscosity of blood because of microcytic red blood cells, or oxidative stress causing platelet aggregations due to anemia [18,19]. Therefore, further investigation is required to determine MPV as a risk factor of thromboembolic complication in IDA.

Iron parameters had inhibitory effect on platelet production especially with the cases of IDA [20]. Also, iron supplements in the early part of treatment caused transient thrombocytopenia in iron deficiency patients [21]. Iron parameters play the major and an essential role in the late stages of thrombopoiesis [22]. It was reported that duration and severity of iron deficiency directly affects megakaryopoiesis [23]. In moderate IDA, the megakaryocyte mitosis index was increased and the maturation time got shortened. In severe IDA, the megakaryocyte number was decreased whereas the size increased. This suggests that megakaryocytes with higher ploidy are correlated with higher MPV [24]. Bilic's study suggested that erythropoietin (EPO) can attribute to changes in platelet parameters due to uniform homology of amino acid sequence between thrombopoietin (TPO) and EPO [25]. In contrast, few other studies have shown that the homology of amino acid sequence between TPO and EPO causes the cross-reactivity at the level of Mpl and do not explain the relationship between iron deficiency and thrombocytosis [26,27].

The present study can be correlated to few other studies which have reported that increased EPO would stimulate megakaryopoiesis in moderate IDA, whereas high EPO response could cause thrombocytopenia in severe IDA [28,29]. Further studies on EPO and platelet parameters may be helpful to state the role of EPO in megakaryopoiesis. In this study, the important iron parameters affecting PLT were found to be serum iron and Tfsat and patients with severe IDA had higher PLT, PCT, and MPV.

Conclusion

Both thrombocytosis and thrombocytopenia may occur with IDA. Important iron parameter affecting platelet was serum iron and transferrin saturation. Several changes thatoccur in platelet parameters are due to morphological features of platelets. When the

level of tissue iron decrease, the platelet count will get increased. It was also found that iron affects thrombopoiesis by inhibiting plateletproduction.

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