

## Platelet Parameters in Children with Iron Deficiency Anemia before and After Treatment

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### Abstract

#### Background

In iron deficiency anemia (IDA), several changes in platelets indices have been reported in a number of studies. The aim of this study was to evaluate the platelet parameters in children with iron deficiency anemia before and after treatment.

**Materials and Methods:** This cross-sectional study was conducted over a period of 18 months. A total of 110 IDA subjects were selected from those who referred to the pediatric hematology clinic, Zahedan, Iran, during the study period. Age range was 12 months to 16 years were selected. Children in the study were given a 3 month course of oral iron as ferrous sulfate with a daily dose of 4mg/kg/day in 2 divided doses. Platelet parameters including platelet count and mean platelet volume (MPV) were measured before and after treatment. The obtained data were analyzed using SPSS software version 20.0.

**Results:** The mean age of the boys and girls was 4.30±4.55 years and 2.46±3.21 years, respectively. The results of the paired t- test showed that platelet means were 409±120 × 10<sup>3</sup> /mm<sup>3</sup> and 384±99 × 10<sup>3</sup> /mm<sup>3</sup> before and after treatment (p<0.001), respectively. The means of MPV increased from 8.07±1.01 fL before treatment to 8.86±1.05 fL after treatment (p<0.001), respectively.

#### Conclusion

The result of this study showed that treatment of iron deficiency anemia leads to decreased platelet count and increased MPV.

**Key Words:** Children, Iron deficiency anemia, Platelet parameters.

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## 1- INTRODUCTION

Iron deficiency (ID) is the most common global nutritional deficiency and the highest populations at risk are infants and young children (1). Developmental delays and behavioral disturbances are some of the iron deficiency indicators that increase in young children compared to other age groups of population (2). IDA in young children is recognized as a major public health issue and the most prevalent form of micronutrient deficiency worldwide (3). Children aged 12- 24 months have the highest risk of iron-deficiency anemia. In this age group, the prevalence of anemia is very high because this is the period of rapid growth, which requires a high intake of iron that may not be covered by their diet (1).

Akbari et al., in a study reported that the prevalence of IDA in the age group of less than 6 year-old from 0.2% to 57.3%, in age group of 6–18 years from 1.7% to 53.6% (4). There is conflicting evidence with regard to the relationship between sex and IDA in children. Yemen and India found a higher prevalence of IDA in girls than boys (5). But Western Kenya and Haiti found boys to be more at risk (6, 7). Pasricha reported that the prevalence of IDA among boys was varied between 2.4% and 37.8% and among girls from 1.7% to 21.4%. (8). Some factors for childhood anemic condition are folate, vitamin A, and vitamin B12 deficiency, malaria infection, hookworm infestation, and hemoglobinopathies (9, 10).

IDA contributes substantially to childhood mortality and morbidity and is linked to impaired brain development and cognitive functions. IDA is also ranked as the third leading cause of disability worldwide and the 13th leading risk factor for the global disability adjusted life years (11). The most common cause of microcytosis is iron deficiency; Mean platelet volume is comparable to the mean corpuscular volume of red blood cells (12). Moreover

factors such as limited access to iron rich food, inadequate infant and young child feeding practices including lack of exclusive breast feeding, prolonged breast feeding and inappropriate weaning food and recurrent illnesses increase the chance of young children developing IDA (13). A study concluded that the odds of IDA increased when the child was stunted and food insecure, and suggested that malnutrition is a contributing factor for IDA (14). Currently iron supplementation and wheat flour fortification are successful strategies being used worldwide. There is good evidence to suggest that iron supplementation improves hemoglobin level and reduces IDA prevalence in children (15). Studies conducted in Pakistan also reveal iron supplementation to children and mothers results in improved iron stores (16). Further a recent pooled analysis and studies in Central Asia, Venezuela and Iran suggest that wheat flour fortification can significantly improve iron status at the population level (17-19). The present study aimed to evaluate the platelet parameters in children with iron deficiency anemia before and after three months' treatment.

## 2- MATERIALS AND METHODS

### 2-1 Study design and population

This cross-sectional study was conducted over a period of 18 months. A total of 110 IDA subjects were selected from those who referred to the pediatric hematology clinic of Ali Asghar hospital, Zahedan, Iran, during the study period. The age range was 12 months to 16 years. There was no specific predilection for race, religion, and socioeconomic status. Informed parental consent was taken before enrolling the children in the study.

### 2-2. Laboratory measurements

This cross-sectional study was conducted over a period of 18 months. A total of 110 IDA subjects were selected from those

who referred to the pediatric hematology clinic of Ali Asghar hospital, Zahedan, Iran, during the study period. The age range was 12 months to 16 years. There was no specific predilection for race, religion, and socioeconomic status. Informed parental consent was taken before enrolling the children in the study.

### 2-3. Intervention

Children in the study were given 3 months course of oral iron as ferrous sulfate with a daily dose of 4mg/kg/day in 2 divided doses. At the initiation of treatment and the end of treatment, blood sample was collected for measurement of CBC and platelet parameters.

### 2-4. Exclusion criteria

Children with history of blood transfusion during last 4 months, hereditary anemia, chronic anemia, acute infection, inflammatory disorders, no response to treatment after 3 months and patients already on iron therapy were excluded.

### 2-5. Definition

Iron deficiency is defined as ferritin <12 ng/ml and <15 ng/ml for the children younger and older than 5 years, respectively. Iron deficiency anemia is referred to Hb<11 gr/dl in the age less than 4 years, Hb<11.5 gr/dl for the age 5-7 years, Hb<12 gr/dl for the age 8-11 years, Hb<12 gr/dl for the 12-17 years-old girls, Hb<12.5 gr/dl for the 12-14 year-old boys, and Hb<13 gr/dl for the 15-17 year-old boys (7).

### 2-6. Data Analysis

The independent t-test and paired t-test were used to compare quantitative variables. The obtained data were analyzed using SPSS software version 20.0. Values were shown as means  $\pm$  standard

deviation. There was a significant relationship between data evaluated with p-value <0.05.

## 3- RESULTS

Mean age of patients was higher in boys (4.30 $\pm$ 4.55 years) compared to girls (2.46 $\pm$ 3.21 years), significantly (p=0.03) (**Table.1**). The mean ferritin level was 8.6 $\pm$ 4 ng/ml and 19 $\pm$ 6 ng/ml before and 3 months after iron therapy, respectively (p<0.001). The results of the paired t- test showed that platelet means were 409 $\pm$ 120  $\times 10^3$  /mm<sup>3</sup> and 384 $\pm$ 99  $\times 10^3$  /mm<sup>3</sup> before and after treatment with significant decrease (p<0.001), means of MPV increased from 8.07 $\pm$ 1.01 fL before treatment to 8.86 $\pm$ 1.05 fL after treatment significantly (p<0.001), mean of WBC count without any changes remained constant after treatment, RBC mean increased significantly (p<0.001) from 4.7 $\pm$ 0.5 $\times 10^6$  /mm<sup>3</sup> to 5.0 $\pm$ 0.7 $\times 10^6$  /mm<sup>3</sup>, means of HCT (%) were 33.7 $\pm$ 3.2 and 42.1 $\pm$ 2.1 in the before and after states respectively with significant change (p<0.001), Hb had 9.2 $\pm$ 1.5 g/dL and 11.6 $\pm$ 1.0 g/dL values of mean in before and after intervention respectively, the difference between means showed a significant increase (p<0.001), means of MCV was 64.8 $\pm$ 7.9 fL before intervention and increased significantly to 74.2 $\pm$ 5.7 fL after intervention (p<0.001), means of MCH were 19.6 $\pm$ 3.1 pg/ml and 24.3 $\pm$ 2.9 pg/ml before and after treatment, respectively (p<0.001), means of MCHC were 29.5 $\pm$ 2.1 g/dL and 32.2 $\pm$ 2.0 g/dL before and after treatment, respectively (p<0.001). RWD (%) decreased significantly after treatment, from 17.0 $\pm$ 2.1 to 15.8 $\pm$ 3.5 (p<0.001) (**Table.2**).

**Table-1:** Mean age of participants.

Gender	Mean± SD (years)	P-value
Girls	2.46±3.21	0.030
Boys	4.30±4.55	

SD: Standard Deviation.

**Table-2:** Platelet, WBC and RBC parameters in participant before and 3 months after intervention.

Parameters	Mean ± SD		P- value
	Before Treatment	After Treatment,	
Platelet, (10 <sup>3</sup> /mm <sup>3</sup> )	409±120	384±99	<0.001
MPV (fL)	8.07±1.01	8.86±1.05	<0.001
WBC (10 <sup>3</sup> / mm <sup>3</sup> )	9465±2989	9307±2741	0.545
RBC (10 <sup>6</sup> / mm <sup>3</sup> )	4.7±0.5	5.0±0.7	<0.001
HCT (%)	33.7±3.2	42.1±2.1	<0.001
Hb (g/dl)	9.2±1.5	11.6±1.0	<0.001
MCV (fl)	64.8±7.9	74.2±5.7	<0.001
MCH (pg/ml)	19.6±3.1	24.3±2.9	<0.001
MCHC (g/dl)	29.5±2.1	32.2±2.0	<0.001
RWD (%)	17.0±2.1	15.8±3.5	<0.001

MPV: Mean Platelet Volume, WBC: White Blood Cell, RBC: Red Blood Cell, HCT: Hematocrit, Hb: Hemoglobin, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, RDW: Red Cell Distribution Width, SD: Standard Deviation.

#### 4- DISCUSSION

The main aim of this study was to measure the platelet parameter in patients diagnosed with anemia deficiency in Iran and to compare the parameters before and after treatment by Iron in this group. The results of our study showed that, Platelet count, WBC and RDW decrease after treatment reversely, MPV, RBC, HCT, Hb, MCV, MCH and MCHC ranges increased after IDA treatment. IDA is a common condition that rapidly improves with oral iron supplementation. The diagnosis is made by taking the nutritional history, performing a physical examination, and identifying hypochromic, microcytic anemia on peripheral blood smear. Morris et al., reported that treatment with oral iron usually increased the hemoglobin concentration by at least 1 g/dL within 1 month of starting iron supplementation (20). Murray-Kolb et al., resulted that ID and anemia are associated with impaired

psychomotor and neurocognitive development as well as impaired immune function in children and often these consequences are irreversible (21, 22). Therefore, prevention of ID in early childhood should remain a public health priority. In the present study, in the present study, results of 110 IDA children aged less than 18 years were analyzed and it was shown that mean age of patients was higher in boys. Platelet count means and RDW decreased after intervention, means of MPV, RBC, HCT, Hb, MCV, MCH and MCHC increased while mean of WBC count without any changes remained constant. The literature expressed many factors of high consumption of evaporated milk and cow's milk after six months of age, prolonged exclusive breastfeeding and significant burden of *Helicobacter pylori* infection that are associated with the increased prevalence of IDA, for this reason, the population at risk are children

from families of low socioeconomic status, infants of low birth weight, and children who consume whole cow's milk before 12 months of age (23). Gupta et al., compared the prevalence of ID, anemia, and IDA among children 1–5 years-old and resulted that the prevalence of ID was much higher than anemia and IDA. They concluded that the prevalence of both ID and anemia was higher among children aged 1–2 years. In addition, about half of anemic children less than two years-old were iron deficient (24). Children are introduced to solid foods after six months and it is evident that from the 6th to 12th month, iron requirement increases with body weight as the infant's weight is tripled by the end of first year of life. For this, sufficient amount of iron is required from food (25).

Sumitha et al., revealed that the majority of 6-59 months-old children were anemic (1). In this regard, Monteiro also reported that the percentage of anemic children was very high in the age interval of 6-23 months and then it decreased with the age (26). It would be resulted that if this supplementation is not fulfilled, children in this age group have a high chance of becoming anemic. After the first two years of life, as growth becomes stable and the requirements of iron become less, the percentage of anemic children goes down. Thus, iron requirement in the food for children's bodies varies nonlinearly with age. Although the cause of IDA among young children can be multifactorial, the consumption of foods with low bioavailable iron is likely the primary contributing factor. Before 24 months of age, rapid growth coincident with frequent inadequate intake of dietary iron places children at the highest risk of any age group for ID. In full-term infants, the iron stores can meet the iron requirements until age four to six months, and IDA generally does not occur until approximately nine months of age. Comparatively, preterm and low-birth-weight infants are born with

lower iron stores and grow faster during infancy. Consequently, their iron stores are often depleted by two to three months of age and they are at greater risk for ID. Ashwini Kalantri et al., conducted a study to determine the diagnostic accuracy of pallor for anemia by using hemoglobin as the reference standard. They concluded that the mean hemoglobin of the study population was about eleven when severe anemia and moderate anemia had the lowest and the highest percentages respectively (27). In Diagne et al.'s study, it has been reported that major thrombocytosis associated with severe anemia is uncommon in pediatrics. They considered the diagnosis of reactive thrombocytosis induced by iron deficient anemia in all cases. Platelet count and red cell indices were progressively normalized with iron treatment and no complication of thrombocytosis was observed (28).

Mujib et al., and the colleagues found that the majority of the patients with IDA were male, aged less than two years. The mean total iron binding capacity was greater in IDA than in control but MPV in females was higher and WBC was lower (29). Khorashadizade and Armat conducted a study on 181 children aged less than 6 years. In their study the prevalence of IDA was estimated 37.8 and 21.4 in boys and girls respectively and 31.5 for both genders (30). Meanwhile, Ramzi et al. (31), found 1.7 in girls aged 6-18 years and Abedini et al. (32), found 53.6 in children and adolescents aged 6-18 years-old. Yuce et al. (33), reported Iron inhibits megakaryopoiesis, so iron deficiency anemia leads to microthrombosis.

In this study, Yuce et al., investigated whether young, active, and large platelets are released into peripheral blood during iron treatment. In their study MPV was measured as an indicator for the presence of these platelets. They defined IDA of the level of ferritin  $1 < 50$  ng/mL with transferrin saturation  $< 20\%$  or ferritin  $< 15$

ng/ml. Daily ferrous sulfate was given orally to patients. They evaluated retrospectively the hematologic and biochemical parameters prior to and 1 month after iron treatment. The levels of ferritin, MPV, MCV, and Hb were significantly increased after one-month treatment. Finally, they concluded that there might be an increase in thrombotic events due to hypercoagulability related to microthrombosis during IDA. Even though thrombosis is corrected during iron treatment, the therapy increases the release of large and active thrombocytes into the peripheral blood. Kürekçi et al., performed a study to investigate the platelet aggregation alterations in whole blood samples of infants with iron deficiency anemia. The differences between the pre-treatment and post treatment mean platelet counts and mean platelet volume values in the study group were statistically significant, whereas those values in the study group after therapy were not significantly different. They concluded that iron deficiency anemia in infants, even without clinically meaningful platelet abnormality, may cause dysfunction of the ex vivo whole blood platelet aggregation, and can be reversed by iron therapy (34).

Mokhtar et al., expressed that several changes in platelets have been reported in patients with IDA, so a relationship between iron metabolism and thrombopoiesis should be considered (35). The largest survey on the prevalence of anemia in children 2–12 year-old in the Islamic Republic of Iran was reported by Sayyari et al. that reported a 15% prevalence rate for anemia in Iranian children (36). Safavi et al., reported the prevalence of anemia and ID in 11 different geographical regions in 2001 to be 21.5% and 42.7%, respectively. The highest prevalence was in South of Kerman, South of Khorasan, Sistan and Baluchestan with average of 44%. The lowest levels of prevalence were 9% in

Isfahan, Yazd, Kohgiluyeh and Boyer-Ahmad provinces (37). In conclusion, the result of this study showed that treatment of iron deficiency anemia leads to decreased platelet count and increased MPV.

## 5- CONCLUSION

Platelet parameter measurement in IDA patients and comparison of the parameter before and after treatment by Iron was the main aim of the present study. The results of our study showed that Platelet count, WBC and RDW decrease after treatment, while MPV, RBC, HCT, Hb, MCV, MCH and MCHC increased after IDA treatment.

## 6- ACKNOWLEDGMENTS

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## 7- CONFLICT OF INTEREST: None.

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