

Influence of Iron Deficiency Anemia on Growth: A Cross-Sectional Study

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Abstract

Background: The most important risk factors for iron deficiency (ID) and ID anemia (IDA) are poor iron intake, low bioavailability of iron, chronic loss from the body, and some specific periods of life when the iron requirement is so much like growth during childhood and pregnancy. **Objective:** In this study, the effect of IDA on physical growth was investigated in children through finding out associations between different growth parameters and IDA. **Materials and Methods:** In this cross-sectional study, we measured growth parameters in fifty children with IDA before and for 6 months' postiron therapy in comparison with fifty age- and sex-matched normal controls. Annualized growth velocity and body mass index (BMI) were calculated from measured growth parameters. Red blood cell indices and serum ferritin were measured. After a 6 months' period (October 1, 2018–March 1, 2019) from starting treatment of the anemic group, growth parameters and the hematological assessment were measured again. **Results:** Mean age and standard deviation for cases were 19.1 ± 12.7 months while that of controls were 19.2 ± 12.4 months, and there was no significant difference regarding age distribution $P > 0.05$. Before the treatment, children with IDA were significantly shorter in comparison to age- and sex-matched controls. The BMI of anemic group increased significantly $P < 0.05$. Weight, length, and occipitofrontal circumference were also significantly increased after iron therapy $P < 0.0001$. After receiving therapy, serum ferritin was significantly correlated with growth velocity and BMI for the anemic group: ($r = 0.853$ $P < 0.0001$) and ($r = 0.460$ $P < 0.001$), respectively. After treatment, the anemic group had a growth velocity 5.2 ± 1.8 which was faster than that of nonanemic one 3.4 ± 1.8 , $P < 0.0001$. **Conclusion:** This study documented a positive effect of IDA on physical growth in children, especially during the first 2 years of life during which growth is fast.

Keywords: Anemia, growth, influence, iron deficiency

INTRODUCTION

Iron deficiency (ID) and its anemia continue to be of worldwide concern. Iron is the most important single nutrient deficiency in developing countries in children.^[1] According to WHO 2011 data, hemoglobin level to make the decision of anemia for children 6–59 months is 11 g/dl, for 5–11 years is 11.5 g/dl, and it is 12 g/dl for 12–14 years.^[2] The most important risk factors for ID and ID anemia (IDA) are poor iron intake, low bioavailability of iron, chronic loss from the body, and some specific periods of life when the iron requirement is so much like growth during childhood and pregnancy.^[3–5]

The clinical manifestations of IDA are those of anemia itself. Children with severe ID are often presented as irritable, apathetic with a poor appetite. The signs of anemia consist of pallor of the conjunctivae, the tongue, the palms, and the nailbeds. When anemia is severe, in more advanced stages,

children may also have signs of congestive heart failure with fatigue, tachypnea, hepatomegaly, and edema.^[6] Half of the anemia among under 4 years age children is due to IDA, and it is estimated that the prevalence of anemia within this age groups is 46% and 66% in developing countries.^[7,8]

Iron is storing in the liver, spleen, and bone marrow in the form of ferritin and hemosiderin (product of ferritin degradation), and is transporting in the body by transferrin.^[9–11] There are different measures to know the iron state in the body, and these measures are indicating different iron depletion phases. Early phase of iron deficiency is reflected by low serum ferritin,^[12] but reduction of serum iron is an advanced stage of iron

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deficiency and means too little body iron to reach and meet the cellular iron need.^[13,14]

In a randomized control trial, there was a catch-up growth in iron-deficient children after treating with iron.^[15] Iron has a vital role in many metabolic processes such as DNA synthesis, oxygen and electron transport,^[16] and also, it is a need for growth, development, normal cellular functioning, and the synthesis of some hormones and connective tissue.^[13,17]

In human, both brain and body growth, especially during the phase of rapid infantile growth, requires relatively high energy supply and metabolism. Cellular energy metabolism is dependent on oxygen. Fe deficiency decreases oxygen-dependent cellular energy metabolism due to decreased heme and hemoglobin (Hb) synthesis, decreased red blood cells' (RBC) synthesis, and decreased RBC survival due to increased oxidative stress in RBC, Hb autoxidation, generation of toxic oxygen radicals' scrambling, and increased removal by the macrophage. Consequently, IDA leads to impaired cognitive abilities and defective linear growth.^[18,19] Infancy is a critical period of growth, which is may be affected by nutritional deficiencies. The magnitude of growth retardation in those who have IDA and degree of catch-up growth after iron therapy is unclear, and this is the purpose of this research to clarify more.

The aim of the study was to find any correlation between IDA and growth in children between 6 months and 5 years old.

MATERIALS AND METHODS

Study design and patients

A cross-sectional, longitudinal, hospital-based study has been conducted at Raparin pediatric teaching hospital outpatient clinic in Erbil city/Kurdistan region/Iraq within 6 months between October 1, 2018, and March 1, 2019. Two sample groups have been selected: first group (anemic, cases) and second group (nonanemic, controls): each of them 50 age- and sex-matched cases using simple randomized sampling. All the cases included in the first and second group were assessed for anthropometric measures (weight, occipitofrontal circumference [OFC], and length) and plotted on Tanner *et al.*'s growth charts;^[20] in addition, complete blood count was sent for all the cases and controls, and then, serum ferritin and serum iron levels for the anemic group were assessed. The anemic group was reassessed and followed up by all the anthropometric measures and investigations, while the control group was followed up only for anthropometric measures, follow-up was done for the anemic group after one, three, and 6 months, while the control group was followed up after three and 6 months.

Full history including nutritional intake was taken, and clinical examination was done for every single participant. Annualized growth velocity by measuring the growth rate in weight for 6 months was calculated. Body mass index (BMI) was calculated; normal population reference data were according to Tanner *et al.*^[20]

Inclusion criteria include clinical manifestation of anemia and low Hb level <11 g/dl,^[2] low serum ferritin <12 µg/l,^[21] low serum iron <25 µg/dl,^[21] and microcytic hypochromic anemia on blood picture.

Children with chronic diseases such as malabsorption, cerebral palsy, liver and renal diseases, and other forms of anemia, also those with IDA not responding to iron therapy hematologically, all of them were excluded.

Ethical consideration

The protocol of the study was approved by the Research Ethics Committee of Kurdistan Board for Medical specialties before the beginning of the study. Informed consent (oral and written) was taken from all children caregivers.

Statistical analysis

Data were analyzed using the statistical package for social sciences version 24 (SPSS, IBM Company, Chicago, USA). Pearson correlation coefficient (*r*) was calculated to assess the strength of correlation between two numerical variables. Paired student *t*-test was used to compare variables before and after treatment. Independent sample *t*-test was used to compare variables of interest between cases and controls. *P* < 0.05 was considered as statistically significant.

RESULTS

One hundred children participated in the study, 50 were anemic and another half were control. For each of the groups, the equal number was included regarding sex of the participants: 25 males and 25 females. 30 preterms were assessed and followed up, as it has been shown in Table 1.

Table 2 which is about age distribution in part, shows no significant difference between cases and controls *P* > 0.05. Among all the growth parameters on the time of presentation,

Table 1: Sample distribution by gender and gestational age

	Anemic (cases), <i>n</i> (%)	Not anemic (controls), <i>n</i> (%)
Sex		
Male	25 (50)	25 (50)
Female	25 (50)	25 (50)
Gestational age		
Term	35 (70)	35 (70)
Preterm	15 (30)	15 (30)
Total	50 (100)	50 (100)

Table 2: Age distribution in month and comparison of growth parameters at presentation

Age and growth parameters	Cases	Controls	<i>P</i>
Age (months)	19.1±12.7	19.2±12.4	0.975
Length/height (cm)	77.2±11.4	81.9±11.4	0.044
Weight (kg)	10.2±3.1	10.9±3.3	0.275
OFC (cm)	45.6±2.4	46.4±2.4	0.150

OFC: Occipitofrontal circumference

there was only significant difference between case and control in length/height which has the mean and standard deviation of 77.2 ± 11.4 cm for the cases and 81.9 ± 11.4 cm for the control group, $P = 0.044$.

Table 3 shows the difference in growth parameters, BMI, and hematological measures at presentation and after treatment which is illustrating that patients with IDA have low Hb (9.3 ± 0.7), mean corpuscular volume (MCV) (65.9 ± 4.8), mean corpuscular hemoglobin (MCH) (20.9 ± 2.2), serum ferritin (10.7 ± 2.06), and serum iron (22.1 ± 4.8) that were corrected significantly after treatment of Hb (11.9 ± 0.5), MCV (76.6 ± 1.4), MCH (26.6 ± 1.7), serum ferritin (27.5 ± 7.5), and serum iron (45.5 ± 6.2), respectively. $P < 0.0005$ for all of them.

Regarding BMI also, there has been significant change during that period, from 16.8 ± 1.4 became 17.3 ± 1.2 , $P = 0.024$. During that 6 months' period, there was significant change for weight – 10.2 ± 3.1 became 12.7 ± 2.6 , $P < 0.0001$; length – 77.2 ± 11.4 became 85.4 ± 10.1 , $P < 0.0001$; and OFC – 45.6 ± 2.4 became 47.1 ± 1.5 , $P < 0.0001$.

Table 4 shows that there is no any difference between anemic and non anemic group regarding growth parameters, while there is a significant difference regarding growth velocity, i.e., anemic group had a faster growth than non anemic group, $P < 0.0001$.

Table 3: Growth parameters: Body mass index and hematological data for the anemic group before and after treatment

Hematological data and growth parameters	Mean $\pm$ SD		P
	Before treatment	After 6 months	
Hb (g/dl)	9.3 ± 0.7	11.9 ± 0.5	<0.0001
MCV (fl)	65.9 ± 4.8	76.6 ± 1.4	<0.0001
MCH (pg)	20.9 ± 2.2	26.6 ± 1.7	<0.0001
Serum ferritin ($\mu\text{g/l}$)	10.7 ± 2.06	27.5 ± 7.5	<0.0001
Serum iron ($\mu\text{g/dl}$)	22.1 ± 4.8	45.5 ± 6.2	<0.0001
BMI	16.8 ± 1.4	17.3 ± 1.2	0.024
Weight (kg)	10.2 ± 3.1	12.7 ± 2.6	<0.0001
Length (cm)	77.2 ± 11.4	85.4 ± 10.1	<0.0001
OFC (cm)	45.6 ± 2.4	47.1 ± 1.5	<0.0001

SD: Standard deviation, Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, BMI: Body mass index, OFC: Occipitofrontal circumference

Table 4: Comparison of growth measures and growth velocity between anemic and nonanemic groups after therapy

Growth indicators	Anemic	Nonanemic	P
Weight growth velocity (kg/year)	5.2 ± 1.8	3.4 ± 1.8	<0.0001
Length/height (cm)	85.4 ± 10.1	85.6 ± 10.1	0.973
Weight (kg)	12.7 ± 2.6	12.7 ± 2.9	1.000
OFC (cm)	47.1 ± 1.5	47.4 ± 1.4	0.420

OFC: Occipitofrontal circumference

Figure 1 shows a strong positive significant correlation between growth velocity and serum ferritin, $r = 0.853$, $P < 0.0005$ after giving iron therapy and correction of the anemia. This means that the more the serum ferritin, the more the growth velocity.

As shown in Figure 2, serum ferritin concentration was correlated positively and significantly with BMI after treating anemia, $r = 0.460$, $P = 0.001$.

DISCUSSION

The most common cause of hypochromic microcytic anemia is IDA, an important health problem worldwide mainly in developing countries.^[22] Iron deficiency has many stages; the first stage is the depletion of ferritin which is the stored iron. second stage is depletion of iron and transferrin but hemoglobin is still normal. The 3rd stage is IDA which is characterized by low hemoglobin, hematocrit, and hypochromic microcytic picture on blood film.^[17]

The primary interest of this study was to know the effect of IDA on growth. In this cross-sectional study, we measured growth parameters in 50 children aged 19.1 ± 12.7 months with IDA before and for 6-month postiron therapy in comparison with normal controls. This study found that children with IDA were significantly shorter in comparison with age- and sex-matched controls before treatment, $P < 0.05$.

After treatment of the anemic group, their BMI increased significantly, $P < 0.05$, also the same significant increase for weight, length, and OFC with $P < 0.0001$ for all of them. After receiving therapy, serum ferritin was significantly correlated with growth velocity and BMI for the anemic group: $r = 0.853$ $P < 0.0001$ and $r = 0.460$ $P < 0.001$, respectively.

After treatment, the anemic group grew faster than non anemic group, $P < 0.0001$. Moreover, these results can tell us that iron is an essential element for normal growth. Iron has many important functions like; carrying oxygen from the lung to the cells, transmission of an electron within the cells, acting as a cofactor for essential enzymatic reactions like synthesis of steroid hormones.^[23] The exact mechanism of IDA effect on growth is not clear, but it may be through insulin-like growth factor-1 (IGF-1)-dependent mechanism which is a

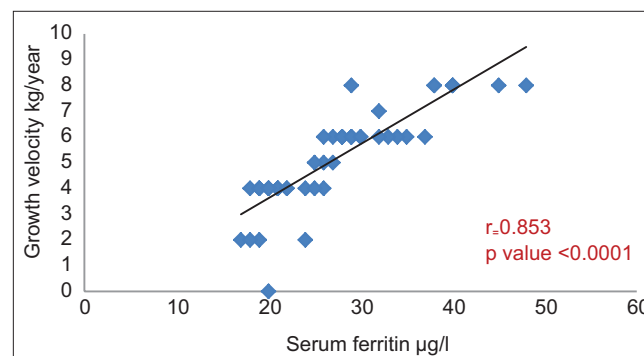


Figure 1: Correlation between growth velocity with serum ferritin after treatment

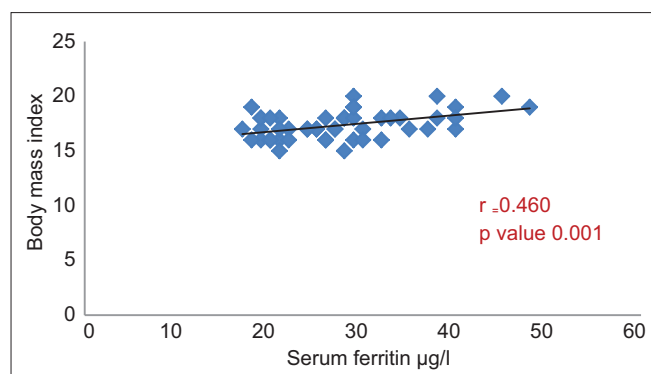


Figure 2: Correlation between serum ferritin and body mass index after correction of the anemia

family of cytokines produced by the liver, osteoclasts, and many other cells; it is illustrated that IGF-1 concentration has an association with iron metabolism and protoporphyrin in children and adolescents.^[24]

Only few studies have investigated the effect of IDA on growth in children with IDA. Bandhu *et al.* studied the effects of IDA, and its treatment with iron, in schoolage children on growth parameters. Pretherapy values of IDA children were significantly lower for mid-arm circumference (MAC) and OFC in girls and for height and MAC in boys, when compared to the control group. Corrected hematological parameters were associated with significant improvement of height, weight, and MAC. Posttherapy, the anemic girls and boys had higher growth velocity than their respective control groups.^[25]

Soliman *et al.* measured anthropometric measures in 40 children with IDA pre- and post-treatment in comparison with normal controls. Before iron therapy, children with IDA were significantly shorter and had slower growth compared with age-matched controls. After treatment, their growth velocity, length standard deviation scores, and BMI increased significantly. Their growth velocity was correlated significantly with mean Hb concentration.^[26] The results of our current study is close to the forementioned study results.

IDA can be prevented through primary and secondary prevention program, primary by iron supplementation of the on-risk groups and secondary prevention by early detection and treatment through special screening programs.^[27,28] The on-risk groups are prematurity and low birth weight, low socioeconomic status, excessive milk intake, early introduction of nonfortified whole cow's milk, prolonged bottle-feeding, and prolonged exclusive breastfeeding.

CONCLUSION

IDA in children, particularly during the period of rapid growth during the first 2 years of life, significantly impairs growth that can be corrected by adequate iron therapy. In view of the significant effect of IDA on growth, pediatricians, hematologists, endocrinologists, and other healthcare providers

should strive to get rid from ID and its anemia through primary and secondary prevention.

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Conflicts of interest

There are no conflicts of interest.

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