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Effect of Iron Deficiency Anemia on IGF-1 Level Among Sample of Children

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Abstract

Background and objectives: Iron-deficiency anemia is a worldwide nutritional problem and an important public health problem especially in developing countries. The aim of this study was to compare the mean insulin like growth factor-1 of anemic children with that of non-anemic children and to correlate the levels of insulin like growth factor-1 with the levels of serum ferritin. **Methods:**cross-sectional study included fifty children. Measurement of levels of insulin like growth factor-1 was done in 25 children with iron deficiency anemia and compared with twenty-five age- and sex-matched non anemic children. **Results:** The mean age + SD were 6.11 + 3.31 years, ranging. There was significant difference detected between the iron deficiency anemia and control group regarding the mean values of insulin like growth factor-1 level as there was more than one third of iron deficiency anemia group had insulin like growth factor-1 levels lower than that of the control group. There was a relatively strong, significant positive correlation between serum ferritin levels with insulin like growth factor-1 levels. **Conclusions:**A significant correlation was observed between serum ferritin and serum insulin growth factor-1 level, since less serum ferritin levels is associated with less insulin growth factor-1 levels among anemic group compared with control group, implying that the effect of IDA on insulin like growth factor-1 level may differ according to body iron status.

Keywords y anemia; Insulin like growth factor-1; Serum ferritin.

Introduction

Iron deficiency anemia (IDA), the most common cause of microcytic anemia, is a worldwide nutritional problem and an important public health problem especially in developing countries[1]. Since the most important indicator of iron deficiency is anemia, the terms “iron deficiency” and “iron deficiency anemia” are often used interchangeably. However, iron deficiency may develop in the absence of anemia and the tissues may be affected from this condition[2]. According to the 2011 World health Organization (WHO) data, anemia in childhood is defined as a hemoglobin (Hb) concentration <11 g/dl in children aged 6–59 months, <11.5 g/dl in children aged 5–11 years and 12 g/dl in older children (aged 12–14). The prevalence of iron deficiency anemia varies among population groups and in different areas of the world3. In infants and young children, severe chronic anemia may lead to delayed growth and long term effects on neurodevelopment and behavior[4, 5].

Iron performs vital functions including carrying of oxygen from lung to tissues, transport of electrons within cells, acting as co-factor for essential enzymatic reactions, including synthesis of steroid hormones and neurotransmission[6]. Iron is reversibly stored within the liver as ferritin and hemosiderin and is transported between different compartments in the body by transferrin. Ferritin is a better measure of available iron levels than serum iron and iron deficiency can negatively affect these functions[7]. Insulin-like growth factor-I (IGF-I) is a family of cytokines produced by the liver, osteoblasts, and many other cells. IGF-I is identical with Somatomedin C (Sm-C)[8]. Its major regulators are growth hormone (GH) and nutrition. Decreased levels of IGF-I are found in states of malnutrition/malabsorption, hypothyroidism, liver disease, untreated diabetes mellitus, chronic inflammatory disease and malignant disease[9,10].

Anemia imposes a hypoxic condition on hepatocytes and hepatic protein synthesis is inhibited by hypoxia. In vitro, low oxygen conditions inhibit insulin-like growth factor-I (IGF-I) activity by increasing IGF binding protein -1 (IGFBP-1), which inhibits IGF-I action. In addition, IGF-I-induced cell proliferation is also inhibited in low oxygen conditions[11-13]. Transferrin (Tf) which is the major circulating iron binding protein, can effect IGFBP-3-induced cell proliferation and apoptosis in different cell lines. On the other hand, the Fe3 + Transferrin complex might facilitate the transport

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of IGFs across the capillary wall by receptor-mediated transcytosis. Therefore, increased Transferrin during iron deficiency anemia may adversely affect the integrity of IGF-I system[14]. The objectives of the study were to compare the mean IGF-1 of the anemic group with the mean of the non-anemic group; to compare the proportions of low IGF-1 in the two study groups, and to correlate the levels of IGF-1 with the levels of serum Ferritin.

Patients and Methods

A cross-sectional study (with a control group) including fifty children between 2-14 years of age who attending the Pediatric Clinic at Raparin Pediatric Hospital in Erbil city between 1 March 2017 and 1 December 2017. Twenty five children with iron deficiency anemia compared with twenty-five age- and sex-matched non anemic (Based on clinical and laboratory results) children.

Patients' inclusion criteria included laboratory manifestations of anemia with low hemoglobin (Hb) (<11 gm/ dl)3, microcytic hypochromic picture in the blood film, serum iron(<25 µg/dl)15, low serum ferritin (<15 µg/l)15 and total iron binding capacity (TIBC) (> 390 µg/dl)15.

All children with chronic systemic illnesses, protein/ calorie malnutrition, rickets, malabsorption, liver disease, renal insufficiency, endocrine disorders or other forms of anemia are excluded from this study.

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 child parents.

All patients were reviewed thoroughly with special reference to the following: detailed history taking including nutritional intake, physical examination including clinical manifestations of Iron deficiency anemia, anthropometric measurements including weight and height, body mass index (BMI) were calculated. Normal population reference data were according to Tanner et al16, 17, measurement of levels of insulin like growth factor-1(IGF-I) in serum by using an enzyme immunoassay for Quantitative Determination of human IGF-I) method also called Sandwich-Assay (ELISA E20). Two cc blood sample taken from all children in different time during a day, since blood samples can be taken at any time of the day18. The samples diluted in an acidic buffer (Sample Buffer PP). The diluted samples are then pipetted into the assay wells. The IGF-I antiserum is dissolved in a buffer, which is able to neutralize the acidic samples. After the IGF-I antibody solution has neutralized the samples, the present excess IGF-II occupies the IGF-binding sites of the binding proteins, thus allowing the measurement of the resulting free IGF-I. The result compared with the normal ranges in various age groups (IGF-I levels are highly age-dependent in children and below 5th percentile proved to be an appropriate cut-off point) and the individuals between 8 and14 years of age were classified according to gender, as the pubertal peak occurs almost 2 years earlier in girls than in boys19. Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 22). Chi square test of association was used to compare proportions. Fisher's exact test was used when the expected count was less than 5 for more than 20% of the cells of the table. Student's t-test of two independent samples was used to compare two means. Pearson correlation coefficient (r) was calculated to assess the strength of correlation between two numerical variables. A p-value of 0.05 was considered statistically significant.

Results

Fifty children were included in the study, 25 were anemic compared with 25 controls. Their mean age + SD were 6.11 + 3.31 years, ranging from 2.16 to 13.50 years. The median was 5.12 years.

No significant difference (p-value=1) was detected between the two groups regarding age distribution as 44% of each group aged less than five years, 44% of each group aged 5-9 years, and 12% of each group aged 10-14 years, Table 1. The same table shows that 54% of the sample were males, with no significant difference in the gender distribution between the two groups (p-value=0.777).

Table (1): Age and gender distribution of the study groups.

	Anemic		Not anemic		Total		
	No.	(%)	No.	(%)	No.	(%)	p-value
Age (years)							
< 5	11	(44.0)	11	(44.0)	22	(44.0)	
5-9	11	(44.0)	11	(44.0)	22	(44.0)	1*
10-14	3	(12.0)	3	(12.0)	6	(12.0)	
Mean (± SD)	6.11	(±3.32)	6.11	(±3.36)			0.986†
Gender							
Male	13	(52.0)	14	(56.0)	27	(54.0)	0.777
Female	12	(48.0)	11	(44.0)	23	(46.0)	
Total	25	(100.0)	25	(100.0)	50	(100.0)	

*By Fisher's exact test. †By t test for two independent samples.

Table 2 shows that the mean Hb (9.92 g/dl) and the mean ferritin (10.52) of the anemic group were significantly less than the means of the non-anemic groups (p-value < 0.001). The mean BMI of the non-anemic group (16.02 Kg/m2) was significantly higher than the mean BMI (15.36 Kg/m2) of the anemic group (p-value = 0.043).

Table (2): Means of Hb, ferritin, BMI, and height of the two study groups.

	Anemic patients		Non-anemic patients		
	Mean	(± SD)	Mean	(± SD)	p-value
Hb (g/dl)	9.920	(±0.763)	12.856	(±0.552)	< 0.001
S. ferritin	10.520	(±2.551)	56.240	(±40.331)	< 0.001
BMI (Kg/m2)	15.360	(±1.122)	16.020	(±1.128)	0.043

Table 3 shows that more than one third (36%) of the anemic group had low IGF-1 levels compared with 0% of the comparison group (p-value = 0.002). The mean IGF-1 level (170.14 ng/dl) of the non-anemic (comparison) group was higher than the mean (102 ng/dl) of the anemic group. The difference was close to the significance level (p-value = 0.063). Significant difference was detected between the two groups regarding the mean IGF-1 percentile where the mean (55.80) of the comparison group was significantly higher than the mean of the anemic group (p-value < 0.001).

Table (3): IGF-1 levels in the two study groups.

	Anemic		Not anemic		Total		p-value
IGF-1	No.	(%)	No.	(%)	No.	(%)	
Low	9	(36.0)	0	(0.0)	9	(18.0)	0.002
Normal	16	(64.0)	25	(100.0)	41	(82.0)	
Total	25	(100.0)	25	(100.0)	50	(100.0)	
Mean IGF-1(±SD)	112.31	(±102.79)	170.14	(±112.04)			0.063
Mean IGF-1% (±SD)	24.74	(±28.20)	55.80	(±22.72)			< 0.001

Figure 1 shows that there was moderately strong, positive, significant correlation between the IGF1 and the BMI (r = 0.533, p-value = 0.006).

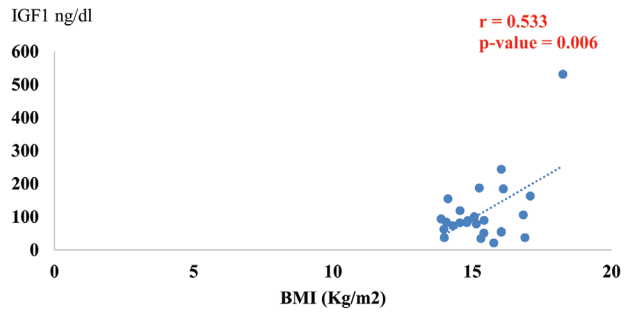

Figure (1): Correlation between the IGF1 with BMI in the anemic group.

Figure 2 shows a relatively strong, significant positive correlation between serum ferritin levels with IGF-1 levels ($r = 0.640$, p-value < 0.001). The less the serum Ferritin levels, the less the IGF-1 levels.

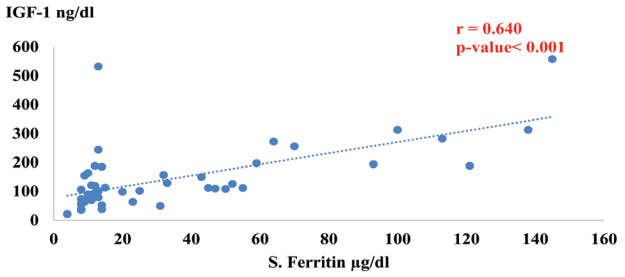

Figure (2): Correlation between serum ferritin and IGF-1.

Discussion

In this study we selected a group of subjects strictly beyond infancy and before puberty. Furthermore, we tried to establish a group of iron deficiency anemia children in whom significant height and weight arrest did not occur.

In present study, significant difference was detected between the Iron deficiency anemia and control group regarding the mean of IGF-1 level. Also there was significant low IGF-1 levels in more than one third of anemic group (36%) compared with (0%) of the control group, which is seem to be similar with other study result[20]. In this study, serum ferritin levels showed significant positive correlations with IGF-1 levels which means the less serum ferritin levels, the less IGF-1 levels in iron deficiency anemia group and vice versa regarding control group. In comparison between Hb and serum ferritin level with serum IGF-1 level in Iron deficiency anemia group, shows that most cases present with low level of IGF-1(9 cases out of 25) belong to children with obvious decreases in Hb and serum ferritin level and it's because of serum iron and serum ferritin differ at different stages of iron deficiency, since in the first stage iron store start to decreased and reflected as decreasing in the level of serum ferritin and ended by more decreasing in the iron store and reflect as decrease in Hb level in the last stage, which is so-called iron deficiency anemia stage[21] which means that prolong untreated iron deficiency anemia have negative effect on the IGF-1 level. In the study done by Soliman, et al. reported growth defect in iron deficiency anemia and explained that by defect in IGF-I secretion and showed that correction of anemia lead to improvement of catch-up growth and a significant increase in IGF-I secretion[22].

Although there was moderately strong, positive, significant correlation between the IGF1 and the BMI, this may be due to not all anemic cases associated with obvious decreases in anthropometric measurements, may be iron deficiency in developing countries related mostly to erroneous nutrition, which is resulting from both difficulties in the supply of protein-rich foods in low-income families and deviations in food composition towards carbohydrates. As reported from previous studies in developing countries, since iron deficiency anemia is also common in overweight and obese children[20].

Conclusions

The results of this study showed significant difference between the iron deficiency anemia and control group regarding the level of IGF-1, this change in IGF-1 level showed high positive correlation with serum ferritin, implying that the effect of iron deficiency anemia on IGF-1 level may differ according to body iron status. In view of these results; there is significant impact of prolonged untreated iron deficiency anemia on IGF-1 level and on growth, pediatricians and endocrinologists should advocate primary prevention and screening for iron deficiency.

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