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Iron Deficiency Anemia in Egypt: Impact on Growth and Relation to Serum Level of Interlukein-2

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ABSTRACT

Background: Iron deficiency is the most common cause of anemia in the developing countries. Late diagnosis and treatment in school aged children lead to stunting and affect neurocognitive development. Iron deficiency may reduce the level of serum interleukin 2 and increase the susceptibility to infections.

Objectives: To study the iron status in children aged 6 to 12 years of both sexes and to investigate the relation of iron deficiency to growth and of serum level of IL2.

Patients and Methods: Three hundred sixty nine children 6 to 12 years were enrolled in the study, 242 (65.6%) were males and 127 (34.4%) were females; M/F ratio 1.9. Anthropometric measures (weight, height and BMI) were studied in all cases and analyzed by growth curves according to their age and sex. Red cell indices and iron profile were measured in all participants. IL2 was measured in the serum of 100 patients with iron deficiency and 50 patients with normal iron profile.

Results: The prevalence of iron deficiency anemia (IDA) among the studied children was 40.4%. Up to 70.5% (n=105) of IDA patients were <10 years, 47.7% (n=71) were short, and one third (n=50) were underweight. Patients with IDA had statistically significant decrease in the level of RBCs count, MCV, MCHC, serum iron, transferrin saturation and raised TIBC when compared to normal subjects (p<0.05). Serum ferritin was lower in IDA group but the difference from normal subjects was marginally insignificant (p=0.058). Serum IL2 was significantly low in the serum of the IDA patients when compared to cases with normal iron status (p=0.001).

Conclusion: Iron deficiency anemia is common in Egyptian children younger than 10 years. Children with IDA looked predominantly short rather than underweight. Low serum iron, low transferrin saturation, and raised total iron-binding capacity might be the reliable markers in diagnosis of IDA. IDA patients had decreased levels of serum IL2 which may increase the risk of infections.

Key Words: *Iron deficiency anemia – Growth – IL2.*

INTRODUCTION

Iron deficiency is the most common cause of anemia worldwide. It has been identified as a modifiable risk factor for the poor development of more than 200 million children in developing countries **[1]**. Failure to investigate iron deficiency anemia (IDA) appropriately in primary care can cause significant delay in the final diagnosis of associated morbidities **[2]**. Malnutrition with underlying multiple vitamin and mineral deficiencies is found to be common among young children and is usually coupled with iron deficiency anemia **[3]**. Among the well described consequences of anemia are impaired physical growth, immune alterations and increased susceptibility to infections **[4]**.

The relation between recurrent infections and iron deficiency is not well studied. Few studies found that mild iron deficiency might be protective against infections; yet other studies showed the opposite results **[5,6]**. They reported that inflammatory cytokines like IL-2 are reduced in children with iron deficiency anemia **[7-9]**; this may cause disturbance of the cell mediated immunity function **[10]**. IL2 is a growth factor secreted from T cells and results into the formation of effector T cells as well as antibody formation hence its important relation to immunity **[11]**. Children with iron deficiency might have abnormally low levels of IL-2. The aim of the study was to assess the iron status in children 6 to 12 years, and to investigate the association of iron deficiency with growth of children and serum level of IL2.

PATIENTS AND METHODS

This was a prospective cross-sectional study carried out on 369 children aged 6-12 years. They were recruited from the outpatient clinics of Abou El-Reesh Hospital, Cairo University during the period from January to December 2017. The study received Institutional Review Board (IRB) approval and was conducted in accordance with the University bylaws for human research and Helsenki declaration for studies on human subjects. A written informed consent was obtained from the legal guardians and assent from children in accordance with the IRB guidelines. A sample size of 369 children was estimated by using anemia prevalence of 20% at 95% confidence level. Patients with chronic diseases, genetic and chromosomal anomalies and active infection proven by elevated CRP were excluded. A detailed clinical history and relevant physical examination were done. The criteria for IDA were combination of hypochromic microcytic anemia with low ferritin, low transferrin saturation, low iron, and raised total iron-binding capacity **[12]**.

Specimen collection and evaluation: Whole blood samples were collected into EDTA tubes for determining the Red blood cell indices automatically using the blood counter (Diagon Ltd D-cell 60). Serum samples were separated and frozen for estimation of serum levels of iron, transferrin saturation, TIBC and IL2. Serum iron and total iron binding capacity (TIBC) were measured using Olympus 400 auto-analyzer. Serum ferritin was measured for all cases by Microparticle Enzyme Immunoassay (AxSYM, Abbott, USA). IL2 was measured by enzyme-linked immune assay (ELISA) technique **[11]**. Transferrin saturation was calculated by following the equation: [Total iron] / [TIBC] x 100 **[13]**.

Statistical analysis: Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 23. Data was summarized using mean, standard deviation, and range in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. The quantitative variables were compared using paired *t*-test. The comparison of qualitative variables was performed using chi-square test or Fisher's exact test. *p*-values less than 0.05 were considered as statistically significant.

RESULTS

Demographics and clinical data: The study included 369 children from 6 to 12 years of age. They were 242 (65.6%) males and 127 (34.4%) females; M/F ratio 1.9. The most common clinical presentation included pallor (85%), fatigue (75%), exertional dyspnea (67%), decreased attention span (45%), lack of concentration (42%), headache (30%), glossitis and angular stomatitis (10%). The prevalence of iron deficiency anemia (IDA) among the studied children was 40.4%. Table (1) illustrates a comparison between patients with IDA deficiency and cases with normal iron profile. Up to 70.5% (n=105) of IDA patients were aged below 10 years, 47.7% (n=71) were short, and one third (n=50) were underweight. The frequency of IDA among males and females was comparable (42.15% and 37.0% respectively; p= 0.339).

Table (1): Comparison between patients with non-IDA and IDA regarding demographic data and anthropometric measures.

Parameter	Non-IDA (n=220)		IDA (n=149)		*p*-value
	No.	%	No.	%	
Age group:					
Age <10 yrs	167	75.9	105	70.5	0.244
Age >10 yrs	53	24.1	44	29.5	
Sex:					
Female	80	63	47	37.0	0.339
Male	140	57.85	102	42.15	
Height for age:					
Normal	142	64.5	78	52.3	0.019*
Stunted	78	35.5	71	47.7	
BMI for age:					
Normal	159	72.3	115	77.2	0.290
Wasted	61	27.7	34	22.8	
Weight for height:					
Normal	107	48.6	99	66.3	0.066
Wasted	113	51.4	50	33.7	
Consanguinity:					
Positive	61	27.7	49	32.9	0.288
Negative	159	72.3	100	67.1	
Family History:					
Positive	31	14.1	13	8.7	0.119
Negative					

*Statistically significant.

Table (2) shows that there was statistically significant decrease in the level of RBCs count, MCV, MCHC, iron, transferring saturation and

raised TIBC in patients with IDA when compared to normal subjects (p<0.05). Patients with IDA had lower serum ferritin in comparison to normal subjects but the difference was marginally insignificant (p=0.058).

Table (2): Comparison of CBC parameters, reticulocyte count and iron profile between IDA patients and non-IDA groups.

Variables	Non-IDA (n=220)	IDA (n=149)	*p*-value
	Mean ± SD	Mean ± SD	
RBC (millions/cmm)	4.20±0.54	3.01±0.49	<0.001*
MCV (fl)	77.47±6.37	60.09±6.53	0.015*
MCH (pg)	27.32±3.53	26.03±3.37	0.190
MCHC (g/dl)	33.56±4.48	31.03±4.15	0.045*
RDW (%)	14.45±1.03	14.52±0.96	0.077
Retics (%)	1.69±1.18	0.9±0.15	0.080
Serum Iron (mg/dl)	75.07±21.86	27.05±10.82	<0.001*
Serum Ferritin (ng/ml)	62.07±19.99	19.80±11.02	0.058
TIBC	240.08±56.87	329.19±42.74	<0.001*
Transferrin saturation (%)	23.06±6.84	14.02±9.41	<0.001*

*Statistically significant.

Serum IL-2 test was carried out to observe the level of cytokine concentration in 100 children with documented IDA in addition to 50 children of non-IDA as a control group. IL2 was significantly lower in the IDA group as compared to the non-IDA group (8.76±0.6, range 3.5-13.9 vs. 31±1.2, range 20.5-195.9 pg/ml respectively; p=0.001).

DISCUSSION

The present study included 369 children aged between 6 and 12 years, none of them had a history of chronic illness or medication. Their main presenting symptoms were pallor (85%), fatigue (75%), and exertional dyspnea (67%). It was reported that nine out of ten anemia sufferers live in developing countries and the most vulnerable, the poorest and the least educated are disproportionately affected by iron deficiency and anemia **[14]**. Poor dietary habits and decreased intake of iron containing food in the study group was reported in up to 65.9% which increased to 95% in IDA group. This was in line with previous reports as Al Ghwass et al., study highlighted the ingestion of low iron containing foods as a significant predictor of IDA **[15]**, which agrees with previous similar studies **[16,17]**.

Detailed interpretation of the iron profile of the studied patients showed that 40.4% had IDA. This is similar to results of a study reporting that anemia with depleted iron stores was identified in 47.1% of children **[18]**. Our rate is lower than that reported in a previous study including 245 5-11 years old children with 58% prevalence of anemia **[19]**. However, a lower rate was reported by Legason et al., who studied 342 children and results revealed that anemia prevalence was 34.4% **[20]**.

Among our patients, the frequency of IDA among males and females was comparable (p=0.339). This was in harmony with results of Murila and associates, studied 403 children aged 6 months to 6 years and found no association between IDA and sex **[20]**. Our results disagree with an Egyptian study carried out by Al-Gawas et al., who reported male predominance (58.3%) in studied patients with a significantly higher prevalence of ID (with or without anemia) among males (85.33%) compared to females (p=0.004) **[15]**.

In our study, nearly half (47.7%) of IDA patients showed decreased height for age and 33.7% had decreased weight for height. This is in line with a study carried out on young Egyptian children which showed that stunting, wasting and underweight were associated with iron deficiency anemia, but the underweight only was statistically significant **[15]**. Similarly, Gosdin et al., reported that the prevalence of decreased height for age in their patients with IDA was 44.2% **[21]**. Moreover, Kishawi et al., who carried out a study on 357 children found that anemia in children was significantly associated with underweight **[22]**. Also Luo et al., mentioned that children with anemia were shorter for their age, and a higher percentage of them had stunted growth **[23]**. Lower rates of abnormal weight or height parameters among anemic children were reported in previous studies. In a study of 184 children with anemia, Gwetu and colleagues reported that the prevalence of decreased height for age was 7.6%, and decreased BMI for age was 1.1% **[24]**.

In our study, we found significantly lower levels of MCV, MCHC, iron level, transferrin saturation and raised TIBC in the IDA patients

when compared to Non-IDA, but no statistical difference found in other parameters (MCH and Ferritin). Another study, El Baroudi et al., **[19]**. reported that ferritin is an inflammatory marker that we should not consider as a reliable marker for diagnosis of iron deficiency anemia. On the other hand, they confirmed that MCV and MCH are the most sensitive parameters for IDA diagnosis. This is not shown in our study, as MCH was not significantly different between the 2 groups and need further studies to be confirmed.

In our present study, we found significantly lower levels of serum IL2 in IDA patients when compared to children with normal iron values. Our study is in agreement with several studies which reported the important role of iron in the process of activation and proliferation of T cells which is needed for the maintenance of the cellular immune response **[8,9]**. In their study, Suegaand and Bakta reported the significant increase in plasma IL2 of iron deficiency patients after treatment with iron tablets for 8 weeks, which confirms the key roles of iron in T cell proliferation, activation and function **[11]**.

In conclusion, iron deficiency anemia is common in Egyptian children younger than 10 years. Children with IDA looked predominantly short rather than underweight. Low serum iron, low transferrin saturation, and raised total iron-binding capacity might be the reliable markers for diagnosis of IDA. IDA patients had decreased levels of serum IL2 which may increase susceptibility to infections.

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