The Effect of Iron Therapy on IQ and School Performance in Anemic Children in Menoufia Governorate

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Abstract: Background: The cause of 30%–50% of anemia in children and other groups is iron deficiency (1) Iron is an important element and it has the most common and best described history between all micronutrients (**2**). **Objective**: This study aimed to evaluate the effect of iron therapy as a treatment for anemia on improvement of IQ and school performance of children (6-12) yrs old. **Material and Methods**: 200 children were divided into two groups: anemic group (100 children) and non anemic group (100 children) the non anemic group were used as control. IQ and school performance were done for both anemic and non anemic group and each group was compared with the other as abase line and iron therapy was given for 3 months until anemia was treated and then IQ and school performance were reassessed for anemic group and compared with the results before the iron supplementation and also compared with the results of the non anemic group. **Results:** There was significant difference in the basic levels of IQ and school performance between anemic and non anemic group and also between the levels between preiron supplementation and postiron supplementation and also between postiron supplementation and non anemic group. **Conclusion:** Iron deficiency anemia affect IQ and school performance of children and treatment of anemia improves them but not reach the level of children who did not suffer from anemia.
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1. Introduction:

Iron deficiency is the most common single nutrient disorder in the world (3) infants are at a special risk due to their rapid growth and decreased dietary sources of iron **(4).**

Iron has a major role in many central nervous system processes that could affect infant behavior and development (5).

Education is one of the most important points of human resource development. Every child should have the chance to achieve his or her academic potential. It is generally noticed that at least 20% of children in any school get poor marks - they are "scholastically backward". Poor school performance should be seen as a "symptom" reflecting a larger underlying cause in children. This symptom not only results in the child having a low self-esteem, but also can cause significant stress to the family. It is essential that this symptom be scientifically analyzed to discover its underlying problem. **(6).**

Intelligence quotient is determined by a number of factors which include genetic and non genetic factors **(7).**

Nutrition has important effect on intelligence prenatally and postnatally. The idea that prenatal nutrition may affect intelligence can be justified by Barker's hypothesis of fetal programming, which states that during critical stages of development the intrauterine environment affects or 'programmes' how the child will develop. Barker put nutrition as being one of the most important intrauterine influences affecting development and that under-nutrition could forever change the physiology and development of the child **(8).**

Early nutrition can also affect brain structures which are actually correlated to IQ levels. Specifically, the caudate nucleus is particularly affected by early environmental factors and its volume correlates with IQ. In an experiment by Isaacs et al., infants born prematurely were either assigned a standard or high-nutrient diet during the weeks directly after labour. When the individuals were assessed later in adolescence, it was found that the high-nutrient group had larger caudate volumes and scored significantly higher on verbal IQ tests **(9).**

In almost all case-control studies comparing otherwise healthy full-term infants who have iron-deficiency anemia to infants with better iron status, their mental development test scores averaged 6 to 15 points lower. **(10).**

2. Materials and methods

The study protocol was approved by the local ethics committee of the Menoufia University and oral consent was obtained from the parents.

This study was conducted from on children aged 6-12 years old randomly selected from different places some of them those who attended the pediatric

outpatient clinics in Menoufia university hospital and others from relatives.

Some of children who attended the out patient clinic in our hospital and others from relatives whose parents accepted to start the study with us were asked to make CBC and according to the result anemic children were used as cases and non anemic children were used as controls until we completed sufficient number of both cases and controls.

Determining the patients was according to inclusion and exclusion criteria which are:

Inclusion criteria**:**

Age (6-12) years and absence of chronic diseases.

Exclusion criteria:

Age<6years or >12 years, chronic diseases or presence of any type of chronic anemia other than iron deficiency anemia.

Patients were divided into two groups:

Anemic group:

100 children with anemia and non anemic group: 100 healthy children without anemia matched as age and sex with anemic children as controls.

The following was done for all patients:

Complete history taking with special concern for:

The most common symptoms and signs of iron deficiency anemia as tiredness, weakness and loss of concentration, pallor, palpitation, irritability, low appetite, dizziness and pica, mode of delivery (normal or cesarian section), birth order of this child, socioeconomic standard level, residence (rural or urban), time of weaning (at 4 months or at 6 months), family history of any type of anemia, past history of any medical or surgical condition, Past history of blood transfusion and Drug and toxin exposure as Possible environmental toxin exposure. The dietary history is focused on assessing iron intake, type of diet, type of formula (if iron fortified), and age of infant at the time of discontinuation of formula or breast milk. In addition, the amount and type of milk the patient is drinking and presence of pica.

General examination:

Pallor is assessed by examining sites where capillary beds are visible (e.g., conjunctiva, palm, and nail beds), vital signs (respiratory rate, heart rate, temperature and blood pressure), anthropometric measurements mainly BMI (body mass index) for age And putting it on z-score, special facial features as thalasemic facies, chest and cardiac examination and abdominal examination mainly organomegally if present to exclude chronic hemolytic anemia.

Lab investigations in the form of:

CBC

Transferrin saturation

So the patients who will be included in our study as anemic group who have: Hgb less than 11.5gm, low MCV, low MCH, low MCHC, increased RDW, and decreased transferrin saturation.

Then after confirmation that our patients are iron deficiency anemia the following was done for anemic and non anemic group:

Stanford Binet IQ test by a specialist: the last version (fifth edition) of Stanford Binet IQ test was used to asses IQ. And assessment of school performance: Assessment of school achievement from subjects school records and grading of it was by using the most common grading scale in USA as there is no standardized system of grading in Egypt then Iron therapy was given to anemic children for 3 months (6mg/kg/day) divided in 2doses per day. Then reevaluation of lab investigation to confirm improvement of anemia was done. After improvement of anemia school performance and IQ were reassed and compared with the pretreatment results and the anemic group was compared with the non anemic group in both lab investigation of anemia, IQ and school performance before and after giving iron therapy.

Statistical Analysis

The collected data were tabulated and analyzed by using an IBM personal computer with Statistical Package of Social Science SPSS, version 20, for Windows (SPSS Inc., Chicago, Illinois, USA). The results were expressed by applying ranges, means ± S.D., Chi-square test, T test, and P values. P value <0.05 was considered to be significant. Pearson correlation was used for normally distributed quantitative variables, while Spearman correlation was used for quantitative variables that were not normally distributed or when one of the variables is qualitative.

3. Results:

Our study included total 200 patients and healthy participants divided into 2 groups: anemic Group 100 patients with iron deficiency anemia (44% male and 56% female) the mean age was 8.57(±1.82) years and non anemic Group: 100 healthy control participants (36% male and 74% female) the mean age was 7.53(±1.3).

Regarding the comparison between anemic and non-anemic children regarding socioeconomic status and residency there was a significant difference between the two groups regarding socioeconomic status and residency (p-value<.001). The anemic children significantly higher in low socioeconomic category (p-value<.001). There was no significant difference between groups in the medium socioeconomic category (p-value=.494). There anemic children where significantly lower in the High socioeconomic category (p-value<.001). Being a rural children, this increase the risk of having anemia. The anemic children were significantly higher in rural

residency compared to urban (p-value<.001) **(Table 1)**. Regarding comparison between the non-anemic children and anemic before iron supplementation regarding iron profile there was a significant difference between the two groups regarding Hg level, MCV, MCH, MCHC, serum iron, TIBC and transferrin saturation. (p-value<.001) **(Table 2).** regarding comparison between the non-anemic children and anemic before iron supplementation regarding IQ and school performance there was a significant difference between the two groups regarding Hg IQ score and School performance. (p-value<.001) **(Table 3)** Regarding comparison between pre-iron and post iron supplementation for anemic group regarding Iron profile there was a significant difference between the two groups regarding Hg level, MCV, MCH, MCHC and transferrin saturation (p-value<.001). This difference indicates that iron supplementation was effective in improving the anemic state of the children **(Table 4)** Regarding comparison between pre-iron and post iron supplementation for anemic group regarding IQ and school performance there is a significant difference between the two groups regarding IQ score and School performance (p-value<.001). This difference indicates that iron supplementation was effective in improving the children **(Table 5)** Regarding comparison between non-anemic and post iron supplementation for anemic group regarding Iron profile there was no significant difference between the two groups regarding Hg level (p-value>0.05. This indicates that the improvement made by iron supplementation in the anemic group was high enough to improve most of their anemia profile levels in comparison with children whom basically didn't suffer from anemia **(Table 6).** Regarding comparison between non-anemic and post iron supplementation for anemic group regarding, IQ and school. performance there was a significant difference between the two groups regarding IQ score and School performance (p-value<.001). This indicates that the improvement made by iron supplementation in the anemic group was not higher enough to improve their IQ and school performance in comparison with children who basically didn't suffer from anemia **(Table 7)**

Table (1): comparison between anemic and non-anemic children regarding socioeconomic status and residence.

Characters	Anemic (N=100)		Non anemic (N=100)		Test	P-value	Post- hoc P-values.
	N	%	N	%			
Socioeconomic status: • Low • Medium • High	 60 35 5	 60 35 5	 33 42 25	 33 42 25	X^2=21.8	<.001***	Low vs. anemia=.006** Medium vs. anemia=.494* High vs. anemia<.001***
Residence: • Rural • Urban	 73 27	 73 27	 32 68	 32 68	X^2=33.7	<.001***	Rural vs. anemia <.001*** Urban vs. anemia <.001***

*"X^2"*means Qui-squared test. *means not significant difference (p-value >.05)
** means significant difference (p-value <.05) ***means highly significant difference (p-value<.001)

Table (2): comparison between the non-anemic children and anemic before iron supplementation regarding iron profile.

Characters	Pre-Iron supplementation For Anemic group (n=100)	Non Anemic (n=100)	t-Test	P-value
	Mean (±SD)	Mean (±SD)		
Hg level, *gm/dL*	9.628(±.469)	12.9 (±.347)	56.04	<.001*
MCV, *fL/red cell*	51.35 (± 3.14)	83.21 (± 2.15)	83.72	<.001*
MCH, *Pg/ red cell*	19.63 (±2.6)	28.2 (±1.2)	29.92	<.001*
MCHC, *gm/dl*	21.46 (±7.8)	33.4(±2.5)	14.57	<.001*
Transferrin saturation, *%*	4 (±1)	35 (±5)	37.57	<.001*

"t" means student test (t-test)
*mean highly significant difference (p-value<.001)

Table (3): comparison between the non-anemic children and anemic before iron supplementation regarding IQ and school performance.

	Pre-Iron supplementation For Anemic group (n=100)	Non Anemic (n=100)	t-Test	P-value
	Mean (±SD)	Mean (±SD)		
IQ score	97.15(±7.402)	118.94(±4.17)	25.65	<.001*
School performance	76.79(±5.19)	94.11(±3.39)	23.1	<.001*

"t" means student test (t-test) *mean highly significant difference (p-value<.001)

Table (4): comparison between pre-iron and post iron supplementation for anemic group regarding Iron profile.

Characters	Pre-Iron supplementation For Anemic group (n=100)	Post-Iron supplementation For Anemic group (n=100)	t-Test	P-value
	Mean (±SD)	Mean (±SD)		
Hg level, *gm/dL*	9.628(±.469)	12.825(±.216)	62.07	<.001*
MCV, *fL/red cell*	51.35 (± 3.14)	75.31(±3.54)	50.63	<.001*
MCH, *Pg/ red cell*	19.63 (±2.6)	24.53(±1.3)	2.6	<.001*
MCHC, *gm/dl*	21.46 (±7.8)	30.1(±1.02)	37.48	<.001*
Transferrin saturation, *%*	4(±1)	25(±3.5)	39.49	<.001*

"t" means student test (t-test) *mean highly significant difference (p-value<.001)

Table (5): comparison between pre-iron and post iron supplementation for anemic group regarding IQ and school performance.

Characters	Pre-Iron supplementation For Anemic group (n=100)	Post-Iron supplementation For Anemic group (n=100)	t-Test	P-value
	Mean (±SD)	Mean (±SD)		
IQ score	97.15(±7.402)	110.05(±7.59)	12.24	<.001*
School performance	76.79(±5.19)	83.9(±5.23)	12.1	<.001*

"t" means student test (t-test)
*mean highly significant difference (p-value<.001)

Table (6): comparison between non-anemic and post iron supplementation for anemic group regarding Iron profile.

Characters	Post-Iron supplementation For Anemic group (n=100)	Non anemic (n= 100)	t-Test	P-value
	Mean (±SD)	Mean (±SD)		
Hg level, *gm/dL*	12.825(±.216)	12.9 (±.347)	1.93	<.061*
MCV, *fL/red cell*	75.31(±3.54)	83.21 (± 2.15)	19.07	<.001***
MCH, *Pg/ red cell*	24.53(±1.3)	28.2 (±1.2)	20.744	<.001***
MCHC, *gm/dl*	30.1(±1.02)	33.4(±2.5)	12.22	<.001***
Transferrin saturation	25(±3.5)	35(±5)	9.19	<.001***

"t" means student test (t-test) *means no significant difference (p-value>.05)
**means significant difference (p-value<.05) ***means highly significant difference (p-value<.001)

Table (7) Comparison between non-anemic and post iron supplementation for anemic group regarding, IQ and school. performance.

Characters	Post-Iron supplementation For Anemic group (n=100)	Non anemic (n= 100)	t-Test	P-value
	Mean (±SD)	Mean (±SD)		
IQ score	110 (±7.59)	118.94(±4.17)	10.27	<.001*
School performance, (%)	83.9(±5.23)	94.11(±3.39)	16.38	<.001**

"t" means student test (t-test) *means significant difference (p-value<.05)
**means highly significant difference (p-value<.001)

4. Discussion:

In our study the prevalence of anemia is higher in rural areas and there is significant relationship between socioeconomic status and anemia and this is in agreement with **Goswmai S (11)** in their study in India that concluded that rural children had a higher prevalence rate of anemia. And in agreement with **Ncogo et al (12)** And also it is in the agreement with **Jamali NH et al (13)** In his study in district Shaheed Benazirabad during the period of August 2015 to March 2016, concluded that monthly income of the volunteers have significant association with Hb, and Serum ferritin. And also in harmony with **Gutema B et al (14)** who concluded that being from a family with low income is a risk factor for anemia.

There was a significant difference in the basic level of IQ and school performance between anemic and non anemic group in our study, this is in the harmony with **Chauhan U et al (15)** which concluded in his study that Mean IQ were found to be significantly low in Iron deficient anemic children as compared to controls (non anemic) and in the agreement with **Beard et al (16)** that concluded that there is a growing body of evidence from animal and human studies that supports a causal relationship between iron deficiency anaemia in early childhood and intelligence in mid-childhood. and also with **Mubarak A et al (17)** who concluded that the mean IQ was lower in the iron deficiency group than the non anemic group and also in agreement with **Jill S (18)** who concluded lower standardized math scores among iron-deficient school-aged children and adolescents and also this is in agreement with **Pollitt et al (19)**, on the other hand IQ tests did not show differences in three studies by **Pollitt et al(20)** and **Soemantri (21)** and **Soemantri et al (22)** At our study IQ and school performance were done as a basic level for both anemic and non anemic children and anemic children were lower than non anemic children and the comparison between them were repeated after improvement of hemoglobin level of anemic children and although the level of IQ and school achievement improved but not reached to the basic level of the non anemic children and this is in harmony with **Betsy Lozoff (23)** that concluded that Infants are at high risk for iron-deficiency anemia and Follow-up studies from preschool age to adolescence report poorer cognitive, motor, and social-emotional function, as well as persisting neurophysiologic differences. Research in animal models points to mechanisms for such long-lasting effects. Potential mechanisms relate to effects of iron deficiency during brain development on neurometabolism, myelination, and neurotransmitter function which have long lasting effect.

In the present study there was improvement of IQ and school achievement records after treatment with iron this is in the agreement with **HPS Sachdev (24) t**hat concluded that Iron supplementation improves mental development score. According to school performance before and after treatment there was significant benefit after treatment this is in the agreement with the Indonesian study as, anemic children showed a clear improvement with treatment **Soemantri et al(22)** On the other hand. In the other study **Pollitt et al (21),** children in Thailand showed no improvement with treatment The criterion for anemia in that study was high, hemoglobin <120 g/L, and the placebo group actually improved by 14 g/L, probably secondary to the deworming. It is possible that the placebo group responding to improved iron status may have threatened the integrity of the trial. In contrast, in the Indonesian study, the criterion for anemia was lower (<110 g/L) and the placebo group's hemoglobin levels declined by 17 g/L during the study. A further consideration is that the children were tested in groups in the Thailand study, which is unlikely to be as accurate as individual testing; it is not clear how testing was conducted in the Indonesian study. And in harmony with **sarika More et al (25)** study, iron deficient student had scored less in scholastic assessment than the normal non iron deficient students Similarly **Sungthong et al (26)** observed that the school performance including Thai language and mathematics score were less in iron deficient children than in non iron deficient children in study done on school children in Thailand. After receiving oral iron therapy and improvement of anemia, IQ and school performance for children was done and compared to the previously done before treatment. **Walter T(27)** concluded that two studies have examined children aged 5 years who had anemia as infants using comparable tools of cognitive development showing persisting and consistent important disadvantages in those who were formerly anemic. These tests were better predictors of future achievement. These children were again examined at 10 years and showed lower school achievement and poorer fine-hand movements**. Logan Set al (28)** concluded that there is no convincing evidence that iron treatment of young children with IDA has an effect on psychomotor development discernable within 5-11 days. The effect of longer term treatment remains unclear but the data would be compatible with clinically significant benefit. And this was updated in 2013 **Wang B et al (29)** by the same conclusion but more studies was identified The study of **Rani NA et al (30)** revealed that There was no association between the anaemic status and students scholastic performance and concluded that the mean

haemoglobin level was higher among low performer, indicating that nutritional anaemia may not \play a major role in educational performance and intelligence in higher education.

Conclusion:

Anemic children have lower IQ and school performance than non anemic children.

Treatment of iron deficiency anemia with iron therapy for adequate period has an important effect on improvement of IQ and school performance.

Iron deficiency anemia has long term effects on intellectual functions if not treated early at life so although the level of IQ and school performance of anemic children improved but not reached to the level of the already non anemic children from the start.

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