

Research Article

Cognitive Function and School Achievement in Adolescent Egyptian Girls with Iron Deficiency and Iron Deficiency Anaemia

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ABSTRACT

Background: Iron deficiency is probably the most prevalent and common micronutrient deficiency. The public health effects of iron deficiency and iron deficiency anemia include decreased intellectual and school performance. Adolescent girls are placed at a high risk level for developing iron deficiency, due to a combination of rapid physical growth adding menstrual iron losses in girls.

Objectives: To evaluate the effect of Iron deficiency and Iron deficiency anemia on school achievement and cognitive functions of adolescent girls in rural Upper Egypt.

Methods: 151 girls from a village school were enrolled in the study, they were divided according to Hb% and serum ferritin into: Group A: 52 non-anemic and non-iron deficient girls. Group B: 49 girls with Iron deficiency. Group C: 50 girls with Iron deficiency anemia. Mathematics score was used to assess school achievement and the Stanford Binet intelligence scale to assess the cognitive functions.

Results: Iron deficient girls with or without anemia had significantly lower mathematics score and lower scores in working memory and knowledge tests than non-iron deficient non-anemic girls ($P<0.05$). Serum ferritin had a significant fair positive correlation with full scale IQ ($r=0.28$, $P= 0.002$) and mathematics score ($r=0.37$, $P=0.001$). While, Hb% had a weak significant positive correlation with full scale IQ ($r=0.19$, $P= 0.03$) and mathematics score ($r=0.22$, $P=0.02$).

Conclusions: Iron deficiency was associated with decreased school achievement and low scores in Stanford Binet IQ test and they were even more affected in Iron deficiency anemia.

Mesh Headings/Keywords: Iron deficiency; Iron deficiency anemia; Adolescent girls; Cognitive function; School achievement

Introduction

Iron deficiency (ID) with or without anemia has important consequences for human health and child development: anemic women and their infants are at greater risk of dying during the perinatal period; children's mental and physical development is delayed or impaired by iron deficiency; and the physical work capacity and productivity of manual workers may be reduced [1]. There have been many efforts to fight iron deficiency and anemia over the past two decades but, despite these efforts, ID is still the most common nutritional disorder in the world and the leading cause of anemia [2]. In Egypt, nutritional anemia is the most common type of anemia. It is mostly caused by ID and less frequently due to folate or vitamin B12 deficiency [3]. Adolescents are considered a high risk group to develop ID and iron deficiency anemia (IDA) because of rapid growth and increased iron demands during puberty [4]. And this is exaggerated by inadequate intake, strenuous exercise, low socioeconomic status and parasitic infestations [5].

School aged adolescent girls are prone more to develop ID than adolescent boys. Their lower total food intake compared to boys, combined with menstrual losses makes them at greater risk of ID and IDA [6].

Prevalence estimates of iron deficiency (ID) in adolescent girls range from 9 to 40%, depending on the population studied and the criteria used to define ID [7].

In our previous study for prevalence of ID and IDA in adolescent girls in rural Upper Egypt, we found the prevalence of IDA 30.2% and that of ID without anemia 11.4% [8], these are relatively high rates.

So, in this study, we aimed to study the effect of ID and IDA on the cognitive functions and school achievement of these school-age adolescent girls.

Subjects and Methods

Subject selection

151 adolescent girls were randomly selected from the participant girls in our previous study which screened 5 village

preparatory schools for girls (from grade 7 to grade 9), in El-Minya governorate at Upper Egypt, for iron deficiency and iron deficiency anemia [8]. Necessary permissions were taken from school's authorities. The study was explained in details to the girls and written consents were taken from their parents or legal guardians. The protocol of the study was approved by the Institutional Review Board and Medical Ethics Committee of Minia University hospital.

Methods

Participant girls' parents completed a questionnaire asking about socio-demographic data, menstrual and medical history of the girls. Illiterate parents were helped to complete the questionnaire.

Anthropometric measures were taken. Wooden height scales were used for height measuring to the nearest 1 cm. Moreover, weight was measured using a scale with a sensitivity of 50 grams and a capacity of 150 kg. BMI was calculated by the use of the following equation: BMI=weight (kg)/height (m^2) [9]. BMI was classified according to BMI classification of the World Health Organization [10].

All the participant girls had undergone the following laboratory investigations: (1) Complete blood count (CBC) using automated blood counter *(Sysmex KX-21N)*. (2) Serum ferritin assay by enzyme-linked immunosorbent assay (ELISA) *(*Ferritin Human ELISA Kit, ab108837, Abcam, Cambridge, USA*)* [11]. (3) C-Reactive Protein (CRP) was analyzed by rapid latex-agglutination assay (CRP latex serology test kit, Omega diagnostics, Scotland, United Kingdom) for the qualitative and semi-quantitative determination of CRP in human serum [12].

Sample collection: About 4 ml of venous blood was withdrawn under complete aseptic technique. 1 ml of which in EDTA coated tubes for CBC evaluation and the other 3 ml in a serum separator tube. The separated serum was stored at -20ºC for measurement of serum ferritin and CRP.

Anemia was diagnosed when Hb<12 gm/dl [13] and ID when serum ferritin<15 ng/ml [2].

Girls with positive CRP were excluded from our study, as presence of inflammation makes the interpretation of normal serum ferritin values more difficult and may mask iron deficiency [2].

To assess the effect of ID and IDA on cognitive function, girls were divided into:

- **Group A (Control group):** 52 girls who were non-anemic (Hb ≥ 12 gm %) and non-iron deficient (serum ferritin levels of 15 ng /ml or more).
- **Group B (ID group):** 49 girls who were non-anemic (Hb ≥ 12 gm%) and iron deficient (serum ferritin less than 15 ng/ml).
- **Group C (IDA group):** 50 girls who were anemic (Hb<12 gm%) and iron deficient (serum ferritin less than 15 ng/ml).

Scholastic achievement assessment by mathematics score: For assessment of scholastic performance, the mathematics score was obtained from the previous month examination report card. The score obtained was from a total of 60 marks.

Cognitive function assessment by Stanford Binet intelligence scale fifth edition: The Arabic version of Stanford Binet test fifth edition for assessment of intelligence was used [14]. This test was translated and standardized for use in Arab countries several years ago with good reliability and validity [15]. The test measures five weighted factors and consists of both verbal and non-verbal sub-tests. The five factors being tested are knowledge, quantitative reasoning, visual-spatial processing, working memory, and fluid reasoning Score [16]. These tests were performed by qualified well trained psychologists.

Statistical methods: The collected data were analyzed using statistical package for social sciences (SPSS) program for windows version 20. Quantitative results were presented as mean ± standard deviation (SD) while qualitative data were presented by frequency distribution as percentage (%). Results were expressed as tables and figures. Chi square test, was used to compare between proportions. Correlation was performed using Pearson and Spearman correlation coefficient (r). The probability of error<0.05 was considered statistically significant.

Results

The age of the participant girls ranged between 12-15 years (13.7 ± 0.9). History of menstruation was positive in 101 girls (66.8%) with a mean age of menarche of 13.5 ± 1.5 years. Table 1 shows that IDA group had significantly lower monthly income than control (p=0.03). Also, there was a significantly higher frequency of underweight, overweight and obese in IDA group than the control group (p<0.001). Heart rate was significantly higher in ID and IDA groups than control group, while the hemoglobin level was significantly lower in IDA group than the other two groups (p<0.001 in all) as this was the criterion used to define IDA. Lastly, serum ferritin was significantly higher in control group than ID and IDA groups (p<0.001) and this was a criterion used to define control group, and it was also significantly higher in ID group than IDA group (p=0.02) (Table 1).

Table 2 shows the mathematics score significantly lower in ID and IDA groups than control group (p=0.03 and 0.02 respectively). IDA group had lower scores than ID group (p=0.02).

Also from Table 2, the control group had significantly higher knowledge score and working memory score than ID and IDA groups, where p=0.02 and 0.001 respectively for knowledge score and P=0.01 in both for working memory score, while control group had a significantly higher full scale IQ (FSIQ) than IDA group only (P=0.01). Serum ferritin had a significant fair positive correlation with both mathematics score (Figure 1) and FSIQ (Figure 2), (r=0.37 and P=0.001) and (r=0.28 and P=0.002) respectively. Hb% had a significant fair positive correlation with both mathematics score and FSIQ, (r=0.22 and P=0.02) and (r=0.19 and P=0.03) respectively. As there were significant differences in monthly income and BMI between IDA group and control group (p=0.03 and <0.001 respectively), we searched for presence of significant correlations between them and FSIQ or Math score, but all the correlations were weak and of statistical insignificance. Correlations of monthly income and FSIQ and Math score were (r=0.16, p=0.24) and (r=0.04, p=0.7) respectively, and correlations of BMI and FSIQ and Math score were (r=0.04, p=0.7) and (r=0.1, p=0.4) respectively.

Table 1: Socio-demographic, Clinical & laboratory findings of the participant girls.

Variable	Group A (Control) n=52 mean ± SD	Group B (ID) n=49 mean ± SD	Group C (IDA) n=50 mean ± SD	p-value
Age (years) (mean ± SD)	12.9 ± 1.3	14 ± 0.3	13.3 ± 0.9	p*=0.4 p#=0.6 p°=0.12
Literate Father: Yes: n (%) No: n (%)	 30 (57.7%) 22 (42.3%)	 29 (59.2%) 20 (40.8%)	 25 (50%) 25 (50%)	p*=0.32 p#=0.12 p°=0.4
Literate Mother: Yes: n (%) No: n (%)	 29 (55.8%) 23 (44.2%)	 27 (55.1%) 22 (44.9%)	 23 (46%) 27 (54%)	p*=0.17 p#=0.1 p°=0.23
Fathers Occupation: Farmer: n (%) Other: n (%)	 37 (71.2%) 15 (28.8%)	 39 (79.6%) 10 (20.4%)	 40 (80%) 10 (20%)	p*=0.2 p#=0.23 p°=0.18
Monthly income: ≤1000 EGP: n (%) >1000 EGP: n (%)	 33 (63.5%) 19 (36.5%)	 36 (73.5%) 13 (26.5%)	 40 (80%) 10 (20%)	p*=0.07 p#=0.03* p°=0.1
Menstruation • +ve n (%) • -ve n (%)	 34(65.4%) 18(34.6%)	 34(68.4%) 15(31.6%)	 33(64.7%) 18(35.3%)	p*=0.52 p#=0.52 p°=0.48
BMI • Normal: n (%) • Underweight: n (%) • Overweight & Obese: n (%)	 37(71.2%) 9(17.3%) 6(11.6%)	 25(51%) 16(32.7%) 8(16.3%)	 18(35.3%) 22(43.1%) 11(21.6%)	 p*=0.32 p#= 0.001* p°=0.37
HR(beat/min) (mean ±SD)	81.8 ± 6.7	89.5 ± 2.1	89.9 ± 7.6	p*=0.001* p#=0.001* p°=0.8
Hb (gm/dl) (mean ±SD)	12.5 ± 0.5	12.3 ± 0.4	10.9 ± 0.8	p*=0.17 p#=0.001* p°=0.001*
Serum ferritin (ng/ml) (mean ±SD)	41.2 ± 15.2	7.9 ± 1.3	6.6 ± 2.1	p*=0.001* p#=0.001* p°=0.02*

p*=Group A versus B; p#=Group A versus C; p°=Group B versus C.

EGP: Egyptian Pound; +ve: Positive; -ve: Negative; BMI: Body Mass Index; HR: Heart Rate; Hb: Hemoglobin.

*statistical significance at p<0.05

Discussion

In our study, the IDA group had significantly lower monthly income than the control group, this may be explained that lower-income families could have limited access to iron-rich foods and are more prone to parasitic infestations [17]. However, there were no statistically significant differences in paternal education and occupation in our study between the three groups, which omits their possible effects on school achievement and on cognitive function.

Also, no statistically significant difference was found regarding history of menstruation, which contradicts with WHO (2011) which stated that menstruation causes ID to be a continuous public health concern through the entire reproductive age [2]. The mean age of the participant girls was 13.7 ± 0.9 years and the mean age of menarche was 13.5 years, so, their short duration of menstruation did not affect their iron status.

The frequency of under-weight, over-weight, and obese girls were significantly higher in the IDA group than control group. This was in agreement with Bandhu et al. [18] and Manios et al. [19] studies, the first reported that IDA children had low anthropometric parameters than controls and they reported relative improvement after iron supplementation. [18] In rural Egypt, the unhealthy eating habits and the lower consumption of foods of animal origin are contributing to the development of anemia [20,21]. Manios et al. [19] stated that ID and IDA incidences in obese girls were higher when compared to their normal-weight peers. Many studies demonstrated that obese adolescents have lower serum iron availability with increasing adipose tissue mass and limited iron uptake from the duodenum when compared to normal weight children [22]. Additionally, ID may impair mitochondrial respiratory chain activity, thereby increasing fatigue, limiting exercise capacity and augmenting insulin resistance which aggravate the overweight problem [19].

Table 2: The mathematics scores and Stanford Binet intelligence scale of the studied girls.

Test	Group A (Control) n=52 mean ± SD	Group B (lD) n=49 mean ± SD	Group C (IDA) n=50 mean ± SD	p-value
Math. Score	47.2 ± 9.4	44.9 ± 9.6	42.6 ± 10.3	p*=0.03* p#=0.02* p°=0.02*
Verbal IQ	91.3 ± 10.175	91.4 ± 8.8	89.6 ± 8.8	p*=0.94 p#=0.39 p°=0.46
Non-verbal IQ	93.2 ± 9.2	93.1 ± 11.7	89.8 ± 16.5	p*=0.97 p#=0.19 p°=0.44
Fluid reasoning	103.5 ± 11.3	103.3 ± 11.4	100.5 ± 10	p*=0.96 p#=0.16 p°=0.32
Knowledge	88 ± 11.7	85.5 ± 15.8	79.4 ± 12.6	p*=0.02* p#=0.001* p°=0.1
Quantitative Reasoning	96.3 ± 8.6	94.6 ± 5.3	94.9 ± 8.1	p*=0.43 p#=0.44 p°=0.84
Visual Spatial	90.5 ± 7.2	88.7 ± 8.1	90.3 ± 8.7	p*=0.82 p#=0.92 p°=0.54
Working memory	96.7 ± 8.2	96.4 ± 4.9	92.1 ± 9.3	p*=0.01* p#=0.01* p°=0.06
Full scale IQ	93 ± 9.6	93 ± 9.3	89.9 ± 10.1	p*=0.98 p#=0.01* p°=0.25

p*=Group A versus B; p#=Group A versus C; p°=Group B versus C.
*statistical significance at p<0.05

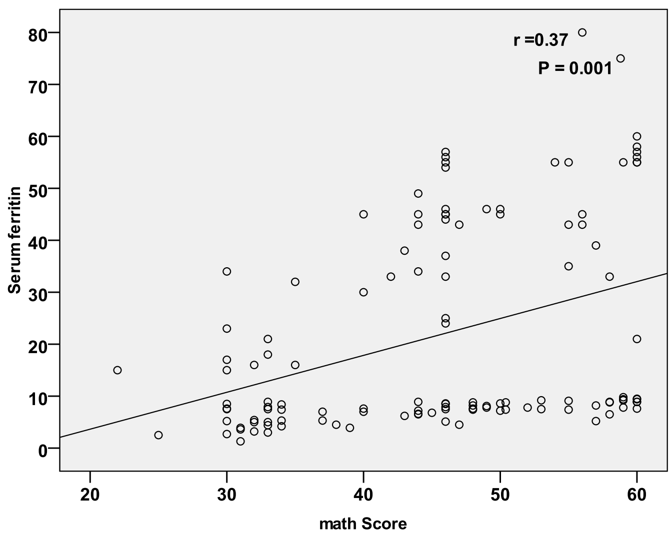

Figure 1: Correlation between Mathematics score and serum ferritin.

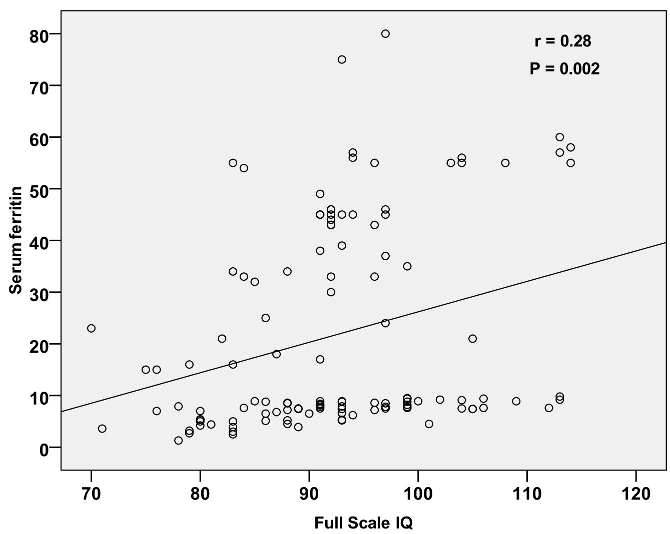

Figure 2: Correlation between Full scale IQ (FSIQ) and serum ferritin.

Assessment of school achievement

The ID and IDA groups had significantly lower mathematics scores than control group, with a positive correlation between serum ferritin and mathematics score. Zafar et al., [23] stated that ID and IDA appear to be associated with lower intellectual performance scores. ID causes impairments in attention span, intelligence, and sensory perception functions, as well as those related to emotions and behavior, which are crucial for school achievement. These impairments were previously related to IDA, but now, it must be noted that ID without anemia may cause these disturbances [24]. Experiments attributed these impairments to ID induced brain mitochondrial damage [25]. These effects may be exaggerated when anemia coexists, leading to low oxygen delivery to the brain causing further impairment of intellectual functions [26]. That was obvious in our study, as we found the IDA group had statistically significant lower mathematics score than the ID group.

Assessment of cognitive function

By using the Stanford Binet Intelligence Scale, the FSIQ was significantly lower in IDA group than control group only. This is in agreement with results of Akramipour et al. [27]. On the other hand, Brooks found significant difference in FSIQ scores between iron deficient girls with or without anemia and non-iron deficient girls. Also, FSIQ had positive correlation with serum ferritin. This was in agreement with many previous studies [6,28-30]. As deficiencies of nutrients like iron, that affect brain functions, have been estimated to shift the world's IQ potential negatively by at least 10 points [31].

The knowledge (long term memory) and working memory (short term memory) were the only two parameters in Stanford Binet intelligence scale which were significantly affected by ID and IDA. This goes with the results of Otero et al. [32] who showed that iron deficiency severely diminishes working memory. A study done in India used the multicomponent test of verbal learning, attention, and memory, which is similar to Stanford Binet IQ test, they found lower scores in the iron deficient with and without anemia groups than non-iron deficient group [6]. In our study, control group had higher verbal IQ score and fluid reasoning score (attention) than both ID and IDA groups but this was not of statistical significance. Many human studies have demonstrated the negative effects of ID on cognitive functions including learning, memory and attention [33]. ID seems to affect the cognitive function by causing mitochondrial damage, changes in brain dopamine receptors and dopamine metabolism, in addition to alterations in serotonergic neurotransmission [34].

Effect of IDA on school achievement and cognitive function

Hb% had a weak significant positive correlation with FSIQ and mathematics score. This was in agreement with results of Akramipour et al. [34] and Jaleel et al. [35], highlighting the effects of anemia on cognitive skills. It has been found in previous studies that cognitive function increases with increased hemoglobin concentration in children with ID but does not change with hemoglobin concentration in children with normal serum ferritin level, and that children with IDA consistently have the poorest cognitive function. Children with non-anemic ID have significantly higher cognitive function. So a dose–response relationship between hemoglobin and cognitive function in children with ID has been found, whereas no similar evidence is found in iron-sufficient children [30].

Conclusion

Iron deficiency was associated with low school achievements and low scores in Stanford Binet IQ test and they were even lower in iron deficiency anemia. This is important as it gives an opportunity for school-based interventions to improve adolescent girls' health stressing on nutritional education. We should screen girls with bad scholastic performance and bad memory for ID and IDA.

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