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Original Article

Assessment of Iron Profile and Its Effect of Deficiency in Growth and Development in Infants at One-Year-Old Age

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ABSTRACT

Background: Anemia is described as a decreased erythrocyte count and or hemoglobin value below the 5th percentile of the usual hemoglobin value specified for that age in healthy individuals.

Aim of the Work: To assess the iron status and evaluate the iron deficiency and their association with the development of motor activity and anthropometric measurement in one-year-old infants.

Patients and Methods: This randomized cross-sectional study is performed on 200 infants aged one year in primary care unit at vaccination set in Damietta governorate. 45% Of them were females and 55% were males all of them underwent laboratory tests (complete blood count (CBC), serum ferritin, total iron binding capacity (TIBC), serum iron), growth and developmental assessment.

Result: 34% of infants were with normal hemoglobin ,serum iron and ferritin ,infants who have deficiency of iron were 25%, infants who have anemia without iron deficiency were 15% and. Infants who have iron deficiency anemia 26%, of them 26.9% were underweight, 23.1% were stunted and 26.9% were delayed development, but growth and development unaffected in other cases.

Conclusion: The percentage of iron deficiency anemia and iron deficiency is high in infants at one year, so we must start iron therapy at the first year to avoid the effects of iron deficiency on growth and development.

Keywords: Iron Deficiency (ID); Hemoglobin; Anemia; Growth; Development

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* Main subject and any subcategories have been classified according to the research topic.

INTRODUCTION

Iron deficiency anemia [IDA] is the commonest type of anemia. It approximately reported in 43% of children during childhood [1].

According to the world health organization [WHO] 2011 and regardless the neonatal age, childhood anemia is usually seen in infants and then again in puberty. Both stages of accelerated growth followed by possible food intake challenges [2].

Infants are the main risk group for dietary iron deficiency anemia. After six months of age, iron reserve is depleted in infants and breast milk is deficient in iron. So, iron therapy [supplementation] must initiated in the first year and foods must be fortified with iron to avoid iron deficiency. Both preterm and low weight during birth are a special risk group as they have a high growth rate [3].

IDA is the most widely reported, global nutritional deficiency in infants [4]. Iron is required in the final stage of hemoglobin formation. Ferrochelatase promotes the incorporation of iron into protoporphyrin. Thus, forming hemoglobin, necessary for the oxygen delivery to various organs and tissues in the body. This leads to microcytic anemia, referred IDA; the most common ID effect. The body's iron reserves must first be depleted before any changes in hemoglobin levels are reduced. Many researchers have studied prevalence of iron deficiency anemia in their community. However, few researchers have studied iron deficiency and their association with motor development and anthropometric measurement. So, we designed the current study.

THE AIM OF THE WORK

This study aimed to measure the iron profile and the effect of iron deficiency [ID] on the development and anthropometric measurement in one-year-old infants.

PATIENTS AND METHODS

This randomized cross-sectional study conducted, after receiving the approval of the ethics committee and parental agreement. Infants were recruited from the primary care units in Damietta Governorate at vaccination set, two days' work per week [from

December 2019 to September 2020]. 200 infants under the study of both sexes, whose all visitor of the vaccination center during this period met eligibility criteria. The mean age is one year at vaccination set. All of them underwent laboratory tests (complete blood count [CBC], serum ferritin, total iron binding capacity [TIBC], and serum iron), with cutoff points (TIBC 2.5-4.5microgram/ml), mean cell volume [MCV 68-85 fl/cell], mean cell hemoglobin [MCH 24 - 30 pg/cell], mean cell hemoglobin concentration [MCHC 32-37g/dl], serum iron (0.33-1.93 microgram/ml) , serum ferritin (7.0-140 Nanogram/ml), red blood cell count [RBC 3,8-6.0x10³cells/ul), red cell distribution width [RDW 11.5-14.5%) growth and development assessment. The study was performed in compliance with the Code of Ethics of the World Medical Association for human research.

The inclusion criteria were infants at one year old of age, of both genders. However, the exclusion criteria were other system disease (liver, kidney and bone marrow diseases); hematological disease other than iron deficiency anemia; congenital heart disease; skeletal deformities leading to limitation of movement; and any symptoms or signs of acute infection/inflammatory condition.

All infants were subjected to medical history taking (type of feeding [breastfeeding, or bottle feeding]), on iron therapy or not, clinical examination [general], pale or not, cachexia or obesity. A systemic evaluation of the vital signs (heart rate, respiratory rate and temperature), cardiac examination, abdominal examination, anthropometric measurements (weight, length and head circumference (HC)). The laboratory analysis, included complete blood cells (CBC), serum ferritin, complete iron-binding power, and serum iron.

The anemia is defined when hemoglobin was less than 11 gm/dl. Types of anemia are known as normochromic normocytic anemia, hypochromic microcytic anemia, macro-cytic normochromic. In addition, anemia classified as iron deficient or not [5].

One blood sample of 4 ml was drawn under a complete aseptic conditions of venous blood in a clean glass tube. Two centimeters for CBC in a clean glass tube containing ethylenetetraacetic acid (EDTA), and two ml of blood for plasma ferritin in a clean glass tube.

The CBC calculation and analysis had been performed by automated blood cell counter. The concentration of plasma ferritin (PF) was measured using a sensitive Sandwich-linked immunosorbent assay (ELISA) technique.

Serum iron and TIBC. Lipemic samples was clarified by means of a detergent. Ascorbate reduces the release of ferric to ferrous ions, which then react with ferro-zinc to form a colored complex. There iron was identified by the color intensity. The analysis was completed by photometer (Roche Fe reagent. Indianapolis, IN, 2010). Anti-transferrin antibodies bind to the antigen in the sample in order to form an antigen/antibody complex. After agglutination, this was assessed turbidimetrically, adding polyethylene glycol (PEG) permits the reaction to reinforces easily to the endpoint and increases the sensitivity. The total iron binding capacity [TIBC] was calculated from the equation $[TIBC = (\text{Transferrin} \times 1.18)]$; and the percentage of saturation = $\text{Iron} / \text{TIBC} \times 100$.

We also measured weight, length, and head circumference and linked to their development. For head circumference, we take light weight, non-stretchable measuring tape used for intervals of one centimeter. Babies weighed while lying in the lap of the caregivers, headgear or another item [e.g. hairpins removed]. The tape was mounted right over the eyebrows (i.e. the supraorbital ridges). The most conspicuous point of the head above the ears, and along the back of the head (i.e. the occiput) such that the full circumference was calculated. The tape on the same plane, on both sides of the head, close enough to compress the scalp. An average of three readings was taken and measurements were read to the nearest millimeter. HC was plotted on the percentage scale of The World Health Organization [WHO] child growth standards (0-36 months).

For measurement of weight, the electronic scale was used and the zero weight on the horizontal beam of the scale shall be tested regularly even after the scale has been shifted. The baby was put in the center of the scale, without wearing any clothing or nappy. If the nappy was worn, the weight shall be reversed by subtracting the weight of the nappy (i.e. the clean nappy was weighed separately). There was little to help the boy. The average of three measurements was

taken and the measurements were read to the nearest value.

Measurement of length was performed as a recumbent length (received when the patient was lying down). Lengths were plotted on the WHO (0-36 months) percentile charts. A wooden board with a solid headboard and a rotating footboard was used, with increments of one millimeter. Two individuals were required to make calculations. No caps, socks, or headgear were worn. One guy holds the crown of the infant head against the headboard with the Frankfort plane forming a 90° angle with the backboard. This person also ensures that the head, shoulders, and buttocks touch the backboard/flat board. The other guy holds the legs parallel to the backboard and slides the footboard to the bottom of the legs with the toes pointed upwards. If the leg/s had troubles, the leg/s were pressed down to the knee to flex the leg upwards and one leg was used. The average of three measurements were taken and the measurements were read to the nearest 0.1 cm. Development was considered normal if the infant was walking alone or with one handheld and sitting alone. However, the development was considered delayed if he/she was not sitting alone, or sit alone, but was not walking alone or with one handheld.

Statistical analysis and data interpretation: Data was fed to the computer and analyzed using IBM SPSS software package version 22.0. (Armonk, NY: IBM Corp, USA). Quantitative data were described using the mean, the standard deviation for parametric data after testing normality using the Kolmogorov-Smirnov test. The significance of the gained results was considered at the (0.05) level. One Way ANOVA test was used to compare more than 2 independent groups with the Post Hoc Tukey test to detect pair-wise comparison.

RESULTS

Table [1] demonstrated that, reduced hemoglobin was discovered among 51.0%. However, TIBC increased in 49% and red cell distribution width was increased among 56.0% of infants. On the extreme side, MCV, MCV, iron, ferritin and red cell blood count were decreased in 32.0%, 69.0%, 69.0%, 51.0% and 18.0% successively. Table (2) showed that, 25.0% of infant had iron deficiency, 26.0% had iron deficiency

anemia, 5.0% had hypochromic microcytic anemia without iron deficiency and 10.0% had normocytic anemia without iron deficiency. Table [3] revealed that, there was significant difference between the normal and different abnormalities of iron deficiency and anemia as regard to infant weight, infant length, and development. Reduced weight was reported in 26.9% of infants with IDA, but other subgroups had normal weight. Also, there was 23.1% of IDA who had lower length than the third percentile. Other subgroups had no abnormality. Finally, the delayed development and

lower HC reported in 26.9% and 15.4% respectively of IDA subgroup. Other subgroups had no abnormalities.

Table [4] describes the correlation between anthropometric measurements and other studied variables. Weight was positively and significantly correlated with hemoglobin, iron, ferritin, MCV, MCH, and MCHC. But, the correlation was negative with TIBC and RDW. The length and HC yielded comparable results.

Table (1): CBC results among studied cases.

		No.	%
Hemoglobin (gm/dl)	Normal	98	49.0
	Decreased	102	51.0
Total Iron Binding Capacity [TIBC]	Normal	102	51.0
	Increased	98	49.0
Mean cell volume [MCV]	Normal	136	68.0
	Decreased	64	32.0
Mean cell hemoglobin (MCH)	Normal	62	31.0
	Decreased	138	69.0
Mean cell hemoglobin concentration (MCHC)	Normal	62	31.0
	Decreased	138	69.0
Serum iron	Normal	98	49.0
	Decreased	102	51.0
Serum ferritin	Normal	98	49.0
	Decreased	102	51.0
Red blood cell count	Normal	164	82.0
	Decreased	36	18.0
Red cell distribution width	Normal	88	44.0
	Increased	112	56.0

Table (2): Distribution of the studied cases according to CBC and iron profile (n=200)

Classification of the studied groups*	No.	%
Normal	68	34.0
Iron Deficiency	50	25.0
Iron deficient anemia	52	26.0
Hypochromic microcytic anemia (but iron status is normal)	10	5.0
Normocytic anemia without iron deficiency.	20	10.0

*Depending on normal average of CBC parameters; Iron deficiency group is defined as normal hemoglobin range (11.2-14.1gm/dl) and low serum iron and low serum ferritin; Iron deficiency anemia group is defined as low hemoglobin, low serum iron, low serum ferritin and high TIBC; Hypochromic microcytic anemia but not iron deficiency is defined as low hemoglobin, low MCV, Low MCH and low MCHC with normal serum iron, and serum ferritin; Normocytic anemia group is defined as low hemoglobin, normal MCV, normal MCH and normal MCHC .normal serum iron and serum ferritin.

Table (3): Comparison of anthropometric measurements and motor development between studied groups

	Normal N=68(34%)	Iron Deficiency N=50(25%)	Iron deficient anemia N=52(26%)	Hypochromic microcytic anemia without iron deficiency N=10(5%)	Normocytic anemia N=20(10%)	p	
Weight (kg)	9.82±0.45 ^{ABC}	9.71±0.56 ^{ADE}	9.18±1.04 ^F	9.62±0.41 ^{BDFG}	9.87±0.45 ^{CEG}	0.005*	
Weight category	Normal <3 rd percentile	68(100.0) 0(0.0)	50(100.0) 0(0.0)	38(73.1) 14(26.9)	10(100.0) 0(0.0)	20(100.0) 0(0.0)	<0.001*
Length (cm)	70.68±0.73 ^{ABC}	70.72±0.74 ^{ADE}	69.88±0.99 ^F	70.40±0.55 ^{BDFG}	70.50±0.53 ^{CEG}	0.001*	
Length category	Normal <3 rd percentile	68(100.0) 0(0.0)	50(100.0) 0(0.0)	40(76.9) 12(23.1)	10(100.0) 0(0.0)	20(100.0) 0(0.0)	0.001*
Head circumference (HC) (cm)	43.97±0.83	44.08±0.76	43.58±1.03	43.80±0.84	44.10±0.88	0.257	
HC category	Normal <3 rd percentile	68(100.0) 0(0.0)	50(100.0) 0(0.0)	44(84.6) 8(15.4)	10(100.0) 0(0.0)	20(100.0) 0(0.0)	0.018*
Development	Delayed Normal	0(0.0) 68(100.0)	0(0.0) 50(100.0)	14(26.9) 38(73.1)	0(0.0) 10(100.0)	0(0.0) 20(100.0)	<0.001*

Similar superscripted letters denote non-significant difference within groups by Post Hoc Tukey test in same row; *statistically significant (if p<0.05)

Table (4): Correlation between anthropometric measurements and CBC results among studied cases.

	Weight		Length		Head Circumference	
	r	p	r	p	r	p
Hemoglobin (gm/dl)	0.503*	<0.001	0.541*	<0.001	0.349*	<0.001
Serum ferritin (ng/ml)	0.290*	0.003	0.179	0.075	0.102	0.313
TIBC(µg/ml)	-0.310*	0.002	-0.190	0.058	-0.072	0.476
Serum iron (µg/ml)	0.269*	0.007	0.173	0.085	0.077	0.446
MCV	0.427*	<0.001	0.426*	<0.001	0.340*	0.001
MCH	0.372*	<0.001	0.384*	<0.001	0.217*	0.030
MCHC	0.251*	0.012	0.298**	0.003	0.198*	0.049
RDW	-0.224*	0.025	-0.208*	0.038	-0.063	0.532
RBCs	0.042	0.679	-0.103	0.310	0.024	0.813

r: Pearson correlation co-efficient *statistically significant

DISCUSSION

This study aims to assess the effect of iron deficiency on growth and development in one-year-old infants. The study showed that the 51% of infants had low hemoglobin, 49% had increased TIBC, 32% had reduced MCV, 69% had reduced MCH & MCHC, 51% had decreased serum iron and serum ferritin, 18% had reduced RBC & 56% had increased RDW. These results are in line with Tawfik *et al.* [6] who studied the prevalence of iron deficient anemia in different groups included children younger than 5 years in Egypt. They indicated that IDA was identified in 18.5%, iron deficiency without anemia reached 26.0% and 20.6% of cases had high ferritin values but still anemic.

In the current study, the infants with IDA had a higher incidence of growth delay, low weight, length, and HC. These results are compatible with Pala *et al.* [7] who established the effect of iron and iron-deficiency anemia on psycho-motor growth in infants. Psychomotor development was tested in stable children with deficiency of iron and IDA. They reported a delay in their personal/social, and fine motor skills. They concluded that IDA affected psychomotor growth during childhood. However, evidence of side effects of IDA was also controversial. The Denver II Developmental Screening Test [DDST] is a helpful test to detect early developmental delays, especially in infants with risk factors. These results are similar to previous evidence that iron deficiency anemia had an effect on children psychomotor development. There is, however, little evidence of adverse effects [7].

Grantham-McGregor *et al.* [5] reported that, an important increase in the Mental Growth Index score (21.6 points) was observed in children aged 9 to 12 months with iron deficiency. These observations

indicated that ID, even in the absence of anemia, results in metabolic changes influencing the babies' behavior. The latest findings have reflected the advantages of iron supply for iron-deficient babies, in particular for motor development and social-emotional behavior.

Also in Lozoff *et al.* [8] suggested that iron supplementation before iron deficiency becomes aggressive or permanent, can prevent such adverse effects. ID classified as poor body iron reserves, is the leading cause of anemia and has been linked with adverse psychomotor, cognitive, and socio-emotional developments.

Beard *et al.* [9] reported that ID and IDA in young children may have long-lasting negative effects on children's actions and development, disrupting their cognitive and socio-emotional control undermining their cognitive and socio-emotional functioning as adolescents and young adults.

Iron is a main component in the metabolism of approximately all living organisms, affects childhood growth, motor development & coordination, language development, and educational attainment in children.

Contrary to the current study, Szajewska *et al.* [10] showed that, limited available evidence suggests that iron supplementation in infants may positively influence children's psychomotor development. Compared with placebo, supplementation with iron had no significant effect on children's Mental Developmental Index approximately at the age of 12 months.

In the current study, there was a positive correlation between the weight of the infants and hemoglobin, serum ferritin, serum iron, MCV, MCH, MCHC, MCHC, and a negative correlation with TIBC and RDW. The

length had a positive correlation with hemoglobin, MCV, MCH, MCHC and a negative association with RDW. The HC indicates an important positive association with hemoglobin MCV, MCH, and MCHC. According to iron deficiency anemia, 26.9% of infants had delayed motor development and 73.1 % had normal motor development. These results are compatible with Stoltzfus *et al.* [11] who showed a substantial increase in motor development after 12 months of supplementary iron was considered as a good evidence that the reprocessing of iron could be posed. The paper also seeks to understand the role of anemia and iron deficiency in developmental delay, indicating that while the effect of iron on motor production is regulated by increased concentrations of hemoglobin and oxygenation. Studies have shown that RDW, in addition to other hematological markers such as (MCV) and hemoglobin, can be used as indicators.

Also Arcanjo *et al.* [12] has shown that the importance and benefits of iron supply for iron-deficient children, especially for motor development and social-emotional behavior. They have indicated that prior iron supplementation can prevent such adverse effects. Children with severe, permanent childhood iron deficiency score lower on emotional and mental performance tests and are at risk for long-lasting developmental drawbacks, such as learning disabilities and socio-emotional problems).

There's a proof that there are differences between males and females in iron status during puberty and adulthood are considered primarily due to the menstrual lack of iron in pregnant women and can be moderated by dietary conditions and iron supplements. In this study, the anemia in males was 53.9%, while the percentage of anemia in females was 46.1%. The prevalence of IDA in this study was higher in males than females. Contrary to Abdel-Rasoul *et al.* [13] showed no significant difference in the prevalence of IDA between girls (57.3%) and boys (42.5%). Mohamed *et al.* [14] showed that, iron deficiency was found in 20.4 % of the children. It was associated with anemia in 85% of the subjects. No gender differences were revealed by these findings according to iron status, though a slight difference is noted, 12.8% for girl's vs 11.4% for boys.

Domellöf *et al.* [15] reported that, at the age of 9

months, male babies are slightly lower in hemoglobin and have a 10-fold greater chance for IDA diagnosis than female infants. They also indicated that the causes of elevated IDA risk of male babies were higher pre-and post-natal growth rates, increased fetal erythropoietin activity resulting in low iron storage. However, these results are inconsistent with Andriastuti *et al.* [16] who showed that, the overall prevalence of anemia was 14.0% and the prevalence of IDA, ID, and iron depletion was higher in females than in males.

In the present study, the percentage of pallor in cases of iron deficiency anemia was 77%, but in Saldivar-Espinoza *et al.* [17] reported that the pallor of the mucous membranes is only 28% sensitive and 87% specific (with high predictive value) in distinguishing children with anemia and 49% sensitive and 79% specific in distinguishing severe anemia (hemoglobin < 7.0 g/dl). Also in Franco [18], 25% of the cases had iron deficiency, 26% of the cases had IDA of them; 10% of the cases were hypochromic microcytic anemia & 5% were normochromic anemia). Hemoglobin was slightly smaller in normocytic anemia than in other categories, except for the iron deficiency.

Results of the current work are compatible with Buttarello who showed that, the total or transferrin iron-binding capacity (TIBC) is a test that measures the blood capacity to bind iron with transferrin [19]. Also in Ogun [20], it is well known for its ability to deliver iron and its concentration of serum transferrin increases when the ID is present. As a transferrin surrogate, TIBC is not an indicator of iron status.

The World Health Organization reported that, total iron-binding ability (TIBC) was a statistically important lower mean for the normal group followed by hypochromic microcytic anemia but not an iron deficiency, and the highest was for the iron-deficiency anemia group. The mean MCV was higher in normocytic anemia than other groups with statistically relevant inconsistencies with other groups, except for normal-group normocytic anemia. In iron-deficient conditions, the relative transferrin content compared to iron content increases, and thus the TIBC values are high. The reverse happens in iron overloaded states of the body; the quantity of free transferrin in the blood decreases, and subsequently, TIBC values are low [21].

Auerbach [22] concluded that TIBC is an assay that measures the amount of iron that can be bound to unsaturated transferrin, i.e. the total number of transferrin-binding sites per unit volume of plasma or serum. Transferrin saturation of <15% in association with elevated TIBC is predictive of iron deficiency anemia. In the case of iron deficiency, the decreased concentration of serum iron leads to an increase in (TIBC) and a decrease in the saturation of the iron transporter transferrin.

Conclusion:

A high prevalence of iron deficiency and IDA in babies aged one year. The percentage of iron deficiency of anemia in our sample was 26% and iron deficiency was 25%. Iron supplementation must begin during the first year of age.

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None to be declared

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The background of the cover is a light blue gradient. It features a faint, stylized ECG (heart rate) line running across the top and bottom. In the center, there is a semi-transparent globe showing the continents. A stethoscope is overlaid on the globe, with its chest piece on the left and its ear pieces on the right. The overall theme is medical and global.

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