Growth Pattern in Anemic Children and Adolescents, aged 12-14 years

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Abstract: Iron deficiency anemia among children and adolescents is a large health problem worldwide. Adolescence is characterized by a large growth spurt and the acquisition of adult phenotypes and biologic rhythms. During this period, iron requirements increase dramatically in both boys and girls. Anemia due to iron deficiency often coexists with zinc deficiency. Deficits in macronutrients or micronutrients can impair growth. Menstruation increases the risk for iron deficiency anemia among girls throughout their adolescence. The aim of the present work is to assess growth pattern in anemic boys and girls and to study relations between anthropometric parameters and hemoglobin, iron and zinc levels. The sample consisted of 60 anemic children and adolescents aged from 12- 14 years (30 boys and 30 girls) and 30 normal healthy children (15 boys and 15girls). Weight, height, mid upper arm circumference (MUAC), waist and hip circumferences were measured and body mass index (BMI) was calculated. Sex- and age-independent SD scores (SDS) were calculated for all anthropometric measurements with the use of the Egyptian reference data. Hemoglobin concentration, serum ferritin, iron and zinc were measured for patients and control. Anemic girls showed significant association between height SDS, weight SDS, BMI SDS and hemoglobin concentration level and also between MUAC SDS and zinc level. Anemic boys showed less marked growth delay. The study showed that growth delay was pronounced among anemic girls during adolescent growth spurt. Thus, age and sex are the factors most predicative of growth delay among Egyptian adolescents. The study emphasized that iron and zinc are essential micronutrients for normal growth and anemia has a negative impact on growth. The study suggests regular nutrition assessment of adolescents and recommends behavior modification to get dietary change among adolescents. The inhibited growth rate, induced by the iron-deficient diet could be reversed by giving a diet supplemented with iron.
[Sanaa Kamal; Moushira Erfan; Shams Mohamad Kholoussi; and karima Abd Elfatta Bahgat. **Growth Pattern in Anemic Children and Adolescents, aged 12-14 years**. Journal of American Science 2010;6(12):1636-1646]. (ISSN: 1545-1003). http://www.americanscience.org.

Key words: Iron deficiency, phenotypes, Growth Pattern.

1. Introduction:

Adolescence is a time of intense physical, psychosocial, and cognitive development. During this period they gain up to 50% of their adult weight, more than 20% of their adult height, and 50% of their adult skeletal mass. Thus the nutritional needs for energy, protein, and many vitamins and minerals are increased. Inadequate stores or intake of nutrients during this period can have adverse effects on the physical growth and cognitive development. So adolescence is a vulnerable period for the development of nutritional anemia (DiMeglio, 2000; Chaudhary and Dhage, 2008).

Deficits in macronutrients or micronutrients can impair growth (Sen and Kanani, 2006). Iron and zinc deficiencies are the main micronutrient deficiencies of public health significance. The deficiency of these nutrients arise from inadequate intakes, impaired absorption and or utilization, excessive losses, or a combination of these factors and are exacerbated during times of greater physiological need such as adolescent (Ijarotimi,2004).

Anemia is a major public health problem at all ages worldwide (Maninder and Kochar, 2010). It may be due to iron deficiency; insufficient hematopoiesis due to deficiencies of folic acid or vitamin B 12; hemorrhagic anemia secondary to blood loss; hemolytic anemia with premature red blood cell plasma membrane rupture; hemoglobinopathies such as sickle cell anemia and thalassemia; or aplastic anemia with destruction of bone marrow. Iron-deficiency anemia is the most common type of several causes of anemia. Deficiencies of folic acid or vitamin B 12 can also cause anemia but are rare, and usually occur because of impaired vitamin absorption. Diseases of the bone marrow will also cause anemia. Fortunately, these conditions are rarer (Hoffman et al., 2008).

Iron deficiency anemia (IDA) is the main micronutrient deficiency that may affect adolescent. It is one of the most universally prevalent diseases in the world today particularly developing countries and it is a major public health .Iron deficiency has been considered an important risk factor for ill health and is estimated to affect 2 billion people worldwide (WHO, 2002). Iron is essential for all tissues in a young child's developing body. It is present in the brain from very early in life, when it participates in the neural myelination processes. Beard (2001) and other authors (Haas and Brownlie, 2001) have been postulated other roles of iron that would affect growth and immune function. It is essential for the expansion of blood volume and muscle mass. Functions of iron include involvement in energy metabolism, gene regulation, cell growth and differentiation, oxygen binding and transport, muscle oxygen use and storage, enzyme reactions, neurotransmitter synthesis, and protein synthesis. Attention deficits, poor performance in intelligence tests, behavioral and mood changes, tiredness, and below-average school performance are associated with iron deficiency in adolescents (Amy et al., 2007).

Iron needs are highest in males during peak pubertal development because of a greater increase in blood volume, muscle mass and myoglobin (Hyder et al., 2007). However, after menarche, iron needs continue to remain high in females to replace menstrual blood loss (Paknahad et al; 2003). So an adolescent girl is 10 times more likely to develop anemia than a boy because of their irregular eating habits (caused by concerns about body image) compounded by normal menstrual blood loss. James et al., (2006) reported that Iron deficiency is the most prevalent micronutrient deficiency disease in the world and occurs in young women in the United States.

The detrimental effects of IDA on physical growth have been attributed to poor appetite, altered endocrinological profile and neurotransmitter metabolism consequent to iron deficiency. The appetite is seen to decrease in IDA independently of plasma leptin levels (Topaloglu et al., 2001). In IDA plasma norepinephrine as well as urinary excretion of epinephrine and norepinephrine is increased .An elevated cortisol and parathormone level along with altered metabolism of calcium, phosphorus and magnesium has also been observed (Campos et al., 1998). The effects of IDA on physical growth have been shown to be resistant even to the administration of growth hormone (Ceppi and Blum, 1994). The thyroid gland metabolism is also affected (Zimmermann et al., 2000) with impaired thermoregulation and a hyperadrenergic state is seen in hypothyroid individuals suffering from iron deficiency (Shakir et al., 2000).

Zinc, which is an essential cofactor for nearly 200 enzymes, participates in cellular growth as a cofactor for enzymes necessary for the synthesis of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), and controls, growth and development. Adolescents need more zinc/kg than adults, due to the role of this metal in growth and maturation. It is important to assess the levels of iron, and zinc in adolescents during the pubertal spurt (Urbano et al., 2002). Zinc deficiency has profound and far-reaching effect on health and well being of humans. There is convincing evidence linking zinc deficiency to childhood growth stunting (villalpando et al., 2003). Growth retardation has been associated with anemia and zinc deficiency in adolescent populations (Wajeunnesa et al., 2009).

Iron and zinc are essential micronutrients for human health. Deficiencies in these 2 nutrients remain a global problem, especially in developing countries. Anemia due to iron deficiency often coexists with zinc deficiency. It was apparently first recorded by Prasad et al., in that year (Nishiyama et al., 1998). Clinical findings included growth stunting, anemia, low serum iron and plasma zinc levels, low urine, sweat and hair zinc levels. Iron and zinc nutrition are often associated. Red meat is the most important common dietary source of bioavailable iron and zinc. Phytate inhibits iron and zinc retention. Consequences of these associations were first described by Prasad, Halsted and their associates in Egyptian and Iranian adolescents whose diets were nearly devoid of meat and were based on bread prepared from whole grain wheat flour rich in phytate (Paknahad et al., 2007). Instead, vegetables, whole grain cereals, legumes and nuts are their major food sources of these trace elements. However, these same foods also contain high levels of phytic acid and dietary fiber; components that may interfere with the absorption of iron and zinc, thus leading to decreased bioavailability The aim of the present study is to assess growth pattern in anemic boys and girls and to study correlations between anthropometric parameters and hemoglobin, iron and zinc levels.

2. Patients and methods:

The subjects of this study comprised a total number of 90 children and adolescents: 60 were anemic (30 boys and 30 girls), and 30 were normal healthy one and randomly chosen of both sexes (15 boys and 15girls). Their age ranged from 12- 14 years. A formal consent letter from the parents of each child included in the study was obtained after explaining to them the whole procedure. This study was approved by the Ethics Committee of the Hospital. They were attending the Pediatric Clinics of Al-Zahraa Hospital, Al-Azhar University complaining of easy fatigability, pale colour and decreased school performance. According to WHO criteria for diagnosis of anemia (Beard and Stoltzfus,

2001) the children with hemoglobin concentration< 12 g/dL were assigned to the anemic group and those with hemoglobin concentration ≥ 12 g/dL were assigned to the control group.

Children suffering from any chronic illness e.g. asthma, rheumatic heart disease etc, or receiving any long term drug treatment were excluded from the study. All Cases were subjected to: appropriate and thorough medical history, physical examination, routine laboratory investigations were also done including: Complete blood picture, erythrocyte sedimentation rate, and C-reactive protein. Hemoglobin concentration values and RBC indices were measured using automated hematology cell counter (Coulter T 890), serum iron values along with peripheral blood smear to study RBC morphology were analyzed. Serum iron was measured by method described by International Committee for standardization in Haematology and TIBC was measured by Ressler and Zak (1958) method. Transferrin saturation was determined by dividing serum iron by total iron binding capacity (looker et al .1995). According to the cut-offs values used by WHO the three indicators of abnormal iron status were applied: serum ferritin < 12 ng/mL, transferrin saturation < 16%, and red blood cell distribution width (RDW) >15%. Calorimetric test for the determination of Zinc in sera of all groups was performed by atomic absorption spectro-photometer (Gupta et al., 1992) using Zinc fluid Monoreagent (Centronic Gmbh-Germany).

The anthropometric measurements and instruments used followed the International Biological Programme (IBP) (Tanner et al., 1969). Measurements were taken on the left side of the body and included: weight, height, mid upper arm circumference (MUAC), waist and hip circumference. Body mass index (BMI; in kg/m2); and waist to hip ratio (WHR) were calculated.

Physical growth was assessed for each child by determining the standard deviation scores of weight, height, BMI and mid-upper arm circumference, using the Egyptian growth reference data (Ghalli et al., 2002), we calculated standard deviation score (SDS) independent of sex and age that is, child measurement minus population mean/population SD.

Waist to hip ratio was also calculated and compared to the control group in the present study. Statistical presentation and analysis of the results were carried out using SPSS software version 11. Statistical tests used included chi-square test, student's't' test , analysis of variance, and tukey tests. Correlations were tested between growth parameters and hemoglobin and serum zinc by linear regression analysis.

3. Results

Table 1 shows means of growth parameters SDS in anemic boys and girls. The values of SDS for the weight, height , BMI, and MUAC lied at the lower limits of reference Egyptian growth data with no statistical significant difference between boys and girls (P<0.188). However, girls had more delyed growth parameters than boys. Also, the waist to hip ratio had lower values, with no statistical significant difference between both sexes as well as when compared to the non anemic control group.

Table 2 shows means of growth parameters SDS in anemic girls. As the age of the girls increase the growth delay is more pronounced in all anthropometric parameters with no statistical significant differences between the age groups.

Table 3 shows means of growth parameters SDS in anemic boys. The values of SDS for height among the studied adolescent boys lied at the lower limits of reference Egyptian growth data nearly with the same lower value in all age groups, with no statistical significant difference between the age groups. However the SDS for weight, BMI, and MUAC showed lower values than Egyptian reference growth data, but at age 14 years the growth delay is more pronounced than that at age 12 years, with no statistical significant difference.

Fig. 1 shows the regression analysis between Hb (gm/dl) and serum zinc levels (μg/dl) among the studied anemic adolescents. The Hb values were negatively correlated with serum zinc in the studied anemic adolescents with significance (P<0.05).

Fig. 2 shows the regression analysis between Hb (gm/dl) and SDS for the weight in anemic girls. It shows significant correlation between Hb (gm/dl) and SDS for the weight in anemic females (P<0.05).

Fig .3 represents the regression analysis between Hb (gm/dl) and SDS for the height in anemic females. The Hb values were negatively correlated with SDS for the height in the studied anemic girls with significance.

Fig. 4 shows the regression analysis between Zinc and MUAC SDS among the anemic girls. Regression analysis shows significant correlation between Zinc and Z MUAC in anemic females (P<0.05).

The linear regression analysis in boys shows no significant correlations between the values of SDS for the weight, height, BMI, and MUAC, hemoglobin and serum zinc (P>0.05).

Table 1: The mean SDS of growth parameters in anemic boys and girls

Gender	Growth Parameters				
	Weight SDS **Mean** ± SD	**Height SDS** **Mean** ± SD	**BMI SDS** **Mean** ± SD	**MUAC SDS** **Mean** ± SD	**WHR** **Mean** ± SD
Boys	-1.5 ± 1.45	-1.8 ± 0.98	-1.76 ± 0.89	-1.23 ± 1.89	. 72 ± .99
Girls	-1.9 ± 1. 38	- 2.6 ± 1.57	-1.68 ± 1.370	-1. 98 ± 0.87	. 69 ± .87

Table 2: The mean SDS of growth parameters in anemic girls by age

Age	**Weight SDS** **Mean** ± SD	**Height SDS** **Mean** ± SD	**BMI SDS** **Mean** ± SD	**MUAC SDS** **Mean** ± SD	**WHR** **Mean** ± SD
12years	-0.15 ± 0.556	0.40 ± 0.67	-0.16 ± 0.74	-0.78 ± 0.49	.63 ± .77
13 years	-0.94 ± 1.07	-0.56 ± 0.267	-0.86 ± 1.49	-1.57± 0.763	.65± .99
14 years	-1.07±1.03	-0.72 ± 1.13	-1.02 ±1.042	-0.55 ± 0.702	.62± .98

Table 3: The mean SDS of growth parameters in anemic boys by age

Age	**WTSDS** **Mean**±SD	**HTSDS** **Mean**±SD	**BMI SDS** **Mean**±SD	**MUAC SDS** **Mean**±SD	**WHR** **Mean** ± SD
12years	-0.07 ± 1.02	-1.14 ± 1.09	-0.37 ± 0.66	-0.17 ±1.57	.67 ± .67
13 years	-0.92 ± 0.65	-1.32 ± 0.45	-0.43±0.85	-1.44 ± 0.88	.68 ± .85
14 years	-1.51 ± 0.66	-1.09 ±1.60	-1.19± 0.64	-1.81 ± 0.41	.77 ± .55

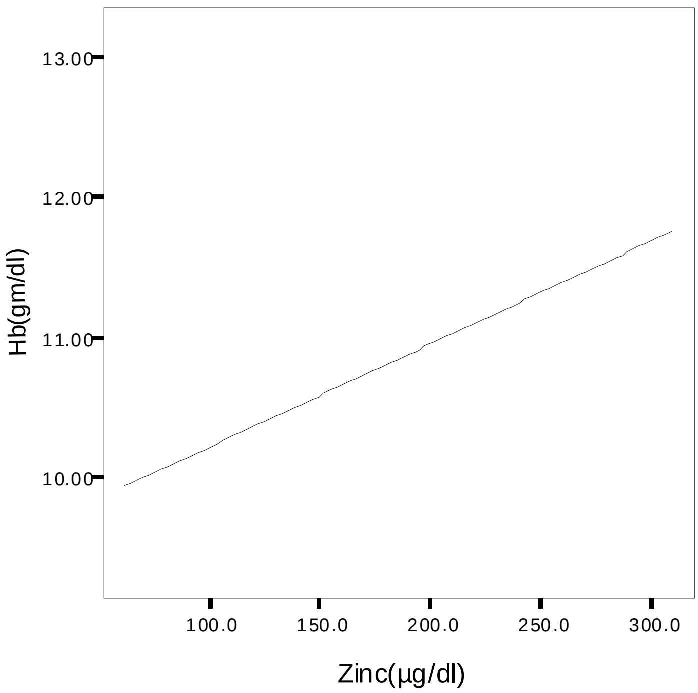

Figure 1 Regression analysis between Hb (g/dl) and serum Zinc levels (µg/dl) among the studied anemic adolescents.

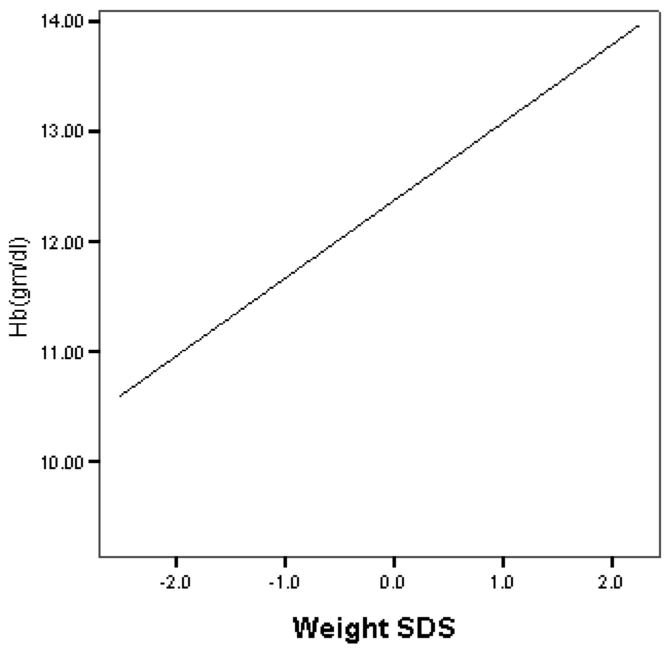

Figure 2 Regression analysis between Hb (gm/dl) and weight SDS in anemic girls

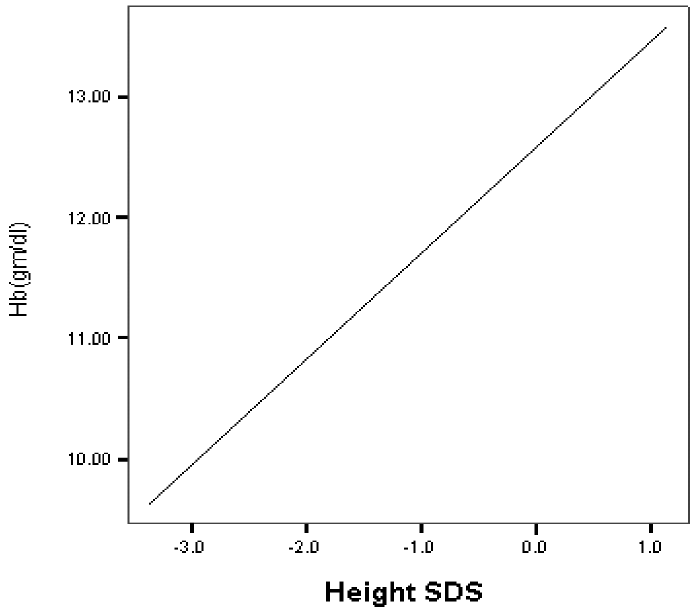

Figure 3 Regression analysis between Hb (gm/dl) and Height SDS in anemic girls

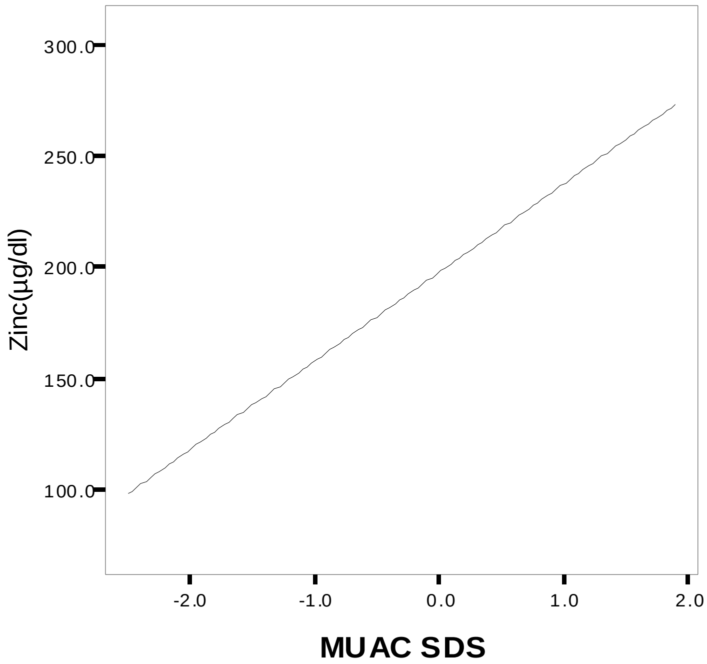

Figure 4 Regression analysis between Zinc and MUAC SDS in anemic girls

4. Discussion:

There exist general feelings in the society that adolescent years are normally free from major health problems. On the contrary it is a crucial period, because adolescent is still a developing child. Significant proportion of young people in developing countries suffers from nutritional anemia, in spite of impressive gains in the field of health and nutrition. Iron deficiency is the most prevalent micronutrient deficiency disease in the world (Stoltzfus, 2001). It affects more than 3.5 billion people in the developing countries (WHO, 2001). Twenty two percent of the Egyptian population is currently adolescents. A survey conducted in 1997 Ibrahim et al., (1999) found that 47% of adolescent girls and boys are anemic. El-Sahn et al., (2000) reported that the prevalence of anemia among adolescents in Egypt was 46.6 %. To address the high anemia rates, the Egyptian government and the Student Health Insurance Program (SHIP) began a targeted program to lower those rates through a dynamic school-based program. The task of improving the health and nutrition of adolescents by strengthening the preventive health program of SHIP was part of this work and was called the Adolescent Anemia Prevention Program. The program is implemented in all governorates all over Egypt.

High rates of anemia have been found in other developing countries, such as India (55%), Nepal (42%) and Cameroon (32%) (Kurz and Johnson-Welch, 1994). Among school children, the prevalence of anemia ranged from 32% in Bahrain to 78% in Oman (Verster and van der Pols; 1995). Irrespective of the severity, the prevalence of anemia ranges between 12-100% in the Region South-East Asian Countries (WHO, 2006). The prevalence of iron deficiency anemia was 6.2 ± 0.8% in Mexican American females and 2.3 ± 0.4% in non-Hispanic white females (Amy et al ,2000).

In the present study, the values of SDS for the weight, height, BMI, and MUAC among the studied anemic adolescents, showed values that represented the extreme lower end of the distribution of reference growth data of the normal age-matched Egyptian reference growth data (Ghalli et al., 2002). This is in agreement with the study of Kanani and Poojara (2000) on Indian adolescents, they recorded that anemia has a negative impact on growth and it may compromise pubertal growth spurt. Beard (2000) has been reported also, that iron deficiency anemia causes poor growth in humans especially among adolescents due to the increased iron requirements and growth spurt. Growth retardation has been associated with anemia in adolescent populations (Alton, 2005). The iron needs are high in adolescents because of the increased requirements for expansion of blood volume associated with the adolescent growth spurt. The low iron status among adolescents may limit their growth spurt. Poor eating habits are the main reason for the high rates of anemia among adolescents in Egypt. The typical Egyptian diet has few iron-rich foods, or foods that enhance iron absorption, and often considerable amounts of foods that inhibit iron absorption such as tea and whole wheat bread. WHO (2006) reported that anemia has a serious negative impact on growth and development. Studies conducted in different countries, reveal that nutritional deprivation affects almost all growth parameters and final adult body size resulting in thinness and stunting (Kanani and Poojara, 2000; Beard 2000; Alton, 2005; Hyder et al., 2007). However, the effect of malnutrition is more pronounced at the time of peak growth.

In the present study anemic adolescents displayed less development of circumferential measurements (waist and hip circumference) as compared to the non anemic control. Likewise, Colin-Ramirez et al., (2003) also observed that anemic subjects had lower waist and hip circumference than the non anemic subjects. Similar finding were noticed by Maninder and Kochar (2010) in anemic rural Haryanvi Jat women in India. It was observed that decrease in hemoglobin concentration reduces the availability of oxygen to the tissues, which in turn affects development of circumferential measurements among anemic subjects.

Muñoz et al., (2009) reported that adolescent iron requirements are higher in developing countries because of infectious diseases and parasitic infestations that cause iron loss, and because of low bioavailability of iron from diets limited in hem iron. Increased iron requirements, limited external supply, and increased blood loss may lead to iron deficiency anemia. Our findings suggest that physical growth spurt may be playing a larger role in causation of growth delay in anemic adolescents.

In our study the growth delay was evident within each gender across age groups in both boys and girls. However, regression analysis shows significant correlation between Hb (gm/dl) and SDS for the weight and height in anemic girls and no significant correlation in boys. This denotes that adverse impact of anemia on growth is more evident in adolescent girls than boys. This is in agreement with the study of Sen and Kanani (2006) on Indian adolescent girls and demonstrated adverse impact of anemia on growth. Bergstrom et al., (1995) evaluated iron status in healthy Swedish adolescents and found that low heme iron intakes increased the risk of low iron stores in girls but not in boys. They suggested that the differences in iron status between boys and girls in adolescence results primarily from biological differences other than menstrual bleeding or insufficient iron intake. Moreover, adolescent girls have high nutrient needs and are susceptible to micronutrient deficiencies (Hyder et al., 2007). So boys are less at risk of growth delay secondary to anemia than girls who lose blood and as a result, iron through menstruation. The World Health Organization (2001) estimated that about 30-55% of adolescent girls suffer from anemia. Egypt Demographic and Health Survey conducted in 2000-2005 recorded the prevalence of anemia in adolescent girls and boys are 35.6% and 26% respectively (El Ashry, 2009). After menarche, iron needs continue to remain high in females to replace menstrual blood loss (Meier et al.، 2003). An adolescent girl is 10 times more likely to develop anemia than a boy because their irregular eating habits, caused by concerns about body image compounded by normal menstrual blood loss. The girl begins her adolescent growth spurt at an average of about 10 years and grows at peak velocity at about 12 years. The boy starts his adolescent growth spurt around 12 years of age and in a year or two overtakes the girl (WHO, 2006).This can explain another superimposed factor for growth delay in adolescent girls in the present study.

Iron and zinc are essential micronutrients for human health and normal growth. Their deficiencies usually coexist in the same individual and make anemia with worst effect on growth. By regression analysis, our study revealed significant positive correlation between Hb values and serum zinc levels in anemic adolescents, which was consistent with the observation of Paknahad et al., (2007) in Iran. However Kogirima et al., (2007) found a positive correlation between zinc intake and serum zinc levels. Serum zinc was significantly correlated with hematocrit and hemoglobin (P was 0.027 and 0.02 respectively). This is in agreement with the study of Cole et al., (2010) who reported that anemic African American children had an increased risk of zinc deficiency, and serum zinc is correlated with hemoglobin ($r = 0.24$, $P < 0.001$). Several studies have highlighted that supplementation of zinc along with iron improves hemoglobin level and is beneficial in iron deficiency anemia (Kolesteren et al., 1999). At the other hand zinc is clearly involved in several aspects of normal hematopoiesis by virtue of its role in many enzyme systems involved with DNA synthesis including thymidine kinase and DNA polymerase (Nishiyama et al., 1998). Zn deficiency should be considered as one of etiologic factors in some children with unexplained short stature. Oral Zn supplementation may be considered as the growth-promoting therapy for children with short stature once marginal zinc deficiency is established. Zinc is well known to be essential for somatic growth of children. Zinc has a close relationship with the endocrine system; it sustains normal growth (Kaji and Nishi, 2006). However, the interrelationships among Zn, growth, and GH-IGF-I axis appear to be complex and deserve further investigation.

In our study we didn't find any relationship between serum zinc and age. Villalpando et al., (2003) findings showed results similar to our study. Regression analysis showed significant correlation of zinc and MUAC SDS in anemic girls only. Consequently, zinc intake influence anthropometric measurements and has effects on the mid-upper arm circumference. Keith et al., (2005) findings showed results similar to our study. MUAC is a useful as an indirect measure of muscle size to determine whether a person has depleted lean body mass and is an excellent indicator of the severity of malnutrition (Rodriguez et al, 2000). An MUAC measurement was easier to perform on severely malnourished adults than BMI assessment. During famine; MUAC may be better suited to screening admissions to adult feeding centers than BMI. In rural Kenya Berkleyet al., (2005) found that MUAC is a practical screening tool that performs at least as well as WHZ in predicting subsequent inpatient mortality among severely malnourished children. Dasgupta et al., (2010) stated that the mid arm circumference measurement is a reliable and a feasible method of assessment of nutritional status of adolescents. The evidence indicates that adolescence boys have greater MUAC than girls in our study and anemic girls showed more growth delay during the adolescent growth spurt.

In conclusion, the anthropometric parameters are low in the anemic children as compared to Egyptian national reference data. Differences were evident within each gender across age groups. Several studies have suggested that lower growth rates and impaired physical performance are the adverse effects of iron deficiency anemia in children (Bandhu et al., 2003; Kanani and Poojara, 2000; Beard, 2000). Age and sex were the factors most predicative of anemia and growth delay among Egyptian adolescents. Boys had higher values of both hemoglobin and zinc concentrations than girls which may be due to the biological difference. Anemic girls were especially at risk of growth delay. A significant correlation between growth parameters and anemia in children, particularly girls during adolescent growth spurt was observed. Iron and zinc are playing a larger role in causation of growth delay in anemic adolescents. The inhibited growth rate, induced by the iron-deficient diet could be reversed by giving a diet supplemented with iron. Aggressive interventions are imperative to correct iron and zinc deficiency and by so doing avoid their deleterious effect on growth. The main strategies suggested for improving adolescent nutrition can be food-based strategies like food fortification, for ensuring adequate nutrition at household level; addressing behavior modification to bring about dietary change in adolescents. This may be achieved through school-based nutrition interventions; regular nutrition assessment and counseling of adolescents; intersectional linkages at community level and building linkages with adolescent friendly health services.

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11/21/2010