Anemia and Iron Deficiency Anemia in Egypt

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Abstract : *Blood hemoglobin and serum ferritin analysis were used to identify the extent of anemia and iron deficiency anemia in Egypt. The study conducted in 2010/11, among 4526 households from eleven governorates and focus on four population groups: mothers (20 – 49.9 yr), children <5 yr (preschool children), children 5-<12 yr (schoolchildren), and adolescents (12-18 yr). The analysis was performed for hemoglobin Hb (18338 subject) and serum ferritin (12293 subjects), and C-reactive protein (CRP) was made for high ferritin sample.*
Median Hb values for mothers, adolescents, schoolchildren and preschool children were 12.0, 12.5, 11.9 and 11.2 g/dl, respectively. The corresponding median ferritin values were 14.9, 15.9, 18.9 and 15.4 µg/l. Iron deficiency was more prevalent among whole sample than anemia (44.7% Vs. 39.1%). Cross tabulation for hemoglobin and ferritin, indicated that iron deficiency anemia (IDA, low Hb and low ferritin) was recognized among 18.5% of whole sample population, with high prevalence for mothers (25.1%). Prevalence of iron deficiency without anemia (low ferritin with normal Hb) reach 26.0% in whole population, and adolescents showed highest prevalence (29.4%). Almost one-fifth (20.6%) of cases had high ferritin values but still anemic (low Hb) and CRP confirm presence of inflammation.
Anemia and Iron Deficiency Anemia must always be taken into consideration for they have a clear impact on the patient's quality of life and they can be the consequence of severe diseases.

Keywords – *adolescents, children, C-reactive protein, ferritin, hemoglobin, mothers.*

I. INTRODUCTION

Iron deficiency is one of the leading risk factors for disability and death worldwide, affecting an estimate of two billion people [1]. The high prevalence of iron deficiency in the developing world has substantial health and economic costs, including poor pregnancy outcome, impaired school performance, and decreased productivity [2]. Nutritional iron deficiency anemia IDA arises when physiological requirements cannot be met by iron absorption from diet. Low iron bioavailability in populations consuming monotonous plant-based diets is another dietary factor for IDA. Although iron deficiency is the most common cause of anemia, deficiencies of other micronutrients (such as folate and vitamin B12) and other factors (such as chronic infection and inflammation) can cause different forms of anemia or contribute to their severity. Because iron deficiency is often accompanied by deficiencies of other nutrients, the signs and symptoms of iron deficiency can be difficult to isolate [3].

The absence of iron stores (iron deficiency) can be diagnosed by showing that there is no stainable iron in the reticuloendothelial cells in bone marrow smears or, more easily, by a low concentration of ferritin in serum (<15mg/l). Even before iron stores are completely exhausted, the supply of iron to the erythrocyte precursors in the bone marrow is compromised, leading to iron deficient erythropoiesis [4]. A possible explanation is that the rate of release of iron from stores is influenced by the amount of iron remaining. It can then be assumed that the supply of iron to other tissues needing iron is also insufficient because the identical transport system is used. During the development of iron deficiency hemoglobin concentration, transferrin concentration, transferrin saturation, transferrin receptors in plasma, erythrocyte protoporphyrin, and erythrocyte indexes are changed. All these indicators, however, show a marked overlap between normal and iron deficient subjects, which makes it impossible to identify the single subject with mild iron deficiency by looking at any single one of these indicators [5].

Ferritin concentration together with that of hemosiderin reflects the body iron stores. They store iron in an insoluble form and are present primarily in the liver, spleen, and bone marrow [6]. The majority of iron is bound to the ubiquitous and highly conserved iron-binding protein, ferritin [7]. Hemosiderin is an iron storage complex that less readily releases iron for body needs. Under steady state conditions, serum ferritin concentrations correlate well with total body iron stores [8]. Thus, serum ferritin is the most convenient laboratory test to estimate iron stores.

Prevalence of anemia among population is commonly used through determination of hemoglobin (Hb) and the cut-off levels of Hb according to age, sex and physiological status has been set by WHO, 2001. The 2004 joint WHO/CDC technical consultation supported the use of serum ferritin as an indicator of depleted iron stores and as an assessment of iron-intervention programmers [9]. However, because serum ferritin is an acute-phase reactant, there are challenges in the applicability of previously established cut-off values (12–15 μg/L) for determining iron deficiency. In 2001, a proposal was made to increase the serum ferritin threshold to 30 μg/l in the presence of infection [10]. However, as summarized in the 2004 consultation, there is a need to validate this threshold in all population groups. An increase in serum ferritin levels has previously been shown to parallel the rise in C-Rective Protein (CRP), particularly at the onset of infection or inflammation [11]. CRP levels initially rise rapidly, but quickly fall, even as ferritin levels remain elevated [12], [13]. Micronutrient deficiencies, especially anemia, were a public health problem in Egypt, where the prevalence of anemia reached 40% [14]. Determination of hemoglobin level was the criteria used by EDHS to identify the prevalence of anemia. It is important to identify iron store status beside hemoglobin values. Therefore, the objective of this study was to use both hemoglobin and serum ferritin to assess the extent of anemia and iron deficiency among Egyptian.

II. METHODOLOGY

Survey was conducted during year 2010 among four target population groups: women of reproductive age 20 – 49.9 yr (mothers); female and male age 12-19 yr (adolescents); children 5 - <12 yr (schoolchildren); children under 5 yr (preschool children). The target groups were covered from 4526 households (HH) obtained through a stratified community cluster sample (about 151 cluster 30 HH each) from eleven governorates representing six geographic regions: Urban governorates: Cairo; Costal governorates: Alexandria; Suez Canal governorates: Suez; Lower Egypt governorates: Kafr Elshaik; Sharkia; and Behaira; Upper Egypt governorates: Bani-suif; Aswan; and Kena and Frontier governorates: New Valley and North Sinai. Urban and rural areas from Lower & Upper regions were considered.

The most recent census data was considered for the selection of villages/cities. The selection of HH in each cluster was randomly selected according to the presence of primary health care facility (PHC), and schools. The selection of HH was based on presence of mother and at least one child (<5yr child or schoolchild). Households' children 6-18yr were selected from the nearest schools (primary, intermediate & secondary schools). Approval of the research and ethical committees and the consent of HH guardian to collect blood sample were obtained. A venous blood sample of 5 ml was collected in heparinized tubes from the target individuals. Blood hemoglobin was immediately determined and the rest of the blood sample was centrifuged to obtain the plasma, divided into two aliquots in Eppendorf vials and stored at -20° C for determination of ferritin and C-reactive protein (CRP). Blood hemoglobin was determined using Cyanmethemoglobin method according to [15]. The quantitative determination of circulating plasma ferritin concentrations were assayed by a microplate immuno-enzymometric assay using Accu Bind Kit according to the method of [16]. The quantitative determination of plasma (CRP) concentrations was done by a microplate immuno-enzymometric assay using Accu Bind Ellisa Microwells, according to [17]. C-reactive protein (CRP) was performed for the samples of high ferritin levels to identify infection and/or inflammation.

The WHO cut-off level to identify anemia is 12 g/dl hemoglobin level for mothers and adolescents. Normal hemoglobin level for children 5-<12 years is 11.5 g/dl while that for children <5 years is 11 g/dl [1].

The cut-off point for ferritin, below which iron stores are considered to be depleted, is < 12 μg/L for <5 years of age and <15 μg/L for >5 years of age [1].

III. RESULTS & DISCUSSION

Blood hemoglobin and serum ferritin biochemical analysis have been used in this study to identify the extent of anemia and iron deficiency anemia through cross tabulation analysis between hemoglobin and ferritin (iron store). The study focus on population groups most at risk for iron deficiency anemia: mothers (20 – 49.9 yr), children <5 yr (preschool children), children 5-<12 yr (schoolchildren), and adolescents (12-18 yr).

3.1 Hemoglobin analysis:

Hemoglobin was determined among 18338 subjects, representing the four target groups. Median hemoglobin values (Table 1) were varied among groups (11.2 - 12.5 g/dl). This variation was expected, where hemoglobin is an iron-containing component of red blood cells that is needed for oxygen transport and its level in the blood depends on age, sex and physiological state. Identifying prevalence of anemia, WHO cutoffs levels of hemoglobin concentration below which anemia may be present were used for the four target groups (Table 1). The prevalence of anemia among mothers was the highest (47.2%), followed by preschool children (39.6%), while other groups (schoolchildren and adolescents) recorded almost similar percentages (35.3% & 35.9%). The overall prevalence (39.1%) would classify anemia as significant public health problem among Egyptian population [18].

The prevalence of anemia reported by EDHS of 2005, was 39.4% for ever-married women (age 15 to 49 yr); 35.6% in never-married female youth (age 11 to19 yr); and 48.5% in preschool children (age 6 to 59 months). This mean that prevalence of anemia considerably increased among mothers in current study than in 2005 (from 39.4% to 47.2%), the opposite picture was observed for young children (prevalence decreased from 48.5% to 39.6%). However, anemia in adolescent remains the same as in 2005.

Table (1): Median hemoglobin level and prevalence of anemia among population segments in Egypt.

Target population	Hemoglobin		Anemic	
	Number	**Median (g/dl)**	**Number**	**(%)**
Mothers	4526	12.0	2135	47.2*
Adolescents	6816	12.5	2436	35.7*
Schoolchildren	2620	11.9	926	35.3**
Preschool children	4376	11.2	1731	39.6***
Total	18338	-	7228	39.1

*Anemia as hemoglobin levels: * <12 g/dl; **<11.5 g/dl; *** <11 g/dl*

3.2 Ferritin analysis:

Serum ferritin was performed for 12255 subjects and the median values (Table 2) for the target groups range between 14.9 ug/l (mothers) and 18.9 ug/l (schoolchildren). The ferritin level is the most specific biochemical test that correlates with relative total body iron stores. A low ferritin level reflects depleted iron stores and hence is a precondition for iron deficiency if there is no concurrent infection. Iron depletion (ferritin level <15ug/L) was recognized among 49.6% of mothers; 47.4% of adolescent and 38.2% in schoolchildren. Low iron level (ferritin <12ug/L) for preschool children accounted for 38.2%.

When infection is present, the concentration of ferritin may increase even if iron stores are low; this means that it can be difficult to interpret the concentration of ferritin in situations in which infectious diseases are common. Therefore, CRP was determined for high serum ferritin samples. CRP analysis showed that a quite high percent of mothers (38.1%) had positive CRP value, while (19.1%) of adolescents had positive CRP value. CRP analysis showed that (24.1%) of schoolchildren and (25.1%) of preschool children had positive CRP values.

Table (2): Median ferritin level and prevalence of iron depletion among population segments in Egypt.

Target population	Ferritin		Iron depletion	
	Number	**Median (ug/L)**	**Number**	**(%)**
Mothers	3037	14.9	1511	49.6*
Adolescents	5020	15.9	2378	47.4*
Schoolchildren	1853	18.9	707	38.2*
Preschool children	2345	15.4	895	38.2**
Total	12293	-	5491	44.7

*Iron depleted as ferritin levels: * <15 ug/l; ** <12 ug/l*

3.3 Anemia and iron deficiency anemia:

Iron deficiency has earned distinction as the most common nutritional deficiency in the world today. Because iron is important for blood formation, iron deficiency often leads to anemia, defined as a blood hemoglobin level below standard. [19] reported that the development of iron deficiency is characterized by sequential changes in the amount of iron in the various iron compartments of the body. In the first stage iron stores becomes depleted but there is enough iron to meet the needs of red cell production. When iron stores are exhausted, the amount of iron in the circulation starts to fall and red cell production becomes compromised (iron deficient erythropoiesis). In the final stage iron stores exhausted, the amount of iron in circulation was very low, red cell production drastically reduced and anemia developed.

Previous Tables (1 & 2) indicated that iron deficiency among almost all studied groups was more prevalent than anemia, and it was clearly shown for the whole sample being (44.7% Vs. 39.4%). Therefore, further analysis for hemoglobin/ferritin cross tabulation was made whereby the studied population can be divided into four groups depending on the presence or absence of anemia (as defined by hemoglobin level) and the presence or absence of iron deficiency (as indicated by iron stores).

Hemoglobin/ferritin cross tabulation for the whole sample of 12023 subjects (Table 3), showed that almost one third (34.7%) of sample population considered normal subjects (having normal hemoglobin and ferritin levels). Iron deficiency anemia IDA (iron depletion with low hemoglobin) was clearly identified among only 18.5% of the whole sample, but iron deficiency without anemia (low ferritin and normal hemoglobin) was recognized in 26.2% of the population. Almost one-fifth (20.6%) of cases had high ferritin values but still anemic (low hemoglobin). CRP analysis showed almost similar percent (25.1%) had positive CRP value, which confirm the presence of inflammation.

Table (3): Percent distribution of all population segments according to hemoglobin and ferritin cross tabulation

			Hemoglobin status		Total
			Anemic	Not-anemic	
Ferritin status	Iron depleted	(No.)	2227	3154	5381
		(%)	**18.5**	**26.2**	**44.7**
	Iron not depleted	(No.)	2476	4166	6642
		(%)	**20.6**	**34.7**	**55.3**
Total		(No.)	4703	7320	12023
		(%)	**39.1**	**60.9**	**100.0**

On the other hand, hemoglobin/ferritin cross tabulation analysis was made for mothers (3065 subjects), adolescents (4823), schoolchildren (1836), preschool children (2345) and the results are demonstrated in "Fig." (1). IDA was identified more among mothers (25.1%), followed by adolescents (17.9%) than other groups (13.6 and 15.1% schoolchildren and preschool children). The hidden iron deficiency expressed in terms of low ferritin but with normal hemoglobin found in higher percent in adolescents (29.4%) than the prevalence among other groups. As adolescence is a time of increased iron needs because of the expansion of blood volume and increases in muscle mass and iron needs are higher in adolescent girls after the onset of menstruation because of monthly blood loss.
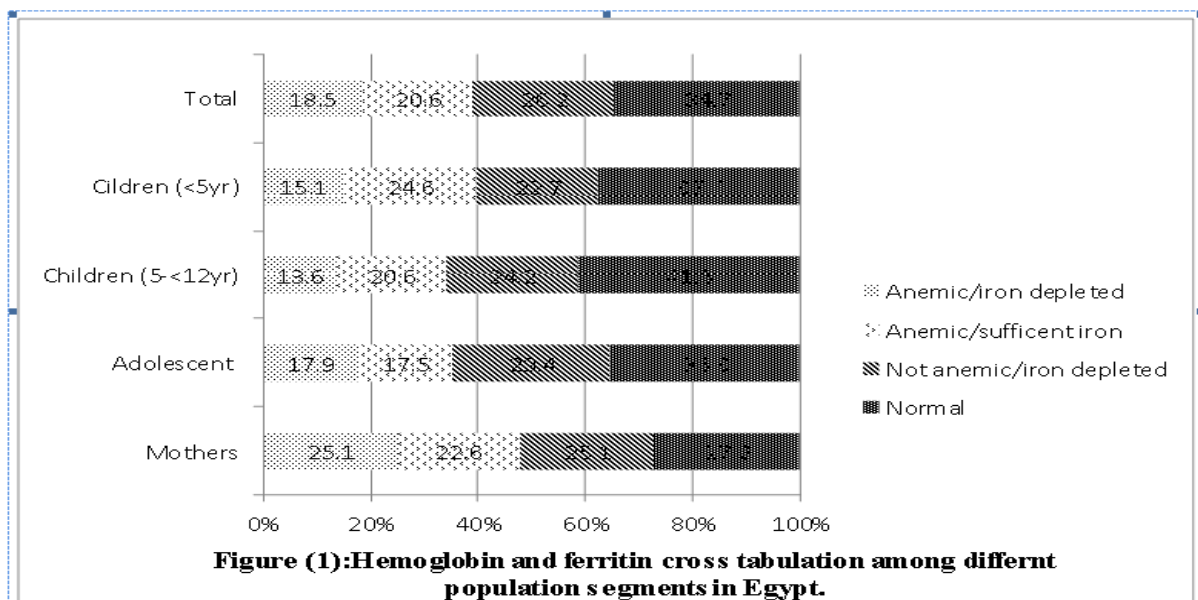

Figure (1):Hemoglobin and ferritin cross tabulation among differnt population segments in Egypt.

IV. CONCLUSION

Anemia and Iron Deficiency Anemia must always be taken into consideration as they have a clear impact on the patient's quality of life, and therefore they require adequate treatment and they can be the consequence of significant or severe diseases, so it is essential to investigate their origin. Hemoglobin and ferritin were chosen in this study to diagnose Anemia and Iron Deficiency Anemia. Further study is recommended including other important indicators as transferrin, serum transferrin receptor and serum iron for in-depth study of Iron Deficiency Anemia and for better management.

Acknowledgements

REFERENCES

[1]. WHO (2001). Iron Deficiency Anemia Assessment, Prevention and Control. A guide for programme managers. Geneva: Switzerland: World Health Organization WHO/UNICEF/UNU. P. 114.
[2]. Zimmermann, M.B. and Hurrell, R.F. 2007 Nutritional iron deficiency. Lancet. Aug 11;370(9586):511-20.
[3]. Aggett, P.J. (2012). Iron. In: Erdman JW, Macdonald IA, Zeisel SH, eds. Present Knowledge in Nutrition. 10th ed. Washington, DC: Wiley-Blackwell:506-20.
[4]. Hallberg, L.; Bengtsson, C.; Lapidus, L.; Lindstedt, G.; Lundberg, P.A. and Hultén, L. (1993). Screening for iron deficiency: an analysis based on bone-marrow examinations and serum ferritin determinations in a population sample of women. Br. J. Haematol. Dec;85(4):787-798.
[5]. WHO & FAO (2004). Vitamin and mineral requirements in human nutrition, 2nd ed. World Health Organization, Food and Agricultural Organization of the United Nations.
[6]. Wood, R.J. and Ronnenberg, A. Iron. In: Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ, editors. Modern Nutrition in Health And Disease. 10th ed. Baltimore: Lippincott Williams & Wilkins; 2005. pp. 248–70.
[7]. Nadadur, S.S.; Srirama, K. and Mudipalli, A. (2008). Iron transport and homeostasis mechanisms: Their role in health and disease. Indian J Med Res.; 128:533–44.
[8]. Hunt, J.R. (2001). How important is dietary iron bioavailability? Am J Clin Nutr.;73:3–4.
[9]. WHO/CDC (2007). Assessing the iron status of populations, 2nd ed. Report of a joint World Health Organization/Centers for Disease Control and Prevention technical consultation on the assessment of iron status at the population level. Geneva: World Health Organization.
[10]. UNICEF/UNU/WHO (2001). Iron deficiency anemia: assessment, prevention and control, a guide for programme managers. Geneva: World Health Organization.
[11]. Baynes, R.; Bezwoda, W.; Bothwell, T.; Khan, Q. and Mansoor, N. (1986). The non-immune inflammatory response: serial changes in plasma iron, iron binding capacity, lactoferrin, ferritin and C-reactive protein. Scand. J. Clin. Lab Invest.;46:695–704.
[12]. Fleck, A. and Myers, M.A. (1985). Diagnostic and prognostic significance of the acute phase proteins. In: Gordon AH, Koj A, editors. The acute phase response to injury and infection. Amsterdam: Elsevier Science Publishers BV (Biomedical Division); 249–71.
[13]. Gabay, C. and Kushner, I. (1999). Acute phase proteins and other systemic responses to inflammation. N Engl J Med.;340:448–54.
[14]. EDHS, 2005. Egypt Demographic and Health Survey. El-Zanaty, Fatma and Ann Way. 2006. Cairo, Egypt: Ministry of Health and Population, National Population Council, El-Zanaty and Associates, and ORC Macro.
[15]. Villanova, P.A. (1994). Reference and selected procedures for the quantitative determination of hemoglobin in blood: approved standards. 2nd ed., National Committee for Clinical Laboratory Standards.
[16]. Tietz, N.W., (1999). Textbook of clinical chemistry, Carl A. Burtis, 3rd ed., WB Saunders, Philadelphia.
[17]. Tietz, N.W., (1995). Clinical guide to laboratory tests. 3rd ed., W.B. Saunders Philadelphia PA.
[18]. WHO (2006). World Health Organization's Worldwide Prevalence of Anemia, and Integrated WHO Nutrition Global Databases.
[19]. MacPhail, A.P. (2012). "Iron" in Essentials of Human Nutrition, 4th ed. Editors, Mann, J. and Truswell, A. S.. Oxford university press, P. (145-158).