Predictors of Gastrointestinal Lesions on Endoscopy in Iron Deficiency Anemia without Gastrointestinal Symptoms

Thesis Submitted in Partial Fulfillment of Master Degree in Pediatrics

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CAIRO 2013

Acknowledgment

First of all, thanks to ALLAH for helping me to achieve this work

I would like to express my deepest gratitude and appreciation to ***Prof. Dr. Hany Ali Hussien Samy, Professor of Pediatrics, Faculty of Medicine,AL Azhar University*** for his valuable advice, constant support, guidance and kind care throughout the accomplishment of this study.

Great appreciation and indebtedness goes to ***Prof. Dr. Zeinab Abdel Aziz El Ramly, Professor of Pediatrics, Faculty of Medicine, Al Azhar University,***for her encouragement , and kind support .

My great thanks and appreciation to***ProfDr. Sameh Mohamad Hussien,Professor of Pediatrics Faculty of Medicine,Al Azhar University,and Prof Dr. Hussien Mohamad EL-Assal,Professor OfPediatrics, Faculty of Medicine, Al Azhar University,***for their kind support, and encouragement.

I would like to express my sincere gratitude and thanks to***Prof.Dr . Wael Refaat Abd EL Hameed Hablas,Professor and Head of ClinicalPathology Department, Faculty of Medicine, Al Azhar University***, for his kind support throughout the completion of this work.

Thanks to all participating children in this study and their parents for their co-operation.

No words can describe the support and the encouragement of my father and my family member

Hany Ahmed aboul soud

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ABBREVIATIONS

CD	Celiac disease
CEM	Confocal endomicroscopy
EGD	Esophago-gastroduodonoscopy
EMA	Antiendomysial antibodies
GALT	Gut associated lymphoid tissue
GFD	Gluten free diet
GIP	Gastric inhibitory peptide
GWA	Genoma-wide association
H Pylori	Helicobactar Pylori
Hct	Hematocrit
HH	Hereditary hemochromatosis
HLA	Human leukocytic antigen
IBD	Inflammatory bowel disease
IDA	Iron deficiency anemia
IELs	Intraepithelial lymphocytes
IRE	Iron responsive element
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
RDA	Recommended dietary allowance
RDW	Red cell disturbution width
RR	Ribonucleotide reductase
TCA	Tricarboxylic acid
TfR	Transferrin receptor
TIBC	Total iron-binding capacity
TTG	Tissue transglutaminase
UC	Ulcerative colitis
WHO	World health organization

1. Introduction

Nutritional anemia, according to the World Health Organization (WHO), is a state in which the hemoglobin concentration in the blood is lower than levels considered normal for the age, gender, physiological state and altitude, as a consequence of shortage of essential nutrients, independent of the cause of this deficiency.(De Maeyer et al .,1989). Nutritional anemia includes a lack of nutrients such as iron, folic acid, vitamin B_{12} and copper (with erythropoietic function), vitamins C and E (related to hemorrhagic states) and vitamin A (related to cellular differentiation of red blood cells and mobilization of the iron of the reticuloendothelial system).(Bloem et al.,1989).

The occurrence of anemia is denominated iron deficiency anemia(Devincenzi et al.,2000). This deficiency is the most common nutritional disorder in infancy, and it affects communities not only in developing nations but also in highly industrialized countries.(Brunken et al ., 1999). Iron deficiency anemia also affects women of childbearing age. These two groups are the ones most affected by shortages of minerals.(Freire et al .,1997).

Iron deficiency adversely affects cognitive development and behavior in infants and children and is the most common micronutrient deficiency among children worldwide (United Nations Administrative 2005). The prevalence of iron deficiency among children in developing countries exceeds 50% and is usually attributed to inadequate nutrition (MMWR Morb 2002).

Iron deficiency among children in most high-prevalence areas has been attributed primarily to poor nutritional intake or parasitosis (Stoltzfus et al., 1997).

The main factors involved in the etiology of anemia in infants under 2 years of age are the iron reserves at birth, growth rate, diet and iron loss(Stekel et al.,1984). Organic physiological loss of iron occurs in bile, urine and cellular desquamation of the skin and intestinal lining. In children, loss also occurs due to blood in the feces and by the use of whole milk in liquid form during the first year of life.(Sigulem et al ., 1988). Another possible cause of iron loss is the presence of intestinal parasites, although several studies have shown that the majority of parasitic diseases have secondary importance in the etiology of iron deficiency anemia in under 5-year-olds(Palupi et al .,1997).

The most significant weight gain and storage of iron by the fetus occurs during the last trimester of pregnancy. Premature births, intrauterine growth restriction and multiple pregnancies are factors that lead to iron deficiency anemia within the first six months of life, caused by low stocks of iron at birth(Brandalise et al., 1981). The average iron concentration per kilogram of body weight at birth is 70 mg/kg for full-term infants(Sigulem et al .,1988). The average daily iron needs are from 0.72 mg to 0.46 mg for children from five months to one year old and from one to three years old, respectively(WHO et al.,2001).

In the diet, the quantity of bioavailable iron is important, and this is determined by stimulation and inhibitory factors that exist within a meal(Bothwell et al .,1989). Among the iron absorption stimulation factors in the diet are organic acids, in particular ascorbic acid, which is found in citric fruits(Bothwell et al ., 1989). Among the iron absorption inhibitory factors are phytic acid, which is found in fibers, whole grains and beans, oxalic acid(Cook et al .,1997). which is found in spinach and beetroot,(Guthrie et al., 1995) and tannin, which is found in tea, coffee and chocolate.(Hurrell et al ., 1997)Calcium, which is present in milk and

dairy products,(Cozzolino et al., 1997) and other minerals that are close to iron in the periodic table, which compete with the same intestinal absorption,(Cozzolino et al., 1997) also inhibit the absorption of iron.

For full-term newborn babies, the iron deposits at birth provide the needs for this mineral until four to six months of age. Breastfeeding alone acts as a protective factor during the first months of life and, in spite of the low iron content of human milk (0.26 to 0.73 mg/l), the mineral in mother'smilk has high bioavailability and absorption around 50%.(Tudisco et al.,1988). Because of the greater physiological requirements within the first two years of life, and specifically from 6 to 12 months because of the accelerated growth during this period, it is rare that the child will manage to ingest the recommended daily amount of iron. This is true even when good sources of bioavailable iron are introduced into the diet. Thus, preventive iron supplements are usually necessary for this age group(Nestel et al., 1996).

Reduced iron absorption is the second category of ID causes of digestive origin, and can be caused by celiac disease, atrophic gastritis, and postsurgical status (gastrectomy, intestinal resection) among others. Celiac disease is very relevant and specific evaluation to exclude it must be performed. In a study on patients referred to a specialized gastroenterological consultation because of ID or IDA, celiac disease was finally the diagnosis in 10% of cases(Corazza et al .,1995) other authors described that at least 2%-3% of patients with IDA are finally diagnosed as celiac disease(Kepczyk et al .,1995). The prevalence of this disease worldwide is approximately 1%, and it is probably under diagnosed(Catassi et al., 2008). Microscopic alterations in the duodenal mucosa in non-treated celiac disease patients will lead to them becoming refractory to oral iron treatment. This has also been described in patients with autoimmune atrophic gastritis and gastritis

due to *Helicobacter pylori (H pylori)*(Hershko et al .,2005).Gastroscopy with biopsies, allowing us to detect the presence of atrophy with or without *H pylori*, is essential. The positivity of autoantibodies (anti-intrinsic factor or anti-parietal cell) supports the diagnosis of autoimmune atrophic gastritis(Carmel et al .,1992). Regarding the possible role of *H pylori* in IDA, a recent meta-analysis indicated that the infection is associated with depleted iron deposits. The mechanism by which *H pylori* induces this alteration is not clear, but it appears to involve gastrointestinal blood loss, diminished iron absorption from the diet, and increased consumption of iron by the bacteria. The authors suggest that the impact of eradication of *H pylori* in the improvement of the iron deposits must be evaluated in large controlled trials(Muhsen et al ., 2008). Finally, it must be pointed out that a deficit of dietary iron not associated with any other pathology may rarely be the cause of ID or IDA.

Common symptoms include:

- Weakness
- Fatigue
- Irritability
- Mood swings
- Headache
- Decreased appetite (especially in children)
- Pale or bluish discoloration of the skin (in dark pigmented persons, this may be seen in the eyes or palms)
- Shortness of breath

- Children have a greater risk of iron deficiency anemia due to rapid growth, particularly in the first two years of life. **:** Women generally consume less iron than

men and may have a greater need for iron, depending on their stage of life. On average, a menstruating woman loses 30 to 45 milligrams of iron per month. Pregnancy and delivery together use about 1 gram of maternal iron. Breast-feeding a child uses a total of about 1 gram of maternal iron in the first year of life.

- **Peptic ulcer disease and gastritis:** These disorders lead to blood loss, which can deplete iron stores. Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) are often contributing factors.
- **Cancer:** Esophageal, gastric, and other gastrointestinal cancers often cause occult bleeding.
- **Excessive exercise:** Rarely, blood losses may occur due to intense exercise. Iron losses also result from increased sweating. In particular, such losses may predispose adolescent female athletes to anemia.
- **Dietary factor**
- A careful history and physical examination, including dietary and menstrual histories are essential.
- Simple blood tests can accurately assess a person's iron status.

Bone marrow biopsy to determine marrow iron stores was a standard means of diagnosis in the past, but this procedure is now only rarely necessary.

Treatment involves resolving the patient's iron deficiency, as well as addressing the underlying cause (e.g., ulcer, malignancy, excess menstrual flow, dietary deficiency, iron malabsorption).

2. Aimof Study

This study is designed to find out the frequency and predictors of endoscopic lesion in iron deficiencies anemia without gastrointestinal symptoms.

3. Epidemiology

According to the United Nations Children's'Fund (Unicef), 90% of all types of anemia in the world are due to iron deficiency(Devincenz et al .,2000). In South and Central America, iron deficiency anemia has been a severe public health problem, affecting as many as 50% of pregnant women and children(Freire et al .,1997).

In Egypt, particularly in rural areas, the prevalence of iron Deficiency Anemia (IDA) is relatively high. It was between 22 and 30 % in rural population groups. It is believed that one of the major causes of such a high prevalence rate is insufficient iron intake. There are about 40 million children around the world who remain in these high risk conditions (Smith et al.,1984). It is notable that a correlation between poverty and occurrence of IDA. The Egyptian rural community has dietary patterns depend on their culture as drinking tea immediately after meal quantity and quality which offer to male rather than female. Egyptian diet inhibit the absorption of iron , because hem iron(in animal flesh) and inorganic iron (in vegetables depend on the mixed diet elements , like the absorption of hem iron is improved by at least 50% of vitamin C is consumed at the same meal .

Tea, coffee and a certain type of fiber, all prevalence in average Egyptian diet can inhibit the absorption of iron (Tatala et al.,1998). Community health nurse has vital role by increasing the health awareness of those target group related to their knowledge. And what is the preventive level to avoid bad health habits and poor nutrition which affect the health of Egyptian people. In addition assessment of

community must be made to ensure that resources exist within the community to sustain the new health education programs. Where ever IDA is usually treatable and preventable through full screening, change cultural differences and increase of education in health promotion activities (El-Zanaty et al.,2004). Anemia is one of the most extensive pandemics, affecting mostly developing countries. About 3.5 billion persons are affected by IDA in developing countries. In most cases it caused by iron deficiency. Some diseases accompanied by blood loss and parasitic infections such filariasis (EL-Zanaty et al.,2001).

In Brazil, studies performed in the State of São Paulo on almost 3,000 infants under 24 months of age, and in the State of Pernambuco on 777 children aged between 6 and 59 months, have demonstrated iron deficiency anemia rates of 59.1% and 40.9% respectively(Osorio et al.,2001). In the city of São Paulo, a study performed on 1,015 children aged between 4 and 59 months reported prevalence of more than 49%, and of pproximately 68% within the 6 to 23-month age range(Brunken et al.,1999). Another Brazilian study performed in the city of Pontal, State of São Paulo, on 115 children aged from 12 to 72 months, confirmed prevalence of 68.7%. In the city of Porto Alegre in the State of Rio Grande do Sul, the prevalence of anemia among 12 to 23-month-olds was 65.6%(Silva et al.,2001). Coutinho et al.,2004 found a prevalence of 75% among 6 to 24-month-old children in a district of the city of São José do Rio Preto, in the State of São Paulo.

Studies performed in other regions of Brazil have revealed great variation in their results, finding prevalences of iron deficiency anemia ranging from 13.3% to 60.5% among preschool-age infants. These studies have also confirmed that the