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Iron Deficiency Anemia Among Kindergarten Children Living in Marginalized Areas in Gaza Strip

Submitted by / Abdallah R. Yaghi

(B.Sc. in Genetics)

Supervisor

Dr. Mahmoud Sirdah

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This thesis was defended and approved on 17th of November 2013 by the thesis defense and approval committee:

Dr. Mahmoud Sirdah

Chairman and Supervisor ……………………………………………..

Dr. Abdel Nasser Abu Shahla

Internal Examiner ……………………………………………..

Dr. Mansour Elyazji

External Examiner ……………………………………………....

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Iron Deficiency Anemia Among Kindergarten Children Living in Marginalized Areas in Gaza Strip

Is my own research work and the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has never been submitted elsewhere for any other degree qualifications nor for any academic titles, nor for any other academic or publishing institutions.

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Signature	Name	Date
Abdallah	Abdallah Rassmy Yaghi	November 2013M
		Muharram 1435 H

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Dedication

To my mother

To my wife who supported me along the time

To my daughters: Yassmin and Nessma

To my sister Haia

To my brothers: Ali, Mazen, Mohammed and Omar

To all my family and those who supported me

To all of them I dedicate this work

Abdellah

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Abdellah Yaghi

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List of Abbreviation

Abbreviation	Full word
UNRWA	United Nations Relief and Works Agency for Palestine Refugees
µg	Microgram
DCT1	divalent cation transporter1
dL	deciliter
DMT1	Divalent metal transporter 1
fl	femtoliters (fl; 10^{-15} liters)
Hb	hemoglobin
Hct	hematocrit
ID	Iron deficiency
IDA	Iron deficiency anemia
Ireg	iron-regulate
KDa	Kilodalton
kg	Kilogram
MCH	mean corpuscular hemoglobin
MCV	mean corpuscular volume
mg	Milligram
MIMP	mucin, integrin and mobilferrin pathway
Nramp2	natural resistance associated macrophage protein 2
pg	Picogram (10^{-12}g)
RBCs	red blood cells
RDW	red blood cell distribution width
SF	Serum Ferritin
SI	Serum Iron
ST	Serum Transferrin
Tf	Transferrin
TfR	Transferrin receptor
TfR	Transferrin Receptor
TIBC	total iron binding capacity
UNICEF	United Nations Children's Emergency Fund
WHO	World health organization

Abstract

***Background*:** Iron deficiency anemia (IDA) is the most common type of nutritional anemias, and is recognized as an important health problem in Palestine. Large numbers of children are suffering from IDA according to previous studies**.** These studies revealed that the nutritional status of the Palestinian children in the West Bank and Gaza is seriously deteriorating due to the prevailing political situation in the area.

Objectives: this study was conducted to estimate the prevalence of IDA among kindergartens' kids living in the marginalized areas in Gaza Strip, to evaluate the level of knowledge, awareness and practices of the parents of the study population regarding the importance of iron on children health. Moreover, the study aims to identify the possible risk factors of IDA among the study population, and to evaluate the effectiveness of oral iron formula (ferrous carbonate 50mg + 100mg vitamin C /5ml) in improving the hemoglobin level in the anemic children.

Material and method: this is a cross sectional study included 735 kids (384 males & 351 females) distributed in 11 kindergartens. Data were collected by a questionnaire, body weight and height of the study sample were also measured. Complete Blood Count (CBC) were measured using cell dyne 1700 electronic counter (Sequoia-Turner Corporation, Santa Clara, CA). The presence of IDA was considered in the microcytic (MCV <80fl) children through the Mentzler mathematical formula MCV/RBC > 13 concomitant to reduced hemoglobin concentration < 11.5g/dl. All IDA children were managed by oral iron supplements, and were checked again for the same parameters of CBC after 3 months of starting the treatment regimen.

Result: The overall prevalence on IDA among the screened children in the marginalized areas was 33.5% (246: 135 M & 111 F), with no significant differences among males (35.2%) and females (31.6%). The majority (68.8%) of the screened kids in the marginalized areas are registered refugees at United Nations Relief and Works Agency (UNRWA). Significantly different prevalences of IDA were reported among the different governorates with highest values reported in Rafah (41.2%) and the Middle (36.2%) governorates.

Also significantly higher prevalence was reported among refugee camp kids (46.4%) as compared to rural (30.9%) and city (31.5%) children. The results also indicated non-significant differences between the numbers of families regarding parents' consanguinity either in the anemic cases or in the overall cases. In regards to the nutritional habits , most of the kids had good nutritional habits with no significant differences between the anemic and the control groups, as the P value > 0.05. Also, It's noticed that most of them had full term pregnancy and natural vaginal delivery. Most of the cases don't suffer from malnutrition, parasitic infection, chronic or frequent diarrhea, nor any diseases. Most of their families don't suffer from any genetic diseases while most of the cases received multivitamins or iron in the last two months of pregnancy. Regarding the anthropometric and socioeconomic characteristics of the cases, there were statistically significant differences between the cases and the normal control in age and height, where the P value < 0.05 and no statistically significant differences were noticed in the other parameters. The results revealed also significant differences between the two groups in all the CBC parameters except for WBC. It was very clear that there were high statistically significant differences between cases before and after treatment in the hematological parameters, except for MCV where the differences were not significant.

Conclusion

This study concluded that more than one-third of the study sample suffering from IDA which significantly affects the growth of children . regarding the risk factors, living in the southern of Gaza Strip and living in refugee camps and the rural areas are considered to be the most important risk factors of IDA. The study also showed that most of the study subjects have good nutritional habits, and this reflects the high education of their parents. Therefore, the study recommends that there is an urgent need to assess the nutritional status of children of school age and replenish their body iron via iron supplements and iron fortified foods to improve their level of hemoglobin.

Keywords: Iron deficiency anemia; Risk factors; Marginalized; kindergartens; Gaza strip

أنيميا نقص الحديد عند أطفال الروضات في المناطق المهمشة في قطاع غزة

ملخص البحث

تعد الانيميا الناتجة عن نقص الحديد من أكثر انواع الانيميا انتشارا، ووصفت على انها مشكلة صحية هامة في فلسطين ،حيث انه ووفقا لدراسات سابقة يعاني اعداد كبيرة من الاطفال من هذا النوع من الأنيميا ، وتظهر هذه الدراسات ان الوضع الغذائي لأطفال فلسطين في الضفة الغربية وقطاع غزة يتدهور بشكل خطير بسبب الوضع السياسي السائد في المنطقة.

هدفت هذه الدراسة لتقدير نسبة انتشار فقر الدم الناتج عن نقص الحديد لدى اطفال الروضات في بعض المناطق التي تعاني نقصا في الخدمات في قطاع غزة . وتقييم مستوى المعرفة والوعي والممارسات من الآباء والأمهات من مجتمع الدراسة فيما يتعلق بأهمية الحديد لصحة الطفل ، وعلاوة على ذلك، تحدد الدراسة عوامل الخطر المحتملة لفقر الدم بسبب نقص الحديد بين عينة الدراسة ، وتقييم فعالية اعطاء الأطفال جرعات من الحديد في تحسين مستوى الهيموغلوبين في الدم

تألفت عينة الدراسة من 735 طفل (384 ذكر–351 أنثى) موزعين على 11 روضة وفي محافظات قطاع غزة. جمعت البيانات الخاصة بالعينة عن طريق استبيان ، وتم قياس الطول والوزن لجميع أفراد عينة الدارسة.

تم إجراء فحص دم شامل لجميع أفراد العينة ، وقد استخدم حجم كريات الدم الحمراء كمؤشر ، حيث ان العينات التي كانت فيها القيمة اقل من 80 فيمتوليتر وخارج قسمة حجم كريات الدم الحمراء الى عددها اقل من 13 بالتوافق مع ان كمية الهيموغلوبين اقل من 11.5 اعتبرت هذه النتيجة فقر دم ناتج عن نقص الحديد، جميع الافراد الذين تبين أن لديهم فقر دم ناتج عن نقص الحديد تم اعطاؤهم جرعات من الحديد وعلى مدى ثلاث اشهر ، وتم اعادة اجراء فحص دم شامل لهم .

أظهرت النتائج أن معدل انتشار فقر الدم الناتج عن نقص الحديد في العينة 33.5%. بنسبة 35.2% ذكور و 31.6% اناث.

تبين من الدراسة أن معظم عينة الدارسة مسجلين في وكاله غوث اللاجئين (68.8) و أن هناك فرق ذو دلاله احصائية بالنسبة لصلة القرابة بين الابوين من عدم وجودها سواء في جميع أفراد العينة او بين الاطفال الدين تبين أنهم مصابون بفقر الدم.

بالنسبة للعادات الغذائية فقد بينت الدارسة تمتع الاطفال بعادات غذائية جيدة ،فليس هناك فرق ذا دلاله إحصائية بين المصابين والعينة الضابطة فيما يخص العادات الغذائية والرضاعة.

أما فيما يتعلق بصحة الام اثناء الحمل والولادة ، فقد اوضحت الدراسة أنه ليس هناك فرق ذو دلاله إحصائية بين عينة المصابين والعينة الضابطه .

معظم الحالات لم تكن تعاني من أمراض سوء التغذية ، الاصابة الطفيلية ، اسهال حاد او امراض اخرى ، كما ان غالبية الحالات لم تتلقى أي فيتامينات خلال الشهريين السابقين للفحص ، ولم تعاني غالبية الحالات او عائلاتهم من أي امراض وراثية.

تم في هذه الدراسة تحديد الطول والوزن لعينة الدراسة وتم من خلال استبيان التعرف على الحالة الاجتماعية والاقتصادية للأسرة وتبين الدراسة انه ثمة فرق ذو دلاله احصائية بين كل من عينة المصابين بفقر الدم والعينة الضابطة بالنسبة للطول والعمر بينما لم يكن هناك فرق ذو دلاله احصائية بما يخص المعايير الأخرى.

فيما يخص تحليل الدم الكامل بينت الدراسة وجود فروق ذات دلالة احصائية بين عينة المصابين بفقر الدم والعينة الضابطة في جميع معايير التحليل باستثناء خلايا الدم البيضاء.

كل طفل تم تشخيصه على ان لديه فقر دم ناتج عن نقص الحديد تم إعطاؤه وعلى مدار ثلاثة أشهر جرعات من الحديد على شكل شراب وتم فحص دم شامل لتقييم هذه المرحلة وتبين من هذه المرحلة وجود فروق ذات دلاله إحصائية في العينات المستهدفة بالعلاج قبل وبعد المعالجة بجرعات الحديد في جميع معايير الخاصة بتحليل الدم الكامل باستثناء حجم خلايا الدم الحمراء.

خلصت هذه الدراسة الى أن أكثر من ثلث العينة يعانون من الأنيميا الناجمة عن نقص الحديد ، وان ذلك أثر بشكل ملحوظ على مستوى النمو لدى الاطفال ، و فيما يتعلق بعوامل الخطورة شكل كل من العيش في جنوب القطاع و العيش في مخيمات اللجوء والمناطق الريفية أهم عوامل الخطورة بالنسبة لفقر الدم الناجم عن نقص الحديد و أظهرت الدراسة أن غالبية عينة الدراسة يتمتعون بعادات غذائية جيدة ؛ وهذا يعكس مستوى الوعي لدى الوالدين الذي يرجع إلى أن غالبيتهم تلقى تعليما ثانويا و جامعيا . وأوصت الدراسة ان هناك حاجة ملحة لتقييم الوضع الغذائي لدى الاطفال دون سن المدرسة وتدعيم وجباتهم الغذائية بجرعات مدروسة من الحديد لتحسين مستوى الهيموجلوبين لديهم .

CHAPTER 1

INTRODUCTION

1.1.Overview

Globally, 1.62 billion people are affected by anemia, and more than 293 million children of preschool age are anemic. Although anemia has a variety of causes, it is generally estimated that 50% of cases are caused by iron deficiency **(Black et al.,2003).**
Iron deficiency (ID) is the most common micronutrient deficiency in the developing world (**Tatala et al., 1998; Asobayire et al., 2001; Abalkhail and Shawky, 2002; Hashizume et al., 2003**). It is considered to be the main cause of anemia **(Ahmed et al.,2005)** which has a negative impact on human health and productivity. ID impairs immune functions and reduces work output (**Committee on Nutritional Status During Pregnancy and Lactation,1990).** Recent evidences indicated that ID during pregnancy negatively affects fetal growth **(Singla et al., 1997)** and increases the risk of infant with ID **(Preziosi et al., 1997 ; Kilbride et al.,1999)** which is associated with lower Apgar scores **(Preziosi et al., 1997)** and potentially irreversible delays in cognitive and psychomotor development **(Lozoff et al.,1996).**

The main risk factors for ID among young children are low intake and the high requirement of iron during child growth. The adverse effects of iron deficiency anemia (IDA) in children as well as adults include poor growth and development **(Soliman et al.,2009 & Falkingham et al., 2010)** and mental and neuromotor malfunction **(Stein et al., 2008 & Fudenberg,2009).** In resource-poor areas, the effects of IDA are frequently exacerbated by infectious diseases (**Wani et al.,2008 , Comité Nacional de Hematología Iron deficiency anemia, 2009**).

In addition to nutritional factors, several studies have shown that socioeconomic factors such as low parental education levels, low household incomes **(Hashizume et al.,2003 & El Hioui et al., 2008)** and demographic factors including age, sex, and family size **(Hashizume et al.,2003, Foo et al.,2004 , Al-Mekhlafi et al.,2008)** affect and worsen the state of anemia.

IDA is a decrease in the total hemoglobin levels caused by a lack of sufficient iron (**Goldenring, 2003).** It is the most common cause of anemia worldwide. According to the World Health Organization (WHO), children are especially vulnerable and exhibit high rates of anemia (**WHO, UNICEF, UNU, 2001).**

1.2. Objectives

1.2.1.General aim of the study

The aim of the present work is to study IDA among kindergarten kids living in marginalized area in Gaza strip and to evaluate an appropriate management plan that include the supplementation of oral iron formula to correct the anemia and to replenish the iron stores in the iron deficient anemic children.

1.2.2. Specific objectives of the study:

1. To determine the prevalence of IDA among kindergarten kids living at marginalized area in Gaza strip.
2. To evaluate the level of knowledge, awareness and practices of parents of the study population concerning the significance of iron for children health.
3. To identify the possible risk factors of iron deficiency anemia among the study Population.
4- To evaluate the effectiveness of oral iron in improving the hemoglobin level in the anemic children.

CHAPTER 2

LITERATURE REVIEW

2.1. Iron

Iron is a very important element for most living organisms, including bacteria, animals and plants **(Roy & Enns, 2000)**. It is inevitable for all cells and has several vital functions in humans . Such as a carrier of oxygen from the lungs to tissues in the form of hemoglobin (Hb), a facilitator of oxygen utilization in muscle tissues as myoglobin, a transport medium for electrons within the cells in the cytochromes, and an integral part of heme (a protoporphyrin ring that contains an iron atom) an enzymes that catalyses fundamental chemical reaction in different tissues **(Conrad & Umbreit, 2000).**

2.1.1. Body Iron

Iron as a micronutrient can be found in a small amount in the human body, the average of iron is 3.8g in men and 2.3g in women **(Bothwell,1995)** this average in males is equivalent to 50mg/kg body weight for healthy 75kg adult males and in females is 42mg/kg body weight for healthy 55kg adult female **(Bothwell et al., 1979; Bothwell & Charlton,1981).**

2.1.2. Body distribution of iron

Iron containing- compounds are the form of iron in human body. Iron is categorized according to the biological role of iron containing compound into functional iron and transport or storage iron. The functional iron presents the majority of iron, while the transport or storage iron presents 30% only **(Food and Nutrition Board, 2001).**

2.1.3 . Functional Iron-containing compounds (Essential Compounds)

The functional iron containing compounds function in the transport and utilization of oxygen to produce cellular energy and include: hemoglobin, myoglobin, heme enzymes (cytochromes, catalases , peroxidases), and iron- sulfur proteins **(Schrier & Bacon ,2012)** 60-70 % of the total body iron is present in hemoglobin of the circulating red blood cells (RBCs) and bone marrow erythroid precursors cells, and about 10% is present in myoglobin of muscle cells. About 3-5% is present in the intracellular respiratory in heme enzymes**(Olsson & Norrby,2008)**. Thus they may serve a metabolic or an enzymatic role.

2.1.3.1. human hemoglobin

The human hemoglobin is composed of four polypeptide chains, which in adults consists of two alpha (a) globin chains and two beta (b) globin chains (i.e. 2a 2b). Each polypeptide has a heme prosthetic group attached, where each heme can bind one oxygen molecule – so there are four heme groups per hemoglobin molecule that together bind four oxygen molecules (**Sadava et al.,2008)**

The main function of the hemoglobin is to transport oxygen from the lungs to the rest of the body. Other minor functions of hemoglobin include acid-base homeostasis and CO_2 transport **(Mahan & S. Escott-Stump,2004).** More details about human hemoglobin are mentioned later.

2.1.3.2. Myoglobin

Both myoglobin and hemoglobin are hemeproteins. They have a physiological significance, as they can bind molecular oxygen.

In contrast to hemoglobin, Myoglobin is a monomeric heme protein. It's found mainly in muscle tissue where it functions mainly as an intracellular storage site for oxygen. During periods of oxygen deprivation oxymyoglobin releases its bound oxygen which is then used for metabolic purposes**.(Nelson & Cox,2000)**

2.1.3.3. Heme Enzymes and Iron Sulphur Proteins

Iron is required for numerous cellular enzymes and coenzymes either as integral part of enzymes or as a cofactor. Cytochromes, catalases, and peroxidases all of which are, like hemoglobin, heme proteins. Iron requires nearly a half of Krebs cycle enzymes. Another important group of iron enzymes which involved in cellular metabolism are the Iron-sulfur proteins and metalloflavoproteins however; their iron is not in the form of heme **(Mahan & S. Escott-Stump,2004).**

2.1.4. Iron Storage and transport compounds

The iron storage compounds are the ferritin and hemosiderin, they are involved in the maintenance of iron homeostasis and contain nearly twenty percent of body iron present primarily in the liver, reticuloendothelial cell, and erythroid precursors of bone marrow. Two other proteins involved in the transport, delivery and regulation of iron uptake to the different tissues are Transferrin and Transferrin receptor **(Beard, 2001).**

2.1.4.1. Iron storage compounds

2.1.4.1.1. Ferritin

Ferritin is the major intracellular storage protein found in all cells, it is a hollow, spherical with the highest concentrations in the liver, spleen and bone marrow. Ferritin binds iron as a ferric complex within a protein shell. Each molecule can theoretically store up to 4500 atoms of ferric iron but, in practice, it is typically less than 2000 atoms **(Kalantar-Zadeh et al.,2006).** It`s store iron which is used for the formation of hemoglobin and other iron-containing protein and enzymes**(Burtis&Ashwood,1994)** that are found in the cells, but the ferritin which is found in the circulating plasma has an unclear function, and the plasma ferritin is used as an index of iron storage deficiency **(Bender & Bender,1997)**

2.1.4.4.2. Hemosiderin

Another iron-storage complex is the hemosidrin. Its molecular nature remains mysterious, however, it's always found within the cells (as opposed to circulating in blood). It seems to be complex of ferritin and denatured ferritin and other material. It occurs by enzymatic hydrolysis of ferritin in lysosomes. **(Brock, 1989).** At normal levels of iron in liver and spleen, the predominant iron storage protein is the ferritin, and when the level of iron increases the percentage of hemosiderin increases **(Bender& Bender, 1997) .**

2.1.4.2. Iron transport compounds

2.1.4.2.1. Transferrin

Transferrin (Tf) is a plasma transport protein, transport iron from one organ to another, it is a monomeric glycoprotein of molecular weight about 80Kda **(Duffy,1996).** The saturation of Tf of iron reflects iron nutritional status ,and provides a sensitive index of the pool of iron that is available and is transported between storage and utilization site **(Bender&Bender,1997)** serum Tf transport iron from absorption sites to utilization sites . Tf found within the cytosol of many cells may play a role as intracellular iron transport protein**(Hirose,2000)**

2.1.4.2.2. Transferrin Receptor

Transferrin receptor(TfR) is a carrier protein for transferrin. It regulates cellular uptake of iron from the plasma glycoprotein Tf **(Punnonen ,1997)** .The TfR helps the uptake of iron into the cells through a cycle of endo- and exocytosis of the iron transport protein Tf .Iron uptake from Tf involves the binding of iron –loaded (diferric) Tf to TfR ,internalization of Tf within an endocytic vesicle by receptor-mediated endocytosis ,and the release of iron from the protein by a decrease in the endosomal pH **(Testa et al.,1993;Ponka & Lok,1999).**

The divalent cation transporter1 (DCT1) allows iron to pass through the endosomal membrane via the endosomal Fe^{+2} transporter after iron release from Tf within endosomes **(Fleming & Andrews,1998) .**And iron is transported to intracellular sites where it`s used or/and stored after iron release from endosomes. The iron-free transferrin which remains receptor-bound returns to the cell surface where it is released from the cells (at extracellular pH)and replaced the diferric Tf from serum**(Lawrence et al.,1999).** TfRs are probably expressed on all cells with the exception of mature erythrocytes and some other terminally differentiated cells**.** Their levels vary greatly with immature erythroid cells showing very high densities of TfR. Erythroid heme synthesis, which uses more than 80% of iron leaving plasma, is critically dependent on iron uptake mediated by high levels of TfR in erythroid cells. In addition to immature erythroid cells, TfR is present in highest concentration on cells with high iron requirements, including the placenta, and on rapidly dividing cells both normal and malignant **(Ponka&Lok, 1999)**.

2.1.5. Iron Metabolism and Recycling

Body iron is strongly regulated in a normal way. The ability to absorb and excrete iron in the body is limited. Controlling iron content is imposed by limiting its entrance into the body rather than by augmenting any excess excretion. The absorption of iron must be controlled in order to compensate the small unavoidable losses (Approximately 1 mg / day mainly from exfoliation skin and gastrointestinal cells), and the increased physiological requirements in association with growth, menstruation of women, and pregnancy, and in the same time avoid any accumulation or iron overload from dietary sources. **(Monsen,1998).** The equilibrium of iron is maintained at each stage of growth and development and the objective is to keep pace with the fluctuation in the requirement in at different developmental stages **(Nathan &Osaki,1993).** Placenta maintains the regulation of iron absorption in embryonic stage, however, after birth regulation of iron absorption is accomplished by the intestinal mucosa.**(Dallman et al.,1996; Andrews,2000a)**

The reuse of iron from senescent RBCs is very important because most of the body iron is found in the hemoglobin of RBCs. The intestinal epithelial cells of the gastro-duodenal junction absorb only 1-2 mg of iron. This amount of iron is balanced by iron output from shed cells **(Andrews, 2000a)**. The efficiency of iron absorption is normally regulated in accordance with body iron status **(Gavin et al.,1994, Wood & Han, 1998)**.In healthy individuals the daily requirements of iron for forming new RBCs is about 20mg, and this iron is provided through macrophage ingestion of aged red blood cells and by the catabolism of their hemoglobin and reuse of released iron **(Andrews, 2000a).**

2.1.5.1. Dietary Iron

There are two forms of dietary iron, non-heme and heme iron. Mainly, iron occurs in food as nonheme iron , a smaller amount is found as heme iron(heme protein, hemoglobin and myoglobin), which is present in meat **(National Institutes of Health Office of Dietary Supplements,2005).**

The two dietary iron differ greatly in the manner of the absorption of the intestinal cells. Thus, nonheme iron has lower absorption rate and is markedly influenced by concomitantly consumed dietary components. On the other hand the absorption of heme iron is not affected by consumed dietary components **(National Institutes of Health Office of Dietary Supplements,2005).**

The absorption of heme iron is mainly diminishes by the formation of insoluble compounds of some dietary components. The most of which are phytates, tannates, polyphenols **(Hurrell et al,.1999; Zijp et al., 2000)**,oxalates, phosphates **(Dallman et al.,1996)**,calcium , lectins **.(Killip et al .,2007) .**

However iron absorption enhanced by the formation of readily absorbed compounds of other dietary components. Such compounds are ascorbic acid (vitamin C) **(National Institutes of Health Office of Dietary Supplements,2005).**

Some studies have concluded that isolated protein extracts from muscle proteins present in chicken and beef enhance non-heme iron absorption by 100% and 180%, respectively **(Hurrell et al.,2006)** Chelators like Na_2EDTA **(Davidsson, et al., 2001)**.

2.1.5.2. Iron Absorption

Iron is essential for multiple metabolic processes particularly in the production of erythrocytes hemoglobin and the production of cellular energy **(Andrew, 2000a)**. Iron can also be potentially toxic. Its ability to produce free radicals lead to tissue damage. That's, tissue iron concentration must be strictly regulated **(Conrad & Umbreit, 2000; &Alpert,2004)**

The sites of entrance of iron into the body play a role of regulation and maintenance of iron homeostasis . The primary mechanism of regulation is the intestinal absorption, particularly the cells of the intestinal crypt which receive the signals from the body to alter iron absorption, and migrate up the villus and differentiate into mature absorptive enterocytes **(Anderson, 1996).**

2.1.5.2.1. Mechanism of intestinal iron absorption

Iron absorption in the duodenum and the upper jejunum is carried out by different proteins and specialized cells **(Muir & Hopfer 1985).** Within the crypts of the intestine are multipotentund on the precursor cells, some of which migrate onto the villus and differentiate into enterocytes. The enterocytes are highly specialized, polarized, absorptive cells found on the intestinal villus that control the passage of dietary iron into the body. The enterocytes differ from their precursor cells in the expression of proteins related to iron uptake and transport.

Precursor cells act only as a sensor of body iron needs, however, upon differentiation, the enterocytes express new proteins that is required for absorption, storage, and export of dietary iron **(Roy & Enns, 2000).** The passage of iron through the intestinal enterocytes is in one direction (vectorial passage) during iron absorption in the intestine. The vectorial passage of iron through the enterocyte entails transport of the iron across three formidable cellular barriers: the apical membrane, intracellular translocation across the cytosol, and release of iron across the basolateral membrane and thence into the circulation. Although some dietary iron is probably absorbed by a paracellular pathway, the transcellular component of iron absorption presumably represents the regulated, carrier-mediated mineral transport pathway. **(Andrews, 2000a).**

Specific proteins are involved in controlling vectorial iron absorption act as membrane carrier or channels and also intracellular transport proteins (chaperones) that are responsible for the delivery of iron to specific cellular locations including the sites of iron exit from the enterocytes basolateral membrane. **(Andrews, 1999a)**.

2.1.5.2.1.1 Apical iron entry

The absorption and transport of heme and nonheme iron take place in the apical membrane of differentiated enterocyte. The most efficient absorbable iron is heme iron followed by the ferrous form and finally the ferric. Each form of iron has its own uptake pathway. At least three pathways have been proposed and reported for iron absorption and transport **(Conrad et al.,1999;Roy &Enns,2000)**.

Divalent metal transporter 1 is a protein that transfers iron across the apical membrane and into the cell through a proton-coupled process **(Gunshin et al., 1997).** DMT1 is not specific to iron; it can transport a wide variety of divalent metals ions, including manganese, cobalt, copper, zinc, cadmium, and lead. (DMT1); formerly called Nramp2 (natural resistance associated macrophage protein 2) or DCT1(divalent cation transporter 1**) (Oates et al., 2000 Wang et al.,2002).**

The most efficient means of iron uptake is that related to heme iron uptake, heme oxygenase enzyme released iron from heme, this means that iron leaves the enterocytes to enter the plasma as a non heme iron, this is the second iron uptake pathway **(Uzel & Conrad, 1998; Conrad & Umbreit; Roy & Enns, 2000)**.

The third pathway explains the uptake of ferric iron, this pathway involves at least three-carrier proteins, which is called mucin integrin and mobilferrin pathway (MIMP).This pathway is characterized by sequential relay of ferric iron from mucin that is found in the intestinal lumen to integrin on the apical cell surface to the intracellular protein mobilferrin **(Nathan & Osaki,1993 & Conrad & Umbreit, 1993& 2000)**

2.1.5.2.1.2. Intracellular Iron Trafficking

Although important molecular details of transferrin-mediated iron uptake and processing within the endosomal compartment in various cell types have been mentioned. However, the molecular details of intracellular trafficking of iron that has been absorbed across the apical membrane of the enterocyte and is destined for absorption into the blood stream remains unknown. Intestinal proteins that can bind iron have been described and may be involved in the vectorial transfer of iron across the intestine or may serve as chaperone proteins to deliver iron to specific cellular organelles or to other intracellular proteins **(Wood & Han 1998)**.

The absorbed iron in the enterocytes has two possible fates : it may be stored as ferritin, or it may be transferred across the basolateral membrane to plasma . Iron that remains in the form of ferritin will be exfoliated with the senescent cell and will leave the body through the gastrointestinal tract when the enterocytes complete their limited life cycle, this process represents an important mechanism of iron loss **(Andrew, 1999a)**.

2.1.5.2.1.3. Basolateral Iron Exit

The transfer of iron from the enterocytes to the rest of the body is mediated by the basolateral membrane. Very little is known about the processes involved in iron exit from the enterocyte. Some proteins on the basolateral membrane of the precursor and mature enterocyte may be involved in this process. These proteins either sense body iron stores or facilitate regulated iron transport into the plasma. These proteins include the basolateral iron-regulated transporter Ireg 1 **(McKie et al, 2000)**, ferriportin **(Donovan et al., 2000)** the transferring receptor-hereditary hemeochromatosis protein complex HFE **(Waheed et al., 1999),** and an accessory muli copper protein which is called hephaestin which presumed to be a form of ferroxidase **(Mahan & Escott-Stump, 2004)**

2.1.5.2.2. Regulation of Intestinal Absorption

The homeostatic regulation of whole body iron primarily takes place in the intestine **(Wood & Han, 1998)**, however, there are other processes that also contribute including interorgan transport and uptake, and cellular utilization **(Eisenstein & Bleming, 1998)**.

The absorption of intestinal iron is regulated by at least three independent regulators: dietary regulator, stores regulator, and The third regulatory mechanism, known as the erythroid regulator **(Andrews, 2000b)**.

2.1.5.2.2.1. The Dietary Regulator

Iron intestinal absorption can be modulated by the amount of iron lately consumed in the diet, this phenomenon has been recognized by **(Hahn et al., 1943)**, a mechanism referred to as the dietary regulator. For several days after a large oral iron dose, absorptive enterocytes are reluctant to obtain additional iron. This phenomenon has previously been called “mucosal block.” This mucosal blocking action probably results from accumulation of iron in the enterocytes, leading the enterocytes to believe that its set-point iron requirement has been met. Moreover this mucosal blocking dietary regulator may occur even in the presence of systemic iron deficiency **(Andrews, 1999a)**.

2.1.5.2.2.2. The Stores Regulator

A second regulatory mechanism which termed the stores regulator, it senses iron levels but responds to total body iron, rather than dietary iron, It is capable of altering the amount of iron absorbed to a limited extent, in the critical level of total iron amount of (storage and circulating) the stores regulator is able to change the amount of absorbed iron over a two or three fold range **(Gavin et al., 1994; Andrews, 2000b)** until the reserves are replete again, which avoid iron overload after ensuring iron needs **(Cox & Peters, 1980; Hunt & Roughead, 2000).**

The store regulator renovates the intestinal epithelium so, iron absorption is decreased in the face of enlarged iron stores. Besides, this reduces the average of iron uptake per day in adulthood as the requirements of growth decrease (**Finch, 1994**). Stores regulator seems to ease significantly a slow accumulation of nonheme iron (1 mg/day) rather than heme iron absorption **(Sayers et al., 1994)**. Components like serum ferritin, transferrin **(Taylor et al., 1998)** and transferrin receptor **(Feelders et al., 1999)** have all been proposed as candidate molecules in the regulation mechanism, since the regulator must work and signal between different organs.

2.1.5.2.2.3. The Erythroid Regulator

The Erythroid Regulator does not respond to iron levels at all. Rather, it modulates iron absorption in response to the requirements for erythropoiesis. **(Finch,1994)** The erythropoietic regulator has a greater ability to enhance iron absorption than the stores regulator. It is known that the erythron should have some effect on the rate of intestinal iron absorption, while most of the body iron is used for erythropoiesis. The daily amount of iron that can be absorbed by an anemic individual is 20-40mg per day this amount is more greater than the capacity of store regulator to produce **(Roy & Enns, 2000).** Yet how it occurs this is unknown. The erythropoietic regulator probably involves a soluble signal that is carried by plasma from the bone marrow to the intestine **(Cazzola et al., 1999).**

2.1.6. Iron requirements

The amount of iron required to meet the daily needs of iron for growth and to afford the normal losses from the body varies due to age and sex. this amount is consequently required more and more during infancy, early childhood, adolescence, pregnancy, and menstruating females **(Bushnell, 1992).**

Iron losses from the body are small and relatively constant; the obligatory losses from the healthy body show a loss of 14µg/kg body weight/day for men, or the total of 1 mg / day for an adult male **(Charlton et al., 1980).** Losses in women are more than in men if we take in consideration the loss of iron in menstruation in addition to the basal loss of 14µg/kg body weight/day. Although menstrual blood loss is relatively constant from one period to another, however there is a wide range of individual variation. That means that the total iron loss for menstruating women (basal and menstrual blood) is about 1.40 – 1.60 mg per day **(Bothwell et al., 1989)**

Although during pregnancy, the menstruation-related losses are reduced to almost nil, however, the requirements of iron during pregnancy are greater than in nonpregnancy state **(Wagener et al.,2000)** during pregnancy, the additional amount of iron is required for fetus, the placenta and the increased maternal blood volume. During the entire period of pregnancy the amount required is approximately 1000 mg. After the first trimester of pregnancy the daily requirements raise steadily to reach the highest value more than 6.0 mg/day in the third trimester **(Bothwell, 2000).**

Iron is necessary for infants, children, and adolescents to enlarge red cell mass and growing body tissue. Overall, adults require iron more than infants and children **(Hokama, 1994).**

Individual must absorb or supply an equivalent amount of iron, that`s needed for the developmental age, to obtain iron balance within the body**.(Bender & Bender 1997).** The amount of dietary iron should be 10 folds greater than the required amount as only 10% of dietary iron is absorbed **(Bender & Bender 1997)**

Both premenopausal and pregnant adult could not maintain normal iron balance because of the menstrual blood loss or the increased demands of iron during pregnancy **(Beard, 2000; Lynch, 2000).**

Because infants, children, and adolescent need iron for their expanding red cell mass and growing body tissue (as mentioned before), and also because of low dietary intakes of iron so they may suffer from negative iron balance. To support the increased iron requirement their diets should be rich in highly bioavailable heme iron and/or they must receive iron supplements. Some countries are supplementing foods with iron to help preventing negative iron balance in target population .these foods include bread, cereal, and bakery products.**(Yip & Ramakrishnan, 2002)**. For individuals at high risk of negative iron balance like infants, children, adolescents, and pregnant women a multivitamins containing iron are recommended **(Hillman, 1998;Hallberg 2002).** Iron fortified food was not implemented yet in the Gaza strip, however, multivitamins containing iron are prescribed for individual at risk **(Palestinian Ministry of Health, 2003).**

2.1.7. Disorders of iron Metabolism

The disorders of iron metabolism could be classified into two main categories: iron overload disorders and iron deficiency disorders **(Conrad& Umbreit, 2000).**

2.1.7.1. Iron Overload

The body is capable to reduce the amount of iron absorption. The process of excreting the excess iron from the body is limited. If the physiological pathway for excreting the excess iron is absent, this means that the patient who has an increased iron is at risk, because of the progressive accumulation of body iron reserves. This leads to high quantity of iron in tissues and thus lethal tissue damage.**(Bacon & Britton, 1990)**

Iron overload usually presents in one of two characteristic patterns. In cases in which erythropoiesis is normal but the plasma iron content surpasses the iron-binding capacity of transferrin (e.g., in cases of hereditary hemochromatosis), iron is deposited in parenchymal cells of the liver, the heart, and a subgroup of endocrine tissues .**(Nathan & Osaki, 1993; Andrew, 1999a & 2000b).**

In contrast, when iron overload results from the increased catabolism of erythrocytes (e.g., in cases of transfusional iron overload), **(Weatherall, 1997)** iron accumulates in reticuloendothelial macrophages first and only later spills over into parenchymal cells.**(Kushner et al., 2001)**.Whether the overload iron is primary or secondary, in both cases it must be treated. If not, it will lead to parenchymal deposition, tissue damage and fibrosis, and finally organ damage **(Andrew, 1999a & 2000b).**

2.1.7.2. Iron Deficiency (ID)

Iron deficiency is the most prevalent and common micronutrient deficiency in the developing world today **(Tatala et al., 1998; Asobayire et al., 2001; Abalkhail and Shawky, 2002; Hashizume et al., 2003).** More than a third of the world`s population are affected by this important public health problem (iron deficiency)**(International Life Sciences Institute,1999).**

2.1.7.2.1 Definition

Conditions of iron lack that of sufficient severity to restrict the production of hemoglobin, it results when the dietary iron intakes do not meet the body`s demands **(Hallberg,2001).** Children in their growing and premenopausal women are at high risk. Although the result of negative iron balance may be the decrease of iron absorption or ingestion, there are other causes of ID are considered to be more common such as, lesions in the gastrointestinal tract, menstruation and pregnancy. In such cases, dietary intake is enabling to keep up with chronic losses **(Duffy, 1996).**

2.1.7.2.2. Stages in the Development of ID

In the development of ID there are three important stages: iron-store depletion, iron deficient erythropoiesis and finally IDA **(Gibson, 2005)**

The first stage is iron store depletion, the depletion of iron store occurs in the hepatocyes and macrophages of the liver, spleen and bone marrow, but the functional iron may not be affected. In this case, if the body requires more iron there are no more iron store to mobilize.

The second stage is iron deficient erythropoiesis, in this stage, the store iron is depleted, the transport of iron is reduced and the amount of iron absorbed is insufficient to replace the amount lost or to provide the requirements of iron to growth and functions, the result in this stage is the reduction of red blood cell production, and certain biochemical abnormalities in iron metabolism are also detected, particularly the reduction of serum ferritin and fall in transferring saturation **(Gibson, 2005)**. Although there is no significant change in red blood cell morphology. However, there is a reduction in bone marrow capacity and a few microcytes in blood smear may be detected **(Nathan,2003).** The useful indicator in this stage (iron-deficient erythropoiesis) is the decrease in reticlocytes hemoglobin level **(Brugnara et al., 1999).** In this stage the hemoglobin level declines to borderline values but remains within the normal limits**(Lee,1999).**

The third stage is the IDA. The most severe form of ID, the reduction of iron amount leads to underproduction of iron containing compounds like Hb, which fall to lower limits of normal. And other iron-containing enzymes such as cytochromes also falls to lower levels. Serum iron and serum ferritin are very low in this stage (IDA), resulting reduction in transferrin saturation. In conclusion poorly hemoglobinized cell begin to enter the circulation **(Gibson, 2005).**

2.1.8. Iron deficiency Anemia

Iron deficiency anemia (IDA) is the most common type of nutritional anemias .It`s considered to be the result of insufficient body iron stores for the needs of normal erythropoiesis, which results the imbalance between iron intake and iron losses or utilization **(Goldenring,2003)**

2.1.8.1. Prevalence of IDA

IDA is the most common medical problem that confronts the general physicians **(Bushnell, 1992; Lee, 1999).** It is most common among the very young, among those on poor diets, among people with intestinal parasitic diseases, and among women in the menstruating age **(Bushnell, 1992).**

In both developing and developed countries microcytosis is resulted mainly by IDA **(Mach-Pascual et al., 1996).** The prevalence of IDA remains high and challenging worldwide. About 2 billion people worldwide are affected by IDA **(International Life Sciences Institute, 1999).**

2.1.8.2. Etiology

The recycling of iron within the body provide a brilliant buffer to satisfy the daily needs of iron or hemoglobin synthesis. IDA is a result of prolonged negative balance between iron intake and losses or utilization. Blood loss, inadequate dietary intake, malabsorption, rapid growth, and repeated pregnancies all are factors of either negative iron balance and IDA **(Frewin et al., 1997; Goddard et al., 2000).** Among these factors blood loss is the most common cause of IDA. In women, excessive menstrual blood loss is accountable for the majority of IDA **(Shaw, 1996 & Guidelines for the management of IDA, & Harper et al., 2011)**. In adult males and postmenopausal females the common cause of IDA is gastrointestinal blood losses mainly due to peptic ulceration, stomach cancer, intestinal parasites and drug ingestion **(Brittenham, 2000).** Malabsorption and iron-poor diet may contribute to the development of IDA **.**The interactions between iron and food substances such as phytates, vegetable fibers, and tea resulting of impairment of iron absorption **(Zimmermann, Hurrell ,2007).**In infants, children and adolescents, the needed iron to grow is more than the available intake from diet and stores **(Brittenham, 2000).**IDA is a common problem in pregnancy, as they require iron for foetus, delivery and lactation. Therefore, pregnant women must be supplied with iron or more than 85% of pregnant will suffer from IDA **(Lipschitz, 1990)**.

2.1.8.3. Clinical Features and Manifestations

The symptoms accompanying iron deficiency anemia depend on how rapidly the anemia progresses. In cases of chronic, slow blood loss, the body adjusts to the increasing anaemia and patients can often tolerate extremely low concentrations of hemoglobin, for example, < 7.0 g/dL, with remarkably few symptoms. Most patients complain of increasing lethargy and dyspnoea. More unusual symptoms are headaches, tinnitus and taste disturbance **(Frewin et al., 1997).**

chronic iron deficiency may be seen in examining skin, nail and other epithelial changes may. About a third of patients suffer atrophy of the skin and (rarely nowadays) nail changes such as koilonychias (spoon-shaped nails) may result in brittle, flattened nails. Patients may also complain of angular stomatitis, in which painful cracks appear at the angle of the mouth, sometimes accompanied by glossitis. Esophageal and pharyngeal webs can be a feature of iron deficiency anemia (consider this in middle aged women presenting with dysphagia), however, it's uncommon. These changes are believed to be due to a reduction in the iron-containing enzymes in the epithelium and gastrointestinal tract **(Marcel & Conrad, 2005).**

Iron deficiency also affects the immune system particularly, cellular immunity, because iron and its binding proteins have immunoregulatory properties. Shifting of immunoregulatory balance is expected during ID, and could result in severe and deleterious physiological effects **(Walker & Walker, 2000; Beard, 2001).**

Furthermore, the RBC of IDA subjects are more susceptible to oxidation **(Bartal et al., 1993)** and are associated with a decreased antioxidant defense system, increased platelets count, platelets aggregation, tendency to thrombosis**(Tekin, 2001)** and increased lipid peroxidation **(Kumerova et al., 1998).**

2.1.8.4. Diagnosis

As a result of iron store depletion, the hemoglobin production becomes restricted, and the normocytic normochromic erythrocyte become microcytic, hypochromic population **(Lipschitz, 1990)**.IDA is the only microcytic hypochromic disorder, in which the mobilized iron stores are absent, and the diagnosis of iron deficiency anemia can almost be verified by assessment of iron store **(Guyatt et al., 1992; Goddard et al., 2000).**

2.1.8.5. Assessment of Iron Stores

The assessment of iron store can be occurred by evaluating iron contents of various iron pools, the assessment can be direct or indirect. Direct methods are either painfully invasive or painfully expensive; however, the indirect methods are noninvasive **(Nathan & Osaki, 1993).**

2.1.8.5.1. Direct Assessment Methods

The most direct method to assessing body iron status is the quantitation of iron in bone marrow or liver biopsy specimens. Although it is considered the most definitive measurement of iron status, it is not used for screening of iron deficiency in major populations because of its invasiveness. It is mainly used to assess iron status in hospitalized patients **(Lewis et al.,2001)**

2.1.8.5.2. Indirect Assessment Methods

There are several laboratory tests for assessing body iron status indirectly: hematological and biochemical, the first based on characteristics of red blood cells [i.e Hemoglobin concentration(Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red blood cell distribution width (RDW)] , the biochemical tests include: serum ferritin concentration, transferrin saturation, and erythrocyte protoporphyrin concentration, these tests detect the earlier changes in iron biochemical tests **(Duffy, 1996; Center For Diseases Control And Prevention, 1998).**

2.1.8.6. Screening and Laboratory Findings

Both biochemical and hematological laboratory parameters can reflect the changes in different body iron compartment and are affected at different levels of iron depletion **(Hastka et al., 1996).**

2.1.8.6.1. Hematological Findings

Hematological measurements include Hb, Hct, MCV, MCH, and more recently RDW**(Center For Diseases Control And Prevention, 1998).**

2.1.8.6.1.1.Hemoglobin (Hb)

Hemoglobin as parameter in diagnosis of IDA is not a reliable parameter because of the lack of specificity and the relative insensitivity as there are different types of nutritional anemia which can result into false estimation of iron deficiency. **(Garby et al., 1969)** The normal Hb levels can vary due to different populations such as age, sex and hydration status. According to WHO, the cut-off level of hemoglobin is 13g/dL for adult men, 12g/dL for non-pregnant women and 11g/dl for pregnant women **(Weatherall, 1996a)**

2.1.8.6.1.2. MCV and MCH

Mean corpuscular volume (MCV) is the average volume of red cells in a specimen. IDA is a microcytic (small average RBC size), and hypochromic (there is a reduced amount of hemoglobin per erythrocytes: reduced MCH), however, hypochromic, microcytic RBCs are also encountered in other anemias like thalassemia and chronic diseases **(Goddard et al., 2000).**

The reference range for MCV is 80FL/red cell in adult. Reference ranges may vary depending on the individual laboratory and patient's age. The mean cell volume indicates the volume of the "average" red cell in a sample. It is expressed in femtoliters (FL; 10^{-15} liters). Traditionally, MCV is calculated by dividing the hematocrit by the red blood cell count, while the MCH is calculated by dividing the hemoglobin by the red blood cell count, a cut-off value of 26pg is accepted as the lower limit normal of MCH in adult **(Jolobe, 2000).**

2.1.8.6.1.3. Red Distribution Width (RDW)

The RDW is an index of the variation in cell volume within the red cell population. It is relatively a new parameter which used in combination with other parameters for classification of anemias **(Lin et al., 1997; Aslan et al., 2002).** Mathematically, it is the coefficient of variation, i.e., RDW(%) = (Standard deviation(fL) ÷ mean cell volume)(fL) x 100 **(Centers For Diseases Control and Prevention, 1998).** High percentage of RDW appears to be the earliest hematological manifestation of iron deficiency. A low MCV together with an increased RDW is strongly suggestive of iron deficiency **(Romero et al., 1999).**

2.1.8.6.2. Biochemical Finding

Biochemical measurements to identify iron deficiency include the quantitation of: Serum iron, serum ferritin, transferrin saturation, serum transferrin, and more recently soluble transferrin receptor **(Punnonen et al., 1997; Mast et al., 1998).**

2.1.8.6.2.1. Serum Iron (SI)

Serum iron is not used as a sole measure of iron status, as it is not specific enough. In addition low serum iron does not always indicate iron deficiency as in the situation of chronic disease. Normal adult value for serum iron 10-30 micromol/l **(Shek & Swaminathan, 1990; Cook et al., 1992).**

2.1.8.6.2.2. Serum Transferrin (TS)

Serum transferrin can be measured indirectly and directly. It can be measured indirectly through the total iron binding iron capacity (TIBC), which is the amount of added iron that can be bound to transferrin molecules in the plasma. On the other hand, serum transferrin can be estimated directly using immunological methods. In IDA the levels of serum transferrin increase, and they can be reduced in acute inflammation, chronic infections, renal malignancy. Normal values for TIBC in serum are 40-75 micromol/l**(Gambino et al., 1997).**

2.1.8.6.2.3. Transferrin Saturation (TS)

Transferrin saturation is a measure of the ratio of serum iron to total iron binding capacity (TIBC). It can be used to assess or to indicate the iron supply to the bone marrow. Transferrin saturations below 16% have been proposed as an undersupply of iron to the bone marrow **(Bothwell et al., 1979).** In the case of inflammatory disease TS is reduced. It is commonly used in population studies combined with other indicators of iron status **(Center For Diseases Control And Prevention, 1998).**

2.1.8.6.2.4. Serum Ferritin (SF)

The ferritin functions as an intracellular molecule, however, just a small amount circulates in the plasma that have a direct relation with the intracellular ferritin, and thus with the iron amount stored in the body **(Lipschitz et al., 1974**). Serum ferritin is an essential reliable and sensitive parameter to assess iron stores in all stages of ID **(Jacobs et al., 1972; Cook et al., 1974; Guyatt et al., 1992)**. Phlebotomy studies have shown a close correlation between SF concentration and the mobilizable iron store, these studies showed that each 1µg/L of SF corresponds to 8-10 mg of storage iron **(Birgegard et al., 1977; Cook & Finch, 1979; Jacob et al., 1980).** A serum ferritin concentration of <12 µg/dl is diagnostic of ID**(Addison et al., 1972).** However, serum ferritin may be raised above 12–15 µg/dl in patients with ID and concurrent chronic inflammation, malignancy, or hepatic disease **(Lipschitz & Cook, 1974**). Independently the consumption of alcohol has been suggested to raise serum ferritin **(Leggett et al., 1990)**

2.1.8.6.2.5. Serum Transferrin Receptor (TfR) Assay

Transferrin receptor is a membrane glucoprotein that mediated cellular uptake of iron from the plasma glycoprotein transferrin, it is most abundant in erythroid cells. A small amount of transferrin receptor exists in the plasma as a soluble fragment **(Ponka & Lok, 1999).** Iron deficiency causes a high regulation of transferrin receptors' cell surface expression that are reflected in an increase concentration of circulating soluble transferrin receptors **(Punnonen et al., 1997; Mast et al., 1998).**

Because of its small amount in serum, soluble TfR can be detected and quantified by sensitive monoclonal ELISA technique. The normal range for serum transferrin receptor is 3-9 mg/l. **(Flowers et al., 1989).** Levels of three to four times normal have been reported for IDA **(Kohgo et al., 1988; Huebers et al., 1990).**

2.1.8.7. Management and Treatment

The aim of treatment should be to restore hemoglobin levels and red cell indices to normal, and replenish iron stores. If this cannot be achieved, consideration should be given to further evaluation. To reach these aims some steps can be followed (a) supplementing sufficient iron to repair the anemia and replenish body iron stores, and (b) identify and correct, if possible, the underlying cause **(Nathan & Osaki, 1993; Duffy, 1996).** Iron can be administrated or parenterally, however, the oral route is the safest and the least expensive **(Lee, 1999; Goddard et al., 2000).**

2.1.8.7.1. Oral Iron Therapy

Treatment of an underlying cause should prevent further iron loss but all patients should have iron supplementation both to correct anemia and replenish body stores. This is achieved most simply and cheaply with ferrous sulfate 300 mg twice daily. Lower doses may be as effective and better tolerated **(Duffy, 1996).** For children the effective dose is 1-2mg of elemental iron per kilogram of body weight three times daily **(Lee, 1999).** Other iron compounds (e.g. ferrous fumarate, ferrous gluconate) or formulations (iron suspensions) may also be tolerated better than ferrous sulphate **(Smith, 1997).** These three components ,however, are associated with high incidence of gastrointestinal distress and side effects, including abdominal pain, nausea, vomiting, constipation, and diarrhea **(Zhou & Gibson & Crowther et al., 2009)**

To enhance iron absorption a number of compounds have been added to standard ferrous sulfate, such compounds vitamin C, vitamin A, zinc+ vitamin A. the restoring of Hb level is more effective in the presence of these compounds than iron alone **(Garcia-Casal & Layrisse, 1998; Kolsteren et al., 1999).**

2.1.8.7.2. Parenteral Iron Therapy

Parenteral iron is used when iron needs are very high cannot be corrected with oral iron therapy (eg, gastrointestinal bleeding), when oral iron cannot be properly absorbed (eg, after gastric bypass or in celiac disease), and in cases where oral iron is not well tolerated because of gastrointestinal side effects and may lead to noncompliance **(Cook ,**

2005 &Clark, 2008). Iron dextran complex intravenous (i.v) is the only parenteral iron formulation indicated for the correction of iron deficiency in patients with either normal or impaired renal function when oral iron use is unsatisfactory or not possible **(Wall & Pauly , 2008).**

2.1.8.7.3. Alternative Treatments

Patients with, or at risk of, cardiovascular instability should recieve blood transfusions according to their degree of anemia. A response from iron treatment is expected if they have endoscopic investigations before. The objective of transfusions should be to restore hemoglobin to a safe level, but not necessarily normal values. Iron treatment should follow transfusion to replenish stores **(Grey & Finlayson ,2008)**

2.1.8.7.4. Prevention Treatment

Iron deficiency and anemia is at risk if iron absorption from the diet is likely to be exceeded by losses or body demands and growth requirements. In particular, infants, pregnant women, adolescents, women of childbearing age, and women with monorrhagia, these people are at such high risk **(Madhavan, 2001; Berger& Dillon, 2002).**

To prevent ID two levels can be considered, primary and secondary level. The primary level based on appropriate dietary intake and food iron fortification. On the other hand, it can be prevented through detecting and treating iron deficient subjects in the secondary level **(Yeung & Kwan, 2002).**

There are several contributing factors to improve dietary iron and reduce iron losses, such as, food fortification, iron supplementation, dietary diversification, and public health measures **(Ramakrishnan & Yip, 2002).**

2.2. Iron Deficiency Anemia in Palestine

IDA was recognized as an important health problem in Palestine. Relatively, large number of children (50%) are suffering from iron deficiency anemia **(Hopkins-Al-Quds University, 2002).** The difficult political situation is reflected strongly on the nutritional status of the Palestinian children in both the West Bank and Gaza. The authors suggested that impaired psychomotor development, coordination, scholastic achievement, and decreased physical activity could be the result of the deteriorating nutritional status. They designed a program in cooperation with the ministry of health and ministry of education to offer iron and vitamins supplementation for schoolchildren. The results also indicated that the majority (60%) of Palestinian families face various difficulties in obtaining sufficient food including closure (60%), curfews (31%), and loss of income (56%). In addition, 61% of families reported borrowing money to secure food, 43% reported using savings, and 32% relying on food aid. Meat consumption decreased by 68% and anemia prevalence reached 50%. The constant restriction, closure, curfews reduce the availability or economical access to fresh fruits and vegetables, as well as micronutrient dens foods, such as poultry, meat, fish, and milk. Reduction in the consumption of such food commodities puts the population at risk to suffer from iron, Vit A, Folate, Zinc, Calcium, Vit B2, Vit B12, and Vit C deficiencies **(Hopkins-Al-Quds University, 2002).**

The Palestinian Ministry of health, WHO, and UNICEF conducted a comprehensive review of nutrition situation among schoolchildren in the West Bank and Gaza Strip in 2005. The findings of this study showed that there is little information on the nutritional status and dietary habits of schoolchildren. Moreover, it appears that food sold at some school canteens are of low nutritional value and all regulations on the quality of food available to students are not forced **(WHO, 2005).**

In Jenin district, 5% of secondary school children reported to suffer from iron deficiency anemia **(Khrewish, 2003)**. According to this study, the anemic students were devided to 16% males, and 84% females. The result of the study showed that the main risk factors of iron deficiency anemia were age, gender, type of diet and economic status.

2.3. Study areas

This study include 9 marginalized areas distributed over the governorates of Gaza Strip, these areas have won the attention of some local and international institutions. The Palestinian medical relief described these areas as marginalized depending on special reports.

Al – Berka area is located in the far south-west of Deir al-Balah city in the middle of Gaza Strip and adjacent to what was called the assembly settlement of Gush Katif .The majority of this area's people work in agriculture. Before 2005, this area suffered from continuous attacks by the Israeli occupation such as, incursions, bulldozing land , depriving from livelihood , bridging the wells that water the agricultural lands , destroying sheep pens and destroying the networks of water and electricity.

Al-Satar al-Gharbi area is adjacent to what was known as the settlement of Gush Katif . this led to the denial of development projects over many years and has recently been working on a project of sanitation in the area. The main source of income of some families of this area was from working in the nearby settlements in construction, agriculture or cleaning . thus, these families lost their main source of income after the withdrawal of the last settlement.

Samouni area is located in the Zeitoun region in Gaza City. The majority of its people work in agriculture and poultry. There are no schools in the area. There are Kindergartens and a mosque, and mobile clinics were carrying out there activities inside the mosque before being destroyed in the massacre which was exposed in the area in January 2009

Al-Salatine area is located in the south-west of Beit Lahiya. The majority of the people of this area depend on agriculture and fishing as the sole source of livelihood. In the war of 2008 – 2009 most of the residents of this area were displaced from their homes, and this area suffered from the white phosphorus shells and toxic gases, and the occupation bulldozed farmland and destroyed irrigation systems. In addition, they damaged the sanitation sector, and electricity grid.

Ezzbat Abed Rabbo area in the north-east of the Gaza Strip suffers from similar circumstances.

Sufa area is located in the south-east of Khan Younis in the southern Gaza Strip. The Israeli occupation is in the east border of sofa and I on the northern border there is a garbage dump .There is no networks of roads, sewerage or water. The Israeli actions led to a marked exodus of families because of the incursions , bulldozing large tracts citizens' agricultural lands, the inability of farmers from reaching their land, and bulldozing roads and water wells on which the people depend in drinking and irrigating crops.

Morag area is located in the east of the road Gaza – Rafah. It's 3 Km far from the beach and 5 km in the west of the eastern borders of the Gaza Strip. Morag settlement was held on its home soil until 2005, most of the inhabitants of this area work in agriculture. This area lacks water networks and relies on wells that are drilled for irrigating crops. It also lacks sewage networks and residents use septic tanks and some discharge water in the streets.

Sreej area is located in the east of Al – Qarara area near the border with the Israeli occupation. It's also an agricultural area. This area lacks sewage, water and health services.

CHAPTER 3
MATERIALS AND METHODS

Materials and Methods:

3.1. Study Design:

The present work was performed according to quasi-experimental research design which includes a pre – post test measurements within a treatment group as well as comparisons between case and control groups for significant differences of the study variables.

3.2. Study area

The study was conducted on 735 kids (384 males & 351 females) representing 11 kindergartens from 9 marginalized areas of the five governorates of the Gaza strip.

3.3. Setting:

This study was carried out in the five governorates of the Gaza strip: North, Gaza, Deir al- Balah, Khanyounis, and Rafah. Sampling and field works were conducted at the five governorates between Jan 1st. 2013 – April 30th - 2013.

3.4. Study population and study subjects:

The study population of the present study includes all kindergarten children (4-5 years old) living in the above mentioned 9 marginalized areas of the Gaza Strip. A total of 735 children (52.2% males, and 47.7 % females) have been screened and represented the overall study subjects. Children were randomly selected from the kindergartens of the marginalized areas.

3.5. Ethical Consideration:

The approvals of the present study were officially obtained from the biology department and the deanship of postgraduate studies and scientific researches, Al Azhar University- Gaza (AUG). The parents or guardians of the children were informed about the aims and objectives as well as the methodology of the study before the day of blood withdrawals. The researcher declared and committed to the participants about the confidentiality of the study. A signed consent form was obtained from the parents or guardians providing their acceptance and full understanding of the study stages and intervention. All parents signed the consent form of the study. The inclusion in the present study was optional and undisclosed. Neither identity nor personal data were presented or discussed. All ethical considerations were maintained, including respect of subjects, legitimacy and confidentiality

3.6. Study stages and tools

The study included different stages of screening, intervention and follow up. The first stage was assigned for screening the children for the presence of iron deficiency anemia, the second stage was the intervention to correct the anemia through oral iron supplements, and the last stage was the follow up and re-evaluation of the treated children.

The tools of present study included main components such as filling the study questionnaire as well as laboratory investigations.

3.6.1 Questionnaire

Part of the data was collected by using close-ended questionnaire which was constructed and performed in Arabic language (Annex 1), and the questionnaire data were collected through home visits and direct interview with the parents or guardians.

The questionnaire was designed to include major items about socio-demographic and general characteristics, as well as items about the health status and health complains of the children as addressed by their parents or guardians. The items and components of the questionnaire were arbitrated and validated at three levels: criterion, content, and piloting. Criterion related validity relied on the construction of questionnaire items based on related literature. For content validity; the questionnaire was reviewed and assessed by university faculty members and experts. For better validity of questionnaire, the objectives of the study were attached to all experts, accordingly, some of the items were added, some modified and some were excluded. Finally the piloting procedure, where the 10 copies where distributed to volunteers and the questionnaire content was also modified for misunderstanding, duplication and time factors.

3.6.2. Blood tests

Blood samples were obtained following standard methods by well trained nurses to prevent hemolysis and clot formation. Venous blood samples (2.5 ml in K_3-EDTA) were collected from the study subjects and then were transferred under appropriate conditions, avoiding exposure to high or low temperature, to Palestinian Medical Relief Society (PMRS) laboratories, where blood tests were performed. Complete blood counts (CBC) was performed on all samples and include: [white blood cell (WBC), red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), and platelets (PLT)] using a Cell Dyne 1700 electronic counter (Sequoia-Turner Corporation, Santa Clara, CA).

3.6.3. Diagnosis of Iron deficiency anemia

The presence of iron deficiency anemia has been considered in the microcytic (MCV <80fl) children through the Mentzler mathematical formula MCV/RBC > 13 concomitant to reduced hemoglobin concentration < 11.5g/dl .

3.6.4. Replenishing the iron stores and correction of anemia

All iron deficient anemic children were managed through oral iron supplements under full supervisor and guidance of practitioner physician at the Palestinian Medical Relief Society (PMRS). In this study the anemic children were treated with 6 ml daily dose of oral Ferrolet syrup (ferrous carbonate 50mg + 100mg vitamin C /5ml) for 3 months.

3.6.5. post-treatment evaluation

All the iron deficient anemic children who have been managed through oral iron supplements, have been checked again for the same parameters of CBC after 3 month of starting the treatment regimen.

3.6.6. Statistical analysis:

Descriptive, frequencies, central tendency, dispersion measurements, cross tabulation and statistical treatment tests like t-test , ANOVA, chi-square, correlation and regression have been used to clarify the relationship between the research variables . The Statistical Package for the Social Sciences (SPSS) version 17 was used in the statistical analysis and treatments.

CHAPTER 4

RESULTS

4.1. Distribution of sample according to locality and kindergarten

The study was conducted on 735 kids (384 males & 351 females) representing 11 kindergartens from marginalized areas of the five governorates of the Gaza strip. The distribution of the study sample according to the governorates is mentioned in Table 4.1. According to the screening protocol of the preset work, 246 kids (135 males & 111 females) were found to be anemic (hemoglobin < 11.5 g/dL) associated with Mentzler index < 13 and therefore assigned for the treatment with (Ferrolet) oral syrup (ferrous carbonate) 50mg/5ml+vitamin C 100mg) (up to 2mg (0.2 ml)/kg body weight three times daily). The distribution of those anemic cases is mentioned in Table 4.1. Significantly different prevalences of IDA were reported among the different governorates with highest values reported in Rafah (108/262, 41.2%) and the Middle (38/105, 36.2%) governorates.

Table 4.1: Distribution of sample according to gender and governorate

	Anemic N= 246 N (%)	**Control N=489** N (%)	**Total N= 735**
Gender			
Males	135 (54.9%)	249 (50.9%)	384
Females	111 (45.1%)	240 (49.1%)	351
Governorate			
Rafah	108 (43.9%)	154 (31.5%)	**262**
Khanyounis	23 (9.3%)	113 (23.1%)	**136**
Middle	38 (15.5%)	67 (13.7%)	**105**
North	56 (22.8%)	110 (22.5%)	**166**
Gaza	21 (8.5%)	45 (9.2%)	**66**

4.2. General characteristics of kids` parents

Table 4.2 demonstrates the general characteristics of the parents of study samples, their education levels, their jobs and smoking. Regarding the education levels, it is noticed that the largest number of kids' parents, father and mother received high education (secondary and university). It can be noticed also that among the fathers, the difference in the percentage of smokers vs nonsmokers are not of a significant value. The mothers were non smokers except one.

Table 4.2: General characteristics of kids` parents

		Father		Mother	
		All cases		All cases	
		No.	(%)	No.	(%)
Education level	University	230	(31.3)	209	(28.4)
	Secondary	239	(32.5)	342	(46.5)
	Preparatory	168	(22.9)	132	(18.0)
	Primary or below	98	(13.3)	52	(7.1)
	Total	735	(100)	735	(100)
Smoking	Yes	311	(42.3)	1	(0.1)
	No	424	(57.7)	734	(99.9)
	Total	735	(100)	735	(100)
Job	Employee	247	(33.6)	61	(8.3)
	Farmer	29	(3.9)	0	(0.0)
	Driver	32	(4.4)	0	(0.0)
	Worker	214	(29.1)	0	(0.0)
	No job	213	(29.0)	674	(91.7)
	Total	735	(100)	735	(100)

4.3. Demographic characteristics of the study sample

As shown in Table 4.3 the majority (68.8%) of the screened kids in the marginalized areas are registered refugees at the United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA). More than half (56.3%) of the study population are living in rural areas or refugee camps. Almost similar distribution was also reported for the anemic cases. Significantly higher prevalence was reported among refugee camp kids (51/110, 46.4%) as compared to rural (94/304, 30.9%) and city (101/321, 31.5%) children

Table 4.3: Demographic data of the study sample

		Anemic cases		Normal cases		All cases	
		No.	(%)	No.	(%)	No.	(%)
Citizenship	Refugee	173	(70.3)	333	(68.1)	506	(68.8)
	Citizen	73	(29.7)	156	(31.9)	229	(31.2)
	Total	246	(100)	489	(100)	735	(100)
Health services provider	UNRWA	177	(72.0)	329	(67.3)	506	(68.8)
	Governmental	63	(25.6)	144	(29.4)	207	(28.2)
	Others	6	(2.4)	16	(3.3)	22	(3.0)
	Total	246	(100)	489	(100)	735	(100)
Registered at UNRWA	Yes	192	(78)	314	(64.2)	506	(68.8)
	No	54	(22.0)	175	(35.8)	229	(31.2)
	Total	246	(100)	489	(100)	735	(100)
Residency	City	101	(41.1)	220	(45.0)	321	(43.7)
	Rural	94	(38.2)	210	(43.0)	304	(41.3)
	Refugee camp	51	(20.7)	59	(12.0)	110	(15.0)
	Total	246	(100)	489	(100)	735	(100)

4.4. Socioeconomic characteristics of kids' families

The Socioeconomic characteristics of kids' families are presented in Table 4.4 which indicates non-significant differences between the numbers of families regarding parents' consanguinity either in the anemic cases (51.2 % vs 48.8%) or in the overall cases (47.5 % vs 52.5 %). It is noticed also from the table that the most of families don't earn a sufficient income that lead to saving. However, the majority of the families are owner of their houses.

Table 4.4: socioeconomic characteristics of kids' families

		Anemic cases No.	(%)	Normal cases No.	(%)	All cases No.	(%)	P value
Consanguinity of parents	consanguineous	126	(51.2)	223	(45.6)	349	(47.5)	0.159
	None consanguineous	120	(48.8)	266	(54.4)	386	(52.5)	
Income sufficiency	Sufficient and savings	47	(19.1)	93	(19.0)	140	(19.0)	1.01
	Just sufficient	87	(35.4)	173	(35.4)	260	(35.4)	
	insufficient	112	(45.5)	223	(45.6)	335	(45.6)	
Home owning	Rent	32	(13.0)	58	(11.9)	90	(12.2)	0.721
	Owner	214	(87.0)	431	(88.1)	645	(87.8)	

4.5. Nutritional habits of the study sample

Most of the kids have good nutritional habits (tables 4.5A and 4.5B), most of them were breast feeders and most of them eat 3 meals a day. However its noticed that the majority of the cases and control are drinking tea (80.9% vs 83.4% respectively), cola (85.4% vs 86.5%) and backed juice (65.4% vs 67.7%) with no significant differences between the anemic and the control groups. Same non-significant differences were reported between anemic and control groups in all other nutritional habits and feedings .

Table 4.5A: Nutritional habits of the study sample

		Normal control No.	(%)	Anemic cases No.	(%)	P value
Drinking tea per day	0	81	(16.6)	47	(19.1)	0.06
	1-3	363	(74.2)	185	(75.2)	
	4-6	44	(9.0)	13	(5.3)	
	7-10	1	(0.2)	1	(0.4)	
	Total	489	(100)	246	(100)	
Daily meals	2	66	(13.5)	20	(8.1)	0.145
	3	316	(64.6)	176	(71.5)	
	4	87	(17.8)	41	(16.7)	
	5	20	(4.1)	9	(3.7)	
	Total	489	(100)	246	(100)	
Weekly meat	0	13	(2.7)	10	(4.1)	0.697
	1-3	411	(84.0)	200	(81.3)	
	4-7	65	(13.3)	36	(14.6)	

	Total	489 (100)	246 (100)	
Weekly crackers	0	20 (4.1)	14 (5.7)	0.246
	1-5	258 (52.8)	124 (50.4)	
	6-10	208 (42.5)	105 (42.7)	
	11-15	3 (0.6)	3 (1.2)	
	Total	489 (100)	246 (100)	
Weekly cola	0	66 (13.5)	36 (14.6)	0.827
	1-3	348 (71.2)	183 (74.4)	
	4-7	75 (15.3)	27 (11.0)	
	Total	489 (100)	246 (100)	
Child appetite	Good	203 (41.5)	96 (39.0)	0.798
	Fair	193 (39.5)	100 (40.7)	
	Poor	93 (19.0)	50 (20.3)	
	Total	489 (100)	246 (100)	
Type of milk feeding	Breast feeding	418 (85.5)	214 (87.0)	0.653
	formula	71 (14.5)	32 (13.0)	
	Total	489 (100)	246 (100)	
Length of breast feeding	≤6months	78 (16.0)	33 (13.4)	0.157
	7-12 months	143 (29.2)	62 (25.2)	
	13-18 months	189 (38.7)	95 (38.6)	
	19-24 months	71 (14.5)	53 (21.5)	
	>24months	8 (1.6)	3 (1.2)	
	Total	489 (100)	246 (100)	

Table 4.5B: Nutritional habits of the study sample

Normal control (N=489)				Anemic cases (N=246)				
Yes		NO		Yes		NO		P value
No.	(%)	No.	(%)	No.	(%)	No.	(%)	
Drinking tea								
408	(83.4)	81	(16.6)	199	(80.9)	47	(19.1)	0.410
Drinking tea with meals								
245	(50.1)	244	(49.9)	131	(53.3)	115	(46.7)	0.435
Drinking packed juice								
331	(67.7)	158	(32.3)	161	(65.4)	85	(34.6)	0.561
Eating fruits								
223	(45.6)	266	(54.4)	110	(44.7)	136	(55.3)	0.875

4.6. Differences in food habits between cases and normal control

Table 4.6 demonstrates the mean values of food habits of the anemic cases and the normal control. It can be noticed that there were no statistically significant differences between cases and the normal control in food habits as, the P value > 0.05.

Table 4.6: Differences in food habits between cases and normal control.

	Anemic cases	Normal control	P value
	Mean ± SD	Mean ± SD	
Tea drinking per day	1.68 ± 1.29	1.77 ± 1.33	0.439
Daily meals	3.15 ±0.60	3.10 ± 0.71	0.407
Weekly meat	2.10 ± 1.53	2.03 ± 1.37	0.568
Weekly crackers	4.61 ± 2.61	4.66 ± 2.47	0.840
Weekly gaseous drink cola	1.71 ± 1.64	1.93 ± 1.82	0.162
Length of milk feeding (month)	14.84 ± 6.14	14.34 ± 6.18	0.352

4.7. Medical history of kids` mothers

Table 4.7 shows the medical history regarding pregnancy and delivery of the study sample's mothers. It's noticed that most of them had full term pregnancy and natural vaginal delivery. In addition most mothers did not suffer from anemia during pregnancy, as they received iron supplements. No significant differences were reported between the mothers of the two groups.

Table 4.7: Medical history of kids` mothers

		Normal control		Anemic cases		P value
		No.	(%)	No.	(%)	
Anemia during pregnancy	Yes	118	(24.1)	73	(29.7)	0.109
	No	371	(75.9)	173	(70.3)	
Iron supplements during pregnancy	Yes	421	(86.1)	224	(91.1)	0.057
	No	68	(13.9)	22	(8.9)	
Full-term or preterm	Full-term	455	(93.0)	230	(93.5)	0.878
	Preterm	34	(7.0)	16	(6.5)	
Delivery method	Natural vaginal	434	(88.8)	208	(84.6)	0.126
	C.S	55	(11.2)	38	(15.4)	

4.8. Medical characteristics of the study sample:

The Medical characteristics of the study sample is presented in table 4.8 which indicated that most of the cases don't suffer from malnutrition, parasitic infection, chronic or frequent diarrhea, nor any diseases. Most of their families don't suffer from any genetic diseases while most of the cases received multivitamins or iron in the last two months. Also non-significant differences were reported between the two groups

Table 4.8: Medical characteristics of the study sample:

Normal control				Anemic cases				P value
Yes		No		Yes		No		
No.	(%)	No.	(%)	No.	(%)	No.	(%)	
Suffering from malnutrition								
89	(18.2)	400	(81.8)	56	(22.8)	190	(77.2)	0.169
Suffering from parasitic infection								
198	(40.5)	291	(59.5)	105	(42.7)	141	(57.3)	0.579
Suffering from chronic or frequent diarrhea								
28	(5.7)	461	(94.3)	22	(8.9)	224	(91.1)	0.120
Receiving multivitamins or iron in the last two months								
43	(8.8)	446	(91.2)	25	(10.2)	221	(89.8)	0.590
Suffering from any diseases								
51	(10.4)	438	(89.6)	28	(11.4)	218	(88.6)	0.706
Genetic diseases in the family								
69	(14.1)	420	(85.9)	38	(15.4)	208	(84.6)	0.658

4.9. The anthropometric and socioeconomic characteristics of the cases and control

The anthropometric and socioeconomic characteristics of the cases and control are mentioned in table 4.9. As shown in the table there are statistically significant differences between the cases and the normal control in age (5.29 ± 0.70 vs 5.45 ±0.61 years) and height (103.61 ± 5.42 vs 105.01 ± 5.14 cm), where the *P* value< 0.05 and no statistically significant differences can be noticed in the other parameters .

Table 4.9: The anthropometric and socioeconomic characteristics of the cases and control

	Anemic cases	Normal control	P value
	Mean ± SD	Mean± SD	
Age (year)	5.29 ± 0.70	5.45 ± 0.61	0.000
Weight of the child now (kg)	15.49 ± 2.29	16.26 ± 6.55	0.084
Weight at birth (kg)	3.14 ± 0.57	3.11 ± 0.54	0.517
Height of the child *(cm)	103.61 ± 5.42	105.01 ± 5.14	0.003
Father age (year)	36.57 ± 7.71	36.44 ± 7.32	0.848
Mother age (year)	31.57 ± 6.18	31.28 ± 6.36	0.602
Marriage years of the parents	12.01 ± 6.03	12.22 ± 6.38	0.702
Number of kids in the family	5.12 ± 2.59	4.99 ± 2.35	0.551
Family income	1349.75 ± 1302.59	1318.44 ± 1678.82	0.814
Family outcome	1488.82 ± 1207.30	1426.53 ± 1290.69	0.572
Family members living together	7.87 ± 3.34	7.90 ± 3.91	0.924

4.10. Hematological parameters of the cases and the normal control

The hematological parameters of the cases and the normal control are presented in Table 4.10 which revealed significant differences between the two groups in all the CBC parameters except for WBC.

Table 4.10: Hematological parameter between cases and normal control

	Anemic cases	Normal control	P value
	Mean ± SD	Mean ± SD	
RBC count X 10^{12} /L	4.18 ± 0.45	4.49 ± 0.26	0.000
Hemoglobin conc mg/dL	10.4 ± 0.45	11.9 ± 0.40	0.000
Hematocrit %	31.34 ± 1.41	35.02 ± 2.29	0.000
MCV fl	75.19 ± 7.77	78.24 ± 3.43	0.000
MCH pg	25.10 ± 2.21	26.50 ± 1.80	0.000
MCHC %	33.17 ± 0.90	33.9 ± 1.03	0.000
RDW	12.9 ± 1.62	12.58 ± 1.00	0.006
WBC x10^9/L	8.50 ± 6.20	8.80 ± 2.50	0.421
PLT x10^9/L	332.7 ± 96.1	355.92 ± 91.52	0.005

4.11. Hematological evaluation of the anemic cases before and after iron supplementation treatment

Table 4.11 shows the mean values of hematological parameters of the anemic cases before and after 3 months treatment with ferrolate It is very clear that there were high statistically significant differences between cases before and after treatment in the hematological parameters, except for MCV where the differences were not significant.

Table 4.11: Hematological parameters among cases before and after treatment

	Before treatment	After treatment	P value
	Mean ± SD	Mean ± SD	
RBC count X 10^{12} /L	4.18 ± 0.45	4.36 ± 0.39	0.000
Hemoglobin conc mg/dL	10.4 ± 0.45	11.37 ± 0.68	0.000
Hematocrit %	31.34 ± 1.41	32.63 ± 1.89	0.000
MCV fl	75.19 ± 7.70	75.19 ± 6.6	0.990
MCH pg	25.10 ± 2.21	26.26 ± 2.31	0.000
MCHC %	33.17 ± 0.90	34.8 ± 0.69	0.000
RDW	12.89 ± 1.58	12.80 ± 1.75	0.000
WBC x10^9 /L	8.50 ± 6.23	8.61 ± 2.86	0.002
PLT x10^9 /L	332.73 ± 96.09	350.95 ± 95.85	0.000

CHAPTER 5

DISCUSSION

Nutritional deficiencies are very important to the overall health of humans in all ages and for both sexes, however in some age groups (infants and children, women in child bearing age) these deficiencies can be critical and then the growth and development will be extremely hindered by scarcities in essential vitamins or nutrients. Iron deficiency (ID) and iron deficiency anemia (IDA) are considered as the commonest and most prevalent nutritional disorder of mankind in the world today. The World Health Organization (WHO) estimates that more than one-third of the world's population suffers from ID and IDA (**World Health Organization (WHO)/ Food and Agricultural Organization (FAO), 1992**). In developing countries every second pregnant woman and about 40% of preschool children are estimated to be anemic due to iron deficiency. ID is the only nutrient deficiency which is significantly prevalent in developed and industrialized countries. Unfortunately, in resource-poor areas, the clinical condition of the iron deficient and anemic subjects is exacerbated by infectious diseases such as worm infections, malaria, HIV and tuberculosis. Previous studies have shown a considerable prevalence of iron deficiency anemia (10.0 %) among the Palestinians in the Gaza strip, Palestine **(Sirdah et al., 1997).** ID and IDA not only constitute a public health nutritional problem, but also their coexistence with other disorders could interfere with the laboratory and clinical diagnosis of the coexisting disorder **(Sirdah et al., 2002).**

We designed the present study to determine the prevalence of IDA among kindergarten kids living at 9 marginalized area in Gaza strip and implement an appropriate management plan that include the supplementation of oral iron formula to correct the anemia through replenishing the circulation iron and iron stores in the iron deficient anemic children. This study include 9 marginalized areas, less fortunate for development, distributed over the different governorates of Gaza Strip, these areas have won the attention of some local and international institutions.

The screening stage of the study included 735 kids (384 males & 351 females) representing 11 kindergartens from marginalized areas of the five governorates of the Gaza strip. Because our target population is the kids of the less fortunate marginalized areas, so in our screening we considered the population in the marginalized area, not the governorate size in determining our sample size.

In the screening stage, the presence of IDA was considered in the microcytic (MCV <80fl) children through the Mentzler mathematical formula MCV/RBC > 13 concomitant to reduced hemoglobin concentration < 11.5g/dl **(Sirdah et al., 1998; Abelson 2001, Bogen et al., 2001).** Although this could be considered as a limitation of the study, however, the financial resources and availability of instruments in these marginalized regions to determine serum ferritin are the main reasons for using the Mentzler mathematical formula.

Our results revealed significantly higher prevalence of IDA among Gaza, Rafah and Middle governorates as compared to the North and Khan Younis governorates. Our results are concomitant to the results of Selmi and Al Hindi 2011 who reported significantly different prevalences of anemia among school children aged 6-11 years old in Gaza Strip, Palestine. However, non-significant differences in the prevalences of ID and IDA among different localities in Gaza strip have been also reported in previous studies of other researchers in different settings **(Abdeen et al., 2002; Radi et al., 2013).**

The educational background of the kids' parents revealed a satisfactory level where more than two-thirds of the parents had received high education (secondary and university). This result is concomitant with the higher educational level of the Palestinian people reported by Palestinian Central Bureau of Statistics where the estimated rate of Illiteracy rate for persons aged 15 years and above was 4.1 **(Palestinian Central Bureau of Statistics (PCBS), 2012)**. Unemployment was reported in nearly one third of the fathers which could significantly affect the ability of the families to supply nutrient foods for their kids **(Pasricha et al., 2010; N. Saluja et al., 2011; Bharati et al., 2013).**

The prevalence of IDA was not significantly different between refugees (34.2) and non-refugees (31.9%), which is concomitant to the national nutritional assessment study performed by Abdeen et al., 2002 and revealed no statistically significant differences in anemia prevalence based on refugee status.

Parents' consanguinity was not found to be a risk factor for IDA in the subjects of the present work. Our results showed that consanguineous vs non-consanguineous marriages represent 51.2 % and 48.8 respectively among the IDA group. However, in the study of Sirdah 2008 the author reported an association between anemia and parents' consanguinity among adolescent males, while no significant differences were observed among the females.

The economic status families reflects a vulnerable one where most of overall families (86.3%) don't earn a sufficient income that lead to savings, and in half of them the income is insufficient. The effects of family income on hemoglobin levels was reported by Sirdah et al., 2008 where the analysis revealed a significant correlation ($r = 0.512$, $p = 0.001$) between hemoglobin level in females and family income also he reported a significant association between small family size and higher incomes on one hand and higher hemoglobin levels on the other hand. . Family size and income may exaggerate the anemic status and increase the gap in hemoglobin level between males and females due to the physiological nature and lifestyle of females. The socioeconomical determinants of anemia have been also reported in adolescent females in other settings (**Kilbride et al., 1999; Bhargava et al., 2001; Beena et al., 2012)**.

A noticeable finding of the present work was the high percentage of females who drinking tea and cola drinks. Tea drinking was found to expressively affect the absorption of iron possibly due to the binding of iron in the gut by polyphenols/tannins in tea (**Siegenberg et al., 1991; Zijp et al., 2000**). Although there are no significant differences between cases and control in the frequency of consuming these drinks, however, the results are distressing which justifying a national awareness programs for kids and for female of the child bearing age, because of the negative effects of these drinks on the kids, mothers and pregnancy outcomes.

The anemic status significantly affected the anthropometric characteristics of the kindergarten children. The anemic children were found to have lower weight and shorter stature. The effect of anemia during pregnancy on the anthropometric measurements of Saudi newborns was studied by Telatar et al., 2009 where the authors revealed significant negative effect of anemia on neonatal anthropometric measurements (**Telatar et al., 2009**). Same finding were also reported by Dakshayani 2013, who showed a significant decrease in the anthropometric parameters in the newborns born to anemic mothers (**Anupama & Dakshayani 2013**). On the other hand, Ayoya et al., 2013 considered short stature and stunting as Predictors of child anemia (**Ayoya et al., 2013)**.

The hematological parameters of the cases and the normal control revealed significant differences between the two groups in all the CBC parameters except for WBC, the mean Hb concentration for cases was 12.5 % lower than those in the control group. Alzain 2012 showed a higher percentage of anemic children in North Gaza with a statistically higher prevalence among males (35%) than female children (30%).

Additionally, **Selmi and Al-Hindi 2011** concluded that anemia constitutes a health problem among schoolchildren with an overall prevalence of 35.3% (36.3 % among girls vs. 34% among boys). However, the recently published work of Radi et al., 2013 estimated the prevalence of anemia among preschoolers to be over 50% (**Selmi and Al-Hindi 2011)**.

An interesting finding of the present work is the success of our intervention to correct the hemoglobin concentration in order to correct anemic status of the children. The mean values of hematological parameters of the anemic cases before and after 3 months of treatment revealed statistically significant improvements in the hematological parameters, except for MCV where the differences were not significant. An improvement in Hb concentration of about 9.3 % was reported with mean Hb conc of 11.37 g/dL. About 10 % increase in Hb conc was reported by Bopche et al., 2009 after one moth treatment in Indian children, however the mean Hb baseline value of their children was much lower (8.53 g/dL) than our study group (10.4 g/dL). In another setting in Guatemala city, 1.8 g/dL improvement in Hb concentration was achieved in infants and young children after 28 days of treatment with ferrous sulfate **(Pineda and Ashmead, 2001).** The better success of these studies over our could be due to different factors that include the commitment of the parents and children in the treatment protocol, the coexistence of parasitic infections among the children, compliance with iron therapy, the bioavailability of the iron formula used **(Stoltzfus and Dreyfuss 1998; UNICEF/UNU/WHO/MI Technical Workshop, 1998; Yip 2002)**

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

This chapter provides the main conclusions of this study as well as some recommendations for decision makers for adopting new strategies to reduce iron deficiency anemia. Recommendations studies for further investigation are also mentioned in this chapter.

6.1. Conclusion

- The prevalence of IDA among kindergarten children living in marginalized areas in Gaza strip was about one third of the study subject, with no significant differences between both genders .
- This study demonstrated that the highest percent of anemia was in Rafah governorate Followed by North and the Middle, whereas, the lowest percent was in Gaza governorate .
- This study showed that more than half of anemic subjects live in rural areas or refugee camps and most of families don't earn a sufficient income that lead to saving.
- There was no significant differences between the number of families according parents' consanguinity neither in anemic cases nor overall cases.
- Most of parents have received a high education (secondary and university), where no significant differences between smokers vs non smokers.
- Most of the children have good nutritional habits, It can be noticed that there were no statistically significant differences between the anemic and the control groups in all nutritional habits and feedings .
- No statistical significant differences were found between normal control and anemic cases in medical history of kids` mothers (Anemia during pregnancy, Iron supplements during pregnancy, Full-term or preterm, Delivery method).
- Concerning the medical characteristics of the study subjects it noticed that there was no statically significant differences between normal control group and anemic

cases in (Suffering from malnutrition, Suffering from parasitic infection, Suffering from chronic or frequent diarrhea, Receiving multivitamins or iron in the last two months, Suffering from any diseases, Genetic diseases in the family).

- It was very clear that IDA affected the height of anemic subjects . with high significant differences between normal control and cases.

- The results also revealed that there is clear relationship between the age and Iron deficiency anemia , where there is significant differences between normal control and anemic cases in age.

- There is no significant differences between normal control and cases in other anthropometric and socioeconomic characteristics (Weight of the child, Weight at birth, Father age, Mother age, Marriage years of the parents, Number of kids in the family, Family income, Family outcome and Family members living together).

- The study demonstrated a statistically significant differences between anemic cases and the normal control in all the CBC parameters except for WBC.

- This study demonstrated the effectiveness of iron supplementation over 3 months of treatment , It is very clear that there were high statistically significant differences between cases before and after treatment in the hematological parameters, except for MCV where the differences were not significant.

6.2. Recommendation

The study provided clear evidence that the prevalence of iron deficiency anemia among children in Gaza Strip become a disturbing .

- Policy makers are advised to develop interventions to improve iron status of the population with emphasis in the sub-populations with higher risks: rural areas, the poorest children.

- Policy makers may collect specific information on population iron status and should use information to develop appropriate intervention programs.

- The results of this study may be used to plan for interventions aimed to improve the iron status of the children.

- We recommend establishing units in primary health care centers to treat malnutrition problems.

6.3. Recommendations for future research

- Further studies are needed to explore the prevalence of IDA among school age children.

- Specific research is recommended to investigate other risk factors associated with IDA among children under 5 years old in Gaza Strip.

CHAPTER 7

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رقم الاستبيان (   )

السيد/ ولي أمر الطفل   تحية طيبه وبعد ،،،

تم إعداد هذا الاستبيان من قبل الطالب /عبدالله رسمي عامر ياغي الطالب في برنامج ماجستير العلوم الحياتية في جامعة الازهر بغزة .

تهدف هذه الدراسة الي تحديد نسبه فقر الدم (الانيميا) الاطفال دون سن الخامسة وتحديد فعالية بعض الفيتامينات والحديد في خفض نسبه الانيميا .

لذا نرجو تعاونكم في ملء بعض البيانات الخاصة بالطفل والأم ، مع العلم أن جميع هذه البيانات تبقي سرية بهدف البحث.

1- بيانات خاصة بالطفل :

اسم الطفل: ....

رقم هاتف المنزل : ....

رقم جوال ولي الامر:...................................

الجنس : ذكر ☐ أنثى ☐ (يرجى وضع إشارة x)

تاريخ الميلاد : ....

وزن الطفل عند الولادة:.......................

وزن الطفل الحالى :..........................

طول الطفل الحالي :...........................

ترتيب الطفل بين اخوته و اخواته :...........

المحافظة : (رفح– خانيونس – الوسطى – غزة – الشمال)

مكان السكن : مدينة ☐ قرية ☐ مخيم ☐ (يرجى وضع إشارة x)

المواطنة : لاجئ ☐ مواطن ☐

الخدمات الصحية التي يتبع لها الطفل : عيادات الوكالة ☐ العيادات الحكومية ☐ أخرى ☐

هل مسجل لدى وكالة الغوث : نعم ☐ لا ☐

2– بيانات خاصة بأسرة الطفل:

عمر الأب : ....

تعليم الأب:.................

عمل الأب :..................

هل الأب مدخن : نعم ☐ لا ☐

عمر الام: ....

تعليم الام :...............

عمل الام:................

هل يوجد صلة قرابة بين الأب و الأم: نعم ☐ لا ☐

(في حال الإجابة نعم ما درجة القرابة؟) :..........................

عدد سنوات الزواج : ....

عدد الابناء :....................

هل عانت الأم من حالات اجهاض سابقة ؟ نعم ☐ لا ☐

هل الأم مدخنة ؟ نعم ☐ لا ☐

الدخل الشهري للأسرة .... شيكل

المصروف الشهري للأسرة .... شيكل

الدخل : يكفي الاحتياجات مع التوفير ☐ يكفي فقط ☐ لا يكفي ☐

ملكية السكن: ايجار ☐ ملك ☐

عدد افراد الاسرة داخل المنزل: (   )

هل عانت الأم من فقر الدم اثناء الحمل: : نعم ☐ لا ☐

هل تلقت الأم الحديد او فيتامينات اثناء الحمل: : نعم ☐ لا ☐

موعد الولادة : مكتمل ☐ مبكر ☐

نوع الولادة: طبيعية ☐ قيصرية ☐

3- بيانات خاصة بصحة و تغذية الطفل :

هل يتناول الطفل الشاي: نعم ☐ لا ☐

(اذا كانت الاجابة نعم كم مرة يوميا ؟) ....

هل يتناول الطفل الشاي بعد الاكل مباشرة او مع الاكل: نعم ☐ لا ☐

كم عدد الوجبات التي يتناولها الطفل يوميا؟...................

كم عدد المرات التى يتناول فيها الطفل اللحوم (عجل/طيور/سمك/كبدة)اسبوعيا؟................

كم مرة يتناول فيها الطفل المقرمشات (الشيبس و مشتقاته) اسبوعيا؟..........................

كم مرة يتناول فيها الطفل الكولا و المشروبات الغازية اسبوعيا؟....................

هل يتناول الطفل العصائر الجاهزة ؟......................

هل يتناول الطفل الفواكه بانتظام؟......................

نوع الرضاعة: طبيعية من الام ☐ غير طبيعية حليب صناعي ☐

في حالة الرضاعة الطبيعية كم استمرت: ....

هل عانى أو يعاني الطفل من سوء تغذية: نعم ☐ لا ☐

هل عانى او يعاني الطفل من الديدان الطفيلية: نعم ☐ لا ☐

هل عانى او يعاني الطفل من اسهال متكرر او مزمن: نعم ☐ لا ☐

هل تلقى او يتلقى الطفل الحديد او الفيتامينات خلال الشهريين الماضيين. نعم ☐ لا ☐

كيف تقيم شهية الطفل: جيدة ☐ مقبولة ☐ ضعيفة ☐

هل يعاني الطفل من امراض ؟ :نعم ☐ لا ☐

(في حال الإجابة نعم اذكرها) ....

هل هناك امراض وراثية في الأسرة/العائلة: نعم ☐ لا ☐

(في حال الإجابة نعم اذكرها)...

انا ولي أمر الطفل ....

اصرح أنه ليس لدي مانع من أخذ عينه دم من طفلي بهدف الدراسة والبحث وليس لدي أي موانع من نشر نتائج هذه الدراسة.

الاسم... ***التوقيع:...................................***
