**Bulletin of Environment, Pharmacology and Life Sciences**
Bull. Env. Pharmacol. Life Sci., Vol 8 [8] July 2019 : 129-138

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.876
Universal Impact Factor 0.9804
NAAS Rating 4.95


**REVIEW ARTICLE** **OPEN ACCESS**

# Iron Bioavailability, Deficiency and its Consequences in Infants and Children: State of the art

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**ABSTRACT**

*Globally, micronutrient deficiency is considered one of the major concerns of public health bodies and institutions in the world. Examples of these greatest public health significance are those of vitamin D, vitamin A, iron, iodine...etc. Iron deficiency is the single most common nutrient deficiency in the world today and affects affluent societies and developing countries. Iron is an essential nutrient for individuals of all ages. Symptoms of the iron deficiency are basically related to the duration and the severity of the deficiency. In addition, iron deficiency affects nervous system and has been reported to cause retardation on cognitive function and detrimental effect on cortical reactivity. Iron is present in food in two forms: (1) heme iron, as found in the hemoglobin or myoglobin of animals, or (2) nonheme iron, which is found in both animal and plant foods, primarily as iron-containing salts. Absorption depends on the body's iron status or level of iron stores and on iron bioavailability from the diet. Iron is an essential nutrient throughout the lifecycle and it remains a serious nutrition concern among important sub-groups of the population. For optimum nonheme iron bioavailability, people should be encouraged to consume at least one source of vitamin C, particularly with meatless meals.*

***Keywords:*** *Iron Bioavailability, Iron deficiency , Micronutrien, Infants , Children*

Received 11.04.2019 Revised 30.04.2019 Accepted 24.06.2019

## INTRODUCTION

Globally, micronutrient deficiency is considered one of the major concerns of public health bodies and institutions in the world. Examples of these greatest public health significance are those of vitamin D, vitamin A, iron, iodine...etc. These nutrients are referred to as micronutrients because the body needs them in minute quantities for growth, development and maintenance. Vitamins and minerals deficiencies adversely affect athird of the world's population[1].

In their article , Tang and Krebs, [2] stated that "Iron is an essential micronutrient that supports hemoglobinsynthesis, oxygen delivery and other important metabolic functions. Iron deficiency is the most common micronutrient deficiency in the world and greatly affects pregnant women and thedeveloping fetus, infants and young children. For these vulnerable life stages, iron needs often cannot be adequately met through diet, due to inadequate total intake and/or low bioavailability".

Iron deficiency anemia during childhood and adolescence impairs mental development and thus learning capacity. In their paper Kwak *et al* [3] stated that "Iron deficiency anemia (IDA) is a common nutritional deficiency in children with a prevalence of 1–15% in the USA depending on ethnicity and socioeconomic status, and a prevalence of 0.5–5% in South Korea". However, Europe is considered to be a developed region in which nutrition is assumed to be adequate to satisfy population requirements[1].

Iron is an essential nutrient for individuals of all ages. Iron deficiency is the most common nutrient deficiency worldwide. Iron is an essential element for all living cells and several metabolic pathways [2]. A growing organism needs much more iron than usual while the adaptation capacity of itself to iron deficiency is exceedingly limited. Thus, the most severe symptoms of iron deficiency are observed in

child-hood. Iron deficiency anemia (IDA) is most frequently seen in the first 2 years, especially in the range of 6 to 24 months, of life. Its incidence is highest in developing countries [4]. Nutritional deficiencies are major contributors to childhood morbidity and mortality, especially in developing countries. Although isolated nutritional deficiencies may occur, it is more common for several to coexist. It is estimated that up to half of all of the children in the world are deficient in iron and/or zinc [5] .

Iron deficiency is the single most common nutrient deficiency in the world today and affects affluent societies and developing countries. The World Health Organization estimated that more than 1.3 billion people have iron deficiency or iron-deficiency anemia and that about 1.2 billion of these people are located in developing countries. Most of the affected individuals are young children who are particularly susceptible because of their rapid growth rates and small, if any, iron reserves. This results in exogenous iron needs that are inadequately met by traditional diets [6]. Nutritional anemia was defined in a 1968 WHO technical report as "a condition in which the hemoglobin content of the blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency." WHO coordinated a series of studies in pregnant women in which anemia, serum folate, transferrin saturation and serum B-12 were assessed. They concluded that "Iron deficiency was present in 40–99% of the pregnant women studied and was undoubtedly responsible for the major proportion of anemia" [7].

In healthy, full-term infants, born from well-nourished mothers, the first 3 to 4 mo of life are characterized by a relative abundance of iron, with 50 mg of the 75 mg Fe/kg of body weight present in their erythrocytes and the remainder in their tissues. The hemoglobin level of a newborn usually declines to about 10 g/dL by postnatal weeks 6 to 8. As rapid growth is established, the iron stores of the infant are mobilized for the production of supporting hemoglobin, myoglobin, and iron enzymes. By 4 mo of age, infant iron stores are generally depleted. Recently published information on iron warrants a revisit of this essential nutrient by health professionals. A review of iron needs in the population has resulted in increased intake recommendations for most individuals, especially infants, adolescent females, women aged 18 to 49 years, and individuals who do not consume meat, fish or poultry; and reduced intake recommendations for men and postmenopausal women [8].

During early infancy, the infant is maintained exclusively by breast-feeding. The quantity of iron in breast milk ranges from approximately 0.05 mg/L to approximately 1.5 mg/L, with the median being 0.47 mg/L, depending on the stage of lactation. The usual daily intake of the baby is approximately 600 mL of milk. Up to 1 y of age, the daily iron requirement of most infants is approximately 0.96 mg/d. By 4 mo of age, the infant's iron stores have been depleted, and the contribution of iron in breast milk is approximately 0.28 mg/d. [6].

## IRON

### Nature (Chemistry)

Iron is a d-block transition element that can exist in oxidation states ranging from 22 to 16. In biological systems, these oxidation states are limited primarily to the ferrous 12, ferric 13 and ferryl 14 states. The interconversion of iron oxidation states is not only a mechanism whereby iron participates in electron transfer but also a mechanism whereby iron can reversibly bind ligands. Iron can bind to many ligands by virtue of its unoccupied d orbitals. The preferred biological ligands for iron are oxygen, nitrogen and sulfur atoms. The electronic spin state and biological redox potential (from 1 1000 mV for some heme proteins to 2550 mV for some bacterial ferredoxins) of iron can change according to the ligand to which it is bound. By exploiting the oxidation state, redox potential and electron spin state of iron, nature can precisely adjust iron's chemical reactivity[9,30,33].

### Forms of dietary iron

Iron is present in food in two forms: (1) heme iron, as found in the hemoglobin or myoglobin of animals, or (2) nonheme iron, which is found in both animal and plant foods, primarily as iron-containing salts. Nonheme iron is found in either the ferrous iron ($Fe^{2+}$) or ferric iron ($Fe^{3+}$) form in many foods. The primary source of nonheme iron in the Canadian diet is Grain Products, many of which are enriched or fortified with iron. Other sources of nonheme iron include beans (e.g. white or kidney beans), lentils, tofu, dried apricots, raisins, nuts, eggs, meat, fish and poultry. Based on a conservative estimate, the average adult Canadian diet includes 10% heme and 90% nonheme iron[9,30,33].

### Iron in the body

The body has two compartments of iron: functional and non-functional. Most of the body iron is considered essential or functional iron, involved in biochemical functions in the form of hemoglobin, myoglobin, and in enzymes. A small amount of iron is transported attached to the protein transferring[10] Non-functional or storage iron is found in the liver, spleen, muscle, or bone marrow . Ferritin accounts for some 95% of the stored iron in liver under normal conditions, with the balance being in the form of hemosiderin[9,30,33].

The minimal concentration of ferritin in the serum is an index of body iron stores and it is unknown whether it serves a specific role. One of the main roles of iron is in the transfer and storage of oxygen, in the form of hemoglobin and myoglobin. Hemoglobin, a major component of red blood cells (erythrocytes), is a protein consisting of four subunits. Each subunit holds one heme molecule, which consists of one atom of ferrous iron (Fe2+) attached to a protoporphyrin molecule. The ferrous iron can bind oxygen and transport it throughout the body. Myoglobin is similar to one subunit of hemoglobin and stores oxygen exclusively in muscle tissue. Iron and the iron containing heme group of hemoglobin and myoglobin are involved as cofactors of enzymes that assist in the oxidation of nutrients for energy and in the proper functioning of cells[10].

The dynamics of iron movement from dietary intake to interorgan distribution are well described by scientists in the fields of clinical science, nutrition and iron biology. The regulation of iron movement across the enterocyte optimizes iron assimilation into the body when an individual is iron depleted and limits iron absorption when iron stores are replete. The exact nature of the feedback signal from body iron status to the enterocyte remains unknown. A prolonged negative iron balance or an acute rapid blood loss both ultimately lead to a depletion of the storage iron pool, which can contain as much as 2–3 g iron (Fig. 1) [9,30,33].

**Importance**

Iron is both an essential nutrient and a potential toxicant to cells; as such, it requires a highly sophisticated and complex set of regulatory approaches to meet the demands of cells as well as prevent excess accumulation. A sufficient supply is essential for the functioning of many biochemical processes, including electron transfer reactions, gene regulation, binding and transport of oxygen, and regulation of cell growth and differentiation. This homeostasis involves the regulation of iron entry into the body, regulation of iron entry into cells, storage of iron in ferritin, incorporation into proteins and regulation of iron release from cells for transport to other cells and organs [9,30,33].

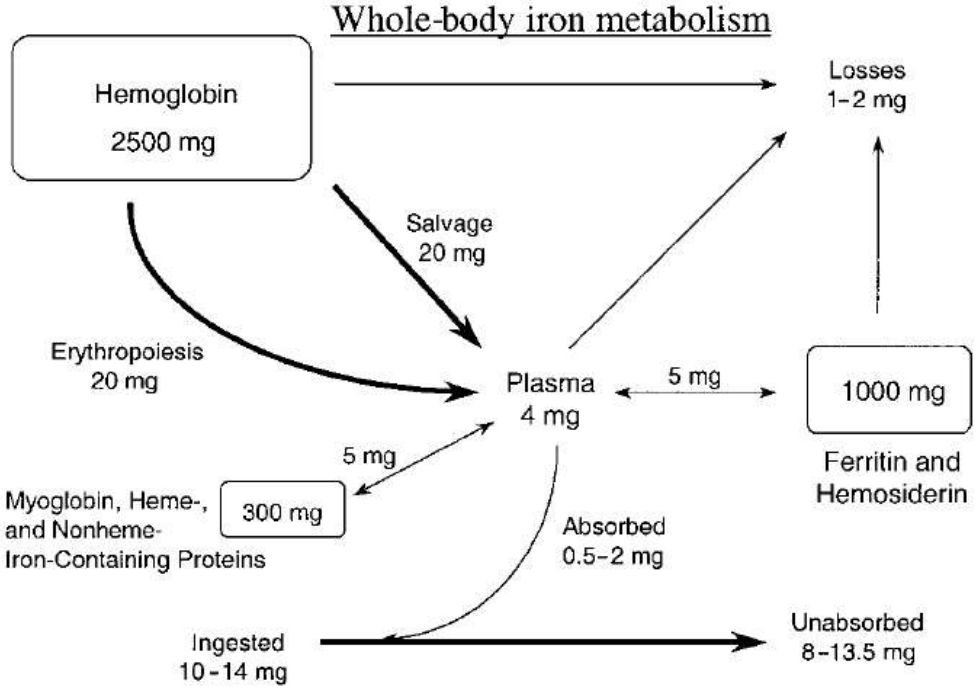


**Figure (1): Iron distribution in the body and quantitative exchange of iron between body pools (adapted from [9])**

Iron deficiency anemia (IDA) due to a dysfunction in iron metabolism is a quite common disorder in almost every community. Iron is a critical and essential element in the function of all living cells since it serves as an oxygen carrier in the hemoglobin molecule and also carries electrons and behaves as a catalytic component in some human enzymes. Epithelial tissue requires iron due to rapid turnover in growth function and proliferation process. Iron has a role in the production and maintenance of myelin and is involved in the function of some neurotransmitters such as dopamine, serotonin, and γ-amino butyric acid[11].

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Symptoms of the iron deficiency are basically related to the duration and the severity of the deficiency. However, on some occasion, symptoms are severe even though there is a mild anemia since symptoms are not only due to loss of oxygen transportation capability of the blood to the living tissues but also due to impaired function of the vital enzymes and epithelial or neural damage. Iron deficiency affects nervous system and has been reported to cause retardation on cognitive function and detrimental effect on cortical reactivity[11].

**Requirements and recommendations**

The Dietary Reference Intakes (DRI) are "a common set of reference values (on macro and micro nutrients) based on scientifically grounded relationships between nutrient intakes and indicators of adequacy, as well as the prevention of chronic diseases, in apparently healthy populations." The DRI recommendations include a Recommended Dietary Allowance (RDA) for iron. This refers to the average daily iron intake level sufficient to meet the needs of almost all healthy individuals in a particular life stage. Table 1 provides the RDA for iron for healthy term infants and young children[12].

The availability of the new DRI values has implications for planning and assessing diets for healthy individuals and populations, the creation of nutrition guidelines and education, and many other applications including judging the need for public health interventions such as food fortification[13]. The DRIs for most nutrients, including iron, have been established and are beginning to be implemented into education programs. As the RNIs are still being used, information on both sets of recommendations is provided (Tables 1 and 2).

**Table (1): Recommended Nutrient Intakes (RNIs) for Iron (mg/d) [13]**

| age | Recommended nutrient intakes (RNIs) | |
|---|---|---|
| | Males | females |
| 5-12 months | 7 | 7 |
| 1-3 years | 6 | 6 |
| 4-9 years | 8 | 8 |
| 10-12 years | 8 | 10 |
| 13-15 years | 10 | 13 |
| 16-18 years | 10 | 12 |
| 19-24 years | 9 | 13 |
| 25-49 years | 9 | 13 |
| 50-74 years | 9 | 8 |
| >75 years | 9 | 8 |
| Pregnant ($2^{nd}$ trimester.$3^{rd}$ trimester) | - | +5. +10 |

**Table (2): Dietary Reference Intakes (DRIs) for Iron (mg/d) [13]**

| age | Recommended dietary allowance (RDA) | | Estimated average requirement (EAR) | | Tolerable upper intake level (UL) |
|---|---|---|---|---|---|
| | Males | females | Males | females | ALL |
| 7-12 months | 11 | 11 | 6.9 | 6.9 | 40 |
| 1-3 years | 7 | 7 | 3 | 3 | 40 |
| 4-8 years | 10 | 10 | 4.1 | 4.1 | 40 |
| 9-13 years | 8 | 8 | 5.9 | 5.7 | 40 |
| 14-18 years | 11 | 15 | 7.7 | 7.9 | 45 |
| 19-30 years | 8 | 18 | 6 | 8.1 | 45 |
| 31-50 years | 8 | 18 | 6 | 8.1 | 45 |
| 51-70 years | 8 | 8 | 6 | 5 | 45 |
| >70 years | 8 | 8 | 6 | 5 | 45 |
| <18 years. Pregnant | - | 27 | - | 23 | 45 |
| 19-50 years. Pregnant | - | 27 | - | 22 | 45 |

**IRON BIOAVAILABILAITY**

**Absorption**

Two pathways for iron absorption exist. One controls the absorption of heme iron from the hemoglobin and myoglobin in meat. The other regulates the absorption of nonheme iron, primarily as iron-containing salts[10].

Absorption depends on the body's iron status or level of iron stores and on iron bioavailability from the diet. Heme iron is the most usable form of iron; it is more easily absorbed than nonheme iron (15% to 35% vs. 2% to 20%, respectively) [14]. Although not yet isolated, it is believed that a receptor exists that binds the heme molecule and is not affected by other dietary factors. The absorption of nonheme iron, on the other hand, is dependent on the level of body iron stores, its solubility and interaction with other dietary components[15].

**Enhancers and inhibitors**

Certain components of the diet can enhance or inhibit the absorption of nonheme iron when consumed in the same meal. Enhancers make the nonheme iron in the diet more soluble or form compounds that are more easily absorbed. Enhancers include ascorbic acid (vitamin C) and meat, fish and poultry (MFP factor). With little or no meat, fish or poultry or vitamin C in the meal, and zero body stores, nonheme iron absorption would be 5%. With 30 g to 90 g of MFP factor or 25 mg to 75 mg of vitamin C present, the absorption of nonheme iron increases to 10%[14].

The exact mechanism by which the MFP factor increases iron absorption is not clear. However, if the MFP factor and/or vitamin C–rich foods such as citrus fruit are consumed with the nonheme iron, absorption can increase by up to a maximum of four times. Inhibitors decrease the amount of nonheme iron absorbed by binding the iron into insoluble complexes that are then excreted from the gastrointestinal tract. The strongest inhibitors are polyphenols, found in many food products. They are especially high in black tea, which can decrease absorption of nonheme iron by up to 70%[15]. Some foods reduce iron absorption. For children with limited diets this a particular problem. A guide to some of the commonly encountered foods that enhance and inhibit iron absorption are given in Table (3) [16]. A recent study showed that many polyphenol containing beverages, such as herb teas, can inhibit iron absorption from a simple bread meal; these have not been tested when consumed with complex meals[17]. To a lesser extent, phytates, found in legumes, rice and grains, can inhibit the absorption of nonheme iron. Additional inhibitors of nonheme iron are listed in Table (3).

Consuming tea or coffee between meals has a much smaller effect, decreasing the amount of iron absorbed by 20%. Consuming vitamin C at the same meal has the ability to neutralize the inhibitory effect of polyphenols and phytates from other foods[15]. Another reason , in addition, cow's milk consumption by toddlers and children. Some families give toddlers and infants frequent bottles of milky tea. This combines micronutrient deficient calories with casein and tannin, which both reduce iron absorption. Cow's milk intake over 24 oz/day must be discouraged. Iron deficiency anemia (IDA) in the absence of inappropriate milk consumption should be investigated for coeliac disease and consideration of causes ofmalabsorption such as *H.pylori*, hookworm infestation, inflammatory bowel disease, chronic kidney disease and malignancy [16].

**Table (3): Factors that Influence Nonheme Iron Absorption [17]**

| | examples |
|---|---|
| **Enhancers** | |
| MFP factor | Meat , fish and poultry |
| Vitamin C (ascorbic acid) | sweet pepper, Broccoli raw, Brussels sprouts, Cabbage, Oranges, Strawberries, papaya, fruit juices |
| **Inhibitors** | |
| Polyphenols | Black tea, herb teas , coffee, cocoa, some grain products , red wine |
| Phytate | Legumes ( Peas, Beans and Lentils), soybeans, whole grains, Rise |
| Oxalate | Spinach, chard, beet greens, rhubarb, sweet potato |
| Non-phytate component of soy protein | Soy protein |
| Calcium | Food and supplements |

Calcium is the only factor that may play a role in inhibiting absorption of heme iron as well as nonheme iron[18]. However, its long-term effect does not seem to be consistent. In one study, a daily supplement of 1000 mg of calcium was given to 11-year-old girls. No effect on their iron status was seen[19]. In another study, calcium intake of both girls and women was measured. A weak inverse association between dietary calcium intake and iron status was found[20].

**Total iron vs. absorbed iron**

Recommendations for iron intake are based on total dietary iron. However, the amount of iron that is actually absorbed is very difficult to determine, as absorption is affected by the quantity of inhibitors and enhancers, as well as the level of body iron stores. Several models and algorithms have been proposed to

determine the amount of iron actually absorbed[18]. Although these calculations are based on experiments involving one meal, not the entire diet, they provide valuable information on absorption.
The availability of iron in diets with restricted intakes of meat, fish or poultry is estimated to be 10%. That is why the new DRI recommendations (RDAs) for individuals who limit those foods are 1.8 times greater than for individuals consuming a mixed diet [8].

**Toxicity**

In the absence of hereditary hemochromatosis, iron overload or toxicity is almost impossible through diet alone because absorption of nonheme iron decreases as body stores increase. Iron toxicity typically occurs through inappropriate intake of iron supplements[13]. or as secondary iron overload resulting from parenteral iron administration, repeated blood transfusions, hereditary hemochromatosis or hematological disorders [8]

**IRON DEFICIENCY**

Nutritional anemia was defined in a 1968 WHO technical report as "a condition in which the hemoglobin content of the blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency." WHO coordinated a series of studies in pregnant women in which anemia, serum folate, transferrin saturation and serum B-12 were assessed. They concluded that "Iron deficiency was present in 40–99% of the pregnant women studied and was undoubtedly responsible for the major proportion of anemia" [7]

**Causes and progression**

As iron is depleted, a gradual sequence of changes occurs. Three levels of iron deficiency are commonly identified [8]

- Depleted iron stores—bone marrow iron is absent, the serum ferritin level is below 12 μg/L, and total iron-binding capacity is above 400 μg/dL, but there is no effect on functional iron;
- Early functional iron deficiency —the supply of iron to the functional compartment is suboptimal but not low enough to identify anemia; biochemical measures indicate that percent transferrin saturation is low, and free erythrocyte protoporphyrin and serum transferrin receptor levels are elevated;
- Iron deficiency anemia—hemoglobin is below 130 g/L in males and 120 g/L in females and mean cell volume is decreased.

**Consequences (symptoms) of iron deficiency**

The key biological processes in each of the consequences of functional outcomes and severity of iron deficiency were shown in the following figure (Figure 2) [9]. The overt physical manifestations of iron deficiency include the generic symptoms of anemia, which are tiredness, lassitude and general feelings of lack of energy (Table 4). Clinical manifestations of iron deficiency are glossitis, angular stomatitis, koilonchyia (spoon nails), blue sclera, esophageal webbing (Plummer-Vinson syndrome) and microcytic hypochromic anemia. Behavioral disturbances such as pica, which is characterized by abnormal consumption of nonfood items such as dirt (geophagia) and ice (pagophagia), are often present in iron deficiency but clear biological explanations for these abnormalities are lacking [9,30,33].

**Table (4) Symptomatology of iron deficiency [9]**

| |
|---|
| Anemia |
| Impaired thermoregulation |
| Impaired immune function |
| Impaired mental function |
| Impaired physical performance |
| Glossitis |
| Angular stomatitis |
| Koilonychia |
| Pica |
| Complications of pregnancy |
| Increased absorption of lead and cadmium |
| Altered drug metabolism |
| Increased insulin sensititvity |
| Blue sclera |
| Fatigue |

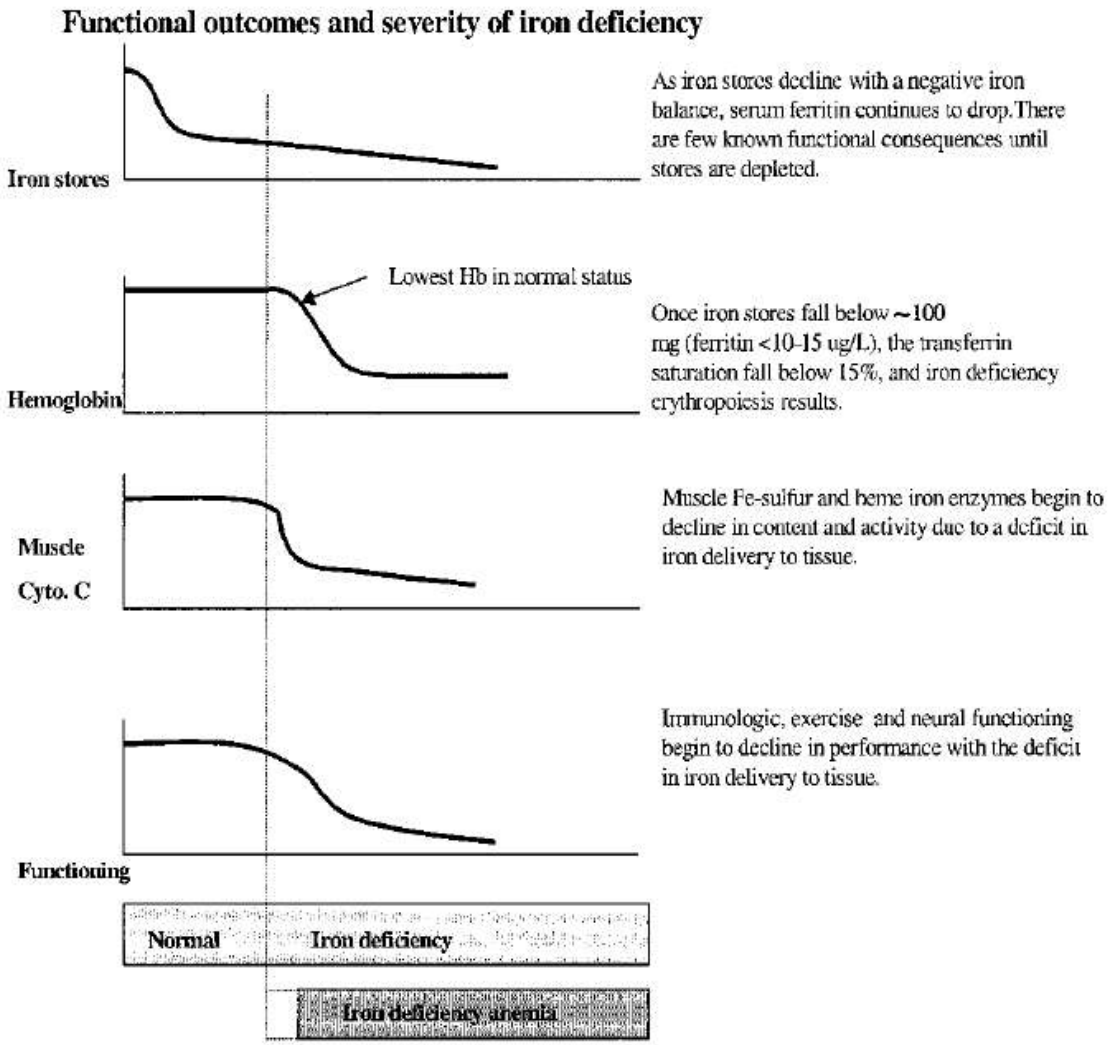


**FIGURE (2) Diagram of changes in functional pools of iron at various stages of iron status.** Reference No.9

**IRON DEFICIENCY IN INFANTS AND CHILDREN**

Anemia prevalence in children is high, especially in developing countries and frequently is multifactorial. It is often associated with childhood malnutrition, producing interlinked factors, several of which could be causally related to mortality risk. These factors include lack of hematinics (e.g., iron, folate, vitamins A, B-12 and C, and copper), impairment of red cell production by acute or subacute inflammation (with an increase in stored iron) and increased red cell destruction either via specific infections (e.g., malaria) or specific nutrients (e.g., vitamin A) [21].

**Early life (pregnant women)**

In a U.S. study, 90% of the pregnant women had iron intakes below two thirds of the former US-RDA for pregnancy; 41% had iron deficiency and 22% had iron deficiency anemia. This is not surprising, as very few women have sufficient iron stores prior to pregnancy to meet the needs of pregnancy[22]. It has been reported that during pregnancy, adolescents and adults have similar low intakes of key nutrients, including iron[23]Iron balance in the second and third trimesters may depend more on adequate intakes of bioavailable iron than on the size of the iron stores at conception. Even so, a symposium held in the United States on improving adolescent iron status before childbearing identified the importance of iron status before and early into pregnancy.

The main findings of the various papers presented at the symposium are [24]:

- Iron status early in pregnancy appears to have a stronger influence on birth outcomes than status later in pregnancy, suggesting the importance of improving iron status before childbearing.

- The prevalence of anemia, requirements for iron and rate of iron absorption into the blood are particularly high in the third trimester of pregnancy, suggesting continued need to provide iron supplementation throughout the entire pregnancy.
- Iron supplementation increases fetal growth significantly in terms of both weight and body mass.
- Schools, community kitchens, low-income communities and marriage registries are important examples of avenues through which to reach adolescent girls before pregnancy, and thereby reduce anemia.
- Dietary iron intake can be increased greatly among adolescent girls.

**Late life (with age progress)**

It is thought that healthy, full-term breastfed infants have sufficient iron stores and circulating hemoglobin to meet their needs until 4 to 6 months of age [25]. If an infant is not breastfed, iron-fortified formulas are recommended until 9 to 12 months of age. After about 6 months of age, iron stores are determined by such factors as intake of iron-fortified infant cereal, meat and iron-fortified formula. To prevent iron deficiency, it is also recommended that all infants should receive iron-containing foods such as iron-fortified cereals as their first foods [25].

Factors that influence iron status in infancy continue in early childhood, with diet playing a major role. Meat intake, more often than any other food group, has been associated with better iron status in children from 6 months to 5 years of age. In addition, the intake of cereals—iron-fortified infant cereal in infants and readyto- eat breakfast cereals in older children—especially when combined with vitamin C, has been effective in maintaining iron status [26]. A Canadian study that examined the dietary intake of preschool children by food groups indicated that most children who ate fortified cereals, the primary source of iron in their diets, would have been expected to meet their iron needs more easily than those who did not.

**Effect on cognitive development**

Most correlational studies have found associations between iron deficiency anemia and poor cognitive and motor development and behavioral problems. Longitudinal studies consistently indicate that children anemic in infancy continue to have poorer cognition, school achievement, and more behavior problems into middle childhood. However, the possible confounding effects of poor socioeconomic backgrounds prevent causal inferences from being made. In anemic children <2 y old, short-term trials of iron treatment have generally failed to benefit development. Most longer trials lacked randomized placebo groups and failed to produce benefits. Only one small randomized controlled trial (RCT) has shown clear benefits. It therefore remains uncertain whether the poor development of iron-deficient infants is due to poor social backgrounds or irreversible damage or is remediable with iron treatment. Similarly, the few preventive trials have had design problems or produced no or questionable benefits only. For children >2 y old, the evidence from RCT is reasonably convincing but not conclusive [27].

Three ideas hide behind the research done on the effects of iron-deficiency anemia (IDA) on mental and cognitive development. One is that the psychometric tools used yield aggregate scores that accurately represent the nature and size of the effect. A second idea is that this comparatively poor psychometric score is explained by particular changes in the architecture and biochemistry of the brain. The third is that randomized clinical trials aimed at the measurement of a main effect (e.g., intergroup difference of an intragroup change) from the nutritional factor are the optimal way in which to assess the effects of iron deficiency on cognition in children. These ideas overlook the complexity of psychobiological development and lead to unrealistic expectations of how much we know about the functional effect of micronutrient deficiencies (e.g., iron or zinc) and about the potential success of intervention programs [28].

The direct impact of compromised iron status is not fully known. However, human and animal studies have shown a direct relationship between iron status and cognitive function[29,30]. A recent review indicates that correlation studies support an association between iron treatment and reversal of developmental delay. However, the review concludes that more randomized control trials are needed to verify the benefits of iron treatment. Longitudinal studies indicate that children who were anemic in early childhood continue to have poor cognitive and motor development and school achievement into middle childhood. In several studies, iron treatment did not result in anemic children catching up to non-anemic children; however, one study did show a clear benefit of long-term treatment [27].

A factor that influences outcome is the length of time the infants were anemic. Anemia for longer than 3 months resulted in significantly lower results in mental and motor development. In children older than 2 years, evidence suggests that iron treatment can improve cognition but not necessarily school achievement. In three preventive trials, some improvement was observed in motor development and attention skills. Interpretation of many cognition studies is difficult because anemic children may have

more psychosocial, economic and biomedical disadvantages than non-anemic children. It is difficult to control for these other variables when studying iron status [27].

The research on cognitive function and iron status has been expanded to examine the relationship in school-aged children, adolescents and dieting adult females. Children and adolescents 6 to 16 years of age in the United States who were participating in the third National Health and Nutrition Examination Survey (NHANES III) were given standardized tests. Math scores were lower in those with iron deficiency compared to those without. In a randomized, double-blind, placebo-controlled clinical trial, adolescent girls with depleted iron stores who were supplemented with iron performed better on a test of memory and verbal learning than the placebo group [31].

In another study, a number of obese women on weight-reducing diets who received sufficient dietary iron had decreased iron measures (hemoglobin and transferrin saturation). The women with the decreased hemoglobin levels had altered cognitive function measured by their ability to concentrate. These studies indicate that iron status throughout life may have an impact on cognitive function [32].

**Effect on platelet agregation**

Iron is also important for platelets that have enzyme systems containing iron. Recently, it has been suggested that symptoms related to iron deficiency result from the dysfunction of the enzyme systems containing iron. Thus, it has been postulated that platelets may also be affected from the iron deficiency [4].

## CONCLUSIONS

From the previous literature the following can be concluded ; (1) Iron-deficiency anemia in infants, if not corrected rapidly, can interfere in normal maturation and development. Children who were anemic as infants may demonstrate measurably lower motor skills and, in some instances, irreversible mental alterations when entering school at about age 7 y.; (2)There is decreased resistance to infections and increased morbidity associated with iron-deficiency anemia. Thus, the need to prevent and/or treat iron-deficiency anemia as rapidly as possible is of great importance in preserving the health and maintaining normal growth and development of the child. ; (3) Because the iron requirements of rapidly growing infants ( ≥ 4 mo) are generally greater than can be met solely by the limited quantity of iron in breast milk, their diets must be augmented with additional food. One widely used method is supplementing the breast milk with iron-fortified cow's milk or specially fortified baby formulations. ; (4) Iron is an essential nutrient throughout the lifecycle. Iron deficiency remains a serious nutrition concern among important sub-groups of the population, including infants and children, adolescent and adult females, and vegetarians who do not eat meat, fish or poultry. At the same time, recommended intakes for these groups have increased. ; (5) For non-vegetarians, the importance of meat, fish and poultry as good sources of iron should be emphasized. Canadians also need practical advice on enhancing the iron availability from nonheme sources. For optimum nonheme iron bioavailability, people should be encouraged to consume at least one source of vitamin C, particularly with meatless meals.

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**CITATION OF THIS ARTICLE**

Ahmad A. Obeidat , Hani J. Hamad, Shamaail A. Saewan and Ashraf O. Khashroom, Omar K Al-Boqai Iron Bioavailability, Deficiency and its Consequences in Infants and Children: State of the art . Bull. Env. Pharmacol. Life Sci., Vol 8 [8] July 2019: 129-138