



ISSN (E): 2277- 7695

ISSN (P): 2349-8242

NAAS Rating: 5.03

TPI 2019; 8(9): 523-527

© 2019 TPI

www.thepharmajournal.com

Received: 13-07-2019

Accepted: 15-08-2019

Aishwarya V Patil

Ph.D. Scholar, Department of Food Science and Nutrition, College of Community Science, University of Agricultural Sciences Dharwad, Karnataka, India

Dr. Usha Malagi

Professor, Department of Food Science and Nutrition, College of Community Science, University of Agricultural Sciences, Dharwad, Karnataka, India

Iron deficiency Anaemia: An overview

Aishwarya V Patil and Dr. Usha Malagi

Abstract

Iron deficiency is the most widespread and frequent nutritional disorder in the world. It affects a high proportion of children and women in developing countries, with a clear predominance in adolescents and menstruating females. Iron is essential for optimal cognitive function and physical performance, not only as a binding site of oxygen but also as a critical constituent of many enzymes. In symptomatic patients with fatigue or in a population at risk for iron deficiency, a baseline set of blood tests including haemoglobin concentration, haematocrit, mean cellular volume, mean cellular haemoglobin, percentage of hypochromic erythrocytes and serum ferritin levels are important to monitor iron deficiency. For healthy males and females aged >15 years, a ferritin cut-off of 30 µg/l is appropriate. For children from 6–12 years and younger adolescents from 12–15 years, cut-offs of 15 and 20 µg/l respectively are recommended. As a first step in treatment, counselling and oral iron therapy is usually combined. Integrating haem and free iron regularly into the diet, looking for enhancers and avoiding inhibitors of iron uptake is beneficial.

Keywords: Iron deficiency anaemia, nutrition, haem and nonhaem iron, treatment, preventive strategies

Introduction

Iron deficiency (ID) is the commonest nutritional deficiency worldwide. Iron deficiency anemia (IDA) is a global health issue. (Lauren H. *et al.*, 2016) [5] Worldwide, the number of non-pregnant women affected by IDA is well over 400 million, making this the population group with the largest number of affected individuals (World Health Organization 2008) [10]. Prevalence of IDA among pregnant women worldwide is 41.8, and 30.2% among non-pregnant women (World Health Organization 2008) [10]. (Lauren H. *et al.*, 2016) [5] The World Health Organization defines anaemia as a haemoglobin (Hb) concentration below 13 g/dl in men over 15 years of age, below 12 g/dl in non-pregnant women over 15 years of age, and below 11 g/dl in pregnant women (Andrew F Goddard. *et al.*, 2015) [2].

IDA is most prevalent among preschool children and women. Among women, iron supplementation improves physical and cognitive performance, work productivity, and well-being, and iron during pregnancy improves maternal, neonatal, infant, and even long-term child outcomes. Among children, iron may improve cognitive, psychomotor, and physical development but the evidence for this is more limited (Sant-Rayn Pasricha., *et al.*, 2016) [8].

Health Organization (WHO) estimates that worldwide, 42% of pregnant women, 30% of non-pregnant women (aged 15 to 50 years), 47% of preschool children (aged 0 to 5 years), and 12.7% of men older than 15 years are anaemic (Sant-Rayn Pasricha., *et al.*, 2016) [8].

Classification of public health significance of anaemia in population on the basis of prevalence estimated from blood levels of haemoglobin

Category of public health significance	Prevalence of Anaemia %
Severe	40 or higher
Moderate	20.0-39.0
Mild	5.0-19.0
Normal	4.9 or lower

(Palihawadana TS, Goonewardene IMR, Motha MBC, Williams HSA)

Correspondence**Aishwarya V Patil**

MHSc (FSN), Department of Food Science and Nutrition, College of Community Science, University of Agricultural Sciences Dharwad, Karnataka, India

Iron Deficiency Anaemia

Iron status can be considered as a wide range form of iron deficiency with anaemia, to iron deficiency with no anaemia, to normal iron status with varying amounts of stored iron, and finally to iron overload which can cause organ damage when severe. Iron deficiency is the result of long-term negative iron balance. Iron stores in the form of haemosiderin and ferritin are progressively diminished and no longer meet the needs of normal iron turnover.

From this critical point onward, the supply of iron to the transport protein apotransferrin is compromised. This condition results in a decrease in transferrin saturation and an increase in transferrin receptors in the circulation and on the surface of cells, including the erythron. All tissues express their need for iron in exactly the same way, i.e. by the same type of transferrin receptors on cell surfaces in proportion to actual iron need. Accordingly, a compromised supply of iron to the erythron is associated with a similarly insufficient supply of iron to all other tissues.

Functionally, the lack of mobilizable iron stores will eventually cause a detectable change in classical laboratory tests, including measurement of haemoglobin, mean corpuscular haemoglobin concentration, mean corpuscular volume, total iron-binding capacity, transferrin saturation, and zinc-erythrocyte protoporphyrin. Iron deficiency is also defined as a condition in which there are no mobilizable iron stores and in which signs of a compromised supply of iron to tissues, including the erythron, are noted. The more severe stages of iron deficiency are associated with anaemia.

When iron-deficient erythropoiesis occurs, haemoglobin concentrations are reduced to below-optimal levels. When individual haemoglobin levels are below two standard deviations (-2SD) of the distribution mean for haemoglobin in an otherwise normal population of the same gender and age who are living at the same altitude, iron deficiency anaemia is considered to be present. The prevalence of iron deficiency anaemia in a population is therefore statistical rather than a physiological concept, although it reflects that proportion of the population that has iron-deficient erythropoiesis. Iron deficiency anaemia should be regarded as a subset of iron deficiency. That is, it represents the extreme lower end of the distribution of iron deficiency. Because anaemia is the most common indicator used to screen for iron deficiency, the terms anaemia, iron deficiency, and iron deficiency anaemia are sometimes used interchangeably. There is, however, mild-to-moderate forms of iron deficiency in which, although anaemia is absent, tissues are still functionally impaired.

In addition, although iron deficiency anaemia accounts for most of the anaemia that occurs in underprivileged environments, several other possible causes should be noted. These include haemolysis occurring with malaria; glucose-6-phosphate dehydrogenase deficiency; congenital hereditary defects in haemoglobin synthesis; and deficits in other nutrients, e.g. vitamins A, B, and C, and folic acid. Blood loss such as that associated with schistosomiasis, hookworm infestation, haemorrhage in childbirth, and trauma, can also result in both iron deficiency and anaemia. Lastly, as with vitamin A deficiency, inhibition of the normal metabolism of iron can result in anaemia.

The prevalence of iron deficiency varies greatly according to host factors: age, gender, physiological, pathological, environmental, and socioeconomic conditions.

Age: Full-term infants are normally born with adequate iron stores in the liver and haematopoietic tissue, because of destruction of foetal red blood cells soon after birth. This leads to deposition of iron in these tissues, especially if the cord is ligated after it stops pulsating. Breast milk is relatively low in iron, although the iron in breast milk is much better absorbed than that in cows' milk. Iron deficiency commonly develops after six months of age if complementary foods do not provide sufficient absorbable iron, even for exclusively breastfed infants. Iron requirements on a body weight basis

are proportional to growth velocity. Accordingly, in addition to women in their reproductive years as a result of physiological losses, iron deficiency is most common in the preschool years and during puberty. Another peak may occur in old age, when diets frequently deteriorate in quality and quantity.

Gender: Following menarche, adolescent females often do not consume sufficient iron to offset menstrual losses. As a result, a peak in the prevalence of iron deficiency frequently occurs among females during adolescence.

Physiological state: Substantial amounts of iron are deposited in the placenta and foetus during pregnancy. This results in an increased need of about 700-850 mg in body iron over the whole pregnancy. Overall, iron absorption is increased during pregnancy, when menstruations stop. Pregnant women still do not absorb sufficient additional iron, however, and the risk of iron deficiency increases. Lactation results in loss of iron via breast milk. Consequently, for some women a deficiency developed during pregnancy may be perpetuated during lactation. In terms of iron balance, however, lactational amenorrhoea more than compensates for iron lost through breast milk.

Pathological state: Common infections, especially those which are chronic and recurrent, may impair haematopoiesis and consequently cause anaemia. Malaria by haemolysis and some parasitic infections, e.g. hookworm, trichuriasis, amoebiasis, and schistosomiasis (both vesical and intestinal forms), cause blood loss directly. This blood loss contributes to iron deficiency. Other important causes of anaemia include genetic factors, e.g. thalassemia, sickle cell trait, and glucose-6-phosphate dehydrogenase deficiency (G6PD). Because these genetic factors are not due to iron deficiency. These other causes of anaemia are mentioned, however, as a reminder that they should be considered when choosing and focusing on population groups for assessment and surveillance purposes. In this way, more appropriate interventions can be developed. It should also be noted that these genetic conditions, except for thalassemia

Environmental factors: A given diet may be low in iron or may contain adequate amounts of iron which are of low bioavailability. Other nutrients necessary for haematopoiesis may also be deficient. These include folic acid, vitamins A, B, and C, protein, and copper and other minerals. Trauma or childbirth can result in acute or chronic blood loss, with consequent iron deficiency and anaemia

Socioeconomic status: Iron deficiency is most common among groups of low socioeconomic status.

Causes

While menstrual blood loss is the most common cause of IDA in premenopausal women, blood loss from the GI tract is the most common cause in adult men and postmenopausal women. Malabsorption (most commonly from celiac disease), poor dietary intake, blood donation and use of non-steroidal anti-inflammatory drugs (NSAIDs) are common causes of IDA (Andrew F Goddard *et al.*, 2011)^[3]

Iron deficiency may result from inadequate iron intake and absorption, increased iron requirements during growth, and excessive iron losses. Women of reproductive age (WRA) are

at particular risk because of menstruation, whereas pregnancy and childbirth result in a net iron loss of 580 to 680 mg because of foetal and placental requirements and bleeding during delivery. In young children, rapid expansion in red cell mass results in very high dietary iron requirements; the US estimated average requirement for iron for a 6- to 12-month-old infant (6.9 mg) exceeds that of an adult male (6 mg). Antenatal and perinatal factors may also influence infant iron status: maternal iron status may influence iron accumulation by the foetus, and maternal haemoglobin and receipt of iron supplementation influence infant iron stores. In addition, maternal iron stores can influence birth weight and duration of gestation: low-birth-weight or premature infants are born with lower iron stores and, thus, are at increased risk for IDA. For these reasons, pregnant and non-pregnant WRA and preschool children are at particular risk for IDA (Sant-Rayn Pasricha. *et al.*, 2016) [8].

Symptoms

Without screening, ID and IDA frequently go unnoticed, as most individuals with low iron stores are asymptomatic. As iron stores continue to be depleted and anaemia worsens. Some of the following, symptoms may be noticed:

- Extreme fatigue
- Pale skin
- Weakness
- Shortness of breath
- Chest pain
- Frequent infections
- Headache
- Dizziness or light headedness
- Cold hands and feet
- Inflammation or soreness of the tongue
- Fast heartbeat
- Unusual cravings for non-nutritive substances, such as ice, dirt or starch
- Poor appetite, especially in infants and children with iron deficiency anaemia
- An uncomfortable tingling or crawling feeling in the legs (restless legs syndrome)
- Brittle fingernails and toenails.
- Cracked lips.
- Smooth, sore tongue.
- Muscle pain during exercise.

Infants and small children with iron deficiency anaemia may not grow as expected and may have delays in developmental skills such as walking and talking. Children may be irritable and have a shorter than normal attention span.

Risk Factors

IDA is associated with a number of adverse health consequences for both women and their children. IDA in pregnancy is associated with preterm delivery and low birth-weight (Scholl and Reilly, 2000) [9]. IDA in pregnancy may also contribute to poorer cognitive development and IDA among children (Radlowski and Johnson, 2013) [7], and has been implicated in the development of post-partum depression (Albacar, *et al.*, 2011) [1]. A recent study showed that IDA was an independent risk factor for maternal transfusion, preterm delivery, 5 min APGAR less than seven, and NICU admission (Drukker *et al.*, 2015) [3], and associated a 1 g/dl increase in haemoglobin with an approximate 8% decrease in

risk for Cesarean section (Drukker *et al.*, 2015) [3]. Most cases of IDA are easily treated by dietary supplementation when identified (Johnson-Wimbley and Graham, 2011) [4].

Functional Consequences of Iron Deficiency: Iron deficiency adversely affects

- The cognitive performance, behaviour, and physical growth of infants, preschool and school-aged children;
- The immune status and morbidity from infections of all age groups; and
- The use of energy sources by muscles and thus the physical capacity and work performance of adolescents and adults of all age groups.

Specifically, iron deficiency anaemia during pregnancy

- Increases perinatal risks for mothers and neonates; and
- Increases overall infant mortality.

Prevention Strategies

Efforts should be targeted to:

- Reduce poverty
- Improve access to diversified diets
- Improve health services and sanitation and
- Promote better care and feeding practices.

These are fundamental elements of any programme to improve nutritional well-being in general, but are especially important in the improvement of iron status in particular.

Food-based approaches

Dietary improvement: Food-based approaches represent the most desirable and sustainable method of preventing micronutrient malnutrition. Such approaches are designed to increase micronutrient intake through the diet. Applied to iron deficiency, efforts should be directed towards promoting the availability of, and access to, iron-rich foods. Examples include meat and organs from cattle, fowl, fish, and poultry; and non-animal foods such as legumes and green leafy vegetables.

Similarly, focus should be upon foods which enhance the absorption or utilization of iron. Examples include those of animal origin, and non-animal foods – such as some fruits, vegetables, and tubers – that are good sources of vitamins A and C, and folic acid. Finally, effective nutrition education – and information on health and nutrition for both supply and demand aspects of programmes – may be needed to increase the demand for and consumption of such foods.

Enhancers of iron absorption include:

- Haem iron, present in meat, poultry, fish, and seafood;
- Ascorbic acid or vitamin C, present in fruits, juices, potatoes and some other tubers, and other vegetables such as green leaves, cauliflower, and cabbage; and
- Some fermented or germinated food and condiments, such as sauerkraut and soy sauce (note that cooking, fermentation, or germination of food reduces the amount of phytates).

Inhibitors of iron absorption include:

- Phytates, present in cereal bran, cereal grains, high-extraction flour, legumes, nuts, and seeds
- Food with high inositol content
- Iron-binding phenolic compounds (tannins); foods that

contain the most potent inhibitors resistant to the influence of enhancers include tea, coffee, cocoa, herbal infusions in general, certain spices (e.g. oregano), and some vegetables and

- Calcium, particularly from milk and milk products.

Examples of simple but effective alterations in meal patterns that enhance iron absorption might include:

- Separate tea drinking from mealtime - one or two hours later, the tea will not inhibit iron absorption because most of the food will have left the stomach
- Include in the meal fruit juices such as orange juice, or another source of ascorbic acid such as tubers, cabbage, carrots, or cauliflower
- consume milk, cheese, and other dairy products as a between-meal snack, rather than at mealtime and
- Consume foods containing inhibitors at meals lowest in iron content, e.g. a breakfast of a low-iron cereal (bread or corn tortilla) consumed with tea or milk products; this meal pattern can provide adequate calcium without hampering iron nutrition.

To address IDA in population; these may include increasing iron stores through supplementation, fortification of processed or staple food, home food fortification, and increased consumption of food with high iron content and bioavailability. In addition, optimizing maternal nutrition before and during pregnancy, prevention of low birth weight and prematurity, control of parasites, and improvements in access to health care, infant feeding, food security, and socioeconomic status are important factors.

Iron supplementation: Iron supplementation has long been advocated for anaemia control. Oral iron is widely available as a single micronutrient supplement in liquid and tablet formulations, as IFA, or in multiple micronutrient preparations. Different iron compounds have varying bioavailability, effect, and cost. Young children may require iron supplements as liquid formulations, which are more expensive and have a limited shelf life. A systematic review of 55 trials administering iron to children orally, parenterally, or in fortified food found that on average, it improves haemoglobin by 0.74 g/dL and reduces anaemia prevalence by 37.9% to 62.3% in non-malaria-endemic settings and 5.8% to 31.8% in malaria-endemic settings. Supplementation may be recommended for daily or intermittent consumption.

Fortification: Fortification is a useful public health intervention if the food to be fortified is widely consumed in sufficient amounts by at-risk individuals and if the fortificants do not have a toxic or unappealing effect on the food or significantly increase food prices. Targets for iron fortification include staple foods such as wheat and maize flour and rice (normally processed rice with a tiny proportion of added, reconstituted, and extruded grains); condiments such as salt, curry powder, and fish and soy sauces; and candies. A range of iron fortificants is available. Ferrous sulfate and fumarate have the highest bioavailability and similar iron content. Ferrous sulfate is cheapest and widely used to fortify flour but may cause rancidity with storage; ferrous fumarate may produce fewer effects on food. Insoluble compounds (ferric pyrophosphate and orthophosphate) have less reactivity with food but poorer bioavailability. Elemental iron compounds have been used but have poor bioavailability and affect taste

at effective concentrations. Fortification of cereals, salt, and sauces has been successfully achieved using iron EDTA, which contains iron protected by a chelating moiety that can also improve absorption of intrinsic nonheme dietary iron. Finally, encapsulated ferrous salts, in which iron is encapsulated in an oil layer, have minimal reactivity with the food and offer high bioavailability, but they are relatively expensive. Iron absorption from fortified food may be improved by addition of an enhancer such as ascorbic acid and by minimizing phytate concentration.

Multiple micronutrient powders: Infants and young children depend on complementary foods to provide the majority of their iron requirement after the first 6 months. However, iron-rich complementary foods are often inaccessible for families in low-income settings. For example, in rural India, the daily iron intake from complementary foods among children aged 12 to 23 months was only 11.7% of that recommended. An important emerging strategy in the control of micronutrient deficiency is the introduction of home-based fortification with micronutrient powders (MNPs) such as “Sprinkles.” In these preparations, iron is encapsulated in a lipid layer that prevents adverse effects on food flavor and appearance. The preparations are supplied as single-dose sachets and added to the child’s meal once it has been served (“home fortification”). Clinical trials have demonstrated that MNPs have efficacy comparable to liquid ferrous sulfate in controlling anaemia and have improved iron and micronutrient status among children in Asia and Africa and in indigenous communities of developed countries.

Anthelmintic therapy: Deworming increases haemoglobin concentrations and reduces the prevalence of anaemia. Periodic, community-wide administration of albendazole or mebendazole for soil-transmitted helminths and praziquantel for schistosomiasis is recommended for communities with high infection burdens.

Assessment of Iron Status

Surveillance of iron deficiency involves an ongoing process of recording and assessing iron status in an individual or a community. Worldwide, the most common method of screening individuals or populations for iron deficiency involves determining the prevalence of anaemia by measuring blood haemoglobin or haematocrit levels. A major limitation of each of these two tests, however, lies in the fact that anaemia is not a specific indication of iron deficiency. Other nutrient deficiencies and most infectious diseases can also result in significant anaemia.

One common practice in assessing whether or not anaemia is due to iron deficiency involves monitoring the response in haemoglobin or haematocrit levels after 1 or 2 months of oral supplementation with iron. An increase of 10 g/l in haemoglobin or 3% in haematocrit is indicative of iron deficiency. Individual management in resource-poor countries is likely to be based mainly upon either haemoglobin or haematocrit assessment or both and upon their response to initial iron therapy. Another limitation of haemoglobin or haematocrit measurements is that levels change only when they are very low at the outset, and when iron deficiency is already severe. In resource-adequate situations, the usual practice involves the use of further, specific, and more sensitive tests for individual assessment. These include serum ferritin, transferrin saturation, and others.

The clinical examinations done for assessing iron are;

- Haemoglobin measurement (cyanmethemoglobin method)
- Haematocrit or packed cell volume
- Serum ferritin
- Erythrocyte protoporphyrin
- Serum iron, transferrin, and transferrin saturation
- Serum transferrin receptors
- Red cell indices
- Bone marrow iron stain

Interpreting laboratory blood test results to assess iron status

Diagnosis	Haemoglobin	Mean cell volume and mean cell haemoglobin	Serum ferritin $\mu\text{g/L}$	Transferrin	Transferrin saturation	Soluble transferrin receptor	Serum iron
Tissue iron deficiency without anaemia	Normal	Normal or low	<15-30	Normal or high	Low-normal or low	High-normal or high	Low
Iron deficiency anaemia (IDA)	Low	Low (or normal in early IDA)	<15-30 adult <10-12 child	High	Low	High	Low
Anaemia of chronic disease or inflammation	Low	Normal (may be mildly low)	Normal or elevated (elevated ferritin does not imply elevated iron stores)	Normal	Low	Normal	Low
IDA with coexistent chronic disease or inflammation	Low	Low	Low or normal, but usually <60-100 $\mu\text{g/L}$	Normal or high	Low	High	Low
Thalassaemia minor	Low (or normal)	Low (or normal)	Normal or elevated	Normal	Normal or elevated	Normal or elevated	Normal
Iron overload	Normal	Normal	Elevated (correlates with body iron stores)	Normal to low	high	Normal	Normal to elevated

References

1. Alleyne M, Horne KM, Miller JF. Individualized Albacar G, Sans T, Martín-Santos R, García-Esteve L, Guillamat R, Sanjuan J *et al*. An association between plasma ferritin concentrations measured 48 h after delivery and postpartum depression. *Journal of affective disorders*. 2011; 131(1-3):136-142
2. Andrew FG, Martin WJ, Alistair SM, Brian BS. Guidelines for the management of iron deficiency anaemia, 2015; 60:1309e1316. doi:10.1136/gut.2010.228874.
3. Drukker L, Hants Y, Farkash R, Ruchlemer R, Samueloff A, Grisaru-Granovsky S. Iron deficiency anemia at admission for labor and delivery is associated with an increased risk for Cesarean section and adverse maternal and neonatal outcomes. *Transfusion*. 2015; 55(12):2799-2806.
4. Johnson-Wimbley TD, Graham DY. Diagnosis and management of iron deficiency anemia in the 21st century. *Therapeutic advances in Gastroenterology*. 2011; 4(3):177-184.
5. Lauren HM, Britta LA, Vanessa RB, Althea MG, Jay S. Screening and Treatment for Iron Deficiency Anemia in Women: Results of a Survey of Obstetrician-Gynecologists, *Matern Child Health J*. 2017; 21(8):1627-1633.
6. Palihawadana TS, Goonewardene IMR, Motha MBC, Williams HAS. Iron deficiency anaemia in pregnancy: diagnosis, prevention and treatment, *Sri Lanka Journal of Obstetrics and Gynaecology*, 2014, 61-65.
7. Radlowski EC, Johnson RW. Perinatal iron deficiency and neurocognitive development. *Frontiers in human neuroscience*, 2013; 7:585.
8. Sant-Rayn P, Drakesmith, James Black, David H, Beverley-Ann B. Control of iron deficiency anemia in low- and middle-income countries, *Blood First Edition paper*, 2016; DOI 10.1182/blood2012-09-453522.
9. Scholl TO, Reilly T. Anemia, iron and pregnancy outcome. *The Journal of nutrition*, 2000; 130(2):443S-447S.
10. World Health Organisation, Distribution, Iron Deficiency Anaemia Assessment, Prevention, and Control, A guide for programme managers. General English only. 2008.