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An Overview on Iron Deficiency Anaemia

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Abstract

"Anaemia'' is defined as a collection of disorders caused by erythropoietin tissues' incapacity to maintain normal haemoglobin concentration due to insufficient availability of one or more nutrients, which lowers the amount of haemoglobin in circulation overall. It can be brought on by a poor vegetarian diet, iron malabsorption, hookworm infections, profuse bleeding during menstruation, or childbirth.Low birth weight, decreased immunological function, poor cognitive development, behavioural issues, decreased job ability, and maternal mortality are among the negative outcomes of anaemia. The most popular and sensitive initial diagnostic test for IDA is serum ferritin. The most effective methods of treating iron deficiency anaemia include dietary variety, supplementation, fortification of staple foods, and nutrition education.

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1. Introduction

At present, Iron Deficit The most prevalent micronutrient deficit in the world, anaemia (IDA) has major negative effects on the economy and impedes the progress of a country. According to data from the National Family Health Survey-3, anaemia affects 79% of children in India, while 56% of teenage girls suffer from the condition [NFHS, 2005-06]. In 5% of American women and 2% of American men, anaemia is caused by an iron deficiency [Wimbley TD et al., 2011]. Almost all living things require iron, which is also necessary for many different metabolic

processes. The transportation of oxygen by haemoglobin is its primary role [Naigamwalla DZ.*et al*., 2012]. The protein called haemoglobin, which is abundant in iron and found in red blood cells, transports oxygen from the lungs to the body's tissues. Red blood cell development is regulated by the glycoprotein hormone erythropoietin, which is produced in the kidneys. The term "anaemia" refers to a group of conditions caused by the erythropoietin tissues' inability to maintain a normal haemoglobin concentration due to an inadequate supply of one or more nutrients, resulting in a reduction in the total amount of circulating haemoglobin. The term comes from the ancient Greek word ἀναιμία, anaimia, meaning "lack of blood." Iron and certain vitamins, such as folic acid, vitamin C, vitamin E, and vitamin B12, are necessary for the production and proper development of red blood cells.
Anaemia can be further subdivided into three categories: sickle cell anaemia, nutritional anaemia, and RBC size (micro, normo, and macrocytic anaemia).

2. Magnitude of the problem

The World Health Organization [WHO, 2008] estimates that 1.62 billion individuals worldwide—or 24.8% of the population—are affected by anaemia. Preschool-age children have the highest prevalence (47.4%), whereas men have the lowest prevalence (12.7%). Nonetheless, non-pregnant women (468.4 million) make up the population group most affected. In underdeveloped nations, anaemia affects approximately 40% of preschool-aged children and every other pregnant woman.

3. Progression of Iron Deficiency to IDA

3.1 Storage and Transport of Iron

Iron deficiency is defined by two or more abnormal values (serum ferritin, transferrin saturation, and/or erythrocyte protoporphyrin) according to data from the National Health and Nutrition Examination Survey-3 [Frith-Terhune AL et al., 1994]. Initially, iron is stored as ferritin, a protein-iron complex. A particular type of globular protein called transferrin travels throughout the plasma pool and uses the transferrin receptor route to deliver iron to cells. Iron is transported by transferring to the bone marrow, where it is integrated into heme to form haemoglobin and absorbed into red blood cells (RBCs) by a transferrin receptor (CD71). Since unbound iron is poisonous, it is crucial that iron be bonded to transferrin. When there is an iron shortage, transferrin concentration rises.

3.2 Stages of IDA

There are three stages that iron insufficiency typically goes through in order:

a)First Stage - Iron Depletion: Depending on the body's need for iron, the body can absorb more iron through the intestines. Reduced serum ferritin, decreased iron concentration in the bone marrow and liver tissue, and an inadequate iron supply as a result of more iron being lost than being absorbed are the characteristics of this stage. Erythropoiesis, haemoglobin, serum iron, total iron binding capacity, and transferrin saturation all remain normal during this time. While most patients at this stage do not exhibit symptoms, they do experience iron insufficiency.

b) Second Stage - Latent Iron Deficiency without Anaemia: Iron-deficient erythropoiesis starts when the bone marrows significantly decreased iron stores start to interfere with haemoglobin synthesis. The production of haemoglobin decreases to the point where anaemia appears. Haemoglobin levels are still normal, though. Serum iron and transferrin saturation drops at this point due to a rise in total iron binding capacity (TIBC) and an increase in free erythrocyte protoporphyrin, in addition to the previously decreased iron storage (decreased serum ferritin). Less than 15% transferrin saturation indicates latent iron deficit since the body is now releasing more iron from the circulating transferrin to sustain erythropoiesis.

c) Final Stage - IDA: This phase starts when normal erythrocytes that have aged and been eliminated from the circulation are replaced by tiny, haemoglobin-deficient cells that are entering the bloodstream in greater numbers. At this point, the emergence of progressive microcytic, hypochromic anaemia is linked to decreased serum iron, elevated TIBC, decreased transferrin saturation, and decreased haemoglobin synthesis as a result of iron deficiency anaemia. The concentration of haemoglobin is below the typical age and sex thresholds.

4. Clinical Features

Many people have anaemia without realizing it, and the symptoms might be mild and ambiguous. The underlying cause or the anaemia itself may be the cause of the symptoms and indications. The majority of anaemia sufferers have vague symptoms including weakness or general malaise, headaches, low appetite, dizziness, fatigue, and shortness of breath. Upon examination, the patient may present with koilonychias, pale conjunctivae, pallor, and a smooth tongue. Other signs and symptoms include twitching muscles, glossitis, angular cheilitis, missing or heavy menstrual cycles, constipation, tiredness, tinnitus, hair loss, depression, and burning, tingling, or numb, feelings. Pica, or eating things that aren't food, such dirt, paper, wax, grass, ice, and hair, can be a sign of iron shortage, even though it frequently happens to people with normal haemoglobin levels [Wintrobe MM et al., 2011].

5. Etiology

In the developing world, anaemia has a variety of reasons. The following are potential causes of iron deficiency:

5.1 Inadequate Iron Intake

The condition known as "nutritional anaemia" is brought on by a lack of one or more nutrients, primarily iron, protein, folic acid, vitamin B12, and possibly pyridoxine, vitamin C, copper, and vitamin E. More people suffer from megaloblastic anaemia (folic acid insufficiency) than from pernicious anaemia (vitamin B12 deficiency), especially during pregnancy when the foetus's needs are combined with the mothers. Except in cases of malabsorption and certain intestinal disorders like tropical sprue, deficits in folic acid and vitamin B12 are uncommon outside of pregnancy. From a public health perspective, iron deficiency ranks as the primary cause of nutritional anaemia globally [Kotecha PV, 2011].A poor diet, such as a vegetarian lifestyle, can lead to insufficient heme iron, which can cause iron deficiency anaemia (IDA), since an average healthy person absorbs only 3-5% of their dietary iron.

5.2 Impaired Absorption

There are two chemical types of dietary iron: non-heme iron, which is found in plant and dairy foods, and heme iron, which is found in meat. Meal and gastrointestinal secretion composition have no effect on heme iron absorption. Vegetarian diets have poorer absorption rates of non-heme iron (1–5%) than heme iron (8–10%). Therefore, vegetarian females have an increased risk of anaemia, particularly after menarche [Srilakshmi B, 2005]. Non-heme iron's bioavailability is dependent on the concentration of enhancers (such ascorbate and meat) and inhibitors (like phytates, phosphates, tannins, calcium, fiber, tea, coffee, and wine) in the diet. It also requires acid digestion. Depleted iron reserves occur from the consumption of iron absorption inhibitors. Infections by parasites such as Helicobacter pylori and anomalies in the gastrointestinal tract can also result in malabsorption of iron. Due to a decline in iron absorption with age, IDA is also common in the elderly.

5.3 Increased Requirements

Anaemia can be caused by a food deficiency in iron during times of accelerated demand, such as infancy (fast blood volume expansion), adolescent (rapid growth and menstrual onset in girls), pregnancy, and lactation. Throughout the perinatal stage, the growing brain experiences fast anatomical and functional changes, necessitating a steady intake of iron. Neurodevelopment appears to be negatively impacted for a long time and frequently permanently by either excess iron or failing to achieve the required amount of iron during this crucial time.
Due to their fast growth, weight gain, and increased blood volume, adolescents of both sexes are more susceptible to developing anaemia. In females, this risk is further increased by the commencement of menstruation. Growth in middle adolescence occurs in girls 12–15 years earlier than in boys 13–16 years [Deshpande NS et al., 2013]. A woman of reproductive age needs at least twice as much iron as a man or a post-menopausal woman because of the elevated need for iron during pregnancy and blood losses during menstruation. Maternal iron deficiency anaemia (IDA) and poor body storage can result in low haemoglobin content in the cord blood, poor fetal stores of iron, and even anaemia in early infancy that can progress to adolescent anaemia in areas where iron deficiency is endemic.

5.4 Blood Loss

Blood loss can result from bleeding, surgery, certain medications, heavy, prolonged, or frequent menstruation; childbirth; chronic diseases of the gastrointestinal tract, such as tuberculosis, ulcers, or intestinal disorders; intravascular haemolyses, which is a condition in which red blood cells break down in the blood stream, releasing iron that is then lost in the urine; and accidents. This can occasionally happen to those who work out hard, especially running.

5.5 Hookworm

Malaria and Infection Chronic intestinal blood loss from hookworm infection, which frequently results in long-term morbidity, is another cause of iron-deficiency anaemia [Steketee RW, 2003]. Extra-corporeal iron loss accounts for a large portion of the hookworm burden, and treatments for hookworm infection have shown considerable increases in haemoglobin [Loukas A, 2005]. Anaemia is largely caused by malaria in the impoverished countries. While haemolytic anaemia is the main cause of anaemia in the context of malaria, research has shown that inflammatory anaemia also plays a significant role by altering iron absorption and distribution [Shaw JG and Friedman JF, 2011]. Apart from the excessive erythrocyte destruction caused by malarial parasites, recurrent malarial infection also causes a chronic anaemia linked to an enlarged spleen.

6. Consequences

According to a direct result of decreased neurological development in infants, chronic anaemia can cause behavioural abnormalities in children. This, in turn, can lead to poor focus and poorer academic performance in children, which can slow down their social development [Wintrobe MM et al., 2011]. Contributing to low birth weight, recurrent infections, lowered immune function, delayed cognitive development, behavioural issues, and diminished job ability, it poses a serious hazard to safe parenthood. The damage that iron deficiency anaemia causes to a mother's and fetus's health is less well understood, but it includes higher risk of sepsis and maternal and neonatal mortality in addition to its well-known detrimental effects on an individual's physical and cognitive function. Iron shortage in infancy seems to be notably linked to deficiencies in reading, writing, and math as well as attention and spatial memory.
The effects of inadequate nutrition and anaemia during pregnancy are generational. Pregnancy, which will bring about the next generation, therefore just makes their pre-existing anaemia worse in these teenage ladies. Severe

anaemia during pregnancy is one of the leading causes of maternal fatalities (20%) in India [Bamji S M et al., 2003]. Women with moderate anaemia account for a significant percentage of maternal mortality from pregnancy-induced hypertension, sepsis, and antepartum and postpartum haemorrhage. Iron deficiency anaemia is commonly linked to a number of chronic illnesses, including cancer, inflammatory bowel disease, chronic heart failure, and chronic kidney disease. Excessive cytokine and leukotriene synthesis interfere with the effects of erythropoietin (EPO) at the bone marrow and the release of stored iron in the reticulo-endothelial system, which is at least largely responsible for anaemia or chronic illnesses [Silverberg DS et al., 2001].

7. Diagnosis

While the etiology and history can aid in the diagnosis, IDA is primarily a laboratory diagnosis that can be achieved through four tests: serum ferritin (SF), serum iron (SI), serum transferrin saturation (TS), or total iron binding capacity (TIBC), and hemoglobin level (Hb). Serum ferritin is the most recommended and sensitive initial diagnostic test among these. Serum iron and total iron binding capacity (TIBC) are frequently assessed simultaneously. Transferrin molecules' prospective ability to bind with serum iron is indicated by this assay. A person's chance of developing diabetes, heart disease, stroke, liver disease, and cancer are increased in direct proportion to the quantity of stored bodily iron that exceeds the recommended range. [WHO, 2001][Knovich MA, 2009][Gomella LG HS., 2007].

8. Prevention and Management

The most effective approach for treating iron deficiency anaemia is to use nutrition intervention strategies that emphasize balanced nutrition over the long term. These strategies include dietary diversification, short-term supplementation, medium-term fortification of staple foods with bioavailable iron, and nutrition education.

8.1 Dietary Diversification

The goal of dietary modification strategies is to enhance intake of micronutrients. In order to improve access to the availability of foods high in iron, kitchen gardens ought to be encouraged. A better diet is necessary to optimize iron absorption. Meat and organs from cattle, poultry, fish, and fowl, as well as non-animal foods such legumes and green leafy vegetables, foods high in vitamins A and C, and folic acid, should be a part of a diet that improves the body's ability to absorb and use iron. Tea and coffee are examples of iron absorption inhibitors that should not be had with meals since they can actually lower the amount of iron that is absorbed. Avoiding raw wheat bran is also advised since it may obstruct the absorption of iron[Gopalan. C et al., 2004]. Every individual has different iron requirements at different age group and conditions; as given in the table below in **Table 1.**

Table:1 Recommended dietary allowance for Indians (ICMR)

Age group (years)	Iron (mg/day)
Men	28
Women	38
Lactating women	30
Non-lactating women	30
Children 1-3 4-6 7-9	 12 18 26

13-15 years Boys Girls	 41 28
16-18 years Boys girls	 50 30

8.2 Dietary Supplementation

Although vitamin C supplementation offers additional benefits, iron and folic acid supplementation is still the mainstay for treating and preventing anaemia. One of the most potent known boosters of non-heme iron absorption—which makes up the majority of an Indian's diet—ascorbic acid also counteracts the effects of dietary inhibitors. The best and least expensive sources of vitamin C are lemons and amla (Indian gooseberry). One of the richest known terrestrial sources of vitamin C is amla; just 100 grams of amla has approximately 700 mg, or thirty times the amount of vitamin C in an orange. Compared to synthetic vitamin C, it is 12 times more assailable and has a stronger therapeutic impact [Rani B, et al., 2013][http://steffysupplement.blogspot.in/2008]. Additionally, studies have demonstrated that 100 mg of synthetic vitamin C is equal to just 8.7 mg of natural vitamin C from Amla . Furthermore, Amla stands out among fruits not only for its high vitamin C concentration but also for the presence of compounds that partially shield the vitamin from deterioration when heated or dried [Anonymous , 2007].

8.3 Food Fortification

As per the World Health Organization's definition [WHO, 2006], fortification is the intentional process of augmenting the number of vital micronutrients, such as vitamins and minerals (including trace elements), in food, regardless of whether these nutrients were present in the food prior to processing, with the aim of enhancing its nutritional quality and minimizing any potential health risks for the public. One of the top four methods for reducing micronutrient deficiency worldwide is food fortification of regularly consumed foods, according to the World Health Organization, the Copenhagen Consensus, and the Food and Agriculture Organization.
Governments, the food sector (producers, processors, and marketers), and consumers must work together to implement an efficient iron fortification scheme. In numerous national initiatives, a number of iron fortifications have proven effective. The general public is the target group when flour is employed as a vehicle, however new-borns and small children, who typically consume little bread, are not reached by this strategy. In order to supply bioavailable iron in a way that is affordable, mostly self-sustaining, palatable to the target population, and commercially feasible, new strategies are obviously required [Abrams SA. 2004].

8.4 Nutrition Education

In order to enhance diet by consuming more fruits and vegetables high in vitamin C, emphasis should also be placed on providing nutrition education. For the first six months of a baby's life, mothers should be trained to only give breast milk. Pre-schoolers should prioritize receiving iron-rich foods in addition to home-based weaning. It is recommended to follow cooking methods that raise the iron content of the meal, such as fermentation, germination of specific foods, and cooking with iron cookware. To improve iron status, for instance, advancements in home or community processing technologies and food preservation techniques can be very helpful. Effective nutrition education and attempts to increase women's income are two ways that these interventions are improved.

8.5 Iron Therapy

The objectives of IDA treatment are to address the underlying cause of the condition and return iron, haemoglobin, and red blood cell levels to normal. The most popular method for managing iron insufficiency at the moment in developing nations is iron supplementation. Folic acid should always be given with iron when pregnant, along with other vitamins. In cases where oral preparations are not tolerated, parenteral iron may be administered. Other non-direct strategies to stop IDA could be:

- The prevention of infectious diseases (such as measles, respiratory and diarrhoeal illnesses).
- Programs to control parasitic diseases (malaria, trichiasis, hookworms, and infestations of schistosomiasis). Ideally, environmental health initiatives to lower parasitism (particularly hookworms) and primary preventative interventions to interrupt the cycle of transmission should be combined with parasite control. Pregnant women should take an adequate anthelminthic after the third month of their pregnancy, thus this is very crucial to them.

The National Nutritional Anaemia Prophylaxis Programme (NNAPP) (INDIA) states that the following iron and folic acid (IFA) daily dosage recommendations are administered as tablets given below in **Table 2.**:-

Table 2: Supplementation dosages recommended by NNAPP

Age group	Dosage schedule	Duration
Children 6-60 months	2o mg elemental iron + 100 µg folic acid (one tablet of paediatric IFA or 5 ml of IFA syrup or 1 ml of IFA drops)	100 days if the child is clinically found to be anaemic
School children 6-10 years	30 mg elemental iron + 250 µg folic acid	100 days
Adolescents 11- 18 years	100 mg elemental iron + 500 µg folic acid	100 days
Pregnant women	One tablet of 100 mg elemental iron + 500 µg folic acid prophylactically If clinically anaemic	Daily 2 such tablets to be given daily for 100 days
Nursing mothers	One tablet OF 100 mg elemental iron + 500 µg folic acid	100 days

Conclusion

Food-based strategies, as opposed to medication-based ones, must be the cornerstone of policies and programs designed to address micronutrient deficiency. Given the negative consequences severe iron shortage has on learning capacity, growth, and development, extra efforts should be taken to diagnose and treat iron deficiency throughout pregnancy and the early years of life. It is recommended to make dietary changes to enhance the total intake of iron, folic acid, and vitamin C-rich foods, as well as foods that facilitate the absorption of iron.

Consequently, the most effective way to return haemoglobin and iron levels to normal and avoid iron deficiency anaemia in the susceptible population is nutrition education combined with iron supplementation from natural sources of vitamin C.

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