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Swetha MP
Department of Food Technology & Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Corresponding Author:
Swetha MP
Department of Food Technology & Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Iron deficiency anemia

Swetha MP

Abstract
Iron deficiency anaemia (IDA) is a widespread and serious public health issue that disproportionately affects women and children in impoverished nations. The prevalence, causes, and effects of IDA, as well as current efforts for diagnosis, treatment, and prevention, are summarised in this review study. Several electronic databases were used to conduct a thorough search of the literature, which included both primary research studies and review articles. Our data suggest that IDA is a complex illness caused by a number of variables such as insufficient iron intake, poor iron absorption, increased iron needs, and chronic blood loss. IDA can have serious implications, such as poor cognitive function, decreased physical performance, and an increased risk of infection. The use of laboratory testing to confirm the diagnosis and the delivery of iron supplements, either orally or intravenously, are effective techniques for the diagnosis and treatment of IDA. IDA prevention is also critical, and it may be accomplished by a mix of dietary interventions, such as iron-fortified foods, and public health measures, such as routine iron supplementation programmes for high-risk groups. Overall, this review emphasises the significance of IDA as a substantial public health concern, as well as the urgency of continuing efforts to address this illness through better prevention, diagnostic, and treatment measures.

Keywords: Iron deficiency, anaemia, fortification, iron, dietary, RBC, vitamin C, vitamin A

Introduction
Iron insufficiency is the most frequent dietary deficit. It is more common among mothers and small children in the United States. Iron deficiency affects up to 19% of women aged 16 to 19. The frequency is 7% in children aged 1-2 years of both sexes (Umbreit, 2005) [71]. Although low iron intake or bioavailability are responsible for the majority of anemia in developed countries, they account for only about half of anemia in developing countries, where infectious and inflammatory diseases (especially malaria), blood loss from parasitic infections, and other nutrient deficiencies (vitamin A, riboflavin, folic acid, and vitamin B12) are also important causes (Hurrell *et al*., 2014) [72]. The majority of the iron in the body is found in erythrocytes as hemoglobin, a molecule made up of four units, each of which contains one heme group and one protein chain. Hemoglobin's structure permits it to be fully loaded with oxygen in the lungs and partially unloaded in the tissues. Myoglobin, the iron-containing oxygen storage protein in muscles, has a structure identical to hemoglobin but only one heme unit and one globin chain (Gupta, 2014) [73]. The human body requires roughly 25 milligrams of iron each day, mostly for hemoglobin production in red blood cells. Iron is also required for various cell and tissue processes, including respiration, energy generation, cell proliferation, DNA repair, and mitochondrial activity, particularly in skeletal and cardiac muscles. The body largely recycles the required iron by breaking down senescent red blood cells in the spleen via macrophages, allowing it to be accessible to plasma transferrin. Hepcidin, a hepatic hormone, strictly controls iron intake and recycling, yet it is readily disturbed, resulting in various types of iron shortage and anaemia (Cappellini *et al*., 2019). Serum ferritin is the most useful measure for diagnosing and monitoring iron shortage and iron excess illnesses. However, the association between serum ferritin and individual iron reserves is low in individuals with significant iron overload. Secondary causes such as illness, inflammation, or the presence of a tumor can also raise blood ferritin levels. Earlier research found that serum ferritin, as opposed to tissue ferritin, had a low iron level even in iron-loaded individuals (ferritin saturation, 2% to 11%). 13-16 As a result, it was considered that serum ferritin did not represent a significant supply of hepatic iron in either normal persons or patients with iron-overload illnesses.
Anemia (ancient Greek 0nai0a, anemia, meaning 'lack of blood') is defined as a reduction in the overall amount of hemoglobin or the number of red blood cells. Iron deficiency anemia is a kind of anemia caused by a lack of adequate iron to generate normal red blood cells.

Iron deficiency anemia is usually caused by insufficient iron intake, chronic blood loss, or a combination of the two. Iron deficiency anemia is the most frequent cause of anemia worldwide. Iron deficiency anaemia occur in phases and may be measured using a variety of biochemical markers. Despite the fact that several iron enzymes are sensitive to iron shortage, their activity has not been employed as a reliable regular assessment of iron status (Abbaspour *et al*., 2014) [75]. Mainly anaemic having quantity of RBCs in the blood is less or the blood cells have less haemoglobin than is usual. Having the proper quantity of RBCs and avoiding anaemia necessitates collaboration between the kidneys, bone marrow, and nutrients throughout the body. Anaemia is a symptom of a disease process, not the disease itself. It is often classified as chronic or acute. Chronic anaemia develops gradually over time. Acute anaemia develops fast (Hurrell *et al*., 2014) [72]. Iron deficiency, which causes anaemia in adults, can result in a wide range of negative health effects, including decreased work capacity, reduced thermoregulation, and fatigue. Immune dysfunction, gastrointestinal problems, and Helicobacter pylori infection are all possible outcomes. Other side effects include neurocognitive impairment in youngsters, which leads to psychomotor and cognitive abnormalities that, if untreated, hinder learning (Clark, 2008) [76].

The most easily absorbable iron comes from foods high in heme iron (meat, meat products, and poultry). Non-heme iron, which is abundant in fruits, vegetables, and grains, is poorly absorbed. The most easily absorbable iron comes from foods high in heme iron. Non-heme iron, which is abundant in fruits, vegetables, and grains, is poorly absorbed. Anormal newborns should consume 1 mg iron per kg per day, while children and male and female teenagers should consume 10, 12, and 15 mg per day, respectively. 15 mg per day for women throughout their reproductive years, adult males, and postmenopausal women just 10 mg daily. Food fortification is frequently recognized as the most cost-effective, long-term solution to lowering iron deficiency prevalence (Camacho *et al*., 2001) [74]. Fortification programs must address social and health concerns, such as protection against iron excess. The most successful technical methods to combating iron deficiency include targeted supplementation paired with a program of food fortification. The production of iron-fortified foods is a cost-effective, long-term method for preventing iron insufficiency. The provision of enough iron content within the recommended dietary norm is a requirement for the formulation of iron-fortified foods. Oral iron supplementation with therapeutic doses produces a quick improvement in symptomatically deficient people. Fortification aims to increase the iron nutritional status of populations throughout time. The key problem is to protect the fortifying iron from possible iron absorption inhibitors found in regularly fortified meals. Dietary supplementation with iron-fortified foods is more feasible and popular. When supplying iron through iron-fortified meals, insufficient or excessive iron supplementation should be avoided. It is critical to continually reinvent processing processes and innovative iron fortification additives.

Types of anemia and its risk factors

Anaemia is a medical disorder characterized by a low quantity of red blood cells or hemoglobin in the blood, which results in decreased oxygen-carrying ability. Nutritional deficiencies, chronic illnesses, genetic problems, certain drugs, pregnancy, blood loss, and ageing are all risk factors. Treatment is individualized and may involve dietary modifications, vitamins, medicines, blood transfusions, or bone marrow transplants. Below mentioned table is about the types of anemia.

Table 1: Types of anemia

Types of anemia	Symptoms	Causes	Diagnosis	Treatment	References
Microcytic	Dizziness Pale skin Weakness	Iron deficiency Thalassemia	Complete blood count test followed by examining peripheral blood smear	Intake of iron and vitamin C Blood transfusion (in severe cases)	(Wang, 2016) [1]
Macrocytic	Brittle nails Rapid heartbeat Memory loss	Chemotherapy Folate deficiency	Determination of vitamin B12 and folate in blood serum followed by examining peripheral blood smear	Intake of food rich in vitamin B12 and folates	(Tettamanti *et al*., 2009)
Normocytic	Lightheadedness Shortness of breath	Acute blood loss Sepsis	Complete blood count test Bone marrow biopsy	Inject shots of erythropoietin Blood transfusion (for severe case)	(Shavelle.*et al*., 2012)

Symptoms of anemia

The symptoms and severity of anaemia are determined by a number of factors, including the degree of anaemia, the speed with which it appears, and the patient's age and physiologic state, the intensity of anaemic symptoms is determined by several factors, including the degree of anaemia, the rate of development, compensatory mechanisms, and, most importantly, the patient's physiologic condition. Anaemia has a significant influence on patients' quality of life. The most common symptom is fatigue, which can occur even with minor reductions in iron levels. Women with ferritin levels less than 50 ng/mL reported alleviation from weariness after taking iron supplements. If they were iron-deficient, non-anemic tired teenagers experienced increased energy levels with iron supplementation. Most women in all nations recognize the signs and symptoms of anaemia and have a local nomenclature for these illnesses, Women perceive weakness and dizziness to be typical pregnancy symptoms, however half of the women polled could identify unfavorable repercussions of the condition, which were mainly related with poor energy and weakness in the mother. In all nations, half of women perceive these symptoms to be a major health problem that must be addressed, while the other half do not. Too much iron might result in too much blood or a large baby, making delivery more difficult. Women's identification of enhanced physical well-being with the reduction of anaemia symptoms, notably weariness, and a greater appetite are facilitators. greater awareness of the advantages to the foetus, and hence increased demand for prevention and treatment of iron deficiency and anaemia (Galloway *et al*., 2002) [77].

The stomach has an impact on dietary iron absorption. Nonheme iron accounts for approximately 80% of dietary iron consumption. Helicobacter pylori infection has been

associated to iron deficient anaemia. Although H. pylori can cause peptic ulcers that result in bleeding and iron deficiency anaemia, most H. pylori infected people develop chronic superficial gastritis rather than ulcers (Annibale *et al*., 2001) [78]. In clinical settings, chronic weariness is an important sign for identifying anaemia. Microcytic and hypochromic anaemia is a main sign of an iron-deficient patient. Tachycardia, shortness of breath, inadequate capillary refilling, weariness, and paleness of the conjunctiva and skin are among signs that can be found during a physical examination. Pica is a condition in which people with anaemia ingest non-food objects such as dirt (pagophagia) and ice (Geophagia). Restless leg syndrome has also been proposed as a probable IDA symptom. Individuals suffering from severe anaemia may experience symptoms of heart failure (Clark, 2008) [76]. The symptoms that are majorly found are shown in the below figure 1.

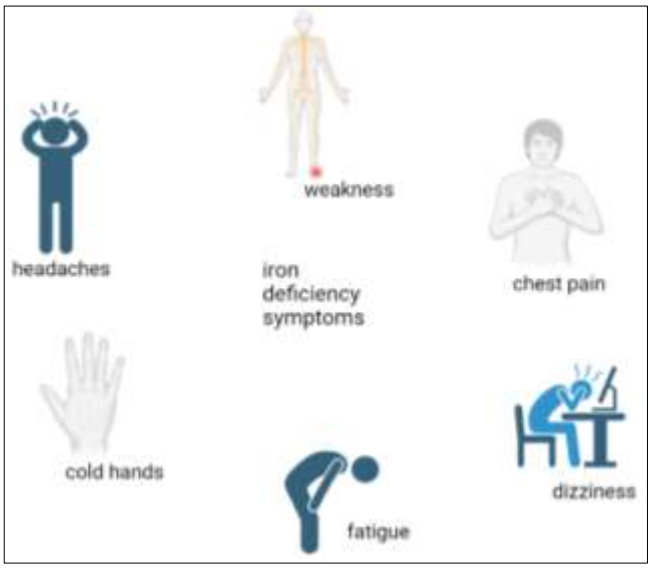

Fig 1: Symptoms of iron deficiency in humans

Diagnosis of anemia

Anaemia is often characterized as hemoglobin 11g/dL in babies and toddlers 6 months to 5 years old, haemoglobin 11.5g/dL in children 5-12 years old, and hemoglobin 12g/dL in teenage females > 12 years old (13g/dL in adolescent men).45 IDA is a microcytic and hypochromic anaemia, defined by low mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC). (Chatterjee *et al*., 2014) [81] Over the last two decades, the proportion of hypochromic erythrocytes, particularly CHr (hemoglobin content of reticulocytes or RET-He), has emerged as a reliable indication of IDA and response to iron treatment. CHr quantifies the functional iron available for erythropoiesis over the past three days and is an early predict of iron-restricted erythropoiesis (Mantadakis E, 2020) [82]. Anaemia is normally diagnosed using a combination of medical history, physical examination, and laboratory investigations. Accurate methods and precise criteria are required for the diagnosis of iron deficiency Hypochromia and microcytosis of red blood cells in circulation have long been thought to be crucial indications of iron deficient anaemia. Hypochromia is characterised by a decrease in the colour or staining intensity of red blood cells, which is often caused by a fall in hemoglobin levels. This can be found in iron deficiency anaemia as well as other kinds of anaemia. Macrocytosis is the enlargement of red blood cells caused by a multitude of reasons such as vitamin B12 deficiency or folate insufficiency. Macrocytic anaemia is a kind of anaemia characterized by larger-than-normal red blood cells. So, while hypochromia may suggest iron deficiency anaemia, macrocytosis may indicate other kinds of anaemia. A full blood count as well as additional laboratory tests are required to diagnose the type and cause of anaemia (Uta *et al*., 2022) Despite the significant frequency and possible negative effects of ID in people with chronic medical conditions, under-diagnosis is common. Under-diagnosis of ID can be attributed to practitioners' lack of identification of ID as a potentially serious illness in patients with inflammatory disorders, but it is mostly due to the lack of harmonized protocols for ID diagnosis. Although studying bone marrow iron reserves is regarded the gold standard, it cannot be done on a regular basis. Among all known indicators, circulating ferritin concentration and transferrin saturation (TSAT) index are extensively utilized in clinical practice and suggested for ID diagnosis (Cacoub *et al*., 2022) [79]. Iron levels in the blood and the development of accurate biomarkers for iron status are influenced by inflammation, diets, environmental stressors, and metabolism. It is challenging to identify reliable biomarkers for iron status in the blood. The serum levels of haemoglobin and iron bound to ferritin decrease, while the total iron-binding capacity in the serum increases due to impaired iron binding to the transport protein (apo-transferrin) and increased soluble transferrin receptor, resulting in low transferrin saturation. Ferritin is used as an indirect indicator of total iron concentration in the body, but it remains an unreliable diagnostic marker during inflammation. The current trend in diagnostics is to use multiple markers to measure iron status. The ratio of serum ferritin to C-reactive protein levels is proposed as an indicator of iron status during inflammation. Alternatively, soluble transferrin receptor (sTfR) is used as an indicator of stored intracellular iron levels, which is independent of inflammation. Low serum iron and ferritin levels with increased TIBC are also used to diagnose iron deficiency (Kumar *et al*., 2022) [80].

Prevention of anaemia

Anaemia can be caused by a number of reasons, including dietary deficiencies (such as iron, vitamin B12, or folate), chronic illnesses (such as renal disease or cancer), hereditary disorders (such as sickle cell anaemia), and others. The prevention of anaemia is dependent on the underlying cause. However, some basic actions that may be done to prevent anaemia include eating healthy and balanced diet rich in iron, folate, and vitamin B12, avoiding excessive alcohol intake, stopping smoking, controlling chronic conditions, and receiving frequent blood count checks. Depending on the patient's Hb level and underlying co-morbid condition, iron deficiency can be treated with dietary or oral iron supplements, intravenous iron treatment, and/or red cell transfusion. Late infantile anaemia is treated with dietary intervention such as iron supplementation and iron fortification of newborn food. Iron is an important dietary component that is required for growth and health. Iron-rich foods include liver, legumes, beans, nuts, green leafy vegetables, and fortified cereals; however, bio-absorption varies greatly. Daily oral iron supplementation is a widely

recommended strategy for both the treatment and prevention of iron deficient anaemia (Sundararajan and Rabe, 2021) [33]. To address ADI anaemia, an educational program will be introduced at primary health care centers that emphasizes the importance of iron supplementation and consuming iron-rich foods during pregnancy and after childbirth. The recommended approach to prevent IDA is through nutritional education, which involves consuming a wider variety of meals and adding more iron-rich foods to the diet, as well as taking iron and folate supplements. To improve the awareness and behavior of pregnant women towards preventing IDA, it is necessary to implement educational programs and regularly assess their knowledge, attitude, and practices. To enhance their awareness, behaviour, and habits regarding the prevention of iron-deficiency anaemia (IDA) during pregnancy, it is recommended that expectant mothers take part in health education programs. One way to achieve this is by distributing educational resources to pregnant women during their prenatal clinic visits. However, it is advisable to replicate this study using larger samples and in various contexts. Teacher support is essential in addition to parental support. Adolescents' awareness and motivation to avoid iron deficiency anaemia might be boosted by empowering instructors. This is confirmed by Crete-based study, which indicated that delivering information to teachers, adolescents, and parents is a good method for combating nutritional difficulties, particularly iron deficiency anaemia. As part of the endeavour to reduce the number of adolescents suffering from iron deficiency anaemia, school-based intervention through health education about the causes of iron deficiency anaemia is critical (Sari *et al*., 2022) [33].

Iron rich foods

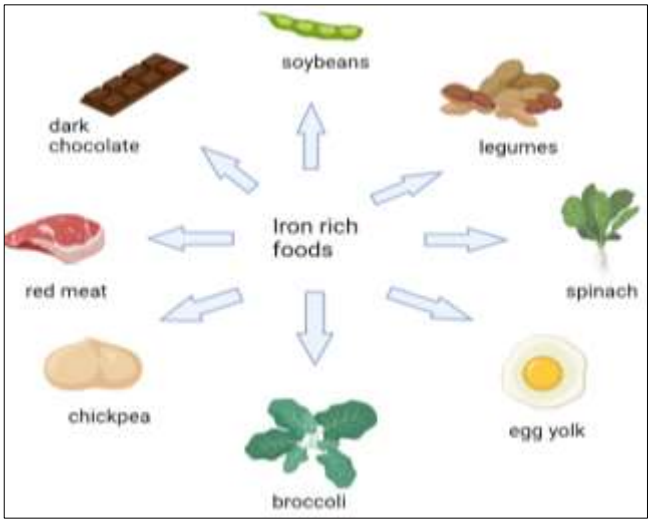

Fig 2: Foods rich in iron content

Foods that we consume contains several nutritional components that are beneficial for the human health in the development and the metabolism. Foods contains mainly vitamins, minerals, carbohydrates, fats etc. which are the major or the general composition of the foods that we consume in daily life. These components that are present are known as the nutritional factors of the food. Nutrients are characterized according to their availability and are classified as the macro nutrients and the micro nutrients which are necessary for the human body (T Gera *et al*., 2012) [70]. Iron is one of the main nutritional contents which are generally found in foods that we consume and some of the foods are very much rich iron which is mentioned in the below figure 2. The necessity of consume these foods that are rich in iron is very much essential for us which help in the prevention of several diseases especially iron deficiency s the major cause of disease which the well-known aneamia.

Conclusion

Iron deficiency anaemia is a major public health issue that affects a large proportion of the world's population, particularly women and children. The different features of iron deficiency anaemia have been reviewed in this review article, including its introduction, kinds, risk factors, symptoms, diagnosis, prevention, and therapy. Iron deficiency anaemia occurs when the body lacks enough iron to make haemoglobin, a protein that transports oxygen to the body's cells. Iron deficiency anaemia may be classified into three types: nutritional, menstruation-related, and pregnancy-related. The review research found many risk factors for iron deficiency anaemia, including insufficient iron intake, persistent blood loss, certain medical disorders, and pregnancy. Iron deficiency anaemia symptoms include tiredness, weakness, and shortness of breath, headache nb, and dizziness. For efficient therapy of iron deficient anaemia, an accurate diagnosis is required. Various diagnostic assays, such as serum iron, ferritin, and transferrin saturation levels, were emphasized in the research. A detailed medical history, physical examination, and other laboratory testing may also be required to identify the illness. The review study also emphasized the significance of preventing iron deficiency anaemia by a healthy iron-rich diet, iron supplementation, and addressing underlying medical disorders that may cause iron deficiency anaemia. Iron supplements, dietary adjustments, and blood transfusions were highlighted as therapeutic options for iron deficiency anaemia in the article. The efficacy of therapy, however, is dependent on the patient's capacity to absorb and accept iron supplementation. As a result, practitioners must educate patients on the significance of iron supplementation and follow-up treatment. In conclusion, iron deficiency anaemia is a widespread health issue that affects a large proportion of the population, particularly women and children. Early detection, appropriate therapy, and preventative initiatives are critical to treating this illness and enhancing the patient's quality of life.

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