A Prospect of Iron Prerequisites - REVIEW

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Abstract: The aim of this survey is to study a primordial element – Iron. For uncountable successive ages of humanity iron has played a noteworthy role. Iron is an essential element for blood production. Iron is required by most organisms as it serves as an essential element for blood production, a prosthetic group for proteins involved in central cellular processes, including respiration, DNA synthesis and oxygen transfer. About 70 percent of our body's iron is found in the red blood cells of our blood called hemoglobin and in muscle cells called myoglobin. Iron concentration in human body is regulated precisely; as iron can contribute to disease development in several ways. Both excess and dearth have harmful consequences causing diseases like Hereditary hemochromatosis and Anaemia respectively. According to WHO, globally Anaemia affects 1.62 billion people. The highest prevalence is in non-pregnant women and pre-school age and the lowest prevalence in men.

Keywords: Iron, Blood, Hemoglobin, Human body, Anaemia.

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1. INTRODUCTION :

Iron is a crucial nutrient required by human body as it plays a significant role in various cellular activities [1]. Iron is required for life[1][2][3]. Iron containing proteins that participate in transport, storage and use of oxygen [5]. Iron proteins are involved in transporting gases, building enzymes, and transferring electrons [3] [4]. Examples of iron-containing proteins in higher organisms include hemoglobin, cytochrome (high-valent iron) and catalase.[1][4] Bio-inorganic iron compounds (biological iron molecules) are the heme proteins [5].

The average adult human contains about 0.005% body weight of iron, or about four grams, of which three quarters is in hemoglobin – a level that remains stable, instead only about one mg of iron being absorbed each day,[3] because the human body recycles its hemoglobin for the iron content [5].

Iron are in much higher prevalence in women than in men and the great variation is in need between women under marked physiological variation in menstrual iron losses and to the effects of pregnancies [12].

The physiological activity of iron on human body are as cofactor in numerous enzymes involved in biosynthesis of amino acid, hormones, neurotransmitter and collegen. The iron aggregate in the body after uptake in human body is strictly controlled, as both excess and deficiency may have harmful outcomes [1][6][8].
Our body needs the right amount of iron, too little iron may lead us to iron deficiency - anemia. The main reason for iron scarcity include blood loss (due to frequent blood donation or menstruation), poor diet, or an inability to absorb enough iron from food intake. According to WHO, People suffering with a scarcity of iron in body are young children and women who are pregnant or have menstruation.

Also excess of iron can cause harm to our body like taking too many iron supplements can cause iron poisoning. Few people have an inherited disease called Hemochromatosis. Increased iron content in certain tissues ie. iron loading leads to infection, neoplasia, cardiomyopathy, arthropathy, and a profusion of endocrine and neurodegenerative disorders [7-11].

2. WHY DO WE NEED IRON?

Iron is an essential element for life. The major reason we need iron is that it helps to transport oxygen throughout the body [13]. About 70 percent of our body's iron is found in the RBC's of our blood called (Hb)hemoglobin and in muscle cells called myoglobin. Iron is an important component of hemoglobin, the substance in red blood cells that carries oxygen from our lungs to transport it throughout our body. Hemoglobin represents about two-thirds of the body’s iron. Every 100 ml of blood has 12-20 grams of Hb in a healthy individual. Hemoglobin has an oxygen-binding capacity of 1.34 mL oxygen per gram [14].

A heme molecule consists of an iron (Fe) ion held in between of a heterocyclic ring, known as a porphyrin. This porphyrin ring consists of four pyrrole molecules cyclically linked together (by methine bridges) with the iron ion bound in the center [15]. The iron ion may be either in the ferrous Fe2+ or in the ferric Fe3+ state, but ferrihemoglobin (methemoglobin) (Fe3+) cannot bind oxygen [16].

Iron has a function to generate energy from nutrients. It also contributes to the transmission of nerve impulses — the signals that coordinate the actions of our body parts. Iron deficiency anemia is caused when there’s not enough iron in our RBC's. A general study on countries may assume that 50% of the cases of anaemia are due to iron deficiency, which can vary according to situation and counties [18]. The main risk elements for IDA include a low consumption of iron, poor absorption of iron from diets high in phytate or phenolic compounds, and period of life when iron requirements are especially high (i.e. growth and pregnancy) [17].

2.1 DAILY IRON REQUIREMENT:

As per WHO expert committee observed in research of 1960 suggested 13 g/dL for men, 12 g/dL for women [23]. Although the amount of iron required may vary according to age, sex and health conditions. Our body doesn’t absorb Non-Heme iron that is present in plant based food and Heme iron that is present in animal foods. This also concludes that Vegetarians require more amount of iron containing food to fulfill the body iron demand.

Daily requirements of iron in human body is given in the below (Table 1), discussed in National Institute of Health - Iron Factsheet
2.2 IRON SOURCES:

Food is a basic necessity of a cell or tissue function. Lack of any particular nutrient is harmful for the health maintenance of living organism. Anaemia globally is a highly prevalent disease, which is due to low iron content in body. Supplementation and addition of nutritional ingredients in the diet is very necessary to increase the advantage with least health issues. Western countries face a major difficulty, that comes across with the low iron intake in diet and especially in Women, having a considerably higher Iron needs, have a meal with low iron.[12]

Iron content in herbal parts - Numerous research and reports have studied that the roots have significantly higher iron content than the stems and leaf. Stems and leaf tend to have similar iron content [7].

To hinder the IDA (Iron Deficiency Anaemia) there are various food resources. Availability of iron is separately studied as Heme iron and Non- heme iron. Heme iron is well absorbed by the body tissues than the Non-heme iron. These resources include both plant and animal resources.

**Plant sources** - Iron-fortified breakfast cereals, breads, White beans, lentils, spinach, kidney beans, peas, Nuts and some dried fruits, such as raisins.

**Animal sources** - Lean meat, seafood, and poultry. [20]

![Iron Rich Foods: Heme Iron and Non- Heme Iron](image)

Animal-based haemoglobin iron is well absorbed (15–40% absorption) compared to plant-based Non- hemoglobin iron (1–15% absorption), despite difference in body iron stores [34]. An alternative food chart of Vegetarians includes 32–36 mg of iron daily in a 2000 calorie diet containing 8 servings of grains, 3 of vegetables, 2.5 of green vegetables and beans ,1.5 of fruits , nuts and seed, protein foods, 3 of dairy or nonfortified dairy products, and 2.5 of oils [20].

2.3 IRON SUPPLEMENT:

Iron in food occurs in two forms - Heme and Non- Heme Iron . Nonheme iron is found in plant foods and iron-enhanced food products. Meat, seafood, and poultry have both heme and nonheme iron [20]. Dietary supplements provide iron in various forms such as iron(II) fumarate, ferrous gluconate, ferric citrate, although iron(II) sulfate is cheaper and is absorbed equally well [20] [25].
The availability of iron increases when cheated to amino acids [27]. A least expensive amino acid, Glycine is most often used to manufacture Iron-glycinate supplements [26].

3. METHOD OF DETERMINING IRON LEVEL IN BODY:

Anaemia is very common disorder, and medical practitioner's have different prospects to determine IDA. These methodologies include transferrin saturation, serum ferritin, RBC volume distribution, RBC photoporphyrin etc. The most useful test for IDA evaluation are:

**Serum Ferritin Test** - It is a routine blood test which uses venous blood to measure ferritin levels. Ferritin is the major iron storage protein in the body [36]. (Table 2) gives the tolerable concentration range of serum ferritin.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Ferritin Level Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12-300 ng/ml</td>
</tr>
<tr>
<td>Female</td>
<td>12-150 ng/ml</td>
</tr>
</tbody>
</table>

2. Haemoglobin Concentration Test -

WHO Hb thresholds were used to classify individuals living at sea level as anaemic (Table 3). Hb concentration is the most reliable indicator of anaemia at the population level [21].

Table 1 Haemoglobin thresholds used to define anaemia

<table>
<thead>
<tr>
<th>Age or Gender group</th>
<th>Haemoglobin threshold (g/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (0.50–4.99 yrs)</td>
<td>110</td>
</tr>
<tr>
<td>Children (5.00–11.99 yrs)</td>
<td>115</td>
</tr>
<tr>
<td>Children (12.00–14.99 yrs)</td>
<td>120</td>
</tr>
<tr>
<td>Non-pregnant women (≥15.00 yrs)</td>
<td>120</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>110</td>
</tr>
<tr>
<td>Men (≥15.00 yrs)</td>
<td>130</td>
</tr>
</tbody>
</table>

Haemoglobin concentration is a broadly used measure of anaemia. A blood drop is collected in a microcuvette for testing anaemia, making adjustments. Serum ferritin are considered more valid than Haemoglobin quantification to measure Iron-deficiency and iron-deficiency anaemia (IDA), a strong link exists between serum ferritin concentration and Hb levels in body [32] [33].

4. RESULT ANALYSIS OF IRON IMBALANCE:

When adequate amount of iron does not reach the body system, no discoverable symptoms arises. The body compensates with the stocked iron from organs like spleen, muscles, liver and bone marrow. But when body's stored iron is imbalanced, Iron Deficiency Anaemia generates. RBC Atrophy takes place, that results in less Hb and decrease in amount of oxygen transportation throughout the body. Hepcidine is a protein regulator of the entry of iron into the circulation in mammals [48].

Iron imbalance in body can be due to reasons like low or high dietary intake. Shedding of Mucosal and skin epithelial cell result in iron loss from body [47]. Hereditary factors are also a reason for impaired iron deposition in body. In cases of genetic history, people are unaware of their medical condition of iron excess and deficiency in body till old age. Iron supplements should be a taken on regular basis to prevent any kind of iron disorder in later ages. Anaemia and Hereditary Haemochromatosis are few such disorders of iron imbalance.

5. HEREDITARY HAEMOCHROMATOSIS:

It is a genetic disease due to excessive absorption of iron. The iron beyond normal levels is stored in organs like liver, heart, skin, joints, adrenal gland, and pancreas affecting their normal physiological function. Patients may get affected by diseases like cirrhosis, polyarthritis, adrenal insufficiency, heart failure, or diabetes [37][38]. Humans and animals do not have a modified excretory system to excrete excess iron. The mandatory daily iron losses are approximately 1-2 mg [39].
Production of RBC is regulated by a hormone erythropoietin, which is secreted by the kidney. In the condition of hypoxia, the kidney regulates synthesis and secretion of erythropoietin. Erythropoietin when floats in the body reaches to bone marrow and leads to the production of RBC's. This not only helps in increasing oxygen binding capacity and correct hypoxia which was the stimulus for it.

Which disease occurs in the age of 50s in males and years later in females. The apparent result of the unregulated iron levels are: [40, 41,42,43]

1. Fatigue
2. Malaise
3. Joint pain
4. Liver cirrhosis
5. Insulin resistance (especially in patients of Diabetes Mellitus) and pancreatic damage due to excessive iron deposition.
6. Erectile dysfunction
7. Congestive heart failure and abnormal heart rhythms
8. Adrenal Insufficiency

5.1 Treatment - When ferritin levels reach up to 500 μg/l, physicians advise treatment. Various practices like -

Phlebotomy (blood is taken out for a regular week interval until ferritin level in body fluid are less than 50 μg/l. To prevent reaccumulation of iron on organs subsequent bloodletting are carried once in 3-4 months and twice in 12 months [45].

For long-term administration, drug named Desferrioxamine mesilate, an iron-chelating agent is highly useful [45].

6. ANAEMIA:

Anemia is stated as “hemoglobin concentration below established cutoff levels” [21]. It is not a disease, but a state of nutritional shortfall [22]. When blood doesn’t have enough healthy red blood cells or due to lack of red blood cells or dysfunctional RBC’s in the body. This leads to reduced oxygen flow to the body’s organs. There are many different types of anemia, but the most common type is iron-deficiency anemia (IDA).

Anaemia impacts around 800 million women worldwide [28]. It is a global health public problem and also a symbol of poor nutrition, this can occur at all stages of life although following cases are more prominent ones: [19]

Women: For many successive years women have been affected by anaemia either on account of blood loss during menstruation or child birth.

Children (Age 1-2): Kids in growing age require more nutrients.

Infants: Infants require more energy after ceasing milk feeding. As solid food iron absorption is not easy.

People over 65: Old age people usually suffer from slow metabolism, low absorption of iron diets or due to some chronic diseases.

People on Blood thinners: Medicines including aspirin, clopidogrel (Plavix®), warfarin (Coumadin®), heparin products, apixaban (Eliquis®), betrixaban are used as blood thinners in Heart Disease and deep Vein Thrombosis cases.

Worldwide, anaemia affects 1.62 billion people (95% CI: 1.50–1.74 billion), which corresponds to affect about 20%–30% of the population [22] [24] [17]. National estimation of Anaemia survey concludes that pre-school age children have severe health issues.

Symptoms of IDA(Iron Deficiency Anaemia)[20] [46]

When body does not get enough amount of iron levels it result in following health instances -

1. Tiredness
2. Problems with concentration and memory
3. GI upset
4. Lack of energy
5. Weak immune system

6. Delayed growth of infants and children

6.1 ANAEMIA PREVALANCY IN WOMEN:

Iron Deficiency Anaemia (IDA) is addressed as a major health problem. It has been assessed that 52% of non pregnant women (NPW) in India are anaemic. The prevalence of anaemia can vary geographically as women in sub-Saharan region of Africa are highly affected by anaemia due to widespread of diseases like HIV, hookworm, malaria and other infectious disease [29]. IDA is a major contributor of 3.7% and 12.8% of maternal deaths in pregnancy and child-birth phase in Africa and Asia respectively [30].

A" 12-by -12 initiative " was started at AIIMS dated on April 24 ,2007 to ensure that every child of nation must have hemoglobin(Hb) of 12 grams by the age of 12 and this measure is together taken by Ministry of Health and family welfare , Govt of India , WHO, and UNICEF. They also discussed main cause of anaemia spread in India as low dietary intake, poor availability of iron, chronic blood loss due to hook-worm infestation, and malaria [31] Three levels of severity of anaemia are specified : Mild Anaemia (10.0–10.9 g/dL for pregnant women, 10.0–11.9 g/dL for Non-pregnant women), moderate anaemia (7.0–9.9 g/dL), and severe anaemia (less than 7.0 g/dL).

Also studies show that low caste / tribes as compared to high caste people are more affected by anaemia. Lower level of fish , egg , meat and chicken and iron - deficit diet are prominent cause of mediating Anaemia in women. And in countries like India , 27% of women have strict regulation of following vegetarian meat and excluding red - meat , eggs , fish and chicken which are highly rich iron content [29]. In rich and literate countries like Australia with more knowledge of iron deficiency and ways to tackle them by adding iron supplements and enhanced food sources have less ratio of anaemic patients than India. Although with the help of biotechnology , biofortification of food can be done and to produce iron rich diet , ferrous sulphate or ferric pyrophosphate for rice and flour may be increased to 40% of the recommended daily intake of iron from the regular basic balanced diet [51,52,53].

7. DISCUSSION:

Iron is a basic nutrient required by human body , responsible for oxygen transfer , building enzymes, and transferring electrons. Iron regulation must be maintained to perform all these functions, as imbalance of it can leads to various diseases. Globally, Anaemia is a very common disease mediated mainly due to the iron deficiency. This is due to many factors like low iron intake, poverty , illiteracy etc. which can be compensated by including iron supplements in diet. Hereditary hemochromatosis is a genetic autosomal recessive disorder due to deposition of excessive iron in organs. Although nowadays they can be treated by various treatments like phlebotomy. To keep a regular check on the iron content in body test like serum ferritin and hemoglobin concentration test must be done at regular intervals. Also for instant check-up of hemoglobin level various analysers like Hb-Quick and HemoCue machines should be used. These instruments give results in 10 seconds by using a few μL blood. In villages and areas with less educated people, Health Care Department should actively keep record of the population especially, children and females. Awareness towards diseases like IDA is a major step towards eradicating the roots of this cause.

8. CONCLUSION:

Iron is a basic necessity of human body and to compensate with Iron deficiency, supplementation and fortification of diet is very necessary. This review work performed concludes the iron requirements, sources, supplementation and imbalance in body due to iron deficiency leading to the most comment anaemia - IDA. This review also gives a brief introduction of Hereditary Haemochromatosis, Anaemia and it's prevalency and severity in females. As women are addressed to be more anaemic than men. Iron Rich diet and supplementation are necessary to deal with IDA. And regular blood test and checkup must be taken to keep control of the nutrients in body.

9. ACKNOWLEDGEMENT:

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10. ABBREVIATION:

RBC - Red Blood Cells

WHO - World Health Organization

PW - Pregnant Women

NPW - Non Pregnant Women

Hb - Hemoglobin
IDA - Iron deficiency Anaemia

AIIMS - All India Institute Of Medical Sciences


mg - milligrams

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