

Iron Deficiency Anemia

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Abstract

Aim: Iron deficiency anemia is a global concern affecting the lives of men and women, young and old even children and infants. Iron deficiency continues to be the top-ranking reason for the advancement of anemia even now. (Camaschella C., 2015). Thereby significantly affecting greater part of the population in nearly every country in the world. Iron plays a vital role and is indispensable from the basic reactions of the cell. Among the varied causes for the development of anemia both in developed and developing countries, nutrition remains the top most reason. (Osungbade & Oladunjoye, 2012) With references to the advances in the study and research of systemic iron homeostasis, this review article aims to re-evaluates iron deficiency and its anemia in and explores the causes, path physiological features, and a variety of treatment alternatives.

Method: The methodology applied is a narrative based descriptive study on articles from PubMed, Google Scholar, web of Science. **Conclusion:** Iron Deficiency anemia when undertaken seriously and detected well in advance can be prevented nonetheless nutrition has a great role to play. **Result:** This study recommends to expand the quality of health services by putting into action more handwork and to evolve with advanced facilities, it also suggests to increase public awareness about anemia.

Keywords: Iron, Iron deficiency anemia, Hcpidin, treatment.

I. Introduction:

Anemia is predominant and widespread in most parts of the world. Iron -deficiency anemia (IDA) is one of the universal reasons of anemia. Insufficient iron intake, poor gastrointestinal absorption, or occult blood loss normally results into Anemia. To differentiate iron deficiency from other causes of anemia is decisive to commence the proper medication, as is to ascertain the primary cause of iron deficiency. (Besarab & Hemmerich, 2018)

Iron performs a vital role as an essential micronutrient in numerous reactions in the human body. Iron is indispensable from the fundamental biochemical activities because of its extraordinary property to readily exchange electrons, correlate with proteins and oxygen binding ability. Certain important proteins such as hemoglobin, myoglobin, and cytochromes, iron-Sulphur clusters such as respiratory complexes and other functional groups has iron integrated in them. Moreover, some of the vital functions including oxygen transport, mitochondrial respiration, nucleic acid replication and repair have these proteins which have iron bound to them as their important constituent. Nonetheless various enzymes such as peroxidases, ribonucleotide reductase and P450 class of detoxifying cytochromes also need iron that serves as an important role in their functions. (Powers & Buchanan, 2014;28)

Young children and premenopausal women particularly those of low income or in developed countries are the worst hit by the iron-deficiency anemia. (McLean, Cogswell, Egli, Wojdyla, & de, 2009;12) Insufficient dietary intake and /or colonization of intestinal worm leading to blood loss, or both in general results in iron deficiency and iron deficiency anemia in developing countries. Whereas selected and specific eating habits in higher-income countries such as vegetarian diet and chronic blood loss or malabsorption are the frequent causes. In elder citizens Iron deficiency is especially high in developed countries. (Kassebaum, Jasrasaria, Naghavi, & al, 2014;123)

II. Anemia - Its prevalence in developing and developed countries

Reduction in the hemoglobin concentration of the peripheral blood below the normal range as expected for age and sex of an individual is termed as Anemia. (Standard treatment guidelines Nigeria, 2008) According to the definition by The World Health Organization (WHO) anemia develops when hemoglobin concentration found less than 12g/dl in non-pregnant women over 15 years of age and below 11g/dl in pregnant women and less than 13g/dl for men over 15 years of age. (Wick, Pinggera, & Lehmann, 2000). There occurs a disparity between the physiological needs and the number of blood cells which results in a state wherein the number of red blood cell or the oxygen carrying capacity is incapable to meet the physiological needs and this differs for age, sex, altitude and pregnancy status. (Nutritional anemia: report of a WHO Scientific Group, 1968) If this criterion is taken into consideration there will be 10-20 percent of women and 6-30 percent of men above the age of 65 who may be anemic. Anemia forms a public health problem in developing countries. About 2 billion people likely to suffer from anemia worldwide and it is stated to account for three quarters of 1 million deaths a year in Africa and south -East Asia. (Zimmermann & Hurrell, 2007) There can be diverse underlying reasons of anemia and are largely escapable; these involve nutritional deficiencies, infections and hemoglobin disorders. Nevertheless, it is evident that the occurrence of anemia in developing countries overdeveloped countries is approximately four times higher. (Allen & Gillespie, 2001).

Children and pregnant women are the most susceptible groups in the population, while next affected are the non-pregnant women and the elderly. In the developed countries it is predicted that 10-20% of the preschool age children whereas in developing countries 30-80% are anemic by the age of 1. (World Health Organization, 2005). The World health Organization (WHO)

projected that of all pregnant women 56% in developing countries are anemic. In North America and Europe, the occurrence of anemia in pregnancy is about 17% in comparison to southern Asia which is about 75% which is a huge contrast. Furthermore, 5% of pregnant women experience adverse from of anemia in the worst affected parts of the world. (World Health Organization, 1992). Tragically, about 20% of maternal deaths are due to anemia; in addition, anemia adds partly to 50% of all maternal deaths. (Rae, Erin, & Leslie, 2002;55(4)) Almost a similar condition is seen in sub-Saharan Africa allegedly where anemia accounts for about 20% of all maternal deaths. Incidentally this is brought about through three main reasons. (Buseri, Uko, Jeremiah, & Usanga, 2008; 2) Firstly, blood loss during or after childbirth resulting in anemia which makes the women more liable to death by lowering their hematological reserves. Secondly, lowered resistance to disease increases susceptibility to infection which is associated with severe anemia; and thirdly, high risk of cardiac failure and death associated when hemoglobin (Hb) level falls less than 4g/dl predominantly during delivery or soon after, if immediate intermediation is not introduced. (Rose & Thomas, 1996).

A very important impact to analyze resulting due to IDA is its effect on the economy. Iron deficiency anemia triggers 25million cases of Disability Adjusted Life Years (DALY's) if we talk in terms of lost years of healthy life, this reports for 2.4% of the entire global DALY's. (World Health Organisation, 2011) Up to 4.05% losses in gross domestic product per annum costs the developing countries due to physical a cognitive loss because of iron deficiency anemia; (Horton & Ross, 2003;28) thereby filibustering social and economic development. Iron Deficiency anemia (IDA) is the third prominent basis of disability-adjusted life years lost for females aged 15-44 years according to The World Health Organization (WHO)/ World Banking Ratings. (Karine & Friedman, 2007(1))

Paradoxically, owing to the aging population it becomes challenging and difficult to decrease iron-deficiency anemia in high-income countries where its prevalence is found to be more as compared to the in low-income countries. Elevated level of iron deficiency in aging populations grounds for this apparent paradox. (Kassebaum, Jasrasaria, & Naghavi, A systematic Analysis of Global Anemia Burden from 1990 to 2010, 2014;123)

III. Modification of Iron homeostasis in Iron deficiency

The hepcidin centered homeostatic control mechanism tightly regulates the iron acquisition. (Hentze, Muckenthaler, Galy, & Camaschella, 2010) Hepcidin hormone which operates as an acute-phase reactant is produced primarily by the liver. Hepcidin unite to ferroportin which is responsible to ship iron from the cell and stimulate its degradation, thereby controlling the fluctuations in plasma iron level triggered by absorptive enterocytes and macrophages in the spleen. (Nemeth, Tuttle, Powelson, Vaughn, Donovan, & Ward, 2004)

There is a considerable and significant surge in the expression of hepcidin due to high circulating and tissue levels of iron and in people suffering with systemic inflammation or infection. The expansion of erythropoiesis, iron deficiency and tissue hypoxia in reply to the signs and symptoms starting in the bone marrow, (Hentze, Muckenthaler, Galy, & Camaschella, 2010) the

liver and probably muscle tissue and adipocytes may result in the obstructing of the making of hepcidin. (Camaschella C., 2013) Increased hepcidin levels, especially interleukin-6 induced due to inflammatory cytokines, justify the act of iron confiscation and downgrade supply of erythropoietic iron that occur during anemia of chronic disease. (Camaschella C., 2015) Usually in a population, the level of hepcidin for girls and young women are at a low level while men- and postmenopausal women have a higher-levels; (Targlia, Girelli, & Biino, 2011) serum levels of ferritin have a strong explicit association with rise and fall of hepcidin levels. (Galesloot, Vermeulen, & GeurtsMoespot, 2011) Moreover in iron deficiency, the transcription of hepcidin is restrained. (Camaschella C., 2015)

IV. Common Causes:

Anemia seldom occurs on its own, it usually co-exists with an underlying disease. In developing countries, anemia mainly occurs due to nutritional disorders and infections predominantly among the most vulnerable groups that is the pregnant women and preschool age children.

Any age group can develop deficiency of iron in the body leading to anemia. In general, it is believed that 50% of instances of anemia are due to iron deficiency, (Moyle, 2002) but this may contrast within population groups or environment.

Low intake of iron, poor absorption of iron from diet rich in phylate or phenolic compounds, and early period of life when iron requirements are expectedly high are the threat factors of IDA. (Osungbade & Oladunjoye, 2012) Likewise, iron requirements for iron in pregnant women are highest accounting to 1.9mg/1000kcal of dietary energy in the second trimester and 2.7mg/1000kcal in the third trimester. The (1.0 mg) for infants, (0.8 mg) for adolescent girls, (0.6 mg) for adolescent boys, (0.6 mg) for non-pregnant women, (0.4mg) for preschool and school age children, and (0.3mg) for adult men follow after the pregnant women in order according to their needs. (Osungbade & Oladunjoye, 2012) Deficiency of Vitamin A can lead to the occurrence of anemia. (Sommer & West, 1996) Animal products are comparatively consumed less in developing countries which again lead to riboflavin deficiency (Camaschella C., 2013) which is an important constituent for the synthesis of red blood cells and may be linked with megaloblastic anemia. (Tolentino & Friedman, An update on anemia in less developed countries, 2007) The formation and maturation of red blood cells and cell growth and repair again essentially requires folic acid. Folate deficiency diminishes the rate of DNA synthesis with subsequent impaired cell proliferation and intramedullary death of resulting abnormal cells; this shortens the lifespan of circulating red blood cells and thereby resulting in anemia. (Tolentino & Friedman, 2007)

In developing countries, in addition to low intake of iron, people also suffer with intestinal infection with nematodes; as a consequence, severe anemia develops, especially in the young children. The real-time polymerase-chain-reaction assays of fecal samples outcome shows that the gravity of iron deficiency intensifies if infection is coupled with *Ancylostoma duodenale* (hookworm) (Jonker, Calis, & Phiri, 2012) Patients with hypermenorrhoea may also have concomitant malabsorption of iron. (Hershko & Camaschella, 2014)

V. Diagnostic Procedure

To ascertain iron status and iron deficiency and associated conditions the traditional laboratory measures and results are used. The most subtle and explicit test used for the detection of iron deficiency is the Serum ferritin level test (indicated by a level of $<3 \mu\text{g}$ per liter). Patients with iron-deficiency anemia have lower levels of serum ferritin; Less than 16% of transferrin saturation level signals an iron supply that is deficient to assist a regular erythropoiesis. (Camaschella C., 2015) However, it is highly recommended not to rely only on a single test to determine the iron status to get the full picture. The differential diagnosis of microcytic anemias guidelines has lately been revised. (Camaschella C., How I manage patients with atypical microcytic anaemia, 2013). Nonetheless it would be a bit demanding to have a single laboratory test for the investigation of iron-deficiency anemia in the perspective of inflammation which perhaps may not be determined. (Camaschella C., 2015). To designate iron-deficiency anemia due by inflammation needs a considerably higher cut-off level for ferritin. (Weiss, Goo, & Goodnough, 2005) with a ferritin level of less than $100 \mu\text{g}$ per liter begins as the best predictor. Ferritin level that has a higher cut offs are used in the diagnosis of iron deficiency in varied conditions e.g., heart failure will have a level that is $<300 \mu\text{g}$ per litre (Anker, Comin, & Filippatos, 2009) transferrin saturation level of less than 30% considered for chronic kidney disease. (Macdougall, Bock, & Carrera, 2014) The iron staining of bone marrow specimen technique for the measurement of iron stores acquired by the process of biopsy is an option that is not popular yet. Presently, there are no trustworthy tests for the accessibility of hepcidin level.

VI. Therapy

Oral Iron Supplements

Iron supplementation should be provided to patients with iron deficiency. Ferrous sulphate, ferrous fumarate or ferrous gluconate given as 200mg twice or thrice a day as an oral iron supplement treatment for Iron deficiency which cannot be cured by dietary iron is the best option. Whenever there is intolerance to oral iron or when diagnosed late in pregnancy there could be an alternative treatment via parenteral as iron dextran. (Osungbade & Oladunjoye, 2012)

The absorption of iron is up regulated when there is an iron deficiency, depending on the iron deficit. In the stomach and proximal duodenum, a bio-availability of 80-97% is accomplished, but it expects that iron is provided in an aqueous solution or discharged promptly from the administered preparation. About 83% of it, is absorbed, if iron is dispensed in enteric-coated pellets. (Wick, Pinggera, & Lehmann, Clinical aspects and laboratory- Iron metabolism, Anemias, 2011) If the iron is fully discharged and iron stocks are depleted, this portion can rise up to 95%. (Wick, Pinggera, & Lehmann, Clinical aspects and laboratory- Iron metabolism, Anemias, 2011) Absorption improves with the addition of Vitamin C. Patients with iron deficiency anemia having a low level of hepcidin certifies efficient iron absorption and speedy progress of hemoglobin concentration level; however for the satiety of iron stores and the regularization of serum ferritin levels approximate 3 to 6 months of medication is required. Thing to be noted is that there can be slight side effects of long-term use of oral administration

like nausea, vomiting, constipation and metallic taste, although these are not very grave side effects but are worrisome for the patients. (Camaschella C., 2015)

Parenteral Iron Supplements

The intravenous dispensation of iron diminished traditionally because of the likelihood of hypersensitivity reactions to high molecular weight iron. This clinical practice has been modified by the newly approved, safer iron formulations. (Onken, Bregman, & Harrington, 2014) Intravenous iron administration is effective and increases hemoglobin level more quickly than oral iron absorption as a result intravenous iron circumvents the problem of iron. (Vadhanraj, Strauss, & Ford, 2014) Another benefit is that in some patients a single infusion can provide the total dose of up to 1000 mg. (Camaschella C., 2015) The dose required by the individual is calculated with the formula i.e. body weight in kilogram * 2.3 * hemoglobin deficiency (hemoglobin level target at–hemoglobin level of the patient) + 500 to 1000mg iron for the repletion of iron stores. The cost is comparatively more for such sort of medication. Anyway, there is a significantly reduced number of hospital or clinic visits over the years. (Bager & Dahlerup, 2010)

Iron deficiency anemia can be considerably prevented by food fortification and dietary diversification with iron which are an important measure (World Health Organization, 2005) for the vulnerable group such as pregnant women and children. Although a number of strategies are used to deliver additional iron to humans, but food fortification has the utmost potential to enhance the iron status of the enormous number of people. (World Health Organisation, 1992)

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