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Research Article

IRON DEFICIENCY AND ANAEMIA

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ABSTRACT
Iron is a vital mineral in our body with many functions but primarily needed in the formation of haemoglobin. Iron deficiency results from an inadequate intake of foods rich in iron. Anaemia, on the other hand, is a disease condition due to decreased red blood cells for circulation to the body. Primary cause of anaemia is iron deficiency. Insufficient iron availability during growth phases or states of increased requirement result in iron deficiency (ID) and eventually iron deficiency anaemia (IDA). Clinically, anaemia is the manifestation of iron deficiency, latter should not be ignored as it is related to adverse functional consequences. This paper examines the various stages of iron deficiency and its ultimate manifestation as anaemia. The seriousness of this scourge is brought to the fore by examining relevant statistics about its prevalence.

Key Words: *Iron, Iron Deficiency, Iron Deficiency Anaemia, Nutritional Anaemia, Anaemia*

INTRODUCTION

Nutritional anaemia is a condition in which the haemoglobin (Hb) content of blood is lower than normal as a result of a deficiency of one or more essential nutrients. Because anaemia is the most common indicator used to screen for iron deficiency, the terms anaemia, iron deficiency (ID), and iron deficiency anaemia are sometimes considered synonymous and used interchangeably. However, there are cases where a person may not be anaemic but is mildly or moderately iron deficient and consequently may be functionally impaired. Iron deficiency anaemia (IDA) is the most common nutritional cause of anaemia and occurs when there is an inadequate amount of red blood cells caused by lack of iron. The prevalence of iron deficiency anaemia is, therefore, less frequent than iron deficiency.

Iron is involved in multiple critical body functions. The predominant use of iron is for the creation of haeme groups that are incorporated into haemoglobin and myoglobin. Iron is additionally involved in the production of cytochromes and other enzymes (Segel *et al.*, 2002; Wu *et al.*, 2002). Immediately, bioavailable iron is bound in the bloodstream to a specific carrier protein called transferrin. Iron in excess of immediate needs will be stored in the liver, spleen, and bone marrow as ferritin (Wu *et al.*, 2002). The majority of iron can be conserved and reused; however, there are some finite losses through the gastrointestinal tract, skin, and urine that ultimately must be replenished.

Iron deficiency is often portrayed as a progressive condition that begins with normal body iron status, which becomes sub normal or depleted because of low dietary iron intake, inadequate intestinal iron absorption or increased iron losses. As this process continues, synthesis of iron containing proteins, such as Hb, is compromised. Finally, when Hb concentration falls below a specified cut-off value, the iron deficiency has progressed to IDA (Haas and Brownlie IV, 2001).

Iron metabolism is unique in several aspects. The body is economical in its handling of iron in the body. When a red cell dies, its iron is reutilised. Iron absorption is in some ways dictated by the requirements of the body. Extra iron can be stored by a specific protein (ferritin), which is utilised at the time of increased iron requirements. The highly reactive properties of iron are balanced by unique control and transport systems. In spite of these ingenious mechanisms, ID is the most common deficiency disorder in the world and also the main remaining deficiency in the industrialised, developed regions of the world (Hallberg, 2001).

Anaemia

Anaemia (British English) or Anemia (American English) from the Greek meaning “without blood”, is defined as a qualitative or a quantitative deficiency of haemoglobin (Hb), a molecule inside red blood

cells (RBCs). The three main classes of anaemia include excessive blood loss (acutely such as haemorrhage or chronically through low-volume loss), excessive blood cell destruction (haemolysis) or deficient red blood cell production (ineffective haematopoiesis). Iron deficiency anaemia is the most common type of anaemia overall and it has many causes. RBCs often appear hypochromic (paler than usual) and microcytic (smaller than usual) when viewed with a microscope. Iron deficiency, the end result of a long period of negative iron balance, develops in three phases: depletion of stores (ferritin and haemosiderin), deficiency of erythropoiesis, and anaemia (Matarese and Gottschlich, 2002).

Nutritional Anaemia

Nutritional anaemia was defined in a 1968 WHO technical report as "a condition in which the haemoglobin content of the blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency." To determine which nutritional deficiencies were most responsible, WHO coordinated a series of studies in pregnant women in which Hb, serum folate, transferrin saturation and serum B_{12} were assessed. They concluded that, "iron deficiency was present in 40-99% of the pregnant women studied and was undoubtedly responsible for the major proportion of anaemia."

In 1985, DeMaeyer and Adiels-Tegman published a landmark paper in which they compiled global data on anaemia from reasonably large studies. In that paper, nutritional anaemia was considered to be a large component of global anaemia prevalence, and iron deficiency was considered the most common cause of nutritional anaemia.

In the late nineties there was a paradigm shift from nutritional anaemia (of which iron deficiency anaemia is one important part) to iron deficiency anaemia as the major public health problem. This is reflected in the title of the 1989 WHO monograph, *Preventing and Controlling Iron Deficiency Anaemia Through Primary Health Care*, which states (DeMaeyer *et al.*, 1989), "Iron deficiency anaemia is the most prevalent nutritional deficiency disorder in the world today….Iron deficiency is by far one of the most common nutritional cause of anaemia; it may be associated with a folate deficiency, especially during pregnancy. Other nutrient deficiencies such as B_{12}, pyridoxine and copper are of little public health significance because of their infrequency."

Nutritional anaemia (UNICEF 2000) refers to a condition in which the haemoglobin content of the blood is lower than normal as result of deficiency of one or more essential nutrients (usually iron, less frequently folate or vitamin B_{12}), regardless of the cause of such deficiency. Stoltzfus and Dreyfuss (1998), opine that, "iron deficiency is not the only cause of anaemia, but where anaemia is prevalent, iron deficiency is usually the most common cause," Severe iron deficiency results in anaemia, which is the most widely used indicator of this deficiency (Ramakrishnan, 2002). Although it is the main cause of anaemia in most settings, anaemia may be the result of other nutrient deficiencies such as vitamin B_{12} and folate as well as non-nutritional causes such as malaria, genetic abnormalities (eg., thalassemia) and chronic disease (Allen and Casterline-Sabel, 2001). Iron deficiency, develops over a period of time. Three stages of iron deficiency have been described: (1) iron depletion during which iron stores are reduced as indicated by lowered values of serum ferritin (2) iron deficient erythropoeisis when iron stores are exhausted and there is a decreased transferrin saturation and increased erythropoietin, and (3) iron deficiency anaemia, which is characterized by low haemoglobin and is usually microcytic, hypochromic anemia (Bothwell *et al.*, 1979).

Iron Deficiency and Anaemia

The nestor in haematology, Maxwell M. Wintrobe, once chairing an expert WHO meeting on nutritional anaemias, defined ID, didactically, as a state (*a*) when an otherwise healthy individual has a Hb below the optimal value for that specific individual, (*b*) when there is no infection or other disorder present, (*c*) when there is no lack of other nutrients required for an optimal hematopoiesis, and (*d*) when laboratory signs are compatible with ID (Hallberg, 2001).

In a bid to define *iron deficiency with and without anaemia,* a WHO/United Nations International Children's Emergency Fund (UNICEF)/United Nations University (UNU) (1993) consultation made the next shift in thinking, i.e., from iron deficiency anaemia to iron deficiency as the problem. In the report (1999) from that meeting, anaemia was considered an indicator of iron deficiency rather than iron deficiency being considered a contributing cause of anaemia (WHO/UNICEF/UNU, unpublished). The authors state, "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 are, however, mild-to-moderate forms of iron deficiency in which, although anaemia is absent, tissues are still functionally impaired" (Stoltzfus, 2001).

Three stages of iron deficiency have been described (Carley, 2003). The initial stage, iron depletion, occurs when stored iron in the bone marrow diminishes due to insufficient supply of iron. Generally, this stage is asymptomatic, creates no overt effect on erythropoiesis, and escapes detection by haemoglobin or haematocrit screening. Continued iron store depletion leads to the second stage, iron deficiency, during which storage levels become substantially reduced and haemoglobin synthesis begins to be affected. The final stage, iron deficiency anaemia, develops when iron stores are insufficient to maintain haemoglobin production. This advanced stage will be reflected in low haemoglobin and hematocrit values (Lesperance *et al.*, 2002).

Sensitivity to iron-restrictive conditions depends on the severity of dietary restriction but also on the stage of development during which iron deficiency occurs and the duration of dietary restriction (Felt and Lozoff 1996; Pinero *et al.*, 2000; Pollitt, 2001; Beard *et al.*, 2003). Iron deficiency anaemia (IDA) is defined as a disease of the reduced erythrocyte production with low content of haemoglobin, because of the lack of iron which is the most important constituent of haemoglobin (Kanamaru, 2008). Dietary iron deficiency results in biochemical changes in the blood and reduced concentrations of iron in tissues. IDA is generally considered to correspond to a degree of dietary iron deficiency sufficient to deplete ferritin stores and to decrease iron concentrations in some tissues, but not sufficient to reduce serum haemoglobin to the point of anaemia. Individuals with depleted iron stores and serum haemoglobin concentrations below the 98th percentile of a normally distributed population are generally considered to be iron deficient anaemic (ID+A) (NAS/DRI 2000; WHO, 2001). Haemoglobin cut off values varied somewhat among human studies, as noted by reviewers (Grantham-McGregor and Ani, 2001; McCann and Ames, 2007).

The recommended cut off values for haemoglobin levels used to define anaemia, however, vary by age, race, and physiologic status (Table 2.1), and adjustments for smoking and altitude have also been recommended (WHO/UNICEF/UNU, 1996).

Iron deficiency may be defined as an absence of iron stores combined with signs of iron-deficient erythropoiesis (the making of red blood cells) implying there is an insufficient supply of iron to various tissues. This occurs at a serum ferritin level <15 mcg/l. Under these conditions, an insufficient amount of iron is delivered to transferrin, the circulating transport protein for iron, resulting in a reduction in transferrin saturation. Formation of haemoglobin is reduced resulting in a reduction in mean corpuscular haemoglobin.

The concentration of transferrin in plasma increases in an effort to compensate. Iron deficiency may be classified according to serum ferritin concentration with depleted iron stores (SF<24 ng/ml), mild iron deficiency (SF=18–24 ng/ml) and severe iron deficiency (SF<12 ng/ml) (Thompson, 2007).

Prevalence

The most severe consequence of iron depletion is iron deficiency anemia (IDA), and it is still considered the most common nutrition deficiency worldwide (Clark, 2008). IDA along with vitamin A deficiency and iodine deficiency disorders continues to pose significant challenge to public health all over India (Vijayaraghavan, 2007).

Table 1: Recommended Cut-Off Values for Haemoglobin Levels Used To Define Anaemia

Age/Sex Groups	**Haemoglobin Level (g/dl)**
Children 6-59 months	11.0
Children 5-11 years	11.5
Children 12-14 years	12.0
Non pregnant women (15 years of age and above)	12.0
Pregnant women	11.0
Men (15 years of age and above)	13.0

Source: UNICEF/UNU/WHO 2001

The summary of numbers begins in 1985 (DeMaeyer and Adiels-Tegman, 1985). The 1985 anaemia estimate and the 50% attribution of anaemia to iron deficiency were cited in two subsequent documents by WHO (DeMaeyer *et al.,* 1989) and the United Nations Subcommittee on Nutrition (Gillespie *et al.,* 1991). However in 1993, two documents (Levin *et al.,* 1993) WHO/UNICEF/UNU, unpublished (quoted in, Stoltzfus, (2001) used De Maeyer and Adiels-Tegman's 1985 anaemia number but named it iron-deficiency anaemia. In Murray and Lopez, (1996) the Global Burden of Disease project adjusted these numbers upward on the basis of a new global population figure but continued to call this the prevalence of iron-deficiency anaemia. In 1997–1998, three expert documents used a higher prevalence number of 2.1 billion people affected; (Draper,1997) used this as the figure for iron deficiency anaemia, whereas the other documents (Gillespie and Johnston, 1998; Stoltzfus and Dreyfuss, 1998) stated this to be the number with iron deficiency. The Technical Workshop (UNICEF/UNU/WHO/MI , 1999) stated that 3.5 billion people suffer from "iron deficiency and its anaemia." Finally, in 1999, a WHO report at an INACG meeting (INACG, 2002) estimated that 2 billion people were anaemic (applying the 30% prevalence figure of DeMaeyer and Adiels-Tegman to a new global population of > 6 billion) and tentatively estimated that the number of iron-deficient people could be as high as 5 billion, or 80% of the world's population. The latter figure was obtained by multiplying the number of anaemic people by 2.5. This factor, discussed in the WHO/UNICEF/UNU consultation (unpublished 1993), is based on U.S. national data for women and children, in which the ratio of iron-deficient people to iron-deficient anaemic people was 2.5 (Yip, 1994). Applying that figure to global data assumes that this relationship found in the United States is generalisable to the world—a troubling assumption that was clearly acknowledged at the INACG meeting. In addition, the factor should rightly be applied only to the number of iron-deficient anaemic people, not to all anaemic people (Stoltzfus, 2001).

Iron deficiency is the most common and widespread nutritional disorder in the world, according to the World Health Organization. WHO estimates that every second pregnant woman, and about 40 percent of pre-school children in developing countries, are anaemic. "The numbers are staggering: two billion people, over 30 percent of the world's population, are anaemic, many due to iron deficiency, and in resource-poor areas this is frequently exacerbated by infectious diseases. Also, WHO reports that it is the only nutrient deficiency which is "significantly prevalent in industrialised countries" (Ringer, 2007).

Iron deficiency is known to affect the lives of more than 1.2 billion people worldwide; many of these individuals are women, children, and infants (Beard and Connor, 2003). Examination of the global prevalence of anaemia among children and women of reproductive age in different regions of the world indicates that more than half the pregnant women (76, 55, 50 per cent) and young children (76, 55, 50 per cent) are anaemic in Southeast Asia, West Pacific and Africa, respectively (WHO 1998). Although the

prevalence of anaemia is slightly lower in school age children (63% in Southeast Asia) and non pregnant women, it is still high enough to deserve intervention strategies These high rates of anaemia, especially in Southeast Asia, clearly indicate that it is likely that almost the entire population has some form of iron deficiency (Ramakrishnan, 2002).

Iron deficiency is believed to affect 20-50% of the world's population, making it the most common nutritional deficiency in the world (Beard and Stoltzfus 2001). In the 15 years since 1985 (Stoltzfus, 2001), as our conceptualization of the problem has evolved from iron deficiency anaemia to iron deficiency with or without anaemia, the number of people supposedly affected has grown from 0.6 million to 3.5 to 5 million.

Anaemia is a major public health problem in India. The prevalence of anaemia is 60-90% in different age groups (Sethi *et al.*, 2003). Under National Family Health Survey 2 (NFHS, 2000) levels of anaemia in ever-married women, 15-49 years of age were studied during 1998-99; the overall prevalence of anaemia in 79662 women was 52%. The percentage of mild, moderate and severe anaemia was respectively 35, 15 and 2 %.

ICMR , (2001) reported an overall prevalence of anaemia in pregnant women from 16 districts as 84.9 %. The overall prevalence among 4,337 non-pregnant adolescent girls from 16 districts was 90.1%; the prevalence of mild (>10-11.9 g %) and moderate (7-10 g %) was 32.1 and 50.9% respectively. Highest prevalence (24.3% against the overall average of 7.1%) of severe anaemia was observed in the adolescent girls of Bikaner.

NFHS- 3 was conducted in 29 states (2005-2006). A total of about 199,000 women aged 15-49 years were studied. Anaemia prevalence among children (< 3 years) (Hb < 11g/dl), pregnant women (Hb < 11g/dl), and women of reproductive age (Hb < 12g/dl) was high at 79%, 59% and 56% respectively and appears to have increased overall since the last survey (1998-1999), though more so in rural than urban areas (Singh and Christian, 2008).

The prevalence of IDA has found to be high in the developing regions of the world. The magnitude of the problem is severe in India with more than half of the populations afflicted by it.

Summing up, it can be said that anaemia remains a major global public health problem. It affects one fourth of the world's population in both industrialized and developing countries and its health consequences affects all age groups to varying degrees. Although it is certainly not the only cause, iron deficiency is by far the primary cause of anaemia and is the most widespread nutrient deficiency in the world.

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