A Biomarker for Iron Deficiency Anemia

P Rajalakshmy*

Lecturer in Nutrition, Kasturba Gandhi Nursing College, India

***Corresponding Author:** P Rajalakshmy, Lecturer in Nutrition, Kasturba Gandhi Nursing College, India.

Received: October 10, 2019; **Published:** November 04, 2019

DOI: 10.31080/ASNH.2019.03.0523

Abstract

Worldwide Anaemia is considered as a major community health problem, about 1.6 billion people are the sufferer of anemia. Dietary iron is usually considered as either heme or nonheme iron to analyse this condition widely haemoglobin is used as a major biochemical test since serum ferritin and transferrin saturation (TSAT) are commonly used as biomarkers for iron status, these markers are not sensitive enough to distinguish functional iron deficiency from iron overload. Recently, Hepcidin, an acute phase reactant protein produced in the liver, is thought to be a central regulator of body iron metabolism. Hepcidin is predominantly synthesized in the liver.

Keywords: Anaemia; Metabolism; Hepcidin

Introduction

Worldwide Anaemia is consider as a major community health problem, about 1.6 billion people are the sufferer of anemia [1]. India is highest among the world, where it exacts a heavy toll in terms of mortality, disability, and lost productivity [1,2]. It is estimated that 56% of women of reproductive age, 59% of pregnant women, 63% of lactating women, and 70% of young children are affected with anaemia in India [1]. Worldwide, Iron deficiency is the leading cause of anaemia, it can be prevented and treated by iron supplementation [1]. It has been estimated that ~50% of anaemia is due to iron deficiency (50%, 95%CI: 47–53%) [1]. Other nutritional factors, such as vitamin B12 and folate, and non-nutritional factors such as inflammation also contribute to the aetiology of anaemia and impact human health [3,4].

Iron metabolism

Dietary iron is usually considered as either heme or nonheme iron [5]. Nonheme iron is seen abundantly plant origins foods like and trace amount can be seen in animal origin foods. Nonheme iron is found in a wide variety of forms and includes soluble iron, iron in low-molecular-weight complexes, storage iron in ferritin, and iron in the catalytic centers of a wide range of other proteins.

Iron is majorly absorbed in the small intestine by the mature enterocytes of the midupper villus [6] Although small amounts of iron can be absorbed by the more distal parts of the gastrointestinal tract, the proximal parts of the small intestine (the duodenum and first part of the jejunum) are particularly adapted for this role.

Storage iron may be defined as the iron which can be mobilized from various body tissues for the formation of hemoglobin when needed. Such iron is stored intracellularly in a protein complex as ferritin and hemosiderin [7].

Iron homeostasis

As an essential element iron play a major part as a component of oxygen-carrying proteins (hemoglobin, myoglobin) and of numerous redox enzymes in cellular metabolism. The average adult human contains 2–4 g of iron. Most of the iron is in hemoglobin of blood erythrocytes, and prolonged systemic iron deficiency results in decreased hemoglobin production that leads to iron deficiency anemia. The supply of iron to erythrocyte precursors in the bone marrow and to other tissues is largely maintained by daily recycling of about 20 mg of iron from senescent erythrocytes [8].

Anemia in chronic disease

ACD is considered the second most common cause of anaemia world wide however detailed statistics on its prevalence are not available. Often the anaemia in individuals with inflammatory diseases is complex and multifactorial and it may be challenging to separate out the component due to ACD. This is especially true in patients with diabetes. Examples of the prevalence of ACD in various inflammatory states include the following Anaemia is observed in 33 to 60% of patients with rheumatoid arthritis [10].

- ACD accounts for about 1/3rd of the cases of anaemia of the elderly because of concomitant inflammatory conditions or chronic kidney diseases.
- Cancer related anaemia occurs in more than 30% of the cases at diagnosis.

Role of ferritin, transferrin and hepcidin in iron metabolism

Ferritin is a highly conserved iron-binding protein. In vertebrates, the cytosolic form consists of 2 subunits, termed H and L. Twenty-four ferritin subunits assemble to form the apoferritin shell. Each apoferritin molecule of 450 000 d can sequester up to approximately 4500 iron atoms [11].

Although serum ferritin and transferrin saturation (TSAT) are commonly used as biomarkers for iron status, these markers are not sensitive enough to distinguish functional iron deficiency from iron overload [12]. Recently, hepcidin, an acute phase reactant protein produced in the liver, is thought to be a central regulator of body iron metabolism [13,14]. Hepcidin controls the plasma iron concentration by inhibiting iron export by ferroportin from enterocytes and macrophages [15]. Hence, increased hepcidin production leads to decrease in plasma iron concentration and to iron-restricted erythropoiesis [16]. Hepcidin expression is upregulated by inflammation [17] and iron loading [18] and down regulated by erythropoietic activity [16,18]. Studies of humans with chronic infection and severe inflammatory disease have shown markedly elevated levels of hepcidin, strongly suggesting that hepcidin level plays a key role in the anemia of inflammation and reticuloendothelial blockade [17].

Figure 1

Inflammation and hepcidin

In case of infection and inflammation there will be massive elevation of interleukin-6 (IL-6), which stimulates Hepcidin production and release from the liver which in turn reduces the Iron Carrier protein, ferroportin [19], so that access of Iron to the circulation is reduced as well as iron absorption in the small intestine, iron transport across the placenta and release from the macrophages are also reduced. Also there is impaired production of erythropoietin (EPO), blunted marrow erythroid response to EPO, Iron restricted erythropoiesis and a diminished pool of EPO- responsive cells [20].

Conclusion

Iron Deficiency Anemia is one of major public health problem In India, since many research are concentrating only on the intake of iron in diet but still other reasons also seen behind this defi-

ciency the biochemical analysis need to analysis the biomarker like of Serum Ferritin, Serum Transferring and Serum Hepcidin which helps to estimate the exact reason for the iron deficiency anemi.

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Volume 3 Issue 12 December 2019

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