Latent Iron Deficiency and Iron Deficiency Anaemia in Hypoferritinemic Patients


*Department of Pathology, Pakistan Atomic Energy Commission General Hospital, Islamabad; **Department of Medicine, Pakistan Atomic Energy Commission General Hospital, Islamabad

Abstract

Background: To find out the frequency of iron deficiency anaemia (IDA) and latent iron deficiency (LID) amongst hypoferritinemic individuals.

Methods: In this descriptive study individuals (n=1821) who were referred for serum ferritin estimation, for a period of one year were included. Ferritin levels were assayed by enhanced chemiluminescence method. Haemoglobin levels were also estimated in all these subjects. Those hypoferritinemic subjects were excluded from the study whose haemoglobin levels were not performed on the same day as serum ferritin assay, with raised C-reactive proteins or had leukocytosis. Male patients having haemoglobin <13g/dl and female patients with haemoglobin <12 g/dl were considered anaemic. Children from 2-12 years were included in this study and children having haemoglobin below 10 g/dl were considered anaemic. Patients with normal haemoglobin, but with low serum ferritin were considered as suffering from latent iron deficiency anaemia. Normal range of serum ferritin for adult male subjects was 12-300 ng/ml, for adult female subjects is 10-150 ng/ml and for children serum ferritin of 17-464 ng/ml was considered normal.

Results: Total number 1821 samples of serum ferritin were assayed by enhanced chemiluminescence method out of which 458 (25.15 %) number of patients had low serum ferritin. 981 (53.87%) subjects had normal ferritin levels and 382 (20.97%) patients had high ferritin levels. In hypoferritinemic patients gender distribution included total of adult males 88 (19.21%) adult females 222 (48.47 %) and 148 (32.31 %) children greater than 2 years. Subjects with low serum ferritin were divided into two groups latent iron deficient group and iron deficiency anaemic patients. Latent iron deficiency (LID) was seen in 19.43%. Mean serum ferritin was low in IDA as compared to LID.

Conclusions: Latent iron deficiency may be missed if hemoglobin levels are taken as sole marker of anemia. Ferritin levels must be assayed for assessing body iron stores.

Key Words: Hypoferritinemia, Iron deficiency anemia, Latent iron deficiency, Haemoglobin, Iron

Introduction

Iron deficiency anemia (IDA) is widely prevalent in Pakistan. IDA is preceded by a stage of latent iron deficiency (LID) where serum ferritin is reduced but the hemoglobin and red cell indices are normal. Iron depletion may be three times as common as iron deficiency anaemia (IDA), which has a prevalence of 2-5% of adult men and postmenopausal women in the developed world. Iron depletion is more common in the developing world like Pakistan especially amongst women because of menstruation, as a result, some workers consider hemoglobin level of 10-11 g/dl as normal. 1,2

Iron depletion is a reduced content of total body iron. Iron deficiency anaemia (IDA) occurs when the iron deficiency is sufficient to reduce erythropoiesis and therefore the haemoglobin (Hb) level falls. However, problems related to iron depletion can develop before this stage diagnosed by hypoferritinemia. This stage is occasionally detected by a routine check of the serum ferritin or transferrin saturation. Iron deficiency, with or without concomitant anaemia also has serious implications and need to be treated. In children this leads to impairment of growth and intellectual development. Iron is the most abundant element on earth, with potential of high toxicity to living cells. Therefore, complex regulatory mechanisms are present in human to ensure adequate intestinal absorption, transportation, utilization, and elimination. Iron balance is regulated by absorption of iron rather than by excretion, because humans cannot actively excrete iron. Iron is absorbed from the small intestine, iron is lost from the body through sloughed skin cells and sloughed enterocytes from the gut, and through any form of blood loss. Males contain about 4,000 mg of iron, of which 2,500 mg is within erythrocytes; 1,000

139
mg is stored in splenic and hepatic macrophages, and the rest is distributed in various proteins such as myoglobin, cytochromes or other ferroproteins. About 1–2 mg of iron is lost every day, through skin and enteric desquamation and minor blood losses. This loss is balanced by intestinal absorption. Therefore, iron recycling accounts for most of the iron homeostasis in human.

For detection of body iron status several tests are available. Nowadays bone marrow examination has been replaced by the measurement of blood ferritin. Other tests, like measurements of transferrin (Tf), of soluble transferrin receptor (sTfr) or of hepcidin, are also available reflecting dynamics of iron metabolism. Hepcidin, is a 25 amino acid peptide hormone, mainly produced by hepatocytes, plays very important role in iron metabolism. Many mechanisms involved in the regulation of hepcidin may therefore regulate availability of iron to erythropoiesis by adaptation of iron absorption and recirculation. Erythrocyte precursors take up iron through transferrin receptors, Tfr. Thus, the Tf cycle is dependent on the Tf-Tfr complex trafficking, involving internalization of the complex within endosome, followed by iron release upon acidification of the endosome and recycling of the Tf-Tfr complex to the cell surface where, Tf dissociates from Tfr, and is used to repeat the iron cycle. Ferrous is reduced to ferric by ferrireductase, as only ferric iron is transported to the enteric desquamation and minor blood losses. This loss is balanced by intestinal absorption. Therefore, iron recycling accounts for most of the iron homeostasis in human.

For detection of body iron status several tests are available. Nowadays bone marrow examination has been replaced by the measurement of blood ferritin. Other tests, like measurements of transferrin (Tf), of soluble transferrin receptor (sTfr) or of hepcidin, are also available reflecting dynamics of iron metabolism. Hepcidin, is a 25 amino acid peptide hormone, mainly produced by hepatocytes, plays very important role in iron metabolism. Many mechanisms involved in the regulation of hepcidin may therefore regulate availability of iron to erythropoiesis by adaptation of iron absorption and recirculation. Erythrocyte precursors take up iron through transferrin receptors, Tfr. Thus, the Tf cycle is dependent on the Tf-Tfr complex trafficking, involving internalization of the complex within endosome, followed by iron release upon acidification of the endosome and recycling of the Tf-Tfr complex to the cell surface where, Tf dissociates from Tfr, and is used to repeat the iron cycle. Ferrous is reduced to ferric by ferrireductase, as only ferric iron is transported to the

Results

Total 1821 samples of serum ferritin were assayed by enhanced chemiluminescence method out of which 458 (25.15 %) number of patients had low serum ferritin. 981 (53.87 %) subjects had normal ferritin levels and 382 (20.97 %) patients had high ferritin levels.

Table 1: Hypoferritinemia- Subjects distribution

<table>
<thead>
<tr>
<th></th>
<th>Latent Iron deficiency (LID)</th>
<th>Iron Deficiency Anemia (IDA)</th>
<th>Total no of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>13 (2.83%)</td>
<td>75 (16.37%)</td>
<td>88 (19.21%)</td>
</tr>
<tr>
<td>Females</td>
<td>21 (4.58%)</td>
<td>201 (43.88%)</td>
<td>224 (48.47%)</td>
</tr>
<tr>
<td>Children</td>
<td>55 (12%)</td>
<td>93 (20.30%)</td>
<td>148 (32.31%)</td>
</tr>
<tr>
<td>Total</td>
<td>89 (19.43%)</td>
<td>369 (80.56%)</td>
<td>458 (100%)</td>
</tr>
</tbody>
</table>

Table 2: Comparison of mean levels of Hemoglobin and Ferritin in hypoferritineic patients (n= 458)

<table>
<thead>
<tr>
<th></th>
<th>IDA (n=201)</th>
<th>LID (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>8.79±1.57</td>
<td>12.54±0.71</td>
</tr>
<tr>
<td>Ferritin (ng/ml)</td>
<td>4.62±1.1</td>
<td>5.84±2.93</td>
</tr>
<tr>
<td>Adult males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>9.20±2.35</td>
<td>13.67±0.93</td>
</tr>
<tr>
<td>Ferritin (ng/ml)</td>
<td>6.82±3.88</td>
<td>10.59±3.56</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>7.89±1.52</td>
<td>11.37±1.08</td>
</tr>
<tr>
<td>Ferritin (ng/ml)</td>
<td>6.09±3.69</td>
<td>8.62±4.60</td>
</tr>
</tbody>
</table>

In hypoferritinemic patients, gender distribution included total of adult males 88 (19.21 %) adult females 222 (48.47 %) and 148 (32.31 %) children older than 2 years. Subjects with low serum ferritin were divided into two groups latent iron deficient group and iron deficiency anaemic patients. Latent iron deficiency

Patients and Methods

In this descriptive study individuals (n=1821) who were referred for serum ferritin estimation, for a period of one year (June 2012 to June 2013) were included. Ferritin levels were assayed by enhanced chemiluminisence method. Haemoglobin levels were also estimated in all these subjects. Those hypoferritinemic subjects were excluded from the study whose haemoglobin levels were not performed on the same day as serum ferritin assay, with raised C-reactive proteins or had leukocytosis. Male patients having haemoglobin <13g/dl and female patients with haemoglobin <12 g/dl are considered anaemic. Children from 2-12 years were included in this study and children having haemoglobin below 10 g/dl considered anaemic. Patients with normal haemoglobin, but with low serum ferritin were considered as suffering from latent iron deficiency anaemia. Normal range of serum ferritin for adult male subjects is 12-300 ng/ml, for adult female subjects is 10-150 ng/ml and for children, serum ferritin of 17-464 ng/ml is considered normal.
(LID) was seen in 19.43% (Table 1). Mean serum ferritin was low in IDA as compared to LID (Table 2).

**Discussion**

Iron is an important micronutrient required for multiple functions in body. Iron deficiency is a major health issue in developing countries like Pakistan where its rates have been reported to vary between 30-69%. Approximately 39% of adolescents, 30% boys and 54% girls, 47% of the children, 30% of the adult females, 40-50 % of preschool and primary school children, and 69% children <2 years, were reported to be affected by IDA. Two different prevalence studies, in semi urban areas of Peshawar found 69% prevalence (Hb <11 g/dl) of anaemia in children under two years and in urban slums of Karachi detected 61 %( Hb <11 g/dl) of anaemia in children aged 6-60 months. A recent study at Abbottabad detected 68 % anaemia prevalence.

No single test can describe iron status accurately, so there are a number of markers that, collectively, describe an individual’s iron “status,” including serum (circulating) iron, red blood cell count, hemoglobin, hematocrit, total iron binding capacity, and serum ferritin. Serum ferritin is a surrogate marker of stored iron. Limitation of ferritin is that as it is a acute phase protein, so high serum ferritin is present with inflammation. When serum ferritin is low, without low haemoglobin, it is called latent iron deficiency, whereas when there is also low hemoglobin, it is iron deficiency anemia. In the population where iron deficiency is common it is important to identify the patients with latent iron deficiency, as these patients also need treatment because iron is also required by other body tissues and enzymes. Moreover, timely treatment will prevent the development of anaemia. In patients with slow developing anaemia have usually very mild symptoms and they do not seek medical advice, as shown in an Indian study where IDA was detected in 20.3% of apparently healthy females aged 18-23 years. Another study conducted in Iran, the prevalence rates of ID and IDA in female university students aged 18-25 years were 40.9% and 3.8%, respectively.

In our study, latent iron deficiency was found amongst 19.43% of hypoferritinemic people while 80.56% had iron deficiency anaemia. Thus latent iron deficiency accounted for significant proportion of hypoferritinemic individuals. Our study of 458 hypoferritinemic individuals noted higher frequency of anemia in females, (48.47 %). This result is comparable to other studies.

**Conclusion**

Latent iron deficiency has clinical implications and it may be missed if hemoglobin levels are taken as sole marker of anemia. Ferritin levels must be assayed for assessing body iron stores.

**References**