Ferritins in iron metabolism investigation

Mariana Pațiu, G. Laszlo, A. Cucuianu

Hematology Laboratory, Oncologic Institute "Ion Chiricuță", Cluj Napoca

Abstract

Ferritin is the main storage form of iron in the body. Ferritin in the serum reflects the extent of the iron stores and is an early indicator of decreasing iron stores. Erythrocyte ferritin, reflecting the balance between iron entering and leaving the red blood cell, can be used in monitoring therapy by bleeding in hemochromatosis patients. Mitochondrial ferritin detection appears to be a promising new means of diagnosing sideroblastic anemia.

Key words: ferritin, serum ferritin, glycosylated ferritin, erythrocyte ferritin, mitochondrial ferritin

Several laboratory tests investigating iron metabolism exist, but none of them is entirely satisfactory. Search for finding the one that best assesses body iron status thus continues.

Ferritin, three major types of which being described, seems to be (though with some limits) quite acceptable. Composed of iron and a protein part (called apoferritin), ferritin is an easily mobilizable storage form of iron in the body, mainly found in the liver and spleen, but also present in serum and other body fluids.

The extent of the iron stores is reflected by serum ferritin\(^3\).

It was held until not long ago that each microgram per liter ferritin in the serum would correspond to about 8 mg tissue storage iron, but it is now quite clear that the ferritin level in the serum actually offers only a guideline, the serum ferritin – storage iron relationship not being linear except for a limited value interval\(^3\).

Serum ferritin measurement is valuable in diagnosing iron deficiency being, in general, the first laboratory test that becomes abnormal when iron stores begins to decrease, and before erythrocyte morphology shows any signs of abnormality.

Among the hypochromic anemias (iron deficiency anemia, anemia of chronic disease, sideroblastic anemias, minor thalassemia) only iron deficiency anemia shows decreased serum ferritin values. Increased (or normal) values do not exclude with certainty the presence of iron deficiency, because ferritin is an acute phase reactant that increases during inflammatory processes.

Serum ferritin can be measured by radioimmunoassay (RIA), enzyme immunoassay (EIA) and immunoradiometric assay. The reference range varies with method, age and sex. It is 20-250 µg/L in men and 10-120 µg/L in women. Its level generally increases in women in menopause and children generally have low ferritin levels, except during the first month of life. Serum ferritin does not have diurnal variations (in contrast to serum iron), and exogenous
iron ingestion does not influence it. Almost all of the circulating ferritin is in a glycosylated form, thus the glycosylated ferritin measurement may reveal a pathological cell lysis that releases non glycosylated ferritin into the circulation and reduces the proportion of glycosylated ferritin in the overall serum ferritin.

Serum ferritin (F), together with soluble transferrin receptor (sTfR, another useful iron metabolism parameter), helps distinguishing iron deficient anemia (IDA) from the anemia of chronic disease (ACD) and the combined presence of these two conditions (IDA&ACD). Ferritin values lower than 30 µg/L are considered to be characteristic of IDA, those higher than 100 µg/L as typical for ACD, while those between 30 and 100 µg/L may represent either ACD or the combined ACD&IDA. Ferritin values lower than 30 µg/L are considered to be characteristic of IDA, those higher than 100 µg/L as typical for ACD, while those between 30 and 100 µg/L may represent either ACD or the combined ACD&IDA. Ferritin values lower than 30 µg/L are considered to be characteristic of IDA, those higher than 100 µg/L as typical for ACD, while those between 30 and 100 µg/L may represent either ACD or the combined ACD&IDA. Ferritin values lower than 30 µg/L are considered to be characteristic of IDA, those higher than 100 µg/L as typical for ACD, while those between 30 and 100 µg/L may represent either ACD or the combined ACD&IDA.

The erythrocyte ferritin represents the storage form of iron in the erythrocyte prior to its use in hemoglobin synthesis. It reflects the balance between the iron entering and leaving the cells (the iron brought by transferrin and that used up for hemoglobin synthesis, respectively). An increased entry of iron, unjustified by increased needs (as happens in hemochromatosis) or its faulty utilization (hemoglobinopathies) increase the ferritin in the erythrocyte, while a reduced delivery or an accelerated utilization of iron (as in hemolytic anemias) decrease it. Although these changes are late manifestations of an affected equilibrium between iron in- and outputs, erythrocyte ferritin has the advantage of not being influenced by inflammatory processes. In iron overloads erythrocyte ferritin shows a remarkable discriminative capacity, differentiating overload in hemochromatosis from that due to alcohol abuse. Erythrocyte ferritin may be used in the surveillance of treatment through repeated bleedings in hemochromatosis, which must be continued even after the collapse of serum ferritin - the iron overload being still important-, until the collapse of the erythrocyte ferritin also takes place, a sign that the treatment has achieved its goal. To eliminate the influence of red cell volume and packed cell volume (hematocrit), the result obtained at the measurement of erythrocyte ferritin in a hemolysate is divided to the number of erythrocytes present. The normal values are 5-38 attog/erythrocyte for men and 3-24 attog/erythrocyte for women. Fertile age women do not have low values, as distinct from serum ferritin.

Attempts exist at present to develop an immunological test for detecting the ring sideroblasts in sideroblastic anemias, more specific and more reliable than the conventional Perls reaction that establishes sometimes with difficulty their presence. The test became possible once it was realized that the iron in the granules encircling the nucleus of the ringed sideroblasts is actually in the form of ferritin.

This novel ferritin type, named mitochondrial ferritin, is structurally and functionally similar to the cytosolic ferritin. Being a protein, antibodies may be raised against it, usable thereafter for ring sideroblast detection.

In addition to the erythroblasts of patients with sideroblastic anemia, high amounts of mitochondrial ferritin are found in the testis, neuronal cells and islets of Langerhans, mitochondrial ferritin expression thus appearing to correlate more with mitochondrial abundance than with iron metabolism.

References


