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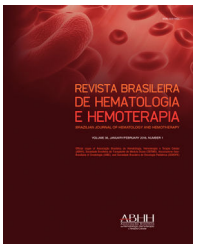

Scientific Comment

Challenges in the diagnosis of iron deficiency anemia in aged people☆

Niele Silva de Moraes[a,b], *Maria Stella Figueiredo*[a,*]

[a] *Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil*
[b] *Universidade do Estado do Pará (UEPA), Belém, PA, Brazil*

In this issue of the Brazilian Journal of Hematology and Hemotherapy, Babaei et al.[1] investigated the cut-off level for serum ferritin that would better discriminate between elderly patients with and without iron deficiency anemia (IDA).

IDA is a common manifestation among the elderly population. It has often been associated to gastrointestinal bleeding caused by esophagitis, gastritis, peptic ulcer, cancer, and intestinal polyps.[2–5] Although a bone marrow examination is the gold standard test to assess iron stores, it is an invasive method with no practical applicability.[6,7] A recent systematic review showed that all guidelines recommend the measurement of serum ferritin to diagnose IDA.[8] Serum ferritin is considered a first-line diagnostic tool not only due to its availability, but also because its plasmatic levels accurately reflect overall iron storage, with 1 ng of ferritin per mL indicating approximately 10 mg of total iron stores.[1,9]

While serum ferritin under 10–15 ng/mL has 99% of specificity in the diagnosis of IDA, normal or elevated ferritin levels do not exclude IDA, since ferritin is an acute phase protein and may increase during inflammation, cancer, and with aging.[8,10] Hence, some studies provide data supporting the use of higher ferritin thresholds for diagnosis, such as 30 or 100 ng/mL.[11,12]

Elderly people often have many morbidities some of which can potentially lead to anemia, making the diagnosis of IDA particularly challenging in this population.[13] Moreover, in individuals with chronic diseases, anemia of inflammation (AI) can be associated with an absolute iron deficiency, especially in cases where there is bleeding.[14]

It is recommended to expand the repertoire of biochemical markers to differentiate between AI and AI with iron deficiency (AI + IDA). These markers include red cell variables (such as hypochromic red cells and reticulocyte-specific indices of volume and hemoglobin content), transferrin saturation, soluble transferrin receptor (sTfR), and hepcidin.[13–17]

Among the red cell variables, hypochromic red cells are used to identify absolute iron deficiency in patients with chronic renal failure, whereas reticulocyte-specific indices are used to assess the iron status of these cells.[8] However, the difficulties in the diagnosis of AI + IDA using these parameters remain.[14]

Transferrin saturation is cheap and available in most laboratories, and is quite suggestive of IDA when below 16%. However, inflammatory illnesses affect transferrin saturation and conclusions may be misleading if used as the sole marker.[8,10,16]

sTfR is an indicator of iron status and is elevated in IDA. It can be useful in the diagnosis of AI + IDA although it is relatively expensive and not widely available.[3,10,18] The TfR index, a ratio between sTfR and log of ferritin, is considered a good indicator of IDA in patients with chronic diseases, but it depends on the viability of the sTfR measurement.[7,18]

Hepcidin, a 25 amino-acid peptide discovered at the beginning of this century, is a regulator of iron metabolism. This

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* *Corresponding author at*: Disciplina de Hematologia e Hemoterapia, Escola Paulista de Medicina da Universidade Federal de São Paulo (EPM/UNIFESP), R Dr. Diogo de Farias, 824, 04037-002 Vila Clementino, São Paulo, SP, Brazil.
E-mail address: stella.figueiredo@unifesp.br (M.S. Figueiredo).
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molecule induces the degradation of ferroportin, a membrane protein responsible for iron transport.[19,20] Low levels of hepcidin are seen in IDA anemia, while the opposite is true in AI. However, this test is most often used in research institutions.[19–21]

The diagnosis of IDA is not always simple. Serum ferritin alone is no longer recommended as the only diagnostic test to assess IDA in the elderly.[8,13] Furthermore, the other laboratorial exams have low sensitivity or are not widely available.[21] The challenge remains and any studies that identify parameters of value during clinical decision-making are welcome.

Conflicts of interest

The authors declare no conflicts of interest.

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