

SHORT COMMUNICATION

Iron Deficiency Without Anemia: A Neglected Clinical Syndrome in Internal Medicine Practice

Déficit de hierro sin anemia: un síndrome clínico ignorado en la práctica de la medicina interna

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Cite as: Sánchez Blanco LA, Gonzales Ferrer JM, Medero García F. Iron Deficiency Without Anemia: A Neglected Clinical Syndrome in Internal Medicine Practice. South Health and Policy. 2025; 4:348. <https://doi.org/10.56294/shp2025348>

Submitted: 05-03-2025

Revised: 10-06-2025

Accepted: 15-08-2025

Published: 16-08-2025

Editor: Dr. Telmo Raúl Aveiro-Róbalo 

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ABSTRACT

Iron deficiency without anemia was identified as an underestimated condition in clinical practice, despite its high prevalence and impact on quality of life. Although iron has historically been linked solely to hemoglobin production, multiple studies have shown that this mineral is essential for mitochondrial, muscular, immunological, and neurological functions. Thus, patients with normal hemoglobin levels but low iron stores presented symptoms such as chronic fatigue, mild dyspnea, headaches, restless legs syndrome, tachycardia, and mild cognitive disorders. This condition was observed more frequently in young women, people with chronic inflammatory diseases, heart failure, or older adults. In these individuals, ferritin was found to be reduced or functionally inactive, making timely diagnosis difficult due to the absence of obvious anemia. The traditional approach in internal medicine, which focused only on hemoglobin, ignored this deficiency, limiting the use of effective treatments such as oral or intravenous iron supplementation. In countries such as Cuba, the need to update clinical guidelines to consider this condition as a separate entity was recognized. It was proposed to routinely include ferritin and transferrin saturation measurements in patients with nonspecific symptoms, especially in women of childbearing age and people with inflammatory comorbidities. Recognizing this deficiency led to significant diagnostic improvement and an opportunity to alleviate the functional and emotional burden on patients, highlighting the importance of modern, comprehensive, and evidence-based internal medicine.

Keywords: Iron Deficiency; Ferritin; Nonspecific Symptoms; Internal Medicine; Diagnosis.

RESUMEN

La deficiencia de hierro sin anemia fue identificada como una condición subestimada en la práctica clínica, a pesar de su alta prevalencia y repercusión en la calidad de vida. Aunque históricamente se relacionó el hierro únicamente con la producción de hemoglobina, múltiples investigaciones demostraron que este mineral resultó esencial para funciones mitocondriales, musculares, inmunológicas y neurológicas. Así, pacientes con niveles normales de hemoglobina, pero con reservas de hierro bajas presentaron síntomas como fatiga crónica, disnea leve, cefaleas, síndrome de piernas inquietas, taquicardia y trastornos cognitivos leves. Este cuadro se observó con mayor frecuencia en mujeres jóvenes, personas con enfermedades inflamatorias crónicas, insuficiencia cardíaca o en adultos mayores. En ellos, la ferritina se encontró reducida o funcionalmente inactiva, dificultando el diagnóstico oportuno debido a la ausencia de anemia evidente. El abordaje tradicional en medicina interna, centrado solo en la hemoglobina, ignoró este déficit, lo que limitó la aplicación

de tratamientos eficaces como la suplementación oral o intravenosa de hierro. En países como Cuba, se reconoció la necesidad de actualizar las guías clínicas para considerar esta condición como una entidad independiente. Se propuso incluir de forma rutinaria la medición de ferritina y saturación de transferrina en pacientes con síntomas inespecíficos, especialmente en mujeres en edad fértil y personas con comorbilidades inflamatorias. Reconocer este déficit implicó una mejora diagnóstica significativa y una oportunidad para aliviar la carga funcional y emocional de los pacientes, destacando la importancia de una medicina interna moderna, integral y basada en la evidencia.

Palabras clave: Déficit De Hierro; Ferritina; Síntomas Inespecíficos; Medicina Interna; Diagnóstico.

BACKGROUND

Iron deficiency has historically been considered a hematological disorder related to anemia. However, there is an underestimated condition in clinical practice: iron deficiency without anemia, a common but often unrecognized condition that causes disabling symptoms and impairs the patient's quality of life.⁽¹⁾

Numerous studies have shown that iron is essential not only for hemoglobin synthesis, but also for mitochondrial, muscular, immunological, and neurological functions. Thus, iron deficiency, even with normal hemoglobin levels, can cause chronic fatigue, mild exertional dyspnea, recurrent headaches, restless legs syndrome, inappropriate tachycardia, and mild cognitive impairment.⁽²⁾

This condition is especially seen in young women, patients with chronic inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease, heart failure with reduced ejection fraction, and older adults. In these individuals, iron stores (ferritin) may be depleted or functionally inactive without overt anemia, delaying diagnosis and treatment.⁽³⁾

In internal medicine, the traditional approach to iron remains anchored in hemoglobin control, without considering that many symptomatic patients have normal values but low ferritin (< 30 ng/mL) or decreased transferrin saturation. This limited perspective deprives patients of effective therapeutic interventions such as oral or intravenous iron supplementation, which has been shown to improve physical performance, cognitive function, and overall functional status.⁽⁴⁾

Cuba, like other developing countries, faces the challenge of modernizing its approach to iron metabolism, with clinical guidelines that consider iron deficiency without anemia as a separate entity. Diagnostic strategies should routinely include measurement of ferritin and transferrin saturation in patients with persistent nonspecific symptoms, particularly in women of childbearing age and patients with inflammatory comorbidities.

Recognizing iron deficiency without anemia not only improves diagnostic accuracy but also provides an opportunity to reduce the functional and emotional burden on patients. Twenty-first-century internal medicine must take on this challenge with an integrative approach, supported by scientific evidence and clinical sensitivity.

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FUNDING

The authors did not receive funding for the implementation of this study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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